April, 1975] BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 48(4), 1237—1239 (1975) 1237

Sugars Containing a Carbon-phosphorus Bond. VI.[1,2) 5-(Alkylphosphinyl)-5-deoxy-D-xylopyranose

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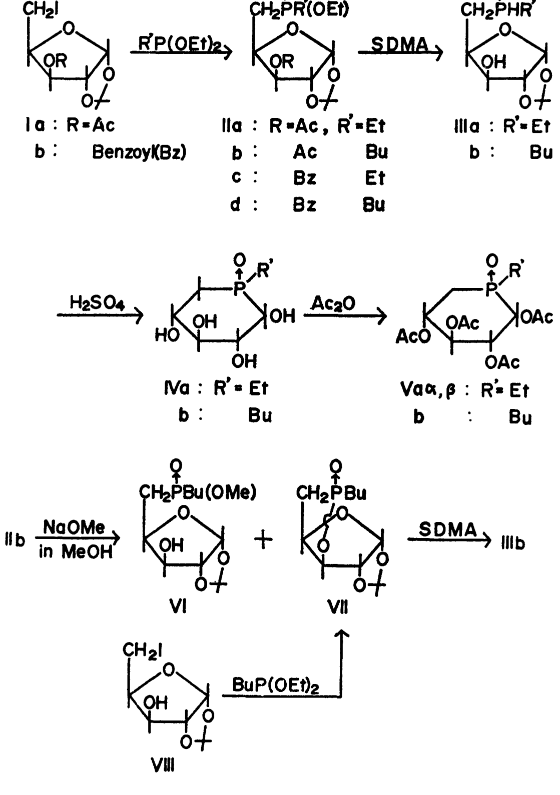
(Received February 22, 1974)

The reactions of diethyl ethylphosphonite with 3-*O*-acetyl-5-deoxy-5-iodo-1,2-*O*-isorpopylidine-α-D-xylofuranose (Ia) or 3-*O*-benzoyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose(Ib) afforded IIa or IIc, respectively. Similarly, using diethyl butylphosphonite in place of diethyl ethylphosphonite, IIb and IId were obtained. Treatment of IIb with methanolic sodium methoxide gave 5-deoxy-1,2-*O*-isopropylidene-5-(methoxybutylphosphinyl)-α-D-xylofuranose together with a small amount of 5-(3-*O*-cyclo-butylphosphinate)-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose(VII). Compound VII was also obtained from the reaction of 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose(VIII) and diethyl butylphosphonite. The reaction of IIa or IIc with sodium dihydrobis(2-methoxyethoxy)aluminate gave 5-deoxy-5-(ethylphosphinyl)-1,2-*O*-isopropylidene-α-D-xylofuranose(IIIa). Similarly, 5-(butylphosphinyl)-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose(IIIb) was obtained from IIb, IId, VI, and VII. Hydrolysis of IIIa and IIIb with sulfuric acid gave 5-deoxy-5-(ethylphosphinyl)-(IVa) and 5-(butylphosphinyl)-5-deoxy-D-xylopyranose(IVb), respectively. Acetylation of IVa and IVb with acetic anhydride in pyridine gave the corresponding *O*-acetates Va and Vb.

Recently, we reported the synthesis of 3-*O*-benzyl-5-deoxy-5-(ethylphosphinyl)-D-xylopyranose,[3) 5-(alkylphosphinyl)-5-deoxy-3-*O*-methyl-D-xylopyranose (alkyl; ethyl, butyl)[4) and 5-deoxy-5-(ethylphosphinyl)-D-ribopyranose,[1) sugar analoges having a phosphorus atom in the hemiacetal ring. In this paper we wish to report the syntheses of 5-deoxy-5-(ethylphosphinyl)-D-xylopyranose(IVa) and 5-(butylphosphinyl)-5-deoxy-D-xylopyranose(IVb).

Results and Discussion

In the present experiments, 3-*O*-acety-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose(Ia) and 3-*O*-benzoyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose(Ib) were used as the starting materials. The Michaelis-Arbuzov reaction[5) of Ia or Ib with diethyl ethylphosphonite gave, almost quantitatively, 3-*O*-acetyl-(IIa) or 3-*O*-benzoyl-5-deoxy-5-(ethoxyethylphosphinyl)-1,2-*O*-isopropylidene-α-D-xylofuranose(IIc), respectively. Similarly, the reaction of Ia or Ib with diethyl butylphosphonite gave 3-*O*-acetyl-(IIb) or 3-*O*-benzoyl-5-deoxy-5-(ethoxybutylphosphinyl)-1,2-*O*-isopropylidene-α-D-xylofuranose (IId), respectively. Reduction of IIa(IIc) or IIb(IId) with 3.3 molar equivalents of sodium dihydrobis(2-methoxyethoxy)aluminate(SDMA) in tetrahydrofuran (THF) gave, almost quantitatively,** syrupy 5-deoxy-5-(ethylphosphinyl)-(IIIa)or 5-(butylphosphinyl)-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose(IIIb), respectively. The PMR spectrum of IIIa(IIIb) in chloroform-*d* showed a characteristic $J_{\text{P-H}}$ value[6) of 469 Hz at δ 6.90 (470 Hz at δ 5.90); the signal disappeared on deuteration. The IR spectrum (KBr) of IIIa(IIIb) showed absorption due to a P–H group at 2350 cm^{-1} (2350 cm^{-1})[7) and absorption due to a P=O group at 1220 cm^{-1} (1220 cm^{-1}).[8) Compound IIIb was also obtained by hydrolysis of IIb and subsequent reduction. Treatment of IIb with sodium methoxide in methanol gave, in good yield, syrupy 5-deoxy-1,2-*O*-isopropylidene-5-(methoxybutylphosphinyl)-α-D-xylofuranose(VI) together with a small amount of crystalline 5-(3-*O*-cyclo-butylphosphinate)-5-deoxy-1,2-*O*-isopropylidne-α-D-xylofuranose(VII). The PMR spectrum of VI on chloroform-*d* showed P–OCH$_3$ ($J_{\text{P-H}}$=10.5 Hz) at δ 3.56 and OH at δ 4.79 (disappearing on deuteration). The PMR spectrum of VII showed an H–3 proton signal at δ 5.18 which was at lower field than that of VI (δ 4.00). No P–OCH$_3$ (or P–OC$_2$H$_5$) and OH signals were found. On reduction with SDMA, VI and VII both gave IIIb in good yield. Compound VII was also obtained, almost quantitatively, by heating 5-deoxy-5-iodo-1,2-*O*-



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** Treatment of IId with lithium aluminum hydride[3) gave IIIb in lower yield.

isopropylidene-α-D-xylofuranose(VIII) in diethyl butylphosphonite.

Hydrolysis of IIIa or IIIb with dilute sulfuric acid (1—2%) for two hr at 80—100 °C afforded, in good yield, a hygroscopic solid, 5-deoxy-5-(ethylphosphinyl)-(IVa) or 5-(butylphosphinyl)-5-deoxy-D-xylopyranose (IVb), respectively. Study of their PMR (DMSO-d_6) and IR(KBr) spectra showed that IVa(IVb) had four OH groups and no P–H group. Acetylation of IVa with acetic anhydride in pyridine gave two kinds of crystalline 1,2,3,4-tetra-*O*-acetyl-5-deoxy-(ethylphosphinyl)-D-xylopyranose: one(Va*β*) had mp 232—234.5 °C, $[\alpha]^{18}_{\mathrm{D}}$ −22° and the other(Va*α*) had mp 176—178 °C, $[\alpha]^{18}_{\mathrm{D}}$ +26°. The PMR spectra of Va*α* and Va*β* showed four acetyl groups and no P–H group. Acetylation of IVb gave only one crystalline tetra-*O*-acetate(Vb), mp 156.5—158.5 °C, $[\alpha]^{19}_{\mathrm{D}}$ +28°. The PMR spectrum of Vb showed four acetyl groups and no P–H group. Attempts to analyze the conformations of Va*α* and Va*β* by 100 MHz PMR have been so faru nsuccessful.

Experimental

Melting points were determined by a Yanagimoto micro melting point apparatus. Infrared spectra were measured on a Hitachi EPI–G2 grating spectrophotometer. Proton magnetic resonance spectra were taken at 60 MHz on a Hitachi-Perkin-Elmer R-20 spectrometer, with tetramethylsilane as an internal standard. Optical rotations (sodium D line) were measured with a Hitachi PO–B polarimeter using a 0.5-dm cell. Thin-layer chromatography (tlc) was carried out on microscope slides coated with silica gel[9] in ethyl acetate–petroleum ether (A) (1 : 1 v/v), (B) (1 : 2 v/v), and (C) (1 : 4 v/v): the spots were visualized with sulfuric acid–ethanol solution.

Materials. *3-O-Acetyl-5-deoxy-5-iodo-1,2-O-isopropylidene-α-D-xylofuranose(Ia)* was prepared in 91% yield by conventional acetylation of 5-deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose(IX)[10]. Mp 65—66 °C, $[\alpha]^{16.5}_{\mathrm{D}}$ −49° (*c* 2.3, $CHCl_3$);

Found: C, 35.11; H, 4.46%. Calcd for $C_{10}H_{15}IO_5$: C, 35.11, H, 4.42%.

3-O-Benxoyl-5-deoxy-5-iodo-1,2-O-isopropylidene-α-D-xylofuranose(Ib) was prepared in 86% yield by conventional benzoylation of IX. Mp 46—48 °C, $[\alpha]^{16}_{\mathrm{D}}$ −40° (*c* 10, CH_3OH);

Found: C, 44.53; H, 4.20%. Calcd for $C_{15}H_{17}IO_5$: C, 44.68; H, 4.25%.

3-O-Acetyl-5-(ethoxyethylphosphinyl)-1,2-O-isopropylidene-α-D-xylofuranose(IIa). A solution of Ia(5 g) in diethyl ethylphosphonite (10 ml) was heated under a nitrogen atmosphere for 10 hr at 140—150 °C, while the phosphonite (2 ml) was added several times. The excess phosphonite was distilled off *in vacuo* and the residue was dissolved in chloroform; the solution was washed with water, dried (sodium sulfate), and evaporated *in vacuo* to give a syrup of IIa (4.8 g, 98%); R_f: 0.25 (Solvent B); $[\alpha]^{20}_{\mathrm{D}}$ −9.1° (*c* 1.3, $CHCl_3$); IR (KBr): 124 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.80—2.16 (16H, m, H-5,5′, P-C_2H_5, O-C-CH_3, $C(CH_3)_2$), 2.19 (3H, s, $COCH_3$), 4.01 (2H, q, $POCH_2$–), 4.47 (1H, d, overlapping with H-4, H-2), 5.10 (1H, d, $J_{3,4}$=3.0 Hz, H-3), 5.81(1H, d, $J_{1,2}$=4.0 Hz, H-1).

*3-O-Acetyl-5-(ethoxybutylphosphinyl)-1,2-O-isopropylidene-α-D-xylofuranose(IIb).**** 98%; R_f 0.20 (solvent B); $[\alpha]^{20}_{\mathrm{D}}$ −9.1° (*c* 13, $CHCl_3$); IR (KBr) 1240 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.69—2.65 (20H, m, H–5,5′, P–C_4H_9, O–C–CH_3, $C(CH_3)_2$, 2.04 (3H, s, $COCH_3$), 3.99 (2H, m, $POCH_2$–), 4.42 (1H, d, overlapping with H–4, H–2), 5.04 (1H, d, $J_{3,4}$=3.0 Hz, H–3), 5.75 (1H, d, $J_{1,2}$=4.0 Hz, H–1).

*3-O-Benzoyl-5-deoxy-5-(ethoxyethylphosphinyl)-1,2-O-isopropylidene-α-D-xylofuranose(IIc).**** 96%; R_f: 0.20 (Solvent B); $[\alpha]^{71}_{\mathrm{D}}$ −13° (*c* 4.3, $CHCl_3$); IR (KBr): 1240 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.74—2.40 (16H, m, H–5,5′, P–C_2H_5, O–C–CH_3, $C(CH_3)_2$), 4.00 (2H, m, $POCH_2$–), 4.64 (1H, d, overlapping with H–4, H–2), 5.41 (1H, d, $J_{3,4}$=3.0 Hz, H–3), 5.96 (1H, $J_{1,2}$=4.0 Hz, H–1), 7.22–8.20 (5H, *m*, COC_6H_5).

*3-O-Benzoyl-5-deoxy-5-(ethoxybutylphosphinyl)-1,2-O-isopropylidene-α-D-xylofuranose(IId).**** 98%; R_f: 0.20 (Solvent B); $[\alpha]^{13}_{\mathrm{D}}$ −7.5° (*c* 14, $CHCl_3$); IR (KBr): 1240 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.63—2.23 (20H, m, H–5,5′, P–C_4H_9, O–C–CH_3, $C(CH_3)_2$, 3.94 (2H, m, $POCH_2$–), 4.54 (1H, d, overlapping with H–4, H–2), 5.28 (1H, d, $J_{3,4}$=3.0 Hz, H–3), 5.80 (1H, d, $J_{1,2}$=4.0 Hz, H–1), 7.20—8.10 (5H, m, COC_6H_5).

5-Deoxy-5-(ethylphosphinyl)-1,2-O-isopropylidene-α-D-xylofuranose (IIIa). To a solution of IIa (0.2 g) (IIb) in tetrahydrofuran (THF) (200 ml) was added THF (100 ml) containing a 70% benzene solution (6.0 g) of sodium dihydrobis(2-methoxyethoxy)alminate (SDMA) under a nitrogen atmosphere in an ice-salt bath. After stirring for 1 hr at room temperature, the reaction mixture was neutralized with THF containing hydrochloric acid and filtered; the filtrate was dried (sodium sulfate) and evaporated, to give a syrup of IIIa (1.4 g, 94%). An analytical crystalline sample was obtained by silica-gel column chromatography (Solvent A and methanol); R_f: 0.1 (Solvent A); mp 120—121 °C, $[\alpha]^{17}_{\mathrm{D}}$ −12.4° (*c* 2.6, $CHCl_3$); IR (KBr): 2350 cm^{-1} (P–H), 1220 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.73—2.58 (13H, m, H–5,5′, P–C_2H_5), $C(CH_3)_2$, 4.12 (1H, d, H–3), 4.53 (1H, d, overlapping with H–4, H–2), 5.15 (1H, broad s, disappearing on deuteration, OH), 5.86 (1H, d, $J_{1,2}$=4.0 Hz, H–1), 6.90 (1H, m, disappearing on deuteration, J_{P-H}=468 Hz, P–H).

Found: C, 47.67; H, 8.04%. Calcd for $C_{10}H_{19}O_5P$: C, 47.98; H, 8.00%.

5-(Butylphosphinyl)-5-deoxy-1,2-O-isopropylidene-α-D-xylofuranose(IIIb). Compound IIb (2.5 g) was treated as described above to give a syrup of IIIb (1.8 g, 94%). R_f: 0.10 (Solvent A); $[\alpha]^{16.5}_{\mathrm{D}}$ −17.3° (*c* 4.4, $CHCl_3$), IR (KBr): 2350 cm^{-1} (P–H), 1220 cm^{-1} (P=O); PMR ($CDCl_3$): δ 0.70—2.55 (17H, m, H–5,5′, P–C_4H_9, $C(CH_3)_2$), 4.18 (1H, d, H–3), 4.56 (1H, d, overlapping with H–4, H–2), 4.95 (1H, broad s, disappearing on deuteration, OH), 5.90 (1H, d, $J_{1,2}$=4.0 Hz, H–1), 6.90 (1H, m, diasppearing on deuteration, J_{P-H}=470 Hz, P–H).

5-Deoxy-1,2-O-isopropylidene-5-(methoxybutylphosphinyl)-α-D-xylofuranose(VI) and 5-(3-O-cyclo-butylphosphinate)-5-deoxy-1,2-O-isopropylidene-α-D-xylofuranose(VII). To a solution of IIb (2.1 g) in methanol (20 ml) was added a small amount of sodium methoxide and the solution stood for two days at room temperature. The solution was neutralized with Amberlite IRC-50 (H$^+$) ion-exchange resin and evaporated *in vacuo* to give a syrup (VI) containing a solid (VII) (1.5 g, 94% as VI) (VI : VII=5 : 1 from the PMR spectrum). The solid (VII) was collected and recrystallized from ethyl acetate. (VI), R_f: 0.30 (Solvent A), $[\alpha]^{16}_{\mathrm{D}}$ −20° (*c* 2.5, $CHCl_3$); PMR ($CDCl_3$): δ 0.61—2.30 (17H, m, H–5,5′, P–C_4H_9, $C(CH_3)_2$), 3.56 (3H, d, J_{P-H}=10.5 Hz, P–OCH_3), 4.00 (1H,

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*** These compounds were prepared by treatment of the corresponding sugars with the phosphonites.

d, H–3), 4.40 (1H, d, overlapping with H–4, H–2), 4.75 (1H, broad s, disappearing on deuteration, OH), 5.73 (1H, d, $J_{1,2}$=4.0 Hz, H–1). (VII), R_f, 0.35 (Solvent A); mp 221.5—222 °C; $[\alpha]_D^{14}$ +32° (*c* 2.3, CH_3OH); PMR ($CDCl_3$): δ 0.80—2.63 (17H, m, H–5,5′, P–C_4H_9, $C(CH_3)_2$); 4.58 (1H, m, H–4), 4.79 (1H, d, H–2), 5.18 (1H, *m*, 1H, m, H–3), 6.02 (1H, d, $J_{1,2}$=4.0 Hz, H–1).

Found: C, 52.19; H, 7.71%. Calcd for $C_{12}H_{21}O_5P$: C, 52.17; H, 7.66%.

The reduction of VI and VII with 1.2 molar equivalents of SDMA gave, almost quantitatively, IIIb.

Compound VII from 5-deoxy-5-iodo-1,2-O-isopropylidene-α-D-xylofuranose (VIII). A solution of VIII (1.4 g) in diethyl butylphosphonite (3 ml) was heated under a nitrogen atmosphere for 2 hr at 130—140 °C; the resulting precipitates were collected by filtration and the filtrate was evaporated *in vacuo*. The conbined precipitates were recrystallized from ethyl acetate to give pure crystalline VII (1.2 g, 93%).

5-Deoxy-5-(ethylphosphinyl)-D-xylopyranose(IVa). A solution of IIIa (1.0 g) and concentrated sulfuric acid (0.5 ml) in water (50 ml) containing a small amount of THF was heated under a stream of nitrogen for 2 hr at 100 °C. The hot solution was neutralized with barium carbonate, followed by filtration and evaporation to give a hygroscopic solid of IVa (0.8 g, 95%); R_f: 0.10 (Solvent C); $[\alpha]_D^{16.5}$ +5.8° (*c* 6.8, H_2O); IR (KBr): 1240 cm^{-1} (P=O); PMR (DMSO–d_6): δ 0.5—2.4 (7H, m, H–5,5′, P–C_2H_5), 3.0—4.5 (7H, m, four of them disappearing on deuteration).

5-(Butylphosphinyl)-5-deoxy-D-xylopyranose(IVb). Compound IIIb (0.9 g) was treated as described above to give a hygroscopic solid, IVb (0.7 g, 91%; R_f: 0.10 (Solvent C); $[\alpha]_D^{16.5}$ +11° (*c* 5.5, CH_3OH); IR (KBr): 1240 cm^{-1} (P=O); PMR (DMSO-d_6): δ 0.5—2.0 (11H, m, H–5,5′, P–C_4H_9), 4.6—5.3 (5H, m, four of them disappearing on deuteration).

1,2,3,4-Tetra-O-acetyl-5-deoxy-5-(ethylphosphinyl)-D-xylopyranose (Va). Treatment of IVa (1.4 g) with acetic anhydride (4.5 ml) in pyridine (20 ml) in the usual way gave a syrupy mixture of Vaα and Vaβ (2.2 g, 88%, $[\alpha]_D^{14.5}$ +20.9° (*c* 2.2, $CHCl_3$)). The syrup was crystallized by standing for several days in a refrigerator. Recrystallization from ethanol gave colorless crystals (Vaβ, 0.06 g), mp 232—234.5 °C, $[\alpha]_D^{18}$ −22° (*c* 1.6, $CHCl_3$). The ethanolic mother solution was evaporated *in vacuo*: recrystallization of the precipitates from ethanol-*n*-hexane gave colorless crystals (Vaα, 0.21 g), mp 176—178 °C, $[\alpha]_D^{18}$ +26° (*c* 1.4, $CHCl_3$).

Vaβ; PMR ($CDCl_3$): δ 0.80—2.82 (7H, m, H–5,5′, P–C_2H_5), 1.95, 1.98, 2.10 (12H, s, 1,2,3,4–$COCH_3$), 5.00–5.75 (4H, m, H–1,2,3,4).

Found: C, 47.32; H, 6.53%. Calcd for $C_{15}H_{23}O_9P$: C, 47.62; H, 6.13%.

Vaβ; PMR ($CDCl_3$): δ 1.00—2.76 (7H, m, H–5,5′, P–C_2H_5), 1.95, 2.00, 2.06 (12H, s, 1,2,3,4–$COCH_3$), 5.04—5.76 (4H, m, H–1,2,3,4).

1,2,3,4-Tetra-O-acetyl-5-(butylphosphinyl)-5-deoxy-D-xylopyranose(Vb). Compound IVb (0.7 g) was treated as described above to give a syrup of Vb (1.0 g, 84%, $[\alpha]_D^{14.5}$ +20.3 ° (*c* 3.5, $CHCl_3$)). Crystals were obtained from the syrup by standing for several days in a refrigerator. Recrystallization from ethanol-*n*-hexane gave colorless crystals (Vb, 0.2 g); mp 156.5—158.5 °C; $[\alpha]_D^{19}$ +28° (*c* 1.4, $CHCl_3$); PMR ($CDCl_3$): δ 1.00—2.76 (11H, m, H–5,5′, P–C_4H_9), 1.96, 2.02, 2.17 (12H, s, 1,2,3,4–$COCH_3$), 5.17—5.93 (4H, m, H–1,2,3,4).

Found: C, 49.80; 6.85%. Calcd for $C_{17}H_{27}O_9P$: C, 50.25; H, 6.70%.

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