Carbohydrate Research, 137 (1985) 89–97
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

ELECTROPHILE-MEDIATED CYCLIZATIONS OF 6-*O*-BENZYL-1,2-DI-DEOXY-3,4-*O*-ISOPROPYLIDENE-D-*ribo*-HEX-1-ENITOL TO DERIVATIVES OF 2,5-ANHYDRO-6-*O*-BENZYL-3,4-*O*-ISOPROPYLIDENE-D-*altro*-HEXITOL

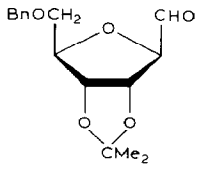
FILLMORE FREEMAN AND KIRK D. ROBARGE
Department of Chemistry, University of California, Irvine, California 92717 (U.S.A.)
(Received May 11th, 1984; accepted for publication in revised form, August 25th, 1984)

ABSTRACT

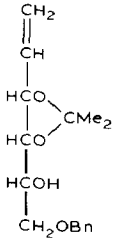
Electrophile (bromine, iodine, mercuric acetate, mercuric trifluoroacetate, phenylselenyl chloride)-mediated cyclization of 6-*O*-benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-D-*ribo*-hex-1-enitol (**2**) led exclusively to 1-substituted derivatives of 2,5-anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-D-*altro*-hexitol (**3**). The synthesis of alkene **2**, together with mechanistic and stereochemical aspects of its cyclization to derivatives of hexitol **3** are discussed.

INTRODUCTION

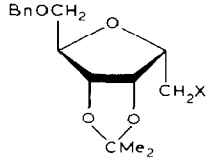
In an ongoing effort toward the synthesis of C-nucleosides and C-nucleoside precursors, an improved synthesis of 2,5-anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-D-allose (**1**) was desired[1,2]. The synthetic strategy envisioned involved stereoselective C-functionalization at the anomeric site of the carbohydrate using derivatives of an acyclic precursor, 6-*O*-benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-D-*ribo*-hex-1-enitol (**2**). Activation of alkene **2** via an electrophile followed by stereospecific trapping from the internal nucleophile would lead to a suitable precursor to the desired compound **1**.



1



2

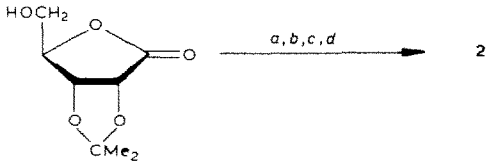


3

4 X = I
5 X = Br
6 X = SePh

0008-6215/85/$ 03.30

D-Ribono-1,4-lactone was protected as the 2,3-isopropylidene acetal[4,5] (72%), benzylated[6,7] at O-6 (70%), and then reduced to the lactol[8] (80%) with Dibal. Treatment of this lactol with 2.0 eq of methylidenetriphenylphosphorane in boiling tetrahydrofuran gave 6-*O*-benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-D-*ribo*-hex-1-enitol, (**2**, 70%).



(a) $Me_2C(OMe)_2$, H^+, DMF, 12 h, 26°, 72 %
(b) Ag_2O, BnBr, DMF, 25°, 70 %
(c) Dibal-H (1.5 eq), 1 h, −78°, Et_2O, 80 %
(d) $Ph_3P{=}CH_2$ (2.0 eq), THF, 18 h, 70 %

The iodine-[9,10], bromine-, and phenylselenyl chloride-[11] mediated cyclization of alkene **2** led to the exclusive formation of 1-substituted derivatives (**4, 5,** and **6**) of 2,5-anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-D-*altro*-hexitol (**3**, Table I); the D-*allo* 2-epimers were not detected. Mercuric acetate[12a] or mercuric trifluoroacetate[12b]-initiated cyclization followed by displacement of the organomercury species with iodine gave the identical product (**4**) obtained from the iodine-mediated cyclization. The reaction of alkene **2** with mercuric trifluoromethanesulfonate–amine complex[13] was unsuccessful.

The stereochemical assignments for 2,5-anhydro-6-*O*-benzyl-1-iodo-3,4-*O*-isopropylidene-D-*altro*-hexitol (**4**) and the other cyclized products (**5** and **6**) were

TABLE I

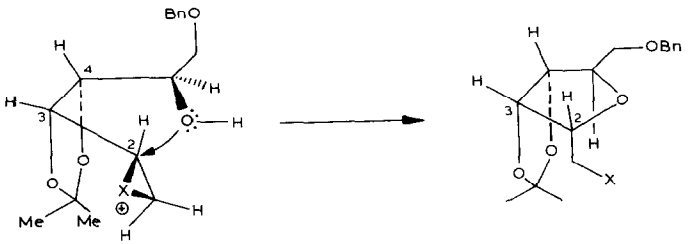
YIELDS OF DERIVATIVES OF 2,5-ANHYDRO-6-*O*-BENZYL-3,4-*O*-ISOPROPYLIDENE-D-*altro*-HEXITOL (**3**) FROM ELECTROPHILIE-MEDIATED CYCLIZATIONS OF **2**

Electrophile	*Experimental conditions*	*X*	*Yield (%)*
I_2 (ref. 9)	10 eq sat'd $NaHCO_3$, 5 eq I_2/THF	I	65
I_2 (ref 10)	3 eq I_2/CH_3CN, 2.5 h, 0°	I	63
Br_2	1.5 eq Br_2/CCl_4, 45 min-1 h, 10°	Br	34
$Hg(OAc)_2$ (ref. 12)	1) 1.5 eq $Hg(OAc)_2$/THF, 15 h, 24° 2) 2.5 eq I_2/THF, 2 h, 24°	I	54
$Hg(OCOCF_3)_2$ (ref. 12)	1) 1.5 eq $Hg(OCOCF_3)_2$/THF, 15 h, 24° 2) 2.5 eq I_2/THF, 2 h, 24°	I	54
$(CF_3SO_3)_2Hg \cdot$ amine (ref. 13)			0
PhSeCl (ref. 11)	1.2 eq PhSeCl/CH_2Cl_2, −78° to 24°	SePh	46
PhSeCl (ref 3)	5 eq sat'd $NaHCO_3$, 1.2 eq PhSeCl/CH_2Cl_2, −78° to 24°	SePh	45

made on the basis of ^{1}H- and ^{13}C-n.m.r. spectra[14–17]. It is well established for structures based on 2,3-*O*-isopropylidene-D-ribofuranose that the isopropylidene methyl groups in β anomers resonate at 25.5 ±0.2 and 27.5 ±0.2 p.p.m. ($\Delta\delta$ = ~1.90 ±0.2), whereas those in α anomers appear at 24.9 ±0.3 and 26.3 ±0.2 p.p.m. ($\Delta\delta$ = ~1.25 ±0.2)[15]. Compound **4** exhibits ^{13}C-n.m.r. resonances at 25.27 and 26.52 p.p.m. ($\Delta\delta$ = 1.25 p.p.m.). Additional support for the "α" configurational assignment (D-*altro* configuration) of **4** comes from examination of the quaternary carbon signal of the *O*-isopropylidene group. Literature precedents[16] show that the resonance for this carbon atom appears at 112.7 ±0.6 p.p.m. for α anomers and at 114.5 ±0.6 p.p.m. for β anomers. Compound **4** exhibits ^{13}C-n.m.r. resonance at 112.8 p.p.m. for the quaternary carbon atom.

The stereochemical outcome of the reaction appears to be independent of the electrophile. When iodine was the electrophile, the same product was obtained regardless of whether the reaction was performed under biphasic[9] "kinetic" conditions or Bartlett's nonaqueous "thermodynamic" conditions[10]. Iodine proved to be the best electrophile, giving **4** in 65% yield. Moderate yields wee obtained with mercuric acetate, mercuric trifluoroacetate, and phenylselenyl chloride, whereas a more reactive electrophile such as bromine led to the cyclized product in lower yield.

Activation of allylic alcohols and ethers, followed by trapping with a suitably disposed internal nucleophile, often results in high stereoselectivity especially in forming 5- and 6-membered rings[18]. Interestingly, in contrast to our results, Mann and Kane[3,19] have recently made use of a selenium-induced cyclization in a system similar to **2** in order to effect exclusive formation of the "β anomer", the key intermediate in a synthesis of showdomycin[3,19]. The stereospecificity of the reaction strongly suggests formation of a bridged species. The observed product **4** ("α anomer") is consistent with a favored conformation in which the terminal methylene group and the allylic ether oxygen are eclipsed (that is H-2 and H-3 are eclipsed). Attack by an electrophile from the least-hindered side, followed by trapping by the internal nucleophile leads to the "α anomer". It is likely that the trapping is synchronous with the formation of iodonium ion in this kinetically controlled process[17]. No product ("β anomer") is observed that would have resulted from a conformation in which H-2 and H-3 are staggered.



3

EXPERIMENTAL

General methods. — Tetrahydrofuran (THF) and ether were distilled from sodium benzophenone anion prior to use. Dichloromethane was distilled from CaH_2 prior to use. *N,N*-Dimethylformamide (DMF) was predried over BaO then distilled under diminished pressure from CaH_2 in the dark and stored over 4-Å sieves.

Other reagents were used as supplied or purified as noted. Butyllithium in hexanes (Alfa) was titrated at 25° in THF with 2,5-dimethoxybenzyl alcohol. Melting points were determined in open capillary tubes with a Thomas–Hoover apparatus and are uncorrected. All reactions were carried out in oven- or flame-dried glassware under argon with magnetic stirring, unless noted otherwise. Solutions and liquids were delivered by syringe or cannula through rubber septa or by pressure-equalizing dropping funnels where appropriate.

Solvents used for extraction and chromatography were nanograde quality or distilled. I.r. spectra were obtained with a Perkin–Elmer 283 spectrophotometer. Spectra were obtained for dilute solutions in CCl_4, neat films, or KBr disks.

Medium-resolution mass spectra were obtained with a Finnigan 9610 g.l.c.–e.i.–c.i. mass spectrometer with a Nova 3 data system operating at an ionization potential of 70 or 100 eV. Chemical ionization mass spectra were obtained by using 2-methylpropane as the reactant gas. Peaks greater than ≈10% relative intensity are generally reported.

^{1}H-N.m.r. spectra were recorded at 250 MHz (Bruker WM-250) with the solvent(s) noted. Chemical shifts (δ) are reported downfield from internal Me_4Si (~0.5% for Fourier transform) at δ = 0.000 p.p.m. The following descriptions are used: Abq = AB quartet, br = broad, d = doublet, m = multiplet, q = quartet, s = singlet, and t = triplet.

Apparent coupling-constants (J) are reported in hertz (Hz). Because of the data digitization with the FT instrument, J values are ±0.40 Hz maximum, but normally are accurate to ±0.20 Hz. ^{13}C-N.m.r. data were obtained with a Bruker WM-250 or WM-90 spectrometers.

Optical rotations were measured with a Perkin–Elmer 241 polarimeter in an unthermostatted, 10-cm glass cell at the sodium D line.

Silica gel 60 (230–400 mesh) was used for flash column-chromatography. T.l.c. was performed on Merck Silica Gel 60 F-254 (0.25 mm, precoated on glass).

Elemental analyses were performed by Robertson Laboratory, Florham Park, NJ.

*2,3-O-Isopropylidene-*D*-ribono-1,4-lactone*[7] was prepared by the procedure of Kiso and Hasegawa[5] in 72% yield after recrystallization from toluene; m.p. 137–138° (lit.[4] m.p. 138–139°) $[\alpha]_D^{25}$ −80.6° (*c* 0.9, $CHCl_3$) [lit. $[\alpha]_D^{26}$ −84.17° (*c* 0.9, $CHCl_3$)]; ^{1}H-n.m.r. ($CDCl_3$): δ 4.82 (ABq, 2 H, $\Delta\nu_{AB}$ 14.0, J_{AB} 5.7 Hz, H-2, H-3), 4.64 (app t, 1 H, $J_{5,4}$ 2.0 Hz, H-4), 3.85 (dABq, 2 H, $\Delta\nu_{AB}$ 44.2, J_{AB} 12.2, $J_{5A,4}$ = $J_{5B,4}$ = 2.0 Hz, H-5), 1.49, 1.38 (s, 6 H, $\Delta\delta$ 23.0 Hz, CMe_2), and 2.35 (br s, OH,

D_2O exchange); ^{13}C-n.m.r. ($CDCl_3$): δ 175.50 (s, C-1), 113.33 (s, CMe_2), 83.23 (d, C-2), 78.51 (d, C-3), 75.90 (d, C-4), 62.01 (t, C-5), 26.89 (q, gem CH_3), and 25.62 (q, gem CH_3).

*5-O-Benzyl-2,3-O-isopropylidene-*D*-ribono-1,4-lactone.* — The benzylation procedure previously described was followed[7]. Chromatography on silica gel with 3:1:1 petroleum ether (35–60°)–diethyl ether–dichloromethane (R_F 0.5) yielded 633 mg (76%) of an off-white, crystalline solid, m.p. 66–64°, $[\alpha]_D^{25}$ −54.0° (*c* 2.7, $CHCl_3$) [lit[7b] $[\alpha]_D^{20}$ −50° (*c* 0.8, $CHCl_3$)]; ^{13}C-n.m.r. ($CDCl_3$): δ 174.53 (s, C-1), 137.20 (s, C-7), 127.1–128.81 (m, C-8–C-12), 113.33 (s, CMe_2), 81.32 (d, C-2), 78.56 (d, C-3), 74.09 (d, C-4), 69.26 (t, C-6), 65.38 (t, C-5), 26.95 (q, gem CH_3), and 25.79 (q, gem CH_3). The product, before chromatography, was contaminated with benzyl alcohol and not dibenzyl ether[7b].

*5-O-Benzyl-2,3-O-isopropylidene-*D*-ribofuranose.* — This compound was prepared by the procedure of Ireland *et al.*[8]. Removal of solvent left a yellow oil (80–91%), which on occasion after chromatography on silica gel (230–400 mesh) with 75% ether in petroleum ether would crystallize (m.p. 52–54°) upon standing (64–80% after chromatography). The oil was a ~4:1 β:α mixture of anomers as determined by ^{1}H-n.m.r. integration of the anomeric protons. The crystalline product was likewise a mixture (^{1}H-n.m.r.), the β anomer being major. The crude product could be used without additional purification; $[\alpha]_D^{25}$ −1.67° (*c* 2.7, $CHCl_3$); R_F 0.23 in 3:1:1 petroleum ether (35–60°)–ether–dichloromethane; ν_{max}^{film} 3429 (br OH), 3098, 3041, 3020 (alkene, arom.), 2995, 2949, 2878, (CH_3), 1501, 1458 (arom. ring), 1392, 1380 (shoulder), 1365 (gem CH_3), 750, and 700 cm^{-1} (monosubst. arom.); ^{1}H-n.m.r. ($CDCl_3$): δ (minor anomer, major anomer), δ 7.2–7.5 (m, 5 H, Ph), 5.48 (dd, $J_{1,2}$ 4.0, $J_{1,\alpha(OH)}$ 11.1 Hz, H-1β, collapses to a doublet upon addition of D_2O), 5.29 (d, $J_{1,\beta(OH)}$ 11.4 Hz, H-1α, collapses to a singlet at δ 5.29 upon addition of D_2O), 4.74 (d, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.59 (ABq, 2 H, $\Delta\nu_{AB}$ 21.2, J_{AB} 11.6 Hz, H-6), 4.51 (d, 1 H, $J_{2,3}$ = 6.0 Hz, H-3), 4.39 (app t, 1 H, $J_{4,5A} = J_{4,5B}$ = 2.4 Hz, H-4), 3.64 (dABq, 2 H, $\Delta\nu_{AB}$ 18.3, J_{AB} 10.2, $J_{5A,4} = J_{5B,4}$ = 2.4 Hz, H-5), 1.56, 1.39 [s, 6 H, $\Delta\delta$ 43.25 Hz, geminal CH_3 (minor)], 1.48, and 1.31 [s, 6 H, $\Delta\delta$ 42.0 Hz, geminal CH_3 (major)]; ^{13}C-n.m.r. ($CDCl_3$, major anomer only): δ 136.61 (s, C-7), 126.82–128.63 (m, C-8,9,10,11,12), 111.98 (s, CMe_2), 103.52 (d, C-1), 87.17 (d, C-2), 85.36 (d, C-3), 82.10 (d, C-4), 73.77 (t, C-6), 71.20 (t, C-5), 26.43 (q, gem CH_3) and 24.90 (q, gem CH_3); *m/z* (c.i.): 263 ($MH^+ - H_2O$), 91; *m/z* (e.i.) 265 ($M^+ - CH_3$), 247, 158, 131, 91.

Anal. Calc. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.05; H, 6.97.

*6-O-Benzyl-5-1,2-dideoxy-3,4-*O*-isopropylidene-*D*-ribo-hex-1-enitol* (**2**). — To a stirred solution of 928 mg (2.6 mmol) of methyltriphenylphosphonium bromide (Aldrich) in 10 mL of dry THF at 24° under argon was added dropwise 1.2 mL (2.4 mmol) of 2.0M butyllithium in hexane during 2 min. A color change from yellow to red occurred. The mixture was stirred for 15 min at 24° and a solution of 290 mg (1.04 mmol) of the preceding lactol in 3 mL of THF was added quickly. Solids began to form in the resulting cream-colored suspension. The mixture was

boiled under reflux for 18 h and quenched upon cooling by the addition of 2 mL of water. The dark-brown mixture was extracted several times with ether, and the combined organic layers were washed with 10 mL of saturated aqueous NaCl, and dried (K_2CO_3). Removal of solvent under diminished pressure and flash column-chromatography of the residue on 25 g of silica gel with 3:1:1 petroleum ether (35–60°)–ether–dichloromethane afforded 202 mg (70%) of alkene **2** (although this reaction worked well on a small scale, the yield decreased to 36–40% upon scaling up). R_F 0.14 (9:1:1 petroleum ether–ether–dichloromethane) 0.31 (3:1:1 petroleum ether–ether–dichloromethane); $\nu_{max}^{CCl_4}$ 3600, 3420–3480 (br OH), 3100, 3080, 3020 (alkene, arom.), 2998, 2940, 2870, (CH_3), 1503, 1458 (arom. ring), 1382, 1372, (gem CH_3), 990 (weak), 925 (term. vinyl), and 690 cm^{-1} (monosubst. aromatic ring); ^{1}H-n.m.r. ($CDCl_3$): δ 7.32–7.37 (m, 5 H, Ph), 6.02 (ddd, 1 H, $J_{1,2(trans)}$ 17.1, $J_{1,2(cis)}$ = 10.4, $J_{2,3}$ 6.7 Hz, H-2, X part of ABX), 5.31 (m, 2 H, H-1), 4.70 (app t, 1 H, $J_{3,4}$ 6.3, $J_{4,5}$ 6.7 Hz, H-3), 4.59 (s, 2 H, H-7), 4.12 (dd, 1 H, $J_{3,4}$ 6.3, $J_{4,5}$ 6.3 Hz, H-4), 3.85 (m, 1 H, H-5, became dt upon irradiating OH), 3.73 (dd, 1 H, $J_{6A,B}$ 9.6, $J_{5,6} \approx$ 4.0 Hz, H-6A or H-6B), 3.59 (dd, 1 H, $J_{6A,B}$ = 9.6, $J_{5,6} \approx$ 7.0 Hz, H-6A or H-6B), 2.43 (d, $J_{(OH),5}$ 4.6 Hz, OH), 1.46 and 1.37 (s, 6 H, $\Delta\delta$ 22.7 Hz, geminal CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 138.22 (s, C-8), 134.22 (d, C-2), 127.14–128.94 (m, C-9-13), 117.87 (t, C-1), 109.00 (s, CMe_2), 78.91 (d, C-3), 77.99 (d, C-4), 73.65 (t, C-7), 72.06 (t, C-6), 69.12 (d, C-5), 27.96 (q, gem CH_3), and 25.60 (q, gem CH_3); *m/z* (c.i.) 279 (MH^+), 221, 203, 185, 161, 131, 113, and 91; *m/z* (e.i.) 263 ($M^+ - CH_3$), 107, and 91.

Anal. Calc. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.26; H, 7.95.

2,5-Anhydro-6-O-benzyl-1-iodo-3,4-O-isopropylidene-D-altro-*hexitol* (**4**). — *Method A.* Compound **4** was prepared by the procedure of Flavin and Lu[9], performing the reaction at 25° instead of 0°. To 199 mg (0.72 mmol) of alkene **2** dissolved in 5 mL of THF was added 6.0 mL (10 eq) of saturated aqueous $NaHCO_3$, followed by dropwise addition of 18.4 mL of a 2.5% solution of iodine in ether (3.58 mmol, 5 eq). The reaction was monitored by t.l.c.; all starting material was consumed in 2 h. The reaction was quenched by addition of solid sodium sulfite. The product mixture was extracted several times with ether. The combined extracts were washed with 25 mL of saturated NaCl, and dried (Na_2SO_4). Removal of solvent under diminished pressure gave 271 mg of a brown oil (94%). Flash column-chromatography of the residue on 8 g of silica gel with 9:1:1 petroleum ether (35–60°–ether–dichloromethane gave 188.1 mg (65%) of the cyclized compound (**4**).

Method B. The cyclization was also carried out in the absence of base under Bartlett's conditions[16] (3 eq iodine, CH_3CN, 2.5 h, 0°) to yield the same cyclization product (**4**, 63%) as obtained by method *A*. In both procedures *only* the *altro* 2-epimer was obtained; R_F (*altro* product) 0.57 (3:1:1 petroleum ether–ether–dichloromethane; R_F 0.30 in 9:1:1 petroleum ether–ether–dichloromethane; $[\alpha]_D^{25}$ −29.58° (*c* 1.8, $CHCl_3$); ν_{max}^{film} 3098, 3070, 3039 (arom., alkene), 2995, 2943, 2864, (CH_3) 1500, 1450, (arom. ring), 1385, 1375 (gem CH_3), 733, and 693 (monosubst.

arom. ring); ^{1}H-n.m.r. ($CDCl_3$): δ 7.28–7.4 (m, 5 H, Ph), 4.84 (dd, 1 H, $J_{3,4}$ 6.1, $J_{4,5}$ 1.0 Hz, H-4), 4.78 (dd, 1 H, $J_{3,4}$ 6.1, $J_{2,3}$ 3.8 Hz, H-3 collapses to a doublet (J 6.1 Hz) upon irradiating H-2), 4.54 (ABq, 2 H, $\Delta\nu_{AB}$ 13.9, J_{AB} 12.1 Hz, H-7), 4.41 (dt, 1 H, $J_{1,2}$ 6.7, $J_{2,3}$ 3.8 Hz, H-2), 4.25 (app. t, 1 H, $J_{5,6}$ 3.7 Hz, H-5), 3.58 (dABq, 2 H, $\Delta\nu_{AB}$ 11.4, J_{AB} 10.2, $J_{5,6}$ 3.7 Hz, H-6), 3.37 (dd, 1 H, $\Delta\nu_{AB}$ 26.8, J_{AB} 9.6, $J_{1,2}$ 7.5 Hz, H-1A or H-1B), 3.29 (ABq, 1 H, $\Delta\nu_{AB}$ 19.8, J_{AB} 9.6, $J_{1,2}$ 6.7 Hz, H-1A or H-1B), 1.5 and 1.36 (s, 6 H, $\Delta\nu$ 36.1 Hz, geminal CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 138.06 (s, C-8), 127.80–128.70 (m, C-9–13), 112.8 (s, CMe_2), 83.67 [d, C-3 and C-4 (off-resonance decoupling shows two doublets barely resolved; single line in ^{13}C spectra indicates coincidence)], 83.19 (d, C-2), 81.51 (d, C-5), 73.80 (t, C-7), 71.63 (t, C-6), 26.52 (q, gem CH_3), 25.27 (q, gem CH_3), and 0.954 (t, C-1); *m/z* (c.i.) 405 (MH^+), 91; *m/z* (e.i.) 389 ($M^+ - 15$), 277 and 91.

Anal. Calc. for $C_{16}H_{21}IO_4$: C, 47.54; H, 5.24; I, 31.39. Found: C, 47.77; H, 5.25; I, 31.71.

*2,5-Anhydro-6-*O*-benzyl-1-bromo-3,4-*O*-isopropylidene-*D*-altro-hexitol* (**5**). — Alkene **2** (178 mg, 0.64 mmol) was dissolved in 5 mL of dry tetrachloromethane, cooled to 0°, and 3 mL of 2.5% bromine in tetrachloromethane (0.937 mmol) was added dropwise with stirring. The reaction was complete (t.l.c.) after 45 min. The product was isolated and chromatographed as described for compound **4** to give 78 mg (34%) of compound **5**.

Compound **5** (*altro* isomer) showed R_F 0.35 in 9:1:1 petroleum ether–ether–dichloromethane; ν_{max}^{film} 3105, 3080, 3045 (arom. alkene), 2998, 2957, 2879 (CH_3), 1502, 1465 (arom. ring) 1390, 1380 (gem CH_3), 738, and 698 cm^{-1} (monosubst. arom.); ^{1}H-n.m.r. ($CDCl_3$): δ 7.29–7.40 (m, 5 H, Ph), 4.84 (dd, 1 H, $J_{3,4}$ 6.2, $J_{4,5}$ 0.8 Hz, H-4), 4.78 (dd, 1 H, $J_{3,4}$ 6.2, $J_{2,3}$ 3.8 Hz, H-3, collapsed to a doublet having J 6.2 Hz upon irradiating H-2), 4.53 (ABq, 2 H, $\Delta\nu_{AB}$ = 16.2, J_{AB} 12.1 Hz, H-7), 4.40 (dt, 1 H, $J_{1,2}$ 6.70, $J_{2,3}$ 3.8 Hz, collapsed to a triplet upon irradiating H-3, H-2), 4.24 (app. t, 1 H, $J_{5,6}$ 3.6 Hz, H-5), 3.43–3.65 (4 H, complex due to the two dd's for H-1A,B overlapping with the doublet of an ABq, for H-6A,B–H-5 coupling; decoupling of H-5 simplified the splitting somewhat but no J values could be determined directly from the spectra; H-1A,B and H-6A,B), 1.50 and 1.36 (s, 6 H, $\Delta\delta$ 36.5 Hz, geminal CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 138.03 (s, C-8), 127.75–128.9 (m, C-9–13), 112.88 (s, CMe_2), 83.60 (d, C-3 and C-4 coincident), 82.63 (d, C-2), 81.51 (d, C-5), 73.81 (t, C-7), 71.72 (t, C-6), 29.29 (t, C-1), 26.49 (q, gem CH_3), and 25.20 (q, gem CH_3); *m/z* (c.i.) 359 (MH^+ ^{81}Br), 357 (MH^+ ^{79}Br), 267, 265, and 91; *m/z* (e.i.) 358 (M^+ ^{81}Br), 356 (M^+ ^{79}Br), 343, 341, 219, 171, and 149.

Anal. Calc. for $C_{16}H_{21}BrO_4$: C, 53.79; H, 5.92; Br, 22.37. Found: C, 53.51; H, 5.78; Br, 22.16.

*2,5-Anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-1-phenylseleno-*D*-altro-hexitol* (**6**). — *Method A.* Compound **6** was made by the method of Nicolau *et al.*[11]. Chromatography with 3:1:1 petroleum ether–ether–dichloromethane yielded 108 mg of a yellow oil (**6**, 46%). No attempt was made to recover unreacted starting material (t.l.c. assay).

Method B. Compound **6** was also made by using 5 eq of solid $NaHCO_3$ in the mixture[3]. Chromatography used the aforementioned solvent-system and no attempt was made to recover unreacted starting-material. After chromatography, 107 mg (42%) of **6** was obtained.

Only the *altro* isomer (**6**) was formed by either method; R_F 0.44 in 3:1:1 petroleum ether (35–60°)–ether–dichloromethane; ν_{max}^{film} 3080, 3050, (arom., alkene), 3000, 2954, 2874, (CH_3), 1590, 1505, 1490 (arom. ring), 1390, 1380 (gem methyl), 740, and 695 (monosubst. arom.); ^{1}H-n.m.r. ($CDCl_3$): δ 7.25–7.68 (m, 10 H, Ph), 4.83 (d, 1 H, $J_{3,4}$ 6.5 Hz, H-4), 4.81 (dd, 1 H, $J_{3,4}$ 6.5, $J_{2,3}$ 3.3 Hz, H-3), 4.52 (ABq, 2 H, $\Delta\delta_{AB}$ 5.8, J_{AB} 11.6 Hz, H-7), 4.36 (dt, 1 H, $J_{2,3}$ 3.3, $J_{1,2}$ 7.0 Hz, collapsed to a doublet upon irradiating H-1A,B and a triplet upon irradiating H-3, H-2), 4.27 (app. t, 1 H, $J_{5,6}$ 3.9 Hz, H-5), 3.58 (dd, 2 H, $J_{5,6}$ 1.0, $J_{6A,6B}$ 3.9 Hz, H-6), 3.20 (d, 2 H, $J_{1,2}$ 7.0 Hz, H-1), 1.55, 1.38 (s, 6 H, $\Delta\delta$ 34.35 Hz, geminal CH_3) (several small resonances and a singlet at δ 4.6 were also observed); ^{13}C-n.m.r. ($CDCl_3$): δ 138.09 (s, C-8), 133.05 (s, C-14), 127.11–132.88 (m, C-9–12, C-15–19), 112.65 (s, CMe_2), 83.49 (d, C-4), 83.27 (d, C-3), 81.87 (d, C-1), 81.74 (d, C-5), 73.69 (t, C-7), 71.66 (t, C-6), 26.50 (q, gem CH_3), 26.40 (t, C-1), and 25.20 (q, gem CH_3); *m/z* (c.i.) 434 (MH^+, ^{79}Se), 377, 91.

Anal. Calc. for $C_{22}H_{26}O_4Se$: C, 60.97; H, 6.05. Found: C, 61.15; H, 6.37.

General procedure for mercury-mediated cyclization[12], *and conversion of alkene* **2** *into* **4**. — Alkene **2** (72.5 mg, 0.261 mmol) was dissolved in 3 mL of dry THF. Solid mercuric acetate (100 mg, 0.313 mmol, 1.5 eq) was quickly added at 24° and the mixture was stirred for 15 h at 24°. A solution of 60 mg (0.47 mmol, 1.8 eq) of iodine in 1 mL of dry THF was added to the mixture at 24° until the red color of iodine persisted[13]. The mixture was stirred at 24° an additional 2 h, during which time an additional 23 mg of solid iodine was added (total, 2.5 eq of iodine). The reaction was quenched by the addition of solid Na_2SO_3. The liquid was decanted and the flask rinsed 3 times with 5-mL portions of ether. The organic layers were combined and the solvent was removed under diminished pressure. Chromatography of the residue on 3 g of silica gel with 3:1:1 petroleum ether–ether–dichloromethane yielded 57 mg (54%) of **4**, which had spectral characteristics and t.l.c. behavior identical with the known iodo compound namely purely the *altro* isomer).

ACKNOWLEDGMENTS

We thank the University of California, Irvine, Research Committee for partial support of this research and the National Science Foundation for financial support toward the purchase of the n.m.r. spectrometers.

REFERENCES

1 H. P. ALBRECHT, D. B. REPKE, AND J. G. MOFFATT, *J. Org. Chem.*, 38 (1973) 1863–1840.
2 J. A MONTGOMERY AND K. HEWSON, *J. Heterocycl. Chem.*, 7 (1970) 443–445.

3 J. MANN AND P. D. KANE, *J. Chem. Soc., Chem. Commun.*, (1983) 224–226.
4 (*a*) L. HOUGH, J. K. N. JONES, AND D. L. MITCHELL, *Can. J. Chem.*, 36 (1958) 1720–1728. (*b*) H. OGURA, H. TAKAHASHI, AND T. ITOH, *J. Org. Chem.*, 37 (1972) 72–75.
5 M. KISO AND A. HASEGAWA, *Carbohydr. Res.*, 52 (1976) 95–101.
6 E. HUNGERBUHLER AND D. SEEBACH, *Helv. Chim. Acta*, 64 (1981) 687–702.
7 (*a*) R. KUHN, I. LOW, AND H. TRISCHMANN, *Chem. Ber.*, 90 (1957) 203–220; (*b*) P. CAMPS, J. CARDELLACH, J. FOUT, R. M. ORTUNO, AND O. PONSATI, *Tetrahedron*, 15 (1982) 2395–2402.
8 R. E. IRELAND, R. C. ANDERSON, R. BADOUD, B. J. FITSIMMONS, G. J. MCGARVEY, S. THAISRIVONGS, AND C. S. WILCOX, *J. Am. Chem. Soc.*, 105 (1983) 1988–2006.
9 M. T. FLAVIN AND M. C. LU, *Tetrahedron Lett.*, 24 (1983) 2335–2338.
10 P. A. BARTLETT AND J. MYERSON, *J. Am. Chem. Soc.*, 100 (1978) 3950–3952.
11 K. C. NICOLAOU, R. L. MAGOLDA, W. J. SIPIO, W. E. BARNETTE, Z. LYSENKO, AND M. M. JOULLIÉ, *J. Am. Chem. Soc.*, 102 (1980) 3784–3793.
12 (*a*) J. R. POUGNY, M. A. M. NASSOR, AND P. SINAY, *J. Chem. Soc., Chem. Commun.*, (1981) 375–376; (*b*) J. J. TUFARIELLO AND M. M. HOVEY, *J. Am. Chem. Soc.*, 92 (1970) 3221–3222.
13 M. NISHIZAWA, H. TAKENAKA, H. NISHIDE, AND Y. HAYASHI, *Tetrahedron Lett.*, 24 (1983) 2581–2584.
14 R. W. MCCLARD, *Tetrahedron Lett.*, 24 (1983) 2631–2634.
15 H. OHRUI, G. H. JONES, J. G. MOFFATT, M. L. MADDOX, A. T. CHRISTENSEN, AND S. K. BYRAM, *J. Am. Chem. Soc.*, 97 (1975) 4602–4613.
16 J. A. SECRIST, III AND T. J. COUSINEAU, *J. Org. Chem.*, 44 (1979) 4351–4358.
17 F. FREEMAN AND K. D. ROBARGE, unpublished results.
18 P. A. BARTLETT, *Tetrahedron*, 36 (1980) 2–72, and references therein.
19 J. MANN AND P. D. KANE, *J. Chem. Soc., Perkin Trans. I*, (1984) 657–660.