Carbohydrate Research, 124 (1983) 195–200
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

FORMATION AND CHARACTERIZATION OF 5-*C*-[(*R*)-(1-ACETOXYETHENYL)PHOSPHINYL]-1,2,4-TRI-*O*-ACETYL-5-DEOXY-3-*O*-METHYL-β-D-XYLOPYRANOSE

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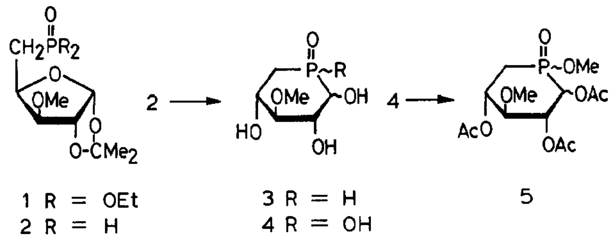
(Received June 18th, 1983; accepted for publication, July 11th, 1983)

ABSTRACT

Treatment of 5-deoxy-3-*O*-methyl-5-*C*-phosphinyl-D-xylopyranose with acetic anhydride in pyridine gave, along with other products, a peracetylated derivative, to which the title structure was assigned on the basis of 400-MHz, ^{1}H-n.m.r. and high-resolution mass spectra. The previous, 5-*C*-[(*S*)-(1-acetoxyethenyl)phosphino] structure, presented for the by-product during the preparation of tri-*O*-acetyl-5-deoxy-5-*C*-(methoxyphosphinyl)-3-*O*-methyl-D-xylopyranoses, is now replaced by the new formulation. Possible structures of other products of the acetylation are discussed. Analysis of the mass spectrum of a sugar analog having a 5-deoxy-5-*C*-(phosphinyl)-D-xylopyranose ring-system is made.

INTRODUCTION

We recently reported[1] an efficient synthesis of 5-deoxy-5-*C*-(hydroxyphosphinyl)-3-*O*-methyl-D-xylopyranoses (**4**) from 5-deoxy-5-*C*-(diethoxyphosphinyl)-D-xylofuranose (**1**) *via* 5-*C*-phosphinyl intermediates **2** and **3**. The product (**4**) was characterized as the peracetylated 5-*C*-(methoxyphosphinyl) derivatives **5**. Besides these four diastereoisomers (with respect to the C-1 and P atoms), the fifth com-



1 R = OEt
2 R = H

3 R = H
4 R = OH

5

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0008-6215/83/$ 03.00

pound was isolated as a minor product (2.7% overall yield from **1**), for which structure **6** was assigned on the evidence of the n.m.r. and mass spectra. These experiments were conducted as the initial part of our study on 5-deoxy-5-*C*-(hydroxyphosphinyl)pyranoses and 4-deoxy-4-*C*-(hydroxyphosphinyl)furanoses, which were considered to be of interest for their potential, biological activities.

Similarly, it seemed to be important from various viewpoints to examine the properties of monosaccharides containing an unsubstituted phosphinyl group in the hemiacetal ring. We now report some reactivities of the 5-deoxy-5-*C*-(phosphinyl)pyranoses, employing **3** as a model compound.

RESULTS AND DISCUSSION

As compound **3** was expected to be a mixture of, at least, two anomers, various attempts were made to separate **3** into single components by recrystallization or chromatography. Although a small portion of **3**, of m.p. 208–210°, had been reported[2] to be available after recrystallization from methanol (in 15% overall yield from **1**), our specimen remained a white, hygroscopic, amorphous solid. Therefore, unambiguous structural assignment was sought in the usual way, by converting **3** into its peracetates by treatment with acetic anhydride–pyridine, and the crude product was carefully separated (by column chromatography on silica gel using ethyl acetate–hexane as the eluant) into three major fractions (R_F 0.45, 0.40–0.30, and 0.28–0.20).

The fastest-eluting fraction (R_F 0.45) afforded mainly a colorless, crystalline compound of m.p. 190° (after recrystallization from ethyl acetate–hexane), which turned out to be identical (by n.m.r. spectra and t.l.c.) with the aforementioned, minor compound that had been assigned structure **6**. Moreover, it was found that

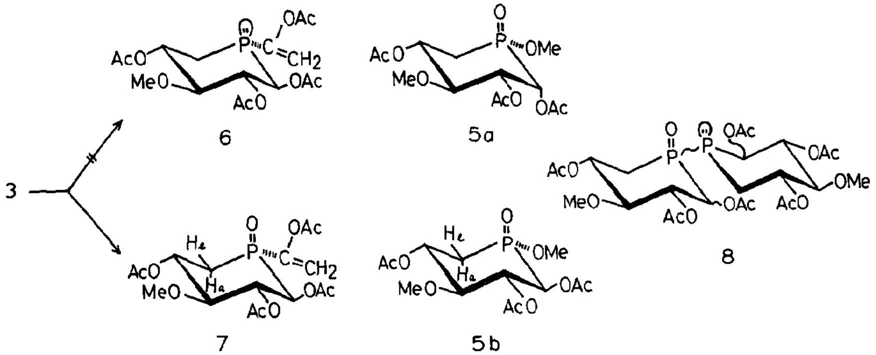
TABLE I

400-MHz, ^{1}H-N M R PARAMETERS FOR **5b** AND **7** IN $CDCl_3$

Compounds	*Chemical shifts (δ)*								
	H-1	*H-2*	*H-3*	*H-4*	*H-5e*	*H-5a*	*AcO-1,2,4*[a]	*MeO-3*	*R-P*
5b[b]	5.27	5.45	3.42	5.24	2.55	1.91	2.16, 2.10, 2.08	3.48	3.77[c]
7[d]	5.43	5.63	3.49	5.40	2.62	1.95	2 11, 2.09, 2 08	3.51	2.26[e], 6.08[f], 6.19[g]

	Coupling constants (Hz)[h]											
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,p}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5a,5e}$	$J_{5e,P}$	$J_{5a,P}$	$^3J_{H,P}$
5b[b]	10.5	5.5	8.7	3.8	8 6	4.5	12.5	0.8	14.8	22.5	11.0	11.2[d]
7[d]	10.8	1.6	9.2	2.6	9.5	4.4	12.0	3.2	14.4	20.0	5.3	[f,g]

[a] Acetoxyl assignments are interconvertible. [b] Ref. 1. [c] MeO–P. [d] These data were incorrectly assigned to structure **6** in ref. 1. [e] P–C(OCOCH$_3$)=C. [f] P–C=C–H(*E*)($^3J_{H,P}$ 29.8, $^2J_{H,H}$ 2.8 Hz). [g] P–C=C–H(*Z*)($^3J_{H,P}$ 10.2, $^2J_{H,H}$ 2.8 Hz). [h] *J* values confirmed by double resonance



6 5a 8

3

7 5b

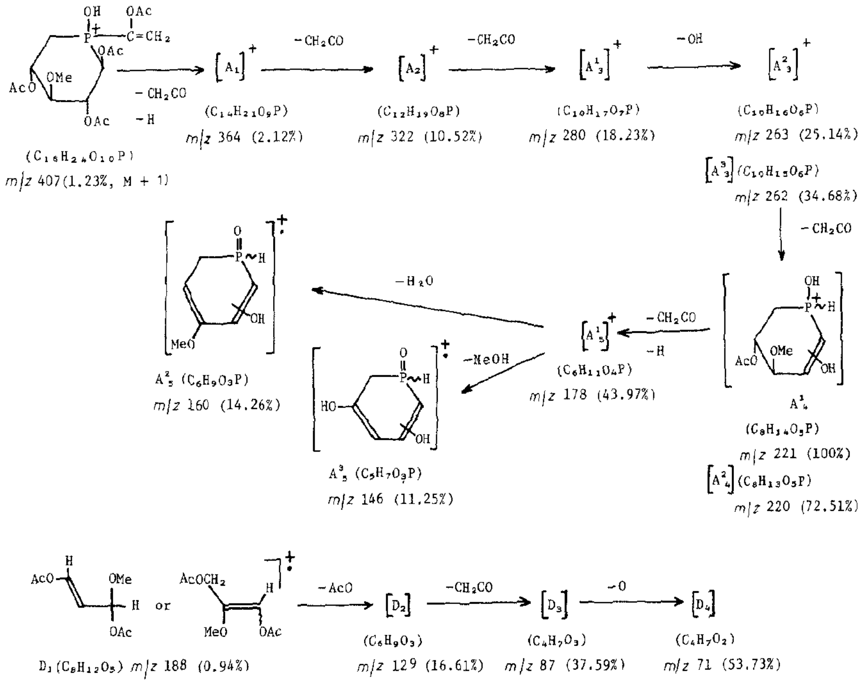
Correct structure

the chemical ionization (NH_3) mass spectrum of this product clearly exhibited its molecular-ion peak at *m/z* 407, corresponding to $C_{16}H_{24}O_{10}P$ (M + 1; 100%). This molecular composition was confirmed by the high-resolution, e.i. mass spectrum at an inlet temperature (150°) lower than that (200°) used during the previous measurement[1], which had given the highest mass-number at *m/z* 378. This newly confirmed molecular weight and the characteristic fragmentation pattern of the mass spectrum (see later), as well as the close resemblance of the 400-MHz, ^{1}H-n.m.r.-spectral signals (see Table I) to those of **5b** (m.p. 194–195°) rather than to those of the α anomer (**5a**; now colorless needles, m.p. 94°, instead of an oil, as had been reported[1]), led to structure **7**, namely, 5-*C*-[(*R*)-(1-acetoxyethenyl)phosphinyl]-1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-β-D-xylopyranose in the $^4C_1$(D) conformation, for this crystalline product (15% yield from **3**). Thus, the previous structure **6** has to be replaced by the revised formula **7**.

The intermediate fraction gave an inseparable mixture of, at least, three compounds as a colorless syrup, the ^{1}H-n.m.r. spectrum of which in $CDCl_3$ was strongly indicative of structures of the diastereoisomers of **7** (with respect to C-1 and the ring-phosphorus atom) for these products (~8% yield).

The slowest-eluting fraction afforded a colorless syrup that was also an inseparable mixture of several compounds. The ^{1}H-n.m.r.-spectral analysis performed on these products (see Experimental section) suggested that their most probable structures would be the diphosphine mono-oxide form (**8**) derived by the facile phosphorus–phosphorus dimerization of **3**, analogous to the formation of tetraphenyldiphosphine mono-oxide from diphenylphosphine oxide in the presence of acetic anhydride and pyridine at room temperature[3]. The formation of a considerable proportion of **8** from **3** (~25% yield) would account for the complexity of the acetylation reaction of phosphine oxide **3**, resulting in the low yield of the anticipated product **7** and its diastereoisomers.

The fact that compound **7** and its diastereoisomers were isolated directly from **3** (to an appreciable extent) suggests that **7** was formed through direct "double" acetylation of the 5-*C*-phosphinyl group of **3** with acetic anhydride–pyridine rather than through the tentatively proposed pathway[1] involving the dispropor-



Scheme 1. Major fragmentation-pathway of compound 7.

tionation reaction of 3. A similar acetylation reaction is known for various primary and secondary phosphine oxides; for example, conversion of $Et_2P(=O)H$ into $Et_2P(=O)\text{-}C(OAc)=CH_2$ with acetic anhydride[4].

Mass spectrum of compound 7. — There has been reported[5] a systematic analysis of the mass spectra of the per-*O*-acetylated derivatives of 5-deoxy-5-*C*-(ethylphosphinyl)-D-glucopyranoses, 5-deoxy-5-*C*-(methoxyphosphinyl)-D-xylopyranoses, and 4-deoxy-4-*C*-(phenylphosphinyl)-L-lyxofuranoses. The mass-spectral analysis of 7 is presented here as the first example of that of the peracetylated derivative of 5-deoxy-5-*C*-(phosphinyl)pentopyranoses.

The molecular ion of 7 is likewise detected at *m/z* 407 [$(M+1)^+$, most likely as the resonance-stabilized hydroxyphosphonium form]. Compound 7 then gives rise to the major fragmentations of the first series A (according to the nomenclature used by Kochetkov and Chizhov[6]), as illustrated in Scheme 1. It is noteworthy that species A_4^1, which is formed from the molecular ion by the four successive losses of three ketene and one acetic acid groups, consisted of the base peak, suggesting the high stability of the phosphorus-containing ring-system. This is in contrast to the spectra[7] of per-*O*-acetylated monosaccharides of oxygen-containing rings, where the intensities of the fragments retaining the hemiacetal ring are generally much lower than those of ring-ruptured fragment-ions. Further elimination of one molecule of acetic acid (or one ketene and one methanol molecule) from species A_4 leads to the species A_5^2 (or A_5^3) having the 1,2-dihydro-λ^5-phosphorin ring system and an appreciable intensity, although the position of the hydroxyl group on this phosphorin ring (at atom 5 or 6) remained unestablished.

The intensities of the fragment-ions due to the subsequent ring-opening fragmentation were relatively weak, whereas the 5-*C*-(methoxyphosphinyl) compounds **5a** and **5b** gave rise to such phosphorus-free ions as the base peak[5]. As in the case of **5b**, degradation of the pyranoid ring of **7** seems to produce phosphorus-free, major fragments D_1–D_4 (see Scheme 1), presumably by the D series of fragmentations that is commonly observed in the mass spectra of per-*O*-methyl derivatives of the usual pentopyranoses[7].

The findings so far described are considered to be of appreciable value in studying the physicochemical properties of sugar analogs having an unsubstituted phosphinyl group in the hemiacetal ring.

EXPERIMENTAL

General methods. — Melting points were measured with a Yanagimoto MP-83 instrument and are uncorrected. T.l.c. was conducted on plates precoated with silica gel (0.25 mm, Merck). ^{1}H-N.m.r. spectra were recorded, for solutions in $CDCl_3$ at 27°, with a Hitachi R-20A (60-MHz) spectrometer. Chemical shifts are reported as δ values relative to tetramethylsilane as the internal standard. Mass spectra were recorded with an A.E.I. MS 50 ultra-high resolution instrument (for accurate measurement of mass) and an A.E.I. MS 12 apparatus (for chemical ionization with NH_3), and the results are given in terms of *m/z* (relative intensity compared with the base peak). All molecular formulas shown in Scheme 1 were supported by the accurate mass of the fragment ions, deviation of which from calculated values was normally within a range of ±3 p.p.m.

*Acetylation of 5-deoxy-3-*O*-methyl-5-*C*-(phosphinyl)-*D*-xylopyranose* (**3**). — Compound **3** was prepared from the phosphonate **1** *via* **2** in 68% overall yield according to the procedures described earlier[1]. The crude product **3** (43 mg) was dissolved in dry pyridine (5 mL), and the solution diluted with cold acetic anhydride (2.5 mL). The mixture was stirred for 2 days at room temperature, and then evaporated *in vacuo* at 20°. A solution of the residue in CH_2Cl_2 was washed with cold water, dried (Na_2SO_4), and evaporated *in vacuo*. The resulting syrup (56 mg) was chromatographed in a column of silica gel (Merck Lobar, prepacked, Size A) using EtOAc–hexane as the eluant, and the three major fractions, namely, A, B, and C [according to their decreasing R_F values (EtOAc)] were collected.

Fraction A (R_F 0.45) gave *5-*C*-[(*R*)-(1-acetoxyethenyl)phosphinyl]-1,2,4-tri-*O*-acetyl-3-*O*-methyl-β-*D*-xylopyranose* (**7**) as colorless prisms (13 mg, 15% yield from **3**); m.p. 190° (after recrystallization from EtOAc–hexane); for 400-MHz, ^{1}H-n.m.r. data, see Table I; c.i. (NH_3) mass spectrum: *m/z* 424 (M + 18, 59.1%), 407 (M + 1, 100%), and 406 (M^+, 24.3%); for high-resolution, e.i. mass spectrum, see Scheme 1.

Anal. Calc. for $C_{16}H_{24}O_{10}P$: mol. wt., 407.1107. Found: mol. wt., 407.1139.

Fraction B (R_F 0.40–0.30) gave the diastereoisomers of **7** (with regard to C-1 and the ring-phosphorus atom) as a colorless syrup (7 mg, 8% yield); ^{1}H-n.m.r.: δ 2.0–2.18 (brs, 9 H, AcO-1,2,4), 2.20–2.28 (brs, 3 H, AcO–C–P), 2.0–2.8 (m, 2 H, H_2-5), 3.35–3.55 (m, 1 H, H-3), 3.50 (brs, 3 H, MeO-3), 5.0–5.8 (m, 3 H, H-1,2,4), and 6.0–6.5 (m, 2 H, CH_2=C–P).

Fraction C (R_F 0.28–0.20) gave a colorless syrup (18 mg, 25% yield), which consisted mostly of the diphosphine mono-oxide (**8**); ^{1}H-n.m.r.: δ 2.0–2.2 (brs, 18 H, 6 AcO), 1.9-2.7 (m, 4 H, H-5), 3.35–3.60 (m, 2 H, H-3), 3.48 (brs, 6 H, MeO-3), and 5.1–5.9 (m, 6 H, H-1,2,4); no P–H signal was observed.

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