A Convenient Procedure for the Deoxygenation and Homologation of D-Ribose Derivatives

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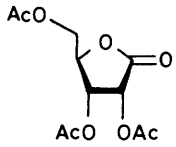
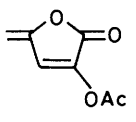
5-*O*-Acetyl- and 5-*O*-diphenyl-t-butylsilyl-2,3-di-*O*-acetyl-D-ribonolactones were converted into the corresponding 3-deoxy-2-*O*-acetyl-D-arabinolactone derivatives (**9a**) and (**9b**) by sequential reaction with 1,8-diazabicyclo[5.4.0]undec-7-ene and hydrogen over palladium on carbon. Reaction of (**9a**) and (**9b**) with sodium borohydride, 2,4,6-tri-isopropylbenzenesulphonyl chloride and potassium cyanide in sequence respectively gave the (3*S*,5*S*)-nitriles [$XCH_2CH(OH)CH_2CH(OH)CH_2CN$ (**10c**; X = CN) and (**10f**; X = Ph_2Bu^tSiO)]. The latter was hydrolysed and silylated to produce (4*S*,6*S*)-4-dimethyl-t-butylsilyloxy-6-[(dimethyl-t-butylsilyloxy)methyl]tetrahydro-2*H*-pyran-2-one (**5b**).

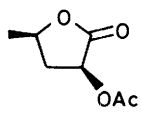
Recently [1] we have described a concise and stereospecific synthesis of a racemic nonactic acid derivative (**4**) from the D-ribose derivative (**1**). The initial key step in this process was the double elimination of acetic acid from the triacetate (**1**) *via* reaction with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to produce the butenolide (**2**). Hydrogenation of (**2**) over palladium on calcium carbonate stereoselectively (>97:3) gave the *cis*-disubstituted lactone (**3**) which was subsequently transformed into the ester (**4**). During a synthetic programme on the milbemycins [2] and avermectins [3] we sought a concise route to the lactones (**5**). We considered (**5**) as a suitable precursor for the spiro-ketal unit that occurs in these important natural products. Herein we report an extension of our work on nonactic acid that readily permits the synthesis of the lactone (**5b**).



(1)



(2)



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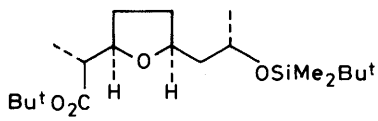
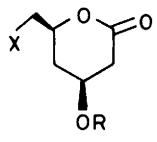
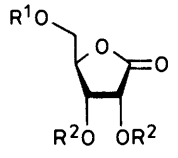


(4)(racemic modification)



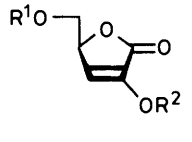
(5)

a; X = CO_2H, R = H
b; X = $OSiMe_2Bu^t$, R = $SiMe_2Bu^t$



(6)

a; $R^1 = R^2 = PhCH_2$
b; $R^1 = R^2 = H$
c; $R^1 = R^2 = Me_2Bu^tSi$
d; $R^1 = Ph_3C$, R^2 = Ac
e; $R^1 = Ph_2Bu^tSi$, R^2 = H
f; $R^1 = Ph_2Bu^tSi$, R^2 = Ac



(7)

a; $R^1 = R^2 = PhCH_2$
b; $R^1 = R^2 = Me_2Bu^tSi$
c; $R^1 = Ph_3C$, R^2 = Ac
d; $R^1 = R^2$ = Ac
e; $R^1 = Ph_2Bu^tSi$, R^2 = Ac

Weidmann and co-workers [4] have shown that 2,3,5-tri-*O*-benzyl-D-ribonic acid γ-lactone (**6a**) may be converted into the butenolide (**7a**) (91%) by reaction with DBU in HMPT at 45 °C. Indeed, our synthesis of (**2**) from (**1**) was based upon this observation. We expected [1,5] that hydrogenation of (**7**) should proceed with high stereoselectivity and thereby should provide a convenient route to the 3-deoxyarabinonic acid derivatives (**9**). In addition, these readily available compounds (**9**) should be easy to transform into the target lactones (**5**) *via* homologation at C-1 and/or C-5. Since the lactone (**6a**) was prepared indirectly [4] from D-ribose, we examined alternative substrates. The tri-*O*-dimethyl-t-butylsilyl ether (**6c**) was treated with DBU in benzene and with lithium di-isopropylamide in tetrahydrofuran (THF). Neither reaction was successful as a route to the butenolide (**7b**). The lactones (**1**), (**6d**), and (**6f**) (95, 45, and 80% respectively) were readily prepared from D-ribonolactone (**6b**). The yields of (**6d**) and (**6f**) were not good on account of incomplete regioselectivity on the initial C-5 tritylation or diphenyl-t-butylsilation of (**6b**). Thus (**8**) and (**12**) were isolated as minor products in these experiments. On reaction with DBU in THF solution (**1**), (**6d**), and (**6f**) were transformed into the butenolides (**7d**), (**7c**) (55%), and (**7e**) (89%) respectively. Both (**7c**) and (**7e**) were stable and were fully authenticated. However, (**7d**) was unstable and all attempts to purify this material gave a product contaminated with the methylenebutenolide (**2**). The facile production of (**2**) from (**7d**) is underscored by the fact that in our original preparation of lactone (**2**) from (**1**) only one equivalent of DBU was employed.[1] The most satisfactory preparation of (**2**) involved the reaction of (**1**) with DBU at −78 °C. Alternative bases were examined, but proved less efficient.

Hydrogenation of the butenolides (**7d**) and (**7e**) over palladium on carbon in ethanol solution proceeded with the

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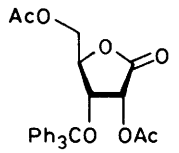
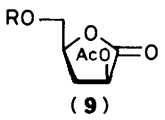
expected high stereoselectivity giving (**9a**) and (**9b**). These lactones (**9a**) (56%) and (**9b**) (84%) were most satisfactorily prepared from (**1**) and (**6f**) without isolating the intermediate butenolides (**7d**) and (**7e**). The stereochemistry of (**9a**) and (**9b**) was fully consistent with n.m.r. data and for (**9a**) confirmed *unequivocally* by nuclear Overhauser effect difference spectroscopy.[6]

Sodium borohydride reduction[7] of the lactones (**9a**) and (**9b**) under acidic conditions respectively gave the tetraol (**10a**) (86%) and the triol (**10d**) (89%). Using 2,4,6-tri-isopropylbenzenesulphonyl chloride the primary hydroxy group(s) of (**10a**) and (**10d**) were selectively functionalised to produce the sulphonates (**10b**) (88%) and (**10e**) (84%). By reaction with potassium cyanide both (**10b**) and (**10e**) were converted into the nitriles (**10c**) (69%) and (**10f**) (83%). Both were characterised by spectral data and microanalysed as the derivatives (**11a**), (**11b**), and (**14**). During the preparation of (**10f**) short reaction times gave rise to formation of the epoxide (**13**). However, this reacted further with cyanide anion to produce the required nitrile (**10f**). The production of (**10c**) and (**10f**) clearly completes the carbon skeletons required for the synthesis of the lactones (**5a**) and (**5b**).



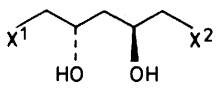
(**8**)



(**9**)

a; R = Ac

b; R = Ph_2Bu^tSi



(**10**)

a; $X^1 = X^2 = OH$

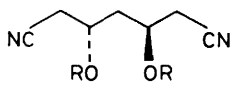
b; $X^1 = X^2 = OSO_2C_6H_2$-2,4,6-Pr^i_3

c; $X^1 = X^2 = CN$

d; $X^1 = Ph_2Bu^tSiO$, $X^2 = OH$

e; $X^1 = Ph_2Bu^tSiO$, $X^2 = OSO_2C_6H_2$-2,4,6-Pr^i_3

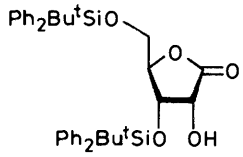
f; $X^1 = Ph_2Bu^tSiO$, $X^2 = CN$



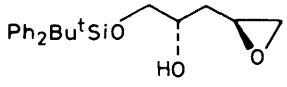
(**11**)

a; R = PhCO

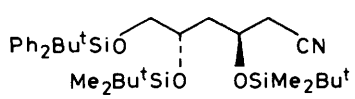
b; R = Me_2Bu^tSi



(**12**)



(**13**)



(**14**)

All attempts to hydrolyse the nitrile (**10c**) under acidic or basic conditions gave intractable mixtures of u.v.-active compounds which could not be isolated. However, hydrolysis of the nitrile (**10f**) under alkaline conditions followed by acidification gave an oil. Subsequent dimethyl-t-butylsilylation[8] gave the expected lactone (**5b**) (40%). Clearly the facile production of the butenolides (**7**) from the ribonolactone derivatives (**1**) and (**6**) provides a convenient route to the 3-deoxylactones (**9**) and the lactone (**5b**).

Experimental

M.p.s were determined using a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 157G, 257, or 298 grating i.r. spectrophotometer. ^{1}H N.m.r. spectra were recorded on a Varian 360A or a Perkin-Elmer R32 spectrometer, at 60 and 90 MHz respectively, and on a Bruker WM250 machine at 250 MHz. Signal allocations in n.m.r. spectra were established by carrying out the appropriate spin-decoupling experiments. ^{13}C N.m.r. spectra were recorded on a Bruker WM250 machine at 62.9 MHz. Tetramethylsilane was used as an internal reference for n.m.r. spectra unless otherwise stated. Optical rotations were determined using a Perkin-Elmer 141 polarimeter. Microanalysis and mass spectral measurements were carried out by the appropriate laboratories at Imperial College. Analytical thin-layer chromatography (t.l.c.) was performed on Merck precoated GF_{254} silica or F_{254} (type E) alumina plates. Preparative layer chromatography (p.l.c.) was performed on GF_{254} silica plates. Medium-pressure chromatography was carried out on Merck Kieselgel H (type 60) silica as described by Still *et al.*[9]

Solvents were purified as follows: benzene and toluene were redistilled and sodium dried; dichloromethane, ethyl acetate, and light petroleum (b.p. 40—60 °C) were redistilled; diethyl ether (ether) was redistilled and dried when required over sodium wire. Tetrahydrofuran (THF) was redistilled from potassium benzophenone ketyl. *N,N*-Dimethylformamide (DMF) was distilled from calcium hydride onto 4A molecular sieves. Pyridine was redistilled from potassium hydroxide and stored over 4A molecular sieves. Reagents were purified according to standard procedures.[10] Organic extracts were routinely dried over anhydrous sodium or magnesium sulphate. Solvents were evaporated at reduced pressure using a rotary evaporator at, or below, 40 °C unless otherwise stated.

Preparation of 2,3,5-*Tris*-O-*dimethyl-t-butylsilyl*-D-*ribonic Acid* γ-*Lactone* (**6c**).—A solution of D-(+)-ribonic acid γ-lactone (**6b**) (4.12 g) and imidazole (16.20 g) in dry *N,N*-dimethylformamide (80 ml) was stirred together with a solution of chlorodimethyl-t-butylsilane (14.80 g) in dry *N,N*-dimethylformamide (25 ml) under an atmosphere of argon.[8] The reaction mixture was maintained at 65—70 °C for 5 h, allowed to cool, and stored at room temperature overnight. The resultant solid was partitioned between diethyl ether (150 ml) and water (150 ml) and the aqueous phase was extracted with diethyl ether (2 × 100 ml). The combined extracts were dried and concentrated under reduced pressure to yield a white crystalline solid which was recrystallized from methanol (150 ml) to afford the *title compound* (**6c**) (13.1 g, 96%) as colourless needles, m.p. 119—120 °C, $[\alpha]_D^{22}$ +28.2° (*c* 0.99, $CHCl_3$), $\nu_{max.}$(Nujol) 2 900, 1 790, 1 170, 1 110, and 840 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 0.06 (3 H, s, $SiCH_3$), 0.08 (3 H, s, $SiCH_3$), 0.09 (3 H, s, $SiCH_3$), 0.10 (3 H, s, $SiCH_3$), 0.14 (3 H, s, $SiCH_3$), 0.18 (3 H, s, $SiCH_3$), 0.88 (9 H, s, $SiBu^t$), 0.89 (9 H, s, $SiBu^t$), 0.94 (9 H, s, $SiBu^t$), 3.78 (1 H, dd, J_{gem} 11.7, $J_{4,5}$ 2.1 Hz, 5-H), 3.86 (1H, dd, J_{gem} 11.7, $J_{4,5'}$ 3.0 Hz, 5-H'), 4.25—4.30 (2 H, m, 4-H and 3-H), and 4.57 (1 H, d, $J_{2,3}$ 5.0 Hz, 2-H); *m/z* 490 ($M^{+\cdot}$), 489, 475 ($M^{+\cdot}$ − 15), 474, 433 ($M^{+\cdot}$ − 57), 432, 404, 301, 300, 273, 272, 146, 116, 114, and 73 (Found: C, 56.5; H, 10.4. $C_{23}H_{50}O_5S_{13}$ requires C, 56.25; H, 10.25%).

Attempted Preparation of (5S)-3-*Dimethyl-t-butylsilyloxy*-5-[(*dimethyl-t-butylsilyloxy*)*methyl*]*furan*-2(5H)-*one* (**7b**).—(i) 2,3,5-Tri-*O*-dimethyl-t-butylsilyl-D-ribonic acid γ-lactone (**6c**) (2.94 g) in dry benzene (10 ml) was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.9 g) at room temperature. After 30 min no elimination product could be detected by n.m.r. spectral analysis.

(ii) The protected lactone (**6c**) (1.47 g, 3.0 mmol) in dry tetrahydrofuran (10 ml) was added to a solution of lithium diisopropylamide (2.96 mmol) in dry tetrahydrofuran (30 ml) at −78 °C. After 30 min the reaction was quenched by the addition of water and the mixture partitioned between diethyl ether (× 2) and the combined extracts were dried and concentrated under reduced pressure to afford a white crystalline solid (1.2 g), identified as mainly the starting lactone (**6c**) by n.m.r. spectral analysis.

Preparation of 2,3-*Di*-O-*acetyl*-5-O-*triphenylmethyl*-D-*ribonic Acid* γ-*Lactone* (**6d**).—D-(+)-Ribonic acid γ-lactone (**6b**) (5.92 g) was treated with chlorotriphenylmethane[11] (11.65 g) in dry pyridine (25 ml). Warming the mixture produced a clear solution which was rapidly converted into a gelatinous solid. The reaction mixture was allowed to stand at room temperature overnight after which it was treated with acetic anhydride (10 ml). The mixture was stirred at room temperature for 5 h, partitioned between diethyl ether (150 ml) and water (200 ml), and quenched by the addition of solid sodium hydrogencarbonate. The aqueous layer was extracted with diethyl ether (3 × 100 ml) and the combined extracts were dried and concentrated to yield a white solid. Medium-pressure chromatography on silica [Kieselgel H, eluant dichloromethane–light petroleum (1:1)] afforded the *title compound* (**6d**) (8.60 g, 45%) as a white crystalline solid, m.p. 109—110 °C (from dichloromethane–light petroleum) $[\alpha]_D^{22}$ +18.6° (*c* 1.59, $CHCl_3$), $\nu_{max.}$(Nujol) 1 800, 1 755, 1 245, 1 215, 1 090, 1 000, 770, 750, 715, and 705 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 2.03 (3 H, s, $COCH_3$), 2.11 (3 H, s, $COCH_3$), 3.29 (1 H, dd, J_{gem} 11.0, $J_{4,5}$ 2.2 Hz, 5-H), 3.65 (1 H, dd, J_{gem} 11.0, $J_{4,5'}$ 2.6 Hz, 5′-H), 4.49 (1 H, distorted t, 4-H), 5.37 (1 H, dd, *J* 6.2 Hz, 3-H), 6.14 (1 H, d, $J_{2,3}$ 5.8 Hz, 2-H), and 7.17—7.46 (15 H, m, aryl-H); *m/z* 474 ($M^{+\bullet}$), 397, 260, 243, 183, 165, 154, 105, 77 (100%), 51, and 43 (Found: C, 70.9; H, 5.5. $C_{28}H_{26}O_7$ requires C, 70.85; H, 5.5%), and the regioisomer 2,5-*di*-O-*acetyl*-3-O-*triphenylmethyl*-D-*ribonic acid* γ-*lactone* (**8**) (1.76 g, 10%) as a white crystalline solid, m.p. 165—166 °C (from dichloromethane–light petroleum), $[\alpha]_D^{22}$ +42.9° (*c* 1.26, $CHCl_3$), $\nu_{max.}$(Nujol) 1 800, 1 755, 1 750, 1 230, 1 140, 1 060, 710, and 700 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.76 (3 H, s, $COCH_3$), 1.93 (3 H, s, $COCH_3$), 3.35 (1 H, dd, *J* 5.9 Hz, 3-H), 3.98 (1 H, dd, J_{gem} 12.5, $J_{4,5}$ 3.3 Hz, 5-H), 4.10 (1 H, dd, J_{gem} 12.5, $J_{4,5'}$ 3.3 Hz, 5-H′), 4.29 (1 H, distorted t, 4-H), 4.64 (1 H, d, $J_{2,3}$ 5.9 Hz, 2-H), 7.23—7.39 (10 H, m, aryl-H), and 7.57—7.67 (10 H, m, aryl-H); *m/z* 474 ($M^{+\bullet}$), 397, 259, 243 (100%), 228, 215, 183, 165, 105, 77, and 43 (Found: C, 70.85; H, 5.5. $C_{28}H_{26}O_7$ requires C, 70.85; H, 5.5%).

Preparation of (5S)-3-*Acetoxy*-5-[(*triphenylmethoxy*)*methyl*]-*furan*-2(5H)-*one* (**7c**).—2,3-Di-*O*-acetyl-5-*O*-triphenylmethyl-D-ribonic acid γ-lactone (**6d**) (0.5 g) in dry THF (5 ml) was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.17 g) for 15 min at room temperature. The solution rapidly turned very dark. The mixture was partitioned between diethyl ether and water, and the highly coloured aqueous phase extracted several times with diethyl ether (× 3). The combined extracts were dried and concentrated under reduced pressure to yield a dark solid (0.38 g). Medium-pressure chromatography on silica [Kieselgel H, eluant dichloromethane–light petroleum (1:1)] afforded the *title compound* (**7c**) (240 mg, 55%) as a white solid, m.p. 148—152 °C (decomp.) (from dichloromethane–light petroleum), $\nu_{max.}$(CCl_4) 1 784, 1 195, 1 110, 1 080, and 705 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 2.27 (3 H, s, $COCH_3$), 3.38 (2 H, ddd, OCH_2), 5.02 (1 H, ddd, 5-H), and 7.12—7.47 (16 H, m, 4-H and aryl-H); *m/z* 414 ($M^{+\bullet}$), 371 ($M^{+\bullet}$ − Ac), 337, 243 (100%), 183, 165, 105, and 43 (Found: C, 75.4; H, 5.4. $C_{26}H_{22}O_5$ requires C, 75.35; H, 5.35%).

Preparation of 2,3,5-*Tri*-O-*acetyl*-D-*ribonic Acid* γ-*Lactone* (**1**).—D-(+)-Ribonic acid γ-lactone (**6b**) (25 g) dissolved in acetic anhydride (200 ml) containing dry pyridine (6 drops) was stirred, after initial cooling at room temperature, overnight. The solvent was removed under reduced pressure and the reaction mixture partitioned between diethyl ether (750 ml) and water (500 ml), and basified by the addition of solid hydrogencarbonate. The aqueous phase was extracted with diethyl ether (3 × 500 ml) and the combined extracts dried and concentrated under reduced pressure to yield the title compound (**1**) (44.3 g, 95%) as a white crystalline solid, m.p. 54—55 °C (from acetic acid–water), $[\alpha]_D^{22}$ +14.5° (*c* 1.44, $CHCl_3$) (lit.,[12] m.p. 54—56 °C, $[\alpha]_D$ +27°).

Preparation of (5S)-3-*Acetoxy*-5-*acetoxymethylfuran*-2(5H)-*one* (**7d**).—2,3,5-Tri-*O*-acetyl-D-ribonic acid γ-lactone (**1**) (10.0 g) in dry THF (100 ml) was cooled to −78 °C and treated with DBU (5.56 g). The reaction mixture was stirred at −78 °C for 4 h; the appearance of a flocculent white precipitate was noted after 3 h. The mixture was partitioned between diethyl ether and water, and the highly coloured aqueous phase was extracted with diethyl ether (× 3). The combined extracts were concentrated, under reduced pressure at low temperature, to afford a yellow crystalline solid (6.14 g) which was shown to be a >2:1 mixture of the title compound (**7d**), δ_H (60 MHz) ($CDCl_3$) 2.07 (3 H, s, $COCH_3$), 2.29 (3 H, s, $COCH_3$), 4.20—4.40 (2 H, m, 6-H,H′), 5.05—5.35 (1 H, m, 5-H), and 7.12 (1 H, d, *J* 2 Hz, 4-H); *m/z* 215 ($M^{+\bullet}$ + 1), and the previously characterised[1] 3-acetoxy-5-methylenefuran-2(5*H*)-one (**2**). Compound (**7d**) was used in this form in the subsequent reaction. Similar reactions employing either aqueous hydrochloric acid or aqueous sodium hydrogencarbonate work-up resulted in the isolation of a more highly coloured mixture of crude products.

Preparation of (3S,5S)-3-*Acetoxy*-5-*acetoxymethyldihydrofuran*-2(3H)-*one* (**9a**).—(i) The previously prepared mixture of (5*S*)-3-acetoxy-5-acetoxymethylfuran-2(5*H*)-one (**7d**) and 3-acetoxy-5-methylenefuran-2(5*H*)-one (**2**) (5.79 g) in ethanol (60 ml) was hydrogenated at atmospheric pressure over 10% palladium on carbon. The catalyst was removed by filtration through Celite, and the solvent removed under reduced pressure to afford a dark oil (4.41 g). Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane) afforded the *title compound* (**9a**) [3.63 g, 46% from the triacetate (**1**)] as a white crystalline solid, m.p. 71—72 °C (from dichloromethane–diethyl ether), $[\alpha]_D^{22}$ +51.1° (*c* 1.09, $CHCl_3$), $\nu_{max.}$($CHCl_3$) 1 795, 1 745, 1 380, 1 250, 1 170, and 1 110 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 2.11 (3 H, s, $COCH_3$), 2.17 (3 H, s, $COCH_3$), 2.12 (1 H, ddd, $J_{4\alpha,4\beta}$ 12.5, $J_{3,4\alpha} = J_{4\alpha,5}$ 10.3 Hz, 4α-H), 2.79 (1 H, ddd, $J_{4\alpha,4\beta}$ 12.5, $J_{4\beta,5}$ 5.9, $J_{3,4\beta}$ 8.8 Hz, 4β-H), 4.18 (1 H, dd, $J_{6,6'}$ 12.5, $J_{5,6}$ 5.8 Hz, 6-H), 4.39 (1 H, dd, $J_{6,6'}$ 12.5, $J_{5,6'}$ 2.9 Hz, 6′-H), 4.72 (1 H, 10 line m, 5-H), and 5.54 (1 H, dd, $J_{3,4\alpha}$10.3, $J_{3,4\beta}$ 8.8 Hz, 3-H); δ_C($CDCl_3$) 20.2 (q, $COCH_3$), 20.3 (q, $COCH_3$) 30.3 (t, CH_2), 64.0 (t, OCH_2) 67.8 (d, OCH ring), 73.9 (d, OCHCO), 169.3 (s, C=O), 170.1 (s, C=O), and 171.4 (s, C=O); *m/z* 259 ($M^{+\bullet}$ + Ac), 217 ($M^{+\bullet}$ + 1), 175, 143, 115 (100%), and 103 (Found: C, 50.0; H, 5.55. $C_9H_{12}O_6$ requires C, 50.0; H, 5.6%).

(ii) 2,3,5-Tri-*O*-acetyl-D-ribonic acid γ-lactone (**1**) (15 g) in dry THF (150 ml) was treated with DBU (9.13 g) at −78 °C dropwise over 15 min. The reaction mixture was stirred at

−78 °C for 1.5 h at which time a white solid was observed and the reaction quenched by addition of water (200 ml). The highly coloured aqueous phase was extracted with diethyl ether (3 × 150 ml) and the volume of the combined organic phases reduced under reduced pressure. After dilution with ethanol (100 ml) the crude material was hydrogenated over 10% palladium on carbon overnight. The catalyst was removed by filtration through Celite and the solvent evaporated under reduced pressure to afford a dark oil (12.3 g). Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane) removed some highly polar base-line material and afforded a yellow oil (10.64 g) which crystallised with time to afford an oily solid. Trituration with diethyl ether afforded the title compound (**9a**) (6.6 g, 56%) as a white crystalline solid, m.p. 71—72 °C (from dichloromethane–diethyl ether) with spectral data identical with those of the previous material.

Investigation of the Possible Use of Alternative Bases in the Preparation of (5S)-3-*Acetoxy*-5-[(*acetoxy*)*methyl*]*furan*-2(5H)-*one* (**7d**).—The course of these reactions was monitored by n.m.r. spectroscopy. Samples from each reaction mixture were quenched with water and extracted with deuteriochloroform. The organic phases were then dried (Na_2SO_4) and directly submitted to n.m.r. spectral analysis. (i) A solution of the lactone (**1**) (2.0 g) in dry THF (20 ml) was treated with potassium t-butoxide [preformed from potassium (285 mg) and t-butyl alcohol (2 ml)] at −78 °C. After 5 h n.m.r. spectral analysis indicated a 2:1 mixture of the starting lactone (**1**) and 3-acetoxy-5-methylenefuran-2(5*H*)-one (**2**).

(ii) A solution of the lactone (**1**) 2.0 g) in dry THF (20 ml) was treated with 100% sodium hydride (175 mg) at room temperature. After 20 h n.m.r. spectral and t.l.c. analysis indicated a mixture of the starting lactone (**1**) and 3-acetoxy-5-methylenefuran-2(5*H*)-one (**2**) plus some polymeric material.

(iii) A solution of the lactone (**1**) (2.74 g) in dry THF (40 ml) at −78 °C, was treated with a solution of lithium hexamethyldisilazide [preformed from 1,1,1,3,3,3-hexamethyldisilazane (1.77 g) in dry THF (20 ml) and 1.5M-n-butyl-lithium in hexane (7.10 ml) at 0 °C for 45 min]. After 3 h n.m.r. spectral analysis indicated no further change in the product ratio. The reaction was quenched by the addition of water and extracted several times with diethyl ether (× 3). The combined extracts were concentrated under reduced pressure to small volume, diluted with ethanol (50 ml), and hydrogenated over 10% palladium on carbon (200 mg) for 12 h. The catalyst was removed by filtration through Celite, and the solvent evaporated under reduced pressure to yield a yellow semi-crystalline solid. Medium-pressure chromatography on silica [Kieselgel H, 40 g, eluant dichloromethane–light petroleum (1:1)] afforded (3*S*,5*S*)-3-acetoxy-5-[(acetoxy)methyl]dihydrofuran-2(3*H*)-one (**9a**) (242 mg, 11%) with spectral data identical with that of an authentic sample.

(iv) A solution of the lactone (**1**) (1.0 g) in dry THF (10 ml) was treated with *N*,*N*-di-isopropylethylamine (0.52 g, 4.01 mmol) at −78 °C. After 3 h n.m.r. spectral analysis indicated a 2:1 mixture of the starting lactone (**1**) and 3-acetoxy-5-methylenefuran-2(5*H*)-one (**2**).

Preparation of (2S,4S)-*Pentane*-1,2,4,5-*tetraol* (**10a**).—The lactone (**9a**) (3 g) in water (20 ml) containing boric acid (0.83 g) and Amberlyte IR 120H$^+$ resin (10.5 ml) was treated with sodium borohydride (5.80 g) over 1.5 h at 0 °C. The reaction mixture was stirred at room temperature overnight and quenched by the addition of Amberlyte IR 120H$^+$ resin to pH 7. The mixture was filtered and the resin washed with water and methanol. Concentration of the combined filtrate and washings under reduced pressure afforded a gummy white solid which was dissolved in methanol and concentrated by heating on a steam-bath. This procedure was repeated several times to ensure the complete removal of boron residues as trimethyl borate. The resulting solid was recrystallised from ethanol to afford the *title compound* (**10a**) (1.62 g, 86%) as colourless platelets, m.p. 106—107 °C, $[\alpha]_D^{22}$ −46° (*c* 1.03, EtOH), δ_H (250 MHz) (D_2O + ref. Bu^{t}OH) 1.54 (2 H, distorted t, CH_2), 2.43—2.70 (4 H, m, 2 × OCH_2), and 2.83—3.00 (2 H, distorted ddd, 2 × OCH); δ_C(D_2O + Bu^{t}OH), 38.3 (t, CH_2), 68.5 (t, 2 × OCH_2), and 70.8 (d, 2 × OCH); *m*/*z* 137 ($M^{+\bullet}$ + 1), 119, 106, 105 ($M^{+\bullet}$ − 31), 88, 87, 69, 61, 57, 45, 43, 41, 31, and 29 (Found: C, 44.2; H, 8.95. $C_5H_{12}O_4$ requires C, 44.1; H, 8.9%).

Preparation of (2S,4S)-2,4-*Dihydroxypentane*-1,5-*diyl Bis*(2,4,6-*tri-isopropylbenzenesulphonate*) (**10b**).—(2*S*,4*S*)-Pentane-1,2,4,5-tetraol (**10a**) (1 g) was dissolved, with warming, in dry pyridine (6 ml) and the resulting solution cooled to 0 °C and treated with 2,4,6-tri-isopropylbenzenesulphonyl chloride (5 g). The reaction mixture was stirred at 5 °C overnight and the solvent removed under reduced pressure at room temperature. The resulting white solid was triturated with dichloromethane and filtered. The filtrate was concentrated under reduced pressure and the residue chromatographed on Kieselgel H (30 g, eluant dichloromethane). Recrystallisation from dichloromethane–light petroleum afforded the *title compound* (**10b**) (4.31 g, 88%) as white crystals, m.p. 154—155 °C; $[\alpha]_D^{22}$ −8.8° (*c* 0.2, EtOH), $\nu_{max.}$(Nujol) 3 300, 1 600, 1 425, 1 345, 1 175, 975, 965, 935, 910, 895, 880, 845, 835, 810, 720, and 665 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.25 [24 H, d, *J* 6.8 Hz, 4 × CH(CH_3)$_2$], 1.26 [12 H, d, *J* 6.8 Hz, 2 × CH(CH_3)$_2$], 1.63 (2 H, dd, *J* 2.6 and 6.6 Hz, CH_2), 2.92 [2 H, septet, *J* 6.8 Hz, 2 × *CH*(CH_3)$_2$], 3.93—4.29 (10 H, m), and 7.19 (4 H, s, aryl-H); δ_C($CDCl_3$) 23.5 (q, 4 × CH_3), 24.7 (q, 8 × CH_3), 29.7 [d, 4 × *C*H(CH_3)$_2$], 34.3 [d, 2 × *C*H(CH_3)$_2$], 35.3 (t, CH_2), 66.5 (d, 2 × OCH), 72.7 (s, 2 × OCH_2), 123.9 (d, 2 × C aryl), 129.0 (s, C aryl), 150.9 (s, 2 × C aryl), and 154.0 (s, C aryl); *m*/*z* $M^{+\bullet}$ absent, 384 ($M^{+\bullet}$ − 284), 284 ($C_{15}H_{24}O_3S$), 269, 267, 266, 251, 218, 203, 202, 188, 187, 161, 159, 145, 131, 129, 128, 117, 115, 105, 101, 91, 87, 83, 69, 55, 43, and 41 (Found: C, 63.0; H, 8.45. $C_{35}H_{56}O_8S_2$ requires C, 62.85; H, 8.45%).

Preparation of (3S,5S)-3,5-*Bis*(*benzoyloxy*)*heptane*-1,7-*dinitrile* (**11a**).—A solution of the disulphonate (**10b**) (1.33 g) in methanol (10 ml) was treated with potassium cyanide (0.39 g) for 3 h at reflux. T.l.c. analysis (silica, 10% diethyl ether in dichloromethane) indicated the absence of starting material (**10b**). The solvent was removed under reduced pressure to yield a light brown solid which was treated with dry pyridine (5 ml) and benzoyl chloride (0.70 g, 5 mmol) at room temperature overnight. The mixture was concentrated under reduced pressure and the residue partitioned between diethyl ether and aqueous sodium hydrogencarbonate. The aqueous phase was extracted with diethyl ether (× 3) and the combined extracts dried and concentrated under reduced pressure to yield a crystalline white solid (674 mg). Preparative-layer chromatography on silica (Merck GF_{254}H, eluant dichloromethane) afforded the *title compound* (**11a**) (244 mg, 34%) as a white crystalline solid, m.p. 94—95 °C (from dichloromethane–light petroleum), $[\alpha]_D^{22}$ −148.3° (*c* 1.19, $CHCl_3$), $\nu_{max.}$(Nujol) 2 260 m (C≡H str.), 1 740, 1 730, 1 280, 1 120, 1 100, 1 070, 1 040, 1 030, and 720 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 2.49 (2 H, dd, *J* 7.3 and 5.7 Hz, CH_2), 2.82 (2 H, dd, J_{gem} 17.0, *J* 4.0 Hz, 2 × *CH*H′CN), 3.02 (2 H, dd, J_{gem} 17.0, *J* 5.5 Hz, 2 × CH*H*′CN), 5.37—5.47 (2 H, m, 2 × OCH), and 7.40—8.03 (10 H, m, aryl-H); δ_C($CDCl_3$) 23.5 (t, *C*H_2CN), 37.2 (t, CH_2), 65.6 (d, OCH), 115.8 (s), 128.6 (d, 4 × *C*H aryl), 128.9 (s, 129.8 (d, 4 × *C*H aryl), 133.7 (d, 2 × *C*H aryl), and 165.4 (s, *C*=O); *m*/*z* 362 ($M^{+\bullet}$), 322, 257, 240, 200, 123, 122, 106, 105, 91,

84, 77, 69, and 51 (Found: C, 69.35; H, 5.0; N, 7.9. $C_{21}H_{18}N_2O_4$ requires C, 69.6; H, 5.0; N, 7.75%).

Preparation of (3S,5S)-3,5-*Dihydroxyheptane*-1,7-*dinitrile* (**10c**).—(i) A solution of the disulphonate (**10b**) (3.20 g) in methanol (50 ml) was treated with potassium cyanide (1.17 g) with stirring at room temperature. An homogeneous solution was produced after 4 h. After 2.5 days the reaction mixture was diluted with water, filtered through a column of Amberlyte IR 120H$^+$ resin, and stirred with Amberlyst A-21(OH$^-$) resin overnight. After filtration the resin was washed with water and the combined filtrate and washings concentrated under reduced pressure to yield a yellowish brown oil (743 mg). Medium-pressure chromatography on silica (Kieselgel H, 15 g, eluant diethyl ether–ethyl acetate) afforded the crude title compound (**10c**) (510 mg, 69%) as a pale yellow oil, $\nu_{max.}$(liq. film) 3 420, 2 940, 2 250, 1 415, 1 300, 1 215, 1 080, and 965 cm^{-1}; δ_H (250 MHz) (D_2O + ref. Bu^{t}OH) 1.64 (2 H, dd, *J* 5.8 and 7.2 Hz, CH_2), 2.56 (2 H, dd, J_{gem} 12.8, *J* 6.3 Hz, 2 × C*H*H′CN), 2.65 (2 H, dd, J_{gem} 12.8, *J* 4.6 Hz, 2 × CH*H*′CN), and 3.97—4.13 (2 H, m, 2 × OCH); δ_C(D_2O + ref. Bu^{t}OH), 28.5 (t, *C*H_2CN), 44.2 (t, CH_2), 66.1 (d, OC*H*), and 122.0 (s, CN); *m/z* 154 ($M^{+\bullet}$), 136, 126, 118, 113, 95, 69, 67, 45, 42 (110%), and 41.

(ii) A solution of the disulphonate (**10b**) (3.82 g) in methanol (50 ml) was treated with potassium cyanide (1.11 g) with stirring at room temperature. An homogeneous solution was produced after 5 h. After 2 days the solvent was removed under reduced pressure to yield a white solid. Medium-pressure chromatography on silica (Kieselgel H, 15 g, eluant diethyl ether–ethyl acetate) afforded the crude title compound (**10c**) (517 mg, 59%) as a pale yellow oil.

Attempted Preparation of (2S,4S)-*Tetrahydro*-4-*hydroxy*-6-*oxo*-2H-*pyran*-2-*ylacetic Acid* (**5a**).—The selective hydrolysis and subsequent lactonisation of (3*S*,5*S*)-3,5-dihydroxyheptane-1,7-dinitrile (**10c**) was attempted using a variety of reaction conditions. (i) A solution of the dinitrile (**10c**) (76 mg) in deuterium oxide (1 ml) was treated with sodium deuterioxide (20 mg) at 70 °C for 16 h. N.m.r. spectral data at this time were found to be too complicated to interpret. The reaction mixture was acidified by filtration through a column of Amberlyte IR 120H$^+$ resin (10 ml) and the solvent removed under reduced pressure to afford a brown oil (56 mg). T.l.c. analysis (silica, ethyl acetate) showed this material to be a complex mixture of u.v.-active compounds from which the title compound (**5a**) could not be isolated.

(ii) A solution of the dinitrile (**10c**) (11 mg, 0.071 mmol) in water (2 ml) was stirred with Amberlyte IR 120H$^+$ resin (41 mg) at room temperature. After 6 days t.l.c. analysis (silica, ethyl acetate) showed that no detectable reaction had occurred.

(iii) A solution of the dinitrile (**10c**) (15.4 mg) in water (3 ml) was stirred with sodium hydroxide (4 mg) at room temperature. After 6 days some starting material was still present as detected by t.l.c. analysis. The reaction mixture was acidified with Amberlyte IR 120H$^+$ resin (2 ml) and the solvent removed under reduced pressure to afford a brown oil. T.l.c. analysis (silica, ethyl acetate) indicated a complex mixture of polar products from which the required compound (**5a**) could not be isolated.

(iv) A solution of the dinitrile (**10c**) (15.4 mg) in water (3 ml) was stirred with Amberlyst A-26(OH$^-$) resin (30 mg) at room temperature. After 6 days no significant reaction had occurred as detected by t.l.c. analysis (silica, ethyl acetate).

(v) A solution of the dinitrile (**10c**) (35 mg) in water (3 ml) containing concentrated sulphuric acid (5 drops) was heated, at reflux point, for 16 h. T.l.c. analysis (silica, ethyl acetate) indicated a complex mixture of u.v. active compounds from which the required product (**5a**) could not be isolated.

Preparation of (3S,5S)-3,5-*Bis*(*dimethyl-t-butylsilyloxy*)-*heptane*-1,7-*dinitrile* (**11b**).—The dinitrile (**10c**) (0.52 g) in dry *N*,*N*-dimethylformamide (5 ml) was treated with chloro-dimethyl-t-butylsilane (1.11 g) and imidazole (1.01 g). The reaction mixture was stirred at room temperature for 2 days and partitioned between diethyl ether (50 ml) and water (50 ml). The aqueous phase was extracted with ether (3 × 50 ml) and the combined extracts were dried and evaporated under reduced pressure to yield a pale oil (2.05 g). Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane–light petroleum) afforded the *title compound* (**11b**) (1.23 g, 96%) as a white crystalline solid, m.p. 43—45.5 °C, $[\alpha]_D^{22}$ −30.2° (*c* 1.61, $CHCl_3$), $\nu_{max.}$(Nujol) 2 245, 1 255, 1 110, 1 100, 840, 810, and 780 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 0.13 (6 H, s, 2 × $SiCH_3$), 0.16 (6 H, s, 2 × $SiCH_3$), 0.92 (18 h, s, 2 × SiBu^t), 1.90 (2H, dd, *J* 5.7 Hz, CH_2), 2.52 (2H, dd, J_{gem} 16.7, *J* 5.0 Hz, 2 C*H*H′CN), 2.62 (2 H, dd, J_{gem} 16.7, *J* 5.5 Hz, 2 × CH*H*′CN), and 4.05—4.11 (2 H, m, 2 × CHO); δ_C($CDCl_3$) −4.4 (q, $SiCH_3$), −4.3 (q, $SiCH_3$), 17.9 [s, *C*(CH_3)$_3$], 25.7 [q, C(*C*H_3)$_3$], 27.1 (t, *C*H_2CN), 44.9 (t, CH_2), 66.2 (d, CHO), and 116.9 (s, CN); *m/z* ($M^{+\bullet}$ absent, 367 ($M^{+\bullet}$ − CH_3), 325 ($M^{+\bullet}$ − Bu^t), 299, 285, 231, 224, 189, 184, 147, 129, 115, 101, 89, 75 (100%), 73, 59, 57, and 55 (Found: C, 59.8; H, 10.05; N, 7.15. $C_{19}H_{38}N_2O_2Si$ requires C, 59.65; H, 10.0; N, 7.3%).

Preparation of 5-O-*Diphenyl-t-butylsilyl*-D-*ribonic Acid* γ-*Lactone* (**6e**).—D-(+)-Ribonic acid γ-lactone (**6b**) (3.0 g) was stirred with chlorodiphenyl-t-butylsilane (6.13 g) and imidazole (3.0 g) in dry *N*,*N*-dimethylformamide (20 ml) at room temperature for 20 h. The reaction mixture was partitioned between diethyl ether (150 ml) and water (150 ml) and the aqueous phase extracted with diethyl ether (3 × 100 ml). The combined extracts were dried and concentrated under reduced pressure to yield a white solid (9.51 g). T.l.c. analysis (silica, dichloromethane) showed this to be a mixture of two major products. Medium-pressure chromatography on silica (Kieselgel H, 250 g, eluant dichloromethane–diethyl ether) afforded the *title compound* (**6e**) (6.62 g, 85%) as a microcrystalline solid, m.p. 65—70 °C (from dichloromethane–light petroleum), $[\alpha]_D^{22}$ +46.3° (*c* 0.84 $CHCl_3$), $\nu_{max.}$(Nujol) 3 300, 1 790, 1 430, 1 180, 1 135, 1 110, 1 080, 970, 940, 855, 820, 765, 725, and 700 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.03 (9 H, s, SiBu^t), 3.78 (1 H, dd, $J_{5,5'}$ 12.0, $J_{4,5}$ 2.5 Hz, 5-H), 3.87 (1 H, dd, $J_{5,5'}$ 12.0, $J_{4,5'}$ 2.5 Hz, 5′-H), 4.03 (1 H, br s, D_2O exch.), 4.49 (1 H, m distorted t, 4-H) 4.54 (1 H, dd, *J* 5.5 Hz, 3-H), 4.62 (1 H, br s, D_2O exch.), and 4.87 (1 H, d, $J_{2,3}$ 4.0 Hz, 2-H); *m/z* No $M^{+\bullet}$ peak, 329 ($M^{+\bullet}$ − Bu^t), 283, 242, 241, 224, 223, 199, 183, 181, 164, 163, 145, 139, 135, 105, 91, 87, 77, 57, 50, 49, 48, 47, and 35 (Found: C, 65.1; H, 6.8. $C_{21}H_{26}O_5Si$ requires C, 65.26; H, 6.78%), and 3,5-*bis*(O-*diphenyl-t-butylsilyl*)-D-*ribonic acid* γ-*lactone* (**12**) (1.15 g, 9%) as a white crystalline solid, m.p. 143—146 °C (from dichloromethane–light petroleum), $[\alpha]_D^{22}$ +44.2° (*c* 0.56, $CHCl_3$), $\nu_{max.}$(Nujol) 3 480, 1 755, 1 430, 1 215, 1 200, 1 165, 1 110, 1 100, 940, 820, 800, 760, 740, and 700 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 0.73 (9 H, s, SiBu^t), 1.17 (9 H, s, SiBu^t), 3.07 (1 H, s, D_2O exch.), 3.55 (1 H, dd, J_{gem} 11.7, $J_{4,5}$ 1.5 Hz, 5-H), 3.75 (1 H, dd, J_{gem} 11.7, $J_{4,5}$ 2.5 Hz, 5-H′), 3.94 (1 H, dd, $J_{2,3}$ 5.5 $J_{3,4}$ 1.2 Hz, 3-H), 4.38 (1 H, m, 4-H), 4.86 (1 H, d, $J_{2,3}$ 5.5 Hz, 2-*H*), and 7.20—7.90 (20 H, m, aryl-H); *mz* $M^{+\bullet}$ absent, 568 ($M^{+\bullet}$ − Bu^t), 551, 550, 523, 522, 491, 490, 463, 462, 384, 320, 260, 243, 223, 205, 183, 163, and 77 (Found: C, 71.1; H, 7.15. $C_{37}H_{44}O_5Si_2$ requires C, 71.1; H, 7.1%).

Preparation of 2,3-*Di*-O-*acetyl*-5-O-*diphenyl-t-butylsilyl*-D-*ribonic Acid* γ-*Lactone* (**6f**).—(i) 5-*O*-Diphenyl-t-butylsilyl-D-ribonic acid γ-lactone (**6e**) (2.0 g) was dissolved in acetic anhydride (50 ml) at 0 °C and the solution treated with pyridine (2 drops). The reaction mixture was stirred at room temperature

overnight and the solvent removed under reduced pressure. The residue was partitioned between diethyl ether and aqueous sodium hydrogencarbonate and the aqueous phase was extracted with diethyl ether (× 3). The combined extracts were dried and concentrated under reduced pressure to afford the *title compound* (**6f**) (2.28 g, 94%) as a colourless oil; t.l.c. analysis (silica, dichloromethane; R_F 0.5) indicated the oil to be a single homogeneous compound, $[\alpha]_D^{22}$ +4.9° (*c* 1.51, $CHCl_3$), $\nu_{max.}$(liq. film) 2 960, 2 935, 2 860, 1 805, 1 755, 1 430, 1 375, 1 240, 1 210, 1 180, 1 110, 825, 730, and 7.05 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.07 (9 H, s, SiBu^t), 2.12 (3 H, s, $COCH_3$), 2.18 (3 H, s, $OCOCH_3$) 3.85 (1 H, dd, $J_{5,5'}$ 11.8 $J_{4,5}$ 1.8 Hz, 5-H), 3.92 (1 H, dd, $J_{5,5'}$ 11.8, $J_{4,5'}$ 2.3 Hz, 5'-H), 4.52 (1 H, distorted, t, 4-H), 5.58 (1 H, dd, *J* 6.1 Hz, 3-H), 6.06 (1 H, d, $J_{2,3}$ 6.1 Hz, 2-H), and 7.36—7.50, and 7.60—7.73 (10 H, m, aryl-H); *m/z* 471 ($M^{+\cdot}$ + 1), 413 ($M^{+\cdot}$ − Bu^t), 371, 311, 283, 241, 223, 199, 181, 163, and 43 (100%) (Found: C, 64.0; H, 6.45. $C_{25}H_{30}O_7Si$ requires C, 63.8; H, 6.4%).

(ii) D-(+)-Ribonic acid γ-lactone (**6b**) (2.11 g) was treated with chlorodiphenyl-t-butylsilane[13] (3.91 g) and imidazole (1.94 g) in dry *N*,*N*-dimethylformamide (16 ml) at room temperature overnight. The reaction mixture was partitioned between diethyl ether (100 ml) and water (100 ml) and the aqueous phase was extracted with diethyl ether (3 × 100 ml). The combined extracts were dried and concentrated under reduced pressure to yield a colourless oil (6.72 g). The oil was dissolved in acetic anhydride (25 ml) containing pyridine (3 drops) and the solution stirred at room temperature overnight. The solvent was removed under reduced pressure and the reaction mixture partitioned between diethyl ether and aqueous sodium hydrogencarbonate. The aqueous phase was extracted with diethyl ether (× 3) and the combined extracts were dried and concentrated under reduced pressure to afford a colourless oil (5.85 g). Medium-pressure chromatography on silica [Kieselgel H, 100 g, eluant dichloromethane–light petroleum (1:1)] afforded the title compound (**6f**) (4.08 g, 61%), with spectral data identical with those of an authentic sample.

Preparation of (5S)-3-*Acetoxy*-5-[(*diphenyl-t-butylsilyloxy*)*methyl*]*furan*-2(5H)-*one* (**7e**).—A solution of 2,3-di-*O*-acetyl-5-*O*-diphenyl-t-butylsilyl-D-ribonic acid γ-lactone (**6f**) (1.99 g) in dry THF (40 ml) was treated with DBU (0.64 g) with stirring at 0 °C for 0.75 h. The reaction was quenched by the addition of Amberlyte IR 120H$^+$ resin, and the mixture filtered and evaporated under reduced pressure to dryness. Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane) afforded the *title compound* (**7e**) (1.54 g, 89%) as a colourless oil, t.l.c. analysis (silica, dichloromethane R_F 0.75) indicated a single homogeneous material, $\nu_{max.}$(thin film) 1 775, 1 190, 1 105, 700, and 600 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.02 (9 H, s, SiBu^t), 2.29 (3 H, s, $COCH_3$), 3.84 and 3.88 (2 H, ddd, J_{gem} 16.0 $J_{5,6}$ 4.5, $J_{5,6'}$ 4.6 Hz, 6-H,H'), 5.02—5.09 (1 H, m, 5-H), 7.18 (1 H, d, $J_{4,5}$ 1.9 Hz, 4-H), 7.33—7.48 and 7.58—7.68 (10 H, m, aryl-H); *m/z* 412 ($M^{+\cdot}$ + 2), 410 ($M^{+\cdot}$), 377, 353 ($M^{+\cdot}$ − 57), 311, 256, 199 (100%), 181, 77, and 43 (Found: C, 67.2; H, 6.6; $M^{+\cdot}$, 410.1557. $C_{23}H_{26}O_5Si$ requires C, 67.3; H, 6.4%; $M^{+\cdot}$, 140.1549).

Preparation of (3S,5S)-3-*Acetoxy*-5-[(*diphenyl-t-butylsilyloxy*)*methyl*]*dihydrofuran*-2(3H)-*one* (**9b**).—The lactone (**7e**) (5.17 g) in dry THF (150 ml) was treated with DBU (2.01 g) with stirring at 0 °C for 20 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride, and partitioned between diethyl ether (150 ml) and water (150 ml). The aqueous phase was extracted with ether (3 × 100 ml) and the combined extracts were concentrated under reduced pressure to small bulk, diluted with ethanol (100 ml), and hydrogenated over 10% palladium on carbon (200 mg), at atmospheric pressure overnight. After filtration through Celite the solvent was removed under reduced pressure to yield a yellow oil (4.37 g). Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane) afforded the *title compound* (**9b**) (3.80 g, 84%) as a yellow oil; t.l.c. analysis (silica, dichloromethane; R_F 0.7) indicated a single homogeneous material, $\nu_{max.}$(liq. film) 2 940, 2 860, 1 800, 1 750, 1 430, 1 375, 1 230, 1 115, 825, 745, and 705 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.06 (9 H, s, SiBu^t), 2.16 (3 H, s, $COCH_3$), 2.27 (1 H, ddd, $J_{4\alpha,4\beta}$ 12.8, $J_{4\alpha,5} = J_{3,4\alpha}$ 10.0 Hz, 4α-H), 2.69 (1 H, ddd, $J_{4\alpha,4\beta}$ 12.8, $J_{3,4\beta}$ 9.1, $J_{4\beta,5}$ 6.1 Hz, 4β-H), 3.74 (1 H, dd, $J_{6,6'}$ 11.6, $J_{5,6}$ 3.9 Hz, 6-H), 3.92 (1 H, dd, $H_{6,6'}$ 11.6, $J_{5,6'}$ 3.4 Hz, 6-H'), 4.53 (1 H, 10 line m, 5-H), 5.52 (1 H, dd, $J_{3,4\alpha}$ 10.0 Hz, $J_{3,4\beta}$ 9.1 Hz, 3-H), and 7.34—7.73 (10 H, m, aryl-H); *m/z* 455 impurity, 413 ($M^{+\cdot}$ + 1), 355 ($M^{+\cdot}$ − 57), 313, 297, 267, 241, 207, 199 (100%), 181, 77, and 43 (Found: C, 66.95; H, 6.85. $C_{23}H_{28}O_5Si$ requires C, 66.95; H, 6.85%).

Preparation of (2S,4S)-1-(*Diphenyl-t-butylsilyloxy*)*pentane*-2,4,5-*triol* (**10d**).—A solution of the lactone (**9b**) (12.41 g) in THF (190 ml) and water (60 ml) containing boric acid (1.70 g) and Amberlyte IR 120H$^+$ resin (26 ml) was treated with sodium borohydride (11.0 g) over 30 min. The temperature of the reaction mixture was maintained in the range 20—30 °C with the aid of external ice-cooling. T.l.c. analysis (silica, dichloromethane) indicated an absence of starting material after 2 h. The reaction mixture was quenched after 2.5 h by addition of glacial acetic acid. The solvent was removed under reduced pressure and the residue partitioned between diethyl ether (200 ml) and water (200 ml). The aqueous phase was extracted with ether (3 × 150 ml) and the combined extracts concentrated under reduced pressure to afford a colourless oil which was dissolved in methanol (100 ml) and stirred with potassium carbonate (0.75 g, 5.43 mmol) for 2 h. The solvent was removed under reduced pressure to yield an amber oil. Medium-pressure chromatography on silica (Kieselgel H, eluant diethyl ether–dichloromethane) afforded the *title compound* (**10d**) (8.82 g, 89%) as a colourless oil which solidified with time to yield a waxy white solid, m.p. 34—40 °C, $[\alpha]_D^{22}$ − 3.0° (*c* 4.07, $CHCl_3$), $\nu_{max.}$(Nujol) 3 360, 1 430, 1 110, 1 080, 740, 700, and 610 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.06 (9 H, s, SiBu^t), 1.47 (2 H, distorted t, CH_2), 3.40—4.10 (9 H, m), and 7.30—7.45 and 7.57—7.75 (10 H, m, aryl-H); *m/z* 343 ($M^{+\cdot}$ − 31), 299, 281, 241, 221, 199 (100%), 181, 143, 139, 135, 101, 83, 77, 57, and 43 (Found: C, 67.15; H, 8.1. $C_{21}H_{30}O_4Si$ requires C, 67.35; H, 8.07%). In a separate series of reactions D-(+)-ribonic acid γ-lactone (**6b**) (22.2 g) was converted into the alcohol (**10d**) in 48% overall yield without isolation of any of the intermediates.

Preparation of (2S,4S)-5-*Diphenyl-t-butylsilyloxy*-2,4-*dihydroxypentyl* 2,4,6-*Tri-isopropylbenzenesulphonate* (**10e**).—A solution of the triol (**10d**) (8.68 g) in dry pyridine (90 ml) was cooled to 0 °C and treated with 2,4,6-tri-isopropylbenzenesulphonyl chloride (11.13 g). The reaction mixture was allowed to warm up to room temperature and stirred for 40 h. The solvent was removed under reduced pressure and the residue partitioned between diethyl ether (300 ml) and dilute hydrochloric acid (200 ml). The aqueous phase was extracted with diethyl ether (3 × 100 ml) and the combined extracts dried and concentrated under reduced pressure. The residue was subjected to medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane–light petroleum) to afford the crude title compound (**10e**) (12.48 g, 84%) as a yellow oil, $\nu_{max.}$(thin film) 3 380, 2 960, 2 930, 2 890, 2 860, 1 600, 1 460, 1 430, 1 385, 1 365, 1 350, 1 180, 1 110, 820, 740, and 700 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.05 (9 H, s, SiBu^t), 1.10—1.40 [19 H, m, 3 × $-CH(CH_3)_2$ + 3-H], 1.50—1.65 (1 H, m, 3-H'), 2.80—3.00 [1 H, m, $CH(CH_3)_2$], 3.42—3.75 (2 H, m), 3.87—4.30 [6 H, m,

2 × -C*H*$(CH_3)_2$], 4.55—4.90 (2 H, m), 7.19 (2 H, s, aryl-H), and 7.30—7.47 and 7.55—7.67 (10 H, m, aryl-H).

Preparation of (3S,5S)-6-*Diphenyl-t-butylsilyloxy*-3,5-*dihydroxyhexanenitrile* (**10f**).—(i) A solution of the sulphonate (**10e**) (1.49 g) in ethanol (20 ml) was treated with potassium cyanide (0.22 g, 3.28 mmol) at room temperature with stirring for 48 h. T.l.c. analysis (silica, 10% diethyl ether–dichloromethane) indicated the presence of two non-polar u.v.-active materials. The solvent was removed under reduced pressure to yield a brown oil. Medium-pressure chromatography on silica (Kieselgel H, eluant 10% diethyl ether–dichloromethane) afforded the crude title compound (**10f**) (486 mg, 55%) as a colourless oil, $\nu_{max.}$(Nujol) 3 460, 2 250, 1 105, 910, 815, 735, and 700 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 1.07 (9 H, s, SiBu^t), 1.66 (2 H, ddd, 4-H,H′), 2.52 (1 H, d, $J_{2,3}$ 1.5 Hz, 2-H), 2.55 (1 H, d, $J_{2',3}$ 1.2 Hz, 2-H′), 2.91 (1 H, br s, D_2O exch.), 3.56 (1 H, dd, $J_{6,6'}$ 10.2, $J_{5,6}$ 7.3 Hz, 6-H), 3.66 (1 H, dd, $J_{6,6'}$ 10.2, $J_{5,6'}$ 4.0 Hz, 6-H′), 3.94—4.10 (1 H, m, 5-H), 4.14—4.30 (2 H, m, 3-H and D_2O exch.), and 7.30—7.77 (10 H, m, aryl-H); *m/z* No $M^{+\bullet}$ peak, 326 ($M^{+\bullet}$ − 57), 299, 281, 246, 228, 226, 199 (100%), 181, 163, 143, 139, 135, 117, 105, 57, 43, and 41; and (2S,4S)-5-(*diphenyl-t-butylsilyloxy*)-4-*hydroxy*-1,2-*epoxypentane* (**13**) (345 mg, 42%) as a colourless oil [t.l.c. analysis (silica, 10% diethyl ether–dichloromethane); R_F 0.6], $[\alpha]_D^{22}$ −9.4° (*c* 2.24, $CHCl_3$), $\nu_{max.}$(liq. film) 3 450, 2 925, 2 860, 1 470, 1 460, 1 425, 1 100, 1 090, 820, 800, 740, 700, and 610; δ_H (250 MHz) ($CDCl_3$) 1.09 (9 H, s, SiBu^t), 1.42—1.52 (1 H, ddd, $J_{3,3'}$ 14.3, $J_{2,3}$ 7.1, $J_{3,4}$ 3.9 Hz, 3-H), 1.74 and 1.85 (1H, ddd, $J_{3,3'}$ 14.3, $J_{3',4}$ 8.8, $J_{2,3'}$ 4.2 Hz, 3-H′), 2.48 (1 H, dd, $J_{1,1'}$ 5.0, $J_{1,2}$ 2.7 Hz, 1-H), 2.75 (1 H, dd, $J_{1,1'}$ 5.0, $J_{1',2}$ 4.1 Hz, 1-H′), 2.80 (1 H, br s, D_2O exch.), 3.05—3.13 (1 H, m, 2-H), 3.55 (1 H, dd, $J_{5,5'}$ 10.2, $J_{4,5}$ 7.0 Hz, 5-H), 3.69 (1 H, dd, $J_{5,5'}$ 10.2 $J_{4,5'}$ 4.0 Hz, 5-H′), 3.90—4.04 (1 H, br m, 4-H), and 7.32—7.50 and 7.60—7.78 (10 H, m, aryl-H); δ_C($CDCl_3$ 19.3 [s, Si*C*$(CH_3)_3$], 27.0 [q, SiC(*C*$H_3)_3$], 36.1 (t, central CH_2), 47.2 (t, CH_2OSi), 49.7 [d, CH(OH)], 68.0 (t, $\overline{CH_2OCH}$), 69.9 (d, $\overline{CH_2OCH}$), 127.9 (d, CH-aryl), 129.9 (d, CH-aryl), 133.3 (s, aryl), and 135.6 (d, CH-aryl); *m/z* $M^{+\bullet}$ absent, 341 ($M^{+\bullet}$ − 15), 299 ($M^{+\bullet}$ − 57), 281, 241, 220, 199 (100%), 181, 163, 139, 135, 116, 105, 91, 77, 57, and 41 (Found: C, 70.55; H, 8.1. $C_{21}H_{28}O_3Si$ requires C, 70.75; H, 7.9%).

(ii) A solution of the sulphonate (**10e**) 1.0 g) in ethanol (20 ml) was stirred with potassium cyanide (0.35 g, 5.35 mmol) at room temperature for 2 days. T.l.c. analysis (silica, 10% diethyl ether in dichloromethane) indicated the presence of a quantity of the epoxide (**13**) (R_F 0.5). Potassium cyanide (0.2 g, 3.08 mmol) was added to the reaction mixture and stirring continued for 2 days. The solvent was removed, under reduced pressure, to yield a brown oil. Medium-pressure chromatography on silica (Kieselgel H, eluant diethyl ether–dichloromethane) afforded the title compound (**10f**) (413 mg, 69%) as a colourless oil. Spectral data were identical with those of an authentic sample.

(iii) A solution of the sulphonate (**10e**) (0.61 g) in dry dimethyl sulphoxide (3 ml) was stirred with potassium cyanide (0.12 g, 1.89 mmol) at room temperature for 7 days. The solvent was removed under reduced pressure to yield a dark oil (387 mg). Preparative-layer chromatography on silica [GF_{254}, eluant diethyl ether–dichloromethane (1:1)] afforded the title compound (**10f**) (301 mg, 83%) as a colourless oil. Spectral data were identical with those of an authentic sample.

Preparation of (3S,5S)-3,5-*Bis*(*dimethyl-t-butylsilyloxy*)-6-(*diphenyl-t-butylsilyloxy*)*hexanenitrile* (**14**).—A solution of the nitrile (**10f**) (0.77 g) in dry *N*,*N*-dimethylformamide (6 ml) was stirred with imidazole (0.75 g) and chlorodimethyl-t-butylsilane (0.66 g) at room temperature for 2 days. The solvent was removed under reduced pressure and the residue partitioned between diethyl ether (50 ml) and water (50 ml). The aqueous phase was extracted with diethyl ether (3 × 50 ml) and the combined extracts dried and concentrated under reduced pressure to yield a colourless oil. Purification by medium-pressure chromatography on silica [Kieselgel H, eluant dichloromethane–light petroleum (1:2)], afforded the *title compound* (**14**) (1.03 g, 84.5%) as a colourless oil, $\nu_{max.}$(thin film) 2 950, 2 925, 2 890, 2 855, 2 250w, 1 465, 1 430, 1 255, 1 100, 830, 775, 740, 705, and 610 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) −0.11 (3 H, s, $SiCH_3$), −0.01 (3 H, s, $SiCH_3$), 0.12 (3 H, s, $SiCH_3$), 0.14 (3 H, s, $SiCH_3$), 0.82 (9 H, s, SiBu^t), 0.93 (9 H, s, SiBu^t), 1.06 (9 H, s, SiBu^t), 1.55—1.73 (1 H, ddd, $J_{4,4'}$ 14.1, $J_{4,5}$ 8.2, $J_{3,4}$ 6.1 Hz 4-H), 2.03—2.16 (1 H, ddd, $J_{4,4'}$ 14.1, $J_{3,4'}$ 5.7 $J_{4',5}$ 3.7 Hz, 4-H′), 2.47 (1 H, dd, $J_{2,2'}$ 16.6, $J_{2,3}$ 6.0 Hz, 2-H), 2.61 (1 H, dd, $J_{2,2'}$ 16.6, $J_{2',3}$ 4.5 Hz, 2-H′), 3.38 (1 H, dd, $J_{6,6'}$ 10.0, $J_{6,5}$ 7.8 Hz, 6-H), 3.58 (1 H, dd, $J_{6,6'}$ 10.0, $J_{6',5}$ 4.6 Hz, 6-H′), 3.70—3.86 (1 H, m, 5-H), and 4.04—4.16 (1 H, m, 3-H) (Found: C, 67.05; H, 9.45; N, 2.05. $C_{34}H_{57}NO_3Si_3$ requires C, 66.7; H, 9.4; N, 2.3%).

Preparation of (4S,6S)-4-*Dimethyl-t-butylsilyloxy*-6-[(*dimethyl-t-butylsilyloxy*)*methyl*]*tetrahydro*-2H-*pyran*-2-*one* (**5b**).—A solution of the nitrile (**10f**) (9.38 g) in 1M-sodium hydroxide solution (90 ml) was heated at 60—70 °C for 44 h; the reaction mixture was stirred by passage of a constant stream of nitrogen gas. After cooling, the mixture was washed with diethyl ether (2 × 50 ml) and acidified by the addition of Amberlyte IR 120H$^+$ resin. The aqueous phase was filtered and the solvent removed under reduced pressure to afford a white solid. The solid was heated at reduced pressure (65—70 °C/1 mmHg) for 17 h and the residue stirred with chlorodimethyl-t-butylsilane (22.14 g) and imidazole (24.98 g) in dry *N*,*N*-dimethylformamide (50 ml) at room temperature for 2 days. The solvent and the excess of chlorosilane were removed under reduced pressure and the residue partitioned between diethyl ether (200 ml) and water (200 ml). The aqueous phase was extracted with diethyl ether (3 × 100 ml) and the combined extracts dried and concentrated under reduced pressure to afford a white crystalline solid. Medium-pressure chromatography on silica (Kieselgel H, eluant dichloromethane) yielded an amber oil (6.76 g), which was subjected to bulb-to-bulb distillation to afford the *title compound* (**5b**) (3.70 g, 40%) as a pale yellow oil, b.p. 150 °C at 0.4 mmHg, $[\alpha]_D^{22}$ +0.5° (*c* 1.07, $CHCl_3$), $\nu_{max.}$($CHCl_3$) 2 920, 2 850, 1 730, 1 085, and 830 cm^{-1}; $\nu_{max.}$(thin film) 2 950, 2 850, 1 745, 1 465, 1 250, 1 135, 1 090, 840, 780, 740, and 670 cm^{-1}; δ_H (250 MHz) ($CDCl_3$) 0.07 [6 H, s, $Si(CH_3)_2$], 0.08 (18 H, s, 2 × SiBu^t) 0.87 (18 H, s, 2 × SiBu^t), 1.71—1.78 (1 H, ddd, $J_{5,5'}$ 13.6, $J_{5,6}$ 11.3, $J_{4,5}$ 9.7 Hz, 5-H), 2.13—2.17 (1 H, 16 line m, 5-H′), 2.42 (1 H, dd, $J_{3,3'}$ 17.2 $J_{3,4}$ 8.5 Hz, 3-H), 2.74—2.85 (1 H, ddd, $J_{3,3'}$ 17.2, $J_{3',4'}$ 5.6, $J_{3',5'}$ 1.6 Hz, 3-H′), 3.76—3.77 (2 H, ddd, $J_{\alpha,\alpha'}$ 10.9, $J_{\alpha,6}$ 4.9, $J_{\alpha',6}$ 4.3 Hz, C_α-H,H′), 4.07—4.23 (1 H, m, 4-H), and 4.17—4.33 (1 H, m, 6-H); *m/z* 375 ($M^{+\bullet}$ + 1), 358, 318, 316, 289, 243, 236, 211, 146, 116, 75, and 73 (Found: C, 57.75; H, 10.3. $C_{18}H_{38}O_4Si_2$ requires C, 57.7; H, 10.2%).

Note added in proof: Recently a laevoglucosan-based route for the synthesis of lactones related to (**5b**) has been reported (R. Baker, R. H. O. Boyes, D. M. P. Broom, J. A. Devlin, and C. J. Swain, *J. Chem. Soc., Chem. Commun.*, 1983, 829).

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