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Preliminary communication

A novel method for the synthesis of sugar derivatives containing a phosphorus atom in the hemiacetal ring

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In preceding papers,we reported the synthesis of 5,6-dideoxy-6-nitro-5-(phenylphosphino)-D-glucopyranose and 5,6-dideoxy-6-nitro-5-(phenylphosphinyl)-D-glucopyranose[1] by the addition of phenylphosphine to 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose, and subsequent steps.

There are several methods for introducing a bond between a phosphorus atom and a secondary carbon atom of a sugar derivative. Addition reactions of phosphite to unsaturated sugars give phosphonates[2]. The reaction of phosphite with glyculoses affords (2-hydroxyalkane)phosphonate derivatives of sugars[3] and that of sodium diphenylphosphinide with a 2,3-anhydroallose derivative gave a 2-(diphenylphosphino) derivative[4].

Recently, we reported a new synthetic method for preparing secondary alkanephosphonates[5]. The results seemed to suggest that the method might be applicable to sugar derivatives, *i.e.*, glyculoses. This communication deals with a new method for preparing sugar derivatives containing a phosphorus atom in the hemiacetal ring.

Treatment of 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranos-5-ulose 5-(*p*-tolylsulfonylhydrazone) (**1**) with methyl phenylphosphonite in the presence of *p*-toluenesulfonic acid afforded a mixture of (5*R*)- and (5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-5-*C*-(*N*-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranose (**2**) in quantitative yield. The reaction of **2** with sodium borohydride in tetrahydrofuran gave 5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-α-D-*xylo*-hexofuranose (**3**) in 70% yield. Compound **3** was reduced by treatment with an excess of sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA), to give (5*R*)- and (5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-(phenylphosphinyl)-3-*O*-methyl-α-D-*xylo*-hexofuranose (**4**) in 41% yield. The i.r. and ^{1}H-n.m.r. spectra of compound **4** showed the presence of a P–H group therein. Compound **4** was hydrolyzed with 0.5M hydrochloric

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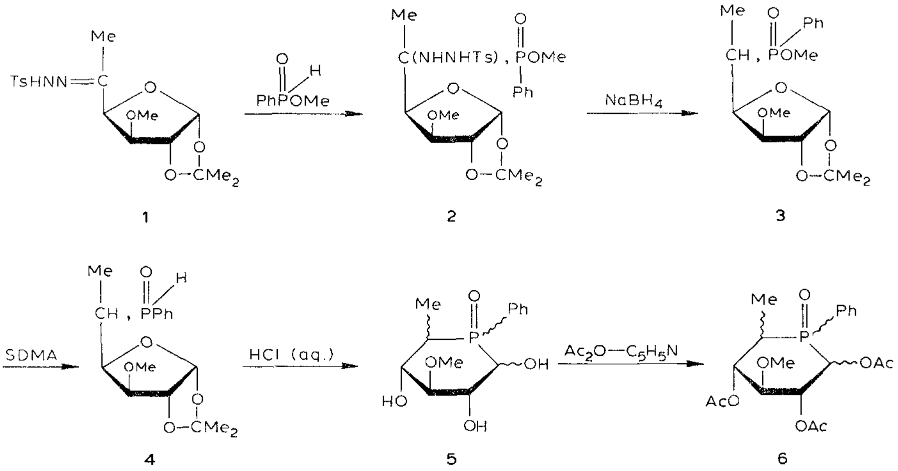
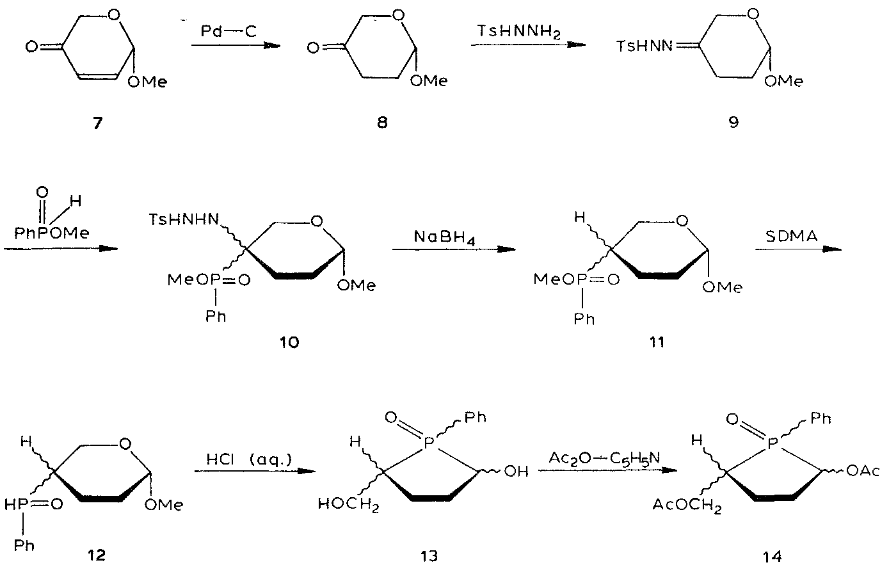
acid, and the product (**5**) acetylated with acetic anhydride–pyridine, to give a mixture (**6**) of 1,2,4-tri-*O*-acetyl-5,6-dideoxy-3-*O*-methyl-5-*C*-(phenylphosphinyl)-D-glucopyranose and -L-idopyranose as a syrup (yield 53%) that afforded a crystalline material (m.p. was 289–291°) from ethanol. The formula was determined to be $C_{19}H_{25}O_8P$ by mass spectrum [*m*/*e* 412 (M^+)], elemental analysis (Calc. for $C_{19}H_{25}O_8P$: C, 55.34; H, 6.11. Found: C, 55.03; H, 6.02), and ^{1}H-n.m.r. spectrum. The configuration at C-5, and the conformation, of the crystalline component are now under investigation.



In a similar way we tried to synthesize a pentofuranose derivative having a phosphorus atom as the ring heteroatom. Methyl 2,3-dideoxy-(1*S*)-DL-pent-2-enopyranosid-4-ulose (**7**) was synthesized by the method of Achmatowicz and co-workers[6], and converted, by catalytic hydrogenation in the presence of Pd–C, into methyl 2,3-dideoxy-(1*S*)-DL-pentopyranosid-4-ulose (**8**) in almost quantitative yield. The *p*-tolylsulfonylhydrazone (**9**) of **8** (yield 81% from **8**) reacted with methyl phenylphosphonite to give methyl (4*RS*)-2,3,4-trideoxy-4-*C*-[(methoxy)phenylphosphinyl]-4-*C*-(*p*-tolylsulfonylhydrazino)-(1*S*)-DL-pentopyranoside (**10**) in 91% yield. Compound **10** was treated with sodium borohydride to afford methyl 2,3,4-trideoxy-4-*C*-[(methoxy)phenylphosphinyl]-(1*S*)-DL-*glycero*-pentopyranoside (**11**, 66% yield), which was treated with SDMA to give methyl 2,3,4-trideoxy-4-*C*-(phenylphosphinyl)-(1*S*)-DL-*glycero*-pentopyranoside (**12**) in 51% yield. Treatment of **12** with 0.5M hydrochloric acid gave **13**; reaction thereof with acetic anhydride–pyridine afforded 1,5-di-*O*-acetyl-2,3,4-trideoxy-4-*C*-(phenylphosphinyl)-DL-*glycero*-pentofuranose (**14**) in 74% yield from **12**. Compound **14**, which is the first such compound having a furanose ring to be synthesized, was identified by ^{1}H-n.m.r. spectral data.

This method constitutes a convenient procedure for preparing various sugars containing a phosphorus atom as the ring heteroatom bonded to secondary, skeletal carbon atoms.



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