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Chemical Ionization Mass Spectra of the Stereoisomeric 1,5-Anhydropentofuranoses, 1,6-Anhydrohexofuranoses and 1,6 : 3,5-Dianhydrohexofuranoses

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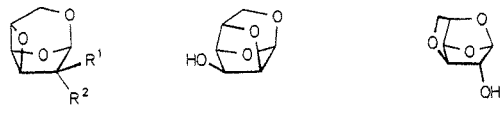
The isobutane and methane direct chemical ionization (DCI) mass spectra of mono- and dianhydrosugars are substantially influenced by their stereochemistry at temperatures of 150–250°C. The best results are obtained under isobutane CI at 200 or 250°C. 1,6:3,5-Dianhydrogulofuranose gives proton-bridge stabilized MH^+ ions and fewer fragment ions compared with its *ido* epimer. The four diastereomeric 1,5-anhydropentofuranoses show increased MH^+ and M_2H^+ abundances for the *lyxo* and *ribo* isomers with *cis*-1,2-diol sites capable of proton bridging. The *xylo* isomer gives a dominant $[M - OH]^+$ ion. All isomers, but especially *xylo* and *ribo*, give abundant $[C_3H_5O_2]^+$ skeleton cleavage ions. They are attributed to an RDA fragmentation of pyranoglycosyl-type MH^+ ions. The eight diastereomeric 1,6-anhydrohexofuranoses with *endo/exo* configured triol structures show very characteristic MH^+ abundances (4–41% Σ). They parallel the amount of proton solvation in *cis*-diol sites of the isomers (*gluco* ⩽ *ido* ⩽ *altro* < *gulo* < *galacto* < *talo* < *allo* < *manno*). The $[M - OH]^+$ ion abundances (15–47% Σ) are also very characteristic (*galacto* ⩽ *talo* < *manno* ⩽ *altro* ⩽ *allo* < *gluco* ⩽ *ido* ⩽ *gulo*). They reflect the possible H_2O or C_4H_9OH loss from the MH^+ and $[M \cdot C_4H_9]^+$ ions, respectively, with formation of protonated 1,6:3,5-and 1,6 : 2,5-dianhydrohexofuranose species; the slightly flattened C(5) site of M might favour the departure of the 5-OH group. In addition, there are especially high abundances of skeleton fragment ions, 15% Σ $[MH - HCOOH]^+$, 10% Σ $[M - OH - H_2O - CH_2O]^+$ and 42% Σ $[M - OH - C_2H_4O_2]^+$, for the *ido*, *galacto* and *gluco* isomers, respectively.

INTRODUCTION

Anhydro derivatives of sugars are of special interest in synthetic carbohydrate chemistry and are thermal degradation products of mono-, oligo- and polysaccharides. Chemical ionization (CI) mass spectrometry has proved to be useful in investigating the stereochemistry of this varied category of compounds. Kadentsev *et al.*[1] reported the characteristic methane and isobutane CI of the deoxy and the *O*-acetyl derivatives of the 1,6:2,3- and 1,6:3,4-dianhydro-β-D-hexopyranoses. Also applying isobutane CI mass spectrometry, Köll and coworkers[2,3] differentiated a series of 1,2:3,4:5,6-trianhydrohexitol isomers and the 1,3:2,5-dianhydro-iditol/glucitol and 1,3:2,5:4,6-trianhydro-iditol/galactitol isomers. Examples of CI studies of related polycyclic alkanes include camphane-2,3-diols,[4] protoadamantane-4,9-diols[5] and [4.3.3]propellane-8,11-diols.[6] General reviews on the CI of organic stereoisomers and sugars can be found in Refs 7–9.

This paper deals with the isobutane and methane direct chemical ionization (DCI) of the 1,6:3,5-dianhydrohexofuranoses **1a** and **b**, 1,5-anhydropentofuranoses **4a–d**, and 1,6-anhydrohexofuranoses **5a–h** (Schemes 1 and 2). The compounds are rigid polycyclic systems which have one, two and three free hydroxy groups and comprise two, four and eight diastereomers, respectively. For the dianhydrosugar group two constitutional isomers, 1,6:2,5-dianhydro-α-L-gulofuranose (**2**) and 1,5:3,6-dianhydro-β-D-glucofuranose (**3**), were included. The aim is to differentiate the stereoisomers and to shed some light on the fragmentation reactions of the protonated anhydrosugars in the gas phase.



1	R^1	R^2
a	OH	H
b	H	OH

2 **3**

Scheme 1

† Dedicated to Professor Dr H.-F. Grützmacher on the occasion of his 60th birthday.

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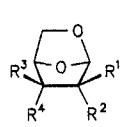
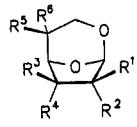


4	R^1	R^2	R^3	R^4
a	OH	H	OH	H
b	OH	H	H	OH
c	H	OH	OH	H
d	H	OH	H	OH



5	R^1	R^2	R^3	R^4	R^5	R^6
a	OH	H	OH	H	OH	H
b	OH	H	OH	H	H	OH
c	OH	H	H	OH	OH	H
d	H	OH	OH	H	OH	H
e	OH	H	H	OH	H	OH
f	H	OH	OH	H	H	OH
g	H	OH	H	OH	OH	H
h	H	OH	H	OH	H	OH

Scheme 2

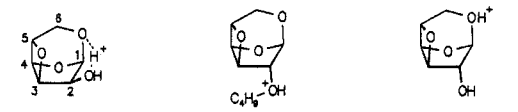
EXPERIMENTAL

The CI measurements were done on a Finnigan-MAT 212 mass spectrometer with isobutane, methane and isobutane-d_{10} as reagent gases (0.1 Torr; 1 Torr = 133.3 Pa) and at ion source temperatures in the range 150–250 °C; emission 0.1 mA, electron energy 200 eV. The samples were introduced by a temperature-programmable solids probe under direct exposure of the compound to the ionizing plasma (DCI). Scans of 40–400 u were taken at a rate of 5.1 s per decade. The data from ten scans were averaged; constant sample evaporation was controlled by total ion current monitoring above *m/z* 60. The spectra of metastable transitions in the first field-free region were taken by linked scanning at constant *B/E*. The syntheses of compounds **1**,[10–12] **2**,[12,13] **3**,[14] **4**[15] and **5**[16,17] have been reported earlier. Samples of *O*, *O'* – d_2 – **4** and *O*, *O'*, *O''* – d_3 – **5** were prepared by exchange with D_2O. Isobutane-d_{10} (98%) was obtained from Cambridge Isotope Laboratories (Woburn, MA, USA).

RESULTS AND DISCUSSION

1,6:3,5-Dianhydrohexofuranoses

The epimeric dianhydrides **1a** and **b** with 2,5,7-trioxatricyclo[4.2.1.0^{3,8}]nonane skeletons are *endo* and *exo* configured monoalcohol species (Scheme 3). X-ray diffraction studies of crystalline **1a** (*endo*) indicate intramolecular bifurcated H bridging of the OH group to the oxygen atoms O(1) and O(3).[11] The OH···H distances are 223 and 238 pm and the O—H···O angles are 122° and 109°, respectively. The isobutane CI spectra of **1a** and **b** measured at different ion-source temperatures (170, 200 and 250 °C) are summarized in Table 1, together with reference data (200 °C) for two constitutional isomers, 1,6:2,5-dianhydro-α-L-gulofuranose (**2**) and 1,5:3,6-dianhydro-β-D-glucofuranose (**3**).



endo – **1** · H^+ *exo* – **1** · $C_4H_9^+$ *exo* – **1** · H^+

Scheme 3

Under isobutane CI, proton transfer from the $[C_4H_9]^+$ reagent ions to the hydroxy group of alkanols (ROH) is endothermic and the formation of R^+ or $[M - OH]^+$ fragment ions occurs by OH^- abstraction by the $[C_4H_9]^+$ ions within intermediate $[M + C_4H_9]^+$ adduct ions.[7] However, intramolecular hydrogen bonding in difunctional alcohols enhances the proton affinity compared with the monofunctional compounds and direct proton transfer from the $[C_4H_9]^+$ ions to the alcohol molecules gives $[M + H]^+$ ions with internal proton solvation. These ions can subsequently lose H_2O to form the analogous $[MH - H_2O]^+$ or R^+ fragment ions. The presence or absence of internal solvation in the substrate molecule can be efficiently used to probe its stereochemistry.[7,9]

Thus, the proton cyclized $[\mathbf{1a} + H]^+$ (*'endo'*) ions, or *endo*-**1** · H^+ ions, were unusually abundant at all ion-source temperatures. A proton-bridged structure is not probable for *exo*-**1** and this was reflected in a lower M · H^+ ion intensity and greater intensity of the $[M - OH]^+$ ions. The configurational discrimination of *endo*- and *exo*-**1** · H^+ is analogous to that observed in the isobutane CI of *cis*- and *trans*-cyclopentane-1,2-diols[9,18] which represent the relevant epimeric partial structures.

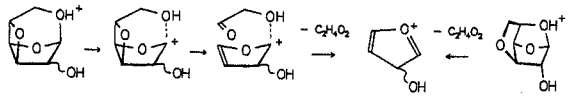
The dianhydrosugar skeleton undergoes protolytic degradation to give additional differences. The $[M - OH]^+$ ions from *endo*-**1** lost H_2O and those from *exo*-**1** lost CO. The *exo* $[M - OH - CO]^+$ ions could even be directly formed as $[MH - HCOOH]^+$ species under loss of the C(1) site. There was also a skeletal cleavage ion, $C_4H_5O_2^+$, for *endo*- and *exo*-**1** (Eqn. (1a)). The MH^+ precursor releases the terminal C(5)–C(6) portion as CH_2OHCHO to give this ion. Although of

Table 1. Isobutane CI mass spectra of dianhydrohexofuranoses 1–3 (% Σ)[a]

Sugar	Configuration	OH type	M · $C_4H_9^+$	MH^+	$[M - OH]^+$	*m/z* 109[b]	*m/z* 99[c]	$C_4H_5O_2^+$
1a	α-L-*gulo*	*endo*[d]	–/–/–	66/44/20	14/24/29	6/11/24	1/1/4	2/3/7
1b	α-L-*ido*	*exo*[e]	2/1/–	34/25/11	32/44/31	1/1/2	5/7/7	3/5/7
2	α-L-*gulo*	*endo*	2	57	10	—	—	5
3	β-L-*gluco*	*exo*	9	33	10	—	—	12

[a] Temperature 170/200/250 °C.
[b] *m/z* value of $[M - OH - H_2O]^+$ ion.
[c] *m/z* value of $[MH - HCOOH]^+$ ion.
[d] Substrate ion percentage versus total ionization: 31/34/–.
[e] Substrate ion percentage versus total ionization: 24/47/–.

low abundance, the intensity of its peak was slightly greater in the spectrum of *exo*-**1**.

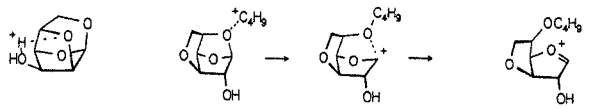


endo/exo-**1** · H^+ $C_4H_5O_2^+$ **3** · H^+

(1*a*/*b*)

The ion-source temperature strongly influences the abundances of the different stereospecific fragmentations and the contrast for the two isomers is always very pronounced, but is highest at 200 °C.

In the constitutionally isomeric dianhydrohexopyranoses **1**, **2** and **3**, the C(5)—C(6) entity is oxygen linked to C(3) and C(1), C(2) and C(1) and C(1) and C(3) of the furanose ring, respectively. The oxetan ring in **1** is changed to a less strained tetrahydropyran ring in **2** and this is reflected in an increased stability of the **2** · H^+ ions (exemplified by the *endo* epimer) compared with that of the *endo*-**1** · H^+ ions. However, in spite of the unstrained skeleton the **3** · H^+ ions (*exo* epimer) show enhanced reactivity. There is anomeric assistance[9,19] for $C_2H_4O_2$ loss to give $[C_4H_5O_2]^+$ ions (Eqn. (1b)) and also for an unusual glycosyl cleavage of the $[M \cdot C_4H_9]^+$ (O(1)) adduct ions to give stable $[\mathbf{3} \cdot C_4H_9]^+$ (*furano*) ions (Eqn (2)). The latter reaction includes backside assistance by the 2-*exo*-OH group. A similar alkylation was observed in the $[M \cdot C_4H_9]^+$ ions of *trans*-configured 3-*O*-acetyl-1,6:2,3-dianhydrohexopyranoses.[1]

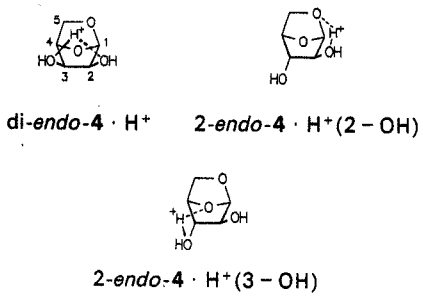


2 · H^+ **3** · $C_4H_9^+$(O(1)) **3** · $C_4H_9^+$(*furano*)

(2)

1,5-Anhydropentofuranoses

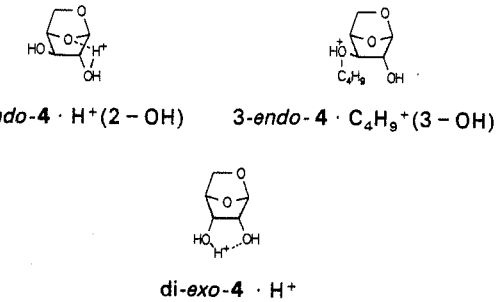
This class of anhydrosugars belongs to the norbornane systems with oxygen-substituted skeletons of the 2,7-dioxabicyclo[2.2.1]heptane type. The isobutane and methane CI mass spectra of the 1,5-anhydro-β-D-pentofuranose group (**4**) are shown in Tables 2 and 3. These diol compounds include four *endo*/*exo*-configurational isomers (Schemes 4 and 5).



di-*endo*-**4** · H^+ 2-*endo*-**4** · H^+(2 − OH)

2-*endo*-**4** · H^+(3 − OH)

Scheme 4



3-*endo*-**4** · H^+(2 − OH) 3-*endo*-**4** · $C_4H_9^+$(3 − OH)

di-*exo*-**4** · H^+

Scheme 5

The high abundance of the MH^+ ions (Table 2) in high-temperature isobutane CI (250 °C), and similarly in low-temperature methane CI, indicates proton-bridged ions. The 3-*endo*-**4** isomer (=**4c**) can form proton cyclized ions only with participation of the *exo*-2-OH but not of the *endo*-3-OH group. This is shown by the decreased 3-*endo*-**4** · H^+ abundance and increased $[M - OH]^+$ ion abundance. The latter ions in isobutane CI result from loss of C_4H_9OH from the $[M \cdot C_4H_9]^+$ adduct ions and originate from loss of H_2O from the unstable fraction of bridged MH^+ ions. The H_2O loss from metastable **4** · H^+ ions from the isobutane CI could be detected for all isomers. Specifically, as a minor process some unbridged 3-*endo*-**4** · H^+(3-OH) ions can be formed by protonation under attack of high thermal energy $[C_4H_9]^+$ reagent ions which overcome the activation energy barrier.

The decreased stability of *endo*-**4** · H^+ is similar to that of *exo*-**1** · H^+ above. Also, the MH^+ ions from the 1,3-diol-type 1,3:2,5-dianhydro-L-iditol[3] with an *exo*-4-OH group which is unable to proton bridging shows slightly more fragmentation compared with the MH^+ ions from its 4,5-di-*exo* D-glucitol epimer, which can undergo 4-OH/6-OH proton cyclization. A very marked

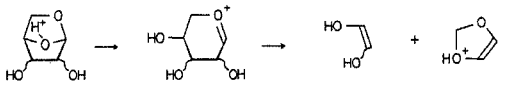
Table 2. Isobutane CI mass spectra of 1,5-anhydropentofuranoses (% Σ)[a]

Sugar	Configuration	Diol type	P[b]	M_2H^+	MH^+	$[M-OH]^+$	$C_3H_5O_2^+$
4a	β-D-*lyxo*	Di-*endo*	24/40/–[c]	1/1/0.2	87/82/66	1/3/9	0.5/1.7/5.0
4b	β-D-*arabino*	2-*endo*	38/40/–	–/–/–	92/86/67	1/2/5	1.8/4.0/9.3
4c	β-D-*xylo*	3-*endo*	41/43/–	1/–/–	81/66/40	5/14/23	2.3/6.4/17
4d	β-D-*ribo*	Di-*exo*	38/53/–	1/2/0.3	84/76/50	2/4/7	4.6/8.2/19

[a] Temperature 160/200/250 °C. M · $C_4H_9^+$ ions: 2–4/1–2/0–1% Σ.
[b] Percentage of substrate ions relative to total ionization.
[c] Not determined.

contrast is seen between the behaviour of the **4** · H^+ isomers and the behaviour of the MH^+ isomers from the analogous camphane-2,3-diols.[4] In isobutane (and methane) CI at 170 °C, the MH^+ ions of the *trans* isomers, 2-*endo* and 3-*endo*, completely decomposed, the proton-bridged di-*endo*-MH^+ ions showed substantial (or at least distinct) abundances and the crowded proton-bridged di-*exo*-MH^+ ions showed only minor (or even no) abundance. The general suppression of the MH^+ ion abundances of the camphane-2,3-diols emphasizes the stabilizing role of the skeleton oxygen atoms in the **4** · H^+ ions.

There was also a characteristic skeletal cleavage ion, $[C_3H_5O_2]^+$. It was accompanied by a metastable transition of the **4** · H^+ precursor ion. The $[C_3H_5O_2]^+$ ion abundances were greater in the spectra of 3-*endo*- and di-*exo*-**4** than in those of di-*endo*- and 2-*endo*-**4**. These ions apparently originated from the RDA reaction of the pyrano-type MH^+ ions (Eqn. (3)). Thus, the $[C_3H_5O_2]^+$ peak heights (Table 2) should reflect initial protonation on the O(4) atom. A strong and direct temperature dependence was observed for the $[C_3H_5O_2]^+$ abundances of the stereoisomers. This indicates that thermal excitation induces the cycloreversion of the stereospecific intermediate ions. In the high-energy methane CI spectra (Table 3) and EI spectra[20] of **4**, similar $[C_3H_5O_2]^+$ abundances were found.

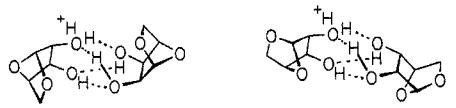


4 · H^+ (O(4)) (*pyrano*) $C_3H_5O_2^+$

(3)

The stereospecific differences of the $[C_3H_5O_2]^+$ ion abundances could be explained as follows. Besides direct O(4) protonation, additional formation of MH^+(O(4)) ions could occur by proton migration of initially OH protonated MH^+ species. Such shifts are possible in the bridged species 2-*endo*-**4** · H^+(3-OH) and 3-*endo*-**4** · H^+(2-OH) from the 3-*exo*- and 2-*exo*-OH, respectively, and in di-*exo*-**4** · H^+ even from both OH groups. This statistical increase in favourable H^+ shifts agrees with the $[C_3H_5O_2]^+$ intensity increase in this sequence of isomers. It is generally possible to trace the proton migration by specific deuterium labelling. As the reagent proton of the decomposing **4** · H^+(O(4)) ions remains on the neutral fragment in Eqn (3), the corresponding RDA ion should have an unchanged $[C_3H_5O_2]^+$ composition under isobutane-d_{10} CI and a shifted $[C_3H_4DO_2]^+$ composition for labelled $M(OD)_2$ samples under isobutane-d_0 CI. However, the experiments were difficult to quantify because of partial H/D interchange in the $M(OH)_2D^+$ and $M(OD)_2H^+$ precursors. This agrees with proton migrations in related MD^+ ions such as those from tri-*O*-acetylglucopyranosyl fluorides[21] and maleic acid.[9,22]

The methane CI spectra of **4** (Table 3) were measured with very high substrate concentrations in the ion source. Therefore, the stereochemical effects on the formation of protonated dimers, M_2H^+, are more pronounced than in the isobutane CI spectra with less high substrate concentrations. The *cis*-1,2-configured isomers, di-*endo*- and di-*exo*-**4**, show unusually stable protonated dimers. This agrees with the increased stability of the M_2H^+ ions from *cis*-cyclopentane-1,2-diol because a di-chelate can be formed and the corresponding *trans*-M_2H^+ ions are mono-chelates.[9,18] The interfering pseudo-rotation of the cyclopentane ring is absent in the bicyclo[2.2.1] heptane skeleton and the *cis*-2, 3 substituents are synclinal. As Dreiding molecular models show (OH···H distance 200 pm; H bridge angle 120°), the M_2H^+ ions of di-*endo*- and di-*exo*-**4** can adopt a circular H-bridge structure which includes all four OH groups. The slightly crowded di-*endo*-$\mathbf{4}_2$ · H^+ cluster ions are slightly less stable than the di-*exo*-$\mathbf{4}_2$ · H^+ clusters (Table 3) (Scheme 6). The 2-*endo* and 3-*endo* isomers cannot adopt M_2H^+ conformations of similar stability.



di-*endo*-$\mathbf{4}_2$ · H^+ di-*exo*-$\mathbf{4}_2$ · H^+

Scheme 6

1,6-Anhydrohexofuranoses

The skeleton of these anhydrosugars is the chiral (1*R*)/(1*S*)-2,8-dioxabicyclo[3.2.1]octane.[17] The compounds are free triols and there is a total of eight diastereomeric pairs of enantiomers which show different *endo*/*exo* configurations of the OH groups.

The conformation of the 1,6-anhydrohexofuranoses (**5**) in the crystalline state is known from x-ray diffraction studies.[17] In all isomers the furanoid ring adopts an envelope near to E_0 or ^0E, respectively, and the 1,3-dioxane bridge is a slightly distorted chair; its slightly flattened $C(6)H_2$ unit has a syn orientation towards the C(2)—C(3) site; *cis*-2,3 oxygen atoms are near synclinal. This was also deduced from ^1H nuclear magnetic resonance experiments on isomeric 1,6-anhydrohexofuranoses (**5**) and their acetates in solution.[16,23]

Table 3. Methane CI mass spectra of 1,5-anhydropentofuranoses (% Σ)[a]

Sugar	Diol	P[b]	M_2H^+	$[M_2H-H_2O]^+$	$[M_2H-2H_2O]^+$	MH^+	$[MH-H_2O]^+$	$[MH-2H_2O]^+$	$C_3H_5O_2^+$
4a	Di-*endo*	59/93	1.5/12	0.3/2.0	0.4/2	33/13	5/5	2/3	7/2
4b	2-*endo*	57/95	0.9/5.6	1.0/5.6	0.9/4	42/24	7/8	2/3	10/3
4c	3-*endo*	58/91	1.4/0.4	0.4/1.8	1.2/5	26/18	16/16	5/14	9/3
4d	Di-*exo*	63/95	6/14	1.3/3.1	0.9/2	30/27	6/6	2/4	11/4

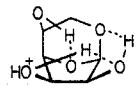
[a] Temperature 150 °C; minor isobutane content (incidental admixing).
[b] Percentage of substrate ions relative to total ionization (% Σ_{35}).

In the crystal state of **5** there is generally intermolecular H bridging and there is also one intramolecular H bridge in four of the isomers.[17] The corresponding donor/acceptor sites, OH···O distances and O—H···O bridge angles are as follows:

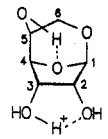
5a (*gulo*; tri-*endo*)	5 – OH···O – 3	289 pm	108°
5d (*ido*; 3,5-di-*endo*)	5 – OH···O – 3	279 pm	129°
5g (*talo*; 5-*endo*)	2 – OH···O – 3	267 pm	101°
5h (*allo*; tri-*exo*)	2 – OH···O – 3	263 pm	127°

In Tables 4 and 5 are shown the isobutane and methane CI mass spectra of the eight diastereomeric 1,6-anhydrohexofuranoses **5a–h**. Fragment ion structures were confirmed by the isobutane CI spectra of 1,6-anhydro-α-D-galactofuranose-$(OD)_3$ and 1,6-anhydro-α-L-idofuranose-$(OD)_3$. Metastable ion spectra were measured of the MH^+, $[M - OH]^+$ and $[M - OH - H_2O]^+$ ions from *galacto-* and *ido-***5** (=**5c** and **5d**); the *galacto*-$[M - OH - H_2O]^+$ ion showed a loss of 30 (0.1% of the precursor intensity) to give the ion of *m/z* 97. For both reagent gases the fragmentation of the protonated anhydrosugars, $\mathbf{5} \cdot H^+$, was strongly influenced by their stereochemistry. Under near thermoneutral protonation in the isobutane CI the abundance of the stereospecific ions was greater than their abundance under exothermic methane CI.

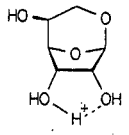
Under isobutane CI all of the isomers of **5** show substantial peaks for MH^+ ions, in the 4–41% Σ range. Very favourable proton bridging in MH^+ of three of the four isomers with *cis*-vicinal diol groups, 2,3-di-*endo*-/tri-*exo*-/5-*endo*-**5** (*manno/allo/talo*) (Scheme 7), gives well spaced abundances of 41, 31 and 26% Σ, respectively. This sequence parallels the corresponding numbers of possible proton cyclization modes.



2,3-di-*endo*-**5** · H^+ (*manno*)



tri-*exo*-**5** · H^+ (*allo*)



5-*endo*-**5** · H^+ (*talo*)

Scheme 7

However, proton bridging is unfavourable in the remaining *cis*-vicinal diol isomer, tri-*endo*-**5** (*gulo*). The rigid skeleton causes 3-OH/5-OH di-*endo* crowding in the tri-*endo* isomer and also in its 2-epimer, 3,5-di-*endo*-**5** (*ido*). The corresponding intramolecular H bridges in the crystalline state have unfavourable H-bridge distances (>220 pm) and/or angles (<120°) as shown above. Both isomers are characterized by very abundant $[M - OH]^+$ ions. Their stability can be attributed to internal dehydration of M^+ to give protonated 1,6:3,5-dianhydrosugar species (Eqns (4a) and (5a)).

Table 4. Isobutane CI mass spectra of 1,6-anhydrohexofuranoses (200 °C; % Σ)[a]

Sugar	Configuration	Triol type	M_2H^+	MH^+	$[M - OH]^+$	*m/z* 127[b]	*m/z* 99[c]	*m/z* 97[d]	$C_4H_5O_2^+$
5a	α-L-*gulo*	Tri-*endo*	<0.1	12	47	7	0.5	8	20
5b	β-D-*manno*	2,3-Di-*endo*	6	41	21	7	0.1	2	16
5c	α-L-*galacto*	2,5-Di-*endo*	2	18	15	5	0.4	10	16
5d	α-L-*ido*	3,5-Di-*endo*	—	6	37	8	15	1	27
5e	β-D-*altro*	2-*endo*	3	8	23	11	0.1	1	26
5f	β-D-*gluco*	3-*endo*	—	4	35	10	0.3	3	42
5g	α-L-*talo*	5-*endo*	1.6	26	16	6	0.4	5	28
5h	β-D-*allo*	Tri-*exo*	0.1	31	31	11	1.4	—	25

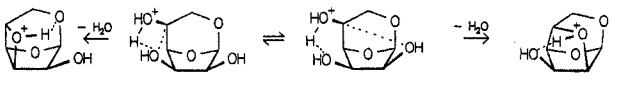
[a] Additional ions: 0–3% Σ $[MC_4H_9 - H_2O]^+$.
[b] *m/z* value of $[M - OH - H_2O]^+$ ion.
[c] *m/z* value of $[MH - HCOOH]^+$ ion.
[d] *m/z* value of $[M - OH - H_2O - CH_2O]^+$ ion.

Table 5. Methane CI mass spectra of 1,6-anhydrohexofuranoses (150 °C; % Σ)[a, b]

Sugar	Triol type	MH^+	$[MH - H_2O]^+$	$[MH - 2H_2O]^+$	$[MH - HCOOH]^+$	*m/z* 91	$C_4H_5O_2^+$
5a	Tri-*endo*	2	6	5	4	9	15
5b	2, 3-Di-*endo*	6[a]	3	5	3	1	23
5c	2, 5-Di-*endo*	7	5	5	4	7	14
5d	3, 5-Di-*endo*	4	10	7	7	3	19
5e	2-*endo*	1.4	6	6	7	3	20
5f	3-*endo*	1.5	4	8	3	1	35
5g	5-*endo*	1.5	3	3	4	3	20
5h	Tri-*exo*	2	3	5	9	2	18

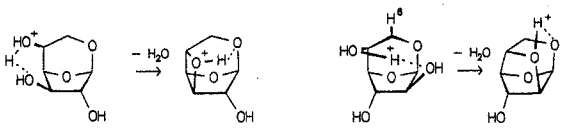
[a] Additional ions: 2–4% Σ *m/z* 97; 3–8% Σ *m/z* 71; 2% Σ manno-M_2H^+.
[b] In further spectra measured at very high sample concentrations there was increased formation of protonated dimers (39, 54, 2, 8, 5, 28, 48 and 18% Σ M_2H^+ for **5a–h**, respectively) which were especially stable for the isomers with *cis*-1, 2-*diol* sites (see M_2H^+ ions of **4**).

These species should be identical with the MH^+ ions of the above *endo*- and *exo*-**1** compounds. Further, only the MH^+ ions of the latter isomer of **5**, 3,5-di-*endo*-**5** · H^+, gave the degradation under HCOOH loss to a unique $[MH - H_2O - HCOOH]^+$ ion; this is analogous to the $[MH - HCOOH]^+$ formation from the *exo*-**1** · H^+ ions. In addition, the tri-*endo*-**5** · H^+ ion could also lose H_2O with participation of the 2-OH group. This reaction (Eqn (4b)) might give $[\mathbf{5a} \cdot H - H_2O]^+$ ions which have the structure of the MH^+ ions of the constitutionally isomeric 1,6:2,5-dianhydrogulofuranose **2**. The distorted C(5) site observed in the crystal state of **5** (see above) is close to the conformation of the S_Ni transition states in the reactions in Eqns (4a/b) and (5a). It might favour this stereospecific elimination. A related H_2O loss from an H-bridged site has been reported for the MH^+ ions in the isobutane CI of di-*endo*-[4.3.3]propellane-8,11-diol.[6]



endo-**1** · H^+ (*gulo*) tri-*endo*-**5** · H^+ (*gulo*) **2** · H^+ (*gulo*)

(4*a*/*b*)

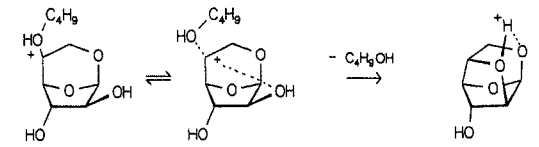


3,5-di-*endo*-**5** · H^+ (*ido*) *exo*-**1** · H^+ (*ido*) 2,5-di-*endo*-**5** · H^+ (*galacto*) **2A** · H^+ (*galacto*)

(5*a*/*b*)

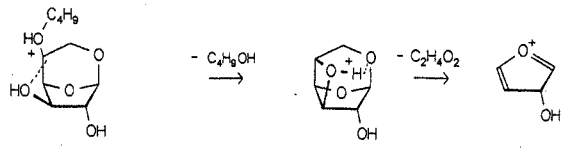
The 2,5-di-*endo* (*galacto*) isomer **5c** shows MH^+ ions of intermediate stability. The 2 – OH/5 – OH proton bridge is not very stable because of the flagpole interaction with the 6-*endo* H atom (Eqn (5b)). The 2,5-di-*endo*-**5** · H^+ ion might also dehydrate by an S_Ni reaction. The resulting protonated 1,6:2,5-dianhydrogalactofuranose ion, **2A** · H^+, is the 3-epimer of the **2** · H^+ ion. However, only 15% Σ $[\mathbf{5c} - OH]^+$ ions are observed, but there is a unique $[\mathbf{5c} - OH - H_2O - CH_2O]^+$ skeleton fragment ion, with a metastable transition for the CH_2O loss (see above).

The remaining 2-*endo* and 3-*endo* (*altro* and *gluco*) isomers show only 8% Σ and 4% Σ MH^+ ions. Proton bridging is only possible with participation of an acetal oxygen. The relatively high stability of the 2-*endo* and 3-*endo* $[M - OH]^+$ ions can be attributed to stable dianhydrosugar structures with an inverted C(5) configuration. In both cases the *exo*-5-OH group might accept a $C_4H_9^+$ reagent ion and undergo loss of C_4H_9OH (Eqns (6) and (7a)). The resulting cationic site could be stabilized by the 2-*endo*- and 3-*endo*-OH group to give the protonated 1,6:2,5-dianhydrogalactofuranose (**2A** · H^+) and 1,6:3, 5-dianhydroidofuranose (*exo*-**1** · H^+), respectively. For this S_N2-type elimination the skeletal distortion at C(5) (see above) also provides a conformation close to the transition state. Similar displacement reactions leading to protonated cage ether structures have been reported for the isobutane CI spectra of the *endo*-/*exo*-protoadamantane-4, 9-diols.[5]



2-*endo*-**5** · $C_4H_9^+$(5 – OH)(*altro*) **2A** · H^+(*galacto*)

(6)



3-*endo*- **5** · $C_4H_9^+$ (5 – OH)(*gluco*) *exo*-**1** · H^+ $[\mathbf{5f} - OH]^+$ (*ido*) $-C_2H_4O_2]^+$

(7*a*/*b*)

Finally, the 2-*endo*- and 3-*endo*-**5** isomers (*altro* and *gluco*) can be distinguished as follows. The spectrum of the *gluco* isomer **5f** shows an unusually abundant $C_4H_5O_2^+$ ion at *m*/*z* 85. In analogy with Eqn (1a), it might be formed by $C_2H_4O_2$ loss from the $[\mathbf{5f} - OH]^+$, or *exo*-**1** · H^+, intermediate to give the $[\mathbf{5f} - OH - C_2H_4O_2]^+$ ion (Eqn (7b)). Hence all of the eight isomers of **5** can be differentiated by their isobutane CI spectra.

CONCLUSION

The spectral data obtained from the isobutane DCI of the stereoisomeric 1,5-anhydropentofuranoses and 1,6-anhydrohexofuranoses can be efficiently applied to differentiate the isomers. The values in Table 6 show that two parameters are sufficient for a distinct identification (except for one additional ion needed in one case). The $MH^+/[M - OH]^+$ parameter is the intensity ratio, which shows the stability of the MH^+ ions towards H_2O loss. The second parameter is indicative of the stability of the bicyclic skeleton. It is the sum of intact skeleton ions normalized to a typical skeleton-cleavage product ion, (% Σ MH^+ + % Σ $[M - OH]^+$)/(% Σ $C_3H_5O_2^+$), for the 1,5-anhydropentofuranose isomers or normalized to the substrate total ionization, % Σ MH^+ + % Σ $[M - OH]^+$, for the 1,6-anhydrohexofuranose isomers, respectively.

Another aspect of the DCI results concerns the gas-phase ion chemistry of the anhydrosugar isomers. As indicated by the discussion about the stereospecific formation of protonated dimers, M_2H^+, of the 1,5-anhydropentofuranoses **4**, these compounds are of interest for other stereochemical approaches in mass spectrometry. These include the specific formation of protonated mixed dimers, M · A · H^+, which is known from studies on complementary binding in systems such as aminoethanol adducts of difunctional oxygen compounds,[24] mixed chiral dialkyl tartrate dimers[25,26] and glycerol adducts of sugars.[8,27] The characteristic behav-

Table 6. Stereochemical differentiation of 4 and 5 isomers[a]

Compound	Configuration	Type	$MH^+/[M-OH]^+$	$(MH^+ + [M-OH]^+)/X^b$
4	*lyxo*	Di-*endo*	7	15
	arabino	2-*endo*	15	7.6
	xylo	3-*endo*	1.7	3.7
	ribo	Di-*exo*	7	3.0
5	*gulo*	Tri-*endo*	(0.25)	(59)[c]
	manno	2,3-Di-*endo*	(1.9)	(62)
	galacto	2,5-Di-*endo*	⟨1.2⟩	⟨33⟩[c]
	ido[d]	3,5-Di-*endo*	[0.15]	[42][c]
	altro	2-*endo*	⟨0.35⟩	⟨31⟩
	gluco	3-*endo*	[0.12]	[39]
	talo	5-*endo*	[1.6]	[42]
	allo	Tri-*exo*	(1.0)	(62)

[a] Intensity ratios calculated from % Σ values of given ions.
[b] $X(\mathbf{4}) = C_3H_6O_2^+$; $X(\mathbf{5}) \equiv 1$.
[c] Three groups with a near ⟨30⟩, [40] and (60) level.
[d] Additional ion: 15% Σ *m/z* 99.

iours of alkali cation-bound mixed dimers of sugars[28] and of transition metal cation-coordinated decalin[29] and dimethoxycyclopentane[30] isomers are other examples of recent studies which are promising for molecules with very complicated stereochemistry.

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