

Studies Related to Cyclopentanoid Natural Products. Part 2.¹ An Improved Route to (4*R*)-4-Hydroxy-2-hydroxymethylcyclopent-2-en-1-one and its *O*-Substituted Derivatives²

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(3*R*,4*S*,5*R*)-3,4-*O*-Cyclohexylidene-3,4,5-trihydroxycyclohexan-1-one (11a), prepared from *D*-quinic acid (4a) by a published three-step sequence, was converted into the 5-*O*-benzoyl derivative (11b) by the action of benzoyl chloride. Simultaneous protection of the ketonic carbonyl group and removal of the cyclohexylidene moiety occurred when the compound (11b) was treated with ethane-1,2-dithiol and boron trifluoride-diethyl ether. The derived (7*R*,8*R*,9*R*)-9-benzoyloxy-7,8-dihydroxy-1,4-dithiaspiro[4.5]decane (15a), when treated sequentially with lead(IV) acetate and pyrrolidinium acetate, underwent an oxidative ring contraction to give (8*R*)-8-benzoyloxy-1,4-dithiaspiro[4.4]non-6-ene-6-carbaldehyde (17a).

The aldehyde (17a) reacted with lithium aluminium hydride to give (8*R*)-8-hydroxy-6-hydroxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18a) and with sodium cyanoborohydride to yield (8*R*)-8-benzoyloxy-6-hydroxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18b). Sodium methoxide effected the transformation of the hydroxybenzoate (18b) into the diol (18a) which underwent benzylation with benzyl bromide to give the dibenzyl ether (18c). Benzoylation of the hydroxybenzoate (18b), to give the dibenzoate (18d), was achieved by the action of benzoyl chloride. Removal of the dithiolane moiety from compounds (18a–d), to give the cyclopent-2-en-1-ones (1a–d), was brought about by copper(II) chloride–copper(II) oxide.

The cyclohexanone (11b) also reacted with propane-1,3-dithiol and boron trifluoride-diethyl ether to give (8*R*,9*R*,10*R*)-10-benzoyloxy-8,9-dihydroxy-1,5-dithiaspiro[5.5]undecane (20), which underwent an oxidative ring contraction to (9*R*)-9-benzoyloxy-1,5-dithiaspiro[5.4]dec-7-ene-7-carbaldehyde (22) when treated with lead(IV) acetate followed by dibenzylamine trifluoroacetate.

The outcome of the reaction of the cyclohexanone (11b) with ethane-1,2-diol depended upon the reaction conditions. In refluxing benzene and in the presence of toluene-*p*-sulphonic acid, 1-hydroxy-4-(2-hydroxyethoxy)benzene (24) was formed. At room temperature and in the presence of sulphuric acid, (7*R*,8*R*,9*R*)-9-benzoyloxy-7,8-dihydroxy-1,4-dioxaspiro[4.5]decane (15c) was the major product. Although the oxidative ring contraction of the last-mentioned derivative was also effected by the action of lead(IV) acetate followed by dibenzylamine trifluoroacetate, the resultant (8*R*)-8-benzoyloxy-1,4-dioxaspiro[4.4]non-6-ene-6-carbaldehyde (17c) was an unstable entity.

Compounds (17a) and (22) inhibited the growth of *Staphylococcus aureus* at concentrations of 2 and 32 $\mu\text{g cm}^{-3}$, respectively.

Compounds of type (1) are expected to be versatile precursors of bioactive cyclopentanoids, such as the prostaglandins, *e.g.* PGE₂ (2), and the pentenomycins, *e.g.* pentenomyacin I (3). Recently, we described¹ a synthesis of the cyclopentenone (1a) from *D*-quinic acid (4a). Although the route demonstrated, for the first time, the feasibility of utilising *D*-quinic acid (4a) as a forerunner of functionally substituted cyclopentenones, the sequence was a lengthy one (requiring 10 steps) and proceeded in poor overall yield (*ca.* 3.5%).

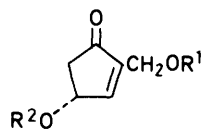
The cyclopentenecarbaldehyde (5a), a key intermediate in the aforementioned synthesis, was prepared from the cyclohexanediol (6) by an oxidation–cyclodehydration sequence. In turn, the cyclohexanediol (6) was elaborated from *D*-quinic acid (4a) by way of compounds (4b), (4c), (7a), and (7b). The conversion of the cyclopentenecarbaldehyde (5a) into the cyclopentenone (1a) involved the intermediacy of compounds (5b), (5c), (8a), and (8b).

In this paper, we examine a modified strategy for effecting the synthesis of functionally substituted cyclopentenones from *D*-quinic acid (4a). In this modification, the oxidative decarboxylation of *D*-quinic acid (4a) is brought about prior to the oxidative ring contraction. The procedure provides a more efficient route to cyclopentenones of the type (1).

Results and Discussion

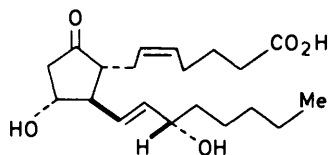
To examine the feasibility of deriving cyclopentenecarbaldehydes of the type (9) (where Z¹ and Z² represent heteroatomic substituents), it was necessary to prepare cyclohexanediols of the type (10). At the outset of our studies, the cyclohexanone (11a) had been described.³ It was therefore selected as a possible precursor of compounds of the aforementioned type. The published route to the cyclohexanone (11a) from *D*-quinic acid (4a) proceeds by way of compounds (12) and (13). Using modifications to the published conditions (see Experimental section), it was possible to prepare the cyclohexanone (11a) in up to 70% overall yield, after recrystallisation, from *D*-quinic acid (4a). Moreover, the three-step sequence required no chromatography and was readily conducted using 100 g of the starting material.

Initial efforts were directed towards the synthesis of the dithiolane (14a), since it was envisaged that removal of its diol-protecting group, to give the diol (15a), would be a trivial matter. In the event, treatment of the crystalline cyclohexanone (11b), prepared in 90% yield from the alcohol (11a) by the action of benzoyl chloride in pyridine, with ethane-1,2-dithiol and boron trifluoride-diethyl ether in dichloromethane

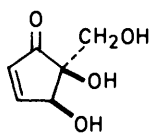


(1)

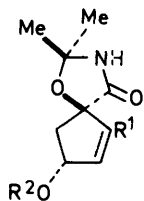
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 b ; R¹ = H, R² = PhC=O
 c ; R¹ = R² = PhCH₂
 d ; R¹ = R² = PhC=O



(2)

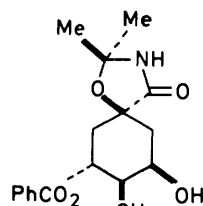


(3)

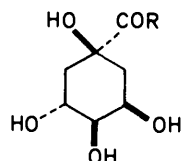


(5)

- a ; R¹ = HC=O, R² = PhC=O
 b ; R¹ = CH₂OH, R² = PhC=O
 c ; R¹ = CH₂OH, R² = H

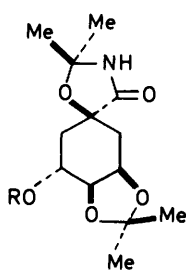


(6)



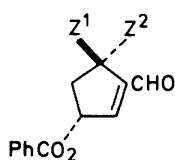
(4)

- a ; R = OH
 b ; R = OMe
 c ; R = NH₂

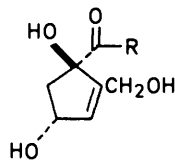


(7)

- a ; R = H
 b ; R = PhC=O

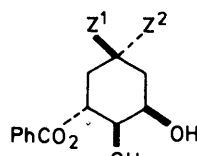


(9)

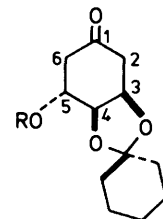


(8)

- a ; R = NHH₂
 b ; R = N₃

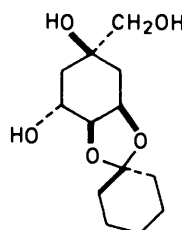


(10)

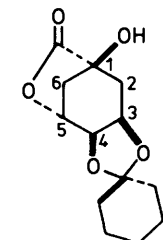


(11)

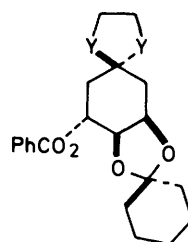
- a ; R = H
 b ; R = PhC=O



(13)

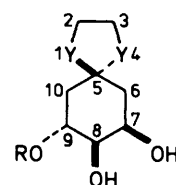


(12)



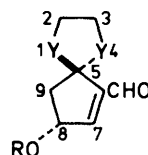
(14)

- a ; Y = S
 b ; Y = O



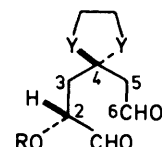
(15)

- a ; Y = S, R = PhC=O
 b ; Y = S, R = PhCH₂
 c ; Y = O, R = PhC=O



(17)

- a ; Y = S, R = PhC=O
 b ; Y = S, R = PhCH₂
 c ; Y = O, R = PhC=O



(16)

- a ; Y = S, R = PhC=O
 b ; Y = S, R = PhCH₂
 c ; Y = O, R = PhC=O

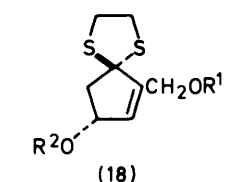
triplet (separation 2 Hz) at δ 9.80, owing to coupling with the adjacent methylene protons.

Without purification, the crude dialdehyde (16a) was heated at 50 °C in benzene with pyrrolidinium acetate⁴ to give the cyclopentencarbaldehyde (17a) in 62% yield [based upon (5a)] (after SiO₂ chromatography and recrystallisation). The structure of compound (17a) followed from its analytical and spectroscopic properties. In particular, its n.m.r. spectrum (CDCl₃) featured two one-proton double doublets at δ 2.72 (*J* 15 and 5 Hz) and δ 3.17 (*J* 15 and 7 Hz), attributed to the methylene groups of the cyclopentene ring, a one-proton multiplet at δ 5.79–6.02, assigned to the methine proton of the cyclopentene ring, a one-proton doublet (*J* 2 Hz) at δ 6.72, ascribed to the olefinic proton, and a one-proton singlet at δ 9.68 for the aldehydic proton. The carbaldehyde (17a) showed a large optical rotation $\{[\alpha]_D +280^\circ$ (CHCl₃) $\}$.

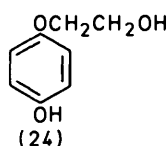
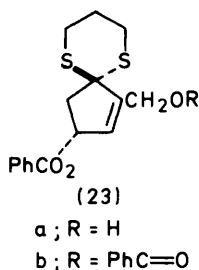
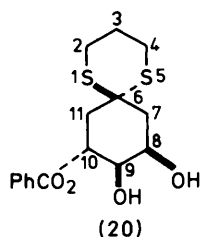
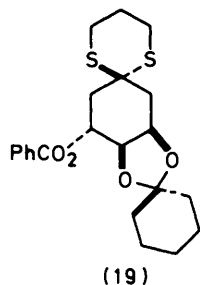
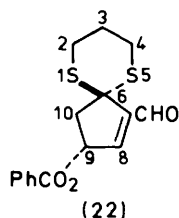
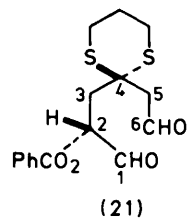
During the course of our work, Barton and his co-workers⁵

gave the crystalline diol (15a) in 87% yield (after SiO₂ chromatography).

When treated with lead(IV) acetate in dichloromethane, the cyclohexanediol (15a) was quantitatively converted into a foamy product which, on the basis of n.m.r. spectroscopy (CDCl₃), contained ca. 70% of the dialdehyde (16a). Although no coupling was observed between the 1-aldehydic proton (which appeared as a singlet at δ 9.65) and the neighbouring methine proton, the 6-aldehydic proton was present as a



- a ; R¹ = R² = H
 b ; R¹ = H, R² = PhC=O
 c ; R¹ = R² = PhCH₂
 d ; R¹ = R² = PhC=O



described the preparation of compounds (11b) and (15a); the dialdehyde (16a) was also generated *in situ* by oxidation of the diol (15a) with triphenylbismuth carbonate. The oxidative cleavage of the diol (15b) to the dialdehyde (16b) and its cyclodehydration to the cyclopentenecarbaldehyde (17a) was also communicated by Barrière *et al.*⁶

Conversion of the aldehyde (17a) into the crystalline diol (18a) $\{[\alpha]_D +100^\circ$ (EtOH) $\}$ (90% yield after SiO₂ chromatography) was achieved by using lithium aluminium hydride in tetrahydrofuran (THF). Although a number of reagents effected the reduction of the aldehyde (17a) to the syrupy alcohol (18b), only the reaction involving sodium cyanoborohydride in acetic acid afforded the product (94% yield after SiO₂ chromatography) in an optically pure state. Thus the alcohol (18b), obtained from the last-mentioned reaction, was re-oxidised to the cyclopentenecarbaldehyde (17a) $\{[\alpha]_D +274^\circ$ (CHCl₃) $\}$ by the action of freshly prepared manganese(IV) oxide⁷ in chloroform. Moreover, when treated with methanolic sodium methoxide, the alcohol (18b) was converted into the diol (18a) $\{[\alpha]_D +101^\circ$ (EtOH) $\}$, establishing that no racemisation had accompanied the lithium aluminium hydride reaction. The optical purities of the alcohols (18b), obtained from the aldehyde (17a) by reduction at -20°C with sodium borohydride in ethanol and with lithium tri-*t*-butoxyaluminium hydride in THF, were assessed at 67 and 79%, respectively [by measuring the optical rotations of the derived crystalline diols (18a)].

Treatment of the optically pure diol (18a) with benzyl

bromide and sodium hydride in THF under reflux afforded the syrupy dibenzyl ether (18c) (79% yield after SiO₂ chromatography). The crystalline dibenzoate (18d) was prepared in 93% yield (after SiO₂ chromatography) from the reaction of the optically pure hydroxybenzoate (18b) with benzoyl chloride in pyridine.

Replacement of the ethylenedithio group of compounds (18a—d) by the oxo moiety was achieved by heating with copper(II) chloride and copper(II) oxide in aqueous acetone.⁸ Following silica-gel purification, the cyclopentenones (1b) and (1c) were isolated as chromatographically homogeneous oils in yields of 70% and the cyclopentenone (1d) as a crystalline solid in 66% yield; all the samples showed positive optical rotations $\{[\alpha]_D +149^\circ$ (CHCl₃) for (1b), $[\alpha]_D +23^\circ$ (EtOH) for (1c), and $[\alpha]_D +48^\circ$ (EtOH) for (1d) $\}$. The cyclopentenone (1a) could not be completely purified by silica-gel chromatography, the sample showing an optical rotation $\{[\alpha]_D +12^\circ$ (EtOH) $\}$ that was substantially lower than that of the material obtained by way of the cyclopentenecarbaldehyde (5a) $\{[\alpha]_D +50^\circ$ (EtOH) $\}$.¹ When a solution of the chromatographed cyclopentenone (1a) in methanol was saturated with hydrogen sulphide, a black precipitate of copper(II) sulphide resulted; however, the cyclopentenone (1a) was destroyed.

It was also possible to convert the compound (18a) into the cyclopentenone (1a) by the action of mercury(II) chloride and calcium carbonate in aqueous methanol.⁹ Again, however, the chromatographed material showed a low optical rotation $\{[\alpha]_D +22^\circ$ (EtOH) $\}$. The presence of a mercury-containing material in the sample was demonstrated by the formation of a black precipitate with hydrogen sulphide in dichloromethane, a treatment which also partially destroyed the cyclopentenone (1a).

The overall yields of the cyclopentenones (1b—d) from *D*-quinic acid were *ca.* 22, 17, and 20%, respectively. Clearly, these represent a marked improvement over the *ca.* 3.5% overall yield achieved for the cyclopentenone (1a) by way of the cyclopentenecarbaldehyde (5a). Moreover, the enone moieties of compounds (1b—d) are, in principle, ready for further manipulation; in the case of the diol (1a), protection of the alcohol moieties would probably be necessary prior to such manipulation.

Interestingly, the cyclopentenecarbaldehyde (17a) was endowed with moderate antibacterial activity, inhibiting the growth of *Staphylococcus aureus* at 2 $\mu\text{g cm}^{-3}$ and *Streptococcus faecalis* at 8 $\mu\text{g cm}^{-3}$. Since compounds (5a), (18a), and (18b) showed no corresponding activity, it was decided to prepare other cyclopentenecarbaldehydes of the type (9) (where Z¹ and Z² represent heteroatomic substituents) and to examine their antimicrobial profiles.

The cyclohexanone (11b) reacted with propane-1,3-dithiol and boron trifluoride-diethyl ether in dichloromethane to give, following silica-gel fractionation, two products. The more mobile material, isolated as a crystalline solid in 8% yield, was the dithiane acetal (19). The less mobile product, obtained as a foam in 89% yield, was the dithiane diol (20).

In dichloromethane, the diol (20) reacted with lead(IV) acetate to afford a foamy product which, on the basis of n.m.r. spectroscopy (CDCl₃), contained *ca.* 50% of the dialdehyde (21). The 1-aldehydic proton appeared as a singlet at δ 9.63 and the 6-aldehydic proton was present as a triplet (separation 2 Hz) at δ 9.80.

An attempt to effect the cyclodehydration of the dialdehyde (21) to the cyclopentenecarbaldehyde (22) by using pyrrolidinium acetate in benzene at room temperature, led to a complex mixture of products which contained very little of the required material by n.m.r. spectroscopy. A cleaner outcome ensued when the reaction was conducted in toluene in the presence of dibenzylamine trifluoroacetate¹⁰ and, following

silica-gel chromatography, compound (22) was isolated as a syrup in 52% yield. The spectroscopic characteristics of compound (22) were similar to those of its counterpart (17a), showing in the n.m.r. spectrum (CDCl_3) a one-proton multiplet at δ 5.90–6.20, assigned to the methine proton of the cyclopentene ring, a one-proton doublet (J 2 Hz) at δ 6.92 attributed to the olefinic proton, and a one-proton singlet at δ 9.82 for the aldehydic proton. The optical rotation of the aldehyde (22) $\{[\alpha]_D +178^\circ$ (EtOH) $\}$ was substantially lower than that of its counterpart (17a) $\{[\alpha]_D +287^\circ$ (EtOH) $\}$. Accordingly, it was deemed worthwhile to inter-relate the compounds by chemical means.

The hydroxybenzoate (23a), obtained as a syrup in 58% yield (after SiO_2 chromatography) from the reaction of the aldehyde (22) with sodium cyanoborohydride in acetic acid, was transformed into the syrupy dibenzoate (23b) (73% yield after SiO_2 chromatography) by the action of benzoyl chloride in pyridine. Removal of the dithiane protection from compound (23b), using copper(II) chloride–copper(II) oxide in aqueous acetone, gave the crystalline cyclopentenone (1d) (59% yield after SiO_2 chromatography) whose optical rotation was identical with that of the material derived from the cyclopentenecarbaldehyde (17a).

Clearly, compounds (17a) and (22) are of comparable optical purity. Since it would seem to be unlikely that the different cyclodehydration procedures used in the syntheses of these compounds would result in the same degree of racemisation, we infer that the compounds are enantiomerically pure. Evidently, the chirality at position 2 of the dialdehydes (16a) and (21) is preserved during the aldolisation–dehydration sequence.

The antibacterial activity of the cyclopentenecarbaldehyde (22) was less than that of its counterpart (17a), the MIC value against *Staphylococcus aureus* being $32 \mu\text{g cm}^{-3}$.

With a view to preparing the cyclopentenecarbaldehyde (17c), the behaviour of the cyclohexanone (11b) towards ethane-1,2-diol under acidic conditions was also investigated. It was expected that the synthesis of the diol intermediate (15c) would prove to be troublesome since a selective deprotection of the cyclohexylidene acetal moiety of the intermediate (14b) would seem to be required.

When the cyclohexanone (11b) was heated in boiling benzene with ethane-1,2-diol and a trace of toluene-*p*-sulphonic acid, a crystalline product, identified as the hydroquinone ether (24)¹¹ by its elemental composition, m.p., and spectroscopic properties, was obtained in 26% yield. Since hydroquinone itself was not converted into the compound (24) under similar reaction conditions, it is clear that the 2-hydroxyethoxy group is introduced prior to aromatisation.

In ethane-1,2-diol containing a trace of concentrated sulphuric acid, the cyclohexanone (11b) was slowly converted into three products, which were separated by silica-gel chromatography. The first-eluted material, isolated as a crystalline solid in 10% yield, was the diacetal (14b). The second-eluted product, which was obtained in 23% yield, was the crystalline hydroquinone ether (24). The third-eluted material, isolated as a crystalline solid in 60% yield, was the required diol (15c).

In dichloromethane, the diol (15c) reacted with lead(IV) acetate to give a syrupy product in quantitative yield which, on the basis of n.m.r. spectroscopy (CDCl_3), was the dialdehyde (16c). Again, the 1-aldehydic proton appeared as a singlet at δ 9.60 and the 6-aldehydic proton as a triplet (separation 2 Hz) at δ 9.70.

Attempts to effect the cyclodehydration of the dialdehyde (16c) to the cyclopentenecarbaldehyde (17c), using pyrrolidinium acetate in benzene, were unrewarding. However, by using dibenzylamine trifluoroacetate in toluene at 60°C , some

of the desired compound was produced. Although the material (17c) could be purified by rapid silica-gel chromatography (after which it was isolated as an oil in 9% yield), it quickly decomposed at room temperature. The n.m.r. spectrum (CDCl_3) of a freshly chromatographed sample featured two one-proton doublets at δ 2.40 (J 14 and 5 Hz) and δ 2.85 (J 14 and 7 Hz), ascribed to the methylene protons of the cyclopentene ring, a one-proton multiplet at δ 5.85–6.15, attributed to the methine proton of the cyclopentene ring, a one-proton doublet at δ 7.05 (J 2 Hz), for the olefinic proton, and a one-proton singlet at δ 9.85, assigned to the aldehydic proton. The sample was optically active $\{[\alpha]_D +143^\circ$ (EtOH) $\}$.

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; benzene and toluene were distilled from calcium hydride and stored over sodium wire; THF was stored over calcium hydride and, immediately prior to use, distilled; ethanol was refluxed over magnesium (activated with iodine) and distilled; ethane-1,2-diol was stored over molecular sieves (Type 4A). Boron trifluoride–diethyl ether was distilled under reduced pressure from calcium hydride, prior to use. Sodium hydride (50% dispersion in mineral oil) was washed ($3\times$) with sodium-dried light petroleum (b.p. 40 – 60°C) and stored *in vacuo* (over CaCl_2). For chromatographic and instrumental details, see Part 1.¹ Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 40 – 60°C .

Reaction of D-Quinic Acid (4a) with Cyclohexanone.—D-Quinic acid (4a) (116 g, 0.604 mol) was heated under reflux with cyclohexanone (130 cm^3 , 1.26 mol) containing conc. sulphuric acid (4 drops) for 30 min. The mixture was distilled until the boiling point of the distillate was $>150^\circ\text{C}$. Heating was continued for a further 30 min, when the yellow solution was left to cool and ethyl acetate (100 cm^3), potassium hydrogen carbonate (10 g), and anhydrous sodium sulphate (10 g) were added. After being stirred for 30 min, the mixture was filtered and the filtrate evaporated to leave a yellow solid. Recrystallisation of the solid from chloroform–light petroleum gave 3,4-*O*-cyclohexylidene-D-quinide (12) (130 g, 85%) as colourless needles. The sample showed the following properties: m.p. 153 – 155°C (lit.,³ 139 – 144°C); $[\alpha]_D -28^\circ$ (1.6% in EtOH) [lit.,³ -33° (EtOH)]; ν_{max} (KBr) *inter alia* 3 420br (OH) and 1 765 cm^{-1} (γ -lactone C=O); δ (CDCl_3) 1.24–1.88 [10 H, m, $(\text{CH}_2)_5$], 2.00–2.84 (4 H, m, 2- and 6- H_2), 3.35br (1 H, s, OH), and 4.20–4.84 (3 H, m, 3-, 4-, and 5-H); m/z *inter alia* 254 (M^+) and 211 ($M^+ - \text{C}_3\text{H}_7$, base peak).

Reaction of the Quinide (12) with Sodium Borohydride followed by Sodium Periodate.—To a stirred solution of the quinide (12) (90.5 g, 0.356 mol) in dry ethanol (500 cm^3) was added sodium borohydride (14.9 g, 0.394 mol). After 12 h, the mixture was evaporated to half its volume and stirred with a solution of ammonium chloride (57.5 g, 1.07 mmol) in water (200 cm^3) for 1 h. The solution was then extracted with chloroform ($4\times$). The combined extracts were dried (Na_2SO_4) and evaporated to give 3,4-*O*-cyclohexylidene-D-quinol (13) as a light-yellow oil. A stirred solution of the oil in ethanol (250 cm^3) was ice-cooled and treated with sodium periodate (76.3 g, 35.7 mmol) dissolved in water (200 cm^3). After 15 min, the mixture was diluted with water and extracted with chloroform ($5\times$). The combined chloroform extracts were

dried (MgSO_4) and evaporated. Recrystallisation of the resultant product from chloroform–light petroleum gave (3*R*,4*S*,5*R*)-3,4-*O*-cyclohexylidene-3,4,5-trihydroxycyclohexan-1-one (11a) (65.7 g, 82%) as fine needles. The sample showed the following properties: m.p. 112–113 °C (lit.,³ 98 °C); $[\alpha]_D^{20} +120^\circ$ (1.7% in EtOH) [lit.,³ $+103^\circ$ (CHCl_3)]; ν_{max} (KBr) *inter alia* 3 470br (OH) and 1 710 cm^{-1} (ketone ($\text{C}=\text{O}$)); δ (CDCl_3) 1.30–1.80 [10 H, m, (CH_2)₅], 2.18–2.95 (4 H, m, 2- and 6- H_2), 3.05br (1 H, s, OH), 4.10–4.40 and 4.57–4.80 (2 and 1 H, each m, 3-, 4-, and 5-H) (addition of D_2O caused the signal at δ 3.05 to disappear); *m/z inter alia* 226 (M^+) and 183 ($M^+ - \text{C}_3\text{H}_7$, base peak) (Found: C, 63.5; H, 7.9. Calc. for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.70; H, 7.95%).

Reaction of the Cyclohexanol (11a) with Benzoyl Chloride.—To a stirred, cooled (CCl_4 –solid CO_2) solution of the cyclohexanol (11a) (37.2 g, 16.5 mmol) in dry pyridine (150 cm^3), benzoyl chloride (19 cm^3 , 16.4 mmol) was added in drops during 10 min. After a further 15 min, the mixture was allowed to warm to room temperature and stirred overnight. Water (5 cm^3) was added to the mixture which, after 0.5 h, was poured into water and extracted with ethyl acetate. The organic extract was washed with dilute hydrochloric acid (until the aqueous layer showed pH < 2), sodium hydrogen carbonate solution, and brine. After being dried (MgSO_4), the organic phase was evaporated to give (3*R*,4*R*,5*R*)-5-benzoyloxy-3,4-*O*-cyclohexylidene-3,4,5-trihydroxycyclohexan-1-one (11b) (48.9 g, 90%). A sample of the benzoate (11b), recrystallised from light petroleum, showed the following properties: m.p. 131–133 °C (lit.,⁵ 120–121 °C); $[\alpha]_D^{20} +80^\circ$ (1.5% in EtOH) [lit.,⁵ $+68^\circ$ (CHCl_3)]; ν_{max} (KBr) *inter alia* 1 720 cm^{-1} (ester and ketone $\text{C}=\text{O}$); δ (CDCl_3) 1.30–1.90 [10 H, m, (CH_2)₅], 2.40–3.15 (4 H, m, 2- and 6- H_2), 4.40–4.90 (2 H, m, 3- and 4-H), 5.40–5.60 (1 H, m, 5-H), 7.30–7.60 (3 H, m, C_6H_3), and 7.85–8.07 (2 H, m, C_6H_2); *m/z inter alia* 330 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: C, 69.2; H, 6.4. Calc. for $\text{C}_{19}\text{H}_{22}\text{O}_5$: C, 69.10; H, 6.65%).

Reaction of the Cyclohexanone (11b) with Ethane-1,2-dithiol.—To an ice-cooled solution of the cyclohexanone (11b) (36.4 g, 11 mmol) in dry dichloromethane (200 cm^3) was added ethane-1,2-dithiol (18.5 cm^3 , 22 mmol) and boron trifluoride-ether (27 cm^3 , 22 mmol). After 18 h, the solution was poured into water and the mixture was extracted with ethyl acetate. The organic layer was washed with sodium hydrogen carbonate solution (until the aqueous layer showed pH > 7), water, and brine. Evaporation of the dried (Na_2SO_4) organic phase gave a yellow oil which was subjected to silica-gel chromatography. The column was eluted with ether–light petroleum (1 : 2) to remove impurities and then with ether–light petroleum (2 : 1) to give (7*R*,8*R*,9*R*)-9-benzoyloxy-7,8-dihydroxy-1,4-dithiaspiro[4.5]decane (15a). After recrystallisation from chloroform–light petroleum the dithioacetal (15a) (31.4 g, 87%) was obtained as fine needles which showed the following properties: m.p. 115–117 °C (lit.,⁵ 115–116 °C); $[\alpha]_D^{17} +17^\circ$ (1.2% in EtOAc) [lit.,⁵ 0° (CHCl_3)]; ν_{max} (KBr) *inter alia* 3 400br (OH) and 1 720 and 1 710 cm^{-1} (ester $\text{C}=\text{O}$); δ (CDCl_3) 2.00–2.80 (4 H, m, 6- and 10- H_2), 2.90–3.60br (4 H, s, 2 \times OH, 2- and 3- H_2), 3.73–3.95 and 4.05–4.35 (each 1 H, m, 7- and 8-H), 5.20–5.50 (1 H, m, 9-H), 7.29–7.60 (3 H, m, C_6H_3), and 7.90–8.15 (2 H, m, C_6H_2) (addition of D_2O caused the signal at δ 2.90–3.60 to sharpen to a two-proton s at 3.23); *m/z inter alia* 326 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: C, 55.1; H, 5.6; S, 19.8. Calc. for $\text{C}_{15}\text{H}_{18}\text{O}_4\text{S}_2$: C, 55.20; H, 5.50; S, 19.65%).

Reaction of the Cyclohexanediol (15a) with Lead(IV) Acetate.—To a stirred solution of the cyclohexanediol (15a) (0.326 g,

1 mmol) in dry dichloromethane (5 cm^3), lead(IV) acetate (0.443 g, 1 mmol) was added. The orange-coloured solution, formed on addition of the oxidant, progressively decolourised and a white precipitate was soon deposited. After 12 h, the mixture was filtered and the filtrate was washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried (MgSO_4) organic layer left a white foam (0.323 g) considered to contain ca. 70% of (2*R*)-2-benzoyloxy-4,4-ethylenedithiohexane-1,6-dial (16a). The material showed the following properties: $[\alpha]_D^{29} +29^\circ$ (1% in EtOAc); ν_{max} (film) *inter alia* 1 715 cm^{-1} (aldehyde and ester $\text{C}=\text{O}$); δ (CDCl_3) *inter alia* 2.65–2.80 (1.4 H, m, 3- H_2), 3.15 (1.4 H, d, separation 2 Hz, 5- H_2), 3.37 (4 H, s, $\text{SCH}_2\text{CH}_2\text{S}$), 5.60 (0.7 H, dd, *J* 7 and 5 Hz, 2-H), 7.35–7.60 (3 H, m, C_6H_3), 7.90–8.15 (2 H, m, C_6H_2), 9.65 (0.7 H, s, 1-H), and 9.85 (0.7 H, t, separation 2 Hz, 6-H); *m/z inter alia* 324 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: M^+ , 324.0483. $\text{C}_{15}\text{H}_{16}\text{O}_4\text{S}_2$ requires M , 324.0490).

Reaction of the Cyclohexanediol (15a) with Lead(IV) Acetate followed by Pyrrolidinium Acetate.—To a stirred solution of the cyclohexanediol (15a) (10.0 g, 30.7 mmol) in dry dichloromethane (150 cm^3), lead(IV) acetate (13.6 g, 30.7 mmol) was added. After 12 h, the mixture was filtered and the filtrate evaporated to dryness. The crude dialdehyde (16a) was dissolved in dry benzene (100 cm^3) and to the solution was added magnesium sulphate (2.0 g). The stirred mixture was heated to 50 °C and treated with a solution of pyrrolidine (8 drops) and acetic acid (4 drops) in dry benzene (10 cm^3). After 1.5 h, at 50 °C, the mixture was filtered and the reddish-brown filtrate was diluted with ethyl acetate and washed successively with dilute hydrochloric acid, sodium hydrogen carbonate solution, and brine. Evaporation of the dried (MgSO_4) organic layer gave a dark-brown oil which was purified by silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] to give (8*R*)-8-benzoyloxy-1,4-dithiaspiro[4.4]non-6-ene-6-carbaldehyde (17a) (7.27 g, 77%). After recrystallisation from light petroleum, the aldehyde (17a) (5.85 g, 62%) was obtained as fine needles with the following properties: m.p. 93–94 °C; $[\alpha]_D^{280} +280^\circ$ (0.7% in CHCl_3) and $+287^\circ$ (1% in EtOH); ν_{max} (KBr) *inter alia* 1 712 (ester $\text{C}=\text{O}$) and 1 690 cm^{-1} (aldehyde $\text{C}=\text{O}$); λ_{max} (EtOH) 232 (ϵ 21 500), 274 (2 200), and 281 nm (2 100); δ (CDCl_3) 2.72 (1 H, dd, *J* 15 and 5 Hz, 9-H), 3.17 (1 H, dd, *J* 15 and 7 Hz, 9-H), 3.17–3.75 (4 H, m, 2- and 3- H_2), 5.79–6.02 (1 H, m, 8-H), 6.72 (1 H, d, *J* 2 Hz, 7-H), 7.27–7.55 (3 H, m, C_6H_3), 7.87–8.12 (2 H, m, C_6H_2), and 9.68 (1 H, s, $\text{CH}=\text{O}$); *m/z inter alia* 306 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: C, 58.5; H, 4.6; S, 21.2. $\text{C}_{15}\text{H}_{14}\text{O}_3\text{S}_2$ requires C, 58.80; H, 4.60; S, 20.90%).

Reaction of the Aldehyde (17a) with Lithium Aluminium Hydride.—To a stirred, cooled (CCl_4 –solid CO_2) solution of the aldehyde (17a) (2.92 g, 9.5 mmol) in dry THF (20 cm^3) was added lithium aluminium hydride (0.82 g, 21.6 mmol) in portions during 5 min. After 30 min, the mixture was allowed to warm to room temperature and stirred for a further 1.5 h, when it was cooled in an ice-bath and treated with ethyl acetate (10 cm^3). After 15 min, the mixture was added to dilute hydrochloric acid and extracted with ethyl acetate (3 \times). The combined organic extracts were washed with water and brine, dried (Na_2SO_4), and evaporated to leave a light-brown oil. Purification of the product by silica-gel chromatography (EtOAc as eluant) gave (8*R*)-8-hydroxy-6-hydroxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18a) (1.75 g, 90%) as an oil which crystallised on standing. A sample of the diol (18a), recrystallised from ethyl acetate–hexane, showed the following properties: m.p. 106–108 °C; $[\alpha]_D^{100} +100^\circ$ (0.5% in EtOH); ν_{max} (KBr) *inter alia* 3 300br cm^{-1} (OH); δ (CD_3COCD_3) 2.30 (1 H,

dd, J 14 and 5 Hz, 9-H), 2.90 (1 H, s, OH), 2.95 (1 H, dd, J 14 and 7 Hz, 9-H), 3.35 (4 H, s, 2- and 3-H₂), 3.93 (1 H, dd, J 6 and 4 Hz, CH₂OH), 4.30–4.50 (2 H, m, CH₂O), 4.60–4.90 (1 H, m, 8-H), 5.78–5.90 (1 H, m, 7-H) (addition of D₂O caused the signals at δ 2.90 and 3.93 to disappear and those at 4.30–4.50 to sharpen); m/z *inter alia* 204 (M^+) and 186 ($M^+ - H_2O$, base peak) (Found: C, 46.7; H, 6.2; S, 31.4. C₈H₁₂O₂S₂ requires C, 47.05; H, 5.90; S, 31.35%).

Reaction of the Aldehyde (17a) with Metal Hydrides.—(a) To a stirred solution of the aldehyde (17a) (1.53 g, 5 mmol) in acetic acid (20 cm³) was added sodium cyanoborohydride (0.320 g, 5.1 mmol). After 30 min, dilute hydrochloric acid was added and the mixture was poured into ethyl acetate. The mixture was washed with water, sodium hydrogen carbonate solution (until the aqueous layer showed pH > 7), and brine. Evaporation of the dried (MgSO₄) organic phase left a syrup which was subjected to silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] to give (8R)-8-benzoyloxy-6-hydroxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18b) (1.44 g, 94%) as a chromatographically homogeneous syrup. The alcohol (18b) showed the following properties: $[\alpha]_D^{25} +179^\circ$ (1.3% in CHCl₃); v_{\max} (film) *inter alia* 3 440br (OH) and 1 715 cm⁻¹ (ester C=O); λ_{\max} (EtOH) 210sh (ϵ 5 800) and 230 nm (11 000); δ (CDCl₃) 2.80br (1 H, s, OH), 2.80 (1 H, dd, J 14 and 4 Hz, 9-H), 3.15 (1 H, dd, J 14 and 7 Hz, 9-H), 3.40 (4 H, s, 2- and 3-H₂), 4.50br (2 H, s, CH₂O), 5.75–5.98 (1 H, m, 8-H), 6.00–6.08 (1 H, m, 7-H), 7.30–7.60 (3 H, m, C₆H₅), and 7.95–8.15 (2 H, m, C₆H₂) (addition of D₂O caused the signal at δ 2.80 to disappear and that at 4.50 to sharpen); m/z *inter alia* 308 (M^+) and 105 (C₇H₅O⁺, base peak) (Found: M^+ , 308.0558. C₁₅H₁₆O₃S₂ requires M , 308.0541).

(b) To a stirred, cooled (CCl₄–solid CO₂) solution of the aldehyde (17a) (0.306 g, 1 mmol) in dry ethanol (3 cm³) was added sodium borohydride (0.038 g, 1 mmol). After 30 min, the mixture was acidified with dilute hydrochloric acid and poured into ethyl acetate. Work-up after 30 min and silica-gel purification of the product, as in experiment (a), gave a syrupy product (0.291 g, 94%), identical with the alcohol (18b) by n.m.r. and i.r. spectroscopy; $[\alpha]_D^{25} +116^\circ$ (2% in CHCl₃).

(c) To a stirred, cooled (CCl₄–solid CO₂) solution of the aldehyde (17a) (0.306 g, 1 mmol) in dry THF (3 cm³) was added lithium tri-*t*-butoxyaluminium hydride (0.508 g, 2 mmol). Work-up after 30 min and silica-gel purification of the product, as in experiment (a), gave a syrupy product (0.253 g, 82%), that was identical (n.m.r. spectroscopy) with the alcohol (18b); $[\alpha]_D^{25} +155^\circ$ (2% in CHCl₃).

Reaction of the Allylic Alcohol (18b) with Manganese(IV) Oxide.—To a stirred solution of the allylic alcohol (18b) (0.374 g, 1.2 mmol) [obtained from the aldehyde (17a) by reduction with NaB(CN)H₃] in chloroform (10 cm³) was added freshly prepared manganese(IV) oxide (3.74 g). After 3 h, the mixture was filtered through 'hyflo' and the solid residue was washed well with chloroform. Evaporation of the dried (MgSO₄) filtrate and purification of the product by silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] gave a solid (0.297 g, 80%) that was identical (n.m.r. spectroscopy) with the aldehyde (17a). The sample, recrystallised from light petroleum, showed m.p. 92 °C and $[\alpha]_D^{25} +274^\circ$ (1% in CHCl₃).

Reaction of the Hydroxybenzoate (18b) with Sodium Methoxide.—(a) To a solution of the hydroxybenzoate (18b) (0.410 g, 1.3 mmol) ($[\alpha]_D^{25} +179^\circ$ (CHCl₃), obtained from the reduction of the aldehyde (17a) with NaB(CN)H₃) in methanol (5 cm³) was added a solution of sodium methoxide (0.144 g

in methanol (0.6 cm³). After 2 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 subjection of the residue to silica-gel chromatography (EtOAc as eluant) gave methyl benzoate (n.m.r. spectroscopy) and the diol (18a) (0.152 g, 56%) (n.m.r. spectroscopy). The diol (18a), recrystallised from ethyl acetate, showed $[\alpha]_D^{25} +101^\circ$ (1% in EtOH).

(b) The hydroxybenzoate (18b) (0.270 g, 0.88 mmol) ($[\alpha]_D^{25} +116^\circ$ (CHCl₃), obtained from the reduction of the aldehyde (17a) with NaBH₄) was converted into the diol (18a) (0.083 g, 46%) as described in (a). The recrystallised diol (18a) showed $[\alpha]_D^{25} +68^\circ$ (1% in EtOH).

(c) The hydroxybenzoate (18b) (0.253 g, 0.82 mmol) ($[\alpha]_D^{25} +155^\circ$ (CHCl₃), obtained from the reduction of the aldehyde (17a) with LiAl(OBu^t)₃H) was debenzoylated to the diol (18a) (0.098 g, 58%) as described in (a). The recrystallised diol (18a) showed $[\alpha]_D^{25} +80^\circ$ (1% in EtOH).

Reaction of the Diol (18a) with Benzyl Bromide.—To a solution of the optically pure diol (18a) (2.67 g, 13.1 mmol) in dry THF (30 cm³) were added benzyl bromide (4.50 g, 26.3 mmol) and sodium hydride (0.942 g, 39.3 mmol). The mixture was heated under reflux for 1.5 h, cooled, and treated cautiously with water. The mixture was then poured into ethyl acetate and the organic layer was separated and washed with dilute hydrochloric acid and brine. Evaporation of the dried (MgSO₄) organic phase gave a brown syrup which was purified by silica-gel chromatography [ether–light petroleum (1 : 3) as eluant] to yield (8R)-8-benzoyloxy-6-benzoyloxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18c) (3.95 g, 79%) as a chromatographically homogeneous oil. The dibenzyl ether (18c) showed the following properties: $[\alpha]_D^{25} +56^\circ$ (1% in EtOH); λ_{\max} (EtOH) 219 nm (ϵ 2 800); δ (CDCl₃) 2.60 (1 H, dd, J 14 and 5 Hz, 9-H), 3.00 (1 H, dd, J 14 and 7 Hz, 9-H), 3.30 (4 H, s, 2- and 3-H₂), 4.45br (2 H, s, CH₂O), 4.50–4.70 (5 H, m, 2 × CH₂O and 8-H), 6.00–6.08 (1 H, m, 7-H), and 7.30br (10 H, s, 2 × Ph) [irradiation at δ 4.60 caused the signals at 2.60 and 3.00 to collapse to d (J 14 Hz) and that at 6.00–6.08 to collapse to an s]; m/z *inter alia* 384 (M^+), 276 ($M^+ - C_7H_8O$), and 91 (C₇H₇⁺, base peak) (Found: $M^+ - C_7H_8O$, 276.0632. C₁₅H₁₆OS₂ requires m/z 276.0643).

Reaction of the Hydroxybenzoate (18b) with Benzoyl Chloride.—To a stirred ice-cooled solution of the optically pure hydroxybenzoate (18b) (0.330 g, 1.1 mmol) in dry pyridine (3 cm³), benzoyl chloride (0.166 g, 1.2 mmol) was added in drops. After 30 min, the mixture was allowed to warm to room temperature, stirred for a further 2 h, and treated with water (1 cm³). The mixture was diluted with ethyl acetate and washed with dilute hydrochloric acid (until the aqueous layer showed pH < 2) following by brine. After being dried (MgSO₄), the aqueous phase was evaporated and the syrupy product subjected to silica-gel chromatography [ether–light petroleum (1 : 2) as eluant] to give (8R)-8-benzoyloxy-6-benzoyloxymethyl-1,4-dithiaspiro[4.4]non-6-ene (18d) (0.409 g, 93%), as a crystalline solid. A sample, recrystallised from chloroform–light petroleum, showed the following properties: m.p. 91–93 °C; $[\alpha]_D^{25} +72^\circ$ (1% in EtOH); v_{\max} (KBr) *inter alia* 1 715 cm⁻¹ (ester C=O); λ_{\max} (EtOH) 210sh (ϵ 11 500) and 230 nm (28 000); δ (CDCl₃) 2.88 (1 H, dd, J 16 and 4 Hz, 9-H), 3.25 (1 H, dd, J 16 and 7 Hz, 9-H), 3.45 (4 H, s, 2- and 3-H₂), 5.22–5.32 (2 H, m, CH₂O), 5.80–6.10 (1 H, m, 8-H), 6.10–6.18 (1 H, m, 7-H), 7.40–7.70 (6 H, m, 2 × C₆H₅), and 8.00–8.30 (4 H, m, 2 × C₆H₂); m/z *inter alia* 412 (M^+) and 105 (C₇H₅O⁺, base peak) (Found: C, 63.9; H, 4.8. C₂₂H₂₀O₄S₂ requires C, 64.10; H, 4.85%).

Reaction of the Dithiolane (18a) with Copper(II) Salts.—A mixture of the dithiolane (18a) (0.280 g, 1.37 mmol), copper(II) oxide (0.437 g, 5.49 mmol), and copper(II) chloride dihydrate (0.468 g, 2.74 mmol) in acetone (20 cm³) containing water (2 drops) was heated under reflux. After 1.5 h, the mixture was diluted with ethyl acetate and filtered through 'hyflo', the insoluble material being washed well with ethyl acetate. Evaporation of the dried (MgSO₄) filtrate and purification of the residue by silica-gel chromatography (EtOAc as eluant) gave an oily material (0.090 g) that was identical (n.m.r. spectroscopy) with 4-hydroxy-2-hydroxymethylcyclopent-2-en-1-one (1a). The sample showed $[\alpha]_D +12^\circ$ (1% in EtOH) [lit.,¹ +50° (EtOH)].

Reaction of the Dithiolane (18a) with Mercury(II) Chloride.—To a solution of the dithiolane (18a) (0.110 g, 0.54 mmol) in a 9 : 1 mixture of methanol and water (10 cm³) was added calcium carbonate (0.115 g, 1.15 mmol) and mercury(II) chloride (0.295 g, 1.09 mmol). A dense off-white precipitate formed and the mixture was stirred vigorously under reflux for 2 h. The cooled mixture was filtered through 'hyflo' and the filtrate was evaporated. Purification of the resultant oil by silica-gel chromatography (EtOAc as eluant) gave an oily material (0.041 g) that was identical (n.m.r. spectroscopy) with the cyclopentenone (1a). The sample showed $[\alpha]_D +22^\circ$ (1% in EtOH) [lit.,¹ +50° (EtOH)].

Reaction of the Dithiolane (18b) with Copper(II) Salts.—A mixture of the dithiolane (18b) (1.09 g, 3.54 mmol), copper(II) chloride dihydrate (1.21 g, 7.1 mmol), and copper(II) oxide (1.13 g, 14.2 mmol) in acetone (10 cm³) and water (10 drops) was heated under reflux for 2 h. After evaporation, ether was added to the dark-brown residue and the mixture was filtered through 'hyflo'; the insoluble material was washed well with ether. Evaporation of the dried (MgSO₄) filtrate and purification of the dark-brown residue by silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] gave (4R)-4-benzoyloxy-2-hydroxymethylcyclopent-2-en-1-one (1b) (0.577 g, 70%), as a chromatographically homogeneous oil. The cyclopentenone (1b) showed the following properties: $[\alpha]_D +149^\circ$ (1% in CHCl₃); ν_{\max} (film) *inter alia* 3 440br (OH), 1 715 (ester and enone C=O), and 1 650 cm⁻¹ (C=C); λ_{\max} (EtOH) 210sh (ϵ 3 300) and 229 nm (6 300); δ (CDCl₃) 2.50 (1 H, dd, *J* 19 and 3 Hz, 5-H), 3.10 (1 H, dd, *J* 19 and 6 Hz, 5-H), 4.05br (1 H, s, OH), 4.45br (2 H, s, CH₂O), 5.90–6.10 (1 H, m, 4-H), 7.35–7.60 (4 H, m, C₆H₅ and 3-H), and 7.85–8.10 (2 H, m, C₆H₂) [addition of D₂O caused the signal at δ 4.05 to disappear and that at 4.45 to sharpen; irradiation at 6.00 caused the signals at δ 2.50 and 3.10 to collapse to d (each *J* 19 Hz)]; *m/z inter alia* 232 (*M*⁺) and 105 (C₇H₅O⁺, base peak) (Found: *M*⁺, 232.0720. C₁₃H₁₂O₄ requires *M* 232.0734).

Reaction of the Dithiolane (18c) with Copper(II) Salts.—A mixture of the dithiolane (18c) (3.84 g, 10 mmol), copper(II) chloride dihydrate (3.41 g, 20 mmol), and copper(II) oxide (3.20 g, 40 mmol) in acetone (35 cm³) containing water (10 drops) was heated under reflux for 45 min. After evaporation, ether was added to the residue and the mixture was filtered through 'hyflo'; the insoluble material was washed well with ether. Evaporation of the dried (MgSO₄) filtrate left a residue which was purified by silica-gel chromatography [ether–light petroleum (1 : 3) as eluant] to give (4R)-4-benzoyloxy-2-benzoyloxymethylcyclopent-2-en-1-one (1c) (2.16 g, 70%), as a chromatographically homogeneous oil. The cyclopentenone (1c) showed the following properties: $[\alpha]_D +23^\circ$ (1% in EtOH); ν_{\max} (film) *inter alia* 1 710 cm⁻¹ (enone C=O); λ_{\max} (EtOH) 217 nm (ϵ 16 000); δ (CDCl₃) 2.35 (1 H, dd, *J* 18 and 3 Hz,

5-H), 2.75 (1 H, dd, *J* 18 and 5 Hz, 5-H), 4.10–4.20 (2 H, m, CH₂O), 4.47–4.65 (5 H, m, 2 × CH₂O and 4-H), 7.25 (10 H, s, 2 × Ph), and 7.40–7.50 (1 H, m, 3-H) [irradiation at δ 4.15 caused the signal at 7.40–7.50 to collapse to a d (*J* 2 Hz)]; *m/z inter alia* 309 (*MH*⁺) and 91 (C₇H₇⁺, base peak).

Reaction of the Dithiolane (18d) with Copper(II) Salts.—A mixture of the dithiolane (18d) (4.95 g, 12 mmol), copper(II) chloride dihydrate (4.09 g, 24 mmol), and copper(II) oxide (3.84 g, 48 mmol) in acetone (25 cm³) and water (15 drops) was heated under reflux for 2 h. After evaporation, ether was added to the brown solid and the mixture was filtered through 'hyflo'; the insoluble material was washed well with ether. Evaporation of the dried (MgSO₄) filtrate left a brown residue which was subjected to silica-gel chromatography [ether–light petroleum (1 : 3) as eluant] to yield (4R)-4-benzoyloxy-2-benzoyloxymethylcyclopent-2-en-1-one (1d) (2.67 g, 66%), as a crystalline solid. A sample, recrystallised from chloroform–light petroleum, showed the following properties: m.p. 77–79 °C; $[\alpha]_D +45^\circ$ (1% in EtOH); ν_{\max} (KBr) *inter alia* 1 730 and 1 715 cm⁻¹ (ester and enone C=O); λ_{\max} (EtOH) 210sh (ϵ 7 600) and 228 nm (23 200); δ (CDCl₃) 2.62 (1 H, dd, *J* 19 and 3 Hz, 5-H), 3.05 (1 H, dd, *J* 19 and 6 Hz, 5-H), 5.05–5.15 (2 H, m, CH₂O), 5.95–6.15 (1 H, m, 4-H), 7.30–7.65 (7 H, m, 2 × C₆H₅ and 3-H), and 7.85–8.15 (4 H, m, 2 × C₆H₂) [irradiation at δ 6.05 caused the signals at 2.62 and 3.05 to collapse to a d (each *J* 19 Hz)]; *m/z inter alia* 336 (*M*⁺) and 105 (C₇H₅O⁺, base peak) (Found: C, 71.8; H, 4.8%; *M*⁺, 336.0992. C₂₀H₁₆O₅ requires C, 71.45; H, 4.75%; *M*, 336.0998).

Reaction of the Cyclohexanone (11b) with Propane-1,3-dithiol.—A stirred solution of the cyclohexanone (11b) (1.07 g, 3.2 mmol) in dry dichloromethane (15 cm³) at 0 °C was treated with propane-1,3-dithiol (0.65 cm³, 6.5 mmol) and boron trifluoride–ether (0.80 cm³, 6.5 mmol). After 30 min at 0 °C and 6 h at room temperature, the mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with sodium hydrogen carbonate solution (until the aqueous layer showed pH > 7) followed by water and dried (MgSO₄). Evaporation and purification of the residue by silica-gel chromatography (ether as eluant) gave two fractions.

The first-eluted material, isolated as a crystalline solid (0.100 g, 8%), was (8R,9R,10R)-10-benzoyloxy-8,9-O-cyclohexylidene-8,9-dihydroxy-1,5-dithiaspiro[5.5]undecane (19). A sample, recrystallised from chloroform–light petroleum, showed the following properties: m.p. 146 °C; $[\alpha]_D -62^\circ$ (1% in CHCl₃); ν_{\max} (KBr) *inter alia* 1 710 cm⁻¹ (ester C=O); λ_{\max} (EtOH) 208sh (ϵ 6 700), 229 (14 000), 272sh (1 400), and 280sh nm (1 100); δ (CDCl₃) 1.40–3.30 [20 H, m, (CH₂)₅, 2-, 3-, 4-, 7-, and 11-H₂], 4.20–4.60 (2 H, m, 8- and 9-H), 5.40–5.75 (1 H, m, 10-H), 7.35–7.62 (3 H, m, C₆H₅), and 7.95–8.25 (2 H, m, C₆H₂); *m/z inter alia* 420 (*M*⁺) and 188 (base peak) (Found: C, 62.6; H, 6.5. C₂₂H₂₈O₄S₂ requires C, 62.85; H, 6.65%).

The second-eluted material, isolated as a foam (0.980 g, 89%), was (8R,9R,10R)-10-benzoyloxy-8,9-dihydroxy-1,5-dithiaspiro[5.5]undecane (20). It showed the following properties: $[\alpha]_D -32^\circ$ (1% in CHCl₃); ν_{\max} (KBr) *inter alia* 3 420br (OH) and 1 715 and 1 700 cm⁻¹ (ester C=O); λ_{\max} (EtOH) 209sh (ϵ 3 600), 229 (6 500), 272sh (680), and 280sh nm (510); δ (CDCl₃) 1.70–3.05 (10 H, m, 2-, 3-, 4-, 7-, and 11-H₂), 3.65–3.95 (3 H, m, 2 × OH and 8- or 9-H), 4.05–4.40 (1 H, m, 9- or 8-H), 5.20–5.50 (1 H, m, 10-H), 7.15–7.50 (3 H, m, C₆H₅), and 7.80–8.05 (2 H, m, C₆H₂) (addition of D₂O caused the signal at δ 3.65–3.95 to simplify to a one-proton m at 3.70–3.90); *m/z inter alia* 340 (*M*⁺) and

105 ($C_7H_5O^+$, base peak) (Found: M^+ , 340.0804. $C_{16}H_{20}O_4S_2$ requires M , 340.0803).

Reaction of the Diol (20) with Lead(IV) Acetate.—To a stirred solution of the diol (20) (0.122 g, 0.36 mmol) in dry dichloromethane (3 cm³), lead(IV) acetate (0.160 g, 0.36 mmol) was added. After 25 h, the precipitated material was removed by filtration and the filtrate was evaporated to leave a foam, considered to contain ca. 50% of (2*R*)-2-benzoyloxy-4,4-propylenedithiohexane-1,6-dial (21). The material showed the following properties: ν_{max} (film) *inter alia* 1715 cm⁻¹ (ester and aldehyde C=O); δ (CDCl₃) *inter alia* 1.85–3.10 (10 H, m, SCH₂CH₂CH₂S, 3-, and 5-H₂), 5.55 (0.5 H, dd, J 6 and 4 Hz, 2-H), 7.30–7.60 (3 H, m, C₆H₅), 7.90–8.15 (2 H, m, C₆H₂), 9.63 (0.5 H, s, 1-H), and 9.80 (0.5 H, t, separation 2 Hz, 6-H); m/z *inter alia* 338 (M^+) and 105 ($C_7H_5O^+$, base peak) (Found: M^+ , 338.0662. $C_{16}H_{18}O_4S_2$ requires M , 338.0646).

Reaction of the Diol (20) with Lead(IV) Acetate followed by Dibenzylamine Trifluoroacetate.—To a stirred, ice-cooled solution of the diol (20) (2.68 g, 7.9 mmol) in dry dichloromethane (30 cm³), lead(IV) acetate (3.50 g, 7.9 mmol) was added. After 30 min at 0 °C and 2.5 h at room temperature, the precipitated material was removed by filtration and the filtrate evaporated. The crude dialdehyde (21) was dissolved in dry toluene (30 cm³) and to the solution was added magnesium sulphate (1.0 g) and dibenzylamine trifluoroacetate (0.100 g). After 4 h, the mixture was filtered and the filtrate was diluted with ethyl acetate and washed with dilute hydrochloric acid followed by water. Evaporation of the dried (MgSO₄) organic phase and purification of the residue by silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] gave (9*R*)-9-benzoyloxy-1,5-dithiaspiro[5.4]dec-7-ene-7-carbaldehyde (22) (1.32 g, 52%), as a chromatographically homogeneous syrup. The aldehyde (22) showed the following properties: $[\alpha]_D^{+178}$ (1% in EtOH); ν_{max} (film) *inter alia* 1715 (ester C=O), 1695 (enone C=O), and 1660 cm⁻¹ (C=C); λ_{max} (EtOH) 207sh (ϵ 7800), 233 (16800), 272 (1500), and 297sh nm (4300); δ (CDCl₃) 1.95–2.30 (2 H, m, 3-H₂), 2.50–3.60 (6 H, m, 2-, 4-, and 10-H₂), 5.90–6.20 (1 H, m, 9-H), 6.92 (1 H, d, J 2 Hz, 8-H), 7.30–7.60 (3 H, m, C₆H₅), 7.90–8.15 (2 H, m, C₆H₂), and 9.82 (1 H, s, CH=O); m/z *inter alia* 320 (M^+) and 105 ($C_7H_5O^+$, base peak) (Found: M^+ , 320.0526. $C_{16}H_{16}O_3S_2$ requires M , 320.0541).

Reaction of the Aldehyde (22) with Sodium Cyanoborohydride.—To a stirred solution of the aldehyde (22) (0.478 g, 1.49 mmol) in acetic acid (5 cm³), was added sodium cyanoborohydride (0.094 g, 1.49 mmol). The residue, obtained by evaporation after 0.5 h, was dissolved in ethyl acetate and the solution was washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried (MgSO₄) organic layer and purification of the residue by silica-gel chromatography [ether–light petroleum (1 : 1) as eluant] gave (9*R*)-9-benzoyloxy-7-hydroxymethyl-1,5-dithiaspiro[5.4]dec-7-ene (23a) (0.279 g, 58%), as a chromatographically homogeneous syrup. The alcohol (23a) showed the following properties: $[\alpha]_D^{+184}$ (0.9% in EtOH); ν_{max} (film) *inter alia* 3450br (OH) and 1715 cm⁻¹ (ester C=O); λ_{max} (EtOH) 207 (ϵ 8800), 233 (15100), 272sh (1000), and 279sh nm (730); δ (CDCl₃) 1.90–3.25 (8 H, m, OH, 2-, 3-, and 4-H₂ and 10-H), 3.50 (1 H, dd, J 14 and 6 Hz, 10-H), 4.53br (2 H, s, CH₂O), 5.80–6.05 (1 H, m, 9-H), 6.10–6.20 (1 H, m, 8-H), 7.35–7.65 (3 H, m, C₆H₅), and 7.90–8.15 (2 H, m, C₆H₂) [irradiation at δ 5.90 caused the signal at 3.50 to collapse to a d (J 14 Hz); addition of D₂O caused the signal at δ 1.90–3.25 to simplify to a two-proton m at 1.90–2.30 and a five-proton m at 2.70–3.25]; m/z *inter*

alia 322 (M^+) and 105 ($C_7H_5O^+$, base peak) (Found: M^+ , 322.0715. $C_{16}H_{18}O_3S_2$ requires M , 322.0697).

Reaction of the Alcohol (23a) with Benzoyl Chloride.—To a stirred solution of the alcohol (23a) (0.480 g, 1.49 mmol) in dry pyridine (5 cm³) at 0 °C, benzoyl chloride (0.208 cm³, 1.79 mmol) was added. After 30 min, the mixture was allowed to warm to room temperature. After 16 h, water (1 cm³) was added and the mixture (after 15 min) was partitioned between ethyl acetate and water. The organic layer was washed with dilute hydrochloric acid (until the aqueous layer showed pH < 2) followed by water. Evaporation of the dried (MgSO₄) organic phase left a residue which was purified by silica-gel chromatography [ether–light petroleum (1 : 2) as eluant] to give (9*R*)-9-benzoyloxy-7-benzoyloxymethyl-1,5-dithiaspiro[5.4]dec-7-ene (23b) (0.461 g, 73%). The sample possessed the following properties: $[\alpha]_D^{+80}$ (1.5% in EtOH); ν_{max} (film) *inter alia* 1720 cm⁻¹ (ester C=O); λ_{max} (EtOH) 207 (ϵ 11100), 229 (22900), 272 (2100), and 279 nm (1600); δ (CDCl₃) 1.80–2.50 (2 H, m, 3-H₂), 2.70–3.30 (5 H, m, 2- and 4-H₂ and 10-H), 3.55 (1 H, dd, J 14 and 7 Hz, 10-H), 5.20–5.30 (2 H, m, CH₂O), 5.90–6.20 (1 H, m, 9-H), 6.17–6.26 (1 H, m, 8-H), 7.32–7.67 (6 H, m, 2 × C₆H₅), and 8.00–8.30 (4 H, m, 2 × C₆H₂) [irradiation at δ 6.1 caused the signal at 3.55 to collapse to a d (J 14 Hz)]; m/z *inter alia* 426 (M^+) and 105 ($C_7H_5O^+$, base peak) (Found: M^+ , 426.0959. $C_{23}H_{22}O_4S$ requires M , 426.0959).

Reaction of the Dithiane (23b) with Copper(II) Salts.—A mixture of the dithiane (23b) (0.182 g, 0.43 mmol), copper(II) chloride dihydrate (0.145 g, 0.85 mmol), and copper(II) oxide (0.136 g, 1.72 mmol) in acetone (5 cm³) and water (3 drops) was heated under reflux for 1 h. After evaporation of the solvent, ether was added to the residue which was filtered through 'hyflo' (the insoluble material was washed well with ether). Evaporation of the dried (MgSO₄) filtrate and purification of the residue by silica-gel chromatography [ether–light petroleum (1 : 2) as eluant] gave a crystalline material (0.085 g, 59%), which was identical (i.r., n.m.r., and mass spectroscopy) with the cyclopentenone (1d) obtained by way of the dithiolane (18d). The crystallised material (from CHCl₃–light petroleum) showed m.p. 76–78 °C and $[\alpha]_D^{+45}$ (1.9% in EtOH).

Reaction of the Cyclohexanone (11b) with Ethane-1,2-diol.—(a) A mixture of the cyclohexanone (11b) (0.819 g, 2.48 mmol), dry ethane-1,2-diol (2 cm³), dry benzene (20 cm³), and a catalytic quantity of toluene-*p*-sulphonic acid was heated under reflux with azeotropic removal of water. After 10 h, the solution was partitioned between ethyl acetate and water. The organic layer was washed with sodium hydrogen carbonate solution, water, and brine. Evaporation of the dried (MgSO₄) organic phase and purification of the product by silica-gel chromatography (EtOAc as eluant) gave 1-hydroxy-4-(2-hydroxyethoxy)benzene (24) (0.100 g, 26%), as a crystalline solid. The hydroquinone ether (24), obtained as flaky crystals after recrystallisation from ethyl acetate–light petroleum, showed the following properties: m.p. 88–90 °C (lit.,¹¹ 88 °C); δ (CD₃COCD₃) 3.70–4.10 (5 H, m, CH₂CH₂-OH), 6.70 (4 H, s, C₆H₄), and 7.90 (1 H, s, OH) (addition of D₂O caused the signal at δ 3.60–4.10 to simplify to a four-proton m and that at 7.90 to disappear); m/z *inter alia* 154 (M^+) and 110 (base peak) (Found: C, 62.0; H, 6.6. Calc. for C₈H₁₀O₃: C, 62.35; H, 6.50%).

(b) To a vigorously stirred suspension of the cyclohexanone (11b) (0.681 g, 2.1 mmol) in dry ethane-1,2-diol (7 cm³) was added conc. sulphuric acid (3 drops). After 75 h, the mixture was diluted with water and extracted with ethyl acetate. The

organic phase was washed with sodium hydrogen carbonate solution, dried (MgSO_4), and evaporated. Purification of the residue by silica-gel chromatography [ether-light petroleum (1:2) as eluant] gave three fractions.

The first-eluted material (0.076 g, 10%) was (7R,8R,9R)-9-benzoyloxy-7,8-O-cyclohexylidene-7,8-dihydroxy-1,4-dioxaspiro[4.5]decane (14b). The compound, recrystallised from light petroleum, showed the following properties: m.p. 106–108 °C; $[\alpha]_D^{25} +62^\circ$ (0.5% in EtOH); ν_{max} (KBr) *inter alia* 1715 cm^{-1} (ester C=O); λ_{max} (EtOH) 205sh (ϵ 4 500), 230 (16 100), and 275 nm (1 100); δ (CDCl_3) 1.30–2.50 [14 H, m, (CH_2)₅, 6- and 10-H₂], 3.90–4.05 (4 H, m, 2- and 3-H₂), 4.15–4.75 (2 H, m, 7- and 8-H), 5.27–5.60 (1 H, m, 9-H), 7.30–7.60 (3 H, m, C_6H_5), and 7.90–8.20 (2 H, m, C_6H_2), *m/z inter alia* 374 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: C, 67.3; H, 7.1%; M^+ , 374.1748. $\text{C}_{21}\text{H}_{26}\text{O}_6$ requires C, 67.35; H, 6.95; M , 374.1729).

The second-eluted material (0.073 g, 23%) was the hydroquinone ether (24) (n.m.r. spectroscopy); m.p. 90 °C (from EtOAc-light petroleum) (lit.,¹¹ 88 °C).

The third-eluted material (0.362 g, 60%) was (7R,8R,9R)-9-benzoyloxy-7,8-dihydroxy-1,4-dioxaspiro[4.5]decane (15c). A sample, recrystallised from chloroform-light petroleum, showed the following properties: m.p. 63–65 °C; $[\alpha]_D^{25} 0^\circ$ (2% in EtOH); ν_{max} (KBr) *inter alia* 3 420br (OH) and 1 710 cm^{-1} (ester C=O); λ_{max} (EtOH) 208sh (ϵ 2 900), 230 (10 000), and 273 nm (800); δ (CDCl_3) 1.60–2.45 (4 H, m, 6- and 10-H₂), 3.40br (2 H, s, 2 × OH), 3.60–4.30 (6 H, m, 2- and 3-H₂ and 7- and 8-H), 5.15–5.55 (1 H, m, 9-H), 7.30–7.60 (3 H, m, C_6H_5), and 8.10–8.25 (2 H, m, C_6H_2) (addition of D_2O caused the signal at δ 3.40 to disappear); *m/z inter alia* 294 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: C, 61.2; H, 6.3. $\text{C}_{15}\text{H}_{18}\text{O}_6$ requires C, 61.20; H, 6.10%).

Reaction of the Diol (15c) with Lead(IV) Acetate.—To a stirred solution of the diol (15c) (0.147 g, 0.5 mmol) in dry dichloromethane (7 cm^3) was added lead(IV) acetate (0.222 g, 0.5 mmol). After 2 h, the mixture was filtered. Evaporation of the dried (MgSO_4) filtrate gave a syrup (0.145 g, 100%), which was considered to be (2R)-2-benzoyloxy-4,4-ethylenedioxyhexane-1,6-dial (16c). The material showed the following properties: $[\alpha]_D^{25} 0^\circ$ (2% in EtOH); ν_{max} (film) *inter alia* 1 715br cm^{-1} (ester and aldehyde C=O); λ_{max} (EtOH) 210 (ϵ 3 700) and 228 nm (10 500); δ (CDCl_3) 2.50 (2 H, d, separation 6 Hz, 3-H₂), 2.90 (2 H, d, separation 2 Hz, 5-H₂), 4.02 (4 H, s, $\text{OCH}_2\text{CH}_2\text{O}$), 5.43 (1 H, t, separation 6 Hz, 2-H), 7.30–7.60 (3 H, m, C_6H_5), 7.95–8.20 (2 H, m, C_6H_2), 9.60 (1 H, s, 1-H), and 9.70 (1 H, t, separation 2 Hz, 6-H); *m/z inter alia* 274 ($M^+ - \text{H}_2\text{O}$) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: $M^+ - \text{H}_2\text{O}$, 274.0867. $\text{C}_{15}\text{H}_{14}\text{O}_5$ requires *m/z* 274.0841).

Reaction of the Diol (15c) with Lead(IV) Acetate Followed by Dibenzylamine Trifluoroacetate.—To a stirred solution of the diol (15c) (0.441 g, 1.5 mmol) in dry dichloromethane (20 cm^3) was added lead(IV) acetate (0.665 g, 1.5 mmol). After 2 h, the mixture was filtered and the solid washed well with dichloromethane. Evaporation of the dried (MgSO_4) filtrate gave the dialdehyde (16c) which was dissolved in dry toluene (10 cm^3).

To the solution was added magnesium sulphate (0.2 g) and dibenzylamine trifluoroacetate (0.20 g). The mixture was heated at 60 °C for 70 min and filtered. The insoluble material was washed well with ethyl acetate and the combined filtrates were diluted further with ethyl acetate and washed with dilute hydrochloric acid and brine. Evaporation of the dried (MgSO_4) organic phase and purification of the residue by silica-gel chromatography [ether-light petroleum (1:1) as eluant] gave (8R)-8-benzoyloxy-1,4-dioxaspiro[4.4]non-6-ene-6-carbaldehyde (17c) as a slightly impure oil (0.037 g, 9%), which decomposed when left to stand at room temperature overnight. A sample of the freshly prepared aldehyde (17c) showed the following properties: $[\alpha]_D^{25} +143^\circ$ (0.9% in EtOH); λ_{max} (film) *inter alia* 215sh (ϵ 6 100), 232 (9 900), and 275 nm (550); δ (CDCl_3) *inter alia* 2.40 (1 H, dd, *J* 14 and 5 Hz, 9-H), 2.85 (1 H, dd, *J* 14 and 7 Hz, 9-H), 3.90–4.35 (4 H, m, 2- and 3-H₂), 5.85–6.15 (1 H, m, 8-H), 7.05 (1 H, d, *J* 2 Hz, 7-H), 7.35–7.65 (3 H, m, C_6H_5), 7.95–8.20 (1 H, m, C_6H_2), and 9.85 (1 H, m, CH=O), *m/z inter alia* 274 (M^+) and 105 ($\text{C}_7\text{H}_5\text{O}^+$, base peak) (Found: M^+ , 274.0843. $\text{C}_{15}\text{H}_{14}\text{O}_5$ requires M , 274.0841).

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