Carbohydrate Research, 110 (1982) 326–329
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

A convenient synthesis of 3-deoxy-D-*erythro*-pentose

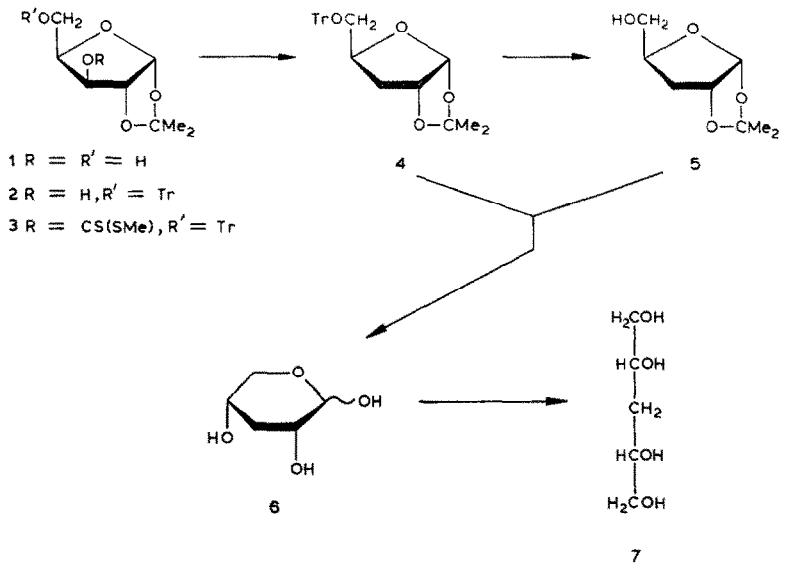
ZBIGNIEW J. WITCZAK* AND ROY L. WHISTLER
Department of Biochemistry, Purdue University, West Lafayette, Indiana 47907 (U.S.A.)
(Received March 1st, 1982; accepted for publication, May 10th, 1982)

In connection with a program to develop noncariogenic sweeteners, as well as dietary sucrose substitutes, a convenient and efficient synthesis of 3-deoxy-D-*erythro*-pentose was developed.

This deoxy sugar was first prepared by Kent, Stacey, and Wiggins[1] by cleavage of the epoxide ring of methyl 2,3-anhydro-β-D-ribopyranoside; later it was synthesized by Allerton and Overend[2] by a similar method. Szabó and Szabó[3] reported the synthesis of the sugar by oxidation of 3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose by sodium metaperiodate, followed by hydrogenation and hydrolysis. Defaye and Hildesheim[4] synthesized the sugar by displacement of the *p*-tolylsulfonyloxy group in 1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-D-xylofuranose by a thiocyanate anion, followed by desulfurization. The synthesis of the L-sugar has been described by Mukherjee and Todd[5].

We describe herein a four-step, convenient synthesis of 3-deoxy-D-*erythro*-pentose with an overall yield of 25% calculated from the starting 1,2-*O*-isopropylidene-α-D-xylofuranose[6] (**1**). Treatment of the 5-*O*-trityl derivative[6,7] (**2**) with sodium hydroxide, carbon disulfide, and methyl iodide in dimethyl sulfoxide, according to the procedure of Descotes and Faure[8], afforded crystalline 1,2-*O*-isopropylidene-3-*O*-[(methylthio)thiocarbonyl]-α-D-xylofuranose (**3**) in 75% yield. Reduction of **3** with tributylstannane in toluene at reflux, according to an improved sequence of reactions[9–11], produced 3-deoxy-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-*erythro*-pentofuranose (**4**) in 85% yield. Deprotection of the deoxy sugar **4** by detritylation with 80% acetic acid for 24 h at 40° yielded, after column chromatography, crystalline 3-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranose (**5**). Treatment of **4** and **5** for 3.5 h with 80% acetic acid at 75° afforded free 3-deoxy-D-*erythro*-pentose (**6**) as a syrup, in 25% overall yield after purification by column chromatography. The ^{1}H-n.m.r. spectrum and elemental analysis of **6**, and the preparation of the *p*-tolylsulfonylhydrazone[3] support the identity of **6**.

*On leave of absence from the Department of Organic Chemistry, Medical Academy, Lodz, Poland.



Compound **6** was reduced, according to the established procedure[12,13], to give crystalline 3-deoxy-D-*erythro*-pentitol (**7**), having properties identical with those reported by Kent *et al.*[1], and Szabó and Szabó[3].

EXPERIMENTAL

General. — The purity of products was determined by t.l.c. on Silica gel G (Merck), and detection effected by charring with 5% sulfuric acid. Column chromatography was performed on silica gel (60–200 mesh, Davidson Grade 62). Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. ^{1}H-N.m.r. spectra were recorded for solutions in chloroform (internal standard, Me_4Si) and deuterium oxide (internal standard, sodium 4,4-dimethyl-4-silapentane-1-sulfonate) with a Varian T-60A spectrometer. All organic solutions were dried with sodium sulfate and evaporated, generally $<40°$, under reduced pressure.

1,2-O-Isopropylidene-3-O-[(methylthio)thiocarbonyl]-5-O-trityl-α-D-xylofuranose (**3**). — To a solution of 1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranose (**2**, 2.5 g, 5 mmol) prepared according to the literature procedure[6,7], in dimethyl sulfoxide (10 mL) were added 5M aqueous sodium hydroxide (1.5 mL, 7.5 mmol) and carbon disulfide (0.5 g, 6.5 mmol). The mixture was stirred for 30 min, and then methyl iodide (0.87 g, 6.1 mmol) was added. Stirring was continued for 30 min, and the yellow solution was poured into water. The organic product was decanted and extracted from the aqueous phase with hexane, washed with water, and dried with calcium chloride. The solvent was evaporated and the residual syrup was chromatographed in a column of silica gel with 4:1 (v/v) hexane–acetone. The eluate was evaporated, and the residue crystallized from ethanol to give **3** as fine, colorless

needles (2.26 g, 75%), m.p. 107–108°, $[\alpha]_D^{20}$ −14° (*c* 1.2, chloroform); t.l.c. (4:1, v/v, hexane–acetone) R_F 0.33; ^{1}H-n.m.r. (chloroform-*d*): δ 7.4–7.1 (m, 15 H, Ph_3C), 5.85 (d, 1 H, H-1), 5.65 (d, 1 H, H-3), 4.35 (d, 1 H, $J_{1,2}$ 4 Hz, H-2), 4.1 (m, 1 H, $J_{3,4}$ 2.5 Hz, H-4), 3.25–2.95 (m, 2 H, H-5), 1.45 (s, 3 H, CH_3 isopr.), and 1.25 (s, 3 H, CH_3 isopr.).

Anal. Calc. for $C_{29}H_{30}O_5S_2$: C, 66.64; H, 5.78; S, 12.26. Found: C, 66.59; H, 5.68; S, 12.00.

*3-Deoxy-1,2-*O*-isopropylidene-5-*O*-trityl-*α*-*D*-erythro-pentofuranose* (**4**). — To a boiling solution of **3** (1.5 g, 2.8 mmol) in dry toluene (60 mL) was added dropwise, within 30 min, a solution of tributylstannane (1.162 g, 4 mmol) in dry toluene (40 mL). Refluxing under nitrogen was continued for 60 h. The time of the reaction was monitored by t.l.c. in 3:2 (v/v) ether–hexane. The solvent was removed *in vacuo* to give a crystalline product. The crude product was dissolved in hot acetonitrile (3 × 30 mL), and the combined extracts were washed with hexane (4 × 50 mL) to remove tin-containing compounds. After concentration of the acetonitrile layer under reduced pressure, the crude deoxy sugar was chromatographed on a column of silica gel with 3:2 (v/v) ether–hexane. The eluate was evaporated and the residue was crystallized from 2:3 (v/v) hexane–acetone to give **4** as fine, colorless needles (1.0 g, 85%) m.p. 130–131°, $[\alpha]_D^{20}$ −7.5° (*c* 1.2, chloroform); t.l.c. (4:1, v/v, hexane–acetone), R_F 0.41; ^{1}H-n.m.r. (chloroform-*d*): δ 7.4–7.1 (m, 15 H, Ph_3C), 5.6 (d, 1 H, H-1), 4.65 (h, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 4.3 (m, 1 H, H-4), 3.35–3.0 (m, 2 H, H-5), 2.1–1.9 (m, 2 H, $J_{2,3}$ 2, $J_{3,3}$ 13 Hz, H_2-3), 1.4 (s, 3 H, CH_3 isopr.), and 1.2 (s, 3 H, CH_3 isopr.).

Anal. Calc. for $C_{27}H_{28}O_4$: C, 77.85; H, 6.77. Found: C, 77.84; H, 6.85.

*3-Deoxy-1,2-*O*-isopropylidene-α-*D*-erythro-pentofuranose* (**5**). — Compound **4** (2.08 g, 5 mmol) was stirred in aqueous 80% acetic acid (200 mL) for 24 h at 40°. The mixture was cooled and then filtered, and the filtrate was evaporated under reduced pressure. The residue was chromatographed in a column of silica gel with 3:2 (v/v) ether–hexane. The eluate was evaporated, and the crude product was crystallized from ether–hexane to give **5** as a colorless, crystalline product (0.95 g, 85%), m.p. 76–77° (lit.[3] m.p. 74–76°), $[\alpha]_D^{20}$ −3.2° (*c* 0.1, chloroform) {lit.[3] $[\alpha]_D$ −3.0° (*c* 0.106, chloroform)}; t.l.c. (3:2, v/v, ether–hexane) R_F 0.11; ^{1}H-n.m.r. (chloroform-*d*): δ 5.65 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.7–4.5 (m, 1 H, H-2), 4.15–4.0 (m, 1 H, H-4), 3.7–3.5 (m, 2 H, H-5), 2.9 (s, 1 H, OH-5), 2.1–1.8 (m, 2 H, H_2-3), 1.4 (s, 3 H, CH_3 isopr.), and 1.26 (s, 3 H, CH_3 isopr.).

*3-Deoxy-*D*-erythro-pentose* (**6**). — Compound **5** (1.7 g, 10 mmol) or **4** (2.08 g, 5 mmol) was stirred for 3.5 h in aqueous 80% acetic acid (200 mL) at 75°. The mixture was filtered, and the solution evaporated under reduced pressure. Toluene (6 × 50 mL) was successively added to and evaporated from the residue. The crude syrupy product was chromatographed in a column of silica gel with 4:1 (v/v) chloroform–methanol. The eluate was evaporated to dryness to give a syrup (yield 1.1 g, 82%), $[\alpha]_D^{20}$ −6.8° (*c* 0.4, water) {(lit.[1] $[\alpha]_D^{24}$ −6.3° (*c* 1.3, water), lit.[3] $[\alpha]_D^{25}$ −11.2° (*c* 1.94, water)}; t.l.c. (4:1, v/v, chloroform–methanol) R_F 0.3; ^{1}H-n.m.r. (D_2O):

δ 5.1–4.94 (m, 2 H, H-1,2), 4.4–4.2 (m, 4 H, H-4), 3.9–3.23 (m, 2 H, H-5), and 2.23–1.9, (m, 2 H, H_2-3).

Anal. Calc. for $C_5H_{10}O_4$: C, 44.77; H, 7.51. Found: C, 44.65, H, 7.63.

The *p*-tolylsulfonylhydrazone had m.p. 144–145° (lit.[3] m.p. 143–144°).

3-Deoxy-D-erythro-*pentitol* (**7**). — To a solution of **6** (2.6 g, 20 mmol) in water (150 mL) was added dropwise a solution of sodium borohydride (1.89 g, 50 mmol) in water (30 mL). The mixture was stirred overnight at room temperature. Acetic acid was added to bring the pH to 5, and the solution was decationized with Amberlite IR-120 (H^+) resin. The solution was evaporated, and methanol (8 × 50 mL) and toluene (5 × 50 mL) were successively added to and evaporated from the residue. The crude syrupy product was homogenous by t.l.c. (R_F 0.23; 4:1, v/v, chloroform–methanol). Crystallization from ether–hexane gave pure **7** (yield 2.1 g, 80%), m.p. 68–69° (lit.[3] m.p. 66–67°); ^{1}H-n.m.r. (D_2O): δ 4.1–3.8 (m, 3 H, H-1,2), 3.73–3.26 (m, 3 H, H-4,5), and 1.83–1.6 (m, 2 H, H_2-3). The 1,2,4,5-tetra-*O*-benzoyl derivative[1,2] had m.p. 108–109° (lit.[1] m.p. 104–105°, lit.[2] m.p. 104°).

ACKNOWLEDGMENTS

This work was supported by Contract No. NO1-DE-02427 of the National Institutes of Health. Journal Paper No. 9026 of the Purdue Agricultural Experiment Station.

REFERENCES

1 P. W. Kent, M. Stacey, and L. F. Wiggins, *J. Chem. Soc.* (1949) 1232–1235.
2 R. Allerton and W. G. Overend, *J. Chem. Soc.*, (1951) 1480–1484.
3 P. Szabó and L. Szabó, *J. Chem. Soc.*, (1965) 2944–2947.
4 J. Defaye and J. Hildesheim, *Carbohydr. Res.*, 4 (1967) 145–156.
5 S. Mukherjee and A. R. Todd, *J. Chem. Soc.*, (1947) 969–973.
6 P. A. Levene and A. L. Raymond, *J. Biol. Chem.*, 102 (1933) 331–339.
7 W. Sowa, *Can. J. Chem.*, 46 (1968) 1586–1589.
8 G. Descotes and A. Faure, *Synthesis*, (1976) 449–450.
9 D. H. R. Barton and S. W. McCombie, *J. Chem. Soc. Perkin Trans. 1*, (1975) 1574–1585.
10 C. Copeland and R. V. Stick, *Aust. J. Chem.*, 30 (1977) 1269–1273.
11 J. R. Rasmussen, C. J. Slinger, R. J. Kordish, and D. D. Newman-Evans, *J. Org. Chem.*, 46 (1981) 4843–4846.
12 C. Westphal and S. Stirm, *Justus Liebigs Ann. Chem.*, 620 (1959) 8–12.
13 D. Horton and C. G. Tindall, Jr., *Carbohydr. Res.*, 8 (1968) 328–339.