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Preliminary communication

Synthesis and the structural analysis of 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*,*S*)-methoxyphosphinyl]-α,β-D-xylopyranoses

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Various sugar analogs possessing a phosphorus atom in the hemiacetal ring have been prepared[1–3], because of the interest in their physicochemical properties and also the potential utility of their biological activity. Compared with a large number of the analogs having an alkyl- or aryl-phosphinyl group in the ring, such as 5-deoxy-5-*C*-(ethylphosphinyl)-D-glucopyranoses[4] and 4-deoxy-4-*C*-(ethylphosphinyl)-D-ribopyranoses[5], only two derivatives containing a hydroxyphosphinyl group therein have been reported, namely, 4-deoxy-4-*C*-(hydroxyphosphinyl)-3-*O*-methyl-D-xylopyranose[6,7] and 4-deoxy-4-*C*-(hydroxyphosphinyl)-D-ribopyranose[8]. We now report the synthesis of the first, unsubstituted 4-deoxy-4-*C*-(hydroxyphosphinyl)-D-xylopyranose (**6**), and the n.m.r.-spectral analysis of its four diastereoisomeric derivatives (**7a–d**), which provides an effective way for establishing the structures of 5-deoxy-5-*C*-(hydroxyphosphinyl)pyranoses.

The Michaelis–Arbuzov reaction of 3-*O*-acetyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylopyranose[9] (**1**) with triethyl phosphite afforded the 5-*C*-(diethoxyphosphinyl) derivative (**2**; 87% yield), which was reduced with sodium dihydrobis(2-methoxyethoxy)-aluminate to give the 5-*C*-phosphino compound (**3**). This was either oxidized with hydrogen peroxide to the 5-*C*-phosphinyl derivative **4**, prior to acid-catalyzed ring-enlargement, or immediately hydrolyzed with 1:1 0.5M sulfuric acid–2-propanol for 1 h at 100° under nitrogen, followed by the usual work-up[7]; however, the latter method provided a better yield of the 5-deoxy-5-*C*-phosphinyl-D-xylopyranose **5**. Oxidation of **5** with 3% hydrogen peroxide overnight afforded the 5-*C*-(hydroxyphosphinyl) compound **6** as a colorless solid in 82% overall yield from **2**.

The unambiguous structural assignment of **6** was made by converting it into the 5-*C*-(methoxyphosphinyl) tetraacetates **7** by treatment with ethereal diazomethane in 1:1

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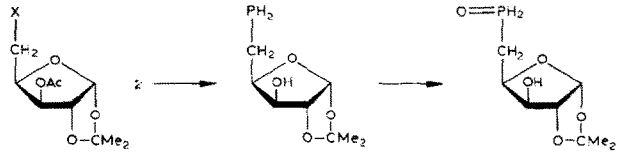

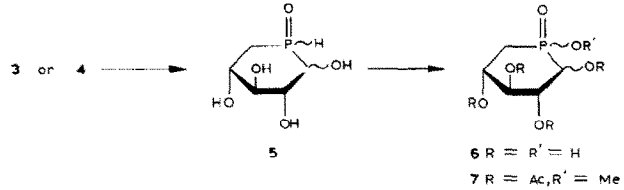

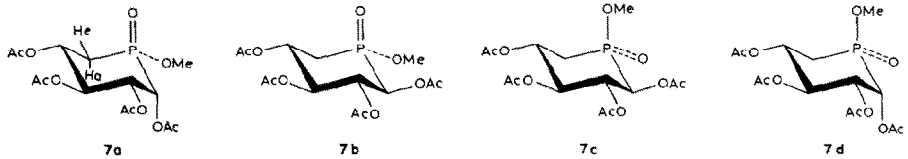

dimethyl sulfoxide–methanol, and then acetic anhydride–pyridine. Purification of the crude mixture by column chromatography on silica gel using ethyl acetate–hexane as the eluant gave three diastereoisomers: **7a** (colorless amorphous solid; 5.0% overall yield from **2**), **7b** (colorless needles, m.p. 183°; 6.4%), and **7c** (colorless prisms, m.p. 151°; 6.8%) as pure components, besides another isomer **7d** (colorless syrup; 2.3%) contaminated by a minor proportion of inseparable **7c**. The molecular composition of these compounds was confirmed by the e.i., high-resolution, mass spectra, all of which clearly gave the (M + 1) ions at *m/z* 381 (2.3–3.4%) corresponding to $C_{14}H_{22}O_{10}P$. The precise configurations and the $^4C_1$(D) conformation of **7a–d** were established by complete analysis of their 400-MHz, ^{1}H-n.m.r. spectra; see the assignments of all signals, summarized in Table I. It should be noted that, as was observed for **7a** and **7b**, a slight, downfield shift (0.2–0.4 p.p.m.) of the H-2 and H-4 signals (and an upfield shift of the P-OMe signal) indicated the axial orientation [(*R*)] of the ring P=O group, whereas the anomeric orientation at C-1 is readily perceived by considering the values of H-1, H-3, and H-5*a*, and the magnitudes of $J_{1,2}$, $J_{1,P}$, and $J_{1,5e}$. This method would also be applicable to the determination of the configuration of C-5 of hexopyranoses, even those having such a ring-phosphinyl group.

The present work thus demonstrates an effective way for preparation and structural analysis of 5-deoxy-5-*C*-(hydroxyphosphinyl)-D-xylopyranose.

TABLE I

400-MHz, ^{1}H-N.M.R. PARAMETERS FOR 5-DEOXY-5-*C*-(METHOXYPHOSPHINYL)-D-XYLOPYRANOSES IN $CDCl_3$ [a]

Compounds	*Chemical shifts* (δ)								
	H-1	*H-2*	*H-3*	*H-4*	*H-5e*	*H-5a*	*AcO-1,2,3,4* [b]		*MeO-P*
7a	5.64	5.48	5.49	5.32	2.47	2.20	2.20, 2.02, 2.01, 1.99		3.73
7b	5.35	5.54	5.24	5.32	2.61	2.02	2.16, 2.05, 2.04, 2.02		3.80
7c	5.53	5.32	5.24	5.09	2.57	2.05	2.14, 2.06, 2.04, 2.02		3.97
7d	5.71	5.13	5.46	5.05	2.54	2.34	2.26, 2.08, 2.06, 2.02		3.93

	Coupling constants (Hz)												
	$J_{1,2}$	$J_{1,P}$	$J_{1,5e}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5a,5e}$	$J_{5e,P}$	$J_{5a,P}$	J_{POMe}
7a	2.3	14.4	2.2	10.0	0	10.0	4.6	12.0	1.5	−14.2	23.4	8.4	11.3
7b	10.5	5.0	0	9.3	3.2	9.7	4.5	11.2	0	−14.7	22.8	9.5	11.5
7c	10.2	3.2	0	10.0	1.8	10.0	4.5	11.5	1.2	−14.8	23.5	9.5	10.5
7d	3.0	15.3	2.3	10.6	0	10.3	4.8	11.7	1.3	−14.8	22.5	12.3	10.5

[a] The assignments of all signals were made by employing a first-order analysis with the aid of a decoupling technique, except for **7a**, some of its parameters being obtained by computer-assisted analysis (see ref. 10). [b] Acetoxyl assignments may have to be interchanged.

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