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for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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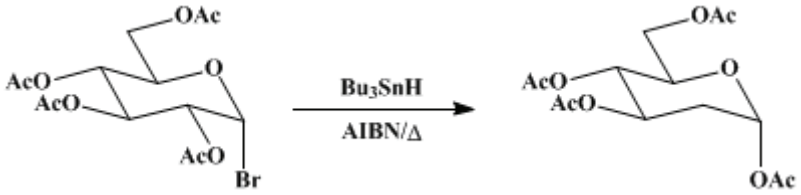
Organic Syntheses, Coll. Vol. 8, p.583 (1993); Vol. 69, p.66 (1990).

1,3,4,6-TETRA-*O*-ACETYL-2-DEOXY-α-D-GLUCOPYRANOSE

[α-D-*arabino*-Hexopyranose, 2-deoxy-, tetracetate]



Submitted by Bernd Giese and Kay S. Gröninger[1].
Checked by Matthew R. Sivik and Leo A. Paquette.

1. Procedure

A 1-L, round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser with a Claisen head on top fitted with a septum and a dry nitrogen inlet is charged with 20.6 g (50 mmol) of 2,3,4,6,-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (Note 1) and 400 mL of anhydrous toluene. The mixture is flushed with nitrogen and brought to reflux with a hot oil bath. A nitrogen atmosphere is maintained over the well-stirred reaction mixture during this and the ensuing steps. Meanwhile, a solution of 1.64 g (10 mmol) of azobisisobutyronitrile (AIBN) and 16.0 g (55 mmol) of tributylstannane in 90 mL of anhydrous toluene is prepared and filtered if necessary (Note 2). This solution is added to the refluxing, well-stirred reaction mixture during 6 hr by a syringe pump through a long needle that pierces the septum and ends at least 3 cm above the lower end of the cooling zone of the reflux condenser (Note 3). Ten minutes after all of the solution is added, the reaction mixture is cooled and the solvent is removed with a rotary evaporator (bath 40°C); 100 mL of hexane and 100 mL of acetonitrile are added, and the resulting two-phase solution is stirred vigorously for 5 min and then transferred to a separatory funnel. The lower, acetonitrile layer is separated and the hexane phase washed with 10 mL of acetonitrile (Note 4). This extraction of the combined acetonitrile solutions is repeated twice using 100 mL of hexane each time. The combined acetonitrile phases are then filtered and distilled (rotary evaporator, bath temp. 40°C). Coevaporation with 40 mL of hexane yields crude solid material that is dissolved in 120 mL of boiling *tert*-butyl methyl ether. Then 30 mL of hexane is added and the mixture is left for 4 hr at room temperature. To complete crystallization of the product, another 20 mL of hexane is added and the mixture is kept for 12 hr at 5°C. The long, colorless needles are filtered and washed once with 30 mL of hexane/*tert*-butyl methyl ether (2:1) and two times with 30 mL of pentane to yield 13.2–13.4 g (79–81%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose, mp 109–110°C; $[\alpha]_D^{20}$ + 113°C (C_2H_5OH, *c* 1.2).

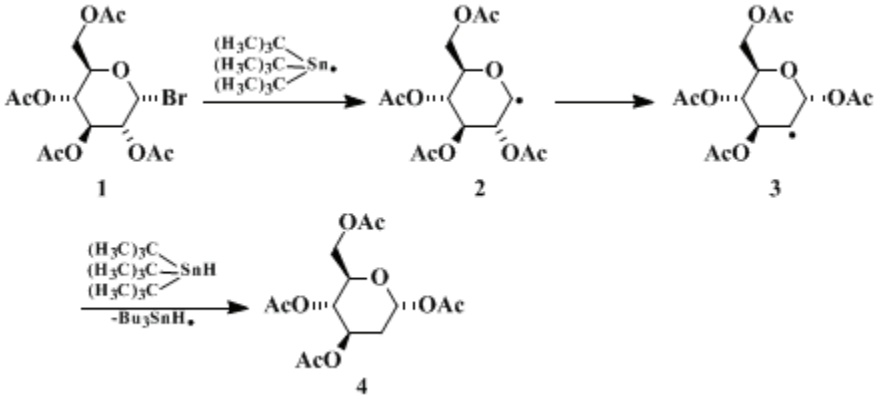
2. Notes

1. This material was obtained form the Sigma Chemical Company and was recrystallized from diethyl ether/pentane before use. It can also be prepared by the procedure of Redemann, C. E.; Niemann, C. *Org. Synth., Coll. Vol. III*, **1955**, 11.
2. Azobisisobutyronitrile (AIBN) and tributylstannane were obtained from the Aldrich Chemical Company, Inc. The amount of AIBN can be reduced to 0.82 g (5 mmol) without affecting yields. A small excess (1.1–1.2 equiv) of tributylstannane must be used to ensure total consumption of starting material.
3. This method ensures that AIBN is not thermolyzed in the needle and that tributylstannane is diluted by the refluxing solvent before reaching the reaction mixture. It is also possible to add the tributylstannane solution by a dropping funnel (l drop every 2 sec) that replaces septum and syringe pump. This method gives only slightly lower yields (75%) if the stannane solution runs down slowly on the glass surface of the condenser and does not enter the reaction mixture undiluted.
4. By this procedure most of the tributylbromostannane and other stannyl compounds are removed. It is important to wait for complete separation of the phases.

5. The product is analytically pure. Anal. calcd. for $C_{14}H_{20}O_9$: C, 50.60; H. 6.07. Found: C, 50.71; H, 6.25. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.97 (ddd, 1 H, H-2a; $J_{1,2a}$ = 3.7, $J_{2a,2c}$ = 13.6, $J_{2a,3}$ = 11.6); 2.04, 2.05, 2.09, 2.14 (4 s, 12 H, acetyl); 2.28 (ddd, 1 H, H-2e, $J_{1,2e}$ = 1.4, $J_{2e,3}$ = 5.3); 4.00–4.11 (m, 2 H, H-5, H-6); 4.36 (m, 1 H, H-6"); 5.08 (t, 1 H, H-4, $J_{3,4} = J_{4,5}$ = 9.7); 5.32 (ddd, 1 H, H-3); 6.26 (br d, 1 H, H-1).
6. Concentration of the mother liquors gives another 0.4–0.6 g of impure product that can be recrystallized from *tert*-butyl methyl ether/hexane to give another 0.3–0.5 g (2–3%) of analytically pure product.

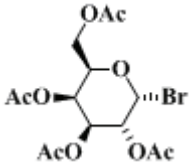
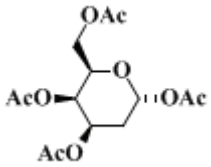
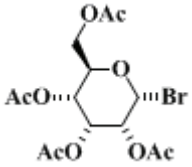
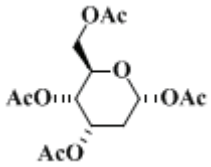
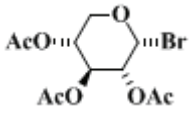
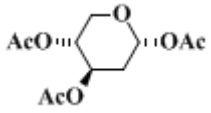
3. Discussion

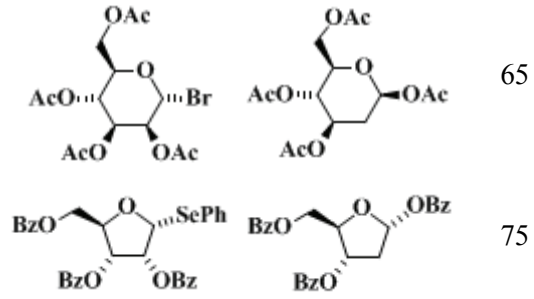
The main reaction step of this synthesis of 2-deoxy sugars is a radical rearrangement (**2** → **3**).[2] Bromine abstraction from the glucosyl bromide **1** by tributyltin radicals yields glucosyl radical **2** that undergoes acetoxy migration and gives the rearranged radical **3**. This rearrangement is a stereoselective one-step reaction that occurs with rate coefficients of about 10^3 at 75°C in benzene.[3] The driving force of the rearrangement **2** → **3** is the formation of the acetal structure at C-1 of **3**.[4] Hydrogen abstraction from tributyltin hydride yields 2-deoxy sugar **4** and the tributyltin radical that starts another chain.



This rearrangement offers a general synthesis of α- and β-2-deoxy sugars with pyranoid and furanoid ring systems (Table I).[5]

TABLE I
SYNTHESIS OF 2-DEOXY SUGARS VIA REDUCTIVE REARRANGEMENT OF GLYCOSYL DERIVATIVES[5]

Glycosyl Bromide	2-Deoxy Sugar	Yield(%)
		71
		70
		81



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References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Benzene (71-43-2)

diethyl ether (60-29-7)

hydrogen (1333-74-0)

acetonitrile (75-05-8)

bromine (7726-95-6)

nitrogen (7727-37-9)

toluene (108-88-3)

Pentane (109-66-0)

hexane (110-54-3)

tributyltin hydride,
tributylstannane,
tributyltin (688-73-3)

azobisisobutyronitrile (78-67-1)

tributylbromostannane (1461-23-0)

tert-butyl methyl ether (1634-04-4)

2,3,4,6,-tetra-O-acetyl-α-D-glucopyranosyl bromide

1,3,4,6-Tetra-O-acetyl-2-deoxy-α-D-glucopyranose

α-D-arabino-Hexopyranose, 2-deoxy-, tetracetate (16750-06-4)