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Preliminary communication

Synthesis of 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-*C*-[(*R*,*S*)-ethylphosphinyl]-α,β-D-ribofuranoses: the first D-ribofuranose derivatives having phosphorus in the hemiacetal ring

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We have previously reported[1] the synthesis of 1,2,3-tri-*O*-acetyl-4,5-dideoxy-4-*C*-[(*R*,*S*)-phenylphosphinyl]-α,β-D-ribo- and -L-lyxo-furanoses (**4**) by the sequence of **1** → **2** → **3** → **4**. However, this method could not be applied to a synthesis of 4-deoxy-4-*C*-phosphinyl-D-ribofuranoses, because of the various difficulties in preparing the open-chain precursors.

We now describe a new, convenient route for preparation of such compounds (**11** and **12**). Methyl 2,3-*O*-isopropylidene-α-L-lyxopyranoside (**5**), prepared[2] from D-galacturonic acid, was oxidized with dimethyl sulfoxide–oxalyl chloride–triethylamine in dichloromethane at −70° to give methyl 2,3-*O*-isopropylidene-β-D-*erythro*-pentopyranosid-4-ulose (**6**; 74% yield). According to a well established method[3], **6** was converted into the *p*-tolylsulfonylhydrazone (**7**; 91% yield). The addition of methyl ethylphosphinate to **7** in the presence of trifluoromethanesulfonic acid, followed by reduction with sodium borohydride in oxolane, gave **8** in 42% overall yield.

The phosphinate **8** was reduced with sodium dihydro(2-methoxyethoxy)aluminate, and then, without isolation, the product was refluxed with ethanolic 0.5M HCl, affording 4-deoxy-4-*C*-[(*R*,*S*)-ethylphosphinyl]-D-ribo- and -L-lyxo-furanoses (**9**), which were characterized by conversion into the peracetates (**10**) with acetic anhydride in pyridine. Purification in a column of silica gel with benzene–ethyl acetate (and then with ethyl acetate–ethanol) as the eluant gave **10** (in 48% overall yield from **8**) as a colorless oil that consisted of at least seven components (R_F 0.45, 0.40, 0.36, 0.32, 0.27, 0.25, and 0.16 with ethyl acetate). By rechromatography with the same system, two pure components, **11** (a colorless oil, 13% yield; R_F 0.45) and **12** [colorless prisms, m.p. 145–146° (from ethyl acetate–hexane), 4% yield; R_F 0.27], were separated from the mixture.

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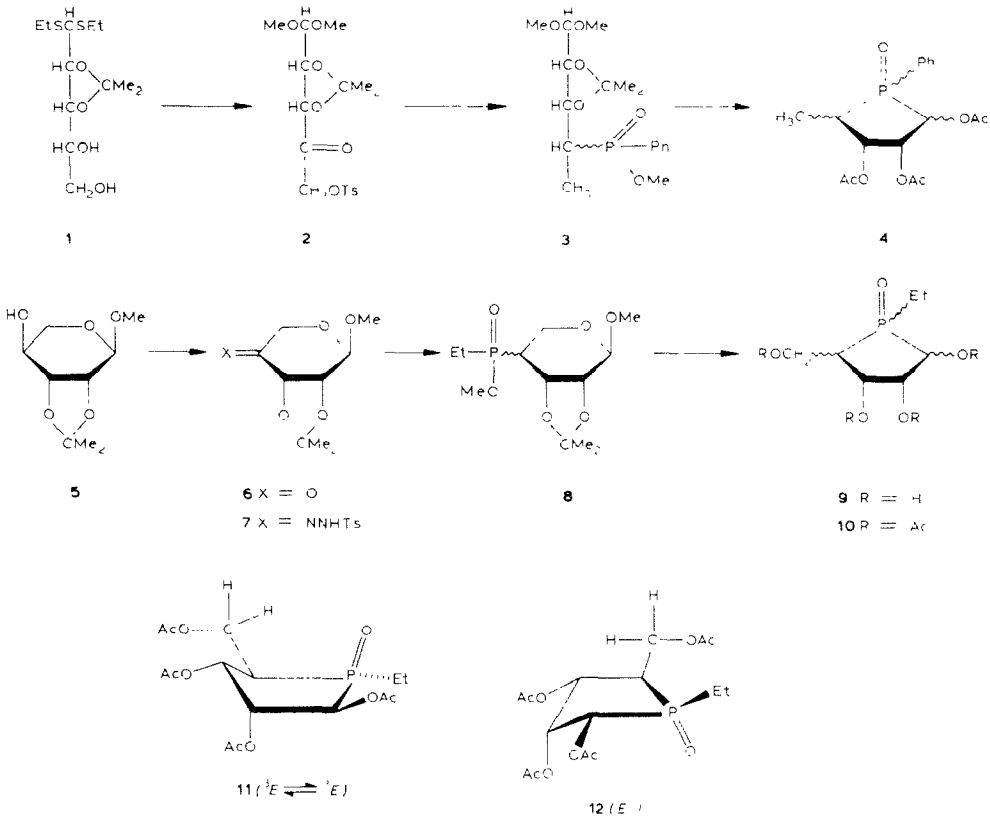

The molecular composition of these compounds was confirmed by examining the relative intensities of the (M + 2) and (M + 3) ions of the c.i. (NH_3) mass spectra, which clearly gave the (M + 1) ions, both at *m/z* 379 (100%), corresponding to $C_{15}H_{24}O_9P$. The precise structures of **11** and **12**, as well as the most probable conformations in chloroform for these two products, were established on the evidence of the 400-MHz, ^{1}H-n.m.r. spectra, which closely resembled those of structurally similar analogs[1]; the assignments of all signals are summarized in Table I.

Although complete separation of the remaining diastereoisomers has not been achieved, their n.m.r. spectra strongly indicated that the pentofuranoses having the D-*ribo* configuration were the preponderant components, among the rest of the products. This is in contrast to the result of the previous, similar cyclization of the open-chain precursor **3** to yield equal amounts of D-ribo- and -L-lyxo-furanoses (**4**). Thus, the present work demonstrates an effective way for preparation of 4-deoxy-4-*C*-phosphinyl-D-ribofuranoses from D-galacturonic acid.

TABLE I

^{1}H-N.M.R.-SPECTRAL (400 MHz) PARAMETERS FOR 4-DEOXY-4-*C*-(ETHYLPHOSPHINYL)-D-RIBOFURANOSES (**11** AND **12**) IN $CDCl_3$

Compound	*Chemical shifts (δ)*									
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*	*AcO-1,2,3,5* [a]		*P CH$_2$*	*P–C–CH$_3$*
11	4.97	5.66	5.54	2.62	4.53	4.30	2.23	2.13	2.27	1.35
							2.12	2.10	2.01	
12	4.97	5.75	5.00	3.12	4.47	4.34	2.22	2.19,	2.10 [b]	1.30
							2.11	2.09	2.07 [b]	
	Couping constants (Hz) [c]									
	$J_{1,2}$	$J_{1,4}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,P}$	$J_{5,P}$	$^2J_{H,P}$	$^2J_{H,H'}$	$^3J_{H,P}$
	$J_{1,P}$		$J_{2,P}$	$J_{3,P}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5',P}$	$^2J_{H',P}$		$^3J_{H,H}$
11	6.0	0.5	3.6	6.0	7.3	6.5	9.2	15.0	15.0	19.0
	2.5		10.5	13.5	7.5	12.0	12.2	11.5		7.5
12	4.8	0	3.0	12.0	4.8	22.0	14.8			17.0
	2.6		24.6	1.0	7.0	11.9	17.0			7.5

[a] Assignments may have to be interchanged. [b] Approximate value, because of overlapping with the acetoxyl signals. [c] The values were confirmed by double resonance.

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