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Preliminary communication

Synthesis of 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-β-D-glucopyranose: A new route for preparation of D-glucopyranoses having phosphorus in the hemiacetal ring

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We have previously reported[1] the synthesis of 1,2,4-tri-*O*-acetyl-3,6-di-*O*-benzyl-5-deoxy-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose (**9**) by the sequence of **1**→**2**→**3**→**9**. However, the yield of the three-step conversion of **3** into **9** was very low (2% overall), because of the appreciable decomposition of **3** during the reaction.

We now describe a new, convenient route for preparation of the first, unsubstituted 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses (**7**). The addition of methyl ethylphosphinate to **2** in the presence of trifluoromethanesulfonic acid, followed by reduction with $NaBH_4$ in oxolane (THF) gave **4** in 50% yield. Debenzylation of **4** was effected by hydrogenolysis, first over Raney Ni in ethanol for 30 min at 55°, and then over 10% Pd–C in ethanol for 12 h at 55°. The product proved to be the tricyclic compound **5**, which, on treatment with chlorotriphenylmethane in pyridine, provided **6** as a diastereoisomeric mixture (with regard to C-5 and the phosphorus) in 17% overall yield from **4**.

Compound **6** was reduced with sodium dihydrobis(2-methoxyethoxy)aluminate; and then, without isolation, the product was refluxed with ethanolic 0.5M HCl, affording the 5-deoxy-5-*C*-phosphinyl-hexopyranoses **7**, which were characterized by conversion into the peracetates (**8**) with acetic anhydride in pyridine, as before[1]. Purification in a column of silica gel with 1:19 (v/v) methanol–dichloromethane as the eluant gave **8** (in 30% overall yield from **6**) as a colorless oil which consisted of almost equal amounts of three components (R_F 0.45, 0.40, and 0.37 with the same eluant). On diluting the mixture with ethyl acetate–hexane, the fastest-eluting fraction (R_F 0.45) crystallized as colorless prisms, m.p. 233° (dec.). The molecular composition of this compound was confirmed by the e.i., high-resolution, mass spectrum, which clearly gave the (M + 1)

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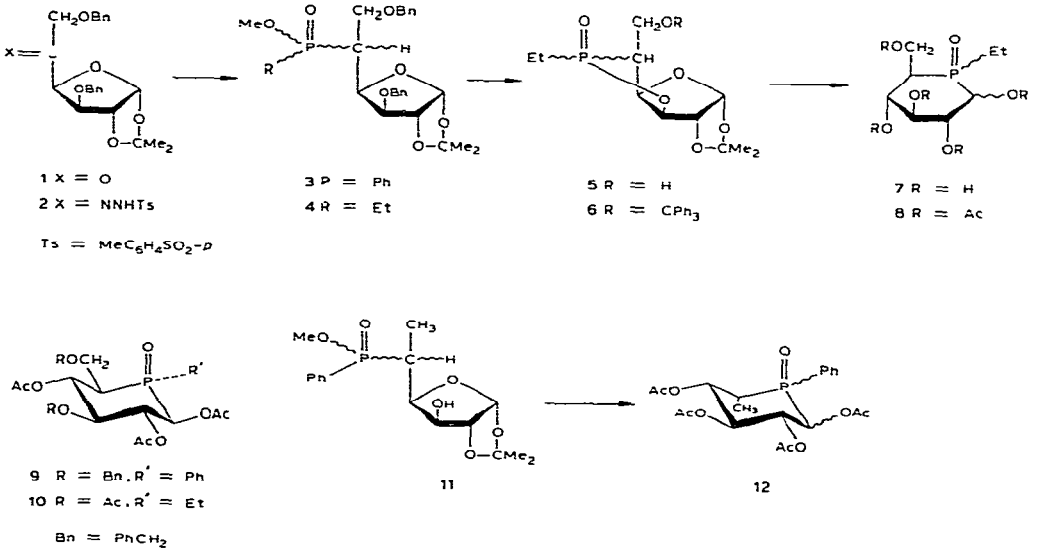
TABLE I

^{1}H-N.m.r. (400 MHz) PARAMETERS[a] FOR 5-DEOXY-5-*C*-(ETHYLPHOSPHINYL)-β-D-GLUCOPYRANOSE (10) IN $CDCl_3$

AcO-1[b] *H-1*	*Ac-2*[b] *H-2*	*AcO-3*[b] *H-3*	*AcO-4*[b] *H-4*	*H-5*	*AcO-6*[b] *Ha-6*	*Hb-6*	P–CH_2–*C*	P–*C*–CH_3
2.16[b] s	2.07[b] s	2.01[b] s	2.06[b] s;		1.99[b] s			
5.38 ddd	5.72 ddd	5.22 t	5.58 ddd	2.37 ddddd	4.49 td	4.45 ddd	2.04 dq[c]	1.19 dt
$J_{1,2}$ 11.0	$J_{2,3}$ 10.0	$J_{3,4}$ 10.0	$J_{4,5}$ 11.5	$J_{5,6a}$ 7.4	$J_{6a,P}$ 11.5	$J_{6b,P}$ 15.0	$^2J_{H,P}$ 15[c]	$^3J_{H,P}$ 19.3
$J_{1,P}$ 3.6	$J_{2,P}$ 3.0		$J_{4,P}$ 2.7	$J_{5,6b}$ 5.0	$J_{6a,6b}$ 11.5			$^3J_{H,H}$ 7.6
$J_{1,5}$ 0.2				$J_{5,P}$ 3.5				

[a] Chemical shifts (δ values) are in p.p.m. from Me_4Si; coupling constants (*J*) are in Hz. [b] Acetoxyl (assignments may have to be interchanged). [c] Approximate value, because of overlapping with the acetoxyl signals.



ion at *m/z* 451 (2.5%) corresponding to $C_{18}H_{28}O_{11}P$ (Calc. for M + 1: 451.138. Found: 451.136). The precise structure, **10**, for this product was established on the evidence of the 400-MHz, ^{1}H-n.m.r. spectrum, which closely resembled those of the structurally similar analogs[1]; the assignments of all signals are summarized in Table I.

Although complete separation of the remaining two 5-deoxy-5-*C*-phosphinyl-hexopyranoses (**8**) has not been achieved, their n.m.r. spectra strongly indicated that these were diastereoisomers of **10** having the *gluco* configuration. This is in striking contrast to the result of the previous, similar ring-transformation[2] of **11** to the L-ido-pyranoses (**12**) solely.

The present work demonstrates an effective way for preparation of the 5-deoxy-5-*C*-phosphinylglucopyranoses from *xylo*-hexofuranoses.

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