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Sugars Containing a Carbon-Phosphorus Bond. IV.[1] 5-(Alkylphosphonyl)-5-deoxy-*O*-methyl-D-xylopyranose[2]

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The synthesis[1,3] of the sugar analogs, in which the ring oxygen is replaced by phosphorus, is intriguing, not only from the point of view of the chemistry, but also from that of biochemistry. In the present paper we will report on the syntheses of 5-deoxy-5-(ethylphosphonyl)-3-*O*-methyl-D-xylopyranose (IVa) and 5-(butylphosphonyl)-5-deoxy-3-*O*-methyl-D-xylopyranose (IVb).

Result and Discussion

As a starting material, we used 5-bromo-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose (I).[4] Ethyl ethyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphinate (IIa) and ethyl butyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphinate (IIb) were obtained almost quantitatively by the Michaelis-Arbuzov reaction of I with diethyl ethylphosphonite and diethyl butylphosphonite respectively. The reduction of IIa and IIb with sodium bis(methoxyethoxy) aluminum hydride (Red Al) in tetrahydrofuran (THF) gave a syrup of ethyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphine oxide (IIIa, 97%) and butyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphine oxide (IIIb, 77%) respectively. The PMR spectrum of IIIa (IIIb) in chloroform-*d* showed a characteristic $J_{\mathrm{P-H}}$ value[5] of 458 Hz at τ 3.08 (459 Hz at τ 3.07); it disappeared on deuteration. The IR spectrum of IIIa (IIIb) showed the absorption of a P–H group at 2320 cm^{-1} (2310 cm^{-1})[6] and that of a P=O group at 1240 cm^{-1} (1240 cm^{-1}).[7]

The hydroysis of IIIa (IIIb) with diluted hydrochloric acid (3 N) in water at 80—100 °C for 6 hr afforded a syrup of IVa (IVb) in a 61% (65%) yield. The studies of PMR (D_2O and DMSO-d_6) and the IR spectra of IVa (IVb) showed that IVa (IVb) had three OH groups and no P–H group. Moreover, the acetyla-

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1) Part III: S. Inokawa, Y. Tsuchiya, K. Seo, H. Yoshida, and T. Ogata, This Bulletin, **44**, 2279 (1971).

2) We have tentatively used this name for the sugar in which O was replaced by RP(0) in the hemiacetal ring of 3-*O*-methyl-D-xylopyranose.

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3) R. L. Whistler and C.-C. Wang, *J. Org. Chem.*, **33**, 4455 (1968).

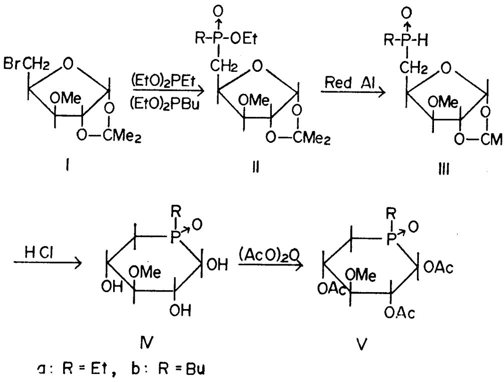
4) S. Inokawa, H. Yoshida, C.-C. Wang, and R. L. Whistler, This Bulletin, **41**, 1472 (1968).

5) H. R. Hays *J. Org. Chem.*, **33**, 3690 (1968).

6) R. A. Chittenden and L. C. Tomas, *Spectrochim. Acta*, **20**, 861 (1964).

7) L. C. Tomas and R. A. Chittenden, *ibid.*, **20**, 467 (1964).

tion of IVa (IVb) with acetic anhydride in pyridine gave, in good yields, crystals of the tri-*O*-acetylated compound, Va (Vb), the PMR data and elemental analysis of which showed that Va (Vb) was 1,2,4-tri-*O*-acetyl-5-deoxy-(ethylphosphonyl)-3-*O*-methyl-D-xylopyranose [1,2,4-tri-*O*-acetyl-5-(butylphosphonyl)-5-deoxy-3-*O*-methyl-D-xylopyranose]. Therefore, IVa and IVb must be 5-deoxy-5-(ethylphosphonyl)-D-xylopyranose and 5-(butylphosphonyl)-5-deoxy-D-xylopyranose respectively.



Experimental

The melting points were determinted by means of a Yanagimoto micro melting point apparatus. The infrared spectra were mesured on a Hitachi EPI-G-2 grating spectrophotometer. The nuclear magnetic resonance spectra were taken at 60 MHz on a Hitachi R-2 spectrometer, using tetramethylsilane as the internal or external standard. Thin-layer chromatography (tlc) was carried out on microscope slides coated with silica gel,[8] using ethyl acetate–petroleum ether ((1: 1 v/v) (A); (3: 7 v/v (B)) and methanol–chloroform ((1: 7 v/v) (C)), and the spots were visualized with a sulfuric acid–ethanol solution (10%).

*Ethyl Ethyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphinate (IIa).* A mixture of 5-bromo-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose (6 g) and diethyl ethylphosphonite (15 ml) was refluxed under nitrogen for 6 hr at 130—145 °C. During the reaction, diethyl ethylphosphonite (2 ml) was added several time. The excess of the phosphonite was then distilled *in vacuo* to give colorless needles of IIa (6.9 g, an almost quantitative yield), which was sufficiently pure for the subsequent conversion; mp 67.5—70.0 °C (from ethyl acetate–*n*-hexane (1: 4 v/v); R_f (Solvent B) 0.2; $[\alpha]^{12}_{D}$ −50° (*c* 6.2, chloroform); IR (KBr): 1240 cm^{-1} (P=O); PMR (CDCl$_3$): τ 4.20 (1H, d, $J_{1,2}$=4 Hz, H–1), 4.45 (1H, d, overlapping with H–4, H–2), 5.97 (2H, q, POCH$_2$–), 6.35 (1H, t, H–3), 6.63 (3H, s, OCH$_3$).

Found: C, 50.04; H, 8.51%. Calcd for $C_{13}H_{25}O_6P$: C, 50.64; H, 8.17%.

*Ethyl Butyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphinite (IIb).* Compound I (5.5 g) was treated with diethyl butylphosphonite as has been described above to give crystals pf IIb in an almost quantitative yield: mp 45.0—46.0 °C (from ethyl acetate–*n*-hexane (1:5 v/v)); $[\alpha]^{19}_{D}$ −39° (*c* 1.1, chloroform); IR (KBr): 1240 cm^{-1} (P=O); PMR (CDCl$_3$): τ 4.2 (1H, d, $J_{1,2}$=4 Hz, H–1), 5.45 (1H, d, overlapping with H–4, H–2), 5.95 (2H, q, P–OCH$_2$–), 6.34 (1H, t, H–3), 6.60 (3H, s, OCH$_3$).

Found: C, 52.39; H, 9.08%. Calcd for $C_{15}H_{29}O_6P$: C, 53.56; H, 8.68%.

*Ethyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphine Oxide (IIIa).* To IIa (2.2 g) in THF (150 ml) Red Al (70% benzene solution) (2.8 g) in THF (100 ml) was added under a nitrogen atmosphere in an iced-salt bath for 30 min. After 1 hr's stirring at room temperature, the reaction mixture was neutralized with hydrochloric acid in THF and a few drops of water were added. The filtration and evaporation of the filtrate gave a syrup of IIIa (1.8 g, 97%) which was sufficiently pure for the subsequent conversion. An analytical sample was obtained by tlc separation; R_f 0.05 (Solvent A): $[\alpha]^{19}_{D}$ −44°[9] (*c* 2.9, chloroform); IR (KBr); 2320 cm^{-1} (P–H), 1240 cm^{-1} (P=O); PMR (CDCl$_3$): τ 3.08 (1H, *m*, disappearing on deuteration, J_{P-H}=458 Hz, P–H), 4.18 (1H, d, $J_{1,2}$=4 Hz, H–1), 5.41 (1H, d, overlapping with H–4, H–2), 6.32 (1H, t, H–3), 6.60 (3H, s, OCH$_3$).

*Butyl-(5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose-5)-phosphine Oxide (IIIb).* Compound IIb (3.0 g) was treated as has been described above, and the reaction product was separated by silica gel-column chromatography (Solvent C) to give a syrup of IIIb (2.0 g, 77%): R_f 0.05 (Solvent C); $[\alpha]^{19}_{D}$ −43°[9] (*c* 4.3, chloroform); IR (KBr): 2310 cm^{-1} (P–H), 1240 cm^{-1} (P–O): PMR (CDCl$_3$): τ 3.07 (1H, *m*, disappearing on deuteration, J_{P-H}=459 Hz, P–H), 4.12 (1H, d, $J_{1,2}$=4 Hz, H–1), 5.51 (1H, d, overlapping with H–4, H–2), 6.34 (1H, t, H–3), 6.65 (3H, s, OCH$_3$).

*5-Deoxy-5-(ethylphosphonyl)-3-*O*-methyl-D-xylopyranose (IVa).* A solution of IIIa (0.5 g) and concentrated hydrochloric acid (1.0 ml) in water (25 ml) containing small amounts of THF was heated at 80—100 °C under a nitrogen atmosphere. The THF was evaporated during the reaction. The hot solution was neutralized with silver carbonate; subsequent filtration and evaporation gave a colorless syrup of IVa (0.3 g, 71%); hydroscopic solid; R_f 0.20 (Solvent C): $[\alpha]^{14}_{D}$ 0.0°[9] (*c* 2.6, water); IR (KBr): 1240 cm^{-1} (P=O); PMR (D$_2$O): τ 6.40 (3H, s, OCH$_3$), 7.3—9.5 (7H, m, H–5,5′, P–C$_2$H$_5$); (DMSO-d_6): τ 6.0—7.0 (8H, m, three of them disappearing on deuteration).

*5-(Butylphosphonyl)-5-deoxy-3-*O*-methyl-D-xylopyranose (IVb).* Compound IIIb (1.0 g) was treated as has been described above to give a hydroscopic solid of IVb (0.5 g, 65%); R_f 0.20 (Solvent C); $[\alpha]^{17}_{D}$ 0.0°[9] (*c* 3.4, water); IR (KBr): 1240 cm^{-1} (P=O); PMR (DMSO-d_6): τ about 6.4 (4H, three of them disappearing on deuteration), 6.72 (3H, s, OCH$_3$), 7.8—9.8 (11H, m, H-5,5′, P–C$_4$H$_9$).

*1,2,4-Tri-*O*-acetyl-5-deoxy-5-(ethylphosphonyl)-3-*O*-methyl-D-xylopyranose (Va).* The treatment of IVa (0.30 g) with acetic anhydride in pyridine in the usual way gave a colorless solid (0.44 g, 94%); R_f 0.95 (Solvent C); mp 227—229 °C (from ethanol); $[\alpha]^{17}_{D}$ 0.0 ° (*c* 0.87, chloroform); IR (KBr): 1240 cm^{-1} (P=O); PMR (CDCl$_3$); τ 4.5—5.1 (3H, m), 6.57 (3H, s, overlapping with one proton, OCH$_3$(, 7.90, 7.94, 7.95 (9H, s, 1,2,4-OCOCH$_3$).

Found: C, 47.95; H, 6.85%. Calcd for $C_{14}H_{28}O_8P$: C, 48.00; H, 6.62%.

*1,2,4-Tri-*O*-acetyl-5-(butylphosphonyl)-5-deoxy-3-*O*-methyl-D-xylopyranose (Vb).* Compound IVb (0.50 g) was treated as has been described above to give crystals of Vb (0.70 g, 93%); R_f 0.95 (Solvent C); mp 218.5—220 °C; $[\alpha]^{17}_{D}$ −8.1° (*c* 4.2, chloroform); IR (KBr): 1240 cm^{-1} (P=O); PMR (CDCl$_3$): τ 4.1—5.1 (3H, m), 6.50 (3H, s, overlapping with one protone, OCH$_3$), 7.86, 7.92, 7.95 (9H, s, 1,2,4-OCOCH$_3$).

Found: C, 50.47; H, 7.43%. Calcd for $C_{16}H_{27}O_8P$: C, 50.79; H, 7.19%.

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[8] Silica-Layer G-10, Nakarai Chemicals, Ltd.

[9] This sample seemed to be fairly pure from the observation of its PMR spectrum and tlc, but it was not enough pure for an elemental analysis.