ELSEVIER

Carbohydrate Research 278 (1995) 227–238

CARBOHYDRATE
RESEARCH

A ^{13}C and ^{183}W NMR study of D-*glycero*-D-*gulo*-heptonic acid as a multisite ligand in tungstate complexes

Miloudi Hlaïbi [a,b], Mohammed Benaïssa [b], Catherine Busatto [c], Jean-François Verchère [a], Stella Chapelle [c,*]

[a] *Université de Rouen, URA 500 du CNRS, Faculté des Sciences, F-76821 Mont-Saint-Aignan, France*
[b] *Université Hassan II, Faculté des Sciences d'Aïn Chock, B.P. 5366, Maârif, Casablanca, Morocco*
[c] *Université de Rouen, Laboratoire de RMN, URA 464 du CNRS, Faculté des Sciences, F-76821 Mont-Saint-Aignan, France*

Received 5 June 1995; accepted 7 July 1995

Abstract

The formation of complexes (x,y,z) between x tungstate ions, y D-*glycero*-D-*gulo*-heptonate ions, and z protons was studied in aqueous solution by ^{13}C and ^{183}W NMR spectroscopy. The overall equilibrium constant for the complex-forming reaction was obtained by a competition method, showing that a (2,2,2) species prevails at pH 4–5. Depending on the pH, various species are formed that involve chelating oxygen atoms originating from hydroxyl groups only, or from the carboxyl and the α-hydroxyl groups. In acidic medium, three types of complexes are formed: a (2,1,2) complex at the *arabino* site (O-4,5,6,7), two complexes at the O-1,2 site which have either (1,2,2) or (2,2,2) compositions, and a mixed 5:2 complex involving O-1,2,4,5,6,7 of each ligand. In alkaline medium, the carboxylate group is not involved in chelation and a single (2,1,1) complex of the pentadentate ligand (O-2,3,4,5,6) was characterized.

Keywords: D-*glycero*-D-*gulo*-Heptonic acid; Tungstate complexes; ^{13}C NMR; ^{183}W NMR

1. Introduction

It is now well known that carbohydrates form metal complexes through their vicinal hydroxyl groups. For most metal cations, such complexes are weak and are unlikely to

---

[*] Corresponding author.

0008-6215/95/$09.50 © 1995 Elsevier Science Ltd. All rights reserved
SSDI 0008-6215(95)00266-9

possess any biological significance [1]. However, transition elements like Mo and W that exist as oxo anions yield much stronger complexes in which the sugars act as multidentate ligands. The stability of such compounds depends on the configuration of the ligand and hence on the structure of the site of chelation. The molybdate complexes are believed to be models for the active species in the C-2 epimerization of aldoses [2–4]. Recent studies have specified the structures of molybdate and tungstate complexes of aldoses [5,6], ketoses [7,8], and related alditols [9,10].

The corresponding complexes of hydroxyacids derived from carbohydrates (aldonic and aldaric acids) have not received so much attention, although the complexes of gluconic and galactaric acids were used in the separation of tungsten and molybdenum by ion-exchange chromatography [11]. The glycuronic acids were demonstrated to adopt an acyclic form in their complexes of V(IV) and Cu(II) [12–14]. Studies of the tungstate and molybdate complexes of aldaric acids have recently been reported [15–18].

In a continuing series of papers, our team has been investigating the structures and stabilities of carbohydrate complexes of tungsten and molybdenum. For this purpose, the use of ^{183}W NMR was recently developed and proved useful in the study of tungstate complexes of alditols [19–22] and aldaric acids [17,18]. The interest of this technique lies in tungsten being a dipolar nucleus for which coupling constants may exist with protons of the ligand, allowing the unambiguous assignment of the sites of chelation of each tungsten atom. We are now extending this work to aldonic acids $HOCH_2$–$(CHOH)_n$–COOH, for which two types of tungstate complexes may be expected with pH-dependent stabilities. The first type should resemble the complexes of α-hydroxyacids like lactic acid and involve only the CHOH–COOH part of the ligand [23]. Complexes of the second type would involve hydroxyl groups only, like those formed by alditols. Unexpectedly, preliminary results with a hexonic acid (D-gluconic acid) revealed the presence of many complexes, whereas a heptonic acid gave a simpler system. D-*glycero*-D-*gulo*-Heptonic acid was used because of its commercial availability, in relation with its use in pharmaceuticals. The structure of the ligand in each complex was determined by ^{1}H and ^{13}C NMR. The overall thermodynamic formation constant for the complex-forming reaction was determined by indirect photometry, using a novel method based on the bleaching of a coloured tungstate complex of known stability [23].

2. Experimental

All chemicals were commercial products of analytical grade and were used as received. The heptonic acid (Aldrich) was supplied in the form of the sodium salt dihydrate. Aqueous solutions of the complexes were prepared by mixing the sodium heptonate (1 mmol) and disodium tungstate dihydrate (2 or 2.5 mmol) in deuterium oxide (1 mL) and adding concentrated HCl (1 mmol). The values of pH were measured using a Radiometer MI-412 combined glass micro electrode (external diameter 2 mm) and a Metrohm 632 pH-meter standardized with commercial buffers.

The ^{1}H, ^{13}C, and ^{183}W NMR spectra were obtained at 297 K on a Bruker ARX 400 spectrometer equipped with 5- or 10-mm multinuclear probes. Experimental details for 1D spectra have been published elsewhere [19–22]. For the mixture of tungstate complexes at pH 5.9, the preliminary proton assignment could not be completed by performing only a 2D COSY spectrum [24]. Thus, a HOHAHA [25,26] experiment was made with a mixing time of 80 ms and a spin-locking period of 2 ms. In this experiment, the magnetization of a spin system is locked with a strong radiofrequency field during the spin-locking period, in order to allow a coherence transfer between spins that belong to the same coupling network as the initially excited spin. The overall process is equivalent to a multiple relay experiment, but is easier to perform experimentally.

All 2D heteronuclear correlation spectra were obtained using the indirect mode [27] through a HMQC pulse sequence that generates heteronuclear multiquantum coherences [28,29]. This sequence is useful for the detection of nuclei of low sensitivity that have a low natural abundance. Because it is very sensitive to temperature changes, all experiments were run with the sample temperature at 297.0 ± 0.1 K. This experiment is also sensitive to the calibration of the ^{1}H pulse, which must be directly measured on the sample. The durations of the ^{1}H 90° pulses were between 10 and 12 μs, 14 μs for ^{13}C and 47 μs for ^{183}W. All 2D experiments were run with presaturation of the HDO signal during relaxation delay and mixing time.

The formation constant was determined by indirect photometry following a published method [23]. The tungstate complex of 2,5-dihydroxy-1,4-benzoquinone ($c = 6 \times 10^{-5}$ M) was dissociated by the stepwise addition of aliquots (200 μL) of a solution of sodium heptonate (c = 10.00 g L^{-1}). The initial volume of solution was 100 mL and the overall added volume of solution of ligand was 3 mL, ensuring negligible dilution. The decrease of the absorbance (accuracy ± 0.005) was measured at λ 320 nm in 1-cm quartz cells. All measurements were made at 25.0°C. Experimental data were processed on a microcomputer using a laboratory-written routine in QBasic.

3. Results

Formation constant.—Since heptonic acids and their tungstate complex(es) do not possess strong absorption bands in their electronic spectra, direct photometric procedures cannot be used for the determination of the formation constant of the complex. Therefore, a competition method by ligand exchange was applied, in which a weak, coloured tungstate complex is dissociated when the stronger tungstate complex of heptonic acid is formed, with corresponding bleaching of the solution. This method may be used when a mixture of complexes is formed, if one of them is strongly prevailing [23].

The chosen sacrificial species was the tungstate complex of 2,5-dihydroxy-1,4-benzoquinone (H_2D) which is formulated as $(1,1,2)^{2-}$ from the complex-forming reaction (1) [30]:

$$WO_4^{2-} + D^{2-} + 2H^+ \rightleftarrows (1,1,2)^{2-} + H_2O \qquad (1)$$

D^{2-} is the dibasic anion of the dihydroxyquinone. The value of the formation constant determined under the present experimental conditions was log $K_{112} = 15.98 \pm 0.14$. The conditions for optimal ligand exchange were found to be pH 4–5 (acetate buffer), with equal concentrations of tungstate and H_2D, $c = 6 \times 10^{-5}$ M. In this pH range, the heptonic acid (HL) is ionized and the formation equilibrium of its complex may be written:

$$x\mathrm{WO_4^{2-}} + y\mathrm{L^-} + z\mathrm{H^+} \rightleftarrows (x,y,z)^{(2x+y-z)-} + n\mathrm{H_2O} \quad (2)$$

The decrease of absorbance due to the dissociation of the (1,1,2) complex by stepwise addition of the heptonic acid was measured at λ 320 nm, where the largest variations occurred. Knowing the initial and final absorbances, it gave the concentrations of D^{2-} and (1,1,2). The concentration of uncomplexed tungstate was calculated from the known formation constant K_{112}:

$$[\mathrm{WO_4^{2-}}] = \left[(1,1,2)^{2-}\right]/[\mathrm{D}^{2-}][\mathrm{H}^+]^2 K_{112}$$

Then, using mass-balance relations, the concentrations of the (x,y,z) complex and of uncomplexed heptonate (L^-) at equilibrium were obtained from the analytical concentrations of tungstate c_W and ligand c_L.

$$[(x,y,z)] = \left(c_W - \left[(1,1,2)^{2-}\right]\right)/x$$

$$[\mathrm{L}^-] = c_L - y[(x,y,z)]$$

Finally, the thermodynamic and conditional formation constants, K_{xyz} and K'_{xyz} respectively, were determined by applying the law of mass action:

$$K_{xyz} = [(x,y,z)]/[\mathrm{WO_4^{2-}}]^x[\mathrm{L}^-]^y[\mathrm{H}^+]^z = K'_{xyz}/[\mathrm{H}^+]^z$$

$$\log K'_{xyz} = \log K_{xyz} - z(\mathrm{pH})$$

The conditional formation constant K'_{xyz} was calculated at several pH values for different integer values of x and y. Only $x = y = 2$ gave a constant value (Table 1). The variations of log K'_{xyz} were plotted vs. pH and gave a straight line with slope $-z$, indicating $z = 2$. Thus, the formula of the major complex is $(2,2,2)^{4-}$, and its formation constant, log K_{222}, was calculated (mean value 24.30) as shown in Table 1.

NMR data.—In acidic medium (pH < 6), preliminary ^{13}C NMR data revealed the presence of several complexes, the nature of which were readily determined by examination of the ^{183}W NMR spectra (Table 2). By comparison with data obtained in previous work on tungstate complexes of α-hydroxyacids [23], three tungsten signals appeared with chemical shifts characteristic for complexes involving the CHOH–COOH site (intensity 40% of total). The signal at δ −120 (15%) was attributed to a dimeric

Table 1
Conditional formation constants K'_{222} and formation constant K_{222} of the (2,2,2) tungstate complex of heptonic acid

pH	3.80	4.00	4.20	4.40	4.60
log K'_{222}	16.70	16.30	15.90	15.50	15.05
log K_{222}	24.30	24.30	24.30	24.30	24.25

K_{222} is the equilibrium constant for reaction: 2 $\mathrm{WO_4^{2-}}$ + 2 L^- + 2 H^+ $\rightleftarrows$ $(2,2,2)^{4-}$ + n H_2O.
log K_{222} = log K'_{222} + 2 pH. Accuracy log K_{222} ±0.20.

Table 2
^{183}W NMR (16.67 MHz) chemical shifts δ (ppm) and vicinal coupling constants $^{3}J_{W,H}$ (Hz) for the tungstate complexes of heptonic acid [a]

Type of complex	pH	W [b]	W-1	W-2	Type
(1,2,2)	2–6	39.6			L, bidentate
(2,2,2)	2–6		−120.0 (nc)	−120.0 (nc)	L, bidentate
(2,1,2)	2–6		−70.5 (J 9.6)	−79.9 (J 7.7)	E, tetradentate
(5:2)	2–6	38.5	−73.2 (J 10.0)	−74.1 (J 8.0)	E+L, mixed
(2,1,1)	10.25		108.1 (nc)	102.3 (nc)	P″, pentadentate [c]

[a] Reference: Na_2WO_4 in alkaline D_2O. Accuracy δ ±0.1 ppm, $^{3}J_{W,H}$ ±0.1 Hz.

[b] Tungsten atom bis-chelated by two CHOH–COOH sites.

[c] In the xylitol complex of type P, δ 93.3 for both tungsten atoms [22].

nc: Not coupled.

(2,2,2) complex and two other signals (25%) near δ 40 to a pair of monomeric (1,2,2) complexes. In the subsequent discussion, such species will be designated as type L (for lactic). Other signals (intensities 60% of total) were observed near δ −75, which is the characteristic range for (2,1,2) complexes of tetradentate alditols in sickle conformation (type E) [19,20]. Such complexes generally display two signals each, hence the finding of four signals suggested the presence of two complexes of type E. In the spectrum represented in Fig. 1, the corresponding multiplet is poorly resolved in a triplet with a high central peak (signals for the major complex) and two smaller peaks for the minor complex.

Further characterization of the complexes was achieved by ^{13}C NMR spectroscopy. In an initial step, in the absence of literature data, the ^{13}C NMR spectrum of the free ligand at pH 8.6 (acyclic heptonate) was assigned by 2D NMR experiments. We checked that the chemical shifts of the non-carboxylic carbon atoms were not modified at lower pH values, as is shown in Tables 3–5. Since the spectrum of the lactone should contain a characteristic C-4 signal close to δ 80, similar to those found in many furanoses, it may be concluded that no conversion of the acyclic acid to the 1,4-lactone occurred in the short time needed for the experiments.

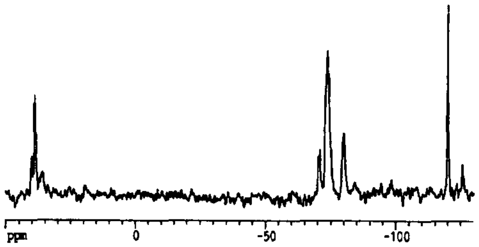


Fig. 1. ^{183}W NMR (16.67 MHz) spectrum of the mixture of tungstate complexes of heptonic acid at pH 4.4 (23,000 scans, 24 h). The signals at ca. −75 ppm correspond to the complexes of type E, those at 40 to the 1:2 complexes of type L, and that at − 120 ppm belongs to the 2:2 complex of type L.

Table 3
^{13}C NMR (100.61 MHz) chemical shifts δ (in ppm) for the (2,2,2) tungstate complex of heptonic acid (type L) at pH 2.8 [a]

Carbon atom	1	2	3	4	5	6	7
u, δ	179.5	74.6	74.8	70.1	72.3	73.3	64.0
(2,2,2), δ	184.2 [b]	85.3	75.6	70.3	72.7	72.9	63.4
$\Delta\delta$	**4.7**	**10.7**	0.8	0.2	0.4	−0.4	−0.6

[a] u, Uncomplexed. Accuracy δ ±0.1 ppm. Data for carbon atoms that bear chelating oxygen atoms are in bold type.
[b] Smaller carboxyl signals are observed at δ 183.8 and 183.0 and are probably due to the minor (1,2,2) complex and to the mixed complex.

Concerning the complexes formed in acidic media, it is obvious that any complex in which the carboxylic group is part of the site of chelation involves the ligand in acyclic form (Scheme 1). In such a case, complex formation should prevent lactonization.

The assignments of the spectra of the complexes were simplified by selecting pH values at which one or two species only were prevailing. Thus, at pH 2.8, seven signals of high intensity were attributed to the (2,2,2) and (1,2,2) species of type L in which only C-1,2 are deshielded (Table 3). Accordingly, several signals for complexed carboxylate groups were observed near δ 185, indicating the presence of more than one complex. On the contrary, six signals only are found for C-2 to C-7, probably because they overlap. In fact, because the sites of chelation are the same in all complexes of type L (Fig. 2), the chemical shifts for all carbon atoms of the ligands are likely to be practically identical. One may notice that the fast formation of these complexes at pH 2.8 agrees with the free ligand being in acyclic form.

The relative proportions of complexes of type E and L do not depend on pH up to 6. Besides, the proportion of type L decreases sharply above pH 6, showing that complexes of type E are favoured at the expense of type L when the acidity decreases. At pH 5.9, where complexes of type E seem to prevail as seen from ^{183}W NMR data, 21 signals are found in the ^{13}C NMR spectrum, indicating the presence of three complexes (Table 4). The relative proportions of complexed ligand are 45:35:20, according to the integration

Table 4
^{13}C NMR (100.61 MHz) chemical shifts δ (in ppm) for the tungstate complexes of heptonic acid at pH 5.9 [a]

Carbon atom	1	2	3	4	5	6	7
u, δ	179.5	74.6	74.7	70.0	72.1	73.2	63.6
Type L, δ	184.2	84.8	75.6	70.3	72.2	72.6	64.1
Type E, δ	179.1	75.8	77.8	81.2	82.2	91.5	70.0
Mixed type, δ	183.8	85.9	77.1	83.8	91.0	82.0	72.2
Type L, $\Delta\delta$	**4.7**	**10.2**	0.9	0.3	0.1	−0.6	0.5
Type E, $\Delta\delta$	−0.3	1.2	3.1	**11.2**	**10.1**	**18.3**	**6.4**
Mixed type, $\Delta\delta$	**4.3**	**11.3**	2.4	**13.8**	**18.9**	**8.8**	**8.6**

[a] u, Uncomplexed. Accuracy δ ±0.1 ppm. Data for carbon atoms that bear chelating oxygen atoms are in bold type. All assignments are made from 2D experiments.

Table 5
^{13}C NMR (100.61 MHz) chemical shifts δ (in ppm) and direct coupling constants $^1J_{C,H}$ (in Hz) for the tungstate complex of heptonic acid (type P″) at pH 10.25 [a]

Carbon atom	1	2	3	4	5	6	7
u, δ	179.75	74.7	74.9	70.2	72.4	73.2	64.6
u, $^1J_{C,H}$	—	142	143	143	143	143	142
(2,1,1), δ	181.65	88.2	84.6	75.2	83.4	87.1	64.0
(2,1,1), $^1J_{C,H}$	—	**147**	**149**	**143**	**145**	**146**	142
$\Delta\delta$	1.9	**13.5**	**9.7**	**5.0**	**11.0**	**13.9**	−0.6
ΔJ	—	**5**	**6**	**0**	**2**	**3**	0

[a] u, Uncomplexed. Accuracy δ ±0.1 ppm; $^1J_{C,H}$ ±1 Hz. Data for carbon atoms that bear chelating oxygen atoms are in bold type. All assignments are made from 2D experiments.

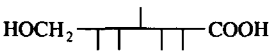
of the carbon signals. The minor complex is certainly a species (or a mixture of species) of type L, since its ^{13}C NMR spectrum is close to that prevailing at pH 2.8.

The second species (35% of ligand) is a complex of type E in which the site of chelation is the *arabino* O-4,5,6,7 system, on the basis of the characteristic CIS pattern given in Table 4, which matches closely that of complexes of alditols that involve the same site [19,20]. In this complex, the more deshielded carbon atom, C-6, is usually surrounded by those that bear the bridging oxygen atoms, C-5 and C-7. Thus, we assume that one tungsten atom is chelated by O-5,6,7 and the other one by O-4,5,7 (Fig. 3). Although the carboxylic group does not chelate tungstate, this complex cannot involve the ligand in 1,4-lactone form, because O-4 is part of the site of chelation.

The major species (45% of ligand) is not, as initially expected, the isomer of the above complex of type E, but a complex of a previously unreported type. The CIS pattern calculated in Table 4 indicates that C-1,2 and C-4,5,6,7 bear chelating oxygen atoms, suggesting that the complex is of a mixed E + L type. A possible structure would possess the skeleton of the (1,2,2) complex of type L, in which the *arabino* sites of each ligand would chelate a ditungstate group. The corresponding W:L stoichiometry is 5:2. This assumption was checked by examination of the corresponding ^{183}W NMR spectrum, which displays the expected signals near δ 40 (for the central tungsten atom, intensity unity) and near δ −75 (for the two ditungstate groups, intensity four).

The structures of these species were drawn in agreement with those determined for other complexes of type E. In the mixed complex, the more deshielded atom is C-5 and thus, the sites of chelation should be, respectively, O-4,5,6 for W-1 and O-4,6,7 for W-2 (Fig. 4).

Between pH 6.5 and 10, the ^{13}C NMR spectra are less easily assigned because some signals are broadened due to chemical exchange between the above complexes and a new species, the proportion of which increases in alkaline medium. At pH 10.25, the ^{13}C NMR spectrum indicates that this species is present alone and the assignments were



Scheme 1. Fischer projection of D-*glycero*-D-*gulo*-heptonic acid.

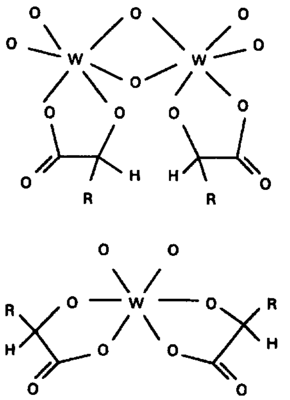


Fig. 2. Proposed structures for the complexes of type L. Top: the (2,2,2) complex. Bottom: the (1,2,2) complexes. R = $(CHOH)_4$–CH_2OH.

made by 2D experiments. The data in Table 5 indicate that four carbon atoms at least, C-2,3,5,6, belong to the site of chelation, and that the CIS pattern is quite symmetrical. It was noted that the central atom, C-4, is little deshielded ($\Delta\delta$ 5 ppm) and its participation in the site of chelation might be questioned. In such a case, the values of the direct coupling constants $^1J_{C,H}$ are often examined since they are generally enhanced by 2–10 Hz for carbon atoms that bear a chelating oxygen atom. In the present case, ΔJ for C-4 is nil. The low CIS value ($\Delta\delta$ 5 ppm) seemed to indicate that C-4 would not bear a chelating oxygen atom.

The ^{183}W NMR spectrum of the same solution (Fig. 5) displays two signals of equal intensities above δ 100 (Table 1) in agreement with a dinuclear stoichiometry and a +VI oxidation state. The small difference between the chemical shifts reveals that both tungsten atoms have similar environments and agrees with the symmetry of the CIS pattern, suggesting that the site of chelation must be roughly symmetrical and in zigzag conformation. Moreover, this ^{183}W NMR spectrum presents an obvious analogy with those of species of type P formed at high pH with xylitol and iditol, in which the ligands are undoubtedly pentadentate [22]. Specifically, the range for the chemical shifts is characteristic and cannot match any other known complex of alditol. We consider that

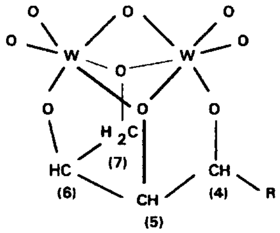


Fig. 3. Proposed structures for the complex of type E. R = CHOH–CHOH–COO(H).

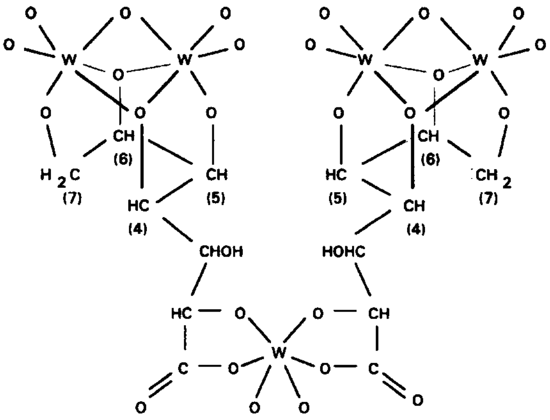


Fig. 4. Schematic representation of the mixed complex. The stereochemistry of the tungsten atom chelated by two lactic sites is arbitrary.

this finding points to the tungsten atoms of the heptonate complex being chelated by the pentadentate ligand (O-2,3,4,5,6), with O-4 being weakly bound to both tungsten atoms.

4. Discussion

Acidic and neutral media.—Our results clearly demonstrate that the heptonic acid forms various types of tungstate complexes in which the ligand uses several sites of chelation. In acidic medium, a competition occurs between the "lactic" site CHOH–COOH and the *arabino* site C-4,5,6,7, showing that the ligand has the dual nature of a α-hydroxyacid and a polyol. An unexpected result is that a mixed complex is formed in which the ligand binds tungstate at both sites. The complexes of type L that involve the carboxylate group are absent in neutral media, indicating that they probably dissociate when the acid function is ionized. The stabilities of the complexes may be compared from their relative proportions at equilibrium, with the result that complexes of types E, L, and mixed type possess quite similar stabilities. Because α-hydroxyacids are gener-

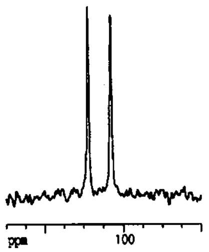


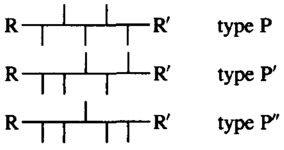
Fig. 5. ^{183}W NMR (16.67 MHz) spectrum of the tungstate complex of heptonic acid at pH 10.25 (2000 scans, 1 h).

ally regarded as efficient ligands [23], one may find it surprising that chelates that involve only donating alcoholic oxygen atoms may be as stable. However, it may indicate that the stabilities of carbohydrate complexes are generally underestimated. A possible reason is the lack of published data on their stability constants. In an attempt to fill this absence of data, the formation constant for one of the type L species, namely the dimeric (2,2,2) species, was determined for the first time.

The existence of the mixed species may be rationalized by considering that the sites of chelation of type L and E are separated by a CHOH group and that no interaction will occur between the chelated tungstate groups. Another type of mixed complex has been characterized earlier in the tungstate complexes of perseitol, that contained a bis-dinuclear species in which the single ligand molecule used two sites of chelation at O-1,2,3 and O-4,5,6,7 [20]. Moreover, a synergistic effect was suspected because of the high proportion of this complex.

It may be noticed finally that, contrary to most asymmetric alditols that yield isomeric pairs of complexes of type E, the heptonic acid affords a single complex of type E and the mixed complex instead of the second isomer. Usually, in such a pair of isomers, the major species is that in which the more deshielded carbon atom is located near the shortest side chain [20]. It is also the case for the heptonate complexes, since C-6 is the atom at δ 91 in the complex of type E. In contrast, the minor species is not formed, but probably exists as the mixed complex, in which C-5 is the atom at δ 91 of the *arabino* site. The stabilization of the minor species when the O-1,2 site chelates a tungsten atom is probably a consequence of the synergistic effect mentioned above.

Alkaline medium.—The chemical shifts of the tungsten atoms of the single dinuclear complex lie in the range characteristic for complexes of pentadentate alditols like xylitol and L-iditol (type P) that are also formed in very alkaline medium, in agreement with the carboxylate group not being involved in the pentadentate O-2,3,4,5,6 site of chelation. The composition of this complex was deduced from the known formulae of the species of type E that are $(2,1,2)^{3-}$ ions [the corresponding complexes of neutral alditols are written $(2,1,2)^{2-}$]. Since the new complex is formed at higher pH, its formula involves a smaller number of protons and should be $(2,1,1)^{4-}$. A similar composition, $(2,1,1)^{3-}$, was proposed for species of type P formed with neutral alditols [22]. However, differences in the CIS pattern and in the tungsten chemical shifts show that the heptonate complex is of a type P″, slightly different from type P. The chemical shifts of the tungsten atoms are ca. 82–94 ppm in type P [22] and > 100 ppm in type P″. The CIS patterns, in ppm, are 13–10–5–11–14 in type P″ and 14–10–13–10–14 in type P [22], showing that the larger difference is found at the central carbon atom. We attribute the origin of these differences to the reversed configurations of the lateral carbon atoms,



Scheme 2. Configurations of carbohydrates (in the D series) in relation to the complexes of the pentadentate ligands.

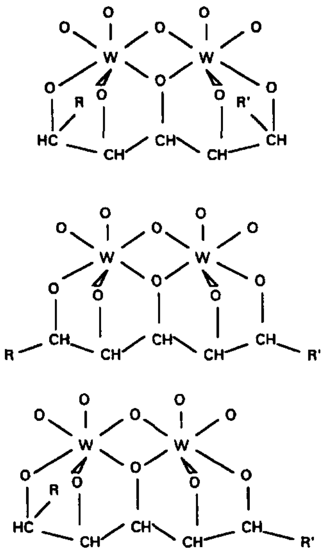


Fig. 6. Proposed structures for the pentadentate tungstate complexes. For D-*glycero*-D-*gulo*-heptonate, R = $HOCH_2$ and R′ = COO^-. From top to bottom: type P″, type P, and type P′.

which probably create a steric strain in the complex. By consideration of molecular models, the postulated steric strain would open the central angle C-3,4,5 of the heptonate ligand. It would decrease the parallelism between the CO-4 and the CO-3,5 bonds, with simultaneous lengthening of the bonds between O-4 and the tungsten atoms, which would be weakened. Consequently, the C-4 atom would be less deshielded in type P″ than in type P. Moreover, comparison of the structures proposed for types P and P″ suggests that complexes of an intermediate type, P′, might be formed with a pentadentate ligand possessing a central *xylo* system with one *threo* and one *erythro* lateral diol groups. The corresponding formulae are shown in Scheme 2 and the structures proposed for complexes of types P, P′, and P″ are shown in Fig. 6. In all these complexes involving pentadentate sugar ligands, the inorganic moiety is made of two WO_6 octahedra sharing an edge [22], which appears to be a very common subunit of most polytungstate anions [31]. In contrast, the dinuclear complexes formed with tetradentate alditols in more acidic medium, like those of type E, are made of two octahedra sharing a face. It may be important to recall that in alkaline medium, free tungstate only exists as monomeric tetrahedral WO_4^{2-} ions. Thus, carbohydrate ligands that possess five vicinal hydroxyl groups and a zigzag conformation can stabilize, by chelation, a dimeric tungstate ion that has not been detected in the uncomplexed state.

5. Conclusions

The nature of the tungstate complexes of the heptonic acid depends on the pH. In acidic medium there exist simultaneously a (2,1,2) complex formed at the tetradentate *arabino* site (O-4,5,6,7), two complexes formed at the CHOH–COOH site, namely a monomeric (1,2,2) species and a dimeric (2,2,2) complex, and a mixed complex (5:2) in which one tungsten atom is chelated by two CHOH–COOH sites, whereas two ditungstate groups are chelated at the *arabino* sites of both ligands. All these complexes disappear at pH > 7 and at pH 10.25, a single dinuclear complex (type P″) becomes predominant in which the ligand is pentadentate (O-2,3,4,5,6) and in zigzag conformation. The type P″ differs from the type P, previously described for two alditols, by the substituents borne at the C-2,6 atoms being oriented towards the site of chelation. In consequence, a steric strain exists that weakens the bond formed with O-4. The absence of complexes involving the carboxyl group in neutral or alkaline medium probably results from the ionization of this group.

References

[1] S.J. Angyal, *Adv. Carbohydr. Chem. Biochem.*, 47 (1989) 1–43.
[2] V. Bílik, *Chem. Zvesti*, 26 (1972) 76–81; 183–186; 187–189; 372–375.
[3] M.L. Hayes, N.J. Pennings, A.S. Serianni, and R. Barker, *J. Am. Chem. Soc.*, 104 (1982) 6764–6769.
[4] E.L. Clark, Jr, M.L. Hayes, and R. Barker, *Carbohydr. Res.*, 153 (1986) 263–270.
[5] J.P. Sauvage, S. Chapelle, A.M. Dona, and J.F. Verchère, *Carbohydr. Res.*, 243 (1993) 293–305.
[6] M. Matulová and V. Bílik, *Carbohydr. Res.*, 250 (1993) 203–209.
[7] J.P. Sauvage, S. Chapelle, and J.F. Verchère, *Carbohydr. Res.*, 237 (1992) 23–32.
[8] M. Matulová and V. Bílik, *Chem. Pap.*, 44 (1990) 97–103.
[9] S. Chapelle, J.F. Verchère, and J.P. Sauvage, *Polyhedron*, 9 (1990) 1225–1234.
[10] M. Matulová, V. Bílik, and J. Alföldi, *Chem. Pap.*, 43 (1989) 403–414.
[11] M. Maruo, N. Hirayama, A. Shiota, and T. Kuwamoto, *Anal. Sci.*, 8 (1992) 511–516.
[12] G. Micera, A. Dessì, H. Kozlowski, B. Radomska, J. Urbanska, P. Decock, B. Dubois, and I. Olivier, *Carbohydr. Res.*, 188 (1989) 25–34.
[13] M. Branca, G. Micera, A. Dessì, and H. Kozlowski, *J. Chem. Soc., Dalton Trans.*, (1989) 1283–1287.
[14] M. Branca, G. Micera, D. Sanna, A. Dessì, and H. Kozlowski, *J. Chem. Soc., Dalton Trans.*, (1990) 1997–1999.
[15] M.L. Ramos, M.M. Caldeira, and V.M.S. Gil, *Inorg. Chim. Acta*, 180 (1991) 219–224.
[16] M.M. Caldeira, M.L. Ramos, V.M.S. Gil, H. van Bekkum, and J.A. Peters, *Inorg. Chim. Acta*, 221 (1994) 69–77.
[17] M.L. Ramos, M.M. Caldeira, V.M.S. Gil, H. van Bekkum, and J.A. Peters, *Polyhedron*, 13 (1994) 1825–1833.
[18] M.L. Ramos, M.M. Caldeira, V.M.S. Gil, H. van Bekkum, and J.A. Peters, *J. Coord. Chem.*, 33 (1994) 319–329.
[19] S. Chapelle and J.F. Verchère, *Inorg. Chem.*, 31 (1992) 648–652.
[20] S. Chapelle, J.P. Sauvage, and J.F. Verchère, *Inorg. Chem.*, 33 (1994) 1966–1971.
[21] S. Chapelle and J.F. Verchère, *Carbohydr. Res.*, 266 (1995) 161–170.
[22] S. Chapelle, J.P. Sauvage, P. Köll, and J.F. Verchère, *Inorg. Chem.*, 34 (1995) 918–923.
[23] M. Hlaïbi, S. Chapelle, M. Benaïssa, and J.F. Verchère, *Inorg. Chem.*, 34 (1995) 4434–4440.
[24] W.P. Aue, E. Bartholdi, and R.R. Ernst, *J. Chem. Phys.*, 64 (1976) 2229–2246.
[25] L. Braunshweiler and R.R. Ernst, *J. Magn. Reson.*, 53 (1983) 521–528.
[26] D.G. Davis and A. Bax, *J. Am. Chem. Soc.*, 107 (1985) 2821–2822.
[27] A. Bax, R.H. Griffey, and B.L. Hawkins, *J. Magn. Reson.*, 55 (1983) 301–315.
[28] L. Mueller, *J. Am. Chem. Soc.*, 101 (1979) 4481–4484.
[29] V. Sklenár and A. Bax, *J. Magn. Reson.*, 71 (1987) 379–383.
[30] J.M. Poirier and J.F. Verchère, *J. Chem. Res.*, (1980) S 80–81, M 0908–0940.
[31] F.A. Cotton and G. Wilkinson, *Modern Inorganic Chemistry*, 5th ed., Wiley, New York, 1988.