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USE OF SELENIUM IN CARBOHYDRATE CHEMISTRY: PREPARATION OF *C*-GLYCOSIDE CONGENERS

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ABSTRACT

3,4,5,7-Tetra-*O*-benzyl-D-*gluco*-hept-1-enitol was submitted to a selenocyclisation–oxidation–elimination sequence to provide 2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-1-deoxy-D-*gluco*-hept-1-enitol in 54% yield. Treatment of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside with *N*-phenylselenophthalimide gave methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-phenylseleno-α-D-glucopyranoside which was transformed to methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*xylo*-hex-5-enopyranoside.

INTRODUCTION

Functionally substituted *C*-glycopyranosides occur as sub-units of a variety of natural products. As a consequence, intensive efforts are currently being devoted to the direct formation of C–C bonds at the anomeric center of carbohydrates[1]. 1-Methylene sugars are *C*-glycoside congeners of particular biochemical interest. For instance, "1-methylene-D-galactose" interferes with the formation of D-galactose 1-phosphate and thus with the biosynthesis of glycoconjugates[2]. 1-Methylene sugars have been prepared by a multistep process culminating with an elimination reaction[3]. Recently, metal carbene-mediated methylenation[4] of aldonolactones has provided a direct route to these compounds, which are intermediates for the synthesis of furanoid or pyranoid rings having a methyl group and a second alkyl group adjacent to the ring oxygen atom. We now describe a new synthesis of pyranoid rings that have an exo-methylene group adjacent to the ring oxygen, either at C-1 or on C-5.

RESULTS AND DISCUSSION

When 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) was submitted to a Wittig reaction with methylenetriphenylphosphorane, 3,4,5,7-tetra-*O*-benzyl-D-*gluco*-hept-1-enitol[5] (**2**) was obtained (75% after purification on silica gel). It was impor-

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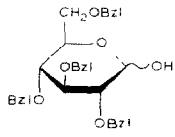
tant to convert **1** into its lithium salt prior to the Wittig reaction. Under these conditions, the formation of **2** was reproducible and the reaction could be conducted on a large scale without particular problems, making the useful synthon **2** easily available. Various selective transformations of **2** have been reported[5-7]. The mercuri-induced cyclisation[5] favours the formation of α anomers almost exclusively[6]. In order to test selenium-induced cyclisation, *N*-phenylselenophthalimide[8] (N-PSP) was selected because it is a superior reagent to phenylselenenyl halides for carrying out organoselenium-induced ring closures of unsaturated substrates[9]. The enitol **2** cyclised in dichloromethane, in the presence of N-PSP and camphorsulfonic acid, to give mainly the hepitol derivative **3**. The stereochemistry at C-2 in **3** was determined when deselenation with tributyltin hydride gave the α-D-glucopyranosylmethane derivative **5**, identical with the derivative previously prepared by another route[5] and the configuration of which had been ascertained by an X-ray diffraction study[10]. The model **12** is proposed in order to rationalise the observed diastereofacial selectivity of both mercuri- and selenium-induced cyclisation.

A by-product formed (30%) during the reaction of **2** with N-PSP was 2,5-anhydro-3,4,7-tri-*O*-benzyl-1-deoxy-1-phenylseleno-D-*glycero*-D-*gulo*-hepitol (**6**). The proposed absolute configuration was inferred from the 300-MHz ^{1}H-n.m.r.



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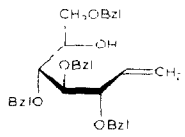

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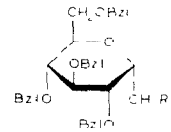

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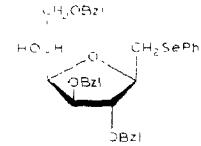
4 R = Se(O)Ph
5 R = H



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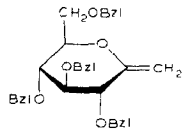

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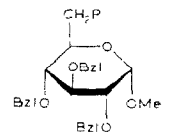
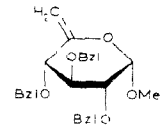


8 R = OH
9 R = SePh
10 R = Se(O)Ph



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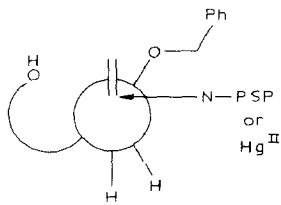

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data. The signal for H-3 (δ 3.98, d, $J_{2,3}$ 1 Hz) favours a *trans*-relationship of -CH_2SePh and BzlO-2. Benzyloxy participation in carbohydrate chemistry is well known[11] and the formation of **6** provides a new example. In accordance with well-established selenium chemistry, oxidation of **3** followed by elimination provided a novel and straightforward route to **7**, an interesting synthon for selective transformations.

Grieco *et al.*[8] have used N-PSP in the presence of tributylphosphine to convert the primary alcohol group of a carbohydrate into an alkyl phenyl selenide. Such a reaction has also been reported in the presence of phenyl selenocyanate[12]. Treatment of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[13] (**8**) with N-PSP and tributylphosphine in tetrahydrofuran at 0° gave 83% of the selenide **9**, which, after oxidation and elimination, afforded 75% of the 6-deoxyhex-5-enopyranoside derivative[14] **11**.

N-PSP is stable, crystalline, and easy to handle, and is the reagent of choice for the preparation of pyranoïd rings that have an exo-methylene group adjacent to the ring oxygen atom.

EXPERIMENTAL

General methods. — Melting points were determined in capillary tubes with a Büchi apparatus and are uncorrected. Optical rotations were measured at 22–25° with a Perkin–Elmer Model 141 polarimeter. ^{1}H-N.m.r. spectra were recorded with a Perkin–Elmer R-32 (90 MHz) or Bruker (300.13 MHz) instrument for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. Mass spectra were recorded with a Ribermag R-10-10 instrument in the desorption chemical-ionisation (d.c.i.) mode, using ammonia as the reagent gas. The purity of products was determined by t.l.c. on silica gel 60 F 154 (Merck) with detection by charring with sulphuric acid. Column chromatography was performed on silica gel 60 (Merck, 63–200 μm) which was used without pre-treatment. Elemental analyses were performed by the Service Central de Micro-Analyse du Centre National de la Recherche Scientifique.

*3,4,5,7-Tetra-O-benzyl-*D-gluco-*hept-1-enitol* (**2**). — A suspension of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (10.8 g) in dry dimethoxyethane (60 mL) was solubilised at 0° under dry argon by the addition of 3M butyl-lithium in hexane (6.6 mL, 1 equiv.). A solution of methylenetriphenylphosphorane in dry dimethoxyethane (40 mL), prepared at −15° under dry argon from methyltriphenylphosphonium bromide (14.3 g) and 3M butyl-lithium in hexane (12.7 mL), was added at room temperature and also under argon. The mixture was then boiled under reflux for 10 min and the excess of Wittig reagent was destroyed by the addition of acetone (50 mL) at room temperature. The mixture was cooled to 0°, filtered, and concentrated. The residue (12.5 g) was eluted from a column of silica gel (380 g) with toluene–ethyl acetate (85:15) to give syrupy **2** (8.32 g, 74%), $[\alpha]_D$ +23° (*c* 1, chloroform). ^{1}H-N.m.r. data (C_6D_6, 90 MHz): δ 2.85 (s, 1 H, OH) and 5.90 (m, 1 H, *J* 7.3, 10, and 18 Hz, vinylic H).

Anal. Calc. for $C_{35}H_{38}O_5$: C, 78.04; H, 7.11. Found: C, 77.42; H, 7.14.

*2,6-Anhydro-3,4,5,7-tetra-O-benzyl-1-deoxy-1-phenylseleno-*D-glycero-D-ido-*heptitol* (**3**). — A solution of **1** (1.205 g) and *N*-phenylselenophthalimide (1.2 g) in dry dichloromethane (15 mL) containing anhydrous (±)-10-camphorsulfonic acid (60 mg) was stirred for 12 h at room temperature under dry argon. The mixture was then neutralised with anhydrous potassium carbonate, filtered, and concentrated. Elution of the residue from a column of silica gel (100 g) with ether–hexane (3:7) gave, first, amorphous **3** (912 mg, 60%), $[\alpha]_D$ +30° (*c* 0.5, chloroform). ^{1}H-N.m.r. data (C_6D_6, 90 MHz): δ 3.25 (d, 2 H, *J* 8 Hz), 3.65 (m, 6 H), 4.15–5.0 (m, 9 H), 7.10 (m, 23 H), and 7.45 (m, 2 H).

Anal. Calc. for $C_{41}H_{42}O_5Se$: C, 70.98; H, 6.10. Found: C, 71.28; H, 6.08.

Further elution gave amorphous **6** (405 mg, 30%), $[\alpha]_D$ +18° (*c* 1.7, chloroform). ^{1}H-N.m.r. data (C_6D_6, 300.13 MHz): δ 3.08 (dd, 1 H, *J* 12.4 and 19.1 Hz, H-1), 3.21 (dd, 1 H, *J* 12.4 and 5.3 Hz, H-1'), 3.58 (dd, 1 H, *J* 9.8 and 6.7 Hz, H-7), 3.73 (dd, 1 H, *J* 9.8 and 2.7 Hz, H-7'), 3.98 (d, 1 H, *J* 1.0 Hz, H-3), 4.11 (d, 1 H, *J* 3.1 Hz, H-4), 4.23 (dd, 1 H, *J* 3.1 and 8.9 Hz, H-5), 4.31 (m, 1 H, H-2), and 4.40 (m, 1 H, H-6). Mass spectrum: *m/z* 605 (100%, $M^+ + 1$) and 622 (6.3%, $M^+ + 18$).

Anal. Calc. for $C_{35}H_{36}O_5Se$: C, 67.65; H, 6.01. Found: C, 67.91; H, 6.13.

*2,6-Anhydro-3,4,5,7-tetra-O-benzyl-1-deoxy-*D-glycero-D-ido-*heptitol* (**5**). — A solution of **3** (27 mg) in toluene (0.6 mL) containing tributyltin hydride (50 μL) and a catalytic amount of azobisisobutyronitrile was heated at 90° for 12 h. Butyl bromide was added to destroy the excess of hydride (10 min at 100°) and the mixture was concentrated. Elution of the residue from a column of silica gel (3 g) with hexane–ether (7:3) gave **5** (6.5 mg, 33%), the m.p. and $[\alpha]_D$ of which were identical with those of the compound previously prepared[5].

*2,6-Anhydro-3,4,5,7-tetra-O-benzyl-1-deoxy-*D-gluco-*hept-1-enitol* (**7**). — A solution of **3** (845 mg) in methanol (50 mL) was diluted with water until turbid, and then stirred for 2 h at room temperature in the presence of sodium periodate (389 mg) and sodium hydrogencarbonate (85 mg). The mixture was concentrated and the residue was extracted with dichloromethane. The extract was dried (Na_2SO_4) and concentrated to give 2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-1-deoxy-1-phenylseleninyl-D-*glycero*-D-*ido*-heptitol (**4**; 835 mg, 97%) which was pure in t.l.c. (two diastereoisomers) and was treated at 50° for 6 h with vinyl acetate (25 mL) and di-isopropylamine (6.5 mL). The mixture was then concentrated and the residue was eluted from a column of silica gel (100 g) with hexane–ethyl acetate (9:1) containing 0.2% of triethylamine, to give **7** (577 mg, 91%), m.p. 65° (from hexane), $[\alpha]_D$ +45.5° (*c* 0.33, chloroform). ^{1}H-N.m.r. data (90 MHz): δ 3.72 (m, 6 H), 4.40–4.90 (m, 10 H, 4 CH_2Ph and 2 vinylic H), and 7.25 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{35}H_{28}O_5$: C, 78.33; H, 6.76. Found: C, 78.36; H, 6.72.

*Methyl 2,3,4-tri-O-benzyl-6-deoxy-6-phenylseleno-α-*D-*glucopyranoside* (**9**). — A solution of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**8**, 500 mg) in dry tetrahydrofuran (5 mL) was stirred in the presence of *N*-phenylselenophthalimide

(650 mg) and tributylphosphine (0.5 mL) at 0° for 2 h under dry argon. Sodium borohydride (40 mg) was then added, and the mixture was stirred at room temperature for 3 h, diluted with ether, washed with aqueous sodium chloride, and concentrated. The residue was eluted from a column of silica gel (20 g) with hexane–ethyl acetate (85:15), to give amorphous **9** (568 mg, 88%), $[\alpha]_D$ +24° (*c* 0.6, chloroform). ^{1}H-N.m.r. data (90 MHz): δ 2.93 (dd, 1 H, *J* 13.5 and 9 Hz, H-6), 3.48 (s, 3 H, OMe), and 3.5 (dd, 1 H, *J* 9 and 4 Hz, H-2).

Anal. Calc. for $C_{34}H_{36}O_5Se$: C, 67.38; H, 6.06. Found: C, 67.68; H, 6.04.

*Methyl 2,3,4-tri-*O*-benzyl-α-*D-xylo-*hex-5-enopyranoside* (**11**). — A solution of **9** (45 mg) in methanol (5 mL) was diluted with water until turbid, and then stirred for 2 h at room temperature in the presence of sodium periodate (24 mg) and sodium hydrogencarbonate (5 mg). The mixture was then concentrated and extracted with dichloromethane, and the extract was dried (Na_2SO_4) and concentrated. The residue (45 mg, 97%) of 2,3,4-tri-*O*-benzyl-6-deoxy-6-phenylseleninyl-α-D-glucopyranoside (**10**), which was pure in t.l.c., was heated at 80° for 5 h in toluene (4 mL) and di-isopropylamine (0.2 mL), and the mixture was then concentrated. The residue was eluted from a column of silica gel (8 g) with hexane–ethyl acetate (85:15) containing 0.1% of triethylamine, to give amorphous **11** (25 mg, 75%), $[\alpha]_D$ −18° (*c* 1.3, chloroform); lit.[14] m.p. 57–58°, $[\alpha]_D$ +18° (*c* 0.5, chloroform). The discrepancy in $[\alpha]_D$ values is emphasised. ^{1}H-N.m.r. data (C_6D_6, 300.13 MHz): δ 3.40 (s, 3 H, OMe), 3.60 (dd, 1 H, *J* 3.6 and 9.2 Hz, H-2), 3.90 (m, 1 H, H-4), 3.97 (t, 1 H, *J* 3.6 Hz, H-3), 4.60 (d, 1 H, *J* 3.5 Hz, vinylic H), 4.62 (d, 1 H, *J* 3.5 Hz, H-1), and 4.70 (d, 1 H, *J* 3.6 Hz, vinylic H).

Anal. Calc. for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.37; H, 6.86.

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