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Note

Synthesis of 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*)- and (*S*)-phenylphosphinyl]-α- and -β-D-xylopyranoses

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In the chemical modification of sugar derivatives, the synthesis of sugar analogs of the pentopyranose type having phosphorus in the hemiacetal ring, prepared from 5-deoxy-5-*C*-phosphinyl-D-pentofuranose precursors afforded by the Michaelis–Arbuzov reaction of 5-deoxy-5-halo derivatives with phosphorus compounds, have already reported[1–7]. We recently described a new method for C–P bond-formation by deoxygenation of an HO-CH-P group at the terminal carbon atom of sugars by 1,1′-thiocarbonyldiimidazole (TCDI), followed by treatment with tributyltin hydride, and an efficient synthesis[8] of 1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-*C*-[(*R*)- and (*S*)-phenylphosphinyl]-α- and -β-D-xylopyranoses (**8**). Synthesis is now reported of 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*)- and -(*S*)-phenylphosphinyl]-α- and -β-D-xylopyranoses (**7**), through a 5-deoxy-5-*C*-(phenylphosphinyl)-α-D-xylofuranose precursor (**4**), which was achieved in the foregoing, convenient way.

3-*O*-Acetyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose (**1**), obtained by glycol-cleavage oxidation of 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose with sodium metaperiodate[9], was used as the starting material for this synthesis.

Compound **1** was treated in a refrigerator with methyl phenylphosphinate and triethylamine, to give 3-*O*-acetyl-1,2-*O*-isopropylidene-5-*C*-[methoxy(phenyl)-phosphinyl]-α-D-xylofuranose (**2**) in 73% yield. Treatment of **2** with TCDI in 1,2-dichloroethane at 90° (bath) afforded 3-*O*-acetyl-5-*O*-(imidazol-1-ylthiocarbonyl)-1,2-*O*-isopropylidene-5-*C*-[methoxy(phenyl)phosphinyl]-α-D-xylofuranose (**3**) in 70% yield. Reductive elimination of the imidazol-1-ylthiocarbonyloxy group of **3** by refluxing with tributyltin hydride in toluene afforded syrupy 3-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-5-*C*-[methoxy(phenyl)phosphinyl]-α-D-xylofuranose (**4**) in 90% yield; compound **4** showed the signals of H-5,5′ at δ 2.0–2.45 in its ^{1}H -n.m.r. spectrum.

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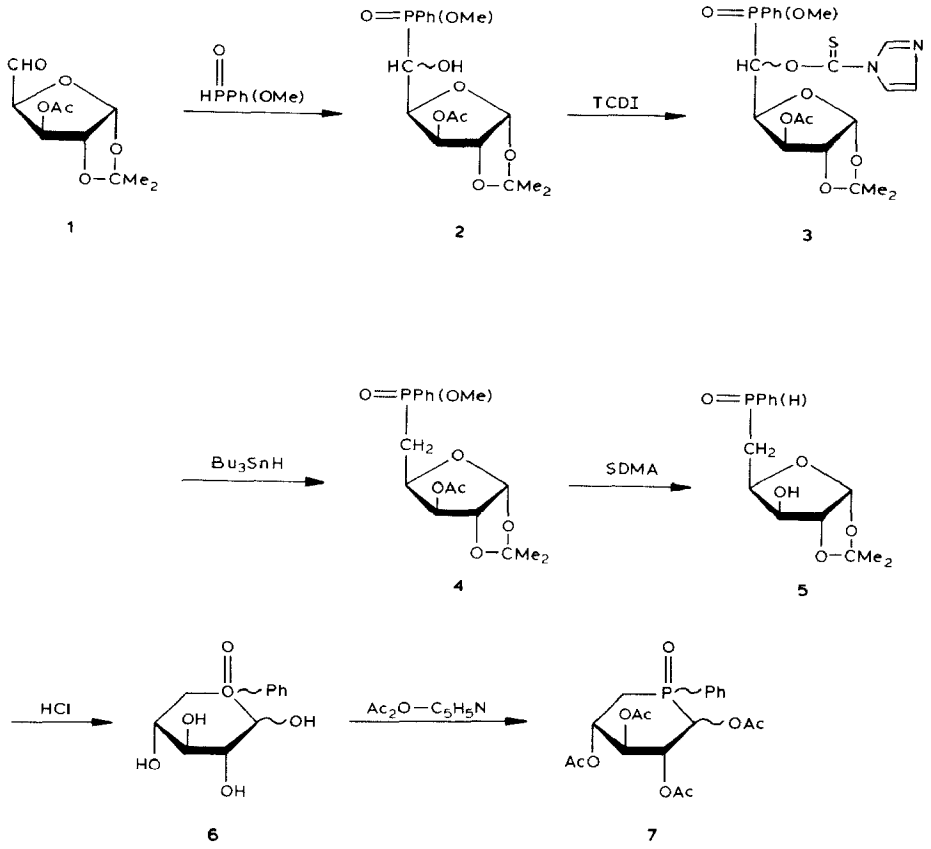
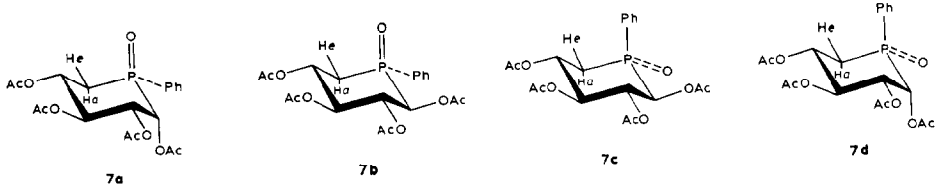
Reduction of **4** with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) in oxolane (tetrahydrofuran; THF) under argon for 1 h at 0° afforded 5-deoxy-1,2-*O*-isopropylidene-5-*C*-(phenylphosphinyl)-α-D-xylofuranose (**5**) in 84% yield; this showed i.r. absorption at 3350 (OH) and 2330 cm^{-1} (P-H), and half a P–H signal at δ 3.5 (disappearing on deuteration) in its ^{1}H-n.m.r. spectrum.



Hydrolysis of **5** with 0.1M hydrochloric acid under argon for 3 h at 110° (bath), and acetylation of the product (**6**) with acetic anhydride–pyridine in the usual way[1–3] afforded crude, syrupy **7** (69% from **5**). Compound **7** was separated by column chromatography on silica gel, using ethyl acetate–methanol as the eluant, into four major fractions, which will be referred to as A, B, C, and D (according to their decreasing R_F values). Fractions A, B, C, and D respectively gave a colorless solid (10% from **5**); colorless plates, m.p. 257–258° (12% from **5**); a colorless syrup (11% from **5**); and a colorless syrup (8% from **5**); each exhibited four acetoxyl groups in the ^{1}H-n.m.r. spectrum, and the molecular-ion peak at *m/z* 426, corresponding to $C_{19}H_{23}O_9P$, in the high-resolution mass spectrum of each, and this formula was supported by the elemental analysis of fraction B. The structural

assignments of these compounds were determined by comparing the ^{1}H-n.m.r. spectra, and the optical rotations, with those of the structurally similar[8] analogs **8**, 1,2,4-tri-*O*-acetyl-5-deoxy-5-*C*-[(*R*)- and (*S*)-methoxyphosphinyl]-3-*O*-methyl-α- and -β-D-xylopyranoses[4] (**9**), 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*)- and (*S*)-isopropylphosphinyl]-α- and -β-D-xylopyranoses[5] (**10**), and 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)- and (*S*)-ethylphosphinyl]-α- and -β-D-glucopyranoses[10] (**11**).

The ^{1}H-n.m.r. spectra of fractions C and D showed relatively high values of δ for the H-2 and H-4 signals (compared with those of fractions A and B). The upfield shift of the H-2 and H-4 signals can be explained in terms of the shielding effect of the phenyl group linked axially to the ring-P atom. The H-1 signal of the β-acetate **7c** consisted of a double doublet at δ 6.22, with $J_{1,2}$ 5.0 and $J_{1,P}$ 2.5 Hz, whereas that of the α anomer **7d** showed a triple doublet at δ 6.15 with $J_{1,2}$ 2.2, $J_{1,P}$ 10.5, and $J_{1,5}$ 1.5 Hz (probably due to 1,5 "W" coupling). These splitting patterns of fractions C and D resembled those of **8** [(*S*); ref. 8], **9** [(*S*), ref. 4], **10** [(*S*); ref. 5], and **11** [(*S*); ref. 10]. The optical rotation of fraction C was smaller than that of



fraction D. Therefore, fractions C and D were respectively identified as the 5-deoxy-5-*C*-[(*S*)-phenylphosphinyl]-β-D-xylopyranose derivative (**7c**) and the 5-deoxy-5-*C*-[(*S*)-phenylphosphinyl]-α-D-xylopyranose derivative (**7d**), both in the $^4C_1$(D) conformation.

The shift patterns in the ^{1}H-n.m.r. spectra of fractions A and B were somewhat similar, and showed relatively low δ values for the H-2 and H-3 signals, compared with those for **7c** and **7d**. The H-1 signal of the α-acetate **7a** showed a triple doublet at δ 5.68, with $J_{1,2}$ 2.0, $J_{1,P}$ 11.0, and $J_{1,5}$ 1.8 Hz (probably due to 1,5 "W" coupling); these splitting patterns resembled those of **9** [(*R*), α; ref. 4], **10** [(*R*), α; ref. 5], and **11** [(*R*), α; ref. 10]. The optical rotation of fraction A was larger than that of fraction B. Therefore, fractions A and B were respectively considered to be the 5-deoxy-5-*C*-[(*R*)-phenylphosphinyl]-α-D-xylopyranose derivative (**7a**) and the 5-deoxy-5-*C*-[(*R*)-phenylphosphinyl]-β-D-xylopyranose derivative (**7b**), both in the $^4C_1$(D) conformation.

EXPERIMENTAL

The general experimental methods have been reported[8]. ^{1}H-N.m.r. spectra were recorded with a Hitachi R-600 (60 MHz) spectrometer, with $CDCl_3$ as the solvent and Me_4Si as the internal standard.

3-O-Acetyl-1,2-O-isopropylidene-5-C-[methoxy(phenyl)phosphinyl]-α-D-xylopyranose (**2**). — Compound **1** (2.44 g) was treated with methyl phenylphosphinate (3 mL) and triethylamine (5 mL), as previously described[8], to give colorless, syrupy **2** (3.00 g, 73%); $[\alpha]_D^{26}$ −13.8° (*c* 2.53, $CHCl_3$); ν_{max}^{KBr} 3450 cm^{-1} (OH); ^{1}H-n.m.r. data: δ 1.28, 1.35 (2 s, 6 H, CMe_2), 1.98, 2.05 (2 s, 3 H, OAc-3), 3.72 (d, 3 H, $J_{P,H}$ 10.8 Hz, P-OMe), 4.0–4.6 (m, 2 H, H-4,5), 4.36, 4.39 (2 d, 1 H, $J_{1,2}$ 3.4 Hz, H-2), 4.9 (broad, 1 H, disappearing on deuteration, OH-5), 5.23, 5.27 (2 d, 1 H, H-3), 5.85 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), and 7.4–7.95 (m, 5 H, P-C_6H_5); *m/z* 386 (M^+).

3-O-Acetyl-5-O-(imidazol-1-ylthiocarbonyl)-1,2-O-isopropylidene-5-C-[methoxy(phenyl)phosphinyl]-α-D-xylofuranose (**3**). — Compound **2** (1.56 g) was treated with TCDI (2.09 g) as described[8], to give syrupy **3** (3.13 g, 70%); $[\alpha]_D^{26}$ −24.1° (*c* 2.91, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.28, 1.34, 1.41, 1.50 (4 s, 6 H, CMe_2), 1.81, 1.90, 1.98, 2.10 (4 s, 3 H, OAc-3), 3.61, 3.71 (2 d, 3 H, $J_{P,H}$ 10.9 Hz, P-OMe), 4.35, 4.38 (2 d, 1 H, $J_{1,2}$ 3.1 Hz, H-2), 4.5–5.35 (m, 3 H, H-3,4,5), 5.82, 5.87 (2 d, 1 H, $J_{1,2}$ 3.1 Hz, H-1), and 5.95–8.1 (m, 8 H, P-C_6H_5, imidazole 3 H).

3-O-Acetyl-5-deoxy-1,2-O-isopropylidene-5-C-[methoxy(phenyl)phosphinyl]-α-D-xylofuranose (**4**). — Compound **3** (3.13 g) was treated with tributyltin hydride (3.4 mL) as described[8], to give syrupy **4** (2.10 g, 90%); $[\alpha]_D^{26}$ −9.1° (*c* 1.10, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.26, 1.40 (2 s, 6 H, CMe_2), 1.89, 2.05 (2 s, 3 H, OAc-3), 2.0–2.5 (m, 2 H, H-5,5′), 3.62, 3.70 (2 d, 3 H, $J_{P,H}$ 10.2 Hz, P-OMe), 4.40, 4.43 (2 d, 1 H, $J_{1,2}$ 4.0 Hz, H-2, overlapping with H-4), 4.95, 5.06 (2 d, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 5.74, 5.79 (2 d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), and 7.45–7.95 (m, 5 H, P-C_6H_5); *m/z* 370 (M^+).

5-Deoxy-1,2-O-isopropylidene-5-C-(phenylphosphinyl)-α-D-xylofuranose (**5**). — Compound **4** (1.3 g) was treated with SDMA (2.5 g; 70% solution in benzene) as described[8], to give syrupy **5** (0.92 g, 84%); $[\alpha]_D^{17}$ −14.8° (*c* 1.35, $CHCl_3$); ν_{max}^{KBr} 3350 (OH) and 2330 cm^{-1} (P-H); ^{1}H-n.m.r. data: δ 1.27, 1.35, 1.46, 1.52 (4 s, 6 H, CMe_2), 2.1–2.95 (m, 2 H, H-5,5′), 3.5 (broad, ½ H, P-H), 4.0–4.3 (m, 1 H, H-4), 4.40, 4.48 (2 d, 1 H, $J_{1,2}$ 4.0 Hz, H-2), 4.7–5.05 (broad, 2 H, one proton disappeared on deuteration, H-3, OH-3), 5.83, 5.98 (2 d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), and 7.35–8.0 (m, 5 H, P-C_6H_5); *m/z* 298 (M^+).

Hydrolysis of **5** *and formation of the 1,2,3,4-tetra-O-acetyl-5-deoxy-5-C-[(R)- and (S)-phenylphosphinyl]-α- and -β-D-xylopyranoses* (**7a–d**). — Compound **5** (318 mg) was treated with 0.1M HCl (20 mL) as described[8], to give syrupy **6**. This was treated with acetic anhydride (5.3 mL) in dry pyridine (20 mL), to give syrupy **7** (314 mg, 69% from **5**). This was separated by chromatography on a column of silica gel by elution with 50:1 EtOAc–methanol, which was gradually changed to 10:1 EtOAc–methanol, to give **7a, 7b,** and a mixture of **7c** and **7d**. The latter mixture was separated in the aforementioned way, to give **7c** and **7d**.

5-C-[(R)-Phenylphosphinyl]-α-D-xylopyranose derivative (**7a**): R_F 0.65 (EtOAc); colorless solid (45 mg, 10% from **5**); $[\alpha]_D^{25}$ +48.9° (*c* 3.56, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.92, 1.95, 2.12 (3 s, 12 H, OAc-1,2,3,4), 2.15–2.85 (m, 2 H, H-5,5′), 5.2–5.6 (m, 3 H, H-2,3,4), 5.68 (td, 1 H, $J_{1,2}$ 2.0, $J_{1,5}$ 1.8, $J_{1,P}$ 11.0 Hz, H-1), and 7.1–7.85 (m, 5 H, P-C_6H_5); *m/z* 426 (M^+).

5-C-[(R)-Phenylphosphinyl]-β-D-xylopyranose derivative (**7b**): R_F 0.57 (EtOAc); colorless plates (58 mg, 13% from **5**); m.p. 257–258° (recrystallized from ethanol–hexane); $[\alpha]_D^{25}$ +16.2° (*c* 4.33, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.90, 1.99, 2.02, 2.05 (4 s, 12 H, OAc-1,2,3,4), 2.2–3.0 (m, 2 H, H-5,5′), 5.2–5.9 (m, 4 H, H-1,2,3,4), and 7.35–7.95 (m, 5 H, P-C_6H_5); *m/z* 426 (M^+).

Anal. Calc. for $C_{19}H_{23}O_9P$: C, 53.52; H, 5.44. Found: C, 53.20; H, 5.32.

5-C-[(S)-Phenylphosphinyl]-β-D-xylopyranose derivative (**7c**): R_F 0.48 (EtOAc); colorless syrup (50 mg, 11% from **5**); $[\alpha]_D^{25}$ +13.5° (*c* 4.81, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.95, 2.01, 2.10 (3 s, 12 H, OAc-1,2,3,4), 2.05–2.7 (m, 2 H, H-5,5′), 4.3–4.8 (m, 1 H, H-4), 5.18 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 7.5 Hz, H-2), 5.36 (dd, 1 H, $J_{2,3}$ 7.5, $J_{3,4}$ 5.5 Hz, H-3), 6.22 (dd, 1 H, $J_{1,2}$ 5.0, $J_{1,P}$ 2.5 Hz, H-1), and 7.2–8.1 (m, 5 H, P-C_6H_5); *m/z* 426 (M^+).

5-C-[(S)-Phenylphosphinyl]-α-D-xylopyranose derivative (**7d**): R_F 0.45 (EtOAc); colorless syrup (34 mg, 8% from **5**); $[\alpha]_D^{25}$ +15.4° (*c* 2.11, $CHCl_3$); ^{1}H-n.m.r. data: δ 1.95, 2.00, 2.14, 2.25 (4 s, 12 H, OAc-1,2,3,4), 1.85–2.5 (m, 2 H, H-5,5′), 4.67 (dd, 1 H, $J_{1,2}$ 2.2, $J_{2,3}$ 9.5 Hz, H-2, overlapping with H-4), 5.53 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3), 6.15 (td, 1 H, $J_{1,2}$ 2.2, $J_{1,5}$ 1.5, $J_{1,P}$ 10.5 Hz, H-1), and 7.3–8.1 (m, 5 H, P-C_6H_5); *m/z* 426 (M^+).

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