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A ROUTE TO FUNCTIONALISED CYCLOPENTANES FROM 6-DEOXYHEX-5-ENOPYRANOSIDE DERIVATIVES*,†

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ABSTRACT

A route to the functionalised cyclopentenone derivative, (2*S*)-(2/3)-dibenzyloxy-5-(hydroxymethyl)cyclopentene-4-enone ethylene acetal, has been developed from a deoxyinososе that is readily accessible. The carbocyclisation procedure was less efficient in affording (2*S*)-(2,3/4,5)-2,3,4,5-tetrahydroxy-2,3-*O*-isopropylidenecyclohexanone from 6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranose. Various reactions were carried out on (2*S*)-(2,4,5/3)-2,3-dibenzoyloxy-5-hydroxy-4-toluene-*p*-sulphonyloxycyclohexanone ethylene dithioacetal.

INTRODUCTION

Carbohydrates have, in recent years, been used as starting materials for the synthesis of an extensive range of enantiomerically pure non-carbohydrate natural products and related substances[2]. Many specifically functionalised acyclic and heterocyclic compounds have been produced in this way, but a special interest in this laboratory has been the use of sugars for the synthesis of carbocyclic derivatives — particularly some of significance in relationship to medicinally important compounds such as aminoglycoside antibiotics[3], prostaglandins[4,5], and anthracycline aglycons[6]. Since several routes from carbohydrates to cyclohexane compounds had been developed, we began, some years ago, a search for efficient methods for obtaining functionalised cyclopentanes, and recently appreciable developments have been reported on this previously neglected possibility[4] which parallel progress in the development of other routes to cyclopentanes[7].

Our first attempts involved base-catalysed reaction of the methyl ketone **1**, obtained from the 6-deoxy-5-enofuranose derivative **2**, and although evidence was obtained[8] for the production of a cyclopentane formed by attack of a C-6 nucleophile at C-2, it was clear that this route was not suitable for the efficient production of the desired products. Indeed, this approach involves an "(enolendo)-exo-tet" cyclisation and is disfavoured as a means of preparing 5-membered rings[9].

*Dedicated to Professor Raymond U. Lemieux.
†Functionalised Carbocycles from Carbohydrates, Part 6. For Part 5, see ref. 1.

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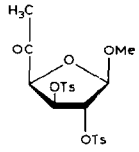

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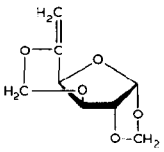

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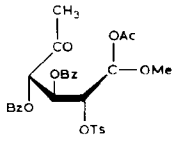

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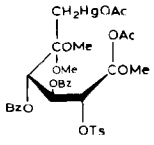

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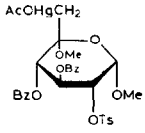

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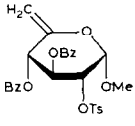

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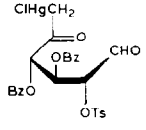

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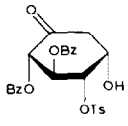

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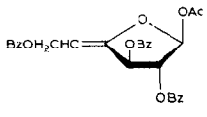

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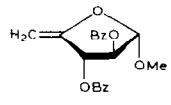

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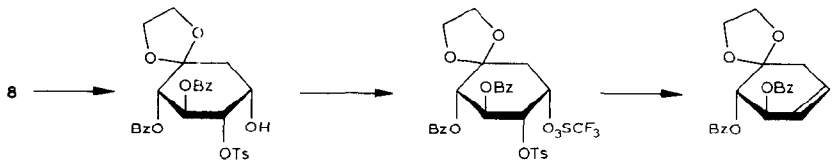
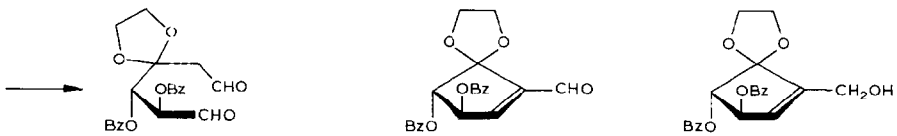
Related attempts with compounds such as **3–5** met with failure[10]. However, the alkene **6**, from which these three compounds were produced, on hydroxymercuration, readily gave an adduct **7** (in equilibrium with its cyclic hydrate) from which the cyclohexanone derivative **8** was easily obtainable in high yield[11]. Then, in the hope that this approach would permit the conversion of ald-4-enofuranose compounds into cyclopentanes, compounds **9** and **10** were treated with mercury(II) salts in aqueous media[12], but no such products resulted which, again, could be ac-



11 12 13



14 15 16

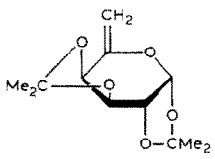
Scheme 1

counted for by Baldwin's generalisations[13]. Having found that the mercury(II) ion-catalysed, ring-closure reaction cannot be used with 4-enofuranoses to give cyclopentanes directly, but that with 5-enopyranoses it affords cyclohexanes very efficiently, our attention was turned to the ring contraction of the latter. We now report a cyclopentane synthesis by use of this strategy (see Scheme 1) which is analogous to that employed by Barrière *et al.*[14] in their use of (−)-quinic acid to produce a variety of enantiomerically pure cyclopentane derivatives and hence 13-oxaprostanoids, and similar to related ring contractions[15,16]. We also describe several reactions investigated during the development of the route illustrated in Scheme 1.

RESULTS AND DISCUSSION

From the readily available ketone **8**, the acetal **11** was made efficiently with ethane-1,2-diol in benzene–1,4-dioxane in the presence of sulphuric acid[17], the use of toluene-*p*-sulphonic acid as catalyst, or 1,2-bis(trimethylsilyloxy)ethane and trimethylsilyl triflate[18], or 2-ethyl-2-methyl-1,3-dioxolane and toluene-*p*-sulphonic acid[19], or *N,N*-dimethylformamide ethylene acetal and acetic acid[15] leading to extensive prior *β*-elimination of water or aromatisation. Conversion of **11** into the alkene **13** was effected in about 60% yield either by way of the derived triflate **12**, which underwent elimination on treatment with sodium iodide in refluxing acetone in the presence of zinc–copper couple[20], or directly, with similar efficiency, by treatment with iodine, imidazole, and triphenylphosphine in refluxing toluene–acetonitrile[21]. Oxidative cleavage of the double bond with sodium periodate and catalytic osmium tetraoxide[22] gave the dialdehyde **14** which was cyclised by use of pyrrolidinium acetate in benzene[16] to give a somewhat unstable product having n.m.r. spectral features consistent with it being the enal **15**. It was stabilised by conversion into the corresponding alcohol **16**.

In the course of the development of the route to cyclopentane derivatives illustrated in Scheme 1, several alternative possibilities were examined. Initially the alkene[23] **17**, available from 1,2:3,4-di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-*α*-D-galactopyranose *via* the 6-iodide[24], was assessed as a precursor of the diol **18** which should be subject to ring contraction. It did not undergo the mercury(II) ion-catalysed carbocyclisation reaction as readily as do analogous D-glucose-based alkenes. However, the diol **18** was obtained (40% after column chromatography) by initial hydroxymercuration of **17** using mercury(II) acetate, followed by treatment with potassium chloride to give the chloromercuric intermediate (*cf.* ref. 7)



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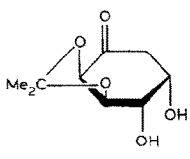

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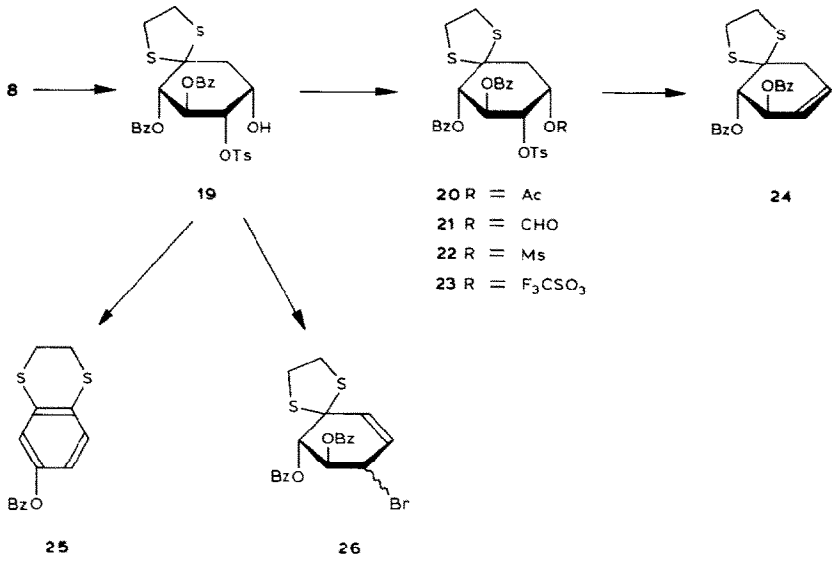


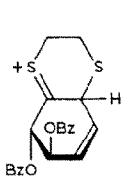
which readily ring closed on heating in solution. This is consistent with the expectation that alkylmercury chlorides are more nucleophilic than the corresponding acetates[25]. The orientation at the new asymmetric centre of the diol **18** was not determined from its 80-MHz ^{1}H-n.m.r. spectrum, and was assigned by analogy, since all of the 6-deoxy-5-enopyranose compounds (*e.g.*, **6**) so far examined have given hydroxycyclohexanones (*e.g.*, **8**) having hydroxyl groups *cis*-related to the adjacent oxygenated groups[3,11,26–28]. In the case of a 2-benzamido-2-deoxy analogue[28] of **6**, and also a 2-deoxy analogue[27], however, mixed epimeric alcohols were produced. Treated with sodium periodate followed by pyrrolidinium acetate, the diol **18** did not give discrete products (presumably protection of the ketonic group could rectify this problem but this proved difficult), and since it was not obtainable with the same high efficiency as was **8**, attention reverted to the use of the latter compound.

Various attempts were made to replace the hydroxyl group of the ethylene dithioacetal **19** of ketone **8** by halogen with a view to facilitating elimination at C-4–C-5. Treatment with methyl iodide in the presence of diethyl azidocarboxylate and triphenylphosphine[29] gave no reaction; but 2,4,5-tribromoimidazole and triphenylphosphine[30] afforded a highly crystalline product that was a 1:1 mixture of the epimeric 4-bromo-5-enes **26** which were characterised by correlation of their ^{1}H- and ^{13}C-n.m.r. spectra with those of 3-bromocyclohexene. Since their H-3 resonances showed strong coupling to the allylic protons, the allylic system is 4-bromo-5-ene rather than 6-bromo-4-ene. The bromides **26** are presumed to have been formed by way of the allylic toluene-*p*-sulphonate, and to preclude the initial elimination, the alcohol **19** was treated with the less basic *N*-bromosuccinimide and triphenylphosphine in *N,N*-dimethylformamide[31], but this resulted only in a good

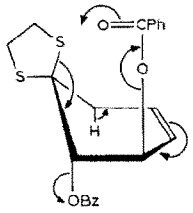
yield of the corresponding formate **21**. Such esters are known to be derivable from this type of reaction, and result from the hydrolysis of forminium salts produced as intermediates in the halogenation of alcohols with various halogenating agents in this solvent[32]. Since halogenation with reagents of this type can be favoured at elevated temperatures[33], the reaction of the alcohol **19** with *N*-bromosuccinimide and triphenylphosphine in *N,N*-dimethylformamide was repeated at 105° but, under these conditions, aromatisation and rearrangement of the dithioacetal took place and 6-benzoyloxy-2,3-dihydro-1,4-benzodithiin (**25**), was produced specifically. It was readily characterised from its n.m.r. spectra, and had λ_{max} 257 nm (ε, 1.75×10^4) which compares with λ_{max} 253 (ε, 1.68×10^4) for the unsubstituted benzodithiin[34]. Therefore, elimination apparently occurred, most probably after the required bromination, to provide an allylic system at C-4–C-6 from which the sulphonium intermediate **25a** could readily be produced, and subsequent aromatisation gave the observed product. Analogous rearrangements of cyclohexanone ethylene dithioacetals to 1,4-dithia-Δ^9-octalins are known with compounds having leaving groups either at (ref. 35) C-2 or on one of the sulphur atoms[36].

With a view to effecting elimination at C-4–C-5 by application of the Tipson–Cohen procedures[20,37], the methanesulphonate **22** was treated with sodium iodide and zinc–copper couple in refluxing *N,N*-dimethylformamide, but a complex mixture of products was formed. The triflate **23**, on the other hand, on heating in acetone with sodium iodide and zinc gave a single product having a ^{1}H-n.m.r. spectrum consistent with it being the required alkene **24**. Unfortunately, this compound proved to be too unstable for preparative work — perhaps because the allylic benzoyloxy group can migrate to a sulphur atom to initiate aromatisation (**24a**) — and the procedures of Scheme 1 were therefore developed to avoid the use of the reactive dithiolane ringsystem.

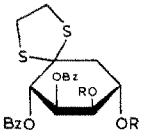
Treatment of the hydroxytoluene-*p*-sulphonate **19** with sodium fluoride in refluxing *N,N*-dimethylformamide[38] gave, by way of a benzoxonium ion, the diols **27**



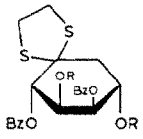
25a



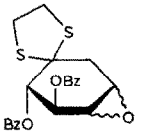
24a



27 R = H
28 R = Ac



29 R = H
30 R = Ac



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and **29** which were characterised as their diacetates **28** and **30**, respectively. Dehydration of the major, vicinal diol **27** by use of diethyl azidocarboxylate and triphenylphosphine in refluxing 1,4-dioxane afforded, in high yield, a crystalline mixture of the epoxides **31** (epimeric ratio 4:1) which, on heating with lithium bromide and *N,N,N',N',N'',N''*-hexamethylphosphoric triamide in toluene, gave mixed products, none of which contained the formyl group, and therefore the possible ring contraction[39] of the derived bromocyclohexanes did not occur.

TABLE I

^{1}H-N.M.R. CHEMICAL SHIFTS (δ)[a]

Compound	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*Others (aromatics excluded)*
11	5.48	5.98	4.75	4.4	←1.9–2.4→		2.18 (Me), 3.42 (OH), 3.8–4.2 (OCH_2)
12	5.53	5.91	4.96	5.45	2.62	2.21	2.21 (Me), 3.8–4.2 (OCH_2)
13	←———	5.6–6.1	——→		2.4	2.7	3.8–4.3 (OCH_2)
15	5.70	6.11	7.05				9.77 (CHO), 3.8–4.3 (OCH_2)
16	5.55	5.95	6.22				2.30 (OH), 4.31 (CH_2, OH), 3.8–4.2 (OCH_2)
18	←———	4.1–4.6	——→		←2.6–2.9→		1.38, 1.43 (Me), 3.2–3.6 (OH)
19	5.50	5.94	4.74	4.5	2.83	2.52	1.74 (OH), 2.15 (Me), 3.1–3.2 (SCH_2)
20	5.52	5.84	4.80	5.5	2.88	2.47	2.18, 2.21 (Me), 3.2 (SCH_2)
21	5.56	5.82	4.88	5.6	2.91	2.53	2.20 (Me), 3.20 (SCH_2), 8.09 (CHO)
22	5.49	5.85	4.74	5.3	3.05	2.62	2.16 (Me), 3.24 (SCH_2, MeS)
23	5.55	5.80	4.92	5.5	3.10	2.68	2.22 (Me), 3.26 (SCH_2)
24	←———	5.8–6.3	——→		←2.7–3.1→		2.7–3.4 (SCH_2)
27	5.75	5.58	←4.0–4.2→		←2.1–2.9→		3.16 (SCH_2), 3.55 (OH)
28	5.7–5.9		5.50	5.26	←2.6–2.8→		2.05, 2.14 (Ac), 3.24 (SCH_2)
29	5.75	4.4	5.35	4.3–4.6	←2.4–2.7→		3.24 (SCH_2, OH)
30	←———	5.5–5.8	——→	5.35	2.75	2.75	1.91, 2.10 (Ac), 3.24 (SCH_2)
31	←5.5–5.8→		←3.2–3.7→		←2.8–3.1→		3.1–3.7 (SCH_2)

[a]For solutions in ^{2}H (chloroform).

TABLE II

^{1}H-N M R. OBSERVED COUPLING CONSTANTS (Hz)

Compound	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	*Others*
11	9.9	9.9	3.3				
12	8.8	8.8	3.2	4.9	3.0	15.4	
13	4.1	2.2					
16	3.0	3.5					$J_{3,5'} = J_{4,5'}$ 1.5
19	8.9	8.9	3.2	4.4	2.9	15.1	
20	8.1	8.4	3.4	5.3	2.6	15.2	
21	7.8	7.9	3.4	5.5	3.2	15.2	
22	8.6	8.9	3.4	5	3	15	
23	7.1	7.7	3.0	6.3	3.0	15.0	
27	5.3	2.2					
28		2.2	6.3	4.7	4.7		
29	6.7	6.7	3.2				
30				4.5	4.5		

TABLE III

^{13}C-N.M R. CHEMICAL SHIFTS (δ)[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*XCH_2*	*Others*
11	108.1	67.3[b]	69.3[b]	73.9[b]	80.8[b]	36.6	65.7, 66.9	
12	106.5	69.0[b]	72.4[b]	75.9[b]	82.1[b]	35.8	65.9, 66.6	108.5 (CF_3)
13	107.8	73.7[b]	73.9[b]	133.0	125.1	36.6	65.7, 66.1	
15	111.8	77.3	80.7	146.5	144.4		66.6, 67.2	192.9 (CHO)
16	113.6	78.5	80.5	129	147.5		65.9, 66.7	57.8 (C-5')
18	207.4	78.4[b]	79.6[b]	69.5[b]	72.3[b]	43.9		26.5, 28.1 (Me), 111.9 (CMe_2)
19	66.6	68.3[b]	70.4[b]	77.4[b]	81.0[b]	38.8[b]	41.2[b], 42.3[b]	
20	66.5	69.2[b]	70.5[b]	76.7[b]	78.8[b]	39.0[b]	39.7[b], 40.8[b]	21.1, 169.8 (Ac)
21	66.6	68.8[b]	70.3[b]	76.4[b]	76.6[b]	39.2[b]	39.6[b], 40.6[b]	159.6 (CHO)
23	66.2	70.0[b]	75.2[b]	75.5[b]	82.7[b]	39.6[b]	40.4[b], 41.0[b]	
27	67.0	69.6[b]	71.9[b]	72.9[b]	75.6[b]	38.3[b]	39.8[b], 44.1[b]	
28	67.0	69.0[b]	69.8[b]	70.9[b]	75.4[b]	39.5[b]	40.0[b], 41.2[b]	20.7, 21.2, 169.5 (Ac)
29	66.8	67.2[b]	69.8[b]	76.2[b]	78.3[b]	39.2[b]	39.2[b], 44.4[b]	
30	67.2	68.9[b]	70.4[b]	70.5[b]	75.3[b]	39.3[b]	39.6[b], 40.1[b]	20.5, 21.0, 169.3 (Ac)
31 (major)	68.6	73.8[b]	73.9[b]	53.3[b]	53.7[b]	39.8[b]	40.1[b], 41.8[b]	
31 (minor)	64.0	71.8[b]	76.7[b]	53.3[b]	52.4[b]	38.2[b]	40.6[b], 41.5[b]	

[a]For solution in (^{2}H)chloroform. [b]Not specifically assigned.

EXPERIMENTAL

General methods. — Optical rotations were determined for chloroform solutions within the concentration range 0.5–1.5%, and temperature range 18–22°. ^{1}H- and ^{13}C-n.m.r. spectra were recorded with a Varian FT80A instrument and, unless otherwise stated, for deuteriochloroform solutions; spectral data are given in Tables I–III.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-5-hydroxy-4-toluene-p-*sulphonyloxycyclohexanone ethylene acetal* (**11**). — The ketone **8** (1 g) and ethane-1,2-diol (1.5 mL) were heated under reflux in 1,4-dioxane (10 mL)–benzene (15 mL) with concentrated H_2SO_4 (0.2 mL) for 5 h with azeotropic removal of water. Pyridine (0.6 mL) was added, and the solvents were removed *in vacuo* to leave a residue which crystallised on trituration with ethanol. The product **11** (0.79 g, 67%) was recrystallised from ethyl acetate, m.p. 175–176°, $[\alpha]_D^{20}$ −3°.

Anal. Calc. for $C_{29}H_{28}O_{10}S$: C, 61.3; H, 4.9; S, 5.6. Found: C, 61.4; H, 5.2; S, 5.6.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-4-toluene-p-*sulphonyloxy-5-trifluoromethanesulphonyloxycyclohexanone ethylene acetal* (**12**). — Trifluoromethane sulphonic

anhydride (0.45 mL, 1.5 mol equiv.) was added with stirring to the alcohol **11** (1.0 g) in dichloromethane–pyridine (40 mL, 3:1) at −40°. The mixture was allowed to warm to 10° over 3.5 h, and then extracted with dilute HCl (30 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ and water, and dried, and on removal of the solvent the product crystallised. Recrystallisation from ethyl acetate–light petroleum gave the pure triflate **12** (1.06 g, 86%), m.p. 163–164°, $[\alpha]_D^{20}$ +15°.

Anal. Calc. for $C_{30}H_{27}F_3O_{12}S_2$: C, 51.4; H, 3.9; S, 9.1. Found: C, 51.6; H, 4.2; S, 9.1.

(2S)-(2/3)-2,3-Dibenzoyloxycyclohex-4-enone ethylene acetal (**13**). — *(a) From triflate* **12**. The triflate **12** (0.36 g), sodium iodide (1.8 g), and zinc-copper couple (3.6 g) were heated in refluxing acetone for 20 min. After filtration, the solvent was removed and the residue partitioned between chloroform (75 mL) and water (100 mL). The product was recovered from the organic phase and purified by preparative t.l.c. After recrystallisation from ethanol, the alkene **13** (0.13 g, 62%) had m.p. 125–126.5°, $[\alpha]_D^{20}$ −196°.

Anal. Calc. for $C_{22}H_{20}O_6$: C, 69.5; H, 5.3. Found: C, 69.5; H, 5.6.

(b) From alcohol **11**. The alcohol **11** (0.49 g), iodine (0.70 g, 3 mol equiv.), triphenylphosphine (0.96 g, 4 mol equiv.), and imidazole (0.25 g, 4 mol equiv.) were heated under reflux in 1:1 toluene–acetonitrile (30 mL) for 11 h. After removal of the acetonitrile under reduced pressure, toluene (50 mL) was added, and the mixture was washed with saturated aqueous $NaHCO_3$, aqueous $Na_2S_2O_3$ solution, water, and then dried. The product was purified by flash column chromatography to give the alkene **13** (0.20 g, 60%), m.p. 125–127°; ^{1}H-n.m.r. spectrum identical to that of the previous sample.

(2S)-(2/3)-Dibenzoyloxy-5-(hydroxymethyl)cyclopent-4-enone ethylene acetal (**16**). — The alkene **13** (0.19 g) in 3:1 1,4-dioxane–water (7 mL) and osmium tetraoxide (8 mg) in 1,4-dioxane (80 μL) were mixed, and treated with sodium periodate (0.51 g) with stirring over 43 h. Water was added and the product was extracted into dichloromethane and, after drying and removal of the solvent, the residue was dissolved in benzene (6 mL). Anhydrous sodium sulphate (1 g), and three drops of a solution of pyrrolidine (0.1 mL) and acetic acid (50 μL) in benzene (1 mL) were added, and the mixture was stirred for 24 h at 20°. Filtration and evaporation of the solvent gave the aldehyde **15** which was purified by preparative t.l.c. (0.11 g, 56%, $[\alpha]_D^{20}$ −190°).

Sodium borohydride (0.15 g) in ethanol (5 mL) was added to aldehyde **15** (0.37 g) in ethanol (6 mL) at −50° under nitrogen. After 0.5 h at this temperature, the mixture was allowed to warm to −10° over 1 h when acetic acid (3 mL) was added, and the solvent removed. The residue was dissolved in dichloromethane (25 mL), washed with water, saturated $NaHCO_3$, and water and the chromatographically discrete product (0.37 g, 100%) was purified by flash chromatography to give the allylic alcohol **16**, $[\alpha]_D^{20}$ −193°.

Anal. Calc. for $C_{22}H_{20}O_7$: C, 66.7; H, 5.1. Found: C, 66.6; H, 5.2.

(2R)-(2,3/4,5)-2,3,4,5-Tetrahydroxy-2,3-O-isopropylidenecyclohexanone (**18**). — A mixture of mercury(II) acetate (3.5 g), in 5:2 1,4-dioxane–water (330 mL) containing acetic acid (3 mL), and 6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranose (**17**) (2.4 g) was kept for 10 min at 20°. Potassium chloride (2 g) was added and the solution heated under reflux for 5 min. Hydrogen sulphide was passed into the solution, the solids were removed, and the filtrate was taken to dryness to give a residue which was extracted with ethyl acetate. The extracted product was fractionated by column chromatography to give the cyclohexanone **18** (0.81 g, 40%), m.p. 113–115° (dichloromethane), $[\alpha]_D^{20}$ −40°.

Anal. Calc. for $C_9H_{14}O_5$: C, 53.5; H, 7.0. Found: C, 53.5; H, 7.1.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-5-hydroxy-4-toluene-p-*sulphonyloxycyclohexanone ethylene dithioacetal* (**19**). — The ketone **8** (1 g) and dichloromethane (100 mL) containing ethane-1,2-dithiol (5 mL) and boron trifluoride etherate (1 mL) were stirred until dissolution was complete (5 min). Dichloromethane (100 mL) was added and the solution washed with aqueous NaOH (5%), and water and dried. Removal of the solvent gave a crystalline residue which on recrystallisation from acetone–ethanol gave the dithioacetal **19** (1.12 g, 95%), m.p. 177°, $[\alpha]_D^{20}$ +8°.

Anal. Calc. for $C_{29}H_{28}O_8S_3 \cdot H_2O$: C, 56.4; H, 4.9; S, 15.6. Found: C, 56.7; H, 5.0; S, 16.1.

(2S)-(2,4,5/3)-5-Acetoxy-2,3-dibenzoyloxy-4-toluene-p-*sulphonyloxycyclohexanone ethylene dithioacetal* (**20**). — Acetylation of the alcohol **19** (2 g) was effected with acetic anhydride (2 mL) and pyridine (10 mL) containing 4-(dimethylamino)pyridine (0.1 mL). The acetate **20** (2.04 g, 95%), recrystallised from acetone–ethanol, had m.p. 208–209°, $[\alpha]_D^{20}$ +19°.

Anal. Calc. for $C_{31}H_{30}O_9S$: C, 57.9; H, 4.7; S, 15.0. Found: C, 58.0; H, 5.1; S, 15.0.

(2S)-(2/3)-2,3-Dibenzoyloxy-4-bromocyclohex-5-enone ethylene dithioacetal (**26**). — A mixture of the alcohol **19** (0.5 g), 2,4,5-tribromoimidazole (1.0 g, 3.9 mol equiv.), and triphenylphosphine (1.7 g, 7.8 mol equiv.) was stirred in refluxing toluene (25 mL) for 50 min. After being cooled, the mixture was stirred with saturated aqueous $NaHCO_3$ for 10 min, and iodine was added in portions until colour persisted in the organic phase. Stirring was continued for 10 min and aqueous $Na_2S_2O_3$ was added until the colour was removed. The organic phase was washed and dried, and removal of the solvent and fractionation of the residue on a column of silica gel gave the epimeric bromides **26**, m.p. 145–146°, in equal proportions; ^{1}H-n.m.r.: δ 3.30 (s, 4 H, CH_2), 4.80 (dt, 0.5 H, $J_{3,4a'}$ 7.5, $J_{4,5} = J_{4,6}$ 1.7 Hz, H-4*a'*), 5.14 (dt, 0.5 H, $J_{3,4e'} = J_{4,5}$ 4.3, $J_{4,6}$ 0.8 Hz, H-4*e'*), 5.50 (dd, 0.5 H, $J_{2,3}$ 10.0 Hz, H-3), 5.6 (m, 3.5 H, H-2,3,5,6), and 7.1–8.1 (m, 10 H, Bz) [3-bromocyclohexene gave: δ 4.7–4.9 (m, 1 H, H-3) and 5.6–6.0 (m, 2 H, H-1,2)]: ^{13}C-n.m.r.: δ 41.0, 41.2 (SCH_2), 46.0, 47.2 (C-4), 67.4, 68.3 (C-1), 71.4, 73.5, 75.5, 75.9 (C-2,3), 123.9, 125.3 (C-6), and ~133 (C-5) [3-bromocyclohexene gave: δ 18.6, 24.7, 32.8 (C-4,5,6), 48.8 (C-3), 129.0 (C-1), and 131.0 (C-2)].

Anal. Calc. for $C_{22}H_{19}BrO_4S_2$: C, 53.8; H, 3.9; Br, 16.3; S, 13.0. Found: C, 53.5; H, 4.1; Br, 16.3; S, 13.0.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-5-formyloxy-4-toluene-p-*sulphonyloxycyclohexanone ethylene dithioacetal* (**21**). — A mixture of the alcohol **19** (0.5 g) and a solution of *N*-bromosuccinimide (0.59 g) and triphenyl phosphine (0.87 g) in *N,N*-dimethylformamide (4 mL) was kept at 20° for 48 h. The solvent was removed, and the residue dissolved in chloroform (50 mL) and washed with dilute aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, and water. The residue obtained on removal of the solvent was fractionated on a column of silica gel to give the formate **21** (0.33 g, 63%) which was recrystallised from acetone–ethanol; m.p. 186–187°, $[\alpha]_D^{20}$ +20°.

Anal. Calc. for $C_{30}H_{28}O_9S_3$: C, 57.3; H, 4.5; S, 15.3. Found: C, 57.2; H, 4.6; S, 15.0.

6-Benzoyloxy-2,3-dihydro-1,4-benzodithiin (**25**). — A mixture of the alcohol **19** (1.5 g), *N*-bromosuccinimide (1.78 g), triphenylphosphine (2.62 g), and *N,N*-dimethylformamide (30 mL) was heated at 105° for 32 h. The solvent was removed, and the residue dissolved in chloroform (50 mL) and washed with aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and water. Removal of the solvent gave a residue which on fractionation on a column of silica gel gave the dithiin **25** (0.70 g, 97%) which, after recrystallisation from ethanol, had m.p. 109–110°; λ_{max}^{MeOH} 257 nm, ε 1.75×10^4; ^{1}H-n.m.r.: δ 3.23 (s, 4 H, CH_2), 6.86 (dd, 1 H, $J_{5,7}$ 2.4, $J_{5,8}$ 8.4 Hz, H-7), 7.05 (d, 1 H, H-5), 7.18 (d, 1 H, H-8), and 7.3–8.2, (m, 5 H, Bz); ^{13}C-n.m.r.: δ 29.1, 29.3 (C-2, C-3), 118.9 (C-5), 121.8 (C-7), 128.6, 130.1 (C-2′,6′ and C-3′,5′), 128.8, 129.3 (C-9, C-1′), 129.6 (C-8), 132.8 (C-10), 133.6 (C-4′), 148.2 (C-6), and 165.0 (C=O).

Anal. Calc. for $C_{15}H_{12}O_2S_2$: C, 62.5; H, 4.2; S, 22.2. Found: C, 62.5; H, 4.2; S, 22.0.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-5-methanesulphonyloxy-4-toluene-p-*sulphonyloxycyclohexanone ethylene dithioacetal* (**22**). — The alcohol **19** (1.0 g) was mesylated with methanesulphonyl chloride (1.5 mL) in pyridine (6 mL) containing 4-(dimethylamino)pyridine (0.1 mL).-Recrystallisation of the product from acetone–ethanol gave **22** (1.02 g, 90%) m.p. 209–209.5°, $[\alpha]_D^{20}$ +27°.

Anal. Calc. for $C_{30}H_{30}O_{10}S_4$: C, 53.1; H, 4.5; S, 18.9. Found: C, 53.2; H, 4.7; S, 19.1.

(2S)-(2,4,5/3)-2,3-Dibenzoyloxy-4-toluene-p-*sulphonyloxy-5-(trifluoromethanesulphonyloxy)cyclohexanone ethylene dithioacetal* (**23**). — The alcohol **19** (3 g) was esterified as was the analogue **11**, and the triflate **23**, obtained after recrystallisation from ethyl acetate–ethanol (2.98 g, 81%), had m.p. 167.5–168°, $[\alpha]_D^{20}$ +30°.

Anal. Calc. for $C_{30}H_{27}F_3O_{10}S_4$: C, 49.2; H, 3.7; S, 17.5. Found: C, 49.2; H, 3.8; S, 17.5.

Reaction of the triflate **23** *in acetone with sodium iodide and zinc.* — A mixture of the ester **23** (0.2 g), sodium iodide (0.5 g), zinc (1 g) and acetone (5 mL) was heated under reflux for 0.3 h to give a single product (t.l.c.). After filtration, the solvent was removed, and the residue dissolved in chloroform (10 mL) and washed with water. Evaporation of the solvent gave a syrup which contained sev-

eral components (t.l.c.), the original being isolated (0.02 g, 22%) by preparative t.l.c. The ^{1}H-n.m.r. spectrum indicated that this unstable compound was the desired alkene **24**.

(2S)-(2,5/3,4)-4,5-Diacetoxy-2,3-dibenzoyloxycyclohexanone ethylene dithioacetal (**28**). — Compound **19** (0.5 g) and sodium fluoride (0.5 g) were heated under reflux in *N,N*-dimethylformamide (25 mL) for 7 h and the solvent was removed. Water was added to give the crystalline mixed diols **27** and **29** which were separated by preparative t.l.c. The less mobile product **27** (0.23 g, 62%), on acetylation, gave the vicinal diacetate **28** (0.21 g, 77%), m.p. 188.5–190° (ethanol–acetone), $[\alpha]_D^{20}$ −7°.

Anal. Calc. for $C_{26}H_{26}O_8S_2$: C, 58.9; H, 4.9; S, 12.1. Found: C, 59.0; H, 5.1; S, 12.2.

(2S)-(2,5/3,4)-3,5-Diacetoxy-2,4-dibenzoyloxycyclohexanone ethylene dithioacetal (**30**). — Acetylation of the minor alcohol **29** (0.11 g, 30%) gave the diacetate **30** (0.11 g, 83%), m.p. 164–165° (ethanol), $[\alpha]_D^{26}$ −15°.

Anal. Calc. for $C_{26}H_{26}O_8S_2$: C, 58.9; H, 4.9; S, 12.1. Found: C, 58.7; H, 4.9; S, 12.1.

(2S)-(2,4,5/3)-and (2S)-(2/3,4,5)-4,5-Anhydro-2,3-dibenzoyloxy-4,5-dihydroxycyclohexanone ethylene dithioacetal (**31**). — The vicinal diol **27** (0.12 g) and triphenylphosphine (0.22 g) were stirred in 1,4-dioxane (2 mL), diethyl azodicarboxylate (0.15 g) was added, and the mixture heated under reflux for 3–5 h. The solvent was removed and preparative t.l.c. gave the mixed epoxides **31** (ratio 4:1) (0.095 g, 80%), m.p. 151.5–153.5° (methanol), $[\alpha]_D^{26}$ −180°.

Anal. Calc. for $C_{22}H_{20}O_5S_2$: C, 61.7; H, 4.7; S, 15.0. Found: C, 61.9; H, 4.9; S, 14.8.

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