Analogues of Methyl D-*Ribo*- and D-*Arabino*-furanosides Having Phosphorus in the Anomeric Position[+]

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Acid-catalysed cyclisation of (1S)- and (1R)-1-C-(dimethoxyphosphinyl)-D-erythritols gave exclusively P-epimeric analogues of methyl D-*ribo*- and D-*arabino*-furanosides with phosphorus in the anomeric position.

Recently, we have completed syntheses of (2R, 3R, 4R)-3-C-(hydroxymethyl)-2-methoxy-2-oxo-1,2-oxaphospholane-3,4-diol as well as of (2R, 3R, 4S, 5R)- and (2S, 3R, 4S, 5R)-4,5[1]-O-benzylidene-3-O-(*tert*-butyldimethylsilyl)-5-C-(hydroxymethyl)-2-methoxy-2-oxo-1,2-oxaphospholane-3,4-diol which were considered as analogues of C-2 branched-chain-D-threose and D-lyxose containing phosphorus in the anomeric position, respectively [1]. Now, we report on the synthesis of the analogues of D-ribose and D-arabinose.

It was anticipated that (1S)-(**1**) and (1R)-2,4-O-benzylidene-1-C-(dimethoxyphosphinyl)-D-erythritol (**2**) could be employed as starting materials for the synthesis of these analogues. Attempts at a base-catalyzed cyclisation [1, 2] of **1** and **2** appeared fruitless. Diequatorial dispositions of the substituents at C-4 and C-5 in the conformationally biased 1,3-dioxane rings of **1** and **2** accounts for this unsuccessful approach [3]. To make formation of 1,2-oxaphospholanes from **1** and **2** possible, these compounds were hydrogenolyzed to (1S)-(**3**) and (1R)-1-C-(dimethoxyphosphinyl)-D-erythritol (**4**), respectively. However, as **3** so **4** are capable of closing 5- as well as 6-membered [4] rings in intramolecular transesterifications. Triethylamine-catalysed cyclisation of **3** in dimethylformamide (DMF) at room temperature afforded a complex mixture of cyclic and acyclic products. On the other hand, in the presence of toluene-*p*-sulfonic acid (5%) cyclisation of **3** in DMF at room temperature proceeded slowly to give a 1:2 mixture of (2S, 3S, 4R, 5R)-(**5a**) and (2R, 3S, 4R, 5R)-5-C-(hydroxymethyl)-2-methoxy-2-oxo-1,2-oxaphospholane-3,4-diol (**5b**) accompanied by *ca.* 40% of unreacted **3.** This process was considerably accelerated by maintaining the reaction mixture at 100 °C for several hours to afford a 1:2 mixture of **5a** and **5b** containing less than 10% of starting **3.** No other compounds were detected by ^{31}P NMR. The ^{13}C NMR spectrum of this mixture (Table I) as well as the ^{31}P NMR shifts of **5a** (39.0 ppm) and of **5b** (37.4 ppm) proved the cyclisation of **3** to P-epimeric 1,2-oxaphospholanes occured.

The configuration at phosphorus in **5a** and **5b** was deduced from their ^{31}P NMR shifts [5] and it was further confirmed by ^{1}H NMR in the following manner. The mixture of **5a, 5b** and **3** was treated with trityl chloride in pyridine to give **6a** (δ^{31}P 39.0 ppm) and **6b** (δ^{31}P 37.1 ppm) and then with acetic anhydride affording after chromatographic separation **7a** (oil, δ^{31}P 30.7 ppm) and **7b** (oil, δ^{31}P 32.0 ppm). In the ^{1}H NMR spectrum of **7b,** H–C-3 resonated at lower field (by 0.13 ppm) than that of **7a** due to the deshielding effect of the phosphoryl oxygen [6].

Table I. ^{13}C NMR (22.63 MHz) parameters[a] (CD_3OD) for compounds **3, 4, 5a, 5b, 8a** and **8b.**

Compound	OCH_3		C-1	C-2	C-3	C-4
3	53.85 d (7.6)	54.47 d (6.8)	70.54 d (165.8)	74.00[b] d (4.9)	74.49[b] d (1.2)	64.45 s
4	53.67 d (7.1)	54.31 d (6.8)	68.51[c] d (166.7)	71.72[b] d (4.2)	71.96[b] d (1.0)	64.65[c] d (4.2)
	OCH_3		C-3	C-4	C-5	C-5[1]
5a	54.11 d (9.3)		65.36 d (143.6)	70.74 d (19.3)	84.74 d (2.9)	62.76 d (4.2)
5b	55.77 d (7.3)		67.13 d (139.6)	70.96 d (17.8)	85.43 d (3.4)	62.35 d (4.2)
8a	53.94 d (6.8)		70.97 d (140.6)	75.68 d (23.7)	82.90 d (1.0)	62.27 d (5.1)
8b	55.04 d (7.1)		72.56 d (141.8)	74.62 d (24.4)	83.06 s	62.09 d (3.9)

[a] Chemical shifts on the δ scale (J in Hz); digital resolution 0.24 Hz/point; [b] assignments may have to be interchanged; [c] due to overlap of signals alternative values [C-1 68.38 (172.6) and C-4 64.78 (1.7)] are possible.

[+] Stereochemistry of 1,2-oxaphospholanes – VI. Part V [5].

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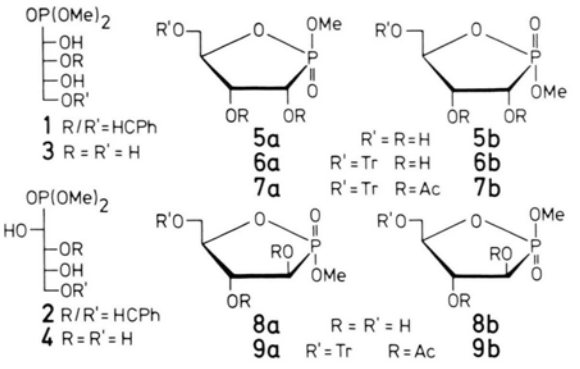
The synthesis of the analogues of *arabino*-configuration was accomplished in the same way as for ribose counterparts. A 2:1 mixture of (2R, 3R, 4R, 5R)-(**8a**) and (2S, 3R, 4R, 5R)-5-C-(hydroxymethyl)-2-methoxy-2-oxo-1,2-oxaphospholane-3,4-diol (**8b**) contaminated by less than 20% of unreacted **4** was produced when a DMF solution of **4** had been maintained at 100 °C for 4 h. The ^{13}C NMR spectrum of this mixture (Table I) supports the structure of the cyclic products. The S configuration at P in **8b** ($\delta^{31}P$ 32.5 ppm) was evident from the upfield shift of its ^{31}P NMR signal [5] in comparison with that of **8a** ($\delta^{31}P$ 35.8 ppm) as well as from the deshielding [6] of H–C-3 in **9b** (oil, $\delta^{31}P$ 30.1 ppm) as compared to **9a** (oil, $\delta^{31}P$ 29.1 ppm).

This paper demonstrates the preference of formation of 5- over 6-membered rings for the analogues of monosaccharides with P in the anomeric position of *ribo*- and *arabino*-configuration.



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