Stereoselective Cyclizations of Unsaturated Esters derived from 2,3-*O*-Isopropylidene-D-ribose

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We describe the preparation of several α,β-unsaturated esters by means of Wittig reactions with 5-*O*-dimethyl-t-butylsiloxy-2,3-*O*-isopropylidene-D-ribose, and methods for the stereoselective cyclization of these compounds to produce 1-β-substituted 1-deoxyribose derivatives. One of these derivatives (**1b**; R = $SiMe_2Bu^t$) was converted into a protected form of dihydroshowdomycin (**8**). Reaction of the diene ester, methyl (6*S*,7*S*,8*R*)-8,9-dihydroxy-6,7-*O*-isopropylidene-3-methyl (2*E*,4*Z*)-non-2,4-dienoate (**1c**; R = H) with benzeneselenenyl chloride produced 2-hydroxymethyl-3,4-*O*-isopropylidene-5-phenylselenenyl-6-[3-methoxycarbonyl-(*E*)prop-2-en-2-yl]pyran (**7**), for which an *X*-ray structure was obtained. Crystals were monoclinic, space group $P2_1$, $Z = 2$, with $a = 10.591(8)$, $b = 10.730(8)$, $c = 9.832(9)$ Å, $\beta = 109.2(1)°$. 1 513 Independent reflections above background were measured on a diffractometer; the structure was refined to *R* 0.074.

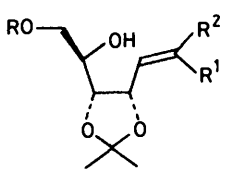
The reactions of P-ylides at the anomeric centre of D-ribose have been widely used for the synthesis of 1-alkyl-1-deoxyribose derivatives,[1] and as key steps in the construction of C-nucleosides.[2] In our earlier paper,[2c] we described a method for the stereoselective cyclization of the Wittig reaction product (**1a**; R = $SiMe_2Bu^t$)† to provide exclusively the 1β-substituted 1-deoxyribose derivative (**2a**; R = $SiMe_2Bu^t$). Here, we report an alternative method of cyclization, and an unexpected mode of cyclization for the diene ester (**1c**; R = H).

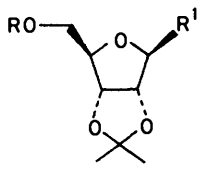
The unsaturated ester (**1a**; R = $SiMe_2Bu^t$) was prepared from 5-*O*-dimethyl-t-butylsiloxy-2,3-*O*-isopropylidene-D-ribose by reaction with ethoxycarbonylethylidenetriphenylphosphorane in dichloromethane (6 h at 40 °C). The major product (85% isolated yield) was shown to be the 2*E* isomer through the use of n.O.e. difference analysis. In particular, there were highly significant effects observed between protons resonating at 1.88 and 4.95 p.p.m. (olefinic methyl and 4-H); and at 6.70 and 3.59 p.p.m. (olefinic H and 6-H). The δ value for 4-H is also similar to those observed by Buchanan *et al.*[3] and Freeman *et al.*[4] for the analogous *E* esters (**3a**) (4.78 p.p.m.) and (**3b**) (4.85 p.p.m.). Values for the *Z* esters (**4a**) and (**4b**) differ significantly (5.65 and 5.68 p.p.m. respectively). Clearly the 4-H is deshielded in the *Z* isomers.

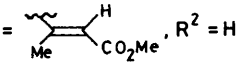
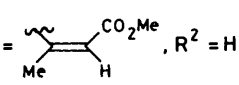
Reaction of this ester with 2 equiv. of tetrabutylammonium fluoride (THF, 2 h, room temp.) provided a good yield (*ca.* 70%) of the C-riboside (**2b**; R = H), albeit as a mixture of stereoisomers at C-2 in a ratio of *ca.* 1:1. Both stereoisomers were 1-β-ribosides since the isopropylidene methyls resonated at δ 1.51 and 1.31 (Δδ 0.20), and δ 1.51 and 1.32 (Δδ 0.19) respectively (*cf.* Moffatt's paper, ref. 1*c*); and the remainder of the ^1H n.m.r. spectrum was assigned with the help of a 2d COSY experiment. No α-ribosides were obtained.

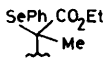
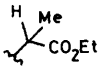
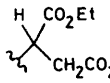
In a similar sequence of reactions, the unsaturated diester (**1b**; R = $SiMe_2Bu^t$) was prepared, and cyclization effected as before. A mixture of β-ribosides (**2c**; R = H), stereoisomeric at C-3, was produced (70%, ratio 3:2). The acetonide methyls resonated at δ 1.29 and 1.48 (Δδ 0.19) and 1.30 and 1.49 (Δδ 0.19). The stereochemistry of the intermediate diester (**1b**; R = $SiMe_2Bu^t$) was again established using n.O.e. difference analysis with significant effects observed between the olefinic proton (6.92 p.p.m.) and 7-H (3.64 p.p.m.), and between 2-H (3.42 p.p.m.) and 5-H (4.91 p.p.m.).

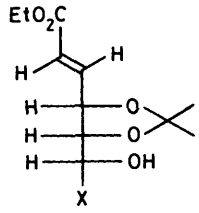
† This was erroneously assigned 2*Z* stereochemistry in this publication.



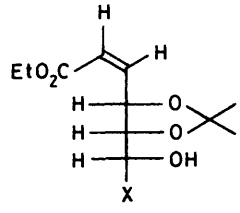


(**1**) **a**; R^1 = Me, R^2 = CO_2Et
b; R^1 = CH_2CO_2Et, R^2 = CO_2Et
c; R^1 =  , R^2 = H
d; R^1 =  , R^2 = H

(**2**) **a**; R′ = 
b; R′ = 
c; R′ = 



(**3**)
a; X = H
b; X = CH_2OBzl

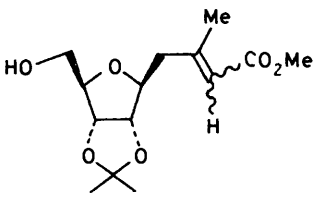


(**4**)
a; X = H
b; X = CH_2OBzl

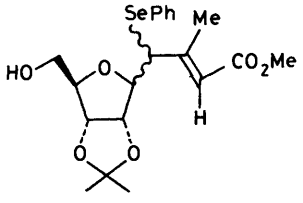
With the results of these model studies in hand, cyclization of the diene ester (**1c**; R = H) was investigated. This compound was prepared most efficiently from 2,3-*O*-isopropylidene-D-ribose and (*E*)-3-methoxycarbonyl-2-methylpropenyl-1-triphenylphosphonium bromide[5] in the presence of 1,2-epoxybutane.[6] Two isomers were obtained (**1c**; R = H) and (**1d**; R = H) in a ratio of 4:1 and in a combined yield of 40% after careful flash chromatography. A similar experiment using the 5-*O*-dimethyl-t-butylsiloxy derivative of ribose acetonide produced a similar ratio of products (**1c**; R = $SiBu^tMe_2$) and (**1d**; R = $SiBu^tMe_2$) but with an improved yield (65%). All four isomers exhibited a 12 Hz coupling between 4- and 5-H, and were thus assigned 4*Z* stereochemistry. The stereochemistry of

the other double bond was assigned on the basis of the δ value for 4-H: 6.2 and 6.16 p.p.m. for the 2*E*,4*Z* isomers (**1c**) and 6.55 and 6.52 p.p.m. for the 2Z,4Z isomers (**1d**). Such deshielding of the γ-protons of 2*Z* sorbate derivatives is well established.[7]

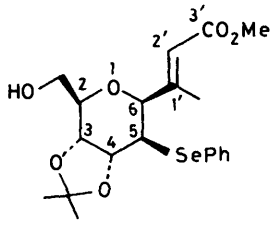
Attempted cyclization of the diene mixture [(**1c**)/(**1d**) ratio 4:1; R = $SiMe_2Bu^t$) was carried out with tetrabutylammonium fluoride, as before, with formation of some of the desired product (**5**) (30% yield), but with obtention of the diene (**1c**; R = H) as the major product (45%). Reaction of this with an excess of methoxycarbonylmethylidenetriphenylphosphorane (as base) in refluxing acetonitrile, yielded compound (**5**) in 55% isolated yield. In both instances, the n.m.r. spectra were consistent[1c] with sole formation of 1-β-alkyl products (δ_H 1.32 and 1.52 p.p.m. Δδ 0.20 p.p.m. for the isopropylidene methyls; δ ^{13}C 25.407 and 27.358 p.p.m. for the isopropylidene carbons) albeit as a mixture of geometrical isomers.



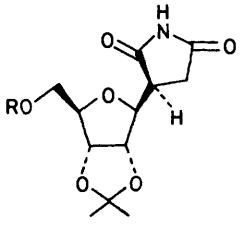
(**5**)



(**6**)



(**7**)



(**8**) R = $SiMe_2Bu^t$

(**9**) R = H

When cyclization of the diene (**1c**; R = H) was attempted using benzeneselenenyl chloride, which we had previously used to good effect for simple unsaturated esters,[2c] the major product was an inseparable mixture of α- and β-isomers (**6**), and the other minor product proved to be the pyranose derivative (**7**). Complete rearrangement of (**6**) into (**7**) could be achieved if a 1:1 mixture in $CDCl_3$ containing a little PhSeCl was set aside for 12 h at room temperature. The n.m.r. spectrum of (**7**) was fully consistent with the structure shown, but an *X*-ray structure determination was also carried out, and this is discussed below.

The synthetic utility of these new compounds (**5**), (**6**), and (**7**) has yet to be investigated, but the diester (**1b**; R = $SiBu^tMe_2$) has been converted into a protected form of dihydroshowdomycin[8] (**8**) by reaction with liquid ammonia–methanol. Interestingly, only one diastereoisomer was produced (3*S*), with spectroscopic data consistent with those already reported for the corresponding acetonide of dihydroshowdomycin (**9**).[9]

Discussion of Crystallographic Data for Compound (**7**).—The structure of the molecule is shown in the Figure and confirms the stereochemistry described above. The CO_2Me and Me groups are mutually *cis* across the double bond. Atoms C(21), C(22), C(23), and C(24) are coplanar within experimental error as indeed are atoms C(25), O(26), C(27), and O(28). The two

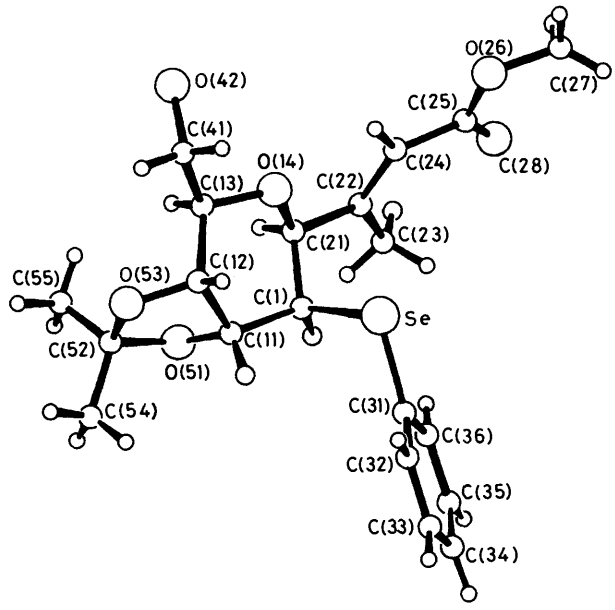


Figure. Structure of compound (**7**) with crystallographic numbering

planes intersect at an angle of 7.2°. The conformation of the five-membered ring is an envelope with C(11) 0.54 Å from the plane of atoms C(12), O(51), C(52), and O(53). These four atoms are coplanar within experimental error. The six-membered ring has a slightly distorted chair conformation with torsion angles of 42.5, −50.7, 66.0, −69.0, 56.1, and −45.3°.

There is an intermolecular hydrogen bond between O(42)–H and O(28) ($-x$, 0.5 + y, $-z$) with an O ••• O distance of 2.73 Å. There are no other intermolecular distances less than the sum of van der Waals radii.

Experimental

I.r. spectra were recorded on a Perkin-Elmer 157 double-beam grating spectrophotometer or a Perkin-Elmer 1420 ratio recording spectrophotometer (liquid films for oils, Nujol mulls for solids). ^1H N.m.r. spectra were recorded with a Varian T-60 (60 MHz), a Varian HA100 (100 MHz) or a Perkin-Elmer R34 (220 MHz) instrument. 400 MHz ^1H N.m.r. spectra were recorded at the Chemistry Department, Warwick University on a Bruker WH400 instrument. Tetramethylsilane was used as the internal standard. ^{13}C N.m.r. spectra were recorded at the City of London Polytechnic on a Jeol FX90Q (90 MHz) instrument.

Accurate mass spectra were obtained from P.C.M.U. (Harwell) using a VG Analytical ZAB-IF Spectrometer and associated data system. Elemental analyses were performed at Butterworth Laboratories Ltd., or at the Chemistry Department, City University.

Analytical t.l.c. was performed on plastic sheets precoated with 0.25 mm of silica gel containing a fluorescent indicator UV_{254} ('Polygram', supplied by Camlab, Cambridge). The t.l.c. strips were viewed under u.v. light and then sprayed with dilute $H_3PO_4 \cdot 12MoO_3 \cdot 24H_2O$ solution (alcoholic) or dilute $KMnO_4$ solution (aqueous). Flash chromatography was performed on silica gel of 32—63 μm particle size ('Woelm' silica gel, supplied by Park Scientific Ltd.).

Purification of solvents and reagents was generally carried out according to Perrin.[11] Solvents were usually dried by refluxing over a drying agent for 2 h followed by distillation: for example, THF was distilled from CaH_2, DME from $LiAlH_4$, and pyridine from BaO. The solvents were then stored in the

dark over 4A sieves, in a tightly stoppered bottle, under an atmosphere of nitrogen. Acetone and DMF were dried over 3A sieves. Unless otherwise stated light petroleum refers to the range with b.p. 40–60 °C.

Ethyl (4S,5R,6R)-7-*Dimethyl-t-butylsiloxy*-6-*hydroxy*-4,5-O-*isopropylidene*-2-*methylhept*-2-*enoate* (**1a**).—A solution of (2,3-*O*-isopropylidene-5-*O*-dimethyl-t-butylsiloxy-β-D-ribofuranose) (1.93 g, 10 mmol) and ethoxycarbonylethylenetriphenylphosphorane (5.43 g, 15 mmol) in dichloromethane (50 ml) was refluxed for 6 h under an atmosphere of nitrogen, and then stirred at room temperature for a further 60 h. The homogeneous reaction mixture was concentrated and purified by flash chromatography using light petroleum–diethyl ether (2:1) as eluant to give an oil (3.62 g, 85%) which was primarily the (*E*)-ester, but which contained small amounts of the (*Z*)-isomer (9:1), R_F 0.43 (light petroleum–diethyl ether, 3:2), m.p. 47 °C; $\nu_{max.}$ 3 500, 2 990, 2 960, 2 940, 2 860, 1 720, 1 660, 1 475, 1 465, 1 385, 1 370, 1 320, 1 250, 1 220, 1 170, 1 120, 1 060, 910, 840, and 780 cm^{-1}; δ_H ($CDCl_3$, 220 MHz), 0.04 (6 H, s, $SiMe_2$), 0.9 (9 H, s, SiBu^t), 1.25 (3 H, t, *J* 7 Hz, ester Me), 1.32 and 1.44 (together 6 H, 2 s, CMe_2), 1.88 (3 H, d, *J* 2.4 Hz, 2-Me), 2.44 (1 H, d, *J* 5.5 Hz, OH), 3.55—3.76 (3 H, m, 6-H + 7-H_2), 4.06 (1 H, dd, *J* 8.9 and 6 Hz, 5-H), 4.14 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.95 (1 H, dd, *J* 9.5, 6 Hz, 4-H), and 6.7 (1 H, dq, *J* 9.5, 2 Hz, 3-H) (Found: C, 58.65; H, 9.4. Calc. for $C_{19}H_{36}O_6Si$: C, 58.73; H, 9.34%).

Ethyl (5S,6R,7R)-8-*Dimethyl-t-butylsiloxy*-7-*hydroxy*-5,6-O-*isopropylidene*-3-*ethoxycarbonyloct*-3-*enoate* (**1b**).—A solution of (2,3-*O*-isopropylidene-5-*O*-dimethyl-t-butylsilyl-β-D-ribofuranose) (308 mg, *ca.* 1 mmol) and 1,2-bis(ethoxycarbonyl)-ethylidenetriphenylphosphorane[12] (663 mg, *ca.* 1.5 mmol) in acetonitrile was refluxed for 1 week under an atmosphere of nitrogen. The reaction mixture was then concentrated and purified by flash chromatography using light petroleum–diethyl ether (3:2) as eluant to afford the acyclic compound as a colourless oil (361 mg, *ca.* 75%) which crystallised with time, R_F 0.37 (light petroleum–diethyl ether, 3:2), m.p. 45 °C; $\nu_{max.}$ 3 500, 2 990, 2 940, 2 890, 1 730, 1 520, 1 380, 1 350, 1 070, 870, 760, and 740 cm^{-1}; δ_H ($CDCl_3$, 400 MHz), 0.07 (6 H, s, $SiMe_2$), 0.89 (9 H, s, SiBu^t), 1.23 (3 H, t, *J* 7 Hz, ester Me), 1.27 (3 H, t, *J* 7.1 Hz, ester Me), 1.35 and 1.49 (together 6 H, s, CMe_2), 2.28 (1 H, d, *J* 5.7 Hz, OH), 3.42 (2 H, dd, J_{gem} 16.8 Hz, 2-H_2), 3.61—3.66 (1 H, m, 7-H), 3.66—3.70 (1 H, dd, *J* 10.1 Hz and 5 Hz, 8-H), 3.78—3.81 (1 H, dd, *J* 10.1, 2.6 Hz, 8-H), 4.08—4.24 (5 H, m, 2 × ester CH_2), 4.89—4.92 (1 H, dd, *J* 9.4, 6 Hz, 5-H), and 6.92 (1 H, d, *J* 9.4 Hz, 4-H); δ_C($CDCl_3$) −5.39 and −5.33 ($SiMe_2$), 14.13 (2 × ester Me), 18.41 (CMe_3), 25.65 and 28.14 (CMe_2), 25.992 (CMe_3), 32.80 (2-C), 61.13 (2 × ester CH_2) 64.68 (C-8), 69.47 (C-6), 74.60 (C-5), 77.85 (C-7), 109.86 (CMe_2), 128.23 (C-3), 139.47 (C-4), and 166.42 and 171.35 (2 × ester CO); *m/z* 403.1788 ($M^+ - C_4H_9$), $C_{18}H_{31}O_8Si$ requires 403.1778) and 299.0961 ($M^+ - 2 \times Me$, $-C_4H_9$, −acetonide, 97%. $C_{13}H_{19}O_6Si$ requires 299.0945) (Found: C, 56.9; H, 8.85. Calc. for $C_{22}H_{40}O_8Si$ C, 57.36; H, 8.75%).

Methyl (6S,7R,8R)-6,7-O-*Isopropylidene*-8,9-*dihydroxy*-3-*methylnon*-2,4-*dienoate:* (2E,4Z)- (**1c**; R = H) and (2Z,4Z)- (**1d**; R = H) *Isomers.*—2,3-*O*-Isopropylidene-D-ribose (1.9 g, 10 mmol), (*E*)-3-methoxycarbonyl-2-methylallyltriphenylphosphonium bromide (5.15 g, 11.3 mmol), 1,2-epoxybutane (a freshly prepared 1M solution in acetonitrile; 11.3 cm^3) were combined in a glass tube (equipped with constriction and B14 ground glass adaptor) diluted with acetonitrile (14 cm^3) and sequentially frozen, evacuated, thawed to effectively de-gas, re-frozen, re-evacuated, and sealed *in vacuo*. The contents were allowed to thaw, the tube heated at 90 °C for 18 h, cooled, frozen, and opened carefully. After concentration of the resultant pale-yellow solution, purification was effected by column chromatography (*a*) on silica, eluant diethyl ether (separated product from triphenylphosphine oxide, excess of ylide, and phosphonium salt); (*b*) the second column, on silica, eluant chloroform–ethanol (10:1) (separated product from unchanged starting material and partially discriminated between isomers), yielding three fractions, *i.e.* pure (**1d**; R = H), a mixture, and pure isomer (**1c**; R = H) in a total yield of 1.15 g (40%) and an overall isomeric ratio of *ca.* 4:1 (**1c**):(**1d**); $\nu_{max.}$ (isomeric mixture) 3 400, 2 960, 1 725, 1 640, 1 620, 1 380, and 1 250 cm^{-1}; *m/z* 271.1189 (5%, M^+ − Me. $C_{13}H_{19}O_6$ requires 271.1176); (**1d**; R = H) R_F ($CHCl_3$–EtOH, 10:1) 0.36; (**1c**; R = H) R_F ($CHCl_3$–EtOH, 10:1) 0.28.

(2Z,4Z)-*Isomer* (**1d**; R = H). δ_H (100 MHz, $CDCl_3$) 1.34 and 1.45 (6 H, 2 × s, CMe_2), 2.08 (3 H, d, *J* 1 Hz, 3-Me), 3.66 (3 H, s, ester Me), 3.4—3.9 (3 H, m, 8- and 9-H), 4.08 (1 H, dd, $J_{7,6}$ 6 Hz, $J_{7,8}$ 8 Hz, 7-H), 4.76 (1 H, d, $J_{6,5}$ 10 Hz, $J_{6,7}$ Hz, 6-H), 5.73 (1 H, dd, $J_{5,4}$ 12 Hz, $J_{5,6}$ 10 Hz, 5-H), 5.80 (1 H, m, 2-H), and 6.55 (1 H, d, $J_{4,5}$ 12 Hz, 4-H).

(2E,4Z)-*Isomer* (**1c**; R = H). δ_H (100 MHz, $CDCl_3$) 1.34 and 1.45 (6 H, 2 × s, CMe_2), 2.24 (3 H, d, 3-Me), 3.7 (3 H, s, ester Me), 3.6—3.9 (3 H, m, 8-H and 9-H_2), 4.1 (1 H, m, 7-H), 5.06 (1 H, dd, $J_{6,5}$ 10 Hz, $J_{6,7}$ 6 Hz, 6-H), 5.72 (1 H, dd, $J_{5,4}$ 12 Hz, $J_{5,6}$ 10 Hz, 5-H), 5.90 (1 H, m, 2-H), and 6.20 (1 H, d, $J_{4,5}$ 12 Hz, 4-H).

2,3-O-*Isopropylidene*-β-D-1′-(1′-*ethoxycarbonyl*)*ethylriboside* (**2b**; R = H).—A solution of (**1a**; R = $SiMe_2Bu^t$) (388 mg, 1 mmol) in distilled THF (3 ml) was treated with tetrabutylammonium fluoride (2 ml, 2 mmol) for 2 h at room temperature. The yellow solution was then concentrated and purified by flash chromatography using petroleum–diethyl ether (1:1) to give the cyclised compound as an oil (260 mg, 70%) and as an inseparable mixture of stereoisomers, A and B: R_F (diethyl ether) 0.43; $\nu_{max.}$ 3 500, 2 990, 2 940, 2 860, 1 740, 1 720, 1 460, 1 370, 1 320, 1 255, 1 220, 1 065, 920, 840, and 780 cm^{-1}. [The numbering system already used for compound (**1a**) has been retained for ease of data comparison.] δ_H($CDCl_3$) 1.21—1.24 (12 H, m, 2 CO_2Et, 2-Me), 1.32 and 1.50 (together 6 H, 2 s, CMe_2), 2.55—2.62 (0.5 H, m, 2-H_A), 2.76—2.82 (0.5 H, m, 2-H_B), 3.57—3.63 (1 H, dd, *J* 12, 3.5 Hz, 7-H_A; dd, *J* 12, 3.7 Hz, 7-H_B), 3.74—3.79 (1 H, dd, *J* 12, 3.5 Hz, 7-H_A; dd, *J* 12, 3.7 Hz, 7-H_B), 3.97—4.04 (2 H, m, 3-H + 6-H, both isomers), 4.09—4.18 (2 H, m, ester CH_2, both isomers), 4.43—4.45 (0.5 H, dd, $J_{3,4}$ 4.5 Hz, $J_{4,5}$ 6.5 Hz, 4-H_A), 4.63—4.67 (0.5 H, dd, $J_{4,5}$ 7 Hz and $J_{3,4}$ 4 Hz, 4-H_B), 4.66—4.69 (0.5 H, dd, $J_{4,5}$ 6.5 Hz and $J_{5,6}$ 4.5 Hz, 5-H_A), and 4.71—4.74 (0.5 H, dd, $J_{4,5}$ 7 Hz and $J_{5,6}$ 4.8 Hz, 5-H_B); *m/z* 259.1180 (65%, M^+ − Me. $C_{12}H_{19}O_6$ requires 259.1176), 229.1067 (28%, M^+ − OEt. $C_{11}H_{17}O_5$ requires 229.1071) (Found: C, 56,9; H, 8.10. $C_{13}H_{22}O_6$ requires C, 56,92; H 8.08%).

2,3-O-*Isopropylidene*-β-D-1′-(1′,2′-*diethoxycarbonylethyl*)-*ribofuranoside* (**2c**; R = H).—A solution of (**1b**; R = $SiMe_2Bu^t$) (384 mg, *ca.* 0.8 mmol) in distilled THF (3 ml) was treated with tetrabutylammonium fluoride for 2 h at room temperature. The yellow solution was then concentrated and purified by flash chromatography using ethyl acetate–petroleum (1:1) as eluant to give the cyclised compound (**2c**; mixture of stereoisomers A and B) as a colourless oil (242 mg, 70%), R_F 0.35 (ethyl acetate–light petroleum, 3:2); $\nu_{max.}$ 3 450, 2 980, 2 930, 1 730, 1 460, 1 375, 1 210, 1 150, and 800 cm^{-1} [The numbering system for (**1b**) has been retained]; δ_H ($CDCl_3$, 400 MHz) 1.23 (3 H, t, *J* 5.5 Hz, ester Me), 1.24 (3 H, t, *J* 7.5 Hz, ester Me), 1.30 and 1.48, 1.30 and 1.49 (6 H, singlets, CMe_2, ratio 6:4), 2.49—2.54 (0.4 H, dd, *J* 16.6, 5.3 Hz, 2-H_A), 2.58—2.64 (0.6 H, dd, *J* 6.2, 16.9 Hz, 2-H_B), 2.73—2.79 (0.6 H, dd, *J* 7.6, 16.9 Hz, 2-H_B), 2.80—2.86 (0.4 H, dd, *J* 9.4, 16.6 Hz, 2-H_A), 3.09 (1 H, m, 3-H both isomers), 3.56—3.78 (2 H, m, 8-H both isomers), 4.00—4.06 (2 H, m, 4- and 7-H

Table 1. Atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
Se(1)	4 733(1)	10 000[a]	1 772(1)
C(31)	6 370(11)	9 132(13)	1 879(13)
C(32)	7 548(13)	9 831(17)	2 242(17)
C(33)	8 721(16)	9 216(18)	2 269(23)
C(34)	8 665(16)	7 984(16)	1 835(20)
C(35)	7 518(15)	7 338(15)	1 462(17)
C(36)	6 346(14)	7 891(12)	1 462(16)
C(1)	4 131(12)	8 927(10)	3 048(13)
C(11)	4 791(14)	9 356(12)	4 647(15)
C(12)	4 191(14)	10 526(13)	5 037(16)
C(13)	2 653(12)	10 512(13)	4 400(14)
O(14)	2 239(8)	10 228(7)	2 889(8)
C(21)	2 597(13)	8 993(12)	2 637(14)
C(22)	1 915(13)	8 593(13)	1 120(17)
C(23)	2 157(17)	7 287(15)	763(19)
C(24)	1 139(13)	9 424(15)	173(15)
O(26)	−104(12)	10 204(14)	−2 053(10)
C(27)	−677(20)	10 104(37)	−3 261(17)
C(25)	453(15)	9 168(17)	−1 397(18)
O(28)	440(16)	8 177(19)	−1 938(16)
O(51)	4 622(9)	8 461(8)	5 599(9)
C(52)	4 855(15)	9 109(15)	6 974(17)
O(53)	4 591(9)	10 428(9)	6 576(8)
C(54)	3 846(17)	8 608(17)	7 583(17)
C(55)	6 282(15)	8 949(16)	7 894(16)
C(41)	2 064(14)	11 771(12)	4 553(15)
O(42)	665(9)	11 692(9)	4 284(11)

[a] Parameter fixed.

Table 2. Molecular dimensions: distances (Å) and angles (°)

Se(1)–C(31)	1.939(12)	C(13)–C(41)	1.516(18)
Se(1)–C(1)	1.958(12)	O(14)–C(21)	1.422(15)
C(31)–C(32)	1.397(19)	C(21)–C(22)	1.490(19)
C(31)–C(36)	1.391(19)	C(22)–C(23)	1.487(21)
C(32)–C(33)	1.399(23)	C(22)–C(24)	1.354(22)
C(33)–C(34)	1.384(25)	C(24)–C(25)	1.500(20)
C(34)–C(35)	1.341(23)	O(26)–C(27)	1.463(18)
C(35)–C(36)	1.375(21)	O(26)–C(25)	1.322(24)
C(1)–C(11)	1.564(17)	C(25)–O(28)	1.187(24)
C(1)–C(21)	1.541(18)	O(51)–C(52)	1.468(18)
C(11)–C(12)	1.512(18)	C(52)–O(53)	1.470(20)
C(11)–O(51)	1.393(16)	C(52)–C(54)	1.487(23)
C(12)–C(13)	1.542(18)	C(52)–C(55)	1.494(19)
C(12)–O(53)	1.435(17)	C(41)–O(42)	1.419(17)
C(13)–O(14)	1.436(15)		
C(31)–Se(1)–C(1)	99.9(5)	C(13)–O(14)–C(21)	111.8(9)
Se(1)–C(31)–C(32)	117.6(10)	C(1)–C(21)–O(14)	108.4(9)
Se(1)–C(31)–C(36)	121.0(9)	C(1)–C(21)–C(22)	111.8(10)
C(32)–C(31)–C(36)	121.1(12)	O(14)–C(21)–C(22)	111.9(11)
C(31)–C(32)–C(33)	117.7(16)	C(21)–C(22)–C(23)	116.3(14)
C(32)–C(33)–C(34)	119.8(15)	C(21)–C(22)–C(24)	118.9(12)
C(33)–C(34)–C(35)	121.4(16)	C(23)–C(22)–C(24)	124.8(14)
C(34)–C(35)–C(36)	120.9(16)	C(22)–C(24)–C(25)	124.5(14)
C(31)–C(36)–C(35)	119.0(13)	C(27)–O(26)–C(25)	114.6(20)
Se(1)–C(1)–C(11)	109.8(8)	C(24)–C(25)–O(26)	109.6(14)
Se(1)–C(1)–C(21)	110.0(8)	C(24)–C(25)–O(28)	123.7(18)
C(11)–C(1)–C(21)	109.5(10)	O(26)–C(25)–O(28)	126.7(16)
C(1)–C(11)–C(12)	114.4(11)	C(11)–O(51)–C(52)	105.8(10)
C(1)–C(11)–O(51)	111.0(9)	O(51)–C(52)–O(53)	104.6(10)
C(12)–C(11)–O(51)	104.2(10)	O(51)–C(52)–C(54)	105.9(12)
C(11)–C(12)–C(13)	111.4(11)	O(53)–C(52)–C(54)	110.9(13)
C(11)–C(12)–O(53)	101.8(10)	O(51)–C(52)–C(55)	109.4(12)
C(13)–C(12)–O(53)	109.5(12)	O(53)–C(52)–C(55)	109.8(13)
C(12)–C(13)–O(14)	110.1(11)	C(54)–C(52)–C(55)	115.6(14)
C(12)–C(13)–C(41)	111.5(11)	C(12)–O(53)–C(52)	108.4(9)
O(14)–C(13)–C(41)	107.3(10)	C(13)–C(41)–O(42)	111.5(10)

both isomers), 4.08—4.19 (4 H, m, ester CH_2, both isomers), 4.53—4.60 (0.4 H, dd, $J_{5,6}$ 6.6 Hz and $J_{5,4}$ 4.6 Hz, 5-H_A), 4.61—4.63 (0.6 H, dd, $J_{5,6}$ 6.7 Hz and $J_{5,4}$ 4.5 Hz, 5-H_B), and 4.67—4.69 (1 H, m, 6-H both isomers); *m/z* 331.1387 (46%, M^+ − Me. $C_{15}H_{23}O_8$ requires 331.1386), 301.1287 (20%, M^+ − OEt. $C_{14}H_{21}O_7$ requires 301.1287), and 255.0846 (45%, M^+ − OEt − EtOH. $C_{12}H_{15}O_6$ requires 255.0864) (Found: C, 56.0; H, 7.45. $C_{16}H_{26}O_8$ requires C, 55.48; H, 7.56%).

Methyl 4-(2′,3′-O-*Isopropylidene*-β-D-*ribofuranosyl*)-3-*methylbutenoate* (**5**).—*Procedure: Part A.* A solution of methyl (6*S*,7*S*,8*R*)-6,7-*O*-isopropylidene-8-hydroxy-9-dimethyl-t-butylsiloxy-3-methylnon-2,4-dienoate [(**1c**) and (**1d**), R = $SiMe_2Bu^t$] (12 g, 30 mmol) in THF (70 cm^3) was stirred under an atmosphere of nitrogen at +5 °C. Anhydrous tetrabutylammonium fluoride (benzene azeotroped) (30 mmol) in THF (50 cm^3) was added dropwise, the bath temperature held at +5 °C for 30 min and then increased to 335—40 °C for a further 1 h. The reaction mixture was poured into saturated brine (100 cm^3) and extracted with dichloromethane (100 cm^3); this extract was washed with further brine (×2) dried, and concentrated. Cyclized and uncyclized products were separated by flash chromatography, eluant diethyl ether to remove the less polar cyclic material (**5**) (2.83 g, 10 mmol) (*ca.* 30% changing to diethyl ether–methanol (10:1) to elute all acyclic products [(**1c**) and (**1d**), R = H] (3.96 g, 13.9 mmol, *ca.* 47%).

Part B. The acyclic desilylated diene (3.96 g, 13.9 mmol) isolated from the previous stage was refluxed in acetonitrile solution with methoxycarbonylmethylidene-triphenylphosphorane (4.7 g, 14 mmol) under a nitrogen atmosphere for 50 h. The solvent was removed under reduced pressure and the product purified by flash chromatography (eluant diethyl ether) to yield an oil (2.195 g, 7.7 mmol, 55%). Total yield for the two stages was 17.7 mmol (59%) and analytical data is given for the *Z*/*E* isomeric mixture; R_F (eluant diethyl ether) 0.33; $\nu_{max.}$ 3 500, 2 990, 2 940, 1 720, 1 650, 1 440, 1 385, 1 375, 1 220, 1 150, 1 080, and 865; δ_H (220 MHz, $CDCl_3$) 1.32 and 1.52 (together 6 H, 2 s, CMe_2), 1.96 and 2.22 [3 H together, d, *J* 1.5 Hz, 3-Me (*Z*-isomer), and d, *J* 1.5 Hz, 3-Me (*E*-isomer)], 2.4 and 2.48 (2 H together, 2 s, 4-CH_2), 3.66 (3 H, s, CO_2Me), 3.6—3.8 (2 H, m, 5′-CH_2), 3.96—4.84 (4 H together, all m, 1′,2′,3′,4′-H), and 5.8 (1 H, m, *J* 1.5 Hz, olefinic CH); δ_C($CDCl_3$) 25.407 and 27.358 (CMe_2), 44.477 (4-C), 50.869 (ester CO), 62.625 (5′-C), 81.315—84.620 (1′,2′,3′,4′-C's), 114.795 (CMe_2), 117.504 (2-C), 155.589 (3-C), and 166.857 (1-C) p.p.m.; *m/z* 271.1189 (1%, M^+ − Me. $C_{13}H_{19}O_6$ requires 271.1182).

Methyl 4-(2′,3′-O-*Isopropylidene*-α,β-D-*ribofuranosyl*)-3-*methyl*-4-*phenylselenenyl*-(E)-*but*-2-*enoate* (**6**) *and* (2R,3R,4R,-5R,6S)-2-*Hydroxymethyl*-3,4-O-*isopropylidene*-5-*phenylselenenyl*-6-[3-*methoxycarbonyl*-(E)-*prop*-2-*en*-2-*yl*]*pyran* (**7**).—A solution of (**1c**) (286 mg, 1 mmol) in dichloromethane (10 cm^3), containing anhydrous, finely divided potassium carbonate (178 mg, 2 mmol) was stirred at −78 °C under a nitrogen atmosphere. Benzeneselenenyl chloride (212 mg, 1.1 mmol) was added in one portion, from a pre-loaded side-arm, and stirring continued at −78 °C for 3 h (t.l.c. analysis revealed two less polar products in addition to starting material. A further equivalent of benzeneselenenyl chloride was added and the existing conditions maintained for a further 2 h. By this time t.l.c. analysis showed an increased intensity of products, but also a substantial u.v./$KMnO_4^-$ base-line spot. The reaction

mixture was washed with saturated aqueous sodium hydrogen carbonate (×2) and saturated brine (×2), dried, and concentrated and the residue purified by flash chromatography (eluant diethyl ether–light petroleum, 5:2) to yield a yellow oil (0.191 g, 0.45 mmol, 45%) consisting of a mixture (*ca.* 2:1) of compounds (**6**) and (**7**). Crystals of (**7**) were obtained after further chromatography (ether), and recrystallisation from light petroleum (b.p. 60—80 °C)–diethyl ether.

Analytical data for (**6**). R_F 0.45 (eluant diethyl ether); δ_H (220 MHz, $CDCl_3$) 1.35 and 1.52 (6 H, 2 s, CMe_2), 2.3 (3 H, d, 3-Me), 3.5—4.7 (7 H, all m, 4-H and 1′,2′,3′,4′,5′-H_2), 3.7 (3 H, s, CO_2Me), 5.5 (1 H, m, 2-H), and 7.0—7.6 (5 H, m, ArH).

Analytical data for (**7**). R_F 0.45 (eluant diethyl ether); δ_H (220 MHz, $CDCl_3$) 1.3 and 1.49 (together 6 H, 2 s, CMe_2), 2.1 (1 H, br s, OH), 2.13 (3 H, d, *J* 1.5 Hz, 1′-Me), 3.7 (3 H, s, CO_2Me), 3.4—4.0 (4 H, 2- and 3-H and 2 CH_2O), 4.18 (1 H, dd, $J_{3,4}$ 8.5 Hz, $J_{4,5}$ 5 Hz, 4-H), 4.45 (1 H, m, $J_{5,6}$ 2.5 Hz, 6-H), 4.63 (1 H, dd, $J_{5,4}$ 5 Hz, $J_{5,6}$ 2.5 Hz, 5-H), 6.12 (1 H, m, 2′-H), and 7.16—7.62 (5 H, m, ArH). The *X*-ray data is given elsewhere.

Crystal data. (i) Compound (**7**), $C_{20}H_{26}O_6Se$, M = 441.4, Monoclinic, space group $P2_1$, a = 10.591(8), b = 10.730(8), c = 9.832(9) Å, β = 109.2(1)°, U = 1 055.2 Å^3, $F(000)$ = 436, D_m = 1.39, D_c = 1.39 g cm^{-3}, λ(Mo-K_α) = 0.7107 Å, μ = 19.5 cm^{-1}. Precession photographs established the preliminary cell constants and space group. A crystal was mounted to rotate around the a axis on a Stoe STADI2 diffractometer and data was collected *via* variable width *w* scan. Background counts were 20 s and a scan rate of 0.033° s^{-1} was applied to a width of (1.5 + 0.5sinμ/tanθ). 1 824 Independent reflections with $2\theta < 50°$ were measured of which 1 513 having $I > 2\sigma(I)$ were used in subsequent refinement. The structure was solved from the Patterson function. The selenium, carbon, and oxygen atoms were refined anisotropically. The hydrogen atoms were included in trigonal or tetrahedral positions. The hydrogen atom on O(42) could not be located. Methyl hydrogen atoms were refined as rigid groups. Hydrogen atoms were given isotropic thermal parameters which were refined. The structure was refined using full-matrix least squares to R 0.074 (R_w = 0.075). The opposite (and rejected) enantiomorph gave R 0.078. In the final cycle of refinement no shift was greater than 0.1σ. There were no significant peaks in a final difference Fourier map. The weighting scheme chosen was $w = 1/(\sigma(F) + 0.003F^2)$ which gave similar values of $w\Delta^2$ over ranges of F_o and sin θ/λ. Calculations were carried out using SHELX 76[10] and local programmes on the Amdahl V7 at the University of Reading. Co-ordinates are given in Table 1 and bond lengths and angles in Table 2.

5-O-*Dimethyl-t-butylsiloxy*-2,3-O-*isopropylidenedihydroshowdomycin* (**8**).—A solution of compound (**2c**; R = Bu^tMe_2Si) (460.5 mg, *ca.* 1 mmol) in THF was treated with methanolic ammonia (10 ml) for 1 week. The reaction was followed by t.l.c., and when most of the starting material had been consumed the mixture was evaporated, prior to purification by flash chromatography using light petroleum–diethyl ether (1:1) as eluant. Further chromatography using diethyl ether–light petroleum (4:1) afforded the pure compound (**8**) as a thick oil (250 mg, 66%); R_F 0.4 (diethyl ether–light petroleum, 4:1); $\nu_{max.}$ 3 200, 2 900, 1 780, 1 720, 1 460, 1 360, 1 250, 1 180, 1 070, 950, and 830 cm^{-1}; δ ($CDCl_3$, 400 MHz) 0.04 and 0.05 (2 s, 6 H, Me_2Si), 0.88 (s, 9 H, Bu^t), 1.34 and 1.55 (2 s, 6 H, CMe_2), 2.62—2.69 (dd, 1 H, J_{gem} 18.1 Hz, $J_{4,3}$ 9.3 Hz, 4-H), 2.89—2.95 (dd, 1 H, J_{gem} 18.1 Hz, $J_{4,3}$ 5.0 Hz, 4-H), 3.14—3.19 (m, $J_{3,4}$ 5 and 9.3 Hz, 3-H), 3.68—3.76 (m, 2 H, J_{gem} 11.3 Hz, $J_{5',4'}$ 2.6 and 2.7 Hz, 5′-H), 4.08—4.10 (dd, 1 H, $J_{4',5'}$ 2.6, 2.7 Hz, 4′-H), 4.31—4.33 (dd, 1 H, $J_{1',2'}$ 5.9 Hz, $J_{1',3}$ 3.4 Hz, 1′-H), 4.37—4.40 (1 H, $J_{2',1'}$ 5.9 Hz, $J_{2',3'}$ 6.4 Hz, 2′-H), 4.67—4.69 (dd, 1 H, $J_{3',2'}$ 6.4 Hz, $J_{3',4'}$ 2.9 Hz, 3′-H), and 8.15 (br s, 1 H, NH); *m/z* 328.1257 (100%, $M^+ - Bu^t$). $C_{14}H_{22}NO_6Si$ requires 328.1210) (Found: C, 55.3; H, 8.0; N, 3.65. $C_{18}H_{31}NO_6Si$ requires C, 56.05; H, 8.1; N, 3.1%).

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