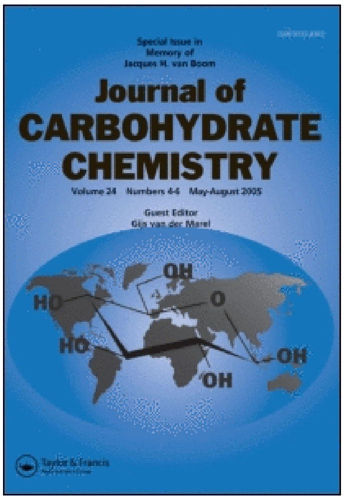

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Thomas W. Flechtner[a]; Bozena Winnik[a]; Michael J. S. Tevesz[b]
[a] Department of Chemistry, Cleveland State University, Cleveland, OH [b] Department of Geological Sciences, Cleveland State University, Cleveland, OH

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GAS PHASE REACTIONS OF 1,2:5,6-DI-*O*-ISOPROPYLIDENE -α-D-GLUCO- AND ALLOFURANOSE WITH ELECTROPHILES DERIVED FROM ACETONE

Thomas W. Flechtner* and Bozena Winnik

Department of Chemistry, Cleveland State University, Cleveland, OH 44115

and Michael J. S. Tevesz

Department of Geological Sciences, Cleveland State University, Cleveland, OH 44115

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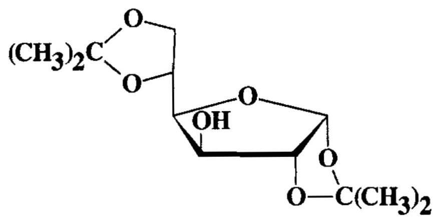
ABSTRACT

In a quadrupole mass spectrometer, under chemical ionization conditions with acetone as the reagent gas, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose form M+1, M+43, and M+59 ions in the gas phase. In addition, the allo isomer produces M+41 ions. These ions and the corresponding ions derived from isotopomers in which the isopropylidene groups were differentiated by deuterium substitution were separately subjected to collisionally activated dissociation conditions. The different reactivities of these ions were attributed to the ability of the allo structure to hydrogen bond internally and the different sizes of the electrophilic groups which formed adducts with the neutral protected sugar molecules.

INTRODUCTION

Electron Ionization (EI) mass spectrometry (MS) of monosaccharides and their derivatives has been shown to be very insensitive to the stereochemistry of the sugars. Chemical Ionization (CI) MS of sugars has the potential to be more selective than EI-MS because it is generally seen as a less energetic technique. Wang and coworkers[1] obtained mixed results when they studied acetone as a reagent gas for CI mass spectrometry of some underivatized monosaccharides. The spectra showed some differences which did not appear in the corresponding CI/ammonia or CI/isobutane mass spectra. However, the spectra were found to be strongly temperature and pressure dependent. In addition, no ions of *m/z* M+43 were reported. This is in contrast to the work of Vairomani and coworkers[2] where the $(M+CH_3CO)^+$ ions were commonly found in the acetone/CI spectra of alcohols, acetates and alkenes.

Because of the complex nature of the CI/acetone mass spectra of underivatized monosaccharides and their strong temperature and pressure dependence, we decided to study the CI/acetone collisionally activated dissociation (CAD) mass spectra of derivatized monosaccharides. In this way we hoped to better understand the gas phase fragmentation patterns of the ions reported in the earlier work. In this paper we report original results



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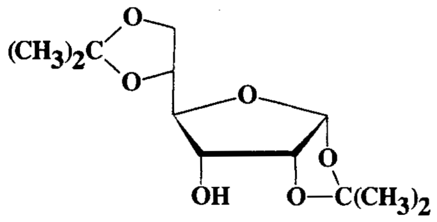

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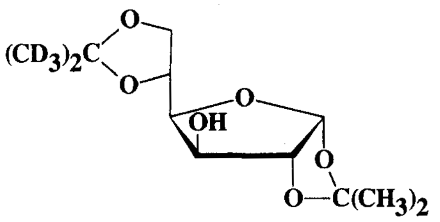

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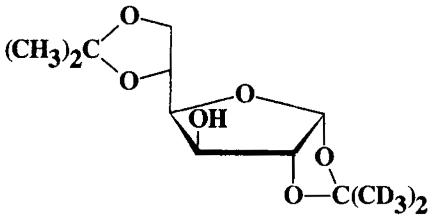

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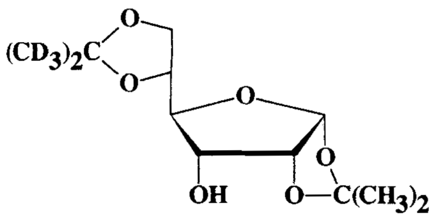

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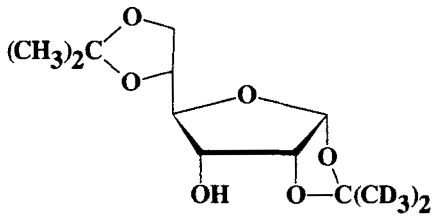

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from the study of CI/acetone-CAD mass spectra of 1,2:5,6-di-*O*-isopropylidene-α-D-gluco- and allofuranoses **1-6**.

The positive ion CI/acetone mass spectra of compounds **1-6** displayed peaks at *m/z* M+1 ($[M+H]^+$), M+43 ($[M+CH_3CO]^+$), and M+59 ($[M+CH_3COHCH_3]^+$). The allofuranose compounds also displayed peaks at *m/z* M+41 (M+59-18, $[M+CH_3COHCH_3-H_2O]^+$). In this paper we report and discuss the positive ion acetone CI CAD of these ions at 0 eV collision energy.

RESULTS AND DISCUSSION

Each of the positively-charged ions examined in this study results from the addition of an electrophile to the sugar derivative. The electrophile should add easily to any site of non-bonded electron density - any one of the six different oxygen atoms in each sugar. Each of the ions selected from a CI/acetone spectrum for CAD examination may consist of a mixture of a number of structures differing in the site of electrophilic addition. While there may be significant differences in the steric environments and electrophilicities of the different oxygen atoms in each structure, there is undoubtedly sufficient energy available to the sugar molecules and the electrophilic species such that each of the oxygen atoms may react with the electrophile.

Daughter Spectra of the M+1 Ions

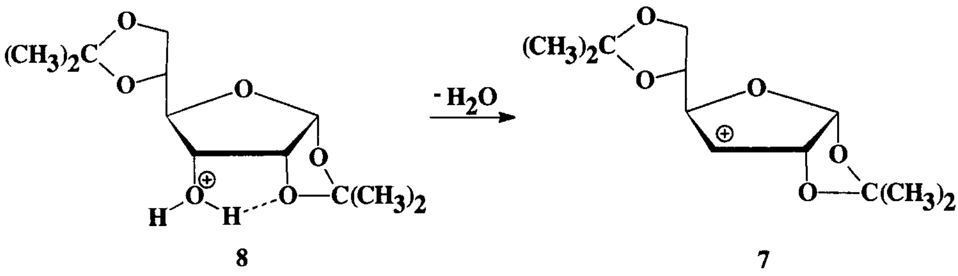
The data for the M+1 ions of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) and 1,2:5,6-di-*O*-diisopropylidene-α-D-allofuranose (**2**) are shown in Table 1.

The protonated allofuranose ion(s) undergo dehydration to form fragment(s) at *m/z* 243. The simplest proposal for this process involves O-3 protonation and then loss of water to produce the secondary cation **7** as shown in Scheme 1.

This ion could also be formed by the analogous dehydration of the O-3 protonated glucofuranose ion. Since the dehydration process is not observed for the gluco ion we propose that the formation of the O-3 protonated allo ion is favored by the presence of the internal hydrogen bond shown in structure **8** (Scheme 1). The stereochemistry of the gluco structure does not allow the formation of the O-2 to O-3 hydrogen bond shown for the allo ion in **8** and we propose that the O-3 protonated glucofuranose ion is not formed to a detectable extent.

Table 1. MS/MS Daughter Data for the $[M+1]^+$ (*m/z* 261) Ions from Compounds **1** and **2**

fragment *m/z*	class	Cmpd. **1** (R.A.)	Cmpd. **2** (R.A.)
261	M+1	100	42
243	M+1-18	0	12
203	M+1-58	48	100



Scheme 1

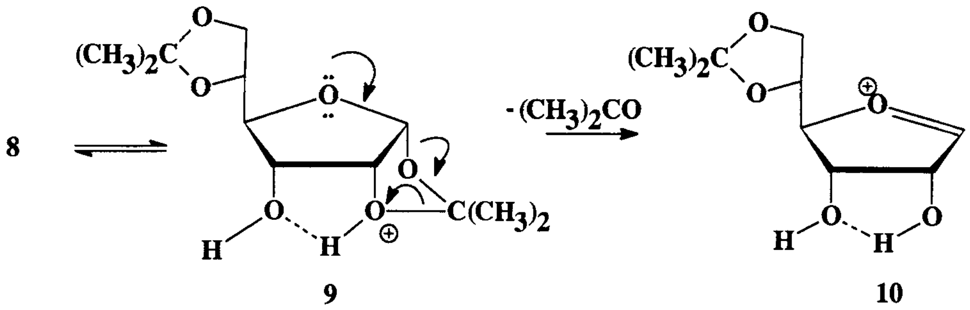
The protonated glucofuranose and allofuranose ions also fragment by the loss of acetone to form ion(s) at *m/z* 203. The acetone expelled in this process must be derived from one of the isopropylidene groups. In order to determine which protecting group is the source of the acetone, the M+1 ions from compounds **3-6** (*m/z* 267) were studied and the data from that study are shown in Table 2.

The shift of the *m/z* 203 peak to *m/z* 209 in the spectrum of the M+1 ion from the allo compound **5** indicates that in this ion it is the 1,2-isopropylidene group which is the source of the acetone. The fact that this peak remains at *m/z* 203 for the M+1 ion from compound **6** confirms this analysis.

Our proposed mechanism for the selective extrusion of acetone from the 1,2 position of the allofuranose ion is shown in Scheme 2. The allofuranose is protonated on O-2 (structure **9**) which activates the ion for the formation of acetone and the stabilized cation **10**. Both the initial protonated allofuranose **9** and the product ion **10** are stabilized

Table 2. MS/MS Daughter Data for the $[M+1]^+$ (m/z 267) Ions from Compounds **3**, **4**, **5**, and **6**

fragment m/z	Class	Cmpd. **3**	Cmpd. **4**	Cmpd. **5**	Cmpd. **6**
267	M+1	100	100	34	84
249	M+1-18	0	0	11	21
203	M+1-64	15	22	0	100
209	M+1-58	24	17	100	81



Scheme 2

by the hydrogen bond to O-3 and the fragmentation process is promoted by electron donation from the endocyclic oxygen atom. We note that ion **9** is a hydrogen bond tautomer of ion **8**.

The protonated glucofuranose ion(s) form daughter ions derived from the loss of acetone at much lower relative abundances than the M+1 ion(s) of the allofuranose. The gluco M+1 ion appears to favor the loss of the 1,2-*O*-isopropylidene over the 5,6, although the low relative abundances of these fragments suggests that the reactions which produce them are relatively unimportant.

Daughter Spectra of the M+59 Ions

The data for the M+59 ions from compounds **1** and **2** are shown in Table 3. These M+59 ions (m/z 319) may consist of a collection of hydrogen bonded structures of the general form shown as structures **11** and **12** shown in Scheme 3. However,

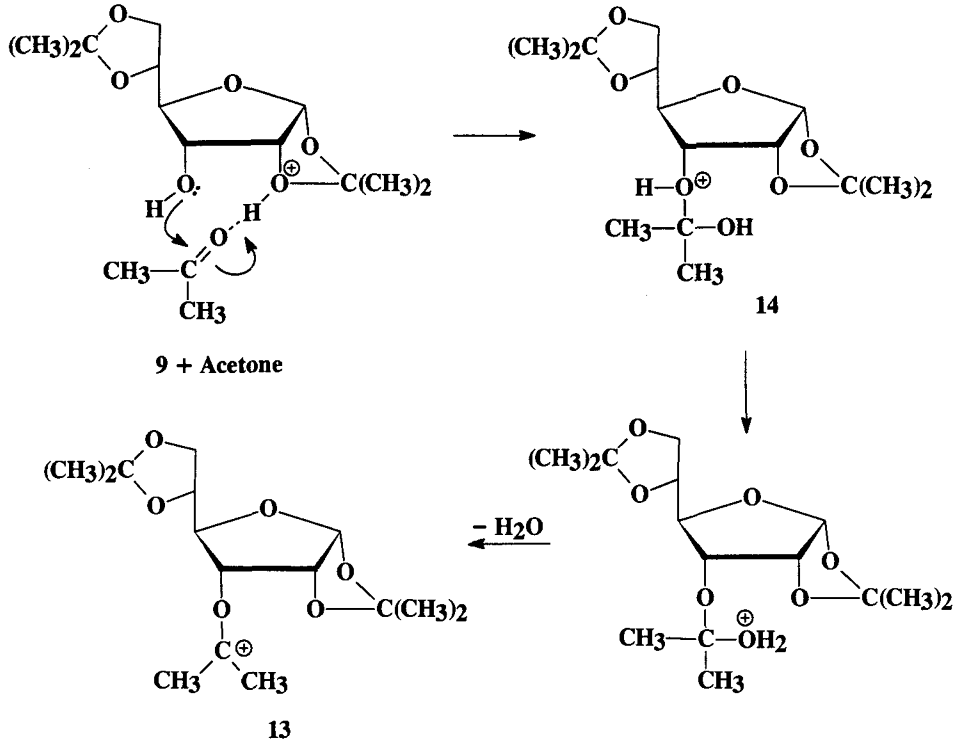
Table 3. MS/MS Daughter Data for the $[M+59]^+$ (m/z 319) Ions from Compounds **1** and **2**

fragment m/z	class	Cmpd. **1** (R.A.)	Cmpd. **2** (R.A.)
319	M+59	3	29
301	M+59-18	0	5
261	M+59-58	100	100
243	M+59-76	0	40
203	M+59-116	2	70

Scheme 3

in the spectrum of the m/z 319 ion from the compound **2** the presence of ions at m/z 301 (M+59-18) indicates that at least some of these m/z 319 ions undergo the loss of a water molecule. This would require the rearrangement of any ions of structures **11** or **12**. Scheme 4 shows our proposal for a process which would provide for the expulsion of the water molecule from an ion of m/z 319.

As shown in Scheme 4, this proposal requires that an oxygen atom be both adjacent and accessible to a free hydroxyl group. The acetone molecule becomes covalently bonded to the hydroxyl oxygen atom as the proton attached to the positively charged isopropylidene oxygen atom is transferred to the acetone oxygen. Then an internal proton transfer is followed by the expulsion of the water molecule with the formation of the stabilized ion **13**. Only the stereochemistry of the allofuranose provides the arrangement of substituents required by this proposal. The protonated ion derived from **2** which would be responsible for this acetone-addition/dehydration process is



Scheme 4

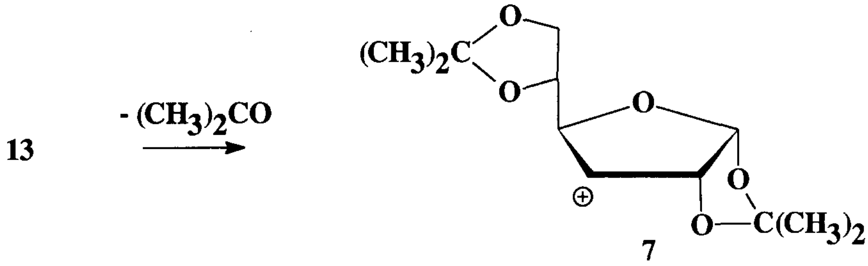
structure **9**. This proposal is also consistent with the fact that no *m/z* 301 fragment is observed in the spectrum of the M+59 ion(s) derived from glucofuranose **1**.

In order to test this model, the acetone-CAD spectra of the M+59 ions (*m/z* 325) from the deuterium-labeled compounds **3-6** were measured. The results are presented in Table 4. The findings are even more dramatic than in the study of the labeled M+1 ions. The M+59 ion from compound **5**, in which the 5,6-*O*-isopropylidene group is deuterated has no peak at *m/z* 203 and has a significant peak at *m/z* 209. The M+59 ion from compound **6**, on the other hand, has a significant peak at *m/z* 203 and a small peak at *m/z* 09. The major process is expulsion of acetone from the 1,2-*O*-isopropylidene group.

The M+59 ions from the allo isomer have two additional fragmentation pathways: the losses of *m/z* 76 and *m/z* 116. The first process is the loss of acetone plus water and the second pathway is the loss of two acetone molecules. The data in Table 4 confirms

Table 4. MS/MS Daughter Data for the $[M+59]^+$ (*m/z* 325) Ions from Compounds **3**, **4**, **5**, and **6**

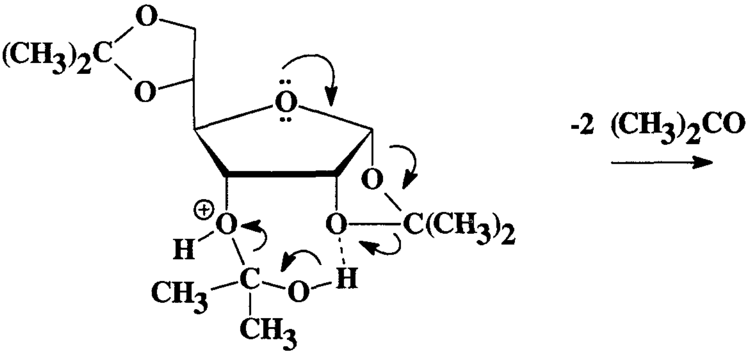
fragment *m/z*	Class	Cmpd. **3**	Cmpd. **4**	Cmpd. **5**	Cmpd. **6**
325	M+59	4	12	18	36
307	M+59-18	0	0	11	7
267	M+59-58	100	100	100	100
249	M+59-76	0	0	55	32
203	M+59-122	2	7	0	20
209	M+59-116	5	2	23	5



Scheme 5

that the acetone molecule expelled in addition to the water is derived from the reagent gas acetone. If the acetone were derived from one of the isopropylidene groups then the M+59 ions from compound **5** and/or compound **6** would have had a peak at *m/z* 243. Presumably the reagent gas acetone is expelled by a simple cleavage in ion 13 as shown in Scheme 5.

The process involving the expulsion of two acetone molecules (without the loss of a molecule of water) must involve the loss of acetone from (at least) one of the isopropylidene groups. The results shown in Table 4 (specificly the relative abundances of the *m/z* 203 and *m/z* 209 ions for compounds **5** and **6**) indicate that it is the acetone from the reagent gas and the 1,2-*O*-isopropylidene group which are the sources of these



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Scheme 6

Table 5. MS/MS Daughter Data for the $[M+43]^+$ (*m/z* 303) Ions from Compounds **1** and **2**

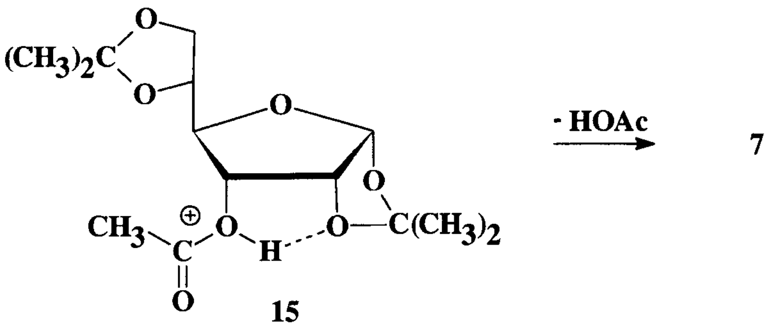
fragment *m/z*	class	Cmpd. **1** (R.A.)	Cmpd. **2** (R.A.)
303	M+43	68	79
243	M+43-60	1	50
245	M+43-58	100	100

two neutral acetone losses. A process which could account for these results is shown in Scheme 6. Ion **14** (a proposed intermediate in the dehydration process as shown in Scheme 4) is proposed to lose the two acetone molecules in a process which may be either concerted (as shown) or stepwise.

Daughter Spectra of the M+43 Ions

The data for the M+43 ions derived from **1** and **2** are shown in Table 5.

The base peak in each case occurs at *m/z* 245 which corresponds to the expulsion of acetone, a process which is discussed below. The expulsion of acetic acid (to form an ion of *m/z* 243) is an important process for these ions derived from allofuranose **2** but quite unimportant for the corresponding ions from **1**. Acetic acid is almost certainly expelled from C-3 (after the acetylation of O-3) with the formation of the secondary



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Scheme 7

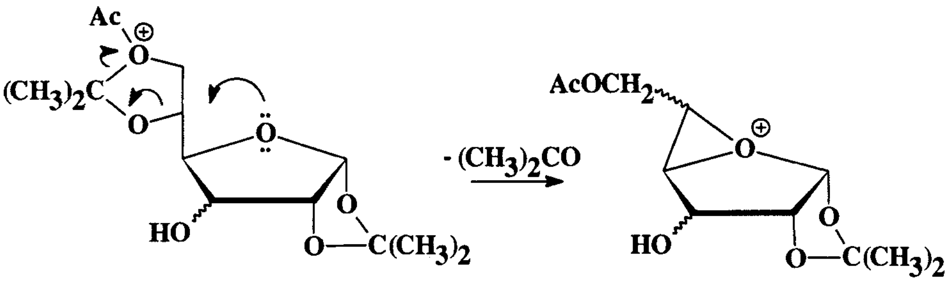
Table 6. MS/MS Daughter Data for the $[M+43]^+$ (*m/z* 309) Ions from Compounds **3**, **4**, **5**, and **6**

fragment *m/z*	Class	Cmpd. **3**	Cmpd. **4**	Cmpd. **5**	Cmpd. **6**
309	M+43	89	83	47	86
249	M+43-60	4	1	33	53
245	M+43-58	100	27	100	24
251	M+43-64	47	100	8	100

cation **7** as shown in Scheme 7. The acetylation of O-3 should be favored for the allofuranose relative to the glucofuranose because of the additional stabilization of the cation by hydrogen bonding to O-2 as shown in **15**. Again, that internal hydrogen bonding cannot take place in glucofuranose **1**.

The origin of the acetone expelled in the formation of the *m/z* 245 ions was determined by examination of the M+43 daughter ion spectra from compounds **3**-**6** and the data is presented in Table 6.

In contrast to the results obtained in examining the M+1 and M+59 ions, the 5,6-*O*-isopropylidene group is now the origin of the expelled acetone. The electrophilic acetyl cation is larger and more sterically demanding than the proton. We believe that for both the gluco- and allofuranose structures the large size of the acetyl group disfavors



Scheme 8

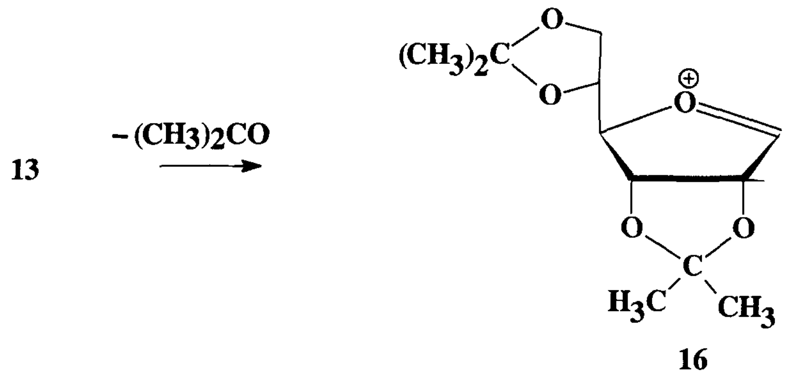
Table 7. MS/MS Daughter Data for the $[M+41]^+$ (*m/z* 307) Ions from Compounds **5**, and **6**

fragment *m/z*	class	Cmpd. **5** (R.A.)	Cmpd. **6** (R.A.)
307	M+41	63	75
243	M+41-64	0	11
249	M+41-58	100	100

the acetylation of all of the sugar oxygens except for O-6. The process that we propose is shown in Scheme 8. As we proposed for the for the loss of the 1,2-*O*-protecting group from the allofuranose structures (Schemes 2 and 6), the endocyclic ring oxygen plays a key roll in providing electron density.

Daughter Spectra of the M+41 Ions from Compounds 2, 5, and 6

The only other ion observed in the CAD spectrum of the M+41 (*m/z* 301) ion from allofuranose **2**, besides the *m/z* 301 ion, was at *m/z* 243. This corresponds to the expulsion of a molecule of acetone. We proposed that the initial *m/z* 301 ion was derived from the M+59 ion ($M+H^+$+acetone) by rearrangement and dehydration to produce **13** as depicted in Scheme 4. Acetone could then be lost from **13** by an S_N1 process to form the cation **7** as illustrated in Scheme 5. In order to examine this proposal we examined the M+41 daughter ion spectra of the deuterated allofuranoses **5** and **6**. The results are shown in Table 7.



Scheme 9

These results confirm the proposal that the acetone expelled from the M+41 ion originates largely from the cationic substituent attached to C-3 (which was, originally, derived from the reagent gas acetone). However, a small portion (approximately 10%) of the acetone molecules expelled originate as the 1,2-*O*-protecting group. We did not detect any loss of the 5,6-*O*-protecting group. We believe that this selective expulsion of acetone from the 1,2-*O*-isopropylidene group is caused by the same factors that led to the selective loss of the 1,2-*O*-isopropylidene from the M+1 ions derived from these same reactants. Electron donation from the endocyclic ring oxygen and bridging from O-2 to the adjacent electrophilic center on O-3 lead to the formation of the stabilized cation **16** as depicted in Scheme 9.

EXPERIMENTAL

General methods. Mass spectra were obtained using a Finnigan TSQ-45 triple quadrupole mass spectrometer under the following conditions: source temperature, 120 °C; reagent gas pressure: acetone (1.0 torr), electron energy, 70 eV. The collision cell pressure (argon) was maintained at 1.4 mtorr and the collision energy was 0 eV.

Compound **1** was purchased from the Aldrich Chemical Company. Compounds **3** and **4** were synthesized according to the procedure involving initial isopropylidenation or deuterioisopropylidenation, selective hydrolysis[3] to remove the 5,6-*O*-isopropylidene group, then introduction of a new protecting group. Compounds **2, 5** and **6** were prepared from **1**, **2** and **3**, respectively, by the method of Horton et al.[4,5] All compounds were introduced into the ion source through the solids probe inlet. To minimize instrumental errors comparative runs were obtained consecutively.

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