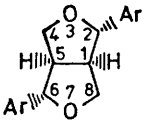
Synthesis and N.m.r. Spectra of 2,6- and 2,4-Diaryl-3,7-dioxabicyclo-[3.3.0]octanes

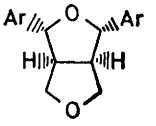
By **Andrew Pelter,* Robert S. Ward, Derrick J. Watson,** and **Ibiba R. Jack,** Chemistry Department, University College of Swansea, Singleton Park, Swansea SA2 8PP

A series of isomeric 2,6- and 2,4-diaryl-3,7-dioxabicyclo[3.3.0]octanes have been prepared *via* the corresponding *threo,* and *erythro*-dioxo-diesters. Comparison of their ^{1}H and ^{13}C n.m.r. spectra reveals small differences in chemical shifts and coupling constants which could be diagnostic in assigning structures to such compounds. The structure of 4-hydroxysesamin has been confirmed by direct correlation with sesamin.

Some lignans of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]-octane series such as pinoresinol (1a) and eudesmin (1b) have been thoroughly characterised.[1-4] It is however difficult without extensive degradation studies to establish whether in any particular compound the aryl groups are attached at the 2,6- or the 2,4-positions. The problem, as with lignans and flavonolignans containing a 1,4-benzodioxan system,[5,6] is that the two oxygen atoms



(1)



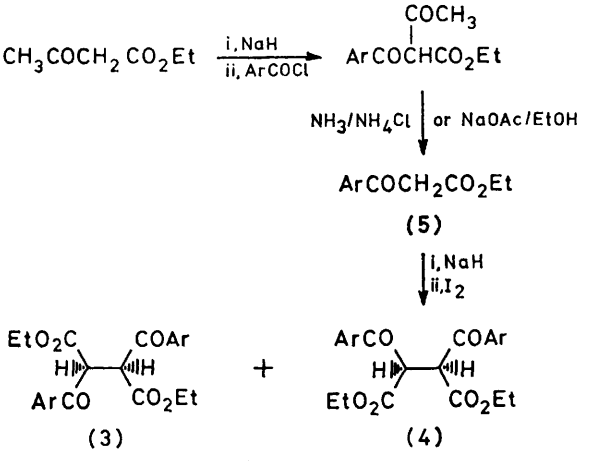
(2)

a; Ar = 4-hydroxy-3-methoxyphenyl
b; Ar = 3,4-dimethoxyphenyl
c; Ar = 4-benzyloxy-3-methoxyphenyl
d; Ar = 3,4-methylenedioxyphenyl
e; Ar = phenyl

of the central bicyclic nucleus insulate the two sides of the molecule from each other with the result that spectroscopic data such as ^{1}H and ^{13}C n.m.r. and mass spectra can as readily be interpreted on the basis of either structure (1) or (2).

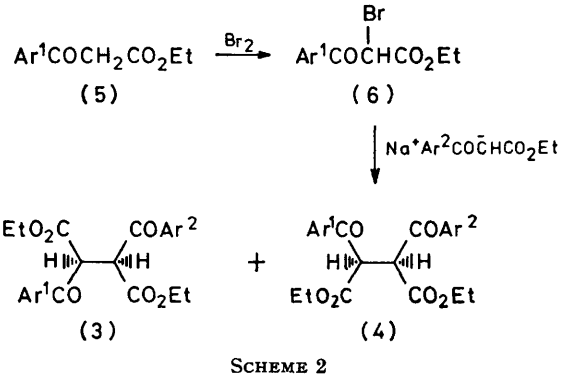
Although it is generally believed that most of the naturally occurring lignans of this type belong to the 2,6-diaryl series,[7] some natural products having interesting physiological properties have recently been assigned structures corresponding to the 2,4-diaryl series.[8,9] One of these claims has since been revised [10] and the other has been seriously questioned,[11] but nevertheless a degree of uncertainty remains.

In order to compare the properties of the 2,6- and the 2,4-diaryl compounds, and in the hope of being able to establish criteria which could be used to distinguish between them, we have prepared isomeric compounds of both types. One potentially very useful method for the synthesis of symmetrically substituted diaryl-3,7-dioxabicyclo[3.3.0]octanes is *via* the dioxo-diesters (3) and (4), which can be produced by coupling together two molecules of a β-oxo-ester (5), as shown in Scheme 1.[12,13] This procedure, which is based on the original work of Knorr,[14] involves the addition of iodine to a suspension of the sodium salt of the β-oxo-ester. A modification which we have also utilised is shown in Scheme 2. This involves the reaction of an α-bromo-β-oxo-ester with the sodium salt of a β-oxo-ester, and has the added attraction that it could in principle be applied to the synthesis of unsymmetrically substituted diaryl-3,7-dioxabicyclo-[3.3.0]octanes.



Scheme 1

Synthesis of Dioxo-diesters.—The β-oxo-ester (5d) was prepared by treating the acid chloride derived from piperonylic acid with the sodium salt of ethyl acetoacetate. This resulted in the sodium salt of the acylated β-oxo-ester, which on warming with aqueous ammonia [15] afforded ethyl piperonoylacetate (5d) as an oil which crystallised. Alternatively the deacetylation could be carried out by refluxing the acylated β-oxo-ester with a catalytic amount of sodium acetate in ethanol: [12] the ethyl piperonoylacetate (5d) crystallised out on cooling.



Scheme 2

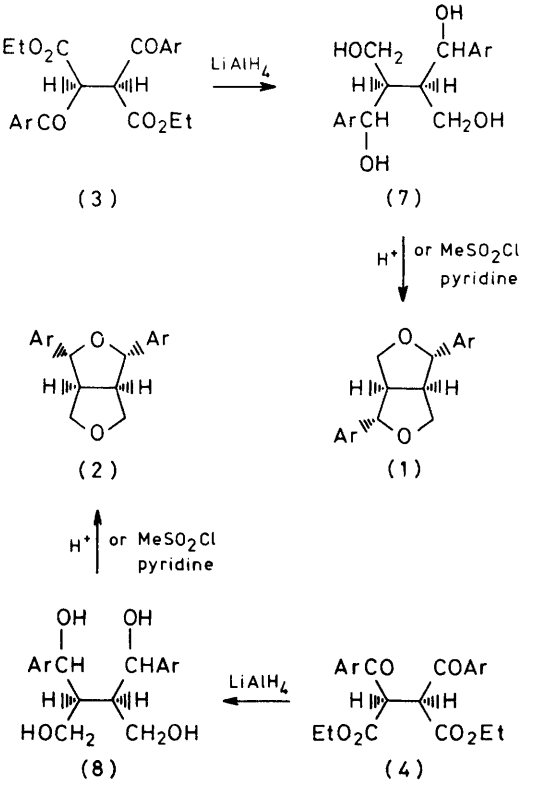
Coupling of the β-oxo-ester (5d) according to Knorr's procedure afforded a white crystalline solid which was shown by n.m.r. and h.p.l.c. to consist of a 2 : 1 mixture of the *threo*- and *erythro*-dioxo-diesters (3d) and (4d). The two isomers were separated by fractional crystallisation from ether, giving the *erythro*-isomer (4d) as a white crystalline solid, m.p. 158—160°. Evaporation of the mother liquor gave the *threo*-isomer (3d) as an oil. Bromination of ethyl piperonoylacetate (5d) using bromine in chloroform[16] yielded ethyl bromo(piperonoyl)acetate (6d), which when added to a suspension of the sodium salt of ethyl piperonoylacetate in ether gave a 2 : 1 mixture of the *threo*- and *erythro*-dioxo-diesters (3d) and (4d). Fractional crystallisation gave the pure *erythro*-isomer (4d), while evaporation of the mother liquors gave the pure *threo*-isomer (3d) as an oil which crystallised, m.p. 93—95°.

Similarly by using Knorr's method and the α-bromo-oxo-ester method the *threo*- and *erythro*-isomers of diethyl 2,3-dibenzoylbutane-1,4-dioate (3e) and (4e) were obtained as white crystalline solids, m.p.s 74—78° and 125—127°,[17,18] respectively.

Application of either Knorr's method or the α-bromo-oxo-ester method to ethyl veratroylacetate (5b) afforded a mixture of the two isomeric dioxo-diesters (3b) and (4b) from which the pure *erythro*-isomer (4b), m.p. 171—172° could be separated by fractional crystallisation. However in this case evaporation of the mother liquors did not give the pure *threo*-isomer. Instead a mixture of the two isomers was always obtained, suggesting that an equilibrium mixture exists from which the *erythro*-isomer (4d) is deposited preferentially on crystallisation. When the *erythro*-isomer was treated with ethanolic sodium ethoxide then acidified it was converted into a mixture containing approximately 50% of the *threo*-isomer (3b). The proportion of the *threo*-isomer in this mixture could be increased by washing with ether, when the feebly soluble *erythro*-isomer was left behind as a solid and the more soluble *threo*-isomer dissolved. In this way a mixture containing approximately 70% of the *threo*-form could be obtained, although it reverted to its original composition in solution.

Applying the same procedure to ethyl 4-benzyloxy-3-methoxybenzoylacetate (5c) gave a mixture of the two isomeric dioxo-diesters (3c) and (4c) from which the pure *erythro*-isomer (4c), m.p. 176—177° could be isolated by fractional crystallisation. Once again the pure *threo*-isomer could not be obtained. Debenzylation of a mixture of (3c) and (4c) gave a mixture of the corresponding diphenols (3a) and (4a).

When an attempt was made to carry out a mixed coupling reaction of ethyl α-bromo-4-benzyloxy-3-methoxybenzoylacetate (6c) with the sodium salt of ethyl veratroylacetate (5b) a white crystalline solid was obtained which was shown by t.l.c. and h.p.l.c. to contain the symmetrical products (3b/4b) and (3c/4c) in addition to the required unsymmetrical products (3/4; Ar^1 = veratryl, Ar^2 = 4-benzyloxy-3-methoxyphenyl). It seems therefore that a halogen transfer reaction, leading to (6b) and (5c), must compete with the coupling reaction. Despite many attempts involving variations of the solvent, cation, time, temperature, and mode of addition of the reagents, in no case was a mixture containing more than 42% of the unsymmetrical product obtained. At this concentration it was not possible to isolate the pure unsymmetrical product from the mixture of dioxo-diesters by either fractional crystallisation or chromatography.



SCHEME 3

Synthesis of Diaryl-3,7-dioxabicyclo[3.3.0]*octanes.*—Reduction of the dioxo-diesters (3e) and (4e) gave two different crystalline tetraols, which could be cyclised by treatment with potassium hydrogen sulphate at 150 °C to give the 2,6- and 2,4-diphenyl isomers (1e) and (2e), respectively.[17,18] Furthermore the structure of the 2,4-diphenyl compound (2e) was confirmed by *X*-ray analysis,[18] thereby also confirming the structure of the *erythro*-isomer (4e) of the dioxo-diester.

Similarly reduction of the *erythro*-isomer (4c) gave a tetraol which on treatment with methanesulphonyl chloride and pyridine gave (2c). The 2,6-isomer (1c) for comparison was conveniently prepared by benzylation of pinoresinol (1a).[19]

Reduction of the *erythro*-isomer (4d) gave a tetraol which was cyclised as above using methanesulphonyl chloride and pyridine. However in this case analysis of the product mixture indicated that it contained both the 2,6- and 2,4-diaryl isomers (1d) and (2d) in a 2 : 1 ratio. In contrast, reduction of the *threo*-isomer (3d) followed

by cyclisation using methanolic HCl gave only (±)-sesamin (1d). Clearly some isomerisation of the *erythro*- to the *threo*-isomer takes place during the reduction step. Indeed when a mixture of both isomers was reduced over a longer period of time, cyclisation yielded only (±)-sesamin (1d). It therefore seems that this is not an ideal or unambiguous method for preparing such compounds since in this case some base-catalysed interconversion of the two series takes place during the reduction.

Comparison of ^{1}H *and* ^{13}C *N.m.r. Spectra.*—The ^{1}H and ^{13}C n.m.r. spectra (Tables 1 and 2) of the pairs of isomers are as expected very similar. There are however small significant and reproducible differences readily apparent which in the case of simple diaryl-3,7-dioxabicyclo[3.3.0]octanes would allow the compounds to be assigned to one or other of the two isomeric series. First, all of the signals in the ^{1}H n.m.r. spectra of the 2,4-diaryl isomers occur at higher field (0.24 p.p.m. on average) than in those of the corresponding 2,6-isomers. Secondly, two of the methylene hydrogens (the two giving rise to the higher-field signal) appear as a simple doublet in the 2,4-series but as a double doublet in the 2,6-series. Thus the coupling between these protons and H-1 and H-5 is zero in the 2,4-series whereas this coupling constant is *ca.* 7 Hz in the 2,6-series. Thirdly, the coupling constants of the benzylic hydrogens to H-1 and H-5 are larger in the 2,4-series.

TABLE 1

Comparison of ^{1}H n.m.r. spectra [a,b]

Protons	(1e)	Protons	(2e)
1/5	3.04m	1/5	2.87m
2/6	4.78d (4)	2/4	4.54d (8)
4(e)/8(e)	4.23dd (9,7)	6(e)/8(e)	3.98d (8)
4(a)/8(a)	3.89dd (9,3)	6(a)/8(a)	3.50dd (8,5)
	(1c)		(2c)
1/5	3.12m	1/5	2.93m
2/6	4.76d (4)	2/4	4.52d (7)
4(e)/8(e)	4.24dd (9,7)	6(e)/8(e)	4.00d (9)
4(a)/8(a)	3.7—3.9m	6(a)/8(a)	3.57dd (9,5)
	(1d)		(2d)
1/5	3.04m	1/5	2.87m
2/6	4.70d (4)	2/4	4.49d(7)
4(e)/8(e)	4.22dd (7,9)	6(e)/8(e)	4.00d (10)
4(a)/8(a)	3.85dd (4,9)	6(a)/8(a)	3.56dd (5,10)

[a] All spectra run in $CDCl_3$ solution. [b] δ Values; coupling constants (in parentheses) in Hz.

TABLE 2

Comparison of ^{13}C n.m.r. spectra [a]

Carbon atoms	(1e)	Carbon atoms	(2e)	Δ[(2) − (1)] (p.p.m.)
1/5	54.38	1/5	55.44	+1.06
2/6	85.79	2/4	87.15	+1.36
4/8	71.92	6/8	71.53	−0.39
1′	141.23	1′	141.20	
2′/6′	128.54	2′/6′	128.58	
3′/5′	125.83	3′/5′	126.17	
4′	127.59	4′	127.87	
	(1c)		(2c)	
1/5	54.15	1/5	55.06	+0.91
2/6	85.76	2/4	86.95	+1.19
4/8	71.72	6/8	71.57	−0.15
1′	134.25	1′	134.24	
2′/5′	109.96, 114.10	2′/5′	110.27, 114.19	
3′/4′	147.82, 149.95	3′/4′	148.02, 149.92	
6′	118.24	6′	118.62	
	(1d)		(2d)	
1/5	54.32	1/5	55.28	+0.96
2/6	85.81	2/5	87.01	+1.20
4/8	71.71	6/8	71.48	−0.23
1′	135.09	1′	134.95	
2′/5′	106.51, 108.29	2′/5′	106.68, 108.17	
3′/4′	147.34, 147.99	3′/4′	147.69, 148.13	
6′	119.36	6′	119.76	

[a] All values in p.p.m. downfield from Me_4Si.

Comparison of Mass Spectra.—The mass spectra of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes were first studied by Pelter [20] and by Duffield.[21] They defined basic fragmentation pathways and put forward structures for the major fragment ions. From a diagnostic point of view the ions (9) and (10) are probably of greatest significance since they correspond to 'vertical' and 'horizontal' cleavage of the molecule. The latter ion (10) and its analogue (11) would clearly be most useful

$ArCH{=}CHCH_2^+$	$ArCH{-}\overset{\cdot\cdot}{O}{-}CH_2$	$ArCH{-}\overset{\cdot\cdot}{O}{-}CHAr$
(9e) *m/z* 117	(10d) *m/z* 120	(11e) *m/z* 196
(9d) *m/z* 161	(10d) *m/z* 164	(11d) *m/z* 284
(9c) *m/z* 253	(10c) *m/z* 256	(11c) *m/z* 468

in distinguishing between the two series. However as can be seen from Table 3 neither of these fragments is present in the spectra of the diphenyl [(1e) and (2e)] or the bis(4-benzyloxy-3-methoxyphenyl) [(1c) and (2c)] derivatives, while (10d) is present in the spectra of both of the bis-(3,4-methylenedioxyphenyl) derivatives (1d) and (2d). Hence in the mass spectra of the simple diaryl-3,7-dioxabicyclo[3.3.0]octanes these ions do not afford a means of distinguishing between the two series. Nevertheless significant differences do exist between the spectra of the isomers. Thus for example the intensity of the $(M - ArCHO)^{+\cdot}$ peak is considerably higher in the 2,4-series.

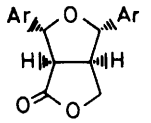
The Structure of 4-*Hydroxysesamin.*—The preparation of 2,4- and 2,6-diaryl isomers of 3,7-dioxabicyclo[3.3.0]-octanes is of particular significance in view of the recent uncertainty surrounding some compounds of this type. Thus, structure (12) was initially assigned to a germination inhibitor isolated from *Aegilops ovata*.[8] This compound was later synthesised by phenolic oxidation of a mixture of coniferyl alcohol and ferulic acid and its structure revised to (13).[10] 4-Hydroxysesamin and its lactone were assigned structures (14) and (15) on the

TABLE 3

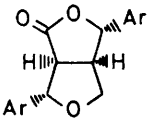
Comparison of mass spectra

m/z	(1e)	(2e)	*m/z*	(1d)	(2d)	*m/z*	(1c)	(2c)	
266	10	34	354	42	25	538	17	88	$M^{+\cdot}$
235	11	15				492	8		
175		12				449	10		
						448	30	21	
						415		14	
						305		20	
						304		100	
161			205		8	297			
160	6	58	204	9	20	296		45	$(M - ArCHO)^{+}$
159	24	14	203	23	14	295			
						271	23		
134	3	13	178	10		270			$ArCH{=}CHCH_2OH^{+\cdot}$
133		36	177	7	7	269			$ArCH{=}\overset{+}{C}HCHOH$
132	3	26	176		16	268			$ArCH{=}CHCHO^{+\cdot}$
131	12	51	175	6	8	267			$ArCH{=}\overset{+}{C}HCO$ and $(M - ArCO - CH_2O)^{+}$
130	5	87	174		16	266			$(M - ArCHO - CH_2O)^{+\cdot}$
129	12	74	173			265			$(M - ArCHOH - CH_2O)^{+\cdot}$
128	4	24	172			264			$(M - ArCH_2OH - CH_2O)^{+\cdot}$
						258	25		
						257	100		
120			164	6	4	256			$ArCH{-}O{-}\overset{+\cdot}{C}H_2$
118	6	19	162	9	7	254			
117	44	100	161	40	22	253			$ArCH{=}CHCH_2^{+}$
116	7	21	160	6	6	252			
115	14	45	159			251			
107			151	8	20	243			$ArC\overset{+}{H}OH$
106	15		150	39	27	242			$ArCHO^{+\cdot}$
105	100	78	149	100	100	241	8	16	$ArCO^{+}$
104	11	83	148	20	25	240			$ArCH{=}CH^{+\cdot}$

basis of a comparison of their spectral properties with those of other sesamin derivatives.[11] At that time lack of material precluded direct chemical correlation with sesamin. However, two other compounds named aptosimol and aptosimone which seem from their physical and spectral data to be identical with (14) and (15) were assigned the 2,4-diaryl structures (16) and (17), respectively.[9]

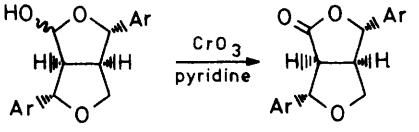


(12)



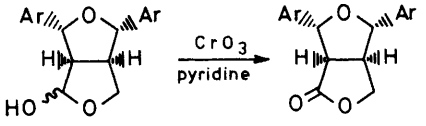
(13)

Ar = 4-hydroxy-3-methoxyphenyl



(14) (15)

Ar = 3,4-methylenedioxyphenyl



(16) (17)

The ^{1}H n.m.r. spectra (Table 4) of aptosimol and 4-hydroxysesamin are virtually identical and show some of the features characteristic of the 2,6-diaryl series. Thus, the methylene hydrogens both give rise to double doublets, as in the case of sesamin itself for example. Furthermore, both compounds show a peak at *m/z* 164 in their mass spectra, but neither shows a peak at *m/z* 284. From this evidence it seems that they are probably the same compound, belonging to the 2,6-diaryl series. The two derived lactones also show almost identical

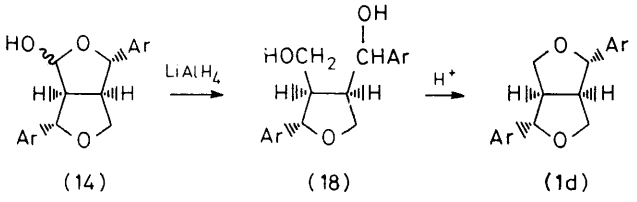
TABLE 4

^{1}H N.m.r. spectra of 4-hydroxysesamin and aptosimol derivatives [a]

	4-Hydroxysesamin (14)	Aptosimol
H-1	6.84m	7.3—6.7m
H-5	7.11m	
H-2	5.11d (6)	5.11d (6.5)
H-6	5.23d (6)	5.22d (6.5)
H-4	4.50m	4.45m
H-8(a)	6.05dd (2,9)	5.9—6.15dd (2.3,9)
H-8(e)	5.82dd (6,9)	5.65—5.9dd (5.5,9)
	Acetate	Acetate
H-1	6.85m	7.3—6.65m
H-5	7.08m	
H-2	5.01d (6)	4.92d (6)
H-6	5.19d (6)	5.10d (6.8)
H-4	3.69br,s	3.62s
H-8(a)	6.05m	5.85—6.1dd (2.5,9)
H-8(e)	5.80dd (6,10)	5.5—5.85dd (5.5,9)
	Lactone (15)	Lactone (17)
H-1	6.77m	6.45—7.0m
H-5	6.58dd (4,9)	
H-2	4.75d (3)	4.72d (3.5)
H-6	4.73d (4)	4.71d (3.5)
H-8(a)	6.02dd (4,10)	5.85—6.15dd (4.5,9)
H-8(e)	5.74dd (6,10)	5.55—6.85dd (6.5,9)

[a] δ Values; coupling constants (in parentheses) in Hz.

n.m.r. and mass spectra. However in this case the problems of structural assignment are complicated by the fact that both compounds show peaks at *m/z* 164 and 284. The structures of these compounds could not therefore be defined unequivocally purely on the basis of their spectral data. We have however now obtained definite confirmation that 4-hydroxysesamin (14) belongs to the 2,6- series by directly converting it into sesamin as shown in Scheme 4.



(14) (18) (1d)

SCHEME 4

EXPERIMENTAL

I.r. and u.v. spectra were recorded on Pye Unicam SP1050 and Perkin-Elmer 402 spectrometers, respectively. N.m.r. (^1H and ^{13}C) spectra were recorded on Varian HA100 and XL100 instruments using tetramethylsilane as internal standard. Mass spectra were obtained on an A.E.I. MS9 double-focusing instrument at 250 °C and 70 eV.

3,4-*Dimethoxybenzoyl Chloride*.—Thionyl chloride was purified by distillation from powdered zinc. 3,4-Dimethoxybenzoic acid (5 g) was dissolved in pure thionyl chloride (15 ml) and refluxed for 3 h. Excess of thionyl chloride was then removed by azeotroping with benzene. The residue was dissolved in ether (40 ml) and used immediately.

4-*Benzyloxy*-3-*methoxybenzoyl Chloride*.—This was prepared as above from 4-benzyloxy-3-methoxybenzoic acid.

3,4-*Methylenedioxybenzoyl Chloride*.—This was prepared as above from piperonylic acid (7 g) and crystallised by treatment with light petroleum (b.p. 40—60°) to give a white solid (6.2 g, 80%); m.p. 79°; $\nu_{max.}$ (KBr) 3 120—2 930, 1 770—1 730, and 1 610 cm^{-1}; $\delta(CDCl_3)$ 6.76—7.74 (m, arom.) and 6.04 (s, OCH_2O); *m/z* 186 (5%), 184 (20), 149 (100), and 121 (22).

Ethyl 2-(3,4-*Dimethoxybenzoyl*)*acetoacetate*.—Sodium hydride (3.4 g; 50% suspension) was washed with dry pentane (3 × 15 ml) and then suspended in diethyl ether (35 ml) under nitrogen. A solution of ethyl acetoacetate (10.6 g) in diethyl ether (35 ml) was added and the mixture stirred under reflux for 1 h. This produced a suspension of ethyl sodioacetoacetate, to which was added a solution of 3,4-dimethoxybenzoyl chloride (prepared as described above from 5 g of 3,4-dimethoxybenzoic acid). The mixture was refluxed for a further 5 h and then stirred overnight. The resulting white solid was collected and dissolved in water (100 ml). Conc. hydrochloric acid was added (to pH 1) and the mixture set aside for 30 min. During this time a yellow oil separated which was collected and dried under vacuum. The *oil* crystallised slowly and was recrystallised from ethanol (yield 6.5 g, 80%); m.p. 80—81.5° (Found: C, 61.4; H, 5.9. $C_{15}H_{18}O_6$ requires C, 61.2; H, 6.1%); $\nu_{max.}$ (KBr) 3 020—2 860, 1 725, 1 710, 1 680, and 1 595 cm^{-1}; $\delta(CDCl_3)$ 5.34 (s, H-2), 2.30 (s, $COCH_3$), 4.20 (q, *J* 7 Hz) and 1.23 (t, *J* 7 Hz) (Et), 3.88 (s, OMe), and 6.8—7.5 (m, arom.).

Ethyl 2-(4-*Benzyloxy*-3-*methoxybenzoyl*)*acetoacetate*.—This was prepared as above from ethyl acetoacetate (10.6 g) and 4-benzyloxy-3-methoxybenzoyl chloride (from 7 g of 4-benzyloxy-3-methoxybenzoic acid); yield 8.4 g (84%); m.p. 105—106 °C (Found: C, 68.6; H, 5.8. $C_{21}H_{22}O_6$ requires C, 68.1; H, 6.0%); $\nu_{max.}$ (KBr) 3 080—2 880, 1 740, 1 720, 1 675, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.34 (s, H-2), 2.30 (s, $COCH_3$), 4.20 (q, *J* 7 Hz) and 1.23 (t, *J* 7 Hz) (Et), 5.14 (s, OCH_2Ph), 3.84 (s, OMe), and 6.8—7.5 (m, arom.).

Ethyl 2-(3,4-*Methylenedioxybenzoyl*)*acetoacetate*.—This was prepared as above from ethyl acetoacetate (7 g) and 3,4-methylenedioxybenzoyl chloride (5 g) and obtained as a brown *oil* (5.9 g, 78%) (Found: C, 60.2; H, 5.3. $C_{14}H_{14}O_6$ requires C, 60.4; H, 5.0%); $\nu_{max.}$ (film) 3 000—2 900, 1 750, 1 720, 1 670, and 1 610 cm^{-1}; $\delta(CDCl_3)$ 6.78—7.75 (m, arom.) 5.98 (s, OCH_2O), 4.08 (q, *J* 7 Hz) and 101 (t, *J* 7 Hz) (Et), 2.30 (s, H-2), and 1.94 (s, $COCH_3$); *m/z* 278 (7%), 149 (100), and 121 (12).

Ethyl (3,4-*Dimethoxybenzoyl*)*acetate* (5b).—Ethyl 2-(3,4-dimethoxybenzoyl)acetoacetate (6 g) was dissolved in ethanol (30 ml; 95%) together with sodium acetate (0.1 g); the solution was refluxed for 6 h, then slowly cooled to 0 °C. The white *crystals* which separated were filtered off and recrystallised from ethanol (yield 4.3 g, 83%); m.p. 34.5—35.5 °C (Found: C, 61.3; H, 6.6. $C_{13}H_{16}O_5$ requires C, 61.9; H, 6.4%); $\nu_{max.}$ (KBr) 3 090—2 850, 1 750, 1 685, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 3.84 (s, H-2), 4.14 (q, *J* 7 Hz) and 1.22 (t, *J* 7 Hz) (Et), 3.88 (s) and 3.86 (s) (OMe), and 6.8—7.5 (m, arom.); *m/z* 252.0998 ($M^{+\cdot}$).

Ethyl (4-*Benzyloxy*-3-*methoxybenzoyl*)*acetate* (5c).—This was prepared as above from ethyl 2-(4-benzyloxy-3-methoxybenzoyl)acetoacetate (7.4 g); yield 6.5 g (68%); m.p. 68—69 °C (Found: C, 69.3; H, 6.35. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.15%); $\nu_{max.}$ (KBr) 3 080—2 880, 1 745, 1 670, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 3.84 (s, H-2), 4.14 (q, *J* 7 Hz) and 1.20 (t, *J* 7 Hz) (Et), 5.14 (s, OCH_2Ph), 3.84 (s, OMe), and 6.8—7.5 (m, arom.).

Ethyl (3,4-*Methylenedioxybenzoyl*)*acetate* (5d).—This was prepared as above from ethyl 2-(3,4-methylenedioxybenzoyl)acetoacetate (3.0 g); yield 1.8 g (72%); m.p. 39—40° (Found: C, 61.2; H, 4.8. $C_{12}H_{12}O_5$ requires C, 61.0; H, 5.1%); $\nu_{max.}$ (KBr) 2 980—2 885, 1 735, 1 670, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 6.7—7.5 (m, arom.), 5.91 (s, OCH_2O), 4.14 (q, *J* 7 Hz) and 1.24 (t, *J* 7 Hz) (Et), and 3.84 (s, H-2); *m/z* 236 (14%), 149 (100), and 121 (11). This compound was also prepared by dissolving ethyl 2-(3,4-methylenedioxybenzoyl)acetoacetate (3.6 g) in ethanol (12 ml) and adding the solution to aqueous ammonia (100 ml; 1%). The mixture was warmed to 50 °C for 45 min and then allowed to cool. The oil which separated was extracted with ether (3 × 50 ml), and the extracts were washed with water (2 × 40 ml), dried ($MgSO_4$), and evaporated to leave an oil which crystallised (2.1 g, 69%) (physical data as above).

Ethyl Bromo-(3,4-*dimethoxybenzoyl*)*acetate* (6b).—Ethyl (3,4-dimethoxybenzoyl)acetate (3 g) was dissolved in chloroform (15 ml) and a solution of bromine (2 g) in chloroform (15 ml) added dropwise with stirring. The mixture was then stirred for 15 min, and washed with saturated aqueous sodium hydrogencarbonate and water. The chloroform solution was dried (Na_2SO_4) and evaporated. The resulting brown oil was dissolved in benzene and treated with decolourising charcoal giving a pale yellow solution which was diluted with light petroleum (b.p. 40—60 °C) and

cooled to 0 °C. White *crystals* were obtained which were recrystallised from benzene; yield 3.0 g (78%); m.p. 66—67.5° (Found: C, 47.0; H, 4.7. $C_{13}H_{15}BrO_5$ requires C, 47.1; H, 4.5%); $\nu_{max.}$ (KBr) 3 070—2 850, 1 760, 1 670, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 5.64 (s, H-2), 4.23 (q, *J* 7 Hz) and 1.23 (t, *J* 7 Hz) (Et), 3.90 (s) and 3.87 (s) (OMe), and 6.8—7.5 (m, arom.).

Ethyl Bromo-(4-benzyloxy-3-methoxybenzoyl)acetate (6c).—This was prepared as above from ethyl (4-benzoyloxy-3-methoxybenzoyl)acetate (6.5 g); yield 6.5 g (80%); m.p. 72—73° (Found: C, 55.8; H, 5.1. $C_{19}H_{19}BrO_5$ requires C, 56.0; H, 4.7%); $\nu_{max.}$ (KBr) 3 080—2 870, 1 750, 1 680, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.77 (s, H-2), 4.18 (q, *J* 7 Hz) and 1.18 (t, *J* 7 Hz) (Et), 5.14 (s, OCH_2Ph), 3.82 (s, OMe), and 6.8—7.5 (m, arom.).

Ethyl Bromo-(3,4-methylenedioxybenzoyl)acetate (6d).—This was prepared as above from ethyl (3,4-methylenedioxybenzoyl)acetate (3.8 g) and obtained as a yellow *oil* (4.5 g, 90%) (Found: C, 45.8; H, 3.2. $C_{12}H_{11}BrO_5$ requires C, 45.7; H, 3.5%); $\nu_{max.}$ (film) 2 980—2 880, 1 750, 1 665, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 6.76—7.58 (m, arom), 6.00 (s, OCH_2O), 5.56 (s, H-2), 4.22 (q, *J* 7 Hz) and 1.24 (t, *J* 7 Hz) (Et), *m/z* 316 (3%), 314 (2), 149 (100), and 121 (11).

Ethyl Bromo(benzoyl)acetate (6e).—This was prepared as above from ethyl benzoylacetate (38.4 g) and obtained as a pale yellow oil (46.6 g, 86%); $\nu_{max.}$ (film) 3 030—2 860, 1 760, 1 690, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.90 (s, H-2), 4.29 (q, *J* 6 Hz) and 1.20 (t, *J* 6 Hz) (Et), and 7.5—8.2 (m, arom.).

Preparation of Dioxo-diesters by Iodine Coupling.

(a) erythro-*Diethyl* 2,3-*bis*-(3,4-*dimethoxybenzoyl*)-*butane*-1,4-*dioate* (4b).—A solution of ethyl (3,4-dimethoxybenzoyl)acetate (7.6 g) in ether (200 ml) was added to a suspension of sodium metal (0.7 g) in ether (50 ml) and the mixture was stirred for 2 days under nitrogen to produce the sodium salt. A solution of iodine (3.6 g) in ether (100 ml) was then added in small portions with vigorous stirring. The mixture was stirred for 4 h and was then filtered. The resulting solid was dissolved in dichloromethane and the solution washed with water and then dried ($MgSO_4$). Evaporation gave a yellow oil which crystallised on washing with ether; yield 5.5 g (72%); m.p. 171—172°; $\delta(CDCl_3)$ 5.51 (s) and 5.47 (s) (H-2/3), 4.12 (q, *J* 7 Hz), 3.95 (q, *J* 7 Hz), 1.17 (t, *J* 7 Hz), and 0.99 (t, *J* 7 Hz) (Et), 3.90 (s, OMe), and 6.8—8.0 (m, arom.). This mixture of isomers was recrystallised four times from ethanol to give the pure *erythro*-isomer (2.5 g, 33%); m.p. 171—172 °C; $\nu_{max.}$ (KBr) 3 080—2 850, 1 730, 1 660, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.51 (s, H-2/3), 3.95 (q, *J* 7 Hz) and 0.99 (t, *J* 7 Hz) (Et), 3.90 (s, OMe), and 6.8—8.0 (m, arom.).

(b) threo- *and* erythro-*Diethyl* 2,3-*Dibenzoylbutane*-1,4-*dioate* (3e) *and* (4e).—These were prepared as above from ethyl benzoylacetate (5.8 g). Evaporation gave a solid (4.3 g, 74%); m.p. 94—118°. Fractional crystallisation from ethanol gave the erythro-*isomer* (4e) (2.2 g, 38%), m.p. 125—127 °C (Found: C, 68.8; H, 5.9. $C_{22}H_{22}O_6$ requires C, 69.1; H, 5.8%); $\nu_{max.}$ (KBr) 3 030—2 900, 1 730, 1 680, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.54 (s, H-2/3), 3.88 (q, *J* 7 Hz) and 0.90 (t, *J* 7 Hz) (Et), and 7.5—8.1 (m, arom.); and the threo-*isomer* (3e) (1.8 g, 30%), m.p. 74—78 °C (Found: C, 69.0; H, 6.2%); $\nu_{max.}$ (KBr) 3 030—2 900, 1 730, 1 680, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 5.48 (s, H-2/3), 4.06 (q, *J* 7 Hz) and 1.08 (t, *J* 7 Hz) (Et), and 7.4—8.1 (m, arom.).

(c) threo *and* erythro-*Diethyl* 2,3-*Bis*-(3,4-*methylenedioxybenzoyl*)*butane*-1,4-*dioate* (3d) *and* (4d).—Ethyl (3,4-methylenedioxybenzoyl)acetate (1.42 g) in dichloromethane (40 ml) was added dropwise to a washed suspension of sodium hydride (0.23 g; 50% suspension) in ether (40 ml) under nitrogen, and then stirred for 2 h (until the sodium salt formed). A solution of iodine (2.8 g) in ether (80 ml) was added dropwise with stirring, and the mixture was stirred overnight, washed with water (2 × 50 ml), aqueous sodium thiosulphate (2 × 50 ml), then water again (2 × 40 ml) and dried ($MgSO_4$). Evaporation gave a semi-solid which on treatment with ether gave white crystals; these were recrystallised from ethanol to give the erythro-*isomer* (4d) (0.45 g, 32%); m.p. 158—160 °C (Found: C, 60.8; H, 4.8. $C_{24}H_{22}O_{10}$ requires C, 61.3; H, 4.7%); $\nu_{max.}$ (KBr) 2 990—2 890, 1 725, 1 660, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 6.88—7.84 (m, arom.), 6.02 (s, OCH_2O) 5.45 (s, H-2/3), 3.96 (q, *J* 7 Hz) and 1.01 (t, *J* 7 Hz) (Et); *m/z* 470 (6%), 149 (100), and 121 (16). Evaporation of the ether solution after separation of the *erythro*-isomer gave the *threo*-isomer (3d) as a brown oil (0.89 g, 63%) (physical data same as those of sample prepared by α-bromo-oxo-ester method).

Preparation of Dioxo-diesters by the α-Bromo-oxo-ester Method.

(a) erythro-*Diethyl* 2,3-*Bis*-(3,4-*dimethoxybenzoyl*)*butane*-1,4-*dioate* (4b).—Sodium hydride (0.57 g, 50% suspension in oil) was washed with dry pentane (3×) and then suspended in dry dichloromethane (5 ml). To this was added a solution of ethyl (3,4-dimethoxybenzoyl)acetate (3 g) in dry dichloromethane (15 ml). This mixture was refluxed for 15 min and then a solution of ethyl bromo-(3,4-dimethoxybenzoyl)acetate (3.93 g) in dry dichloromethane (15 ml) was added. The product was then refluxed with stirring for 3 h. The suspension was cooled, washed with water (2 × 10 ml), and dried ($MgSO_4$). Evaporation gave a yellow oil which crystallised on washing with ether; yield 4.8 g (81%). This solid was again a mixture of isomers from which the pure *erythro*-isomer was obtained by repeated recrystallisation from ethanol.

(b) erythro-*Diethyl* 2,3-*Bis*-(4-*benzyloxy*-3-*methoxybenzoyl*)*butane*-1,4-*dioate* (4c).—This was prepared as above from ethyl (4-benzyloxy-3-methoxybenzoyl)acetate (3.9 g) and ethyl bromo-(4-benzyloxy-3-methoxybenzoyl)acetate (4.9 g); yield 7 g (90%); m.p. 176—177°; $\delta(CDCl_3)$ 5.45 (s) and 5.41 (s) (H-2/3), 4.07 (q, *J* 7 Hz), 3.90 (q, *J* 7 Hz), 1.13 (t, *J* 7 Hz), and 0.93 (t, *J* 7 Hz) (Et), 5.15 (s, OCH_2Ph), 3.86 (s) and 3.79 (s) (OMe), and 6.8—7.8 (m, arom.). The mixture of isomers was recrystallised four times from ethanol to give the pure erythro-*isomer* (4.0 g, 51%); m.p. 176—177 °C (Found: C, 69.3; H, 6.2. $C_{38}H_{38}O_{10}$ requires C, 69.7; H, 5.8%); $\nu_{max.}$ (KBr) 3 080—2 840, 1 730, 1 675, and 1 605 cm^{-1}; $\delta(CDCl_3)$ 5.45 (s, H-2/3), 3.90 (q, *J* 7 Hz) and 0.93 (t, *J* 7 Hz) (Et), 5.15 (s, OCH_2Ph), 3.86 (s, OMe), and 6.8—7.8 (m, arom.).

(c) erythro-*Diethyl* 2,3-*Dibenzoylbutane*-1,4-*dioate* (4e).—This was prepared as above from ethyl benzoylacetate (19.2 g) and ethyl bromo(benzoyl)acetate (27.1 g). A single recrystallisation from ethanol gave the pure *erythro*-isomer (29.8 g, 78%); m.p. 125—127 °C.

(d) threo- *and* erythro-*Diethyl* 2,3-*Bis*-(3,4-*methylenedioxybenzoyl*)*butane*-1,4-*dioate* (3d) *and* (4d).—This was prepared as above from ethyl (3,4-methylenedioxybenzoyl)-acetate (2.8 g) and ethyl bromo-(3,4-methylenedioxybenzoyl)acetate (3.8 g). Recrystallisation from ethanol

gave the *erythro*-isomer (4d) as a white crystalline solid (0.84 g, 30%); m.p. 159—161°. Evaporation of the ether residues after separation of the *erythro*-isomer gave an *oil* which crystallised (1.8 g, 64%); m.p. 93—95 °C (Found: C, 61.0; H, 4.9. $C_{24}H_{22}O_{10}$ requires C, 61.3; H, 4.7%); $\nu_{max.}$ (KBr) 2 980—2 880, 1 730, 1 665, and 1 610 cm^{-1}; $\delta(CDCl_3)$ 6.85—7.79 (m, arom.), 6.00 (s, OCH_2O), 5.39 (s, H-2/3), and 4.11 (q, *J* 7 Hz) and 1.17 (t, *J* 7 Hz) (Et); *m/z* 470 (7%), 149 (100), and 121 (18).

(e) *Diethyl* 2-(4-*Benzyloxy*-3-*methoxybenzoyl*)-3-(3,4-*dimethoxybenzoyl*)*butane*-1,4-*dioate*.—This was prepared as above from ethyl (3,4-dimethoxybenzoyl)acetate (3 g) and ethyl bromo-(4-benzyloxy-3-methoxybenzoyl)acetate (4.9 g); yield 5.5 g (79%). H.p.l.c. (Partisil 10μ, pentane–THF 3 : 1) showed this to be a mixture of the desired compound together with diethyl 2,3-bis-(3,4-dimethoxybenzoyl)-butane-1,4-dioate and diethyl 2,3-bis-(4-benzyloxy-3-methoxybenzoyl)butane-1,4-dioate in approximately equal amounts. A small amount (4 mg) of the title compound was separated by h.p.l.c. using the same system as above; m.p. 173—174 °C; $\nu_{max.}$ (KBr) 3 080—2 840, 1 730, 1 670, and 1 600 cm^{-1}; $\lambda_{max.}$ 278 nm (log ε 5.19).

threo-*Diethyl* 2,3-*Bis*-(3,4-*dimethoxybenzoyl*)*butane*-1,4-*dioate* (3b).—The *erythro*-isomer (1 g) was dissolved in 2M-sodium ethoxide in ethanol (20 ml) and refluxed for 1 h. The resulting solution was poured into dichloromethane (100 ml) and washed with dil. hydrochloric acid (3 × 15 ml) and then water (2 × 15 ml). It was then dried ($MgSO_4$) and evaporated to give an oil consisting of equal amounts of the *threo*- and *erythro*-isomers as shown by ^1H n.m.r. This oil was washed with ether, which left a solid (0.36 g) and yielded on evaporation an oil which contained 70% of the *threo*-isomer and 30% of the *erythro*-isomer as shown by the ratio of the integrals of the signals at 1.17 and 0.99 in the ^1H n.m.r. spectrum.

Diethyl 2,3-*Bis*-(4-*hydroxy*-3-*methoxybenzoyl*)*butane*-1,4-*dioate* (31)/(4a).—Diethyl 2,3-bis-(4-benzyloxy-3-methoxybenzoyl)butane-1,4-dioate (0.65 g) was dissolved in dry dichloromethane (20 ml) and cooled to −78 °C under nitrogen. A 1M-solution of boron trichloride in dichloromethane (5 ml) was added slowly with vigorous stirring. The mixture was stirred for 10 min and then quenched with water (20 ml) and allowed to warm to room temperature. The dichloromethane layer was separated, dried ($MgSO_4$), and evaporated to give a yellow *oil* which crystallised on treatment with ether and was recrystallised from ethanol; yield 0.23 g (48%); m.p. 170—171 °C (Found: C, 60.3; H, 5.6. $C_{24}H_{26}O_{10}$ requires C, 60.8; H, 5.8%); $\nu_{max.}$ (KBr) 3 400—3 200, 3 000—2 800, 1 730, 1 660, and 1 620 cm^{-1}; $\delta[(CD_3)_2SO]$ 5.25 (s, H-2/3), 4.15 (q), 3.85 (q), 1.10 (t) and 0.88 (t) (*J* 6 Hz) (Et), 10.21 (br, s) and 9.45 (br, s) (OH), 3.78 (s) and 3.54 (s) (OMe), and 6.8—7.7 (m, arom.).

erythro-2,3-*Bis*(α-*hydroxybenzyl*)*butane*-1,4-*diol* (8e).—Lithium aluminium hydride (1.9 g) was suspended in ether (160 ml) at 0 °C under nitrogen and a solution of *erythro*-diethyl 2,3-dibenzoylbutane-1,4-dioate (3.8 g) in ether (240 ml) was added at such a rate as to maintain the temperature below 4 °C. The mixture was stirred at 0 °C for 1 h, then at 20 °C for 2 h, and finally under reflux for 1 h. The suspension was cooled to 0 °C and carefully decomposed with water (20 ml) and sulphuric acid (10 ml; 10%). The ether solution was separated from the wet precipitate and dried (Na_2SO_4). Evaporation gave a yellow oil which slowly crystallised. The *product* was recrystallised from dichloromethane; yield 1.4 g (46%); m.p. 139—140 °C (Found: C, 71.5; H, 7.15. $C_{18}H_{22}O_4$ requires C, 71.5; H, 7.35%); $\nu_{max.}$ (KBr) 3 300, 3 000—2 800, and 1 600 cm^{-1}; $\delta[(CD_3)_2SO]$ 2.04 (m, H-2/3), 3.74 (ddd, *J* 3, 4, and 10 Hz) and 3.56 (ddd, *J* 4, 5, and 10 Hz) (H-1/4), 4.79 (t, *J* 4 Hz, CH_2OH), 4.92 (dd, *J* 4 and 5 Hz, CHOH), 5.54 (d, *J* 4 Hz, CHOH), and 7.20 (s, arom) [after D_2O addn. 2.06 (m, H-2/3), 3.78 (dd, *J* 3 and 10 Hz) and 3.52 (dd *J* 5 and 10 Hz) (H-1/4), 4.94 (d, *J* 5 Hz, CHOD), and 7.20 (s, arom.)].

threo-2,3-*Bis*(α-*hydroxybenzyl*)*butane*-1,4-*diol* (7e).—This was prepared as above from *threo*-diethyl 2,3-dibenzoylbutane-1,4-dioate (3.8 g); yield 0.8 g (30%); m.p. 141—144 °C (Found: C, 71.3; H, 7.6. $C_{18}H_{22}O_4$ requires C, 71.5; H, 7.3%); $\nu_{max.}$ (KBr) 3 260—3 140, 3 000—2 800, and 1 600 cm^{-1}; $\delta[(CD_3)_2SO]$ 2.07 (m, H-2/3), 3.44 (dd, *J* 5 and 6 Hz, H-1/4), 5.05 (t, *J* 5 Hz, CH_2OH), 4.66 (t, *J* 5 Hz, CHOH), 5.42 (d, *J* 5 Hz, CHOH), and 6.9—7.3 (m, arom.) [after D_2O addn. 2.07 (q, *J* 5 Hz, H-2/3), 3.44 (d, *J* 5 Hz, (H-1/4), 4.66 (d, *J* 5 Hz, CHOD), and 6.9—7.3 (m, arom.)].

erythro-2,3-*Bis*-(α-*hydroxy*-4-*benzyloxy*-3-*methoxybenzyl*)-*butane*-1,4-*diol* (8c).—Lithium aluminium hydride (0.8 g) was suspended in tetrahydrofuran (50 ml) in an atmosphere of nitrogen and a solution of *erythro*-diethyl 2,3-bis-(4-benzyloxy-3-methoxybenzoyl)butane-1,4-dioate (2.6 g) in tetrahydrofuran (300 ml) was added at a rate sufficient to maintain refluxing. The suspension was refluxed for a further 48 h with vigorous stirring and then cooled. It was carefully decomposed with water (10 ml) and hydrochloric acid (20 ml; 5M); the mixture was filtered and the precipitate washed with warm tetrahydrofuran (3 × 50 ml). The combined extracts were evaporated until the water present separated and were then extracted with ethyl acetate. The solution was dried (Na_2SO_4) and evaporated to give a yellow oil, which was crystallised from dichloromethane; yield 1.2 g (52%); m.p. 78—80 °C; $\nu_{max.}$ (KBr) 3 200, 3 060—2 840, and 1 610 cm^{-1}; $\delta(CDCl_3)$ 2.48 (m, H-2/3), 3.68 (m, H-1/4), 3.20 (br, s, CH_2OH), 4.54 (d, *J* 8 Hz, CHOH), 3.20 (br, s, CHOH), 5.04 (s, OCH_2Ph), 3.77 (s, OMe), and 6.9—7.3 (m, arom.); *m/z* 556.2458 (*M* − H_2O, $C_{34}H_{36}O_7$) and 538.2354 (*M* − $2H_2O$, $C_{34}H_{34}O_6$).

erythro-2,3-*Bis*-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-*butane*-1,4-*diol* (8d).—*erythro*-Diethyl 2,3-bis-(3,4-methylenedioxybenzoyl)butane-1,4-dioate (1.9 g) was placed in a thimble and a solution of lithium aluminium hydride in tetrahydrofuran (24.5 ml; 0.49M) was syringed through a tap adaptor with septum cap into a nitrogen-filled two-neck flask. The mixture was refluxed for 48 h in an oil-bath using a Soxhlet extractor, then cooled, and hydrochloric acid (20 ml; 5M) was added. The resulting mixture was stirred for 1 h and then extracted with dichloromethane (3 × 40 ml); the extracts were washed with water (2 × 50 ml) and dried ($MgSO_4$). Evaporation gave a brown oil (1.1 g, 69%); $\nu_{max.}$ (film) 3 540—3 200, 2 980—2 840, and 1 610 cm^{-1}; $\delta(CDCl_3)$ 2.4 (m, H-2/3), 3.66 (m, H-1/4), 3.95 (br, s, OH), 4.48 (br, d, *J* 8 Hz, CHOH), 5.86 (s, OCH_2O), and 6.62—6.87 (m, arom.); *m/z* 372 (6%), 149 (100), and 121 (15).

threo-2,3-*Bis*-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)-*butane*-1,4-*diol* (7d).—This was prepared as above from *threo*-diethyl 2,3-bis-(3,4-methylenedioxybenzoyl)butane-1,4-dioate (1.5 g); yield 0.93 g (78%); $\nu_{max.}$ (film) 3 480—3 320, 3 010—2 890, and 1 610 cm^{-1}.

2,4-*Diphenyl*-3,7-*dioxabicyclo*[3.3.0]*octane* (2e).—A mixture of *erythro*-2,3-bis-(α-hydroxybenzyl)butane-1,4-diol (3 g) and potassium hydrogen sulphate (2.7 g) was heated at 150 °C and 1 mmHg in a flask equipped with a reflux

condenser for 1 h. The resulting solid was distilled at 1 mmHg (bath temperature 190 °C) and yielded a yellow syrup which crystallised. The product was recrystallised from light petroleum (b.p. 60—80 °C); yield 1.0 g (38%); m.p. 87—88.5 °C; $\nu_{max.}$ (KBr) 3 080—2 860 and 1 610 cm^{-1}; *m/z* 266.1306 ($M^{+\bullet}$, $C_{18}H_{18}O_2$), 160.0888 ($C_{11}H_{12}O$), 131.0857 ($C_{10}H_{11}$), 131.0496 (C_9H_7O), 130.0782 ($C_{10}H_{10}$), 129.0704 ($C_{10}H_9$), and 117.0704 (C_9H_9).

2,6-*Diphenyl*-3,7-*dioxabicyclo*[3.3.0]*octane* (1e).—This was prepared as above from *threo*-2,3-bis-(α-hydroxybenzyl)-butane-1,4-diol (1.5 g); yield 0.35 g (26%); m.p. 73—76°; *m/z* 266.1306 ($M^{+\bullet}$, $C_{18}H_{18}O_2$) and 117.0704 (C_9H_9).

2,4-*Bis*-(4-*benzyloxy*-3-*methoxyphenyl*)-3,7-*dioxabicyclo*-[3.3.0]*octane* (2c).—*erythro*-2,3-Bis-(α-hydroxy-4-benzyloxy-3-methoxybenzyl)butane-1,4-diol (0.57 g) was dissolved in dry pyridine (5 ml) and kept with a solution of methanesulphonyl chloride (0.23 g) in dry pyridine (2 ml) at room temperature overnight. The mixture was filtered and poured into water (20 ml) and then extracted with ethyl acetate (3 × 20 ml). The ethyl acetate solution was washed with 1M-hydrochloric acid (2 × 10 ml) and then water (2 × 10 ml). It was dried ($MgSO_4$) and evaporated to a brown oil. Column chromatography on silicic acid using mixtures of light petroleum (b.p. 60—80 °C) and ethyl acetate gave the pure product (0.06 g, 12%); m.p. 131—135 °C; $\nu_{max.}$ (KBr) 3 030—2 840 and 1 600 cm^{-1}; *m/z* 538.2355 ($M^{+\bullet}$, $C_{34}H_{34}O_6$) and 296.1412 ($C_{19}H_{20}O_3$).

2,4-*Bis*-(3,4-*methylenedioxyphenyl*)-3,7-*dioxabicyclo*[3.3.0]-*octane* (2d).—This was prepared as above from *erythro*-2,3-bis-(α-hydroxy-3,4-methylenedioxybenzyl)butane-1,4-diol (1.1 g) and obtained as an oil (0.96 g). Column chromatography on silica gel using mixtures of light petroleum (b.p. 40—60 °C) and chloroform gave an oil (300 mg) which showed two overlapping spots on t.l.c. Preparative h.p.l.c. [0.5 in Partisil column eluted with pentane–THF (95 : 5)] gave two fractions, the first of which on further purification by preparative t.l.c. gave the required 2,4-isomer as an oil (40 mg, 13%); $\nu_{max.}$ (film) 3 100—2 920 and 1 610 cm^{-1}; *m/z* 354.1104 ($M^{+\bullet}$, $C_{20}H_{18}O_6$), 204.0887 ($C_{12}H_{12}O_3$), 175.0394 ($C_{10}H_7O_3$), and 161.0503 ($C_{10}H_9O_2$).

2,6-*Bis*-(3,4-*methylenedioxyphenyl*)-3,7-*dioxabicyclo*-[3.3.0]*octane* (1d) (*Sesamin*).—*threo*-2,3-Bis-(α-hydroxy-3,4-methylenedioxybenzyl)butane-1,4-diol (0.5 g) was dissolved in dry methanol (5 ml) and cooled to 0 °C. Methanolic hydrogen chloride (15 ml; 3M) was added and the mixture left at 0 °C for 6 h with occasional swirling. The mixture was then poured into ethyl acetate (100 ml), washed with water (2 × 30 ml), dried ($MgSO_4$), and evaporated to give an oil (0.45 g). This was placed on a column of silica gel and eluted with light petroleum (b.p. 40—60 °C). When the solvent was changed through 1 to 10% chloroform a fraction was collected which on evaporation gave a semi-solid. Recrystallisation from ethanol gave a white solid (0.3 g, 44%); m.p. 118—120° (lit.,[22] 123°); $\nu_{max.}$ (KBr) 3 090—2 920 and 1 610 cm^{-1}; *m/z* 354.1103 ($M^{+\bullet}$, $C_{20}H_{18}O_6$), 175.0396 ($C_{10}H_7O_3$), 164.0476 ($C_9H_8O_3$), and 161.0503 ($C_{10}H_9O_2$).

2,6-*Bis*-(4-*benzyloxy*-3-*methoxyphenyl*)-3,7-*dioxabicyclo*-[3.3.0]*octane* (1c).—Pinoresinol (0.36 g) was dissolved in dry acetone (20 ml) together with benzyl chloride (0.5 g) and dry potassium carbonate (0.56 g). This mixture was refluxed with stirring for 6 h and then cooled and poured into water (50 ml). The mixture was extracted with dichloromethane (3 × 40 ml) and the extracts were dried ($MgSO_4$) and evaporated to give a yellow oil. This was placed on a column of silica gel (120 mesh; 40 g) and washed with light petroleum (b.p. 40—60 °C; 500 ml) which removed most of the benzyl chloride. The product was then obtained by elution with ether (200 ml), which deposited white crystals upon concentration; yield 0.39 g (72%), m.p. 148—152 °C; $\nu_{max.}$ (KBr) 3 030—2 840 and 1 600 cm^{-1}; *m/z* 538.2355 ($M^{+\bullet}$, $C_{34}H_{34}O_6$) and 257.1177 ($C_{16}H_{17}O_3$).

2-(3,4-*Methylenedioxyphenyl*)-3-*hydroxymethyl*-4-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)*tetrahydrofuran* (18).—4-Hydroxysesamin (67 mg) was dissolved in dry tetrahydrofuran (2 ml) and refluxed with a suspension of lithium aluminium hydride (36 mg) in dry tetrahydrofuran (15 ml) for 5 h. The excess of lithium aluminium hydride was destroyed by adding wet tetrahydrofuran (10 ml) followed by sulphuric acid (10 ml; 2%). The mixture was filtered and the filtrate extracted with ethyl acetate (3 × 15 ml); the extracts were washed with water (2 × 15 ml) and dried ($MgSO_4$). Evaporation gave an oil (60 mg) which was used directly.

Cyclisation of 2-(3,4-*Methylenedioxyphenyl*)-3-*hydroxymethyl*-4-(α-*hydroxy*-3,4-*methylenedioxybenzyl*)*tetrahydrofuran* (18).—The diol (60 mg) was dissolved in dry methanol (2 ml), methanolic HCl (2 ml; 3M) was added, and the mixture was kept at 0 °C for 1 h with occasional swirling. It was then extracted with ethyl acetate (3 × 20 ml); the extracts were washed with water (2 × 15 ml) and dried ($MgSO_4$). Evaporation gave an oil (50 mg) which had physical and spectral data identical with those of sesamin (1d).

[1/1040 *Received*, 29*th June*, 1981]

REFERENCES

[1] K. Weinges and R. Spanig, 'Oxidative Coupling of Phenols,' ed. W. I. Taylor and A. R. Battersby, Arnold, London, 1967, ch. 7.
[2] E. W. Lund, *Acta Chem. Scand.*, 1960, **14**, 496.
[3] A. M. Villard and J. Wyant, *C. R. Acad. Sci., Ser. C*, 1968, **266**, 1284.
[4] R. F. Bryan and L. Fallon, *J. Chem. Soc., Perkin Trans. 2*, 1976, 341.
[5] R. Hänsel, J. Schulz, and A. Pelter, *Chem. Ber.*, 1975, **108**, 1482.
[6] O. R. Gottlieb, J. G. S. Maia, and J. Mourao, *Phytochemistry*, 1976, **15**, 1289.
[7] A. Pelter and R. S. Ward, 'Chemistry of Lignans,' ed. C. B. S. Rao, Andhra Univ. Press, Visakhapatnam, India, 1978, ch. 7.
[8] D. Lavie, E. C. Levy, A. Cohen, M. Evenari, and T. Gutterman, *Nature*, 1974, **249**, 388.
[9] C. H. Brieskorm and H. Huber, *Tetrahedron Lett.*, 1976, 2221.
[10] R. Cooper, E. C. Levy, and D. Lavie, *J. Chem. Soc., Chem. Commun.*, 1977, 794.
[11] A. S. R. Anjaneyulu, A. Madhusudhana Rao, V. Kameswara Rao, L. Ramachandra Row, A. Pelter, and R. S. Ward, *Tetrahedron*, 1977, **33**, 133.
[12] J. Kratzl and G. Miksche, *Monatsh. Chem.*, 1963, **94**, 434.
[13] M. Beroza and M. S. Schechter, *J. Am. Chem. Soc.*, 1956, **68**, 1242.
[14] L. Knorr, *Liebigs Ann. Chem.*, 1896, **293**, 70.
[15] W. Bradley and R. Robinson, *J. Chem. Soc.*, 1928, 1541.
[16] I. A. Pearl and J. Kratzl, *J. Org. Chem.*, 1962, **27**, 2111.
[17] N. B. Galstukhova, *Zh. Org. Khim.*, 1957, **27**, 1857; *Dokl. Akad. Nauk. S.S.S.R.*, 1957, **113**, 1276.
[18] A. Pelter, R. S. Ward, D. J. Watson, P. Murray-Rust, and J. Murray-Rust, *Tetrahedron Lett.*, 1978, 1509.
[19] A. Pelter, R. S. Ward, D. J. Watson, P. Collins, and I. T. Kay, *Tetrahedron Lett.*, 1979, 2275.
[20] A. Pelter, *J. Chem. Soc.* (*C*), 1967, 1376.
[21] A. M. Duffield, *J. Heterocycl. Chem.*, 1967, **4**, 16.
[22] K. Freudenberg and G. S. Sidhu, *Tetrahedron Lett.*, 1960, 3; *Chem. Ber.*, 1961, **94**, 851.