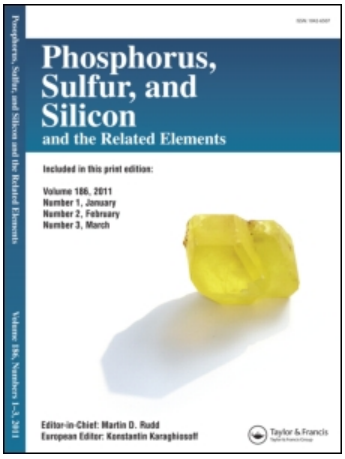

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MASS SPECTRA OF PERACETYLATED DERIVATIVES OF SUGAR ANALOGUES HAVING PHOSPHORUS IN THE HEMIACETAL RING

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MASS SPECTRA OF PERACETYLATED DERIVATIVES OF SUGAR ANALOGUES HAVING PHOSPHORUS IN THE HEMIACETAL RING

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The first, detailed analysis of the mass spectra of the title compounds having a pyranoid or furanoid ring was carried out. The molecular-ion intensities of these phosphorus sugars were shown to be higher compared to the oxygen analogues, thus permitting accurate mass measurement. The main fragmentation pathway was the consecutive loss of the substituents from ring carbon atoms and C-6 (the A series of fragmentation), leading to the formation of 1,2-dihydro-λ^5-phosphorin or -phosphole oxide derivatives. Possible degradation pathways of the phosphorus-containing ring to acyclic fragments are also discussed. These findings are considered to be of use in structural analysis of these phosphorus sugars.

INTRODUCTION

Extensive studies on the preparation of sugar analogues having nitrogen or sulfur in the hemiacetal ring, such as 5-amino-5-deoxy-D-glucose (Nojirimycin)[1,2] and 5-deoxy-5-thio-D-glucose,[3–7] have been carried out not only from the viewpoint of their physicochemical properties but also from that of a wide variety of their biological activities.[8–10] Thus, sugar analogues having a phosphorus atom in the ring are also considered to be of interest, particularly for the potential utility of their biological activities.[11]

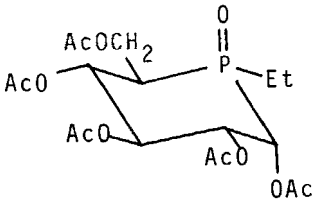
In our effort to prepare such hexopyranoses and pentofuranoses, we recently reported 5-deoxy-5-*C*-[(*R*,*S*)-phenylphosphinyl]-α,β-L-idopyranoses,[12–16] 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses,[17–21] and 4,5-dideoxy-4-*C*-phenylphosphinyl-D-ribo- and -L-lyxo-furanoses.[22,23] The structural assignments of these compounds were mainly based on 400 MHz, proton nuclear magnetic resonance spectroscopy and partly on X-ray crystallographic analysis.

Because of the versatile applicability of mass spectroscopy to the structural assignments, an extensive, systematic investigation of mass spectra of carbohydrate derivatives has been undertaken, and a wide variety of general degradation pathways has been well established.[24–28] We wish to describe in this paper the first, detailed analysis of the mass spectra of some of those phosphorus-containing sugar analogues that have been found to show certain characteristic features in connection with the spectra of the usual monosaccharides having a ring oxygen atom.

RESULTS AND DISCUSSION

The molecular ions of these phosphorus sugars are, in most cases, clearly detected as the protonated species $[(M + 1)^+$, most likely as the resonance-stabilized hydroxy-

phosphonium form], whereas owing to their lability the molecular ions are rarely observed[24] for carbohydrate derivatives having a ring-oxygen atom. Thus, the existence of the molecular-ion peaks of the phosphorus sugars advantageously allows establishment of their accurate molecular composition by high resolution EI mass spectroscopy.



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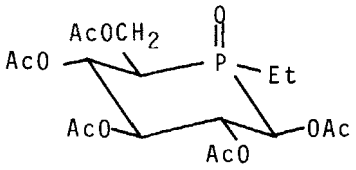


2

The EI mass spectra of penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-α- and -β-D-glucopyranoses[20,21] (**1** and **2**) are shown in Figures 1 and 2, respectively, as representative examples of D-glucose derivatives having phosphorus in the ring; the accurate masses and the intensities of the significant ions are listed in Table I. A

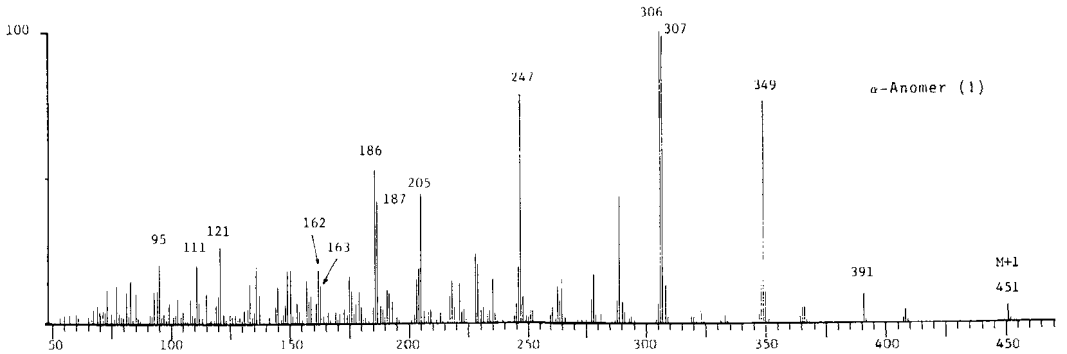


FIGURE 1 Mass spectrum of 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-α-D-glucopyranose (**1**).

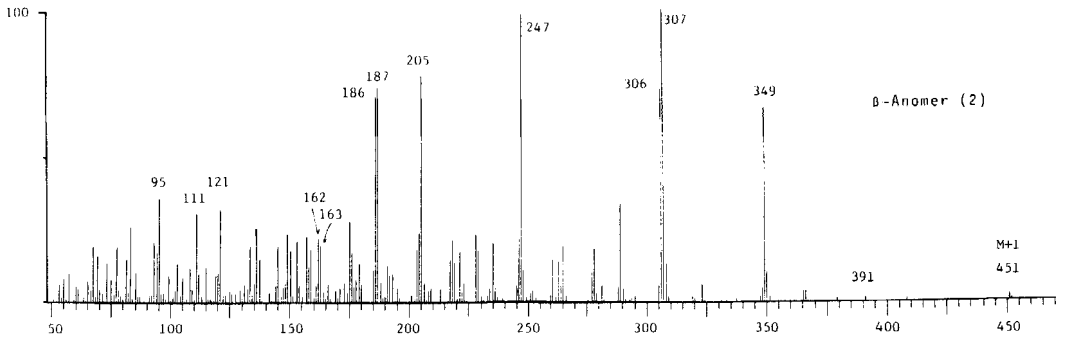


FIGURE 2 Mass spectrum of 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-β-D-glucopyranose (**2**).

TABLE I

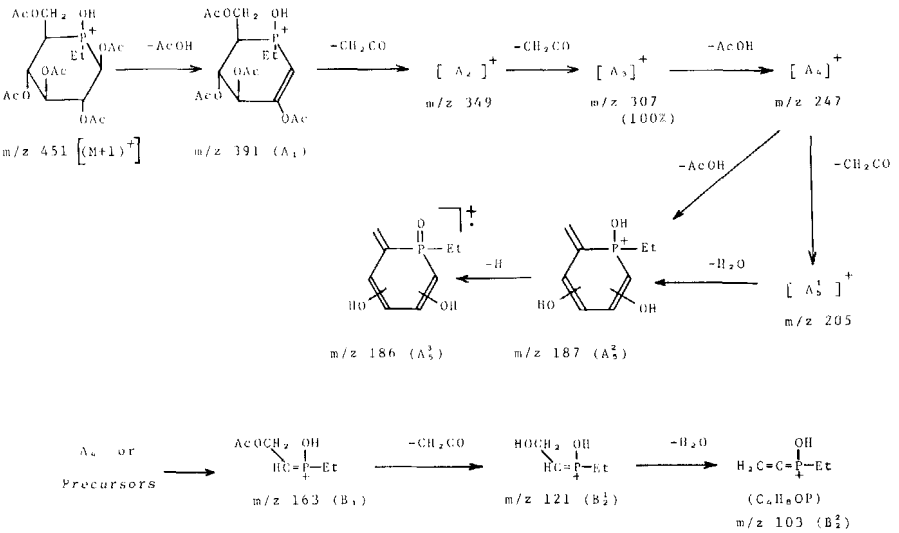
Major fragment ions of penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-α- and -β-D-glucopyranose (**1** and **2**)

Species	Element	*m/z* (Calc.)	*m/z* (Obs.)	Int (%)[a]	*m/z* (Obs.)	Int (%)[b]
M + 1	$C_{18}H_{28}O_{11}P$	451.1369	451.1376	5.60	451.1362	2.56
A_1	$C_{16}H_{24}O_9P$	391.1158	391.1159	10.09	391.1151	1.44
A_2	$C_{14}H_{22}O_8P$	349.1053	349.1056	77.32	349.1059	66.43
A_3	$C_{12}H_{20}O_7P$	307.0946	307.0943	99.06	307.0946	100.00
	$C_{12}H_{19}O_7P$	306.0869	306.0872	100.00	306.0873	72.61
A_4	$C_{10}H_{16}O_5P$	247.0735	247.0736	75.69	247.0740	93.55
A_5^1	$C_8H_{14}O_4P$	205.0629	205.0627	42.36	205.0631	73.00
A_5^2	$C_8H_{12}O_3P$	187.0524	187.0524	40.50	187.0524	70.10
A_5^3	$C_8H_{11}O_3P$	186.0446	186.0446	50.76	186.0449	66.66
B_1	$C_6H_{12}O_3P$	163.0524	163.0523	12.34	163.0522	18.54
	$C_6H_{11}O_3P$	162.0446	162.0447	17.46	162.0446	20.40
B_2^1	$C_4H_{10}O_2P$	121.0419	121.0419	25.44	126.0421	32.43
	$C_6H_7O_2$	111.0446	111.0444	17.39	111.0448	29.03
	C_6H_7O	95.0497	95.0495	20.99	96.0497	33.04

[a]For α-Anomer (**1**).
[b]For β-Anomer (**2**).

highly unique feature of the mass spectra of these peracetylated 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses is that phosphorus-containing ions are the most intense ions (except for CH_3CO^+ ion of a much higher intensity at *m/z* 43); this is in striking contrast to the spectra[24] of peracetylated monosaccharides of oxygen-containing rings, where the intensities of the fragments retaining the hemiacetal ring are generally much lower than those of the ring-ruptured fragment ions. Thus, β-anomer (**2**) gives rise to the major fragment ions of the first series A (according to the nomenclature used by Chizhov and Kochetkov[25]) as illustrated in Scheme 1; the fragmentation is presumed to be initiated by loss of the substituent from C-1 (to give a resonance-stabilized ion A_1) as was commonly observed for peracetylated monosaccharides,[24] but the order of the succeeding acetate losses is uncertain. It should be noted that the species A_3, which is formed from the molecular ion by the three successive losses of one acetic acid and two ketene groups, consisted of the base peak, suggesting the high stability of the phosphorus-containing ring system. Further elimination of two molecules of acetic acid from this species leads to the species A_5^2 and A_5^3 having the 1,2-dihydro-1-methylene-λ^5-phosphorin ring system. Although the position of the acetoxyl or hydroxyl groups on this phosphorin ring remains to be established, the presence of such a set of intense fragments of the A series, in turn, effectively characterizes the structures of peracetylated 5-deoxy-5-*C*-phosphinylhexopyranoses, which are usually prepared[11] by the three-step ring enlargement of the 5-deoxy-5-*C*-phosphinylhexofuranose precursors. The mass spectrum of the α-anomer (**1**) closely resembles that of the β-anomer **2**, but the intensities of the (M + 1) ion and A_1-A_3 species of **1** are higher than those of **2**.

No detailed analysis of the subsequent ring-opening fragmentation was made because of the relatively low intensities of these fragment ions, but the exact molecular compositions of ions at mass 163, 121, and 103 (Table I) suggests that these are presumably derived by simultaneous, or stepwise, rupture of two bonds (at



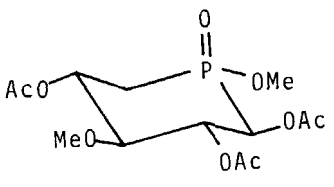
SCHEME 1 Major fragmentation pathway of penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-β-D-glucopyranose (**2**).

C-1—P-5 and C-4—C-5) of the pyranoid ring in species A_4 or its precursors, namely the B series of fragmentation; the most probable forms of these ions (B_1 and B_2) are shown in Scheme 1. Although one can propose another type of cleavage which gives rise to the characteristic six-carbon fragments of appreciable intensities at mass 111 ($C_6H_7O_2$) and 95 (C_6H_7O), the structures of these ions as well as the mode of the fragmentation could not be established.

Only a negligible extent of fragmentations of series C, D, and other types is observed in the spectra of **1** and **2**, whereas these ions are abundantly formed in the degradation of the oxygenated analogues.[24-28]

The high resolution EI mass spectra of other D-gluco- and L-ido-hexopyranoses having phosphorus in the hemiacetal ring[12,14,19] also exhibited appreciable intensities of the molecular ions (as M + 1) which further degraded into the A series ions by consecutive loss of acetic acid or ketene in a manner analogous to those of **1** and **2**.

As a representative example of pentopyranoses having phosphorus in the ring, the mass spectrum of 1,2,4-tri-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-methoxyphosphinyl]-3-*O*-



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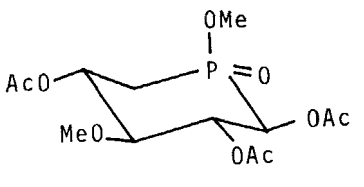

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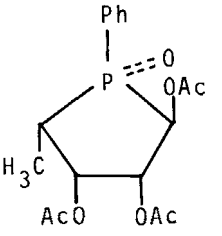

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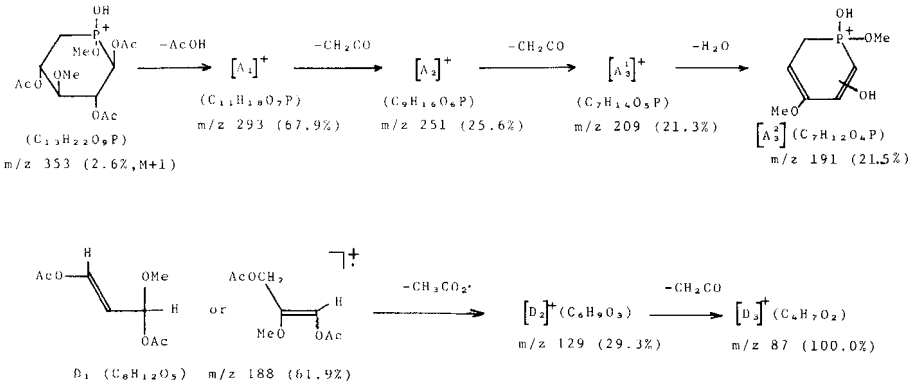
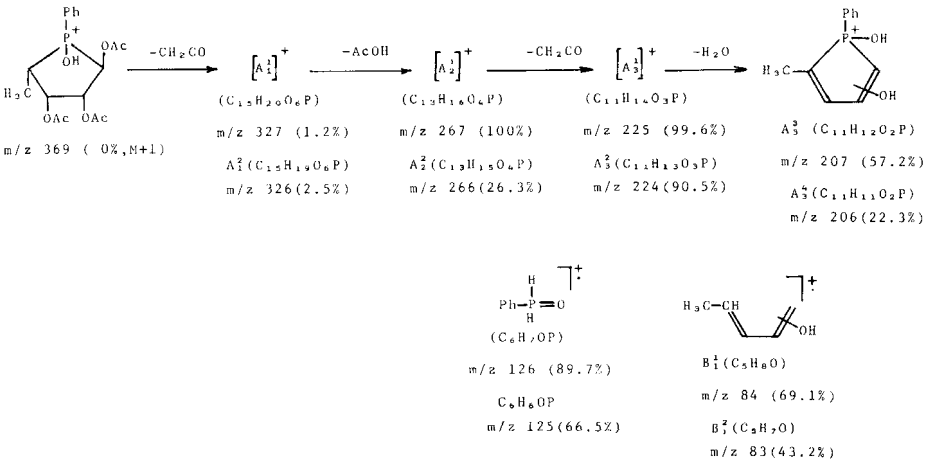


SCHEME 2 Major fragmentation pathway of compound **3**.

methyl-β-D-xylopyranose[29] (**3**) was examined, and again the major fragmentation giving rise to ions A_1-A_3 of dihydro-λ^5-phosphorin structure is observed for this compound as illustrated in Scheme 2; as the precise order of the acetate losses was not clear, the position of the hydroxyl group on the dihydrophosphorin ring remained unestablished. Compared to the aforementioned fragmentation patterns of hexopyranoses **1** and **2**, degradation of the pyranoid ring of **3** seems to take place more readily, producing phosphorus-free major fragments D_1-D_3 (Scheme 2), presumably by the D series of fragmentation which is commonly observed in the mass spectra of per-*O*-methyl derivatives of oxygenated pentopyranoses.[24] No appreciable fragmentations of series B and C are observed for **3**, whereas these are the main fragmentation pathways in the spectrum of structurally similar tri-*O*-acetyl-3-*O*-methyl-β-D-xylopyranose.[24]

The 5-*C*-[(*S*)-methoxyphosphinyl]-epimer **4** and other pentopyranose derivatives[29] show almost identical fragmentation patterns with that of **3**, indicating that the



SCHEME 3 Major fragmentation pathway of 5-phosphinyl-L-lyxofuranose (**5**).

configurations of the C-1 and the ring-phosphinyl group do not seem to play a significant role in these degradation pathways.

Because of the various difficulties in preparing the precursors, only a few derivatives of furanoid compounds having phosphorus in the hemiacetal ring have been prepared.[11] Among these, the mass spectrum of 1,2,3-tri-*O*-acetyl-4,5-dideoxy-4-*C*-[(*R*)-phenylphosphinyl]-α-L-lyxofuranose[22,23] (**5**) is presented. The most important of the series of degradation pathways is shown schematically in Scheme 3. Here again, the fragmentation of series A to give rise to ions A_1-A_3 of the λ^5-phosphole oxide structure is predominant, followed by the exclusive removal of the phenylphosphine oxide from the furanoid ring. The presence of such a type of fragmentation would easily permit us to differentiate the mass spectra of furanoid from those of pyranoid compounds. The molecular ion of **5** was not seen in this EI mass spectrum, but it was clearly shown at *m/z* 368 by ^{23}Na-FD mass spectroscopy.

Although more examples of the spectra of other derivatives including deuterium-labelled compounds are required to rationalize the general degradation pathways proposed in this paper, this initial work clearly demonstrates the utility of high resolution mass spectral studies for the effective characterization of the structures of peracetylated derivatives of monosaccharides having phosphorus in the hemiacetal ring. Moreover, the various fragmentation patterns found by the present spectral analysis provide information concerning the unique reactivities that are potentially important in connection with the physicochemical properties of the phosphorus sugars.

EXPERIMENTAL

Mass spectra. The spectra were measured with an A.E.I. MS 50 ultra-high-resolution instrument, and are given in terms of *m/z* (relative intensity) compared with the base peak. All molecular formulas shown in schemes were supported by the accurate mass of the fragment ions, the deviation of which was normally within a range of ±3 ppm error from the calculated values.

Materials. These were prepared according to the literatures cited in the main text, and the chromatographically (thin-layer) pure specimens were subjected to the spectral measurement.

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