The Chemistry of Fungi. Part 76.[1] The Synthesis and Transformations of Three Stereoisomeric 2-(2,6-Dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo[2,2,1]heptanes

By **Alan D. Borthwick, David J. Curry, Alan Poynton, W. Basil Whalley,*** and (in part) **John W. Hooper**, The School of Pharmacy, The University, 29/39 Brunswick Square, London WC1N 1AX

Condensation of 1-lithio-2,6-dimethoxybenzene with the anhydride (10) of 7-oxabicyclo[2.2.1]heptane-2β,3β-dicarboxylic acid and subsequent esterification of the product gave 2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (8; R^1 = H, R^2 = Me). The isomeric 2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (11; R = Me) was prepared similarly using the anhydride (9) from 7-oxabicyclo[2.2.1]heptane-2α,3α-dicarboxylic acid. Epimerisation of (11; R = Me) or of (8; R^1 = H, R^2 = Me) gave 2α-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (12).

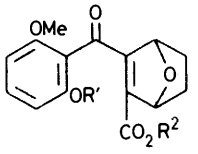
Treatment with boron trichloride of (11; R = Me) gave 1α-chloro-4β-hydroxy-2α-(2-hydroxy-6-methoxybenzoyl)-3α-methoxycarbonylcyclohexane (13; R = H) and 1,7α-dihydroxy-8β-methoxycarbonyl-5aα,5,6,7,8,8aα-hexahydroxanthone (23; R = H); similarly (8; R^1 = H, R^2 = Me) gave 4β-hydroxy-2β-(2-hydroxy-6-methoxybenzoyl)cyclohexane-1β,3β-carbolactone (24; R = H) and 1,7α-dihydroxy-8α-methoxycarbonyl-5aα,5,6,7,8,8aβ-hexahydroxanthone (25; R = H). The third isomer (12) formed 4α-chloro-1β-hydroxy-2α-(2-hydroxy-6-methoxybenzoyl)-3β-methoxycarbonylcyclohexane (31; R = H) together with 1,7α-dihydroxy-8α-methoxycarbonyl-5aα,5,6,7,8,8aα-hexahydroxanthone (32; R = H).

Hydrogenolysis of (1; R^1 = R^2 = Me) or treatment of (11; R = Me) with acid yielded 2-(2,6-dimethoxybenzoyl)-4β-hydroxy-3α-methoxycarbonylcyclohexene (15; R = H); the corresponding acetate (15; R = Ac) was hydroxylated to form 4β-acetoxy-2α-(2,6-dimethoxybenzoyl)-1β,2β-dihydroxy-3α-methoxycarbonylcyclohexane (18) as the major product. The stereoisomeric cyclohexene (34; R = H) was similarly obtained.

Bromination of the ketone (11; R = Me) gave the α-bromoketone (33): similarly the α-bromoketone (8; R^1 = Br, R^2 = Me) was obtained from (8; R^1 = H, R^2 = Me) and (12). Dehydrobromination of each of these bromoketones formed 2-(2,6-dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo[2.2.1]hept-2-ene (1; R^1 = R^2 = Me).

Various further transformations of these products are described.

In an investigation concerning the synthesis of the fungal metabolite, ergoflavin and its congeners, we have shown [2] that base-catalysed cyclisation of the ketone (1; R^1 = H, R^2 = Me) gaves the spiran (2) rather than the hexahydroxanthone, type (3). However, since the interconversion [3] of ergochrysin (4) and isoergochrysin (5) most probably proceeds through an intermediate of type (6), we have investigated the possibility of obtaining such an intermediate from stereoisomers of the system (7).



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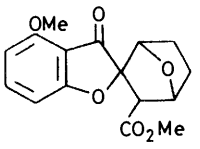

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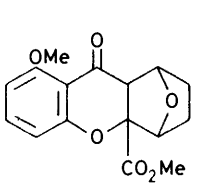
Although our initial objective has not yet been achieved, the investigation has provided routes to a variety of related hexahydroxanthones, some of which are similar in structure to other natural products. Hence our investigations in this area are now reported.

Thus treatment of *exo*-7-oxabicyclo[2.2.1]heptane anhydride (10) with 2,6-dimethoxyphenyl-lithium gave the keto-acid (8; R^1 = R^2 = H). In the n.m.r. spectrum of the methyl ester (8; R^1 = H, R^2 = Me) signals at τ 5.19 (m, 1 H) and 4.90 (m, 1 H) are attributed to the C-4 and C-1 bridgehead methine protons.

In the preparation of ketones from organo-lithium reagents and alicyclic carboxylic acids the absence of epimerisation at the α-carbon atom has been rigorously demonstrated.[4] Thus the *exo*-anhydride (10) would be expected to give the *exo*-ketone (8; R^1 = R^2 = H). This expectation is confirmed by the coupling constant



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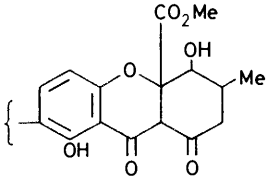

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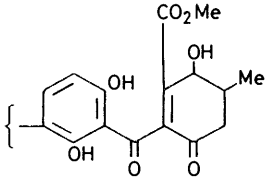

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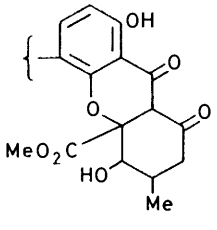


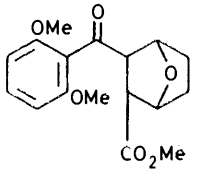
(5)

(*J* 9 Hz) of the C-3 methine proton which indicates that the C-2/C-3 dihedral angle between the C-2 and C-3 protons is ~0°.

Condensation of 2,6-dimethoxyphenyl-lithium with the

* All the structures imply (±)-compounds.

endo-7-oxabicyclo[2.2.1]heptane anhydride (9) similarly furnished the *endo*-ketone (11; R = H), the methyl ester (11; R = Me) of which was identical with the



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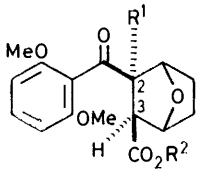

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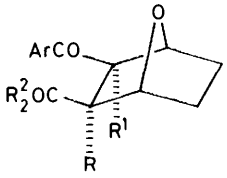
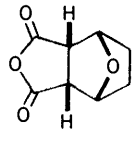


hydrogenation product of the ketone (1; $R^1 = R^2 =$ Me).

The *cis*-ketone (8; R^1 = H, R^2 = Me) was converted quantitatively and rapidly in refluxing acetic acid–sodium acetate into the *trans*-ketone (12). Under similar conditions the *cis*-ketone (11; R = Me) epimerised only very slowly, if at all, but with toluene-*p*-sulphonic acid gradually gave a mixture of the parent ketone (11; R = Me) and the *trans*-isomer (12).



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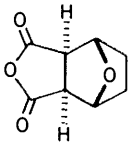

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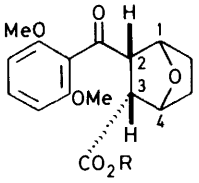

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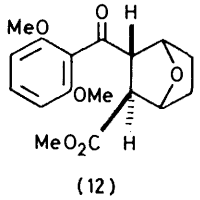

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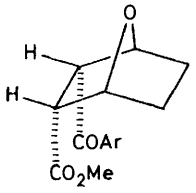

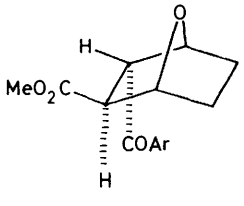

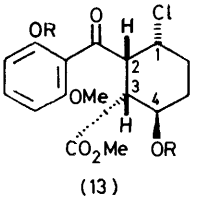

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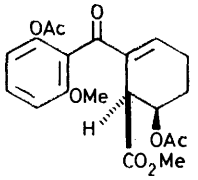
The protons α to the ester residue in (8; R^1 = H, R^2 = Me), (11; R = Me), (12) and (28) resonate about τ 7.2—6.8; hence the signals at τ 6.84 and 5.83 in the n.m.r. spectrum of the *trans*-ketone (12) may be assigned to the C-3 and C-2 protons, respectively. The C-3 proton is adjacent to the C-2 and C-4 protons, but furnishes only a doublet signal with *J* 5 Hz. Models show that this is possible only if the C-3 proton is on the α-face of the oxabicyclo[2.2.1]heptane system, where the dihedral angle between the C-3 and C-4 protons is ≃90°,



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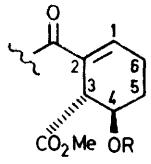

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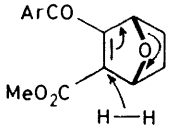

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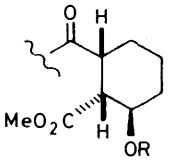


(17)

with a coupling constant of ≃0 Hz. Hence the splitting of the C-3 proton signal (*J* 5 Hz) is to be ascribed to axial-equatorial coupling to the C-2 proton. As the C-2 proton signal is a triplet, this proton must be coupled to *both* the C-3 and C-1 protons and is therefore on the same side of the ring as the oxygen bridge. It thus follows that the *trans*-isomer can be depicted as (12).

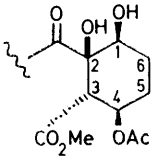
With these three diastereoisomeric 2-(2,6-dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo[2.2.1]-heptanes available, their possible transformation into a synthon, suitable for our purpose was investigated.

Thus, treatment of the *endo*-ketone (11) with boron trichloride, gave two phenolic products, the major of which is formulated as the chloro-alcohol (13; R = H), genesis of which is by way of attack [2] of the chloride nucleophile on the oxido-bridge from the α-face. The n.m.r. spectrum included signals at τ 7.20br (s, O*H*, H, exchangeable with D_2O), 6.64 (s, $OCOCH_3$, 3 H), 6.16 (s, OCH_3, 3 H), and −2.28 (s, O*H*, 1 H, exchangeable with D_2O). The mass spectrum showed *m/e* 334 and 332 in an abundance ratio of 1 : 3 in agreement with the presence of one chlorine atom in the molecule. The di-*O*-acetate showed n.m.r. signals *inter alia* at τ 8.01 (s, $CH{\cdot}OOCH_3$, 3 H), 7.72 (s, $ArOCOCH_3$, 3 H), and 4.80 (*m*, C-4 methine proton, 1 H), in accord with structure (13; R = Ac) where the saturated ring has a chair conformation, in which the chlorine is axial. In accord with this conformation (13; R = Ac) readily eliminated hydrogen chloride with warm pyridine to give the αβ-unsaturated ketone (14). The i.r. spectrum showed $\nu_{max.}$ 1 768 (acetoxy carbonyl), 1 738 (ester carbonyl), and 1 663 cm^{-1} (aryl carbonyl). The

decrease in wavenumber of the aryl carbonyl peak in the i.r. spectrum of (14) by 27 cm^{-1} [from 1 690 cm^{-1} in (13; R = Ac)] together with the similar values (1 742 and 1 738 cm^{-1}) for the methoxyester carbonyl frequencies in (13; R = Ac) and (14), respectively, confirm that the halogen in (13; R = Ac) is β to the aryl ketonic carbonyl. In the n.m.r. spectrum of (14) the $W_{\frac{1}{2}}$ value (15 Hz) for the C-4 proton signal indicates that this proton is probably axial with the ester group equatorial in a half-chair conformation; the epimerisation of C-3 during this dehydrochlorination cannot be excluded.

The minor product from the cleavage of (11; R = Me) with boron trichloride is formulated as 1,7α-dihydroxy-8β-methoxycarbonyl-5aα,5,6,7,8,8aα-hexahydroxanthone (23; R = H), the genesis of which is presumably by way of the intramolecular attack of a phenolic nucleophile upon the oxido-bridge as in ref. 2 to the accompaniment of the normal *trans*-opening of this bridge. The stereochemistry of the xanthone derivative then follows and is confirmed by the spectral data. In accord with this formulation, (23; R = H) gives an intense green ferric reaction. The di-*O*-acetate (23; R = Ac) showed signals in the n.m.r. spectrum at τ 5.78 (m, C-5a proton, H, $W_{\frac{1}{2}} \sim 15$ Hz), and 4.99 (m, C-7 proton, H, $W_{\frac{1}{2}} \sim 16$ Hz). The $W_{\frac{1}{2}}$ of these signals indicate clearly that the C-7 acetoxy-residue and the C-5a aryl ester group must be equatorial and hence *trans*; this is in accord with the established *trans*-opening of the 1,4-oxido-bridge. The relative stereochemistry of C-8 and C-8a remain as in (11; R = Me); hence the total relative stereochemistry may be defined as (23; R = H).

One hydrogenation of the keto-ester (1; $R^1 = R^2 =$ Me), to form (11; R = Me), produced additionally the olefinic alcohol (15; R = H). The formation of this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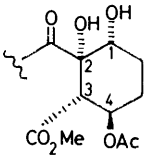
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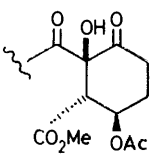
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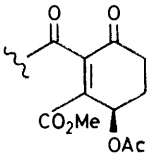
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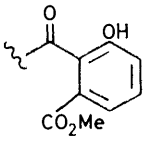
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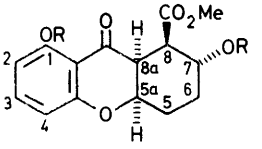
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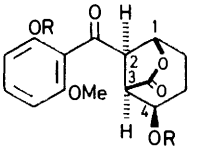
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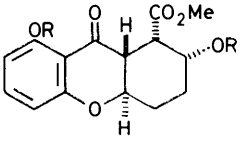
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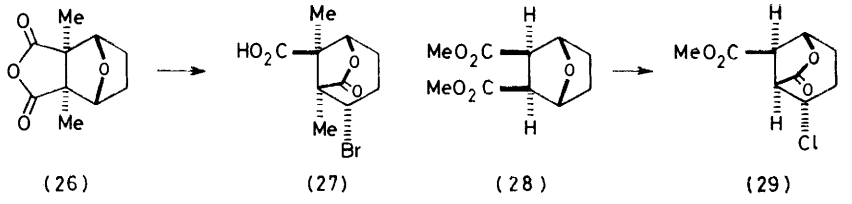
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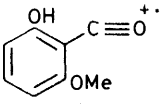
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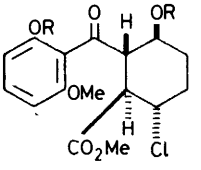

(31)

unsaturated product was traced to the presence of acetic acid in the solvent (ethyl acetate). Quantitative conversion of (1; $R^1 = R^2 = Me$) into (15; R = H) was achieved by conducting the hydrogenation in acetone containing perchloric acid. This reaction is equivalent to an allylic rearrangement, and probably occurs by an S_N2^1 *mechanism* where hydrogen acts as a nucleophile. The S_N2^1 mechanism is stereospecifically [5] a *cis*-process as in (16) ⟶ (15; R = H), and hence the ester and hydroxy residues probably have a *trans*-orientation: this conclusion is confirmed later.

The acetate (15; R = Ac) shows *inter alia* in the n.m.r. spectrum that the C-4 proton signal has $W_{\frac{1}{2}} > 15$ Hz, in agreement with the equatorial disposition of the acetoxy-residue in a half-chair conformation (15; R = Ac). Hydrogenation of (15; R = Ac) gave 2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-4β-acetoxycyclohexane (17) showing no vinylic proton signals in the n.m.r. spectrum.

Hydroxylation of (15; R = Ac) with osmium tetraoxide–pyridine gave (almost quantitatively), a mixture of the two *cis*-diols (18) and (19) in a ratio of 7 : 1, respectively. The major product was formulated as (18), in accord with its formation by approach of the reagent from the less-hindered face of the cyclohexene ring. This diol most probably has the chair conformation in which the methoxycarbonyl and acetate residues are equatorial. In the n.m.r. spectrum the C-3 and C-4 protons are *trans*-diaxial, in accord with the J values of 10.5 Hz; and the $W_{\frac{1}{2}}$ value (12 Hz) for the C-4 methine proton signal indicates the *trans* di-equatorial arrangement of the C-3 methoxycarbonyl and the C-4 acetoxy-residues. It follows that the C-1 hydroxy-group must be equatorial.

The minor diol must therefore have structure (19). The n.m.r. spectrum includes signals at τ 6.66 (d, J 11 Hz, C-3 methine proton, H), 6.35—5.85 (m, C-1 methine proton, 1 H, $W_{\frac{1}{2}} > 13$ Hz), and 4.66 (m, C-4 methine proton, 1 H, $W_{\frac{1}{2}} > 15$ Hz). This diol thus has the cyclohexane ring in a chair conformation (19) where the C-3 and C-4 functions are in a *trans* di-equatorial conformation, and the C-4 acetoxy- and the C-1 hydroxy-groups are both equatorial in agreement with these n.m.r. data.

Oxidation of the diol (18) with *freshly* prepared Jones' reagent gave the ketol (20), but attempts to dehydrate this with various reagents, to yield (21), furnished only the benzophenone (22).

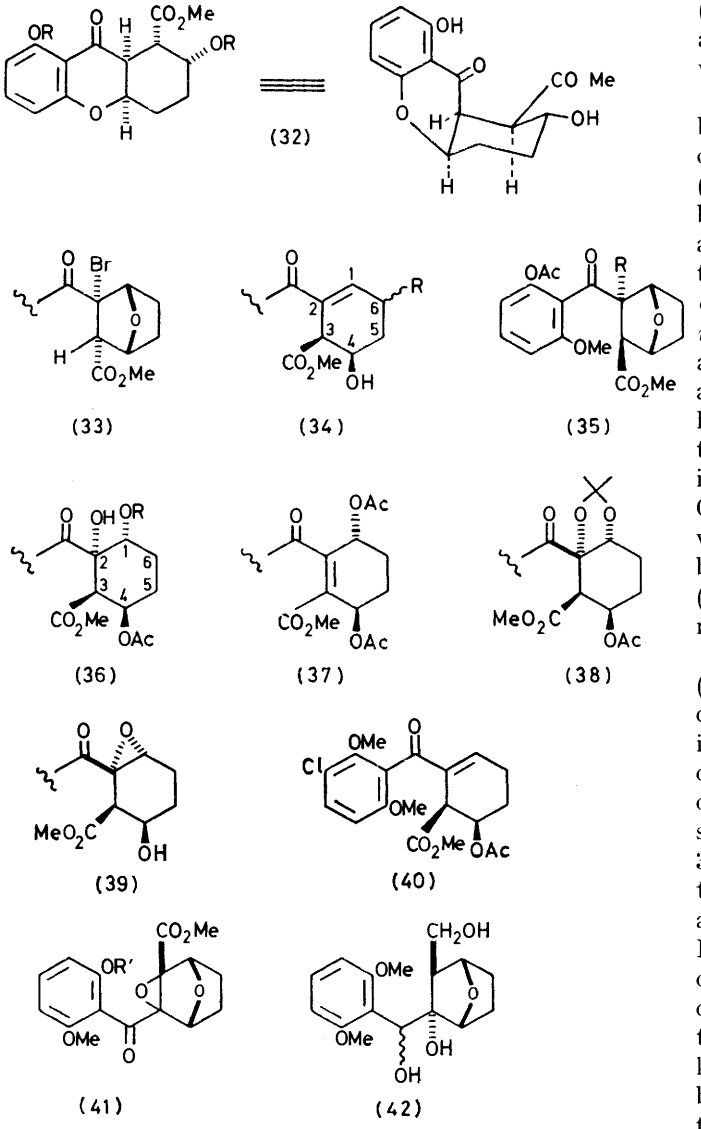
Treatment of the *exo*-7-oxabicyclo[2.2.1]heptane (8; $R^1 = H$, $R^2 = Me$) with boron trichloride gave two phenolic products (24; R = H) and (25; R = H). Thus the i.r. spectrum of the minor product (24; R = H) showed $\nu_{max.}$ 3 440 (OH), 1 753 (γ-lactone), 1 615 (hydrogen bonded aryl ketone), and 1 590 cm^{-1} (aromatic double bonds), whilst the n.m.r. spectrum [in $(CD_3)_2CO$] included signals at τ 8.4—7.6 (m, C-5 and C-6 methylene protons, 4 H), 7.0 (s, O*H*, 1 H; exchangeable with D_2O), and 6.31 (s, OCH_3, 3 H). The mass spectrum of (24; R = Ac) exhibited a base peak at *m/e* 151, corresponding to the fragment (30). The stereochemistry of the cyclohexane ring was further defined by the n.m.r. spectrum of the di-*O*-acetate (24; R = Ac), which had τ 7.90 (s, alkyl-OCOC*H*, 3 H), 7.79 (s, ArOCOCH_3, 3 H), 6.84 (m, C-3 proton, 1 H, $W_{\frac{1}{2}} \sim 15$ Hz), 6.66 (s, C-2 proton, 1 H), 6.10 (s, OCH_3, 3 H), 5.15—4.75 (m, C-4 proton, H, $W_{\frac{1}{2}} \sim 15$ Hz) and 5.02 (m, C-1 proton, 1 H; $W_{\frac{1}{2}} \sim 6$ Hz). The $W_{\frac{1}{2}}$ values of the signals for the C-1 and C-3 protons indicate that these protons are both equatorial: this is in agreement with conclusions from a model of (24; R = Ac) which clearly shows that for the presence of the γ-lactone bridge the functional groups at C-1 and C-3 must be *cis* and axial. The model also indicates that the dihedral angle between the C-2 and C-3 protons is ~90°, and equal to the dihedral angle between the C-2 and C-1 protons. Hence there should be no coupling between the C-2 proton and the C-1 and C-3 protons. This is confirmed by the C-2 proton signal being a sharp singlet. Additionally the $W_{\frac{1}{2}}$ value for the C-4 methine proton indicates that the C-4 acetoxy-group is equatorial. These conclusions are in accord with a *cis*-opening of the oxido-bridge.

Collateral evidence for the structure of the γ-lactone (24; R = H) is provided by the similar conversion [6] of cantharidin (26) into the γ-lactone (27) and by our observation that the 7-oxabicyclo[2.2.1]heptane (28) reacts with boron trichloride to yield the analogous γ-lactone (29).

The major product from *exo*-[2.2.1]heptane (8; $R^1 = H$, $R^2 = Me$) was assigned structure (25; R = H). The mass spectrum was similar to that of the hexahydroxanthone (23; R = H), and was devoid of a peak at *m/e* 198, corresponding to fragment ion (30): the i.r. spectrum had $\nu_{max.}$ 3 515 (OH), 1 700 (ester carbonyl), 1 638 (hydrogen-bonded aryl carbonyl), and 1 613 cm^{-1} (aromatic double bonds): the n.m.r. spectrum included signals at τ 7.24 (q, J 4.5, 8 Hz, C-8 proton, 1 H), 6.4—5.8 (m, C-7, C-8a protons, 2 H; $W_{\frac{1}{2}} > 15$ Hz), and 5.4—4.7 (m, C-5a proton, 1 H; $W_{\frac{1}{2}} > 15$ Hz). The $W_{\frac{1}{2}}$ values for the C-5a, C-8a, and C-7 methine protons indicate that the functional groups attached to these carbon atoms are equatorial. The known relative stereochemistry of C-8 and C-8a and of the oxido-bridge opening combine to define the relative stereochemistry of this hexahydroxanthone as (25; R = H), with ring c in a chair conformation. The n.m.r. spectrum of the di-*O*-acetate (25; R = Ac) confirmed these assignments, with τ 5.00 (m, C-7, and C-5a protons, 2 H). The shift for the signal of the C-7 proton from τ 6.20 in (25; R = H) to 5.00 in (25; R = Ac) further substantiates this, whilst the $W_{\frac{1}{2}}$ of ~16 Hz for this signal establishes the equatorial position of the acetoxy-substituent as in (25; R = Ac). This hexahydroxanthone is similar to the naturally occurring pigment, cochlioquinone A.[7]

Treatment of the *trans*-7-oxabicyclo[2.2.1]heptane (12) with boron trichloride again gave a mixture of a major product (31; R = H), and a minor product (32; R = H). The structure of (31; R = H) is based on the usual criteria. The di-*O*-acetate (31; R = Ac) showed n.m.r. signals at τ 5.82 (m, C-4 proton, 1 H; $W_{\frac{1}{2}}$ 12 Hz) and

5.03 (m, C-1 proton, 1 H; $W_{\frac{1}{2}} > 12$ Hz). The $W_{\frac{1}{2}}$ values indicate that the functional substituents of these carbons are equatorial. From the known relative stereochemistry of the C-2 and C-3 atoms, and the stereospecific opening of the 1,4-oxido-bridge in (12), the relative stereochemistry at C-1, C-2, C-3, and C-4 may be assigned as in (31; R = H). The α-oriented chlorine atom is



placed at C-4 rather than C-1 since (31; R = H) does not eliminate hydrogen chloride readily with warm pyridine (C-3 proton and C-4 chlorine, *cis*). If the α-orientated chlorine were at C-1 then the relationship to the β-proton would be *trans* and axial and dehydrohalogenation would occur readily [*cf.* the case of conversion of (13; R = Ac) into (15; R = Ac)]. The structures of (13; R = H) and (31; R = H) are also compatible with their derivation by attack of the chloride nucleophile upon the boron trifluoride complex of the parent oxido-derivative, at the less-hindered terminus of the oxido-bridge.

The minor product from (12) has been formulated as the hexahydroxanthone (32; R = H). Thus, *inter alia*, the mass spectrum and general properties are very similar to those of (23; R = H) and (25; R = H), whilst the n.m.r. spectrum included signals at τ 5.75 (m, C-7 proton, 1 H; $W_{\frac{1}{2}} > 5$ Hz) and 5.37 (m, C-5a proton, 1 H, $W_{\frac{1}{2}} > 5$ Hz). These $W_{\frac{1}{2}}$ values indicate that the functional groups at these two positions are axial: thus (32; R = H) may be formulated in the chair conformation, in agreement with mechanistic arguments previously advanced.

The direct synthesis [2] of (1; $R^1 = R^2 =$ Me) is impeded by solubility problems. An alternative approach has circumvented this difficulty. Thus bromination of 2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (11; R = Me) with bromine in acetic acid gave the 2α-bromo-derivative (33), in which the presence of one atom of bromine was confirmed by elementary analysis and by the mass spectrum which, *inter alia* exhibited signals of a 1 : 1 intensity at *m/e* 400 and 398 (M^+), 369 and 367 [$M^+ - 31(OCH_3)$], and 341 and 339 [$M^+ - 59(CO{\cdot}CH_3)$]. The n.m.r. spectrum exhibited signals at τ 6.29 and 6.18 which are assigned to the methoxy and methoxycarbonyl protons: since the integral is *ten* protons the hidden proton is assigned to the C-3β proton: if substitution were at C-3 the C-4 proton would been observed at *ca.* τ 5.2. The ease of dehydrobromination of (33; R = Br) with warm pyridine to yield (1; $R^1 = R^2 =$ Me) confirms the *trans*-diaxial arrangement of the leaving atoms, and hence the structure (33).

Bromination of the more easily preparable methyl 2β-(2,6-dimethoxybenzoyl)-7-oxabicyclo[2.2.1]heptane-3β-carboxylate (8; $R^1 =$ H, $R^2 =$ Me) or of the *trans*-isomer (12) gave the same methyl 2α-bromo-2β-(2,6-dimethoxybenzoyl)-7-oxabicyclo[2.2.1]heptane-3β-carboxylate (8; $R^1 =$ Br, $R^2 =$ Me). The mass spectrum showed twin peaks at *m/e* 400 and 398, 369 and 367, and 341 and 339 (of equal intensity) similar to those shown by the isomer (33). In agreement with the stereochemical assignments at C-2 and C-3, dehydrobromination of (8; $R^1 =$ Br, $R^2 =$ Me) to yield (1; $R^1 = R^2 =$ Me) occurred only under vigorous conditions (lithium carbonate–dimethylformamide). These results are compatible with the brominations proceeding through the enol of the ketone and with the stereochemistry of the resultant bromoketone being determined by steric approach control. Thus the enols of (8; $R^1 =$ H, $R^2 =$ Me) and of (12) will be essentially equivalent with approach of bromonium ion proceeding from the less-hindered *endo*-face of the molecule to yield the same product (8; $R^1 =$ Br, $R^2 =$ Me) in each case. With ketone (11; R = Me) however, the bulky *endo*-methoxycarbonyl group will hinder *endo*-approach of the halogen which will thus be introduced on the *exo*-face of the enol to yield (33). Bromination of (11; R = Me) proceeded more readily than bromination of the isomer, (8; $R^1 =$ H, $R^2 =$ Me).

Bromination of methyl 2β-(2,6-dimethoxybenzoyl)-7-oxabicyclo[2.2.1]heptane-3β-carboxylate (8; $R^1 =$ H, $R^2 =$ Me) using copper(II) bromide [8] in ethyl acetate

resulted in a complex mixture; the major component is formulated as (34; R = Br) on the basis of the usual criteria.

Consequent upon our proposed mechanism for the production of (15; R = Me) from (1; $R^1 = R^2 =$ Me) by hydrogenolysis (*q.v.*) a solution of the 7-oxabicyclo-[2.2.1]heptane (11; R = Me) in methanol was refluxed for 1 h with toluene-*p*-sulphonic acid to yield the same ester (15; R = Me). A longer reaction period gave the C-3 epimer (34; R = H), which was obtained directly from (11; R = Me) by treatment with toluene-*p*-sulphonic acid during 1 h. This rearrangement appears to be critically dependent upon the solvent: thus whilst rearrangement occurs in methanol it fails in ethyl acetate; in benzene or acetic acid only epimerisation to (12) occurs (see above).

Bromination of the acetate (35; R = H) gave a monobromo-derivative, which on the basis of spectral evidence, and by analogy with the formation of (8; R^1 = Br, R^2 = Me) from (8; R^1 = H, R^2 = Me) is formulated as (35; R = Br). Attempts to dehydrobrominate (35; R = Br) failed.

Treatment of the αβ-unsaturated ketone (34; R = H) with osmium tetraoxide gave a *cis*-1,2-diol which is formulated as (36; R = H) on the basis that oxidation would occur on the α-face, *i.e.* opposite to the methoxycarbonyl and acetoxy-residues. The coupling constant (9 Hz) of the doublet due to the C-3 proton indicates that the angle between the C-3 and C-4 C–H bonds is small, whilst the $W_{\frac{1}{2}}$ value (>14 Hz) for the C-4 proton signal indicates the axial orientation of this bond. In accord with these conclusions, the acetate (36; R = Ac) could not be dehydrated to (37) with thionyl chloride–pyridine or phosphorus pentaoxide–benzene. Numerous attempts to convert the diol (36; R = H) into the corresponding ketol, with a wide variety of oxidising agents, failed, in contrast to the behaviour of the stereoisomer (18). Oxidation of the acetonide (38) using trityl tetrafluoroborate [9] regenerated the parent diol (36; R = H).

In additional attempts to functionalise the double bond in (34; R = H), this αβ-unsaturated ketone was converted into the epoxide (39). Oxidation of the acetate of (34; R = H) with chromyl chloride [10] did not furnish the α-chloroketone, but the chlorophenol (40).

Epoxidation of (1; $R^1 = R^2 =$ Me) gave the derivative (41; $R^1 = R^2 =$ Me). This epoxide system was very inert; thus the action of boron trichloride gave (41; R^1 = H, R^2 = Me), whilst reduction with lithium aluminium hydride formed the triol (42) which was cleaved with periodic acid to yield 2,6-dimethoxybenzaldehyde.

EXPERIMENTAL

N.m.r. spectra were determined at 60 MHz in deuteriochloroform (unless otherwise indicated); i.r. spectra were obtained in a Nujol mull. Mass spectra were observed using an A.E.I. 902 mass spectrometer at 70 E.V.

2β-(2,6-Dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]*heptane* (8; R^1 = H, R^2 = Me).—A solution of 7-oxabicyclo[2.2.1]heptane-2β,3β-dicarboxylic anhydride [11] (2.1 g) in tetrahydrofuran (50 ml) and ether (200 ml) at 0 °C was treated dropwise with a solution of 1-lithio-2,6-dimethoxybenzene (12 g) in tetrahydrofuran (20 ml) and ether (100 ml) under nitrogen. After ½ h (stir) at 0 °C the reaction mixture was added to an excess of saturated ammonium chloride solution, containing 0.1% hydrochloric acid. The organic phase was separated, washed with 2N-sodium hydrogencarbonate and the washings acidified, and extracted with ethyl acetate to yield *2β-(2,6-dimethoxybenzoyl)-7-oxabicyclo*[2.2.1]*heptane-3β-carboxylic acid* (1.8 g) as needles, m.p. 184—185 °C, from ether–chloroform (Found: C, 62.6; H, 5.9. $C_{16}H_{18}O_6$ requires C, 62.7; H, 5.9%).

Esterification of this acid with diazomethane gave (quantitatively) *2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo*[2.2.1]*heptane* (1.2 g) as needles, m.p. 174 °C from ether; $\nu_{max.}$ 1 738 (ester C=O), 1 698 cm^{-1} (Ar C=O) (Found: C, 63.7; H, 6.2%; M^+ 382. $C_{17}H_{20}O_6$ requires C, 63.7; H, 6.3%; *M* 320). The n.m.r. spectrum exhibited signals at τ 8.8—7.9 (m, 5-/6-H 4 H), 7.19 (d, *J* 9 Hz, 3-H, 1 H), 6.32 (s, $OCOCH_3$, 3 H), 6.4—6.1 (d, 2-H, H), 6.18 (s, 2 × OCH_3, 6 H), 3.41 (d, *J* 8 Hz, 3'-/5'-ArH, 2 H), and 2.69 (t, *J* 8 Hz, 4'-H, 1 H).

2α-(2,6-Dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo[2.2.1]*heptane* (11; R = Me).—(a) Hydrogenation at normal temperature and pressure of a solution of 2-(2,6-dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo-[2.2.1]hept-2-ene [2] (0.6 g) in acetone (25 ml) with 5% palladium–charcoal occurred during ½ h, to yield *2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo*[2.2.1]-*heptane* (0.6 g) which formed prisms, m.p. 115—116 °C from light petroleum (b.p. 40—60 °C); $\nu_{max.}$ 1 735 (ester C=O), 1 688 cm^{-1} (Ar-C=O). The n.m.r. spectrum of (11; R =Me) included signals at τ 8.6—7.7 (m, 5-/6-H, 4 H), 6.92 (q, *J* 5Hz, *J* 11 Hz, 3-methine H, 1 H), 6.39 ($OCOCH_3$, 3 H), 6.20 (s, 2 × OCH_3, 6 H), 5.86 (q, *J* 11 Hz, *J* 5 Hz, 2-methine H, 1 H), 5.27 (m, 4- and 1-bridgehead H, 2 H), 3.45 (d, Ar*H*, *J* 8 Hz, 2 H), and 2.71 (t, *J* 8 Hz, 4'-H, 1 H) (Found: C, 63.9; H, 6.2%; M^+ 320. $C_{17}H_{20}O_6$ requires C, 63.7; H, 6.3%; *M* 320).

(b) Prepared as for the β-isomer from excess of 1-lithio-2,6-dimethoxybenzene and 7-oxabicyclo[2.2.1]heptane-2α,3α-dicarboxylic anhydride [12] (2.2 g), *2α-(2,6-dimethoxybenzoyl)-7-oxabicyclo*[2.2.1]*heptane-3α-carboxylic acid* (1.6 g) formed plates, m.p. 187 °C, from light petroleum (b.p. 40—60 °C) (Found: C, 62.6; H, 5.9. $C_{16}H_{18}O_6$ requires C, 62.7; H, 5.9%).

The methyl ester (prepared with diazomethane) was identical (i.r., n.m.r., m.p. and mixed m.p.) with that prepared by method (*a*).

2α-(2,6-Dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]*heptane* (12).—(*a*) A solution of 2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (1 g) and sodium acetate (10 g) in acetic acid (50 ml) was refluxed for 6 h. Purification of the product from benzene–light petroleum (b.p. 60—80 °C) gave *2α-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo*[2.2.1]*heptane* (0.96 g) as prisms, m.p. 63 °C, $\nu_{max.}$ 1 735 (ester C=O) and 1 685 cm^{-1} (ArC=O) (Found: C, 63.9; H, 6.3. $C_{17}H_{20}O_6$ requires C, 63.7; H, 6.3%).

(*b*) A solution of 2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (1 g) in benzene (50 ml) containing toluene-*p*-sulphonic acid (0.3 g) was refluxed during 72 h. Purification of the product by chromatography on Florisil from benzene–ethyl acetate (49 : 1) gave

(i) the parent compound (0.43 g) (identical by i.r., n.m.r., m.p. and mixed m.p.) and (ii) 2α-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (0.2 g), identical, i.r., n.m.r., mass spectrum, t.l.c., m.p. and mixed m.p. 62 °C, with the product from method (*a*). The n.m.r. spectrum had signals at τ 8.6—7.8 (m, 5-/6-H, 4 H), 6.84 (d, *J* 5 Hz, 3-methine H, 1 H), 6.30 (s, OCOC*H*$_3$, 3 H), 6.22 (s, 2 × OC*H*$_3$, 6 H), 5.83 (t, *J* 5 Hz, 2-methine H, 1 H), 5.40—5.00 (m, 4- and 1-bridgehead H, 2 H), 3.43 (d, *J* 8 Hz, Ar*H*, 2 H), and 2.72 (t, *J* 8 Hz, 4′-Ar*H*, 1 H).

The Cleavage of 2α-(2,6-*Dimethoxybenzoyl*)-3α-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (11; R = Me) *with Boron Trichloride*.—(a) A solution of this bicycloheptane (0.35 g) in dichloromethane (30 ml) was treated with a solution of boron trichloride (1 g) in dichloromethane (5 ml) at 0 °C during 18 h. After the addition of an excess of 10% sodium acetate solution and extraction with chloroform the product was purified from dichloromethane to yield 1,7α-*dihydroxy*-8β-*methoxycarbonyl*-5aα,5,6,7,8,8aα-*hexahydroxanthone* (23; R = H) (0.15 g) which formed stout prisms, m.p. 217 °C; the i.r. spectrum showed bands at ν$_{max.}$ 3 530 (OH), 1 713 (ester carbonyl), 1 658 (hydrogen-bonded aryl carbonyl) and 1 625 cm^{-1} (aryl double bonds). The n.m.r. spectrum included signals at τ 8.5—7.7 (m, 5- and 6-CH$_2$, 4 H), 7.71 (s, O*H*, 1 H, exchangeable with D$_2$O), 7.44 (m, 8-H, 1 H), 6.71 (m, 8a-H, 1 H), 6.14 (s, COOC*H*$_3$, 3 H), 6.3—5.8 (m, 5a- and 7-H, 2 H), and −1.27 (s, hydrogen-bonded phenolic proton, 1 H) (Found: C, 61.3; H, 5.5%; *M*$^+$ 292. C$_{15}$H$_{16}$O$_6$ requires C, 61.6; H, 5.5%; *M* 292). 1,7α-*Diacetoxy*-8β-*methoxycarbonyl*-5aα,5,6,7,8,8aα-*hexahydroxanthone* formed cubes, m.p. 153 °C from ether (Found: C, 60.9; H, 5.4. C$_{19}$H$_{20}$O$_8$ requires C, 60.1; H, 5.4%): ν$_{max.}$ 1 755 (acetate), 1 738 (ester), and 1 690 cm^{-1} (aryl C=O).

The di-*O*-acetate (23; R = Ac) showed signals in the n.m.r. spectrum at τ 7.95 (s, OCOC*H*$_3$, 3 H), 7.78 (s, Ar-OCOC*H*$_3$, 3 H), 7.34 (t, *J* 10.5 Hz, 8-H, H), 6.72 (q, *J* 1.5 Hz, 8 Hz, 8a-H, 1 H), and 6.27 (s, COOC*H*$_3$, 3 H).

Purification by p.t.l.c. of the residue from the mother-liquors gave 1α-*chloro*-4β-*hydroxy*-2α-(2-*hydroxy*-6-*methoxybenzoyl*)-3α-*methoxycarbonylcyclohexane* (13; R = H) (0.2 g) as pale yellow needles, m.p. 137—138 °C from benzene–ether; ν$_{max.}$ 3 520 (OH), 1 742 (ester C=O), and 1 628 cm^{-1} (aryl C=O) (Found: C, 57.1; H, 5.7%; *M*$^+$ 342.086 7. C$_{16}$H$_{19}$ClO$_6$ requires C, 56.1; H, 5.6%; *M* 342.087 0). The 2α,4β-*di*-O-*acetate* (13; R = Ac), formed quantitatively, separated from ethyl acetate–ether as prisms, m.p. 135 °C, ν$_{max.}$ 1 770 (acetate C=O), 1 740 (ester C=O), and 1 690 cm^{-1} (aryl C=O) (Found: C, 56.3; H, 5.4; *M*$^+$ 426. C$_{20}$H$_{23}$ClO$_8$ requires C, 56.3; H, 5.4%; *M* 426).

A solution of this di-*O*-acetate (40 mg) in pyridine (1 ml) heated at 100 °C during 30 min, gave 4β-*acetoxy*-2-(2-*acetoxy*-6-*methoxybenzoyl*)-3-*methoxycarbonylcyclohexene* (14) (35 mg) which formed plates, m.p. 118—120 °C from ether (Found: C, 61.6; H, 5.8%; *M*$^+$ 390. C$_{20}$H$_{22}$O$_8$ requires C, 61.5; H, 5.7%; *M* 390). The n.m.r. spectrum of (14) has signals at τ 7.95 (s, CH·OCOC*H*$_3$, 3 H), 7.78 (s, Ar-OCOC*H*$_3$, 3 H), 6.26 (s, OCOC*H*$_3$, 3 H), 6.22 (s, OC*H*$_3$, 3 H), and 4.64 (m, $W_{\frac{1}{2}}$ ~ 15 Hz, 4-H, 1 H).

(b) Treatment of the title compound (0.23 g) in dichloromethane with boron trichloride as in (a) during 10 min at −70 °C gave 2α-(2-*hydroxy*-6-*methoxybenzoyl*)-3α-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (0.17 g) as yellow plates, m.p. 104 °C from acetone (Found: C, 62.8; H, 5.7%; *M*$^+$ 306. C$_{16}$H$_{18}$O$_6$ requires C, 62.7; H, 5.9%; *M* 306).

2-(2,6-*Dimethoxybenzoyl*)-4β-*hydroxy*-3α-*methoxycarbonylcyclohexene* (15; R = H).—A solution of 2-(2,6-dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo[2.2.1]hept-2-ene (1.6 g) in acetone (100 ml) containing 60% perchloric acid (0.5 ml) and 5% palladium–charcoal (0.15 g) was hydrogenolysed during 12 min: uptake of hydrogen was 113 ml. Purified from ether–methanol 2-(2,6-*dimethoxybenzoyl*)-4β-*hydroxy*-3α-*methoxycarbonylcyclohexene* (1.6 g) formed prisms, m.p. 126 °C; ν$_{max.}$ 3 420 (OH), 1 728 (ester C=O), and 1 655 cm^{-1} (C=O). The n.m.r. spectrum of (15; R = H) has signals at τ 6.38 (m, 3-H, 1 H), 6.25 (s, COC*H*$_3$, 2 × OC*H*$_3$, 9 H), 5.76 (m, 4-H, 1 H), 3.44 (d, *J* 8 Hz, 3′- and 5′- aryl H, 2 H), 3.30 (m, 1-H, 1 H), and 2.70 (t, 8 Hz, 4′-aryl H, 1 H) (Found: C, 63.5; H, 6.2%; *M*$^+$ 320. C$_{17}$H$_{20}$O$_6$ requires C, 63.7; H, 6.3%; *M* 320).

The 4β-*O*-*acetate* formed (quantitatively) prisms, m.p. 97 °C from ether–cyclohexane (Found: C, 62.8; H, 6.2. C$_{19}$H$_{22}$O$_7$ requires C, 63.0; H, 6.1%).

The acetate (15; R = Ac) shows signals *inter alia* in the n.m.r. spectrum at τ 7.95 (s, OCOC*H*$_3$, 3 H), 6.24 (s, 2 × OC*H*$_3$, 6 H), 6.28 (s, COOC*H*$_3$, 3 H), 4.60 (q, *J* 5 Hz, 4-H, 1 H), and 3.27 (m, 1-H, 1 H). Hydrogenation (15 min) of this acetate (0.3 g) dissolved in acetone (25 ml) with 5% palladium–charcoal (0.03 g) gave 4β-*acetoxy*-2β-(2,6-*dimethoxybenzyl*)-3α-*methoxycarbonylcyclohexane* (17; R = Ac), which formed cubes, m.p. 125 °C from ether; ν$_{max.}$ 1 740 (ester C=O), 1735 (acetate C=O), and 1 700 cm^{-1} (C=O) (Found: C, 62.4; H, 6.3%; *M*$^+$ 364. C$_{19}$H$_{24}$O$_7$ requires C, 62.6; H, 6.6%; *M* 364). The n.m.r. spectrum showed signals at τ 7.95 (s, OCOC*H*$_3$, 3 H), 7.02 (q, *J* 6.5 Hz, 3-H), 6.46 (m, 2-H, 1 H), 6.33 (s, COOC*H*$_3$, 2 × OC*H*$_3$, 9 H), and 4.54 (m, 4-H, 1 H, $W_{\frac{1}{2}}$ > 12 Hz).

Hydroxylation of 4β-*Acetoxy*-2-(2,6-*dimethoxybenzoyl*)-3α-*methoxycarbonylcyclohexene*.—A solution of 2-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-4β-acetoxycyclohexene (1.4 g) in pyridine (50 ml) was treated with osmium tetraoxide (1 g) and the mixture stirred for 24 h. After addition of a solution of sodium hydrogensulphite (1.8 g) in water (30 ml) and pyridine (20 ml) stirring was continued for a further 15 min. The product was extracted with chloroform. Purification from dichloromethane–ether gave (a) 4β-*acetoxy*-2α-(2,6-*dimethoxybenzoyl*)-1β,2β-*dihydroxy*-3α-*methoxycarbonylcyclohexane* (18) (1.2 g) as prisms, m.p. 180—182 °C; ν$_{max.}$ 3 575 (OH), 1 753 (ester C=O), 1 723 (acetate C=O), and 1 698 cm^{-1} (C=O). The n.m.r. spectrum showed signals at τ 7.97 (s, OCOC*H*$_3$, 3 H), 7.12 (b, 1- or 2-OH, 1 H, exchangeable with D$_2$O), 6.90 (d, *J* 10.5 Hz, 3-H, 1 H), 6.27 (s, COOC*H*$_3$, 3 H), 6.23 (s, 2 × OC*H*$_3$, 6 H), 5.97 (m, 1-OH, 1 H, $W_{\frac{1}{2}}$ < 10 Hz), 4.65 (s, 1- or 2-OH, 1 H, exchangeable with D$_2$O), and 4.4—4.0 (m, 4-OH, 1 H, $W_{\frac{1}{2}}$ > 12 Hz) (Found: C, 57.5; H, 6.4%; *M*$^+$ 396. C$_{19}$H$_{24}$O$_9$ requires C, 57.6; H, 6.1%; *M* 396) and (b) 4β-*acetoxy*-1α,2α-*dihydroxy*-2β-(2,6-*dimethoxybenzoyl*)-3α-*methoxycarbonylcyclohexane* (19) (0.18 g) as stout prisms, m.p. 157 °C; ν$_{max.}$ 3 510 (OH), 3 480 (OH), 1 750 (ester C=O), 1 738 (acetate C=O), and 1 700 cm^{-1} (aryl C=O) (Found: C, 57.4; H, 6.2%; *M*$^+$ 396). The n.m.r. spectrum includes signals at τ 8.0 (s, OCOC*H*$_3$, 3 H), 6.68 (d, *J* 6 Hz, 1-OH, 1 H, exchangeable with D$_2$O), 6.32 (s, OCOC*H*$_3$, 3 H), 6.17 (s, 2 × OC*H*$_3$, 6 H), 5.52 (d, *J* 1.3 Hz, 1-OH, 1 H, exchangeable with D$_2$O), and 4.66 (m, 4-OH, 1 H, *W* > 15 Hz).

A solution of the 1β,2β-diol (0.2 g) in acetone (70 ml) was treated during 5 min dropwise at 0 °C (stir) with *freshly* prepared Jones' reagent (0.5 ml): after a further 25 min, the excess of reagent was discharged by the addition of methanol, and the product extracted with chloroform. Purific-

ation by chromatography on silica from chloroform–ethyl acetate (17 : 3) gave 4β-*acetoxy*-2α-(2,6-*dimethoxybenzoyl*)-2β-*hydroxy*-3α-*methoxycarbonylcyclohexanone* (20) (0.07 g) as prisms, m.p. 171—173 °C from ether–dichloromethane; $\nu_{max.}$ 3 455 (OH), 1 743 (ester C=O), 1 735 (acetate C=O), 1 730 (cyclohexanone C=O), and 1 719 cm^{-1} (aryl C=O) (Found: C, 57.8; H, 6.0%; M^+ 394. $C_{19}H_{22}O_9$ requires C, 57.9; H, 5.6%; *M* 394), τ 7.98 (s, $OCOCH_3$, 3 H), 7.13 (d, *J* 11 Hz, 3-CH, 1 H), 6.30 (s, 2 × OCH_3, 6 H), 6.25 (s, $COOCH_3$, 3 H), 5.19 (s, 2-OH, 1 H, exchangeable with D_2O), and 3.69 (m, 4-CH, 1 H, $W_{\frac{1}{2}} > 13$ Hz).

Treatment of a solution of this cyclohexanone (55 mg) in pyridine (2 ml) at −5 °C with thionyl chloride (1 ml) during 6 h, gave *methyl* 2-(2,6-*dimethoxybenzoyl*)-3-*hydroxybenzoate* (22) (25 mg) as plates, m.p. 126—127 °C from dichloromethane (Found: M^+ 316. $C_{17}H_{16}O_6$ requires *M*, 316), $\nu_{max.}$ 1 728 (ester C=O) and 1 630 cm^{-1} (aryl C=O); τ 6.76 (s, $COOCH_3$, 3 H), 6.28 (s, 2 × OCH_3, 6 H), and 5.5—2.4 (m, aryl-H, 6 H).

The Cleavage of 2β-(2,6-*Dimethoxybenzoyl*)-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (8; R^1 = H, R^2 = Me) *with Boron Trichloride*.—(a) A solution of this bicyclo[2.2.1]-heptane (1 g) in dichloromethane (25 ml) was treated with a solution of boron trichloride (3.4 g) in dichloromethane (17 ml) at −70 °C. The temperature was allowed to rise to 0 °C during 3 h, when an excess of 10% sodium acetate solution was added. Purification of the extract (chloroform) from acetone–ether gave 4β-*hydroxy*-2β-(2-*hydroxy*-6-*methoxybenzoyl*)*cyclohexane*-1β,3β-*carbolactone* (24; R = H) (0.3 g) as stout prisms, m.p. 225 °C; $\nu_{max.}$ 2 440 (OH), 1 753 (γ-lactone), and 1 615 cm^{-1} (aryl C=O) (Found: C, 61.8; H, 5.6%; M^+ 292. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.52%; *M* 292).

Purification by p.t.l.c. of the residues from the mother liquors gave 1,7α-*dihydroxy*-8a-*methoxycarbonyl*-5aα,5,6,7,8,-8aβ-*hexahydroxanthone* (25; R = H) (0.6 g) as needles, m.p. 168—169 °C from acetone–ether (Found: C, 61.9; H, 5.5%; M^+ 292. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.5%; *M* 292). This xanthone exhibits an intense green colour with ferric chloride in alcohol. The n.m.r. spectrum exhibited signals at τ 7.30 (s, OH, 1 H, exchangeable with D_2O), 6.25 (s, $COOCH_3$, 3 H), 6.4—5.8 (m, 7-, 8a-H, 2 H; $W_{\frac{1}{2}} > 15$ Hz), and −1.47 (s, hydrogen-bonded phenolic H, 1 H).

The *di*-O-*acetate* formed prisms, m.p. 161 °C from ether; $\nu_{max.}$ 1 758 (acetate C=O), 1 740 (acetate C=O), 1 720 (ester C=O), and 1 690 cm^{-1} (aryl C=O) (Found: C, 60.4; H, 5.4. $C_{19}H_{20}O_8$ requires C, 60.6; H, 5.4%).

(b) Treatment of the title bicycloheptane (0.25 g) at −70 °C with boron trichloride in dichloromethane during 20 min, gave 2β-(2-*hydroxy*-6-*methoxybenzoyl*)-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (0.2 g) as yellow prisms, m.p. 144 °C from acetone (Found: C, 62.8; H, 5.8%; M^+ 306. $C_{16}H_{18}O_6$ requires C, 62.7; H, 5.9%; *M* 306).

Cleavage of Dimethyl 7-*Oxabicyclo*[2.2.1]*heptane*-2β,3β-*dicarboxylate* (28) *with Boron Trichloride*.—A solution of boron trichloride (1.6 g) in dichloromethane (8 ml) was added slowly to a solution of the title ester (1 g) in dichloromethane (50 ml) at −70 °C. After 48 h, the product was isolated: 4α-*chloro*-2β-*methoxycarbonylcyclohexane*-1β,3β-*carbolactone* (29) (0.8 g) formed prisms, m.p. 69 °C from ether (Found: C, 49.6; H, 4.9%; M^+ 218. $C_9H_{11}ClO_4$ requires C, 49.5; H, 5.0%; *M* 218): $\nu_{max.}$ 1 788 (γ-lactone) and 1 738 cm^{-1} (ester C=O), τ 8.2—7.6 (m, 4-/5-H, 4 H), 6.71 (d, *J* 4.5 Hz, 1-H, 1 H), 6.47 (s, 2-H, 1 H), 6.22 (s, $COOCH_3$, 3 H), 5.38 (m, 6-H, 1 H, $W_{\frac{1}{2}} \sim 11$ Hz), and 4.88 (m, 3-H, 1 H, $W_{\frac{1}{2}}$ *ca.* 6 Hz).

The Cleavage of 2α-(2,6-*Dimethoxybenzoyl*)-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (12) *with Boron Trichloride*.—A solution of this bicyclo[2.2.1]heptane (0.75 g) in dichloromethane (25 ml) was treated with boron trichloride as for the previous bicycloheptanes. Purification of the product from acetone–ether gave 4α-*chloro*-1β-*hydroxy*-2α-(2-*hydroxy*-6-*methoxybenzoyl*)-3β-*methoxycarbonylcyclohexane* (31; R = H) as prisms (0.4 g), m.p. 161 °C; $\nu_{max.}$ 1 730 (ester C=O) and 1 630 cm^{-1} (aryl C=O) (Found: C, 56.2; H, 5.6%; M^+ 342. $C_{16}H_{19}ClO_6$ requires C, 56.1; H, 5.6%; *M* 342). The n.m.r. spectrum which showed signals at τ 7.8br (s, OH, 1 H, exchangeable with D_2O), 7.2—6.8 (m, 3-H, 1 H, $W_{\frac{1}{2}} > 16$ Hz), 6.60 (s, OCH_3, 3 H), 6.0—5.7 (m, 1-, 2-, and 4-H, 3 H), and −2.22br (s, Ar-OH, 1 H).

The *di*-*O*-*acetate* formed plates, m.p. 153 °C from ether; $\nu_{max.}$ 1 770 (acetate C=O), 1 740 (ester C=O), and 1 692 cm^{-1} (aryl C=O) (Found: C, 56.2; H, 5.3. $C_{20}H_{23}ClO_8$ requires C, 56.3; H, 5.4%). The di-*O*-acetate (31; R = Ac) showed n.m.r. signals at τ 8.25 (s, alkyl $OCOCH_3$, 3 H), 7.81 (s, Ar-$OCOCH_3$, 3 H), 7.05—6.30 (two superimposed multiplets, 2- and 3-H, 2 H), 6.38 (s, $COOCH_3$, 3 H), and 6.13 (s, OCH_3, 3 H).

Purification by p.t.l.c. of the mother-liquors remaining after the separation of (31; R = H) gave stout prisms, m.p. 119 °C, of 1,7α-*dihydroxy*-8a-*methoxycarbonyl*-5aα,5,6,7,8,-8aα-*hexahydroxanthone* (32; R = H) (0.25 g); $\nu_{max.}$ 3 530 (OH), 1 723 (ester C=O), and 1 640 cm^{-1} (aryl C=O) (Found: C, 61.8; H, 5.6%; M^+ 292. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.5%; *M* 292).

2α-*Bromo*-2β-(2,6-*dimethoxybenzoyl*)-3α-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (33).—A solution of bromine (0.2M, 5 ml) in acetic acid was added slowly (½ h) (stir) to a solution of 2α-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (0.32 g) in acetic acid (25 ml). After 15 min an excess of chloroform was added and the solution washed with sodium hydrogensulphite; an excess of solid sodium hydrogencarbonate was then added. The neutral solution gave 2α-*bromo*-2β-(2,6-*dimethoxybenzoyl*)-3α-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (33) as prisms (0.3 g), m.p. 160 °C from methanol (Found: C, 51.3; H, 4.7%; M^+ 400. $C_{17}H_{19}BrO_6$ requires C, 51.2; H, 4.8%; *M* 400).

Dehydrobromination of this ester was carried out as follows: (i) a solution of the bromo-ester (0.2 g) in pyridine (2.5 ml) was kept at 100 °C during ½ h, to yield 2-(2,6-dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo[2.2.1]-hept-2-ene (0.15 g ≡ 94%), identical with an authentic specimen. Purification from acetone–ether gave pale yellow rhombs, m.p. 93—94 °C; when a solution in methanol was seeded with a sample of m.p 114 °C the product of the higher m.p. was obtained and conversely: (ii) a solution of the bromo-ester (2 g) in dimethylformamide (20 ml) containing lithium carbonate (2 g) was refluxed in a stream of nitrogen for 3 h, to give the hept-2-ene (1.2 g ≡ 75%).

2α-*Bromo*-2β-(2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (8; R^1 = Br, R^2 = Me).— (a) A solution of bromine (5 ml, 0.2M) in acetic acid was added, during 30 min, to a stirred solution of 2α-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (0.32 g) in acetic acid (25 ml). After isolation in the normal manner 2α-*bromo*-2β-(2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (0.3 g ≡ 70%) formed prisms, m.p. 208—210 °C from methanol (Found: C, 51.3; H, 4.8%; M^+ 400. $C_{17}H_{19}BrO_6$ requires C, 51.2; H, 4.8%; *M* 400). The i.r. spectrum showed signals at $\nu_{max.}$ 1 740

(ester) and 1 708 cm^{-1} (aryl C=O); the n.m.r. spectrum contained signals at τ 6.19 (s, 2 × OCH_3, 6 H), 6.27 (s, $COOCH_3$, 3 H), 3.46 (d, *J* 9 Hz, aryl-H, 2 H), 2.71 (b, *J* 9 Hz, aryl-H, H), and 6.98 (s, 2-H, 1 H).

(b) Phenyltrimethylammonium perbromide (3.76 g) was added gradually to a suspension of 2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (3.2 g) in tetrahydrofuran (250 ml) at −5 °C. After 4 h the solid was collected and washed with tetrahydrofuran. The filtrate and washings were evaporated *in vacuo* to 50 ml and then added to an excess of saturated sodium hydrogencarbonate and sodium dithionite solutions. The mixture was extracted with chloroform to yield the 2α-bromo-derivative (3 g ≡ 75%), identical with that prepared in (a).

6ξ-*Bromo*-2-(2,6-*dimethoxybenzoyl*)-4β-*hydroxy*-3β-*methoxycarbonylcyclohex*-1-*ene* (34; R = Br).—A solution of 2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane (3.2 g) in hot chloroform (75 ml) was added to a suspension of copper(II) bromide (4.5 g) in hot ethyl acetate (75 ml). The mixture was then refluxed until the green colour had been discharged (*ca.* 3 h). After cooling, the mixture was clarified, and the filtrate evaporated *in vacuo*. Purification of the residue from benzene gave 6ξ-*bromo*-2-(2,6-*dimethoxybenzoyl*)-4β-*hydroxy*-3β-*methoxycarbonylcyclohex*-1-*ene* (2.3 g) as prisms, m.p. 156 °C (Found: C, 51.4; H, 4.8%; M^+ 400. $C_{17}H_{19}BrO_6$ requires C, 51.2; H, 4.8%; *M* 400). The i.r. spectrum showed $\nu_{max.}$ 3 330br (OH), 1 725 (ester C=O), 1 670 (aryl C=O), and 1 600 cm^{-1} (Ar double bonds); the n.m.r. spectrum exhibited signals at τ 2.70 and 3.45 (A_2B system, *J* 7 Hz, Ar-H, 3 H), 3.39 (d, *J* 6 Hz, 1-H, 1 H), 5.00 (m, 6-H, 1 H), 5.7—5.3 (m, 4-H, 1 H)—this signal is coupled (double-resonance determination) to the signal at 5.90 (d, *J* 6 Hz, 3-H, 1 H), 6.23 (s, 2 × OCH_3 and $COOCH_3$, 9 H), 7.4—7.7 (m, 5-CH_2, 2 H), and 6.9—6.3br (s, OH, 1 H, exchangeable with D_2O).

2-(2,6-*Dimethoxybenzoyl*)-4β-*hydroxy*-3α-*methoxycarbonylcyclohex*-1-*ene* (15; R = H).—When a solution of 2α-2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-7-oxabicyclo-[2.2.1]heptane (2 g) in methanol (25 ml) containing toluene-*p*-sulphonic acid (0.1 g) was refluxed during 1 h; 2-(2,6-dimethoxybenzoyl)-3α-methoxycarbonyl-4β-hydroxycyclohex-1-ene (15; R = H) (1.7 g), identical (i.r., n.m.r., m.p. and mixed m.p.) with the previously obtained specimen was obtained.

2-(2,6-*Dimethoxybenzoyl*)-4β-*hydroxy*-3β-*methoxycarbonylcyclohex*-1-*ene* (34; R = H).—A solution of 2β-(2,6-dimethoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]-heptane (4 g) in methanol (150 ml) containing toluene-*p*-sulphonic acid (0.4 g) was refluxed during 24 h, to yield 2-(2,6-*dimethoxybenzoyl*)-4β-*hydroxy*-3β-*methoxycarbonylcyclohex*-1-*ene* (3 g) as needles, m.p. 164 °C from methanol (Found: C, 63.9; H, 6.5%; M^+ 320. $C_{17}H_{20}O_6$ requires C, 63.7; H, 6.3%; *M* 320).

The 4-O-*acetate* formed needles, m.p. 136 °C from ether–hexane (Found: C, 63.0; H, 6.3%; M^+ 362. $C_{19}H_{22}O_7$ requires C, 63.0; H, 6.1%; *M* 362).

2β-(2-*Acetoxy*-6-*methoxybenzoyl*)-2α-*bromo*-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (35; R = H).—The 2-O-*acetate* of 2β-(2-hydroxy-6-methoxybenzoyl)-3β-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane formed needles, m.p. 115—157 °C from methanol (Found: C, 62.1; H, 5.6. $C_{18}H_{20}O_7$ requires C, 62.1; H, 5.8%).

Bromination of this acetate (0.33 g) dissolved in tetrahydrofuran (50 ml) by the addition of phenyltrimethylammonium perbromide (0.36 g) at 0 °C during 18 h, gave 2β-(2-*acetoxy*-6-*methoxybenzoyl*)-2α-*bromo*-3β-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (0.3 g) as needles, m.p. 164 °C from benzene–light petroleum (b.p. 60—80 °C) (Found: C, 50.8; H, 4.5%; M^+ 428. $C_{18}H_{19}BrO_7$ requires C, 50.6; H, 4.5%; *M* 428).

4β-*Acetoxy*-1α,2α-*dihydroxy*-2β-(2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonylcyclohexane* (36; R = H).—A mixture of osmium tetraoxide (1 g), pyridine (15 ml), and 4β-acetoxy-2-(2,6-dimethoxybenzoyl)-3β-methoxycarbonylcyclohex-1-ene (1.4 g) was stirred for 24 h, at room temperature, and then for a further hour after addition of pyridine (20 ml), water (30 ml), and sodium hydrogensulphite (1.8 g). Extraction with chloroform gave 4β-*acetoxy*-1α,2α-*dihydroxy*-2β-(2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonylcyclohexane* (1.25 g) as needles, m.p. 194 °C from acetone (Found: C, 57.6; H, 6.2%; M^+ 396. $C_{19}H_{24}O_9$ requires C, 57.6; H, 6.1%; *M* 396). The i.r. spectrum has $\nu_{max.}$ 3 505 (OH), 1 738 (ester) and 1 700 cm^{-1} (ketone); the n.m.r. had signals at τ 7.01 (s, $OCOCH_3$, 3 H), 6.37 (s, $COOCH_3$, 3 H), 6.20 (s, 2 × OCH_3, 6 H), 5.35—5.00 (m, 1-H, 1 H), 4.90—4.50 (m, 4-H, 1 H), 3.70—3.44 (AB system, *J* 9 Hz, Ar-H, 3 H).

The 1α-*acetate* (36; R = Ac) formed needles, m.p. 152 °C from methanol (Found: C, 57.6; H, 5.8. $C_{21}H_{26}O_{10}$ requires C, 57.5; H, 6.0%).

Prepared from the 1α,2α-diol (0.3 g), toluene-*p*-sulphonic acid (0.03 g) and 2,2-dimethoxypropane (15 ml) in refluxing benzene (100 ml) with continuous removal of water during 4 h, 4β-*acetoxy*-2β-(2,6-*dimethoxybenzoyl*)-1α,2α-O-*isopropylidene*-3β-*methoxycarbonylcyclohexane* (38) (0.3 g) formed prisms, m.p. 134 °C from benzene–light petroleum (b.p. 60—80 °C) (Found: C, 60.3; H, 6.5%; M^+ 436. $C_{22}H_{28}O_9$ requires C, 60.5; H, 6.5%; *M* 436), $\nu_{max.}$ (devoid of OH absorption), 1 740 (ester), 1 705 cm^{-1} (ketone); τ 9.17 and 8.54 (s, 6 H), 7.95 (s, $OCOCH_3$, 3 H), 6.88 (d, *J* 5 Hz, 3-H, 1 H), 6.34 (s, $COOCH_3$, 3 H), 6.19 (s, 2 × OCH_3, 6 H), 5.61 (m, 1-H, 1 H), 4.63—4.26 (m, 4-H, 1 H), 3.42 (d, *J* 7 Hz, Ar-H, 2 H), and 2.46 (t, *J* 7 Hz, Ar-H, 1 H).

2β-(2,6-*Dimethoxybenzoyl*)-1α,2α-*epoxy*-4β-*hydroxy*-3β-*methoxycarbonylcyclohexane* (39).—A solution of 2-(2,6-dimethoxybenzoyl)-4β-hydroxy-3β-methoxycarbonylcyclohex-1-ene (0.5 g) in acetone (25 ml) and water (5 ml) containing potassium carbonate (0.4 g) was cooled to 0 °C and 30% hydrogen peroxide (5 ml) added. Next day the product was isolated with ethyl acetate and purified from methanol to yield 2-(2,6-*dimethoxybenzoyl*)-1α,2α-*epoxy*-4β-*hydroxy*-3β-*methoxycarbonylcyclohexane* (0.5 g) as prisms, m.p. 145 °C (Found: C, 60.8; H, 6.0%; M^+ 336. $C_{17}H_{20}O_7$ requires C, 60.7; H, 6.0%; *M* 336), $\nu_{max.}$ 3 520 (OH), 1 725 (ester), and 1 703 cm^{-1} (C=O); τ 7.05—6.70 (m, OH, 1 H, exchangeable with D_2O), 6.71 (m, 3-H, 1 H), 6.24 (s, $COOCH_3$, 3 H), 6.20 (s, 2 × OCH_3, 6 H), 6.10 (m, 1-H, 1 H), 6.0 (m, 4-H, 1 H, signal sharpens + D_2O), 3.45 and 2.69 (A_2B system, *J* 8 Hz, Ar-H, 3 H).

Prepared in the normal manner, the 4β-*acetate* formed prisms, m.p. 128 °C from methanol (Found: C, 60.4; H, 6.0%; M^+ 378. $C_{19}H_{22}O_8$ requires C, 60.3; H, 5.9%; *M* 378): $\nu_{max.}$ 1740 (acetate), 1 725 (ester) and 1 705 cm^{-1} (C=O).

4β-*Acetoxy*-2-(3-*chloro*-2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonylcyclohex*-1-*ene* (40).—To a solution of 4β-acetoxy-3β-methoxycarbonyl-2-(2,6-dimethoxybenzoyl)cyclohex-1-ene (1 g) in acetone (15 ml) cooled to −70 °C (in nitrogen) was added (stir) chromyl chloride (1.5 ml). The mixture was stirred at −70 °C for 1 h, and then at 0 °C for 1 h. Extraction with ethyl acetate gave 4β-*acetoxy*-2-(3-*chloro*-2,6-*dimethoxybenzoyl*)-3β-*methoxycarbonylcyclohex*-1-*ene*

(0.75 g) as yellow prisms, m.p. 156 °C from methanol (Found: C, 57.3; H, 5.3%; M^+ 398. $C_{19}H_{21}ClO_7$ requires C, 57.5; H, 5.3%; M 398): τ 8.25—7.3 (m, 5-H, 4 H), 7.91 (s, $OCOCH_3$, 3 H), 6.34 (s, 2 × OCH_3, $COOCH_3$, 9 H), 5.84 (m, H), 4.80 (m, H), 3.33 (d, J 9 Hz, H), 3.30 (m, H), 2.60 (d, J 9 Hz, H).

2ξ-(2,6-*Dimethoxybenzoyl*)-2ξ,3ξ-*epoxy*-3ξ-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (41; $R^1 = R^2 =$ Me).—2-(2,6-Dimethoxybenzoyl)-3-methoxycarbonyl-7-oxabicyclo-[2.2.1]hept-2-ene (2.1 g) dissolved in acetone (100 ml) and water (5 ml) containing potassium carbonate (0.4 g) was stirred at 0 °C during the slow addition of 30% hydrogen peroxide (10 ml). Next day, the solution was diluted with water (50 ml) and the crystalline precipitate collected. Purification from methanol gave 2ξ-(2,6-*dimethoxybenzyl*)-2ξ,3ξ-*epoxy*-3ξ-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (2 g) as needles, m.p. 141—142 °C (Found: C, 61.1; H, 5.4%; M^+ 334. $C_{17}H_{18}O_7$ requires C, 61.1; H, 45.4%; M 334).

Reduction of a solution of this epoxide (0.25 g) in ether (30 ml) with lithium aluminium hydride (0.6 g) at room temperature during 5 h, gave 2ξ-(2,6-*dimethoxyphenyl-hydroxymethyl*)-2ξ-*hydroxy*-3ξ-*hydroxymethyl*-7-*oxabicyclo*-[2.2.1]*heptane* (42) (0.4 g) as rhombs, m.p. 139—140 °C from aqueous methanol (Found: C, 61.9; H, 7.2. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.2%).

Cleavage of this triol (50 mg) in methanol (1.5 ml) with periodic acid (40 ml) in water (0.3 ml) gave 2,6-dimethoxybenzaldehyde, identified by its R_F value on t.l.c. with an authentic specimen.

Hydrolysis of the epoxy-ester (41; $R^1 = R^2 =$ Me) (0.25 g) in boiling 1N-potassium hydroxide (1.5 ml) during 10 min (in nitrogen) gave 2ξ-(2,6-*dimethoxybenzoyl*)-2ξ,3ξ-*epoxy*-7-*oxabicyclo*[2.2.1]*heptane*-3-*carboxylic acid* (41; R^1 = Me, R^2 = H) (0.2 g) as needles, m.p. 208 °C from methanol (Found: C, 60.1; H, 5.2%; M^+ 320. $C_{16}H_{16}O_7$ requires C, 60.0; H, 5.0%; M 320).

2ξ,3ξ-*Epoxy*-2ξ-(2-*hydroxy*-6-*methoxybenzoyl*)-3ξ-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane*.—A solution of the epoxide (41; $R^1 = R^2 =$ Me) (1.6 g) in dichloromethane (30 ml) was treated at −70 °C with a solution of boron trichloride (1 g) in dichloromethane (5 ml). After 10 min, the reaction was quenched by the addition of 10% aqueous sodium acetate (20 ml) (0 °C). Purified from ether, 2ξ,3ξ-*epoxy*-2ξ-(2-*hydroxy*-6-*methoxybenzoyl*)-3ξ-*methoxycarbonyl*-7-*oxabicyclo*[2.2.1]*heptane* (41; R^1 = H, R^2 = Me) (1.3 g) formed yellow prisms, m.p. 121 °C (Found: C, 59.9; H, 5.1. $C_{16}H_{16}O_7$ requires C, 60.0; H, 5.0%).

Prepared by the pyridine–acetic anhydride method the 2-O-*acetate* formed prisms, m.p. 124 °C from light petroleum (b.p. 40—60 °C) (Found: C, 59.4; H, 4.8%; M^+ 362. $C_{18}H_{18}O_8$ requires C, 59.7; H, 5.0%; M 362).

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