Studies Related to Cyclopentanoid Natural Products. Part 3.[1] Synthesis of Pentenomycin and its Racemate[2]

Michael Hetmanski, Neil Purcell, and Richard J. Stoodley*
Department of Organic Chemistry, The University, Newcastle upon Tyne NE1 7RU
Malcolm N. Palfreyman
Pharmaceutical Chemistry, May and Baker Ltd., Dagenham, Essex RM10 7XS

(4*R*)-4-Benzyloxy-2-benzyloxymethylcyclopent-2-en-1-one (**9b**) reacted with osmium(VIII) oxide to give (2*S*,3*S*,4*R*)-4-benzyloxy-2-benzyloxymethyl-2,3-dihydroxycyclopentan-1-one (**8b**), the *cis*-hydroxylation occurring *anti* to the 4-benzyloxy group. By a hydrogenolysis–dehydration sequence, compound (**8b**) was converted into pentenomycin (**1a**).

Although the optical rotations of the synthetic pentenomycin (**1a**) and its 4,5,6-tri-*O*-acetyl, 2-bromo-4,5,6-tri-*O*-acetyl, and 6-*O*-benzyl derivatives (**13a**), (**13b**), and (**1d**), were substantially different from those reported in the literature, the compounds were shown to be enantiomerically pure.

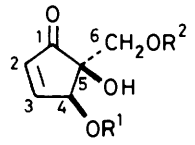
When treated with t-butyldimethylsilyl chloride, (8*R*)-8-hydroxy-6-hydroxymethyl-1,4-thiaspiro-[4.4]non-6-ene (**10b**) was converted into its disilyl ether (**10f**). The last-cited compound reacted with benzeneseleninic anhydride to give (4*R*)-4-t-butyldimethylsilyloxy-2-t-butyldimethylsilyloxymethyl-cyclopent-2-en-1-one (**9d**), which was converted into pentenomycin (**1a**) by sequential reactions involving osmium(VIII) oxide and hydrochloric acid.

The racemate of compound (**9d**), prepared from the racemate of 4-hydroxy-2-hydroxymethyl-cyclopent-2-en-1-one (**9c**) by reaction with t-butyldimethylsilyl chloride, was similarly transformed into the racemate of pentenomycin (**1a**).

As part of a programme aimed at the synthesis of bioactive cyclopentanoids, we have developed an interest in the pentenomycin antibiotics. These compounds, which are produced by *Streptomyces*, show moderate activity against Gram-positive and Gram-negative bacteria. There are four natural representatives: pentenomycin I (**1a**)[3] (herein, referred to as pentenomycin), pentenomycin II (**1b**)[3] (herein, called 4-*O*-acetylpentenomycin), pentenomycin III (**1c**)[4] (herein, named 6-*O*-acetylpentenomycin), and G2201-C (**2**)[5] (herein, referred to as 4-dehydropentenomycin).

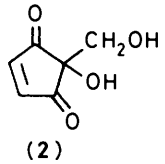
At the outset of our work, Branca and Smith[6] had reported syntheses of (±)-pentenomycin (**1a**), (±)-4-*O*-acetylpentenomycin (**1b**), and of 4-dehydropentenomycin (**2**). The cyclopentenone (**3**), a key intermediate in the syntheses, was elaborated from ethyl 2-oxocyclopentanecarboxylate or, preferably, from cyclopent-2-en-1-one. The conversion of D-glucose into pentenomycin (**1a**) had also been described by Verheyden *et al.*[7] The cyclopentenone (**4**), which served as a precursor of pentenomycin (**1a**), was generated from the keto-aldehyde (**5**) by an aldolisation–dehydration sequence. In turn, the keto-aldehyde (**5**) was obtained from the vinyl ether (**6**) by mild acidic hydrolysis.

In this paper, we report the synthesis of pentenomycin (**1a**) from D-quinic acid (**7**) and of (±)-pentenomycin (**1a**) from ethyl acetoacetate and chloroacetaldehyde.



(**1**)

a; $R^1 = R^2 = H$
b; R^1 = MeCO, R^2 = H
c; R^1 = H, R^2 = MeCO
d; R^1 = H, $R^2 = PhCH_2$



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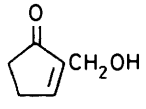
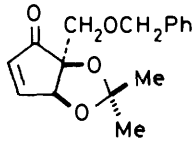
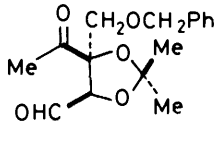


(**3**)



(**4**)



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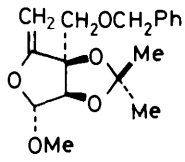
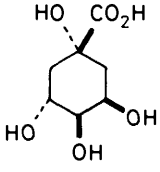


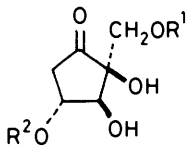
(**6**)



(**7**)

Results and Discussion

Our plan for the synthesis of pentenomycin (**1a**) rested upon effecting the deprotection and dehydration of a precursor of type (**8**). It was envisaged that such a precursor would be available from a cyclopentenone of type (**9**) by a *cis*-hydroxylation process, which would occur *anti* with respect to the 4-oxy substituent. Recently, we described syntheses of the cyclopentenones (**9a**) and (**9b**) by way of the dithiaspirononene (**10a**). The dialdehyde (**11a**), which was converted into the last-cited compound by an aldolisation–dehydration sequence, was obtained by oxidative cleavage of the diol (**12**) which, in turn, was elaborated from D-quinic acid (**7**). Accordingly, compounds (**9a**) and (**9b**) were examined as forerunners of pentenomycin (**1a**).



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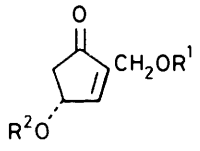
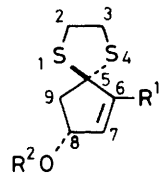


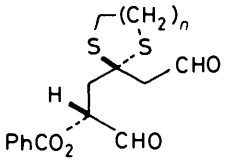
(9)

a; $R^1 = R^2 = PhCO$
b; $R^1 = R^2 = PhCH_2$
c; $R^1 = R^2 = H$
d; $R^1 = R^2 = Bu^tMe_2Si$



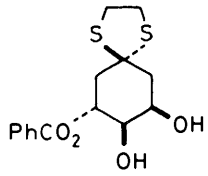
(10)

a; $R^1 = CHO$, $R^2 = PhCO$
b; $R^1 = HOCH_2$, $R^2 = H$
c; $R^1 = PhCO_2CH_2$, $R^2 = PhCO$
d; $R^1 = H$, $R^2 = PhCO$
e; $R^1 = R^2 = H$
f; $R^1 = Bu^tMe_2SiOCH_2$, $R^2 = Bu^tMe_2Si$



(11)

a; $n = 1$
b; $n = 2$



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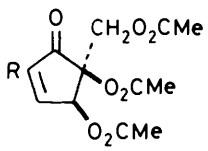
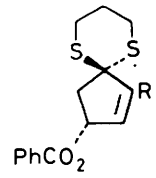


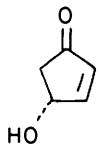
(13)

a; R = H
b; R = Br



(14)

a; R = CHO
b; R = $PhCO_2CH_2$



(15)

Attempts to effect the conversion of the cyclopentenone (**9a**) into the diol (**8a**), by treatment with osmium(VIII) oxide (1 mol equiv.) in pyridine[8] and a reductive work-up with sodium bisulphite,[9] afforded a complex mixture of products containing benzoic acid as a major component. However, the corresponding reaction of the cyclopentenone (**9b**) provided a syrupy diol (77% yield after SiO_2 chromatography), presumed to possess the stereostructure (**8b**). That the diol was a single diastereoisomer was indicated by 360 MHz ^1H and 20 MHz ^{13}C n.m.r. spectroscopy. An attempt to effect the *cis*-hydroxylation with hydrogen peroxide and a catalytic quantity of osmium(VIII) oxide[10] was unsuccessful.

Removal of the benzyl groups from the dibenzyl ether (**8b**) was readily achieved by hydrogenolysis over palladium in ethanol. Following silica-gel chromatography, the tetraol (**8c**) was isolated as a slightly impure oil in *ca.* 72% yield.

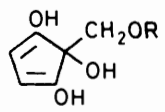
In the presence of tetrahydrofuran (THF) containing dilute hydrochloric acid, the tetraol (**8c**) was transformed into pentenomycin (**1a**) (84% yield after SiO_2 chromatography). Although the spectroscopic properties of the sample were in good agreement with those published,[3] the optical rotation {$[\alpha]_D$ −17° (EtOH)} was significantly lower than the reported values {$[\alpha]_D$ −32° (EtOH)[3] and −27° (EtOH)[7]}. Nevertheless, since the absolute configuration of pentenomycin (**1a**) has been established,[11] the result confirms that the product of *cis*-hydroxylation of the cyclopentenone (**9b**) possesses the stereostructure (**8b**); clearly, the oxidant had attacked the double bond from its least-hindered face.

Pentenomycin (**1a**) was reported to be isolated as a white amorphous powder, in the form of a hemihydrate, which was strongly hygroscopic[3] [our sample of pentenomycin (**1a**) was a syrup]. As the optical rotation of a hygroscopic material is difficult to measure reliably, a crystalline derivative was sought. It has been reported[12] that pentenomycin (**1a**) reacts with acetic anhydride in pyridine to give pentenomycin triacetate (**13a**), m.p. 111—112 °C, $[\alpha]_D$ −24° (EtOH), which is converted into 2-bromopentenomycin triacetate (**13b**), m.p. 107—108 °C, $[\alpha]_D$ +59° ($CHCl_3$), by the action of bromine. Our sample of pentenomycin (**1a**) was similarly converted into the derivatives (**13a**) and (**13b**). An analytically pure sample of the former material showed m.p. 112—114 °C and $[\alpha]_D$ −8° (EtOH); the latter material showed m.p. 108—110 °C and $[\alpha]_D$ +25° ($CHCl_3$).

The foregoing results suggested that our sample of pentenomycin (**1a**) was partially racemic, and the situation was further complicated when an additional chemical correlation was carried out. Thus the compound (**4**), described by Verheyden *et al.*,[7] was reported to be a syrup with $[\alpha]_D$ −66° (EtOH). When treated in THF with dilute hydrochloric acid, the cyclopentanone (**8b**) was converted into 6-*O*-benzylpentenomycin (**1d**) which was isolated as a syrup in 59% yield after silica-gel chromatography. The last-mentioned compound reacted with acetone–2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid to give the isopropylidene derivative (**4**) {$[\alpha]_D$ +33° (EtOH)} as a chromatographically homogeneous syrup (79% yield after SiO_2 chromatography).

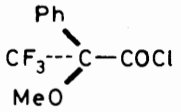
As this juncture, it appeared that there was a step (or steps) in our synthesis where partial racemisation was occurring. Earlier, it was shown that no racemisation had accompanied the (**10a**)→(**10b**) transformation.[1] The dithiaspirononene (**10a**) [derived from the dialdehyde (**11a**) by reaction with pyrrolidinium acetate in benzene at 40 °C] was also considered to be enantiomerically pure since both it and its homologue (**14a**) [obtained from the dialdehyde (**11b**) by the action of dibenzylammonium trifluoroacetate in benzene at 0 °C] were converted into the crystalline cyclopentenone (**9a**), both samples showing an identical optical rotation {$[\alpha]_D$ +45° (EtOH)}.[1] Obviously, the aforecited correlation did not rigorously exclude the possibility that the same degree of racemisation had accompanied the formation of compounds (**10a**) and (**14a**), and/or of the cyclopentenone (**9a**) which was produced from the dithiaspirononenes (**10c**) and (**14b**) by Mukaiyama's method.[13]

It was decided to inter-relate the dithiaspirononene (**10a**) with the hydroxycyclopentenone (**15**).[14–17] Decarbonylation of the aldehyde (**10a**), to give the syrupy compound (**10d**) (50% yield after SiO_2 chromatography), was accomplished with tris(triphenylphosphine)rhodium(I) chloride in refluxing acetonitrile.[18] In the presence of methanolic sodium methoxide, the benzoate (**10d**) was transformed into the alcohol (**10e**) (91% yield after SiO_2 chromatography) which underwent ketone



(16)

a; R = H
b; R = $PhCH_2$



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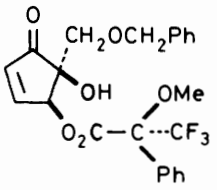

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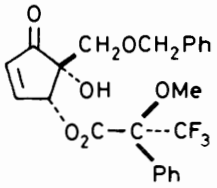

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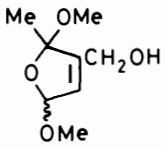

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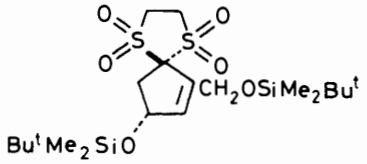


(21)

deprotection when heated with copper(II) oxide and copper(II) chloride in aqueous acetone.[13] The derived hydroxycyclopentenone (**15**), which was isolated as a chromatographically homogeneous oil (37% yield after SiO_2 chromatography), showed $[\alpha]_D$ +84° (MeOH), in moderate agreement with the highest * reported literature value {$[\alpha]_D$ +96° (MeOH)†}.[16]

According to correlations of optical rotations, the enantiomeric purity of the dithiaspirononene (**10a**) was at least 88% whereas those of the derived pentenomycins (**1a**), (**13a**), and (**13b**) were 53, 33, and 42%, respectively.

In principle, the pentenomycins (**1a**) and (**1d**) may undergo racemisation under acidic conditions, *e.g.* by way of the intermediates (**16a**) and (**16b**) (it would, however, be surprising if such a process were not accompanied by epimerisation of the compounds). However, when pentenomycin (**1a**), $[\alpha]_D$ −17° (EtOH), was left in THF and dilute hydrochloric acid for 24 h [a period eight times longer than that required to effect the (**8c**)→(**1a**) transformation], it was recovered in 90% yield with an unchanged optical rotation.

In view of the disparity of our results with those of other workers and the remote possibility that the cyclopentenone (**9b**) had undergone some racemisation prior to the *cis*-hydroxylation [it was shown that the optical rotation of the compound (**9b**) was unaltered in pyridine solution over a 24-h period], it was decided to assess the optical purity of 6-*O*-benzylpentenomycin (**1d**) by Mosher's procedure.[19]

When treated in dichloromethane with triethylamine followed by the acid chloride (**17**), 6-*O*-benzylpentenomycin (**1d**) was transformed into the syrupy ester (**18**) (45% yield after SiO_2 chromatography). On the basis of 90 MHz ^1H and 85 MHz ^{19}F n.m.r. spectroscopy, the material was a single diastereoisomer.

To establish unequivocally that the ester (**18**) could be distinguished from its diastereoisomer (**19**) by n.m.r. spectroscopy, the preparation of the racemate of 6-*O*-benzylpentenomycin (**1d**) was undertaken. The racemate of the hydroxycyclopentenone (**9c**), a compound previously prepared from the dihydrofuran (**20**) by a hydrolysis–aldolisation sequence,[20] was selected as a possible precursor. When treated with benzyl bromide and silver(I) oxide in refluxing ethyl acetate, the racemate of the hydroxycyclopentenone (**9c**) provided the racemate of the dibenzyl ether (**9b**) (25% yield after SiO_2 chromatography). The last-described compound was converted into the racemate of 6-*O*-benzylpentenomycin (**1d**) by treatment with osmium(VIII) oxide followed by hydrochloric acid. Following acylation with the acid chloride (**17**), a 1:1 mixture of the diastereoisomeric esters (**18**) and (**19**) was obtained. These compounds were readily differentiated by 90 MHz ^1H and 85 MHz ^{19}F n.m.r. spectroscopy.

On the basis of the foregoing results, we conclude that enantiomerically pure pentenomycins (**1a**) and (**1d**) had been derived from D-quinic acid (**7**). In consequence, no racemisation had accompanied the cyclodehydrations of the dialdehydes (**11a**) and (**11b**).

The overall yield of pentenomycin (**1a**) from D-quinic acid (**7**) was *ca.* 8% for the eleven-stage sequence. Although this yield was considerably better than that obtained by Verheyden *et al.*[7] from D-glucose (*ca.* 1% for the sixteen-stage sequence), an alternative route was examined. Since it was expected that the disilyl ether (**8d**) would be directly convertible into pentenomycin (**1a**) under acidic conditions, efforts were made to prepare this precursor.

Silylation of the diol (**10b**), to give the syrupy disilyl ether (**10f**) (86% yield after SiO_2 chromatography), was readily effected by using t-butyldimethylsilyl chloride and imidazole in *N*,*N*-dimethylformamide (DMF).[21] In an attempt to effect the *cis*-hydroxylation of its double bond, compound (**10f**) was treated with hydrogen peroxide and a catalytic quantity of osmium(VIII) oxide (1 mol equiv.) in pyridine followed by a tography, the crystalline tetraoxide (**21**) was isolated in 54% yield. A complex mixture of products resulted when the last-mentioned compound was subjected to the action of osmium(VIII) oxide (1 mol equiv.) in pyridine followed by a reductive work-up ($Na_2S_2O_5$).

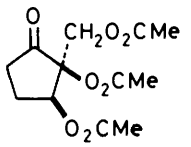
Removal of the ketone-protecting group from compound (**10f**) was next examined. This transformation proved to be troublesome. The use of the procedures devised by Mukaiyama ($CuCl_2$–CuO),[13] Corey ($HgCl_2$–$CaCO_3$ and *N*-chlorosuccinimide–$AgNO_3$),[22] Wynberg (chloramine-T),[23] and Logan (HIO_4)[24] afforded complex mixtures of products. However, Barton's method [$(PhSeO)_2O$][25] afforded the required cyclopentenone (**9d**) (73% yield after SiO_2 chromatography). In the presence of osmium(VIII) oxide, the cyclopentenone (**9d**) was converted into the crystalline diol (**8d**) [shown to be a single diastereoisomer by 360 MHz ^1H and 20 MHz ^{13}C n.m.r. spectroscopy] in 58% yield after silica-gel chromatography. Gratifyingly, in THF containing dilute hydrochloric acid, the cyclopentanone (**8d**) was transformed into pentenomycin (**1a**) (56% yield after SiO_2 chromatography). Using the aforementioned sequence, the overall yield of pentenomycin (**1a**) from D-quinic acid (**7**) was *ca.* 8%.

Although the optical rotations of the last-cited sample of pentenomycin (**1a**) and its derived triacetate (**13a**) were again far lower than the literature values, they were in good agreement with those of our earlier synthetic samples. However, the optical rotation of the crystalline dihydro derivative (**22**), $[\alpha]_D$ −158° (EtOH), prepared from the triacetate (**13a**) by hydrogenation over palladium, was in good agreement with the reported value {$[\alpha]_D$ −152° (EtOH)}.[12]

During the course of our studies, the anomaly regarding the

* In ref. 15, the hydroxycyclopentenone (**15**), of 90% optical purity was claimed to show $[\alpha]_D$ +59° (MeOH).

† In our preliminary communication,[2] this value was incorrectly quoted.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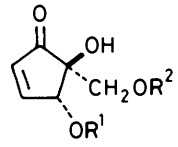
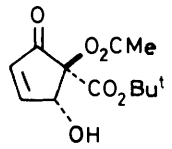

(23)

a; $R^1 = R^2 = H$
b; R^1 = MeCO, $R^2 = H$
c; $R^1 = H$, R^2 = MeCO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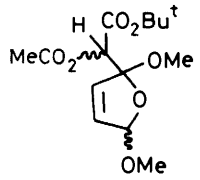
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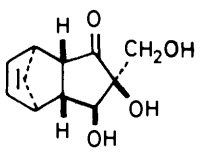
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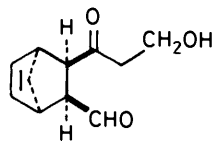
(27)

optical rotation of pentenomycin triacetate (**13a**) has apparently been resolved. Following the isolation of pentenomycin (**1a**) and its 4-*O*-acetyl derivative (**1b**) {which were converted into pentenomycin triacetate (**13a**), $[\alpha]_D$ −24° (EtOH)} from *Streptomyces eurythermus*[5] and of 6-*O*-acetylpentenomycin (**1c**) { which was transformed into pentenomycin triacetate (**6a**), $[\alpha]_D$ −8° (MeOH)} from *Streptoverticillium eurocidicum*,[4] three antibiotics were obtained from *Streptomyces lavenduligriseus*. These antibiotics, which were referred to as C-2554 A-I, C-2554 AII, and C-2554 B, were initially considered[6,26] to be epimers of the pentenomycins (**1c**), (**1b**), and (**1a**), since they afforded an acetylated derivative with $[\alpha]_D$ −6.8° (EtOH). Subsequent studies, however, revealed[27] that the compounds were identical with the pentenomycins (**1c**), (**1b**), and (**1a**). Evidently, the rotation quoted by Umino *et al.* for pentenomycin triacetate (**13a**) {$[\alpha]_D$ −24° (EtOH)}[3] is incorrect.

Finally, in order to complete a synthesis of the racemate of pentenomycin (**1a**), the racemate of the cyclopentenone (**9c**) (itself available[20] in 14% overall yield from ethyl acetoacetate and chloroacetaldehyde diethyl acetal) was converted into the racemate of the disilyl ether (**9d**) (40% yield after SiO_2 chromatography) by the action of t-butyldimethylsilyl chloride and imidazole in DMF. The crystalline racemate of the diol (**8d**), obtained by osmium(VIII) oxide oxidation, reacted under acidic conditions to give (±)-pentenomycin (**1a**), which was analytically characterised as its crystalline triacetate (**13a**). The aforementioned sequence afforded (±)-pentenomycin (**1a**) in *ca.* 14% overall yield.

During the course of our work, there has been further activity in the pentenomycin area. The synthesis of the racemate of 4-*epi*-pentenomycin (**23a**) has been communicated by the groups of Shono[28] and Smith.[29] In the Japanese route, the key precursor (**24**) was elaborated from the dihydrofuran (**25**) by a hydrolysis–aldolisation–dehydration sequence.[28] In Smith's synthesis, the cyclopentenone (**3**) was employed as a precursor; this material was also converted into the racemates of 4-*O*-acetyl- and 6-*O*-acetyl-4-*epi*-pentenomycins (**23b**) and (**23c**).[29] Full details of Smith's work in the pentenomycin area have recently been published.[30] Finally, Zwanenburg and his coworkers have communicated an interesting synthesis of the racemate of pentenomycin (**1a**) in which the key step involved a cyclo-reversion reaction of compound (**26**), prepared by way of the Diels–Alder cycloadduct (**27**).[31]

Experimental

Dry solvents, referred to in the ensuing experiments, were prepared as follows: pyridine was allowed to stand over potassium hydroxide, distilled, and stored over molecular sieves (Type 4A); dichloromethane was stored over calcium chloride flakes; methanol was dried by means of magnesium activated with iodine and distilled; DMF was distilled under reduced pressure from calcium hydride and stored over molecular sieves (Type 4A). Benzeneseleninic anhydride was freshly prepared from diphenyl diselenide by oxidation with nitric acid.[32] (α*R*)-α-Methoxy-α-trifluoromethyl-α-phenyl acetyl chloride was prepared from (α*R*)-(+)-methoxy-α-trifluoromethyl-α-phenylacetic acid and thionyl chloride.[19] All other solvents and chemicals were employed as purchased. Light petroleum refers to the fraction boiling in the range 40—60 °C. For chromatographic and instrumental details, see Part 1.[20] 360 MHz ^{1}H N.m.r. spectra were recorded using a Bruker WH-360 spectrometer. Microanalyses were performed using a Carlo-Erba 1106 Elemental Analyser.

Reaction of the Cyclopentenone (**9b**) *and its Racemate with Osmium*(VIII) *Oxide.*—(*a*) To a stirred solution of the cyclopentenone (**9b**) (0.795 g, 2.58 mmol) in dry pyridine (10 cm^3) at 0 °C was added osmium(VIII) oxide (0.721 g, 2.84 mmol) in dry pyridine (1 cm^3). After 1 h, a solution of sodium bisulphite (1.18 g, 6.21 mmol) in water (20 cm^3) was added. The mixture, after a further 6 h, was poured into ethyl acetate and the organic layer was washed with dilute hydrochloric acid followed by brine. Evaporation of the dried ($MgSO_4$) organic phase left a residue which was purified by silica-gel chromatography [light petroleum–Et_2O (1:2) as eluant] to give (2S,3S,4R)-4-*benzyloxy*-2-*benzyloxymethyl*-2,3-*dihydroxycyclopentan*-1-*one* (**8b**) (0.680 g, 77%), as a chromatographically homogeneous oil. The sample possessed the following properties: $[\alpha]_D$ −48° (1% in EtOH); $\nu_{max.}$(film) *inter alia* 3 420br (OH) and 1 755 cm^{-1} (ketone C=O); $\lambda_{max.}$(EtOH) 218 nm (ε 2 400 nm); δ_H (360 MHz; $CDCl_3$) 2.40 (1 H, ddd, *J* 19, 4, and 1 Hz, 5-H), 2.78 (1 H, dd, *J* 19 and 7 Hz, 5-H), 3.06br (1 H, s, OH), 3.65 and 3.70 (each 1 H, d, *J* 10 Hz, CH_2O), 3.67br (1 H, s, OH), 4.09—4.13 (1 H, m, 4-H), 4.21 (1 H, d, *J* 3 Hz, 3-H), 4.51 (2 H, s, OCH_2Ph), 4.56 and 4.60 (each 1 H, d, *J* 12 Hz, OCH_2Ph), and 7.25—7.37 (10 H, m, 2 × Ph); δ_C (20 MHz; $CDCl_3$) 41.1 (C-5), 70.4, 71.9, 73.8, 74.5, 77.6, and 79.9 (C-2, -3, and -4, 2 × CH_2Ph, and CH_2O), 127.7, 127.8, 128.5, 137.6, and 137.7 (2 × C_6H_5), and 180.1 p.p.m. (C-1); *m/z inter alia* 342 (M^+) and 91 ($C_7H_7^+$, base peak) (Found: M^+, 342.1478. $C_{20}H_{22}O_5$ requires *M*, 342.1467).

(*b*) The racemate of the cyclopentenone (**9b**) (0.500 g, 1.62 mmol) was subjected to the aforecited *cis*-hydroxylation procedure. Following silica-gel purification, (2RS,3RS,4SR)-4-*benzyloxy*-2-*benzyloxymethyl*-2,3-*dihydroxycyclopentan*-1-*one* (**8b**) (0.270 g, 49%) was isolated as a chromatographically homogeneous oil (Found: M^+, 342.1468. $C_{20}H_{22}O_5$ requires *M*, 342.1467). The spectroscopic properties of the sample were indistinguishable from those of the optically active material.

Reaction of the Dibenzyl Ether (**8b**) *with Hydrogen–Palladium.*—A solution of the dibenzyl ether (**8b**) (0.625 g, 1.83 mmol) in ethanol (7 cm^3) was vigorously stirred with 10% palladium on charcoal (0.625 g) under hydrogen (1 atm). After 5 h, the mixture was filtered through 'hyflo' and the insoluble

material was washed well with ethanol. Evaporation of the filtrate gave (2*S*,3*S*,4*R*)-2-hydroxymethyl-2,3,4-trihydroxycyclopentan-1-one (**8c**) (0.214 g, *ca.* 72%) as a slightly impure colourless oil with the following properties; $[\alpha]_D$ −56° (1.5% in EtOH); $\nu_{max.}$(film) *inter alia* 3 400br (OH) and 1 740 cm^{-1} (ketone C=O); δ(60 MHz; D_2O) *inter alia* 2.30 and 2.90 (each 1 H, dd, *J* 18 and 7 Hz, 5-H_2), 3.66 (2 H, d, separation 3 Hz, CH_2O), and 3.95—4.45 (2 H, m, 3- and 4-H).

Reaction of the Tetraol (**8c**) *with Hydrochloric Acid.*—To a solution of the tetraol (**8c**) (0.130 g, 0.80 mmol) in freshly distilled THF (2 cm^3) was added 3M-hydrochloric acid (2 cm^3). After 3 h, the mixture was evaporated and the resultant syrup was purified by silica-gel chromatography [EtOAc–MeOH (9:1) as eluant] to give pentenomycin (**1a**) (0.097 g, 84%) as a chromatographically homogeneous oil. The sample showed the following properties: $[\alpha]_D$ −17° (0.34% in EtOH) [lit., −32° (EtOH)[3] and −27° (EtOH)[7]]; $\nu_{max.}$(film) 3 400 (OH) and 1 715 cm^{-1} (enone C=O); $\lambda_{max.}$(EtOH) 218 nm (ε 2 700); δ(60 MHz; D_2O) 3.60 (2 H, s, 6-H_2), 6.32 (1 H, dd, *J* 6 and 1 Hz, 2-H), and 7.73 (1 H, dd, *J* 6 and 3 Hz, 3-H) (the 4-H was obscured by the HOD signal at δ 4.70); *m/z inter alia* 113 ($C_5H_5O_3^+$, base peak). The foregoing spectroscopic properties were in good agreement with those published.[3]

Reaction of Pentenomycin (**1a**) *and its Racemate with Acetic Anhydride.*—(*a*) Acetic anhydride (0.5 cm^3) was added to a solution of pentenomycin (**1a**) [derived from the tetraol (**8c**)] (0.054 g, 0.38 mmol) in ice-cold pyridine (1 cm^3). After 24 h, a few drops of water were added and the mixture, after 10 min, was poured into ethyl acetate. The mixture was then washed with water, dilute hydrochloric acid, and brine. Evaporation of the dried ($MgSO_4$) organic phase and purification of the residue by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] gave 4,5,6-tri-*O*-acetylpentenomycin (**13a**). After recrystallisation from diethyl ether, the sample (0.040 g, 40%) showed the following properties: m.p. 112—114 °C (lit.,[12] 111—112 °C); $[\alpha]_D$ −8° (0.5% in EtOH) [lit., −24° (EtOH)[12] and −6.8 °C (EtOH)[27]]; $[\alpha]_D$ −6° (0.5% in MeOH) [lit.,[4] −8° (MeOH)]; $\nu_{max.}$(KBr) *inter alia* 1 740br (ester and enone C=O); $\lambda_{max.}$(EtOH) 221 nm (ε 4 000); δ(60 MHz; $CDCl_3$) 2.10 and 2.15 (3 and 6 H, each s, 3 × MeC=O), 4.40 (2 H, s, 6-H_2), 5.85 (1 H, dd, *J* 3 and 1 Hz, 4-H), 6.55 (1 H, dd, *J* 6 and 1 Hz, 2-H), and 7.50 (1 H, dd, *J* 6 and 3 Hz, 3-H); *m/z inter alia* 270 (M^+) and 43 ($C_2H_3^+$, base peak) (Found: C, 53.5; H, 5.15%; M^+, 270.0729. Calc. for $C_{12}H_{14}O_7$: C, 53.3; H, 5.20%; *M*, 270.0739). The foregoing spectroscopic properties were in good agreement with those published.[12]

(*b*) Pentenomycin (**1a**) [derived from the disilyl ether (**8d**)] (0.030 g, 0.21 mmol) was subjected to the aforementioned acetylation. Following silica-gel purification and recrystallisation, the derived triacetate (**13a**) (0.017 g, 30%) showed m.p. 113—115 °C and $[\alpha]_D$ −10° (0.34% in EtOH).

(*c*) The racemate of pentenomycin (**1a**) (0.042 g, 0.29 mmol) was acetylated as described in (*a*). Following silica-gel purification and recrystallisation, the derived triacetate (**13a**) (0.023 g, 29%) showed m.p. 110—112 °C (lit.,[30] 98.5—99.5 °C) (Found: C, 53.5; H, 5.20. Calc. for $C_{12}H_{14}O_4$: C, 53.3; H, 5.20%). The spectroscopic properties of the sample were indistinguishable from those of the optically active material.

Reaction of Pentenomycin Triacetate (**13a**) *with Bromine.*—To a solution of pentenomycin triacetate (**13a**) (0.034 g, 0.13 mmol) in acetic acid (1 cm^3) was added, in drops, bromine (0.021 g, 0.13 mmol) dissolved in carbon tetrachloride. After 3 h, the mixture was diluted with water and dichloromethane. The organic layer was then dried ($MgSO_4$) and evaporated. Purification of the resultant residue by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] gave 2-bromo-4,5,6-tri-*O*-acetylpentenomycin (**13b**) (0.022 g, 50%). The sample, after recrystallisation from diethyl ether, showed the following properties: m.p. 108—110 °C (lit.,[12] 107—108 °C); $[\alpha]_D$ +25° (0.5% in $CHCl_3$) [lit.,[12] +59° ($CHCl_3$)]; $\nu_{max.}$(KBr) *inter alia* 1 740 cm^{-1} (ester and enone C=O); $\lambda_{max.}$(EtOH) 240 nm (ε 5 100); δ (60 MHz; $CDCl_3$) 2.07 and 2.15 (3 and 6 H, each s, 3 × MeC=O), 4.38 (2 H, s, CH_2O), 5.75 (1 H, d, *J* 3 Hz, 4-H), and 7.58 (1 H, d, *J* 3 Hz, 3-H); *m/z inter alia* 350 and 348 (M^+) (Found: M^+, 347.9871. Calc. for $C_{12}H_{13}{}^{79}BrO_7$: *M*, 347.9844). The foregoing spectroscopic properties were in good agreement with those published.[12]

Reaction of the Cyclopentanone (**8b**) *and its Racemate with Hydrochloric Acid.*—(*a*) To a solution of the cyclopentanone (**8b**) (0.170 g, 0.50 mmol) in freshly distilled THF (2 cm^3) was added 3M-hydrochloric acid (2 cm^3). After 24 h, the solution was diluted with ethyl acetate and water. The organic layer, after being washed with brine and dried ($MgSO_4$), was evaporated and the residue fractionated by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] to give 6-*O*-*benzylpentenomycin* (**1d**) 0.068 g, 59%) as a colourless chromatographically homogeneous oil. The sample showed the following properties: $[\alpha]_D$ +7° (1% in EtOH); $\nu_{max.}$(film) *inter alia* 3 420br (OH) and 1 720 cm^{-1} (enone C=O); $\lambda_{max.}$(EtOH) 221 nm (ε 3 800); δ (60 MHz; $CDCl_3$) 3.30—3.70br (2 H, s, 2 × OH), 3.60 (2 H, s, 6-H_2), 4.50 (2 H, s, OCH_2Ph), 4.60—4.80 (1 H, m, 4-H), 6.20 (1 H, d, *J* 6 Hz, 2-H), 7.20 (5 H, s, Ph), and 7.45 (1 H, dd, *J* 6 and 2 Hz, 3-H) (addition of D_2O caused the signal at δ 3.30—3.60 to disappear); *m/z inter alia* 216 ($M^+ - H_2O$) and 91 ($C_7H_7^+$, base peak) (Found: $M^+ - H_2O$, 216.0797. $C_{13}H_{12}O_3$ requires *m/z* 216.0786).

(*b*) The racemate of the cyclopentanone (**8b**) (0.270 g, 0.79 mmol) was subjected to the same reaction conditions. Following silica-gel chromatography, the *racemate of* 6-O-*benzylpentenomycin* (**1d**) (0.109 g, 60%) was isolated as a chromatographically homogeneous oil (Found: $M^+ - H_2O$, 216.0808. $C_{13}H_{12}O_3$ requires *m/z* 216.0786). The spectroscopic properties of the sample were indistinguishable from those of the optically active material.

Reaction of 6-O-*Benzylpentenomycin* (**1d**) *with Acetone–2,2-Dimethoxypropane.*—A solution of 6-*O*-benzylpentenomycin (**1d**) (0.060 g, 0.26 mmol) in a 5:1 mixture of acetone–2,2-dimethoxypropane (3 cm^3) containing toluene-*p*-sulphonic acid (0.01 g) was poured, after 45 min, into sodium hydrogen carbonate solution. The mixture was extracted with dichloromethane (2×) and the organic extracts dried ($MgSO_4$) and evaporated. Purification of the residue by silica-gel chromatography [light petroleum–Et_2O (2:1) as eluant] gave 6-*O*-benzyl-4,5-*O*-isopropylidenepentenomycin (**4**) (0.056 g, 79%) as a chromatographically homogeneous syrup. The sample possessed the following properties: $[\alpha]_D$ +33° (0.5% in EtOH) [lit.,[7] −66° (EtOH)]; $\nu_{max.}$(film) *inter alia* 1 730 cm^{-1} (enone C=O); $\lambda_{max.}$(EtOH)] 216 nm (ε 6 300); δ (60 MHz; $CDCl_3$) 1.30 and 1.40 (each 3 H, s, CMe_2), 3.62 and 3.77 (each 1 H, d, *J* 12 Hz, CH_2O), 4.40 (2 H, s, OCH_2Ph), 5.13 (1 H, d, *J* 2 Hz, 4-H), 6.10 (1 H, d, *J* 6 Hz, 2-H), 7.10 (5 H, s, Ph), and 7.40 (1 H, dd, *J* 6 and 2 Hz, 3-H); *m/z inter alia* 259 ($M^+ - CH_3$) and 91 ($C_7H_7^+$, base peak) (Found: $M^+ - CH_3$, 259.0956. Calc. for $C_{15}H_{15}O_4$: *m/z* 259.0970). The n.m.r. spectroscopic properties of the sample were similar to those reported.[7]

Reaction of the Aldehyde (**10a**) *with Tris(triphenylphosphine)rhodium(I) Chloride.*—A mixture of the aldehyde (**10a**) (0.600 g, 1.96 mmol), acetonitrile (15 cm^3), and tris(triphenylphosphine)rhodium(I) chloride (2.10 g, 2.27 mmol) was heated under reflux. After 2.5 h, the solvent was evaporated and

methanol (10 cm^3) was added. The mixture was filtered through 'hyflo' and the residue washed thoroughly with methanol. Evaporation of the filtrate and purification of the product by silica-gel chromatography [light petroleum–Et_2O (2:1) as eluant] gave (8R)-8-*benzoyloxy*-1,4-*dithiaspiro*[4.4]*non*-6-*ene* (**10d**) (0.272 g, 50%) as a colourless chromatographically homogeneous oil. The sample showed the following properties: $[\alpha]_D$ +205° (1% in EtOH); $\nu_{max.}$(film) *inter alia* 1 715 cm^{-1} (ester C=O); $\lambda_{max.}$(EtOH) 211sh (ε 7 400) and 229 nm (17 400); δ (60 MHz; CCl_4) 2.60 (1 H, d, *J* 14 and 4 Hz, 9-H), 3.03 (1 H, dd, *J* 14 and 6 Hz, 9-H), 3.30 (4 H, s, 2- and 3-H_2), 5.70—6.10 (3 H, m, 6-, 7-, and 8-H), and 7.20—7.50 and 7.85—8.05 (3 and 2 H, each m, Ph) [irradiation at δ 5.90 caused the signals at 2.56 and 3.06 to collapse to d (*J* 14 Hz)]; *m/z inter alia* 278 (M^+) and 105 ($C_7H_5O^+$, base peak) (Found: M^+, 278.0453. $C_{14}H_{14}O_2S_2$ requires *M*, 278.0435).

Reaction of the Benzoate (**10d**) *with Sodium Methoxide.*—To a solution of the benzoate (**10d**) (0.140 g, 0.50 mmol) in dry methanol (10 cm^3) was added sodium methoxide (0.040 g, 0.74 mmol) in methanol (0.75 cm^3). After 9 h, the solution was neutralised by the addition of Amberlite IR 120 (H^+) ion-exchange resin. The resin was filtered off and washed thoroughly with methanol. Evaporation of the filtrate and purification of the product by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] gave two fractions.

The first-eluted material was methyl benzoate (n.m.r. spectroscopy).

The second-eluted material (0.080 g, 91%), isolated as a chromatographically homogeneous oil, was (8R)-8-*hydroxy*-1,4-*dithiaspiro*[4.4]*non*-6-*ene* (**10e**). The sample possessed the following properties: $[\alpha]_D$ +117° (1% in MeOH); $\nu_{max.}$(film) *inter alia* 3 380 cm^{-1} (OH); $\lambda_{max.}$(EtOH) 219 (ε 2 200) and 243sh nm (600); δ (60 MHz; $CDCl_3$) 2.30 (1 H, dd, *J* 14 and 4 Hz, 9-H), 2.60br (1 H, s, OH), 2.90 (1 H, dd, *J* 14 and 6 Hz, 9-H), 3.30 (4 H, s, 2- and 3-H_2), 4.70—4.95 (1 H, m, 8-H), 5.80 (1 H, ddd, *J* 5, 2, and 1 Hz, 7-H), and 6.00 (1 H, d, *J* 5 Hz, 6-H) [addition of D_2O caused the signal at δ 2.60 to disappear; irradiation at δ 4.83 caused the signals at 2.30 and 2.90 to collapse to d (*J* 14 Hz)]; *m/z inter alia* 174 (M^+, base peak) (Found: M^+, 174.0181. $C_7H_{10}O_2S_2$ requires *M*, 174.0173).

Reaction of the Dithiaspirononene (**10e**) *with Copper*(II) *Salts.*—A mixture of the dithiaspirononene (**10e**) (0.100 g, 0.58 mmol), copper(II) chloride dihydrate (0.195 g, 1.15 mmol), copper(II) oxide (0.184 g, 2.31 mmol), acetone (10 cm^3), and water (10 drops) was heated under reflux for 2 h. After evaporation, ethyl acetate was added to the residue and the mixture was filtered through 'hyflo'; the insoluble material was washed well with ethyl acetate. Evaporation of the dried ($MgSO_4$) filtrate and purification of the product by silica-gel chromatography [EtOAc–light petroleum (2:1) as eluant] gave (4*R*)-4-hydroxycyclopent-2-en-1-one (**15**) (0.021 g, 38%) as a chromatographically homogeneous oil. The sample showed the following properties: $[\alpha]_D$ +84° (1% in MeOH) [lit., +66° (MeOH) [15] and +96° (MeOH) [16]]; $\nu_{max.}$(EtOH) 215 nm (ε 5 900); δ(60 MHz; $CDCl_3$) 2.30 (1 H, dd, *J* 18 and 2 Hz, 5-H), 2.70br (1 H, s, OH), 2.80 (1 H, dd, *J* 18 and 5 Hz, 5-H), 5.00—5.20 (1 H, m, 4-H), 6.25 (1 H, d, *J* 5 Hz, 2-H), and 7.60 (1 H, dd, *J* 5 and 2 Hz, 3-H) [addition of D_2O caused the signal at δ 2.70 to disappear; irradiation at δ 5.10 caused the signals at 2.30 and 2.80 to collapse to d (*J* 18 Hz)]; *m/z inter alia* 98 (M^+, base peak) (Found: M^+, 98.0366. Calc. for $C_5H_6O_2$: M^+, 98.0368). The spectroscopic properties of the sample were in good agreement with those published.[14]

Reaction of 6-O-*Benzylpentenomycin* (**1d**) *and its Racemate with* (αR)-α-*Methoxy*-α-*trifluoromethyl*-α-*phenylacetyl Chloride* (**17**).—(*a*) To an ice-cooled solution of 6-*O*-benzylpentenomycin (**1d**) (0.068 g, 0.29 mmol) in dry dichloromethane (3 cm^3) was added triethylamine (0.049 cm^3, 0.35 mmol) followed by (α*R*)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride (**17**) (0.077 g, 0.35 mmol). After 1 h, the mixture was allowed to warm to room temperature. After a further 15 h, it was diluted with diethyl ether and washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and brine. Evaporation of the dried ($MgSO_4$) organic phase and purification of the product by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] gave two fractions.

The first-eluted material (0.059 g, 45%), isolated as a chromatographically homogeneous oil, was 6-O-*benzyl*-4-O-[(αS)-α-*methoxy*-α-*trifluoromethyl*-α-*phenylacetyl*]*pentenomycin* (**18**). The sample showed the following properties: $[\alpha]_D$ +43° (1% in EtOH); $\nu_{max.}$(film) *inter alia* 3 460 (OH), 1 755 (ester C=O), and 1 730 cm^{-1} (enone C=O); $\lambda_{max.}$(EtOH) 214 nm (ε 10 600); δ_H (90 MHz; $CDCl_3$) 2.60br (1 H, s, OH), 3.58—3.61 (3 H, m, OMe), 3.72 and 3.82 (each 1 H, d, *J* 9 Hz, 6-H_2), 4.50 2 H, s, OCH_2Ph), 5.84—5.88 (1 H, m, 4-H), 6.22 (1 H, dd, *J* 6 and 2 Hz, 2-H), and 7.15—7.50 (11 H, m, 2 × Ph and 3-H); δ_F (85 MHz; $CFCl_3$) +72.7br (s, CF_3) (relative to $CFCl_3$); *m/z inter alia* 432 ($M^+ - H_2O$) and 91 ($C_7H_7^+$, base peak) (Found: $M^+ - H_2O$, 432.1188. $C_{23}H_{19}F_3O_5$ requires *m/z* 432.1182).

The second-eluted material (0.017 g, 25%) was 6-*O*-benzylpentenomycin (**1d**) by n.m.r. spectroscopy.

(*b*) The racemate of 6-*O*-benzylpentenomycin (**1a**) (0.109 g, 0.47 mmol) was subjected to the aforementioned acylation. Following silica-gel purification, a 1:1 mixture of compound (**18**) and its diastereoisomer (**19**) was isolated as an oil (0.129 g, 61%). The sample possessed the following properties: $[\alpha]_D$ +23° (2% in EtOH); δ_H (90 MHz; $CDCl_3$) 3.30br (1 H, s, OH), 3.48—3.56 (3 H, m, OMe), 3.63, 3.67, 3.72, and 3.76 (each 0.5 Hz, d, *J* 9 Hz, 6-H_2), 4.50 (2 H, s, OCH_2Ph), 5.82—5.90 (1 H, m, 4-H), 6.14—6.27 (1 H, m, 2-H), and 7.10—7.60 (11 H, m, 2 × Ph and 3-H); δ_F (85 MHz; $CFCl_3$) +72.8br and +72.1br (each s, CF_3) (relative to $CFCl_3$); *m/z inter alia* 450 (M^+), 432 ($M^+ - H_2O$), and 91 ($C_7H_7^+$, base peak) (Found: M^+, 450.1291. $C_{23}H_{21}F_3O_6$ requires *M*, 450.1290). The i.r. and u.v. spectra of the sample were indistinguishable from those of compound (**18**).

Reaction of the Racemate of the Diol (**9c**) *with Benzyl Bromide.*—A mixture of the racemate of the diol (**9c**) (0.671 g, 5.24 mmol), benzyl bromide (2.5 cm^3, 21 mmol), silver(I) oxide (4.87 g, 21.0 mmol), and ethyl acetate (70 cm^3) was heated under reflux for 5 h. The cooled mixture was filtered through 'hyflo' and the insoluble material was washed thoroughly with ethyl acetate. Evaporation of the dried ($MgSO_4$) filtrate and purification of the residue by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] yielded (4RS)-4-*benzyloxy*-2-*benzyloxymethylcyclopent*-2-*en*-1-*one* (**9b**) contaminated with some benzyl alcohol. After azeotropy with water, the sample (0.403 g, 25%) was obtained as a chromatographically homogeneous oil. Its spectroscopic properties were indistinguishable from those of the optically active material.

Reaction of the Diol (**10b**) *with t-Butyldimethylsilyl Chloride* (**with J. D. Elliott**).—To a stirred solution of the diol (**10b**) (0.268 g, 1.31 mmol) in dry DMF (2 cm^3) was added imidazole (0.460 g, 6.75 mmol) followed by t-butyldimethylsilyl chloride (0.520 g, 3.45 mmol). A white precipitate formed and more dry DMF (0.5 cm^3) was added. The mixture was stirred overnight, poured into water, and extracted with diethyl ether (2 ×). The organic phase was washed with water (4 ×) and brine, and dried ($MgSO_4$). Evaporation and purification of the product by silica-gel chromatography [light petroleum–Et_2O (6:1) as eluant] gave (8R)-8-*t-butyldimethylsilyloxy*-6-*t-butyldimethylsilyloxy*-

methyl-1,4-*dithiaspiro*[4.4]*non*-6-*ene* (**10f**) (0.490 g, 86%). A sample, precipitated from acetone by the addition of water, showed the following properties: m.p. 77—80 °C; $[\alpha]_D$ +45° (1.1% in $CHCl_3$); $\nu_{max.}$(KBr) *inter alia* 1 650w cm^{-1} (C=C); δ (60 MHz; $CDCl_3$) 0.20 (12 H, s, 2 × $SiMe_2$), 1.00 and 1.03 (each 9 H, s, 2 × $SiBu^t$), 2.45 (1 H, dd, *J* 14 and 6 Hz, 9-H), 3.03 (1 H, dd, *J* 14 and 7 Hz, 9-H), 3.39br (4 H, s, 2- and 3-H_2), 4.45—4.60 (2 H, m, CH_2O), 4.72—5.05 (1 H, m, 8-H), and 5.80—5.90 (1 H, m, 7-H); *m/z inter alia* 432 (M^+) and 375 ($M^+ - Bu^t$, base peak) (Found: C, 55.5; H, 9.4; S, 14.8. $C_{20}H_{40}O_2S_2Si_2$ requires C, 55.6; H, 9.25; S, 14.8%).

Reaction of the Dithiaspirononene (**10f**) *with Osmium*(VIII) *Oxide–Hydrogen Peroxide.*—To a stirred solution of the dithiaspirononene (**10f**) (0.112 g, 0.26 mmol) in acetone (1 cm^3) was added osmium(VIII) oxide (0.01 g) in t-butyl alcohol (1 cm^3) followed by 30% hydrogen peroxide solution (0.15 cm^3, 1.47 mmol). After 16 h, the solvent was evaporated and the dark-brown residue was purified by silica-gel chromatography (Et_2O as eluant) to give (8R)-8-*t*-*butyldimethylsilyloxy*-6-*t*-*butyldimethylsilyloxymethyl*-1,4-*dithiaspiro*[4.4]*non*-6-*ene* 1,1,4,4-*tetraoxide* (**21**) (0.069 g, 54%) as a white crystalline solid. The material, recrystallised from chloroform–light petroleum, showed the following properties: m.p. 124—126 °C; $[\alpha]_D$ −62° (1% in EtOH); $\nu_{max.}$(KBr) *inter alia*) 1 330 and 1 130 cm^{-1} (SO_2); $\lambda_{max.}$(EtOH) 214 nm (ε 5 600); δ (60 MHz; $CDCl_3$) 0.30 (12 H, s, 2 × $SiMe_2$), 0.90 (18 H, s, 2 × $SiBu^t$), 2.40 (1 H, dd, *J* 14 and 5 Hz, 9-H), 2.96 (1H, dd, *J* 14 and 6 Hz, 9-H), 3.55—3.75 (4 H, m, 2- and 3-H_2), 4.40—4.60 (2 H, m, CH_2O), 4.80—5.05 (1 H, m, 8-H), and 6.40—6.50 (1 H, m, 7-H); *m/z inter alia* 496 (M^+), 481 ($M^+ - CH_3$), and 439 ($M^+ - C_4H_9$, base peak) (Found: C, 48.4; H, 8.1. $C_{20}H_{40}O_6S_2Si_2$ requires C, 48.4; H, 8.05%).

Reaction of the Dithiaspirononene (**10f**) *with Benzeneseleninic Anhydride.*—To a solution of the dithiaspirononene (**10f**) (0.380 g, 0.88 mmol) in dry dichloromethane (20 cm^3) was added freshly prepared benzeneseleninic anhydride (0.299 g, 0.83 mmol). After 2 h, the solvent was evaporated and the residue subjected to silica-gel chromatography.

The first-eluted material [eluted with light petroleum–Et_2O (20:1)] was diphenyl diselenide.

The second-eluted material (0.229 g, 73%) [eluted with light petroleum–Et_2O (9:1)] was (4R)-4-*t*-*butyldimethylsilyloxy*-2-*t*-*butyldimethylsilyloxymethylcyclopent*-2-*en*-1-*one* (**9d**). The sample possessed the following properties: $[\alpha]_D$ +29° in EtOH); $\nu_{max.}$(film) *inter alia* 1 710 cm^{-1} (enone C=O); $\lambda_{max.}$(EtOH) 220 nm (ε 7 300); δ (60 MHz; $CDCl_3$) 0.03 and 0.08 (each 6 H, s, 2 × $SiMe_2$), 0.90 (18 H, s, 2 × $SiBu^t$), 2.28 (1 H, dd, *J* 18 and 3 Hz, 5-H), 2.75 (1 H, dd, *J* 18 and 6 Hz, 5-H), 4.28—4.38 (2 H, m, CH_2OSi), 4.75—4.95 (1 H, m, 4-H), and 7.15—7.30 (1 H, m, 3-H); *m/z inter alia* ($M^+ - CH_3$) and 299 ($M^+ - C_4H_9$, base peak) (Found: $M^+ - CH_3$, 341.1945. $C_{17}H_{33}O_3Si_2$ requires *m/z* 341.1968).

Reaction of the Cyclopentenone (**9d**) *and its Racemate with Osmium*(VIII) *Oxide.*—(*a*) To a stirred solution of the cyclopentenone (**9d**) (0.602 g, 1.69 mmol) in dry pyridine (8 cm^3), cooled in an ice-bath, was added a solution of osmium(VIII) oxide (0.473 g, 1.86 mmol) in pyridine (1 cm^3). After 45 min, a solution of sodium bisulphite (0.771 g, 4.06 mmol) in water (15 cm^3) was added. Work-up, after a further 4 h, consisted of pouring the mixture into ethyl acetate and washing the organic phase with water, dilute hydrochloric acid, and brine. Evaporation of the dried ($MgSO_4$) organic layer and purification of the residue by silica-gel chromatography [light petroleum–Et_2O (1:1) as eluant] furnished, after recrystallisation from cold light petroleum, (2S,3S,4R)-3,4-*dihydroxy*-4-*t*-*butyldimethylsilyloxy*-2-*t*-*butyldimethylsilyloxymethylcyclopentan*-1-*one* (**8d**) (0.379 g, 58%). The sample possessed the following properties: m.p. 77—79 °C; $[\alpha]_D$ −55° (1% in EtOH); $\nu_{max.}$(KBr) *inter alia* 3 460 (OH) and 1 735 cm^{-1} (ketone C=O); $\lambda_{max.}$(EtOH) 222 (ε 720) and 275sh nm (180); δ_H (360 MHz; $CDCl_3$) 0.30, 0.04, 0.08, and 0.10 (each 3 H, s, 2 × $SiMe_2$), 0.86 and 0.87 (each 9 H, s, 2 × $SiBu^t$), 2.25 (1 H, ddd, *J* 19, 3, and 1 Hz, 5-H), 2.75 (1 H, dd, *J* 19 and 7 Hz, 5-H), 2.81br and 3.47br (each 1 H, s, 2 × OH), 3.76 and 3.87 (each 1 H, d, *J* 10 Hz, CH_2O), 3.86br (1 H, s, 3-H), and 4.30 (1 H, ddd, *J* 7, 6, and 3 Hz, 4-H); δ_C (20 MHz; $CDCl_3$) 25.8 (10 × CH_3), 43.9 (C-5), 64.3, 70.8, 76.9, and 78.7 (C-2, -3, -4, and CH_2O), and 178.7 p.p.m. (C-1); *m/z inter alia* 390 (M^+) and 333 ($M^+ - C_4H_9$, base peak) (Found: C, 55.3; H, 10.25. $C_{18}H_{38}O_5Si_2$ requires C, 55.4; H, 9.75%).

(*b*) The aforementioned experiment was repeated using the racemate of the cyclopentenone (**9d**) (0.931 g, 2.62 mmol). Following silica-gel chromatography, (2RS,2RS,3SR)-3,4-*dihydroxy*-4-*t*-*butyldimethylsilyloxy*-2-*t*-*butyldimethylsilyloxymethylcyclopentan*-1-*one* (**8d**) (0.612 g, 60%) was isolated as an oil which slowly solidified. The material, recrystallised from light petroleum, showed the following properties: m.p. 56—58 °C (Found: C, 55.3; H, 10.2. $C_{18}H_{38}O_5Si_2$ requires C, 55.4; H, 9.75%). The i.r., n.m.r., and mass spectra of the sample were very similar to those of the optically active material.

Reaction of the Cyclopentanone (**8d**) *and its Racemate with Hydrochloric Acid.*—(*a*) To a solution of the cyclopentanone (**8d**) (0.170 g, 0.44 mmol) in freshly distilled THF (3 cm^3) was added 3M-hydrochloric acid (3 cm^3). After 4 h, the solvent was evaporated and the oil subjected to silica-gel chromatography [EtOAc–MeOH (9:1) as eluant] to give pentenomycin (**1a**) (0.035 g, 56%) as a syrup; $[\alpha]_D$ −18° (0.35% in EtOH). The i.r. and n.m.r. spectra of the sample were indistinguishable from those described earlier.

(*b*) The aforementioned experiment was repeated with the racemate of the cyclopentenone (**8d**) (0.576 g, 2.35 mmol). Following silica-gel chromatography, the racemate of pentenomycin (**1a**) (0.115 g, 54%) was isolated as a syrup. The i.r., n.m.r., and mass spectra of the sample were indistinguishable from those of the optically active material.

Reaction of the Racemate of the Diol (**9c**) *with t-Butyldimethylsilyl Chloride.*—To a stirred solution of the racemate of the diol (**9c**) (2.11 g, 16.5 mmol) in dry DMF (20 cm^3), imidazole (5.60 g, 82.4 mmol) and t-butyldimethylsilyl chloride (5.95 g, 39.5 mmol) were added. After 5 h, the mixture was partitioned between diethyl ether and water. The organic layer was washed with water (3 ×) and brine. Evaporation of the dried ($MgSO_4$) organic phase left a syrup which was purified by silica-gel chromatography [light petroleum–Et_2O (10:1) as eluant] to give (4RS)-4-*t*-*butyldimethylsilyloxy*-2-*t*-*butyldimethylsilyloxymethylcyclopent*-2-*en*-1-*one* (**9d**) (2.57 g, 40%) as a chromatographically homogeneous oil (Found: $M^+ - CH_3$, 341.1985. $C_{17}H_{33}O_3Si_2$ requires *m/z* 341.1968). The spectroscopic properties of the sample were indistinguishable from those of the optically active material.

Reaction of Pentenomycin Triacetate (**13a**) *with Hydrogen–Palladium.*—To a solution of pentenomycin triacetate (**13a**) (0.057 g, 0.21 mmol) in methanol (3 cm^3) was added 10% palladium on charcoal (0.060 g). The mixture was vigorously stirred under hydrogen (1 atm.) for 3 h and then filtered through 'hyflo'. The insoluble material was washed well with methanol and the filtrate was evaporated. Purification of the residue by silica-gel chromatography [light petroleum-Et_2O (1:1) as eluant] gave (2*S*,3*S*)-2-acetoxymethyl-2,3-diacetoxycyclopentan-1-one (**22**) (0.046 g, 80%) as an oil that slowly crystallised. The sample, recrystallised from diethyl ether, showed the following properties: m.p. 58—60 °C (lit.,[12] 60 °C); $[\alpha]_D$ −158° (0.45% in

EtOH) [lit.,[12] −152° (EtOH)]; $\nu_{max.}$(KBr) *inter alia* 1 745 cm^{-1} (ester and ketone C=O); $\lambda_{max.}$ (EtOH) 213 nm (ε 720); δ (60 MHz; $CDCl_3$) 2.10 and 2.15 (3 and 6 H, each s, 3 × MeC=O), 2.10—2.60 (4 H, m, 4- and 5-H_2), 4.30 (2 H, d, separation 2 Hz, CH_2O), and 5.45 (1 H, t, *J* 6 and 6 Hz, 3-H); *m/z inter alia* 273 (MH^+). The n.m.r. spectroscopic properties of the sample were in agreement with those published.[12]

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