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Synthesis of 5-Deoxy-3-O-methyl-5-phenylphosphinyl-L-fucopyranoses. The First P-in-Ring Sugar Analogs of L-Fucose Type

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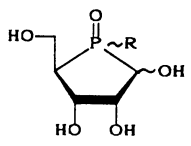
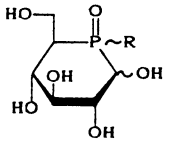
Starting from 1,2:5,6-di-O-isopropylidene-β-D-altrofuranose, 5,6-dideoxy-1,2-O-isopropylidene-5-[(methoxy)phenylphosphinyl]-3-O-methyl-β-D-arabino-hexofuranose was prepared in a 6 step sequence (13% overall yield). It was converted into the title compounds, which were characterized as the 1,2,4-triacetates.

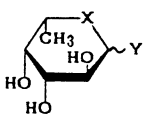
Sugar analogs having a phosphorus atom in the hemiacetal ring have been prepared in recent years;[1] e.g., those corresponding to D-ribofuranoses **1**[2] and D-glucopyranoses **2**.[3] These compounds are of interest in view of their physico-chemical properties and potential biological activity. Meanwhile, 1,5-imino-L-fucitol (**3**)[4] and 5-thio-L-fucose (**4**)[5] were synthesized and both compounds have been shown to inhibit L-fucosidase. We describe here a convenient synthesis of the first P-in-ring sugar analogs with L-fucose type structure having a phenylphosphinyl as a model functional group.



1 R=Et,Ph,OH

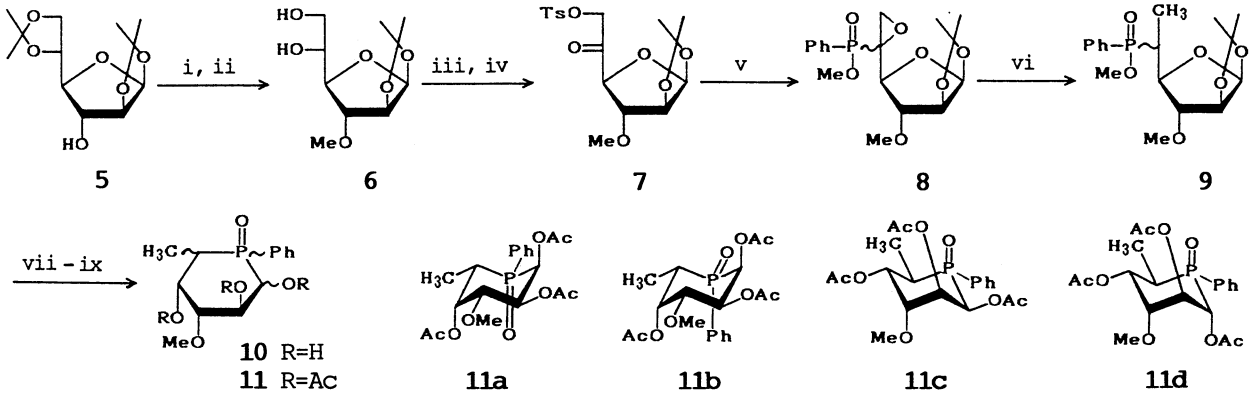


2 R=Et,OH



3 X=NH,Y=H
4 X=S,Y=OH

Thus, D-altrofuranose **5**[6] was converted into the key intermediate 5,6-dideoxy-5-[(methoxy)phenylphosphinyl] derivative **9** by sequence of **5** → **6** → **7** → **8** → **9** (6 steps, 13% overall yield) as illustrated in Scheme 1.[7] Then, **9** was reduced with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA), followed by acid hydrolysis, affording 5,6-dideoxy-



5 **6** **7** **8** **9**

10 R=H
11 R=Ac

11a **11b** **11c** **11d**

Scheme 1. Reagents: i, MeI-NaH/DME, 98% yield; ii, 80% aq AcOH, 78%; iii, TsCl/Py, 76%; iv, PCC, 95%; v, PhPH(=O)OMe-DBU/DME, 55%; vi, H_2/Raney-Ni, 44%; vii, SDMA; viii, aq HCl-EtOH; ix, Ac_2O-Py.

5-phenylphosphinyl-D-arabino-hexopyranoses (**10**), which were converted into their triacetate (**11**) by the usual method (Scheme 1). Chromatography of **11** over silica gel with ethyl acetate-hexane afforded pure 1,2,4-tri-O-acetyl-5-deoxy-3-O-methyl-5-[(R)-phenylphosphinyl]-α-L-fucopyranose (**11a**) (colorless needles, mp 259-261 °C, 13% overall yield from **9**) and its 5-[(S)]-epimer **11b** (syrup, 7% yield), together with a minor proportion of 5,6-dideoxy-5-[(S)-phenylphosphinyl]-β-D-altropyranose **11c** (9%) and its α-anomer **11d** (2%).[8] The configuration of **11a-d**, predominantly in the $^1C_4$(L) or $^4C_1$(D) conformation (Scheme 1), was established by analysis of their 500-MHz ^{1}H NMR spectra (see Table 1),[9] by taking into account the known parameters of structurally related compounds obtained before.[1,3] These NMR data are considered to be highly versatile in determining the structures of other 5-deoxy-5-phosphinyl-L-fucopyranoses, preparation of which is currently under investigation.

Table 1. ^{1}H NMR (500 MHz) Parameters for **11a-d** in $CDCl_3$[a]

	Chemical shifts (δ)										
Compd	H-1	H-2	H-3	H-4	H-5	H_3-6	MeO-3	Ac-1,2,4		Ph(o)	Ph(m)	Ph(p)
11a	5.77	5.85	3.68	5.87	2.61	1.19	3.46	2.23, 2.00, 1,95		7.75	7.75	7.59
11b	6.17	5.57	3.74	5.61	2.73	1.28	3.43	2.24, 2.11, 2.06		7.76	7.51	7.58
11c	5.69	5.77	3.85	5.64	2.70	1.10	3.61	2.23, 2.13, 1.94		7.76	7.51	7.57
11d	5.37	5.49	3.80	5.60	3.02	1.16	3.60	2.18, 2.09, 1.96		7.80	7.51	7.59
	Coupling constants / Hz											
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,P}$	$J_{5,6}$	$J_{5,P}$	$J_{6,P}$	
11a	2.9	11.8	10.4	0	3.8	0	2.7	27.9	7.3	6.7	14.8	
11b	3.1	8.6	9.8	4.2	2.8	0	2.9	29.6	7.3	21.2	14.6	
11c	3.5	0.5	5.2	24.9	2.3	1.8	12.0	4.1	7.2	4.1	14.8	
11d	3.4	9.6	4.7	20.1	2.3	1.0	11.5	6.4	7.2	6.1	14.9	

a) Measured with a Varian VXR-500 instrument (the SC-NMR Lab, Okayama Univ.).

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7) MS (high-resolution) and ^{1}H NMR data (mostly at 500 MHz) of the products described in this paper were in agreement with the structures proposed.
8) Small amounts of the β-anomers of **11a** and **11b** appear to be present in the remaining fractions.
9) The L-fucopyranose configuration was assigned to **11a,b** on the basis of their relatively small $J_{4,5}$ and large $J_{4,P}$ values, whereas the D-altropyranose structure for **11c,d** was derived from the large $J_{4,5}$ and $J_{2,P}$ values.

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