Synthesis of the Unique All-*cis* Cyclopentanetetraol Moiety in Funiculosin

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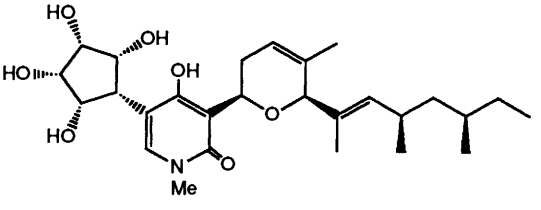
A total synthesis of the all-*cis* cyclopentanetetraol moiety 2,3,4,5-tetrahydroxycyclopentane-1-acetonitrile, present in the antiviral substance funiculosin produced by *Penicillium funiculosum*, is described. Conversion of the known cyclopent-4-ene-1,2,3-triol into the 1-[1-(*t*-butyldimethylsiloxy)vinyl] 2,3-methylene trisether, followed by Claisen–Ireland rearrangement in xylene at 190 °C, first provided the key intermediate all-*cis*-4,5-(methylenedioxy)cyclopent-2-ene-1-acetic acid. Iodolactonisation of this acid then led to the iodo lactone 4β-iodohexahydrofuro[2′,3′:4,3]cyclopenta[*d*][1,3]dioxolan-6-one, which on direct nucleophilic displacement using potassium superoxide in the presence of 18-crown-6 produced the corresponding 4β-hydroxy lactone by an S_N1 mechanism probably *via* the C-4 radical intermediate. The structure and stereochemistry of the hydroxy lactone were determined by X-ray analysis of its *t*-butyldimethylsilyl ether.

The above iodo lactone was converted into the iodohydrin-acetonitrile 2α-hydroxy-3β-iodo-4α,5α-(methylenedioxy)cyclopentane-1α-acetonitrile in three steps, which was then treated with methyl (chloroformyl)acetate to give the corresponding mixed malonate diester. Treatment of this diester with sodium hydride resulted in smooth, intramolecular oxygen nucleophile displacement leading to the all-*cis* ketene acetal methyl [7-(cyanomethyl)-3b,6a,7,7a-tetrahydro-3a*H*-cyclopenta[1,2-*d*;3,4-*d*′]-di[1,3]dioxol-2-ylidene]acetate in 92% yield, hydrolysis of which produced a mixture of positional isomers of all-*cis*-2-(cyanomethyl)-5-hydroxy-3,4-(methylenedioxy)cyclopentyl methyl malonate, which was then saponified to give the all-*cis* cyclopentane-substituted 2,3-dihydroxy-4,5-(methylenedioxy)cyclopentane-1-acetonitrile. The full structure and stereochemistry of this acetonitrile followed from X-ray analysis. The synthesis of (±)-all-*cis*-2,3,4,5-tetrahydroxycyclopentane-1-acetonitrile was then completed following treatment of the 4,5-methylenedioxy compound with ozone, leading to the 4-formate (and its 5-isomer), and saponification.

Funiculosin **1** is a novel and unusual secondary metabolite which has been isolated from the filter cake of *Penicillium funiculosum*.[1] The molecule exhibits antiviral properties and shows antifungal activity against a wide variety of pathogenic fungi; it also exhibits antitumoral activity.[2] Structurally, funiculosin is tricyclic and accommodates a 3-dihydropyran-substituted 4-hydroxy-2-pyridone which is further substituted at C-5 in the pyridone ring by a unique all-*cis* cyclopentanetetraol moiety.†[,3] In addition, funiculosin contains nine chiral centres, five of which are contiguous and associated with the cyclopentanetetraol, the remainder being associated with the *cis*-substituted dihydropyran residue. Although both pyridone[4] and dihydropyran[5] structural units are found quite commonly within natural products, funiculosin is the only natural compound to contain the interesting and unusual all-*cis*-substituted cyclopentanetetraol moiety.[6] The novel and unusual structure of funiculosin, together with its interesting biological profile, attracted us towards synthetic studies with this new antiviral substance. In this paper, we describe a concise and stereocontrolled synthesis of the unique all-*cis* cyclopentanetetraol moiety **36** found in funiculosin.[7]

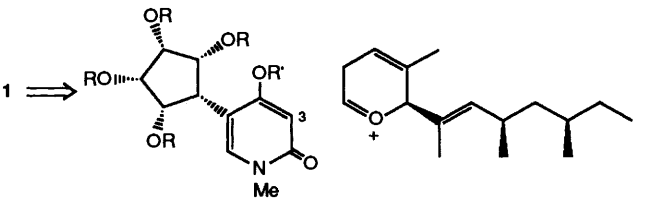
Our general strategy for a total synthesis of funiculosin relied on access to a protected form of the C-5 cyclopentanetetraol-substituted 2-pyridone **2**. Model studies had established that these substituted pyridones undergo specific lithiation at C-3 in the presence of butyllithium at −78 °C, and that the resulting vinyllithium species **4** can be alkylated with a range of electrophiles, leading to the corresponding C-3-alkylated derivatives



1

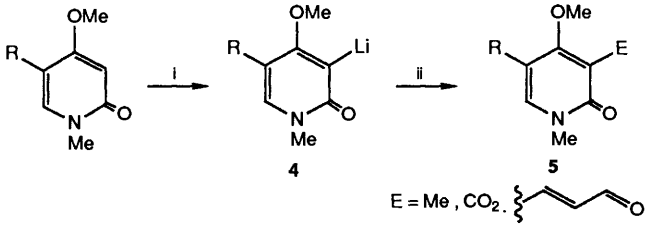
5.[8,9] Thus, alkylation of compound **2** with the oxonium ion (**3**; or an equivalent species) would constitute one of the penultimate steps in the synthesis of funiculosin.

Other model investigations had established that the C-5 cyclopentane-substituted pyridone **8** could be produced from condensation between cyclopentaneacetonitrile and malonyl dichloride, followed by methylation of the resulting chloropyridone **6** (to **7**) and reduction in the presence of tributylstannane and azoisobutyronitrile (AIBN) (Scheme 1).[9] Hence the cyclopentanetetraol acetonitrile **9** became a vital key intermediate in our projected synthesis of funiculosin.

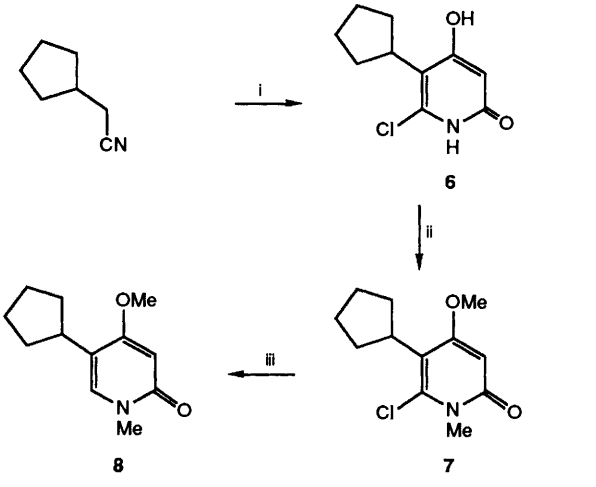


2 **3**

† The C-5 cyclopentanetetraol-substituted pyridone residue in funiculosin bears an interesting structural resemblance to a number of known antiviral agents (ref. 3).

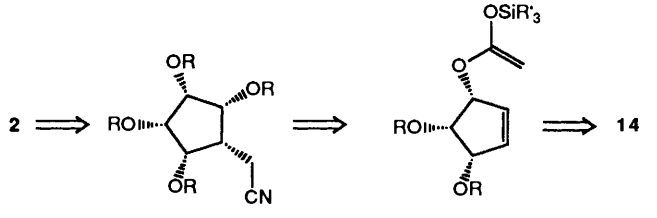


Reagents and conditions: i, BuLi, −78 °C; ii, E^+



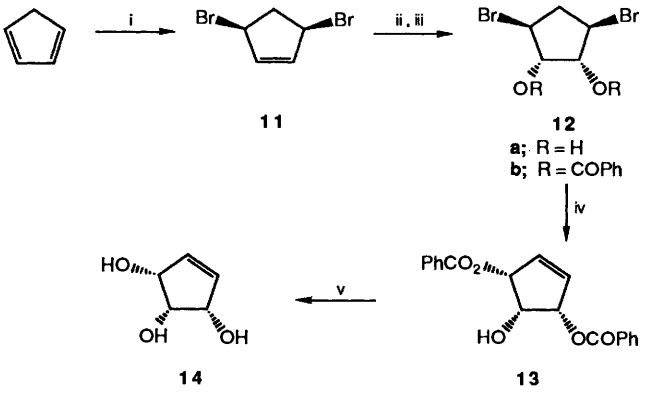
Scheme 1 *Reagents:* i, $CH_2(COCl)_2$, $LiClO_4$; ii, CH_2N_2; iii, Bu_3SnH–AIBN

Analysis of a number of complementary synthetic routes to substituted cyclopentanols led us to design a route to the cyclopentanetetraol acetonitrile **9** which incorporated a Claisen–Ireland rearrangement of the ester enol ether **10**, derived in two steps from the readily available cyclopentenetriol **14**, as a key stage (Scheme 2).



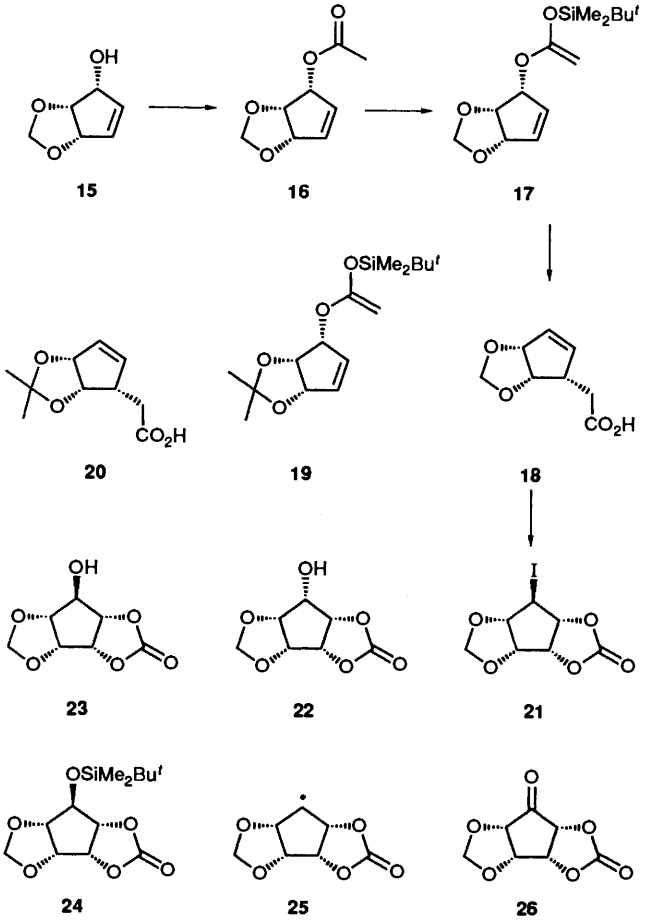
Scheme 2

Thus, optimisation of literature methods first allowed us to prepare the cyclopentenetriol **14** in five steps starting from cyclopentadiene (Scheme 3).[10] Protection of compound **14** as the corresponding methylenedioxy derivative **15**[11] followed by treatment of compound **15** with acetic anhydride in 4-(dimethylamino)pyridine (DMAP) then provided the acetate **16** in 88% yield. Deprotonation of compound **16** by using lithium bis(trimethylsilyl)amide at −78 °C and quenching of the resulting enolate with *t*-butyl(chloro)dimethylsilane in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone[12] next led to the ester enol ether **17** (98%). After some experimentation, it was found that when a solution of compound **17** in dry *m*-xylene was heated in a sealed tube at 190 °C for 18 h, work-up in the presence of tetrabutylammonium fluoride (TBAF) gave the key intermediate cyclopenteneacetic acid **18** as prisms in 89% overall yield from the acetate **16** (Scheme 4). The corresponding isopropylidene acetal enolate **19** was also prepared starting from compound **14**. Under optimum conditions this derivative underwent Claisen–Ireland rearrangement to produce the cyclopenteneacetic acid **20** in 67% yield.*



Scheme 3 *Reagents:* i, Br_2, $CHCl_3$; ii, $KMnO_4$, $MgSO_4$, EtOH; iii, PhCOCl, C_5H_5N; iv, DMSO, $NaHCO_3$; v, NaOMe, MeOH

Iodolactonisation of the cyclopenteneacetic acid **18** in the presence of potassium iodide–iodine–sodium hydrogen carbonate[13] next led to the iodo lactone **21**, which we had hoped that, by simple S_N2 substitution with an appropriate oxygen nucleophile, would produce the all-*cis* cyclopentanetetraol system **22**. This was not to be. Standard conditions[14] led to recovered starting material, and the direct nucleophilic displacement of



Scheme 4

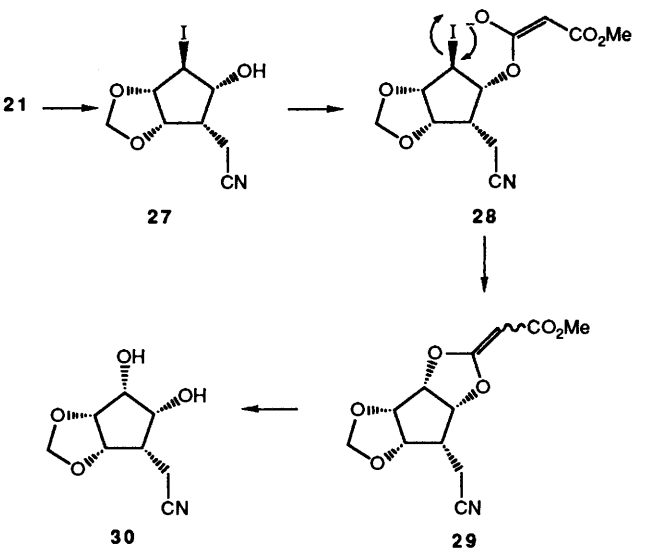
* Earlier we had reported that this rearrangement proceeded in only 5% yield.[7] Under the optimum conditions we have now found that the yield can be increased to 67%.

iodide **21** by using potassium superoxide in dimethylformamide–dimethylsulfoxide (DMF–DMSO) in the presence of one mol equiv. of 18-crown-6,[15] followed by a reductive and aq. work-up, led to an hydroxy lactone derivative whose spectroscopic data did not establish unambiguously that it was the required all-*cis* system **22**. The corresponding crystalline *t*-butyldimethylsilyl ether **24** was therefore prepared, and an X-ray structure determination established that the cyclopentanol was indeed the derivative **23** with the 'wrong' stereochemistry of substituents about the cyclopentane ring. It seems likely that the alcohol **23** arises from the iodide **21** by an S_N1 mechanism with the cyclopentane radical **25** as an intermediate.[16]

Conversion of the cyclopentanol **23** into the corresponding mesate, followed by treatment with superoxide or caesium acetate, both gave starting mesate. Similarly, Mitsunobu conditions [$PhCO_2H$, diethyl azodicarboxylate (DEAD), PPh_3] led to starting cyclopentanol **23**. In addition, we were unable to achieve the oxidation of the alcohol **23** to the corresponding cyclopentanone **26** under a range of conditions; hence it was not possible to examine the reduction of ketone **26** to the required all-*cis* system **22**.

At this stage in our work, we decided to alter our strategy towards the all-*cis*-cyclopentanetetraol acetonitrile **9** in two important ways. First, we decided to relieve steric congestion at the carbon-to-iodine reacting bond in the iodide **21** by opening the lactone ring in the intermediate **21**, thereby leading to nitrile **27**. Secondly we elected to use an *intramolecular* oxygen nucleophile displacement strategy, *i.e.* **28** ⟶ **29**, to introduce the fourth oxygen centre in **27**, using the mixed malonate protocol highlighted by Corey and his colleagues[17] (see Scheme 5).

Thus, the iodo lactone **21** was first converted into the corresponding iodohydrin-acetonitrile **27** following reduction to the hemiacetal **31** on treatment with diisobutylaluminium (DIBAL), formation of the oxime **32** and dehydration of the oxime by using 1,1 -carbonyl diimidazole in refluxing dichloromethane. Reaction between the iodohydrin **27** and methyl (chloroformyl)acetate in the presence of DMAP next produced the mixed ester **33**, which on treatment with sodium hydride at room temperature overnight then gave a satisfying 92% yield of the ketene acetal **29**. Hydrolysis of compound **29** with 1 mol dm^{-3} hydrochloric acid led to a mixture of positional isomers of the malonate diester **34** which was not separated, but instead was saponified in the presence of potassium carbonate to produce the all-*cis* cyclopentane-substituted acetonitrile **30** as a solid (Scheme 6). The structure and stereochemistry of the product **30** were confirmed by a single-crystal X-ray analysis.

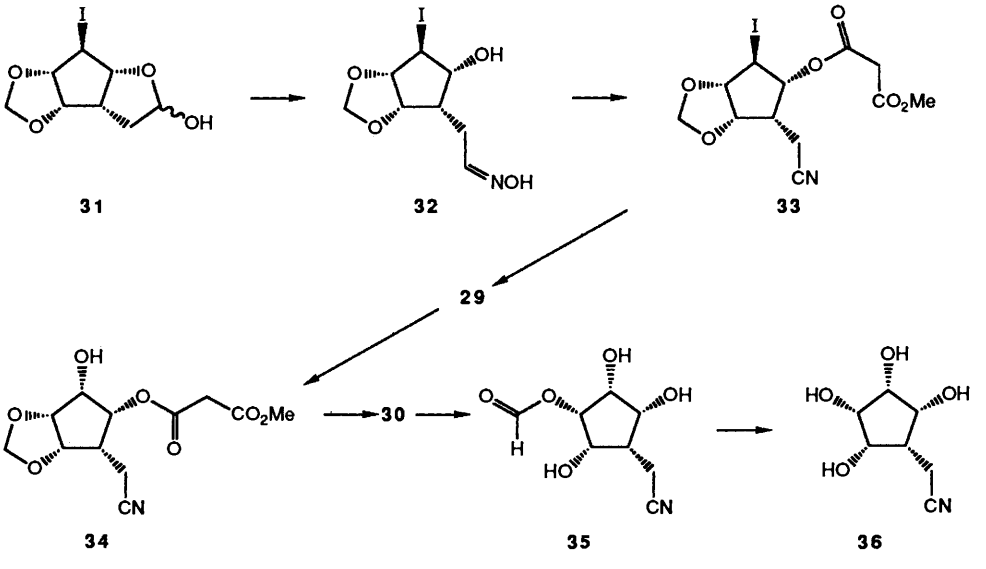


Scheme 5

Finally, when a solution of the methylenedioxy derivative **30** in methanol was treated with ozone at −78 °C,[18] work-up produced a mixture of positional isomers of the expected formate **35**, which on saponification gave rise to the target all-*cis* cyclopentanetetraol acetonitrile **36** as a viscous oil.

Experimental

General Details.—All m.p.s were determined on a Köfler hot-stage apparatus and are uncorrected. UV spectra recorded on a Philips PU 8700 spectrophotometer for solutions in spectroscopic grade ethanol. IR spectra were obtained on a Philips PU 9706, Pye Unicam SP-100 or Perkin-Elmer 1600 series FT-IR instrument. ^1H NMR spectra were recorded on either a Bruker WM 250 (250 MHz) or a Bruker AM 400 (400 MHz) instrument. The spectra were recorded for dilute solutions in deuteriochloroform unless otherwise stated. The chemical shifts were recorded relative to an internal tetramethylsilane



Scheme 6

standard; all coupling constants, *J*, are reported in Hertz. ^{13}C NMR spectra were recorded on either JEOL FX-90 (22.5 MHz), a Bruker WM 250 (62.9 MHz) or a Bruker AM 400 (100.6 MHz) instrument. The spectra were recorded for dilute solutions in deuteriochloroform unless otherwise stated. The chemical shifts are reported relative to internal tetramethylsilane or chloroform standard on a broad-band decoupled mode, and the multiplicities were obtained by using a DEPT sequence. The following abbreviations are used for the multiplicities in ^{13}C spectra: q, methyl; t, methylene; d, methine; s, quaternary.

Mass spectra were recorded on an AE1 MS-902 or a MM-710CF instrument. Microanalytical data were obtained on a Perkin-Elmer 240B elemental analyser.

Flash chromatography was performed on Merck silica gel 60 and the solvents ethyl acetate, light petroleum (boiling range 40–60 °C) and hexanes were redistilled before use. All reactions were monitored by TLC on Merck silica gel 60 F254 precoated aluminium plates which were visualised with UV light and then with either vanillin solution or basic aq. potassium permanganate.

Routinely, dry organic solvents were stored under nitrogen. Benzene, diethyl ether, toluene and xylenes were dried over sodium wire. Other organic solvents were dried by distillation from the following: tetrahydrofuran (THF) (sodium benzophenone ketyl), dichloromethane (phosphorus pentaoxide) and methanol (magnesium methoxide). Other organic solvents and reagents were purified by the accepted literature procedure. Organic extracts were dried over anhydrous magnesium sulfate (unless stated otherwise) and solvents were removed on a Büchi rotary evaporator. Where necessary, reactions requiring anhydrous conditions were performed in a flame- or oven-dried apparatus under nitrogen or argon. A Büchi GKR-50 Kügelrohr apparatus was used for bulb-to-bulb distillations.

3α,5α-*Dibromocyclopentene* **11**.—A solution of bromine (69 cm^3, 215 g, 1.35 mol) in dry chloroform (100 cm^3) was added dropwise, during 50 min, to a stirred solution of freshly distilled cyclopentadiene (90.6 g, 1.37 mol) in dry chloroform (50 cm^3) maintained at −40 °C. The mixture was stirred at −40 °C for 20 min, then pyridine (10 cm^3) was added and the solution was allowed to warm to 0 °C. The resulting mixture was washed with a solution of glacial acetic acid (5 cm^3) and sodium chloride (5 g) in water (50 cm^3) and then the organic layer was separated and dried (Na_2SO_4). The solvent was removed under reduced pressure at < 20 °C and the black oily residue was then triturated with hot light petroleum (3 × 150 cm^3). The petroleum extracts were evaporated to 100 cm^3 and the residue was then cooled to −78 °C for 1 h to give a solid, which was crystallised immediately from light petroleum to yield the dibromide **11** (90.5 g, 30%) as crystals, m.p. 42–45 °C (lit.,[19] 45 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1360 and 890; δ_H 2.77 (d, *J* 16.8, C*H*H), 3.04 (dt, *J* 16.8 and 6.7, CH*H*), 5.07 (dt, *J* 6.8 and 1.3, 2 × CHBr) and 6.16 (d, *J* 1.3, CH=CH); δ_C 44.9 (t), 50.3 (2 d) and 135.8 (2 d) (Found: M^+, 225.8812. Calc. for $C_5H_6Br_2$: M, 225.8815).

3β,5β-*Dibromocyclopentane*-1α,2α-*diol* **12a**.—A solution of 3α,5α-dibromocyclopentene **11** (44 g, 0.19 mol) in dry chloroform (50 cm^3) was added during 10 min to ethanol (2.0 dm^3) which had been cooled to −50 °C. A solution of potassium permanganate (48 g, 0.30 mol) and magnesium sulfate heptahydrate (96 g, 0.39 mol) in water (800 cm^3) was added during 1 h while the temperature was kept below −35 °C. The mixture was stirred at −35 °C for 30 min and was then allowed to warm to 0 °C. Sulfur dioxide was passed through the solution until a white precipitate was formed. The solution was filtered and the ethanol filtrate was evaporated under reduced pressure at < 30 °C. The aq. residue was extracted continuously with diethyl ether (24 h) and the extracts were then dried, and evaporated under reduced pressure to leave a solid. Recrystallisation from dichloromethane–light petroleum gave the diol dibromide **12a** (45 g, 89%) as crystals, m.p. 75 °C (lit.,[19] 75 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3420 and 920; δ_H 240 (dt, *J* 15.2 and 7.4, C*H*H), 3.17 (dt, *J* 15.2 and 7.8 CH*H*), 3.32 (br s, 2 × CHO*H*), 4.07 (dt, *J* 7.4 and 7.4, 2 × CHBr) and 4.43 (br s, 2 × C*H*OH); δ_C 42.3 (t), 47.9 (2 d) and 78.5 (2 d) (Found: C, 23.2; H, 3.2. Calc. for $C_5H_8Br_2O_2$: C, 23.1; H, 3.1%).

3β,5β-*Dibromocyclopentane*-1α,2α-*diyl Dibenzoate* **12b**.—Benzoyl chloride (53.4 cm^3, 0.38 mol) was added during 5 min to a stirred solution of 3β,5β-dibromocyclopentane-1α,2α-diol (54.0 g, 0.21 mol) in dry THF (180 cm^3) containing pyridine (40 cm^3) maintained at 0 °C. The mixture was allowed to warm to 18 °C during 24 h and then the solvent was evaporated off under reduced pressure, with azeotroping of the last of the pyridine with toluene. The solid residue was recrystallised from ethanol to give the dibenzoate **12b** (80 g, 82%) as crystals, m.p. 126 °C (lit.,[10] 122–123 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730, 1280 and 920; δ_H 2.65 (dt, *J* 15.5 and 6.9, C*H*H), 3.36 (dt, *J* 15.5 and 8.3, CH*H*), 4.42 (ddt, *J* 8.3, 6.9 and 4.8, 2 × CHBr), 5.89 (d, *J* 4.8, 2 × C*H*OBz) and 7.35–7.96 (m, 2 × Ph); δ_C 42.7 (t), 44.1 (d), 78.4 (d), 128.4 (d), 128.9 (s), 129.7 (d), 133.5 (d) and 164.9 (s) (Found: C, 48.8; H, 3.5; Br 34.0. Calc. for $C_{19}H_{16}Br_2O_4$: C, 48.7; H, 3.6; Br 34.1%).

Cyclopent-4-*ene*-1α,2α,3α-*triol* 1,3-*Dibenzoate* **13** *and Cyclopent*-4-*ene*-1α,2α,3α-*triol* 1,2-*Dibenzoate*.—A solution of 3β,5β-dibromocyclopentane-1α,2α-diyl dibenzoate **12b** (10 g, 22 mmol) in dry DMSO (150 cm^3) containing sodium hydrogen carbonate (10 g, 119 mmol) was heated at 100 °C for 1.5 h. Water (150 cm^3) was then added, followed by dichloromethane (50 cm^3). The organic layer was separated and the aq. layer was then extracted with dichloromethane (6 × 50 cm^3). The combined organic fractions were washed successively with brine (3 × 50 cm^3) and water (3 × 50 cm^3), then dried, and evaporated under reduced pressure to leave a pale brown oil, which was purified by flash chromatography with 30% ethyl acetate in hexanes as eluant to give the 1,3-dibenzoate **13** (4.1 g, 59%), which was recrystallised from diethyl ether as needles, m.p. 105–106 °C (lit.,[10] 100–101 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 1715 and 1600; δ_H 2.57 (d, *J* 9.5, CHO*H*), 4.63 (dt, *J* 9.5 and 5.5, C*H*OH), 5.77 (dd, *J* 5.5 and 1.3, 2 × C*H*OBz), 6.40 (d, *J* 1.3, HC=CH) and 7.39–8.09 (m, 2 × OBz); δ_C 70.8 (d), 75.4 (d), 128.4 (d), 129.7 (d), 129.9 (s), 133.2 (d), 134.8 (d) and 165.7 (s) (Found: C, 70.2; H, 5.0%; M^+, 324.0990. Calc. for $C_{19}H_{16}O_5$: C, 70.4; H, 5.0%; M, 324.0998). Further elution gave the corresponding 1,2-*dibenzoate* (2.13 g, 30%), which was recrystallised from diethyl ether as needles, m.p. 90–92 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3413, 1716 and 978; δ_H 2.75 (br s, CHO*H*), 4.87 (br s, C*H*OH), 5.56 (td, *J* 5.6 and 11.6, C*H*OBz), 5.92 (br d, *J* 5.6, C*H*OBz), 6.17 (br d, *J* 5.8, C*H*=CH), 6.27 (br d, *J* 5.8, CH=C*H*) and 7.22–7.98 (m, 2 × OBz); δ_C 72.7 (d), 73.1 (d), 74.7 (d), 128.2 (d), 129.6 (d), 129.7 (s), 131.2 (d), 133.0 (d), 137.7 (d), 165.7 (s) and 165.8 (s) [Found: C, 70.4; H, 5.35%; *m/z*, 203.0723. $C_{19}H_{16}O_5$ requires C, 70.4; H, 5.0%; (M − $C_7H_5O_2$), 203.0708].

Cyclopent-4-*ene*-1α,2α,3α-*triol* **14**.—A mixture of the dibenzoate **13** and the corresponding 1,2-dibenzoate isomer (13.1 g, 0.11 mol) was dissolved in a solution of sodium methoxide in methanol (0.1 mol dm^{-3}; 150 cm^3) and the resulting solution was then stirred at room temperature for 1 h. Solid carbon dioxide (5 g) was added portionwise to the mixture and when the effervescence had subsided the solution was filtered and the filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography with 8% methanol in dichloromethane as eluent to give the triol **14** (3 g, 65%), which

was recrystallised from ethyl acetate as needles, m.p. 65 °C (lit.,[10] 65–66 °C); ν_{max}(KBr disk)/cm^{-1} 2960, 1635 and 900; δ_H[$(CD_3)_2SO$)] 3.94 (dt, *J* 6.1 and 5.5, C*H*OH), 4.17 (d, *J* 6.1, CHO*H*), 4.25 (dt, *J* 7.8 and 5.5, 2 × C*H*OH), 4.46 (d, *J* 7.8, 2 × CHO*H*) and 5.80 (s, CH=CH); δ_C[$(CD_3)_2SO$)] 75.5 (d), 77.3 (d) and 138.5 (d) [Found: C, 51.6; H, 7.1%; *m/z* 98.0354. Calc. for $C_5H_8O_3$: C, 51.7; H, 6.9%; (M − H_2O), 98.0367].

4α,5α-(*Methylenedioxy*)*cyclopent*-2-*en*-1α-*ol* **15**.—A solution of cyclopent-4-ene-1α,2α,3α-triol (1.26 g, 10.9 mmol) in hydrochloric acid (1 mol dm^{-3}; 100 cm^3) containing paraformaldehyde (4 g) was heated at 60 °C for 10 h and was then cooled to 18 °C. The solution was extracted with dichloromethane (5 × 50 cm^3) and the extracts were then dried, and evaporated under reduced pressure to give the cyclic acetal **15** (1.24 g, 89%) as an oil, b.p. 78–80 °C/7 mmHg; ν_{max}(liquid film)/cm^{-1} 3400 and 810; δ_H 2.77 (br s, CHO*H*), 4.56 (br d, *J* 4.8, 2 × C*H*OR), 4.67 (s, C*H*HO_2), 5.13 (s, CH*H*O_2), 5.16 (br d, *J* 3.3, C*H*OR), 5.75 (dt, *J* 5.8 and 1.2, C*H*=CH) and 6.15 (dt, *J* 5.8 and 1.1, CH=C*H*); δ_C 74.8 (d), 79.2 (d), 84.0 (d), 94.8 (c), 128.7 (d) and 140.7 (d) [Found: C, 56.1; H, 6.4%; (M^+ + H), 129.0553. $C_6H_8O_3$: Calc. for C, 56.3; H, 6.3%; (M + H), 129.0552].

4α,5α-(*Methylenedioxy*)*cyclopent*-2-*en*-1α-*yl Acetate* **16**.—Acetic anhydride (1 cm^3, 11 mmol) was added dropwise, during 2 min, to a stirred solution of the cyclic acetal **15** (1 g, 7.8 mmol), in dry diethyl ether (30 cm^3) containing pyridine (0.84 cm^3) and DMAP (~ 10 mg) at 0 °C. The mixture was allowed to warm to room temperature during 24 h. The organic layer was washed successively with saturated aq. copper(II) sulfate (3 × 10 cm^3) and water (2 × 5 cm^3), then was dried, and evaporated under reduced pressure (acetic acid was removed by azeotroping with toluene) to leave a pale brown oil, which was purified by Kügelrohr distillation to yield the *acetate* **16** (1.02 g, 88%) as a solid, m.p. 47–49 °C; b.p. 170–172 °C/10 mmHg; ν_{max}(liquid film)/cm^{-1} 1740 and 1570; δ_H 2.13 (s, OAc), 4.57 (s, C*H*HO_2), 4.77 (d, *J* 5.6, C*H*OR), 4.79 (d, *J* 5.6, C*H*OR), 5.08 (s, CH*H*O_2), 5.10 (dd, *J* 5.4 and 1.8, C*H*OR), 5.94 (dt, *J* 5.9 and 1.8, C*H*=CH) and 6.11 (dd, *J* 5.9 and 1.9, CH=C*H*); δ_C 20.6 (q), 75.0 (d), 75.8 (d), 82.6 (d), 93.8 (t), 131.1 (d), 135.0 (d) and 170.4 (s) [Found: C, 56.5; H, 6.1%; *m/z* 140.0477. $C_8H_{10}O_4$ requires C, 56.4; H, 5.9%; (M − CH_2O), 140.0473].

3α-[1-(t-*Butyldimethylsiloxy*)*vinyloxy*]-4α,5α-(*methylenedioxy*)*cyclopentene* **17**.—A solution of the acetate **16** (539 mg, 3.15 mmol) in dry THF (10 cm^3) was added dropwise during 15 min to a stirred solution of lithium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF; 9 cm^3, 9 mmol) maintained at −78 °C. The solution was then stirred for 10 min at −78 °C and then a solution of *t*-butyl(chloro)dimethylsilane (515 mg, 3.4 mmol) in dry 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (5 cm^3) was added dropwise during 5 min. The mixture was maintained at −78 °C for 3 h and was then allowed to warm to −20 °C. Water (10 cm^3) was added and the separated aq. layer was then extracted with pentanes (4 × 10 cm^3). The combined organic layers were washed with water (6 × 10 cm^3) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure left the crude ester enol ether (880 mg, 98%) as an oil, ν_{max}(liquid film)/cm^{-1} 2860, 1650 and 1270; δ_H 0.18 (s, SiMe), 0.19 (s, SiMe), 0.93 (s, SiBu^t), 3.27 (d, *J* 2.8, O_2C=C*H*H), 3.36 (d, *J* 2.8, O_2C=CH*H*), 4.59 (s, O_2C*H*H), 4.72 (dd, *J* 5.4 and 5.4, C*H*OR), 4.77 (dt, *J* 5.5 and 1.7, C*H*OR), 5.08 (dd, *J* 4.8 and 1.9, C*H*OR), 5.08 (s, CH*H*O_2), 5.88 (dt, *J* 6.0 and 1.8, C*H*=CH) and 6.16 (dd, *J* 6.0 and 1.7, CH=C*H*); δ_C −4.6 (q), −4.5 (q), 18.1 (s), 25.6 (q), 62.3 (t), 75.1 (d), 78.6 (d), 82.8 (d), 94.0 (t), 130.1 (d), 135.7 (d) and 160.4 (s) (Found: M^+, 284.1392. $C_{14}H_{24}SiO_4$ requires M, 284.1440), which was used without further purification.

4α,5α-(*Methylenedioxy*)*cyclopent*-2-*en*-1α-*acetic Acid* **18**.—A solution of the ester enol ether **17** (880 mg, 3.1 mmol) in dry xylenes (10 cm^3) was heated in a sealed tube to 190 °C for 18 h. The solution was cooled to 18 °C and then TBAF (1 mol dm^{-3} in THF; 4 cm^3) was added. The mixture was stirred for 1 h and then the solvent was removed under reduced pressure. The residue was purified by flash chromatography with ethyl acetate as eluent to give the *acid* **18** (500 mg, 90%) as a solid, which was recrystallised from diethyl ether–hexanes as rectangular prisms, m.p. 56–58 °C; ν_{max}(liquid film)/cm^{-1} 1715 and 1075; δ_H 2.52 (dd, *J* 17.3 and 7.0, C*H*HCO_2H), 2.62 (dd, *J* 17.3 and 8.8, CH*H*CO_2H), 3.15 (m, RR′C*H*R″), 4.61 (s, C*H*HO_2), 4.69 (dd, *J* 5.8 and 5.8, C*H*OR), 5.02 (s, CH*H*O_2), 5.24 (d, *J* 5.4, C*H*OR), 5.68 (dt, *J* 5.8 and 2.1, C*H*=CH) and 5.96 (d, *J* 5.8, CH=C*H*); δ_C 33.8 (t), 44.0 (d), 77.8 (d), 84.9 (d), 93.4 (t), 127.4 (d), 138.6 (d) and 177.4 (s) [Found: (M^+ + H), 171.0644. $C_8H_{10}O_4$ requires (M + H), 171.0665)].

3α-[1-(t-*Butyldimethylsiloxy*)*vinyloxy*]-4α,5α-(*isopropylidenedioxy*)*cyclopentene* **19**.—A solution of the triol **14** (0.96 g, 8.27 mmol) and toluene-*p*-sulfonic acid (~10 mg) in dry acetone (30 cm^3) containing anhydrous copper(II) sulphate (0.5 g) was stirred at room temperature for 25 h. The copper salts were removed by filtration and were then washed with acetone (3 × 20 cm^3). Evaporation of the solvent under reduced pressure left a pale yellow oil, which was purified by bulb-to-bulb distillation to give the corresponding acetonide (1.01 g, 78%) as an oil, b.p. 65–70 °C/18 mmHg; ν_{max}(thin film)/cm^{-1} 3487, 1213 and 1056; δ_H 1.39 (d, *J* 0.4, CMe), 1.43 (s, CMe), 2.95 (br s, CHO*H*), 4.55 (br d, *J* 5.5, C*H*OH), 4.73 (dd, *J* 5.5 and 5.5, C*H*OR), 5.00 (d, *J* 5.5, C*H*OR) and 5.88 (s, CH=CH); δ_C 26.6 (q), 27.7 (q), 74.2 (d), 77.3 (d), 83.7 (d), 112.4 (s), 131.9 (d) and 136.5 (d) [Found: *m/z*, 141.0548. $C_8H_{12}O_3$ requires (M − CH_3), 141.0552].

Acetic anhydride (0.62 cm^3, 6.6 mmol) was added dropwise during 2 min to a stirred solution of the acetonide alcohol (0.862 g, 5.5 mmol) in dry THF (20 cm^3), containing pyridine (0.62 cm^3) and DMAP (~ 10 mg) at 0 °C. The mixture was allowed to warm to room temperature during 24 h and the separated organic layer was then washed successively with saturated aq. copper(II) sulfate (3 × 10 cm^3). Evaporation of the dried organic extracts under reduced pressure (acetic acid was removed by azeotroping with toluene) left a pale brown oil, which was purified by bulb-to-bulb distillation to yield 4α,5α-(*isopropylidenedioxy*)*cyclopent*-2-*en*-1α-*yl acetate* (0.91 g, 83%) as a solid, m.p. 43–45 °C; b.p. 55–60 °C/13 mmHg; ν_{max}(liquid film)/cm^{-1} 1739, 1241 and 1067; δ_H 1.37 (d, *J* 0.4, CMe), 1.40 (s, CMe), 2.12 (s, OAc), 4.90 (dd, *J* 5.6 and 5.6, C*H*OR), 5.03 (dd, *J* 5.7 and 1.8, C*H*OR), 5.36 (ddd, *J* 5.8, 1.8 and 1.7, C*H*OAc), 5.89 (ddd, *J* 5.8, 1.7 and 0.4, C*H*=CH) and 6.09 (ddd, *J* 5.8, 1.8 and 1.7, CH=C*H*); δ_C 20.6 (q), 26.6 (q), 27.3 (q), 75.7 (d), 76.8 (d), 83.3 (d), 112.5 (s), 131.9 (d), 134.6 (d) and 170.2 (s) [Found: C, 60.25; H, 7.2%; M^+, 183.0645. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.1%; (M − CH_3), 183.0657].

A solution of the acetate (550 mg, 2.78 mmol) in dry THF (10 cm^3) was added dropwise during 15 min to a stirred solution of lithium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF; 8.3 cm^3, 8.3 mmol) maintained at −78 °C. The solution was stirred for 10 min at −78 °C and then a solution of *t*-butyl(chloro)dimethylsilane (468 g, 3.12 mmol) in dry 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (4 cm^3) was added dropwise during 5 min. The mixture was maintained at −78 °C for 3 h and was then allowed to warm to −20 °C. Water (10 cm^3) was added and the separated aq. layer was then extracted with pentanes (4 × 10 cm^3). The combined organic layers were washed with water (6 × 10 cm^3) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure left the crude ester enol ether (860 mg, 98%) as an oil, ν_{max}(liquid film)/cm^{-1} 2931, 1652 and 1270; δ_H

Table 1 Fractional atomic co-ordinates for compound **24** with standard deviations in parentheses

Atom	*x*	*y*	*z*
C(1)	0.389 8(1)	0.649 1(3)	0.144 9(3)
C(2)	0.360 3(1)	0.614 5(3)	0.273 2(3)
C(3)	0.309 5(1)	0.482 4(3)	0.235 4(3)
C(4)	0.305 6(1)	0.443 5(3)	0.084 6(3)
C(5)	0.373 0(1)	0.515 3(3)	0.052 7(3)
C(6)	0.473 8(1)	0.659 7(3)	0.174 8(3)
C(7)	0.498 2(1)	0.508 1(3)	0.168 6(3)
C(8)	0.391 8(2)	0.446 8(4)	0.444 3(3)
C(9)	0.112 5(2)	0.591 1(4)	−0.196 1(3)
C(10)	0.061 6(3)	0.562 6(7)	−0.344 2(5)
C(11)	0.066 0(3)	0.574 2(10)	−0.089 8(6)
C(12)	0.143 5(3)	0.743 1(5)	−0.190 7(6)
C(13)	0.245 5(2)	0.468 0(6)	−0.290 1(4)
C(14)	0.160 1(3)	0.270 8(6)	−0.146 6(7)
O(2)	0.419 0(1)	0.567 0(2)	0.388 5(2)
O(3)	0.347 1(1)	0.374 1(2)	0.328 9(2)
O(4)	0.241 35(9)	0.510 6(2)	−0.001 1(2)
O(5)	0.439 34(9)	0.426 8(2)	0.099 6(2)
O(7)	0.558 73(9)	0.456 4(2)	0.212 1(2)
Si(1)	0.190 84(4)	0.459 2(1)	−0.157 03(8)

Table 2 Fractional atomic co-ordinates for compound **30** with standard deviations in parentheses

Atom	*x*	*y*	*z*
C(1)	0.3950(6)	0.4589(3)	0.1236(2)
C(2)	0.2467(7)	0.4012(3)	0.1703(1)
C(3)	0.1552(6)	0.3067(3)	0.1354(2)
C(4)	0.2363(6)	0.3165(3)	0.0674(2)
C(5)	0.4418(5)	0.3822(3)	0.0703(2)
C(6)	0.5972(7)	0.5030(4)	0.1556(2)
C(7)	0.7573(8)	0.5426(3)	0.1112(2)
C(8)	0.4097(7)	0.2528(4)	0.2068(2)
O(2)	0.3572(4)	0.3562(2)	0.2232(1)
O(3)	0.2412(5)	0.2171(2)	0.1674(1)
O(4)	0.2619(5)	0.2194(2)	0.0366(1)
O(5)	0.6257(4)	0.3199(2)	0.0844(1)
N(1)	0.8870(7)	0.5724(3)	0.0775(2)

0.13 (SiMe), 0.14 (SiMe), 0.87 (SiBu^t), 1.31 (CMe), 1.34 (CMe), 3.20 (d, *J* 2.8, O_2C=CH*H*), 3.30 (d, *J* 2.8, O_2C=C*H*H), 4.73 (d, *J* 6.0, C*H*OR), 4.85 (dd, *J* 6.0 and 5.9, C*H*OR), 4.98 (d, *J* 6.0, C*H*O_2R), 5.88 (d, *J* 6.0, *H*C=CH) and 5.98 (d, *J* 6.0, HC=C*H*); δ_C −4.6 (q), −4.4 (q), 18.2 (s), 25.7 (q), 26.9 (q), 27.4 (q), 62.0 (t), 76.9 (d), 79.0 (d), 83.7 (d), 112.5 (s), 132.3 (d), 133.8 (d) and 160.6 (s).

4α,5α-(*Isopropylidenedioxy*)*cyclopent*-2-*ene*-1α-*acetic Acid* **20**.—A solution of the ester enol ether **19** (860 mg, 2.77 mmol) in dry xylenes (10 cm^3) was heated in a sealed tube to 190 °C for 18 h. The solution was then cooled to 18 °C and TBAF (1 mol dm^{-3} in THF; 4 cm^3) was added. The mixture was stirred for 1 h and then the solvent was removed under reduced pressure. The residue was purified by flash chromatography with ethyl acetate as eluent to give the *acid* **20** (367 mg, 68%) as a solid, which was recrystallised from diethyl ether–hexanes as needles, m.p. 78–80 °C; ν_{max}(liquid film)/cm^{-1} 1779 and 1523; δ_H 1.35 (CMe), 1.40 (CMe), 2.50 (dd, *J* 17.0 and 6.7, C*H*HCO_2H), 2.71 (dd, *J* 17.0 and 6.7, CH*H*CO_2H), 3.11 (m, RR′C*H*CH_2), 4.81 (dd, *J* 5.8 and 5.8, C*H*OR), 5.13 (d, *J* 5.8, C*H*OR), 5.74 (br d, *J* 5.7, *H*C=CH) and 5.82 (d, *J* 5.7, HC=C*H*); δ_C 25.8 (q), 27.1 (q), 33.4 (t), 43.6 (d), 78.6 (d), 85.2 (d), 110.7 (d), 130.7 (d), 135.3 (d) and 178.0 (s) [Found: C, 60.5; H, 7.3%; *m*/*z*, 183.0626. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.1%; (M − Me) 183.0657].

4β-*Iodohexahydrofuro*[2′,3′:4,3]*cyclopenta*[d][1,3]*dioxol*-6-*one* **21**.—A solution of potassium iodide (300 mg, 1.8 mmol) and iodine (150 mg, 0.6 mmol) in water (6 cm^3) was added to a solution of the acid **18** (90 mg, 0.30 mmol) in aq. sodium hydrogen carbonate (0.5 mol dm^{-3}; 6 cm^3). The solution was stirred in the dark for 48 h and was then extracted with dichloromethane (5 × 20 cm^3). The combined extracts were washed successively with aq. sodium thiosulfate (0.5 mol dm^{-3}; 3 × 20 cm^3) and water (20 cm^3), then were dried, and evaporated under reduced pressure to leave the *iodo lactone* **21** (144 mg, 92%) as a solid, which was recrystallised from ethyl acetate–hexanes as needles, m.p. 134–135 °C; ν_{max}($CHCl_3$)/cm^{-1} 1780, 1155 and 1100; δ_H 2.65 (dd, *J* 17.4 and 8.7, RC*H*HCO_2R), 2.90 (d, *J* 17.4, RCH*H*CO_2R), 3.33 (m, RR′C*H*R″), 4.60 (d, *J* 0.5, C*H*OR), 4.79 (s, C*H*HO_2), 4.80 (dd, *J* 6.5 and 5.6, CHI), 5.08 (d, *J* 5.7, C*H*OR), 5.13 (d, *J* 6.5, C*H*OR) and 5.14 (s, CH*H*O_2); δ_C 26.4 (d), 30.3 (t), 41.7 (d), 80.6 (d), 91.5 (d), 92.6 (d), 96.9 (t) and 175.4 (s) [Found: C, 32.6; H, 3.0%; *m*/z (FAB) 297. $C_8H_9IO_4$ requires C, 32.5; H, 3.1%; (MH^+) 297].

4α-*Hydroxyhexahydrofuro*[2′,3′:4,3]*cyclopenta*[d][1,3]-*dioxol*-6-*one* **23**.—A solution of the lactone **21** (33 mg, 1.1 mmol) in dry DMF (7 cm^3) was added dropwise during 5 min to a stirred solution of potassium superoxide (319 mg, 4.4 mmol) and 18-crown-6 (387 mg, 1.6 mmol) in dry DMSO (7 cm^3) at 0 °C. The solution was stirred for a further 3 h and then hydrochloric acid (2 mol dm^{-3}; 5 cm^3) was added. The solvent was removed under reduced pressure and the residue was adsorbed onto silica and purified by flash chromatography with ethyl acetate as eluent to give the *alcohol* **23** (91 mg, 44%) as a solid; ν_{max}($CHCl_3$)/cm^{-1} 1780 and 1310; δ_H 2.63 (dd, *J* 17.5 and 8.9, RC*H*HCO_2R), 2.85 (d, *J* 17.5, RCH*H*CO_2R), 3.18 (m, RR′C*H*R″), 3.66 (br s, CHO*H*), 4.48 (br s, C*H*OR), 4.53 (d, *J* 5.8, C*H*OR), 4.69 (dd, *J* 6.5 and 6.5, C*H*OH), 4.74 (d, *J* 5.9, C*H*OR), 4.79 (s, C*H*HO_2) and 5.05 (s, CH*H*O_2); δ_C 30.0 (t), 41.8 (d), 77.1 (d), 81.2 (d), 88.4 (d), 90.3 (d), 96.4 (t) and 176.4 (s) (Found: M^+, 187.0605. $C_8H_{10}O_5$ requires M, 187.0606).

4β-(t-*Butyldimethylsiloxy*)*hexahydrofuro*[2′,3′:4,3]*cyclopenta*[d][1,3]*dioxol*-6-*one* **24**.—A solution of the alcohol **23** (90 mg, 0.5 mmol), *t*-butyl(chloro)dimethylsilane (108 mg, 0.72 mmol) and imidazole (95 mg, 1.4 mmol) in dry DMF (5 cm^3) was stirred for 14 h at room temperature. Dichloromethane (30 cm^3) was added and the solution was then washed with water (5 × 10 cm^3). The organic extract was evaporated to dryness and the residue was then purified by flash chromatography with 40% ethyl acetate in hexanes as eluent, to give the *silyl ether* **24** (35 mg, 29%) as a solid. The solid was recrystallised from diethyl ether as prisms, m.p. 78–79 °C; ν_{max}($CHCl_3$)/cm^{-1} 1780 and 1103; δ_H 0.13 (s, SiMe), 0.15 (s, SiMe), 0.90 (s, Bu^t), 2.60 (dd, *J* 17.4 and 8.8, RC*H*HCO_2R), 2.82 (br d, *J* 17.4, RCH*H*CO_2R), 3.13 (m, RR′C*H*R″), 4.42 (br s, C*H*OR), 4.43 (br d, *J* 7.2, C*H*OR), 4.60 (br, C*H*OR), 4.67 (dd, *J* 6.4 and 6.2, C*H*OSi), 4.80 (s, C*H*HO_2) and 5.05 (s, CH*H*O_2); δ_C −4.9 (q), 25.7 (q), 29.8 (s), 30.0 (t), 41.8 (d), 77.8 (d), 81.2 (d), 89.0 (d), 90.7 (d), 96.5 (t) and 176.1 (s) [Found: C, 56.1; H, 8.5%; M^+, 213.0571. $C_{14}H_{24}O_5Si$ requires C, 56.0; H, 8.1%; (M − $C_5H_{11}O$), 213.0583].

Crystallographic Analyses of the Furanone **24** *and the Acetonitrile* **30**.—*Crystal data:* **24** $C_{14}H_{24}O_5Si$, M = 300.39. Monoclinic, *a* = 18.585(2), *b* = 9.331(1), *c* = 9.870(1) Å, β = 105.05(1)°, *V* = 1652.92 Å^3, *Z* = 4, D_c = 1.21 g cm^{-3}, *F*(000) = 648. Space group $P2_1/c$. Cu-Kα radiation, λ = 1.541 78 Å, μ(Cu-Kα) = 13.69 cm^{-1}.

Crystal data: **30** $C_8H_{11}NO_4$, M = 185.18. Orthorhombic, *a* = 6.183 (1), *b* = 12.776(2), *c* = 21.312(2) Å, *V* = 1683.62 Å^3, *Z* = 8, D_c = 1.46 g cm^{-3}, *F*(000) = 784. Space group *Pbca*, Cu-Kα radiation, λ = 1.541 78 Å, μ(Cu-Kα) = 10.15 cm^{-1}.

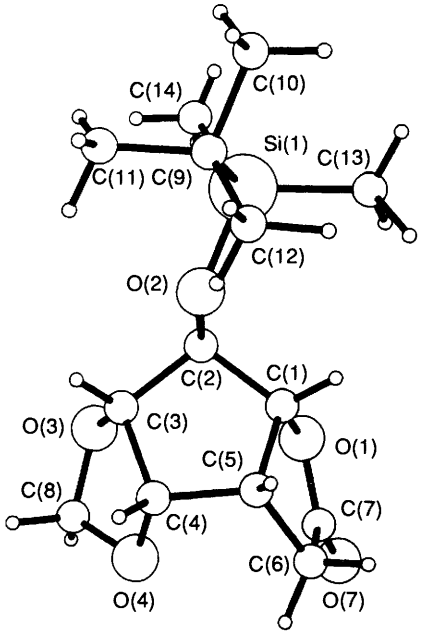


Fig. 1 X-Ray molecular structure of compound **24**

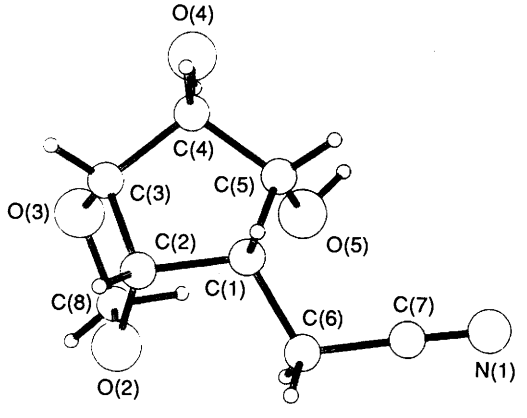


Fig. 2 X-Ray molecular structure of compound **30**

Crystals of approximate dimensions 0.5 × 0.5 × 0.3 mm for **24** and 0.6 × 0.2 × 0.02 mm for **30** were mounted on an Enraf–Nonius CAD4 diffractomer and 25 reflections were used to determine accurate lattice parameters. Intensity data were collected using an ω/θ scan for $1 < \theta < 76$ for **24** and $1 < \theta < 60$ for **30**. Totals of 3445 (for **24**) and 1253 (for **30**) independent reflections were measured of which 2323 and 744, respectively, had $I > 3\sigma(I)$ and were considered observed and were used in the subsequent refinement. Periodic measurement of standard reflections throughout data collection demonstrated their stability. The data were corrected for Lorentz and polarisation factors but no absorption corrections were made. Crystallographic calculations were performed by using the CRYSTALS[20] system of programs. The structures were solved by direct methods by using the SHELX[21] program for compound **24** and the MULTAN[22] program for compound **30**. Least-squares refinement, including anisotropic thermal parameters for non-hydrogen atoms and isotropic refinement of hydrogen atoms located in a difference Fourier synthesis, terminated at R 0.0490 (R_w 0.0637) for compound **24** and at R 0.0331 (R_w 0.0451) for compound **30**. Final difference maps showed no features in excess of 0.3 e Å^{-3} for compound **24**, with the largest near the silicon atom, or 0.1 e Å^{-3} for compound **30**.

The refined fractional atomic co-ordinates are shown in Tables 1 and 2, respectively, and the resulting molecular structures are illustrated in Figs. 1 and 2. In both structures the relative stereochemistries at each centre are clearly revealed. All five-membered rings adopt the envelope conformation with the carbon atoms remote from the ring junctions (C-5 in the cyclopentane and C-8 of the methylenedioxy moiety) out of the planes containing the other four atoms. However, in compound **30** both of these atoms are below the planes while in compound **24** the conformation is different with the methylenedioxy C-8 above the plane. In the lactone ring of compound **24** it is the atom remote from the lactone function (C-1) which is out of the plane. Two intramolecular hydrogen bonds, one to the alcohol oxygen and the other to the cyano nitrogen, control the solid-state packing in a framework arrangement. The remaining geometric data for both structures are unexceptional.*

4β-*Iodohexahydro*-3a*H*-*furo*[2′,3′:4,3]*cyclopenta*[d][1,3]-*dioxol*-6-*ol* **31**.—DIBAL (1 mol dm^{-3} in hexanes; 4.0 cm^3) was added during 2 min to a stirred solution of the lactone **21** (1.13 mg, 3.8 mmol) in dry dichloromethane (100 cm^3) at −78 °C. After 5 min, magnesium sulfate (10 g) and then methanol (2 cm^3) were added, and the mixture was then allowed to warm to room temperature during 1 h. The solution was filtered through a bed of Celite and the filtrate was then evaporated under reduced pressure to leave the crude lactol **31** (0.70 g, 62%) as an oil, ν_{max}(thin film)/cm^{-1} 3420, 1085 and 1025; δ_H 1.85–1.96 (0.8 H, m, CHC*H*HCHO$_2$), 2.44–2.49 (0.2 H, m, CHC*H*H-CHO$_2$), 2.52–2.60 (0.8 H, m, CHCH*H*CHO$_2$), 3.06–3.15 (0.2 H, m, CHCH*H*CHO$_2$), 3.12–3.48 (1 H, m, RR′C*H*CH$_2$), 4.35 (1.8 H, m, C*H*OR), 4.42 (0.2 H, m, C*H*OR), 4.57–4.78 (1 H, m, CHI), 4.83 (s, O$_2$C*H*H), 4.95 (0.8 H, d, *J* 4.9, C*H*OR), 5.03 (s, O$_2$CH*H*), 5.07 (0.8 H, d, *J* 5.9, C*H*OR), 5.12 (0.2 H, d, *J* 5.9, C*H*OR), 5.42–5.50 (0.2 H, m, CH$_2$C*H*O$_2$) and 5.57–5.62 (0.8 H, m, CH$_2$C*H*O$_2$); δ_C (approximately 4:1 isomer ratio) major isomer: 28.9 (t), 33.4 (d), 44.8 (d), 58.5 (d), 80.5 (d), 91.6 (d), 95.6 (t) and 100.8 (d); minor isomer: 28.9 (t), 34.0 (d), 43.9 (d), 58.5 (d), 80.9 (d), 92.3 (d), 94.2 (t) and 100.8 (d) [Found: *m*/*z* (FAB), 281. $C_8H_{11}INO_4$ requires (M − H_2O), 281].

2α-*Hydroxy*-3β-*iodo*-4α,5α-(*methylenedioxy*)*cyclopentane*-1α-*acetaldehyde Oximes* **32**.—A stirred solution of the lactol **31** (700 mg, 2.35 mmol) and hydroxylamine hydrochloride (708 mg, 7.05 mmol) in water (10 cm^3)–THF (3 cm^3) was basified with saturated aq. potassium hydrogen carbonate. The aq. solution was extracted with ethyl acetate (6 × 20 cm^3) and the combined extracts were then dried, and evaporated under reduced pressure. The residue was purified by flash chromatography with 60% ethyl acetate in hexanes as eluent to give the *oxime* **32** (655 mg, 89%) as an oil, ν_{max}(thin film)/cm^{-1} 3404, 1652 and 1081; δ_H 2.58–2.87 (3 H, m), 3.1–3.4 (br s, CHO*H*), 4.30 (m, C*H*OR), 4.33 (s, C*H*OR), 4.65 (dd, *J* 5.7 and 5.8, CHI), 4.70 (0.5 H, s, O$_2$C*H*H), 4.73 (0.5 H, s, O$_2$CH*H*), 4.99–5.03 (m, C*H*OR), 5.20 (0.5 H, s, O$_2$C*H*H), 5.21 (0.5 H, s, O$_2$CH*H*), 6.94 (0.5 H, t, *J* 5.7, C*H*NOH) and 7.58 (0.5 H, t, *J* 5.7, C*H*NOH); δ_C 20.4 (t), 24.4 (t), 31.8 (d), 41.7 (d), 42.1 (d), 81.9 (d), 89.4 (d), 95.5 (t) and 150.2 (d).

2α-*Hydroxy*-3β-*iodo*-4α,5α-(*methylenedioxy*)*cyclopentane*-1α-*acetonitrile* **27**.—1,1′-Carbonyldiimidazole (660 mg, 4.1 mmol) was added to a solution of the oxime **32** (903 mg, 4.07 mmol) heated under reflux in dichloromethane (100 cm^3). The solution was heated under reflux for a further 3 h and was then cooled to room temperature. The solution was extracted with hydrochloric acid (1 mol dm^{-3}; 2 × 20 cm^3) and the combined aq. extracts were then back-extracted with ethyl acetate (3 × 20

* Thermal parameters, fractional atomic co-ordinates of hydrogen atoms, bond lengths and bond angles have been deposited at the Cambridge Crystallographic Data Centre (see section 5.6.3 of Instructions for Authors, January issue).

cm^3). The combined organic extracts were dried, and evaporated under reduced pressure. The residue was purified by flash chromatography with 40% ethyl acetate in hexanes as eluent to give the *nitrile* **27** (600 mg, 75%), which was recrystallised from diethyl ether–hexanes as rectangular prisms, m.p. 106–108 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 2252 and 964; δ_H 2.67–2.83 (3 H, m), 2.97–3.08 (m, RR'C*H*CH_2CN), 4.33–4.38 (2 H, m), 4.71 (s, C*H*HO_2), 4.72 (dd, *J* 6.0 and 4.4, CHI), 5.03 (dd, *J* 5.8 and 0.8, CHOR) and 5.20 (s, CH*H*O_2); δ_C 17.9 (t), 29.8 (d), 41.7 (d), 80.8 (d), 81.8 (d), 89.9 (d), 95.9 (t) and 118.8 (s) (Found: C, 32.75; H, 3.4; N, 4.7. $C_8H_{10}NIO_3$ requires C, 32.5; H, 3.4; N, 4.75%).

Methyl Malonate Ester **33**.—Methyl (chloroformyl)acetate (250 mm^3, 2.3 mmol) was added dropwise during 2 min to a solution of the iodohydrin **27** (570 mg, 1.90 mmol) and DMAP (2.59 mg, 2.1 mmol) in dry THF (30 cm^3) maintained at −78 °C. The solution was allowed to warm to room temperature during 2 h and then the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (30 cm^3) and the solution was then extracted successively with aq. copper(II) sulfate (1 mol dm^{-3}; 10 cm^3) and water (10 cm^3). The dried organic layer was evaporated under reduced pressure, and the residue was then purified by flash chromatography with 40% ethyl acetate in hexanes as eluent to give the diester **33** (480 mg, 64%), which was recrystallised from diethyl ether–hexanes, m.p. 91–93 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 2260, 1740 and 1140; δ_H 2.67 (ddd, *J* 30.8, 16.8 and 7.6, RC*H*$_2$CN), 3.18 (m, RR'C*H*CH_2CN), 3.42 (s, $O_2CCH_2CO_2Me$), 3.76 (s, CO_2Me), 4.36 (br s, C*H*OR), 4.77 (dd, *J* 5.9 and 4.8, CHI), 4.79 (s, C*H*HO_2), 5.05 (d, *J* 5.9, C*H*OR), 5.12 (s, CH*H*O_2) and 5.31 (d, *J* 4.8, C*H*O_2R); δ_C 12.6 (t), 26.7 (d), 40.7 (d), 41.0 (t), 52.5 (q), 80.1 (d), 82.6 (d), 89.3 (d), 96.4 (t), 117.9 (s), 165.0 (s) and 166.0 (s) [Found: *m*/*z*, 222.0752. $C_{12}H_{14}NIO_6$ requires (M − CH_2IO_2), 222.0766].

Ketene Acetal **29**.—A solution of the diester **33** (480 mg, 1.2 mmol) in dry THF (30 cm^3) containing sodium hydride (60% dispersion in mineral oil; 78 mg, 1.8 mmol) was stirred in the dark under nitrogen for 7 days. The solvent was removed under reduced pressure and the residue was then dissolved in ethyl acetate (30 cm^3). The extract was washed with saturated aq. sodium chloride (2 × 5 cm^3), then was dried (Na_2SO_4), and evaporated under reduced pressure to leave an oily residue. The residue was partitioned between acetonitrile and pentanes and the acetonitrile layer was separated and evaporated to leave the crude ketene acetal **29** (296 mg, 92%) as a pale yellow oil, ν_{max}/cm^{-1} 2953, 2250, 1708 and 1634, which was used without further purification.

Methyl Malonate Esters **34** *and its Isomer*.—A solution of the acetal **29** (285 mg, 1.06 mmol) in THF (10 cm^3) containing hydrochloric acid (1 mol dm^{-3}, 1.0 cm^3) was stirred at room temperature for 15 min. The dried solution was then evaporated under reduced pressure to leave a residue, which was purified by flash chromatography with 20% hexanes in ethyl acetate as eluent to give the *title esters* (258 mg, 86%) as an oil, ν_{max}/cm^{-1} 3480, 2250, 1732 and 732; δ_H 2.30 (m, C*H*CH_2CN), 2.57 (m, CHC*H*$_2$CN), 3.34 (br s, CHO*H*), 3.41 (s, $O_2CCH_2CO_2Me$), 3.71 (s, CO_2Me), 4.03 (br s, C*H*OH), 4.46–4.58 (m, 2 × C*H*OR), 4.83 (s, C*H*HO_2), 5.04 (s, CH*H*O_2) and 5.31 (m, C*H*O_2CR) (Found: M^+, 286.0870. $C_{12}H_{15}NO_7$ requires M, 286.0881).

2α,3α-*Dihydroxy*-4α,5α-(*methylenedioxy*)*cyclopentane*-1α-*acetonitrile* **30**.—A solution of the diester **34** and its position isomer (210 mg, 0.8 mmol) in dry methanol (25 cm^3) containing potassium carbonate (~20 mg) was stirred at room temperature for 30 min. The solvent was removed under reduced pressure and the residue was purified by flash chromatography with ethyl acetate as eluent to give the diol (115 mg, 84%) as a solid, m.p. 110 °C (from ethyl acetate); $\nu_{max}(CHCl_3)/cm^{-1}$ 3520, 2260 and 920; δ_H 2.11–2.19 (m, RR'C*H*CH_2CN), 2.25 (br s, CHO*H*), 2.75 (d, *J* 8.5, CH_2CN), 2.96 (br s, CHO*H*), 3.92 (dd, *J* 6.6 and 4.6, C*H*OH), 4.03 (dd, *J* 4.5 and 4.3, C*H*OH), 4.55 (dd, *J* 5.8 and 5.8, C*H*OR), 4.61 (dd, *J* 5.8 and 5.6, C*H*OR), 4.87 (s, C*H*HO_2) and 5.17 (s, CH*H*O_2); δ_C 12.6 (t), 40.7 (d), 73.1 (d), 79.8 (d), 80.0 (d), 96.1 (t) and 118.1 (s) [Found: *m*/*z*, 184.0623. $C_8H_{11}NO_4$ requires (M − H) 184.0610].

Formate Esters **35** *and its Isomer*.—A solution of the diol **30** (50 mg, 0.27 mmol) in dry methanol (20 cm^3) was saturated with ozone at −78 °C for 90 min. The solution was purged with oxygen for a further 30 min and then dimethyl sulfide (100 mm^3) was added. The solvent was removed under reduced pressure and the residue was purified by flash chromatography with 2% methanol in ethyl acetate as eluent to give a mixture of positional isomers of the formate ester **35** (40 mg, 74%) as an oil, ν_{max}(thin film)/cm^{-1} 3444, 2249 and 1716; δ_H([$^2H_6$]acetone) 2.48 (m, RR'C*H*CH_2), 2.68–2.89 (m, CHC*H*$_2$CN), 3.99–4.31 (m, 3 × CHOH), 5.06 (0.5 H, dd, *J* 4.8 and 4.9, C-2 C*H*OCHO), 5.36 (0.5 H, dd, *J* 5.1 and 5.2, C-3 C*H*OCHO), 8.27 (0.5 H, s, OCHO) and 8.30 (0.5 H, d, *J* 1.1, OCHO) [Found: (M^+ + H), 202.0696. $C_8H_{12}NO_5$ requires *m*/*z*, 202.0637).

2α,3α,4α,5α-*Tetrahydroxycyclopentane*-1α-*acetonitrile* **36**.—A solution of the formate ester **35** and its positional isomer (10 mg, 0.05 mmol) in dry methanol (3 cm^3) containing potassium hydrogen carbonate (~5 mg) was stirred at room temperature for 30 min. The solution was filtered and the filtrate was then evaporated to dryness under reduced pressure. The residue was purified by flash chromatography with 5% methanol in acetone as eluent to give the tetraol **36** (7 mg, 70%) as a gum, δ_H([$^2H_6$]DMSO) 2.31 (m, C*H*CH_2CN), 2.56 (d, *J* 8.0, CH_2CN), 3.92 (br d, *J* 6.4, 2 × CHO*H*), 4.04 (br s, 2 × C*H*OH and 2 × CHO*H*) and 4.14 (br s, 2 × C*H*OH); δ_C(CD_3OD) 13.2 (t), 42.7 (d), 73.4 (d) and 73.6 (d) [Found: (M^+ + H), 174.0782. $C_7H_{12}NO_4$ requires *m*/*z*, 174.0766].

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