Calciferol and its Relatives. Part 19.[1] Synthetic Applications of Cyclic Orthoesters: Stereospecific Synthesis of a Bicyclic Alcohol related to the Vitamins D[2]

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Examples are described of Claisen rearrangements using cyclic orthoesters. Their synthetic potential is pointed out and illustrated by a synthesis of the optically active 1β-[(*R*)-2-hydroxy-1-methylethyl]-3aα,6,7,7aβ-tetrahydro-7aβ-methylindane (31),† a compound intended as an intermediate for syntheses of vitamin D_2 and 25-hydroxyvitamin D_3. In the key reaction between 2-hydroxy-4-methylcyclohex-3-enyl benzoate (7) and 2,2-diethoxy-4-methyltetrahydrofuran (24) the asymmetric centre C-1 of the final product (31) is set up stereospecifically by asymmetric induction with the required configuration, and this configuration is maintained throughout the synthesis.

MODERN variants of the Claisen rearrangement [3-5] permit the conversion of an allylic alcohol, A–OH, into the rearranged allyl derivative A′–CHR–CO_2H. If R is a saturated alkyl group this change can be simply accomplished by use of the orthoester $RCH_2{\cdot}C(OEt)_3$,[6] but when R is unsaturated the product of the rearrangement contains two double bonds which, during later stages of a synthetic scheme, may require to be functionalised differentially, a process which often presents difficulties. It appeared that such problems could be avoided by the use of cyclic orthoesters, such as (1) † and (5) and their derivatives, as reagents for Claisen rearrangements. The required reagents can be obtained from γ- or δ-lactones by Meerwein's [7] method, and so count among the most readily available orthoesters. Their mode of use can be illustrated by reference to the reaction of 2,2-diethoxytetrahydrofuran (1), with the allylic alcohol *rac*-(2) to give the γ-lactone *rac*-(3), which was characterised as the *p*-bromophenacyl ester *rac*-(4). In compounds such as (3) and (4) the double bond can conveniently be functionalised, and the primary hydroxy-group which has been set free by the lactone opening can then be used to potentiate an olefination reaction, or for chain extension in other ways. The present paper records the use of this approach in a stereospecific synthesis of the bicyclic alcohol (31), a compound from which it seemed likely that total syntheses of vitamin D_2, 25-hydroxyvitamin D_3, and related compounds could be effected.

As the synthesis was expected to follow a path similar to that taken in an earlier synthesis [6] of de-AB-cholestane derivatives we first explored the reactions of representative cyclic orthoesters with the allylic alcohol *rac*-(7).[8] With 2,2-diethoxytetrahydropyran (5) there was obtained in over 80% yield a single crystalline δ-lactone which, as shown elsewhere,[9] has the relative stereochemistry shown [*rac*-(8)]; the two new asymmetric centres were formed with complete stereospecificity. When the six-membered cyclic orthoester *rac*-(6) was used, approximately equal amounts of two stereoisomeric δ-lactones, *rac*-(9) and *rac*-(10), were obtained as expected; they were separated by chromatography. Reaction between the allylic alcohol *rac*-(7) and 2,2-diethoxytetrahydrofuran (1) gave a single crystalline γ-lactone, *rac*-(12), whose relative stereochemistry is assigned by analogy with that of *rac*-(8). It was formed in *ca.* 65% yield, considerably lower than those attained with the six-membered cyclic orthoesters. All these reactions must proceed through unsaturated cyclic acetal intermediates, similar to that

† All the structures in this paper capable of dissymmetry represent optically active compounds. Racemates are denoted by the prefix *rac*-; thus *rac*-(7) means the racemate corresponding to structure (7),

[1] Part 18, R. G. Harrison, B. Lythgoe, and P. W. Wright, *J.C.S. Perkin I*, 1974, 2654.

[2] Preliminary report, C. B. Chapleo, P. Hallett, B. Lythgoe, and P. W. Wright, *Tetrahedron Letters*, 1974, 847.

[3] A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv. Chim. Acta*, 1964, **47**, 2415.

[4] W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, 1970, **92**, 741.

[5] R. E. Ireland and R. H. Mueller, *J. Amer. Chem. Soc.*, 1972, **94**, 5897.

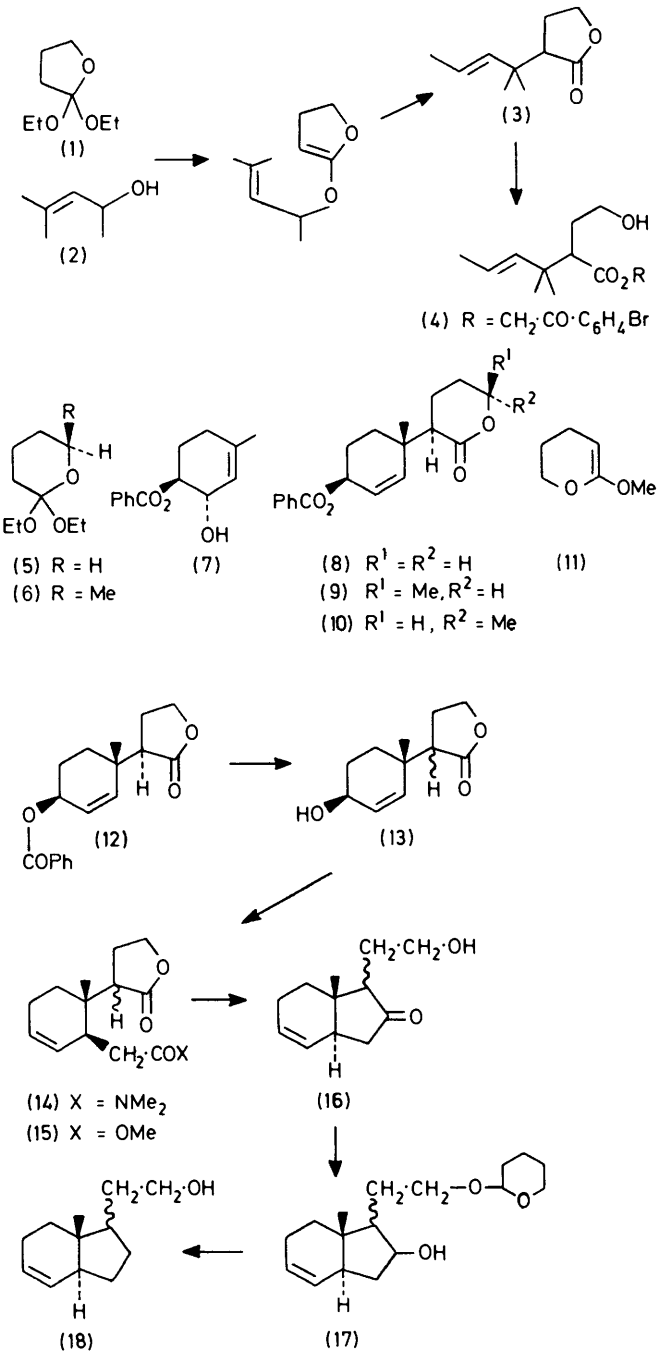
[6] I. J. Bolton, R. G. Harrison, and B. Lythgoe, *J. Chem. Soc.* (*C*), 1971, 2950.

[7] H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, 1956, **89**, 2060.

[8] I. J. Bolton, R. G. Harrison, B. Lythgoe, and R. S. Manwaring, *J. Chem. Soc.* (*C*), 1971, 2944.

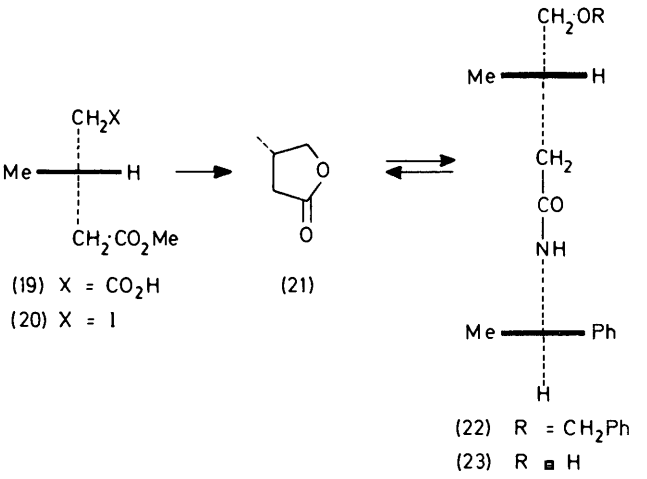
[9] B. Lythgoe and D. A. Metcalfe, *Tetrahedron Letters*, 1975, 2447.

(11) which McElvain [10] obtained by treatment of 2,2-dimethoxytetrahydropyran with aluminium t-butoxide. It may be significant that, although we were able to repeat the preparation of (11), attempts to obtain the



five-membered analogue by similar methods were unsuccessful.

Before undertaking the synthesis of the optically active compound (31), we explored that of the simpler model compound *rac*-(18), starting from the γ-lactone *rac*-(12). By using Zemplén methanolysis [11] the benzoate group was removed from this compound without opening the lactone ring. However, during this reaction, racemisation took place at the asymmetric centre adjacent to the lactonic carbonyl group, and the hydroxy-compound *rac*-(13) was obtained as a mixture of the two stereoisomeric forms indicated by the structure. Their



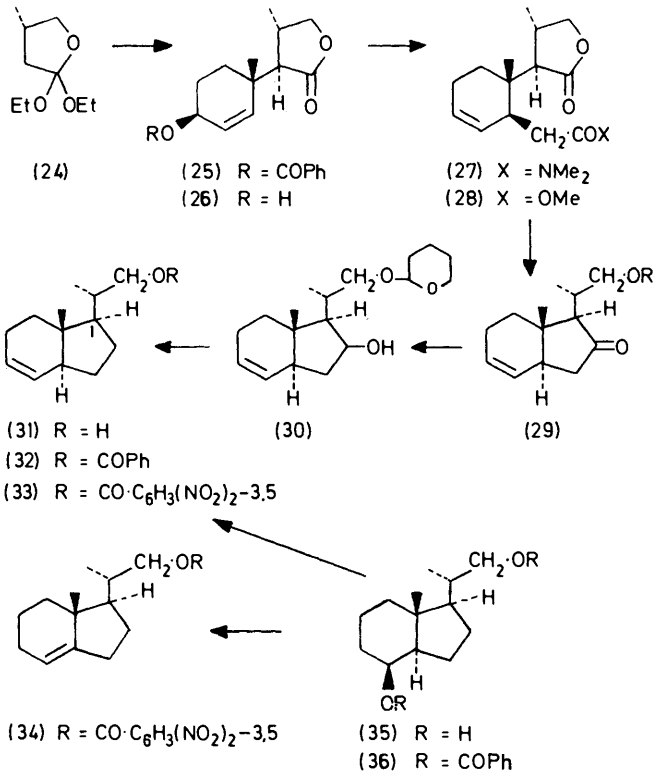
presence was apparent from the observation that re-benzoylation gave a crystalline mixture of two benzoate lactones, the n.m.r. spectrum of which showed the presence of the original benzoate *rac*-(12), and also of an isomer which exhibited different vinyl proton signals; whereas those of *rac*-(12) formed a broadened AB pattern, those of the isomer formed a broadened singlet. Reaction of the mixture *rac*-(13) with 1,1-dimethoxy-1-dimethylaminoethane [3] gave a mixture (*ca.* 1 : 1) of two dimethylamides, *rac*-(14), which were distinguishable by the positions of their quaternary CMe resonances, τ 8.89 and 9.09. The isomer responsible for the resonance at τ 8.89 was obtained pure and crystalline. The circumstance that compound (27) (see later) shows its quaternary CMe resonance at τ 8.89 suggests (but does not prove) that the crystalline dimethylamide in the present series had the configuration shown [*rac*-(14)] in which the hydrogen adjacent to the lactonic carbonyl group is α-oriented.

Vigorous alkaline hydrolysis of the pure dimethylamide (as also of the liquid mixture), followed by conversion of the resulting acids into methyl esters with diazomethane, gave a mixture of approximately equal amounts of two stereoisomeric methyl esters, *rac*-(15), which showed CMe resonances at τ 8.96 and 9.12. That responsible for the resonance at τ 9.12 was obtained pure and crystalline. In view of the fact that the ester (28) (see later) shows its quaternary CMe resonance at τ 8.94 it is probable (but not certain) that the component of *rac*-(15) which resonates at τ 8.96 has the α-configuration for the hydrogen adjacent to the lactonic

[10] S. M. McElvain and G. R. MacKay, *J. Amer. Chem. Soc.*, 1955, **77**, 5601.
[11] G. Zemplén and A. Kuns, *Ber.*, 1923, **56**, 1705.

carbonyl group, whilst the isomer obtained crystalline has the corresponding β-configuration. The mixture of esters was cyclised with potassium t-butoxide in benzene, and demethoxycarbonylation with toluene-*p*-sulphonic acid in acetic acid for 2 h gave a mixture (*ca.* 7 : 3) of the two stereoisomers *rac*-(16), which showed CMe resonances at τ 9.27 and 9.08, respectively. Increasing the period of the demethoxycarbonylation reaction to 16 h altered the ratio of the isomers to *ca.* 85 : 15, so it is probable that the major isomer, showing τ 9.27, represents the more stable 1β-form. This form was obtained as the pure crystalline *p*-nitrobenzoate, which showed its CMe signal at τ 9.22; the isomeric form (not obtained pure) showed this signal at τ 9.05.

The mixed hydroxy-ketones *rac*-(16) were converted into tetrahydropyranyl ethers and reduced with lithium aluminium hydride to give the secondary alcohols *rac*-(17). This mixture was then deoxygenated at C-2 by Barton's [12] method (treatment of the *S*-methyl



xanthate with tri-n-butyltin hydride). Removal of the tetrahydropyranyl group then gave a mixture of the two isomeric hydroxyethyl compounds *rac*-(18). The minor isomer showed its CMe resonance at τ 9.24, the major at τ 9.38. The latter, which is regarded as the 1β-isomer, was obtained as the homogeneous crystalline 3,5-dinitrobenzoate.

With the successful conclusion of these model experiments the way seemed clear for a similar synthesis of the C_{13} compound (31) from the optically active starting materials (7) [8] and (24). It was first necessary to work out a route to (*S*)-3-methylbutyrolactone (21) from which the orthoester (24) was to be prepared. By virtue of Linstead's work,[13] methyl hydrogen β-methylglutarate is readily available in both enantiomeric forms. The (+)-isomer, which has the *R*-configuration (19), was degraded to the iodide (20) by Barton's photochemical conversion [14] with lead tetra-acetate and iodine; acetolysis, hydrolysis, and cyclisation then gave the (—)-(3*S*)-lactone (21) in 53% overall yield from the starting half-ester. As we wished to be satisfied about the optical purity of the lactone (21) so obtained. we converted it, with benzyl chloride and powdered potassium hydroxide in toluene, into the benzyl ether-acid, and then, by reaction with (+)-(*R*)-α-phenylethylamine and *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) [15] into the benzyl ether phenylethylamide (22) (yield 96% from the lactone). Hydrogenolysis over palladium gave the hydroxy-phenylethylamide (23). This was crystallised to constant optical rotation and m.p., and then hydrolysed to give, after acidification, the regenerated lactone (21). This sample and the original sample had, within an error limit of 1.5%, the same optical rotation. Moreover, the equimolar mixture of diastereoisomeric forms, (22) and its (3*R*)-isomer, prepared from the lactone *rac*-(21) and (+)-α-phenylethylamine, showed two equally intense n.m.r. signals corresponding to the benzylic CH_2 group in each of the diastereoisomers, whereas the compound (22), prepared from the regenerated lactone (21), showed only one such signal; scrutiny of the n.m.r. spectrum at 90 MHz showed that, if the undesired isomer was present at all in the sample of compound (22), its content was less than 3%. The lactone (21) was then converted into the orthoester (24) in good yield by Meerwein's method.[7]

The orthoester (24) and the monobenzoate (7) reacted to give as sole product the homogeneous crystalline γ-lactone (25). The corresponding hydroxy-γ-lactone (26) was obtained by Zemplén methanolysis without racemisation at the centre adjacent to the lactonic carbonyl group; compound (26) was crystalline and homogeneous, and on re-benzoylation it gave exclusively the starting benzoate (25). We attribute this difference from the model series to the extra steric hindrance of the centre in question caused by the additional methyl group adjacent to it in the lactone ring. In the Meerwein–Eschenmoser reaction [3] the hydroxy-lactone (26) gave a single crystalline dimethylamide (27), which was hydrolysed to the corresponding acid without configurational change, and treatment with diazomethane then gave the crystalline methyl ester lactone (28) in *ca.* 40% yield from the starting monobenzoate (7).

[12] D. H. R. Barton and S. W. McCombie, *J.C.S. Perkin I*, 1975, 1574.
[13] R. P. Linstead, J. C. Lunt, and B. C. L. Weedon, *J. Chem. Soc.*, 1950, 3333.
[14] D. H. R. Barton, H. P. Faro, E. P. Serebryakov, and N. F. Woolsey, *J. Chem. Soc.*, 1965, 2438.
[15] B. Belleau, R. Martel, G. Lacasse, M. Ménard, N. L. Weinberg, and Y. G. Perron, *J. Amer. Chem. Soc.*, 1968, **90**, 823.

Cyclisation with potassium t-butoxide followed by removal of the methoxycarbonyl group gave the hydroxy-ketone (29). The n.m.r. data (see Experimental section) suggest the presence in this compound of two species; hemiacetal formation may be concerned. No stereochemical heterogeneity was involved; both the acetate and the *p*-nitrobenzoate were homogeneous; the latter was crystalline. Reduction of the tetrahydropyranyl derivative with lithium aluminium hydride gave the secondary alcohol (30). It was deoxygenated by Barton's method [12] to give, after removal of the protecting group, the alcohol (31), which was characterised as the homogeneous crystalline 3,5-dinitrobenzoate (33). It was obtained in a *ca.* 10% overall yield from the monobenzoate (7). An unexpected feature of this reaction series is the complete maintenance of stereochemistry at the future C-1 centre. Steric hindrance seems to be the principal factor operative between compounds (25) and (28); thereafter, a further important factor may be the superior stability of the form actually present.

In order to confirm the structure of the product from the foregoing synthesis its preparation from vitamin D_2 was undertaken. The C_{13} diol (35), first obtained by Inhoffen [16] from ozonolysis of dihydrovitamin D_2I, followed by reductive work-up with lithium aluminium hydride, was converted into its dibenzoate, which was subjected to controlled pyrolysis. The secondary benzoate group was eliminated in preference to the primary, and a 3 : 1 mixture of the benzoate (32) and its $\Delta^{8(14)}$-isomer was obtained. After saponification, and re-esterification with 3,5-dinitrobenzoyl chloride, chromatography on silica gel, impregnated with silver nitrate, followed by crystallisation, afforded both the Δ^{8}-isomer (33) and the $\Delta^{8(14)}$-isomer (34) in pure condition. The Δ^{8}-isomer was identical with the 3,5-dinitrobenzoate derived from the synthetic alcohol (31).

Further transformations of the alcohol (31) are in hand, and will be described in a later paper.

EXPERIMENTAL

N.m.r. data relate to solutions in $CDCl_3$, and, unless otherwise specified, $[\alpha]_D$ values to solutions in $CHCl_3$. T.l.c. and p.l.c. were carried out with Kieselgel GF_{254}. Light petroleum refers to the fraction b.p. 60—80 °C, unless otherwise specified.

The γ-Lactone, rac-(3).—4-Methylpent-3-en-2-ol (310 mg), 2,2-diethoxytetrahydrofuran (1 g), and propionic acid (20 mg) were heated at 135 °C in xylene (10 cm³) for 24 h; dry benzene (1 cm³) was added and removed by distillation after 1, 4, and 7 h. The solvent and excess of reagent were removed under reduced pressure; distillation at 145—150 °C and 12 mmHg gave (RS)-2-(1,1-*dimethylbut*-2-*enyl*)*butan*-4-*olide*, rac-(3) (281 mg), $\nu_{max.}$ (film) 1 147s, 1 174s, and 1 760s cm^{-1}, τ 4.54 (2 H, s, =CH), 5.82 (2 H, m, CH_2·OCO), 8.33 (3 H, m, *Me*CH=), 8.79 (3 H, s, Me_2C), and 8.85 (3 H, s, Me_2C) (Found: M^+, 168.115 794. $C_{10}H_{16}O_2$ requires M, 168.115 023). G.l.c. (6 ft column; 5% PEGA at 140 °C) showed >95% purity (retention time 10.8 min). The presence of a *trans*-double bond [$RCH_B{:}CH_A{\cdot}C(H_X)_3$] was shown by addition of $Eu(fod)_3$ to the $CDCl_3$ solution, with spin-decoupling experiments: τ 3.95 and 4.12 (1 H, d with allylic splitting, J_{AB} 15 Hz, H_A), 4.25 and 4.42 (1 H, 2q, J_{AB} 15, J_{BX} 5.5 Hz, H_B), 8.21 [3 H, d, J_{BX} 5.5 Hz, $C(H_X)_3$].

The lactone *rac*-(3) (70 mg) was kept at 50 °C for 2 h with aqueous 0.668N-sodium hydroxide; the solution was then cooled and brought to pH 6.7 with 0.1N-hydrochloric acid. *p*-Bromophenacyl bromide (120 mg) in ethanol (2 cm³) and water (1 cm³) was added, the solution was kept at 90 °C for 3 h and then cooled, and the product was isolated with ether. After p.l.c., crystallisation from ether–light petroleum gave the p-*bromophenacyl ester*, *rac*-(4) (70 mg), m.p. 78—79°, $\nu_{max.}$ 1 167s, 1 690s, 1 715s, and 3 545s cm^{-1} (Found: C, 56.45; H, 5.95; Br, 21.0. $C_{18}H_{23}BrO_4$ requires C, 56.4; H, 6.0; Br, 20.9%).

Reaction of the Cyclohexenol rac-(7) *and* 2,2-*Diethoxytetrahydropyran* (5).—The cyclohexenol (400 mg), 2,2-diethoxytetrahydropyran (900 mg), and propionic acid (10 mg) were heated together under reflux in dry xylene (10 cm³) under nitrogen for 24 h. Solvent and excess of orthoester were removed under reduced pressure, and the residue was chromatographed on silica gel (45 g); 2% ethyl acetate–benzene eluted material (457 mg) which crystallised from chloroform–light petroleum giving (2RS)-2-[(1SR,4SR)-4-*benzoyloxy*-1-*methylcyclohex*-2-*enyl*]*pentan*-5-*olide*, rac-(8) (407 mg), m.p. 127—129°, $\nu_{max.}$ (Nujol) 718s, 1 114s, 1 280s, 1 711s, and 1 741s cm^{-1}, τ 4.15 (2 H, dd, J 9.5 Hz, =CH), 4.3—4.6 (1 H, m, CH·O·COPh), 5.55—5.87 (2 H, m, O·C*H*$_2$·CH_2) and 8.68 (3 H, s, Me) (Found: C, 72.7; H, 6.95. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.05%).

Reaction of the Cyclohexenol rac-(7) *and* 2,2-*Diethoxy*-6-*methyltetrahydropyran* rac-(6).—The cyclohexenol (350 mg) was brought into reaction with the orthoester *rac*-(6) (850 mg) in the way described for the reaction with the orthoester (5). The crude product (437 mg) was chromatographed on Kieselgel (ethyl acetate–benzene). The less strongly adsorbed material crystallised from chloroform–light petroleum, giving the δ-*lactone* rac-(9) or -(10), m.p. 117—119°, τ 4.13 (2 H, dd, J 10 Hz, =CH), 4.3—4.65 (1 H, m, C*H*·O·COPh), 5.25—5.85 (1 H, m, O·C*H*Me), 8.65 (3 H, d, J 6 Hz, O·CH*Me*), and 8.68 (3 H, s, Me) (Found: C, 73.4; H, 7.2. $C_{20}H_{24}O_4$ requires C, 73.1; H, 7.4%). The more strongly adsorbed material crystallised from chloroform–light petroleum giving the δ-*lactone* rac-(10) or -(9), m.p. 110—112°, τ 4.13 (2 H, dd, J 10 Hz, =CH), 4.3—4.65 (1 H, m, C*H*·O·COPh), 5.35—5.95 (1 H, m, O·C*H*Me), 8.65 (3 H, d, J 6 Hz, O·CH*Me*), and 8.68 (3 H, s, Me) (Found: C, 73.1; H, 7.45%).

The γ-Lactone rac-(12).—The cyclohexenol *rac*-(7) (400 mg) and 2,2-diethoxytetrahydrofuran (850 mg) were heated together in boiling xylene (30 cm³) containing propionic acid (10 mg) for 16 h. Chromatography of the crude product on silica gave unchanged *rac*-(7) (40 mg), and (2RS)-2-[(1SR,4SR)-4-*benzoyloxy*-1-*methylcyclohex*-2-*enyl*]-*butan*-4-*olide*, rac-(12) (300 mg), m.p. 109—111°, $\nu_{max.}$ (Nujol) 712s, 1 118s, 1 274s, 1 600w, 1 704s, and 1 756 cm^{-1}, τ 1.95 (2 H, m, ArH), 2.52 (3 H, m, ArH), 4.1 (2 H, dd, J 9.5 Hz, =CH), 4.3—4.7 (1 H, m, C*H*·O·COPh), 5.4—6.15 (2 H, m, O·C*H*$_2$·CH_2), and 8.75 (3 H, s, Me) (Found: C, 71.85; H, 6.7. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%).

The Hydroxy-lactones rac-(13).—A solution of the benzoate *rac*-(12) (1.37 g) in dry methanol (37 cm³) containing sodium

[16] H. H. Inhoffen, G. Quinkert, S. Schütz, G. Friedrich, and E. Tober, *Chem. Ber.*, 1958, **91**, 781.

methoxide [from sodium (220 mg)] was kept at 20 °C for 18 h and then acidified to pH 5 with glacial acetic acid. The methanol was removed under reduced pressure, and the residue, dissolved in methanol (150 cm^3) and water (50 cm^3), was extracted thoroughly with light petroleum (b.p. 30—40 °C); the extracts were discarded. The aqueous methanolic phase was evaporated to remove the methanol, and the product, an oil (880 mg), was isolated with ether. It did not separate on t.l.c. (ethyl acetate), and had $\nu_{max.}$ (film) 1 760s and 3 400s cm^{-1}, τ 8.78 (3 H, s, Me).

Treatment of a portion (60 mg) of this material with benzoyl chloride and pyridine in the usual way gave the benzoate mixture as a crystalline solid (50 mg), m.p. 84—85° (from chloroform–light petroleum), which did not separate on t.l.c. (5% ethyl acetate–benzene) (Found: C, 71.85; H, 6.85. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%); $\nu_{max.}$ (Nujol) 708s, 1 710s, and 1 762s cm^{-1}, τ [in addition to the signals cited for the benzoate *rac*-(12)] 4.27br (s, =CH). A mixture (4 : 1) of this benzoate and *rac*-(12) had m.p. 84—95°.

The Amide-lactones rac-(14).—The hydroxy-lactone mixture *rac*-(13) (0.85 g) and 1-dimethylamino-1-methoxyethylene (1.95 g) were heated together under reflux under dry nitrogen in xylene (25 cm^3) for 16 h. Evaporation under reduced pressure and chromatography on neutral alumina (grade III; 75 g) (10% ethyl acetate in benzene; elution with ethyl acetate) gave the mixed amide-lactones *rac*-(14) (0.885 g) as an oil, $\nu_{max.}$ (film) 1 642s and 1 763s cm^{-1}, τ 4.1—4.7 (2 H, complex m, =CH), 5.6—6.1 (2 H, m, CH_2O), 6.93 (3 H, two close singlets, NMe), 7.02 (3 H, s, NMe), and 8.89 and 9.09 (3 H, s, Me). Crystallisation from chloroform–light petroleum gave (1SR,6SR)-6,NN-*trimethyl*-6-[(3RS)-2-*oxotetrahydrofuran*-3-*yl*]*cyclohex*-2-*enylacetamide*, rac-(14), as needles (0.237 g), m.p. 108—110°, $\nu_{max.}$ (Nujol) 1 650s and 1 763s cm^{-1}, τ 4.24 (1 H, d, *J* 11.5 Hz, =CH), 4.54 (1 H, d, *J* 11.5 Hz, =CH), 5.6—6.1 (2 H, m, CH_2·O), 6.93 (3 H, s, NMe), 7.02 (3 H, s, NMe), and 8.89 (3 H, s, Me) (Found: C, 67.75; H, 8.7; N, 5.2. $C_{15}H_{23}NO_3$ requires C, 67.9; H, 8.7; N, 5.3%).

The Lactonic Esters rac-(15).—The crystalline amide lactone *rac*-(14) (220 mg) and potassium hydroxide (4 g) were heated together under reflux in ethylene glycol (11 cm^3) and water (3.5 cm^3) for 21 h. The cooled solution was diluted with water (100 cm^3) and acidified with 6N-hydrochloric acid, and the product was isolated with ether and esterified with ethereal diazomethane. Chromatography on neutral alumina (grade III) and elution with 5% ethyl acetate–benzene gave the mixed lactonic esters as an oil (77%) which did not separate on t.l.c.; $\nu_{max.}$ (film) 1 160s, 1 735s, and 1 765s cm^{-1}, τ 4.26br (1 H, d, *J* 11 Hz, =CH), 4.50br (1 H, d, *J* 11 Hz, =CH), 5.50—6.05 (2 H, m, CH_2·O), 6.32 (3 H, s, CO_2Me), and 8.96 and 9.12 (3 H, singlets, Me) (Found: M^+, 252.135 485. Calc. for $C_{14}H_{20}O_4$: *M*, 252.126 150). Crystallisation from ether–light petroleum (b.p. 40—60 °C) gave *methyl* (1SR,6SR)-6-*methyl*-6-[(3SR)-2-*oxotetrahydrofuran*-3-*yl*]*cyclohex*-2-*enylacetate*, m.p. 86—87°, $\nu_{max.}$ ($CHCl_3$) 1 165s, 1 730s, and 1 763s cm^{-1}, τ as for the oily mixture, but only one CMe signal (τ 9.12) (Found: C, 66.9; H, 7.9. $C_{14}H_{20}O_4$ requires C, 66.65; H, 8.0%).

The Bicyclic Hydroxy-ketones rac-(16).—The mixed lactonic esters *rac*-(15) (248 mg) and potassium t-butoxide (2.24 g) were heated together under reflux in dry benzene (35 cm^3) under nitrogen for 4 h and then stirred at 20 °C for 16 h. The solution was shaken with dilute sulphuric acid (50 cm^3), the aqueous layer was extracted with ether, and the combined organic phases were washed, dried, and evaporated. The residual oil was heated under reflux for 16 h with toluene-*p*-sulphonic acid (0.8 g) in glacial acetic acid (8 cm^3) and water (2 cm^3), and then cooled and neutralised with aqueous sodium carbonate. The product, isolated with ether, consisted of a mixture of alcohol and acetate; acetylation with pyridine and acetic anhydride gave the mixed acetoxy-ketones (0.136 g), $\nu_{max.}$ (film) 1 240s and 1 740s cm^{-1}, τ 4.30 (2 H, s, =CH), 5.83 (2 H, m, CH_2·O), 7.95 (3 H, s, O·COMe), and 9.07s and 9.26s (3 H, Me).

Deacetylation with aqueous ethanolic potassium hydroxide gave the mixed hydroxy-ketones *rac*-(16), which showed singlets at τ 9.08 and (major component) 9.27. Crystallisation of the derived *p*-nitrobenzoate mixture from chloroform–light petroleum gave the p-*nitrobenzoate* of (±)-1β-(2-*hydroxyethyl*)-3aα,6,7,7aβ-*tetrahydro*-7aβ-*methylindan*-2-*one*, m.p. 100—102°, $\nu_{max.}$ (Nujol) 712s, 1 527s, 1 710s, and 1 735s cm^{-1}, τ 1.75 (4 H, m, ArH), 4.31 (2 H, s, =CH), 5.38—5.63 (2 H, m, CH_2·O), and 9.22 (3 H, s, Me) (Found: C, 66.55; H, 6.05; N, 4.35. $C_{19}H_{21}NO_5$ requires C, 66.45; H, 6.15; N, 4.1%).

The Bicyclic Alcohols rac-(18).—The mixed hydroxy-ketones *rac*-(16) (100 mg) and 2,3-dihydropyran (110 mg) were allowed to react in dry ether (5 cm^3) containing toluene-*p*-sulphonic acid (5 mg) at 20 °C for 22 h; normal work-up then gave the tetrahydropyranyl ethers as an oil (157 mg), $\nu_{max.}$ (film) 1 745s cm^{-1}. Reduction of this oil (153 mg) with lithium aluminium hydride (61 mg) in ether (5 cm^3) at 20 °C for 1.5 h, followed by work-up with aqueous sodium potassium tartrate, gave the alcohols *rac*-(17) as an oil (154 mg), $\nu_{max.}$ (film) 3 470 cm^{-1}. This was heated under reflux under dry nitrogen for 1.5 h with sodium hydride (31 mg) and imidazole (5 mg) in tetrahydrofuran (6 cm^3). Carbon disulphide (420 mg) was then added, and heating was continued for 0.5 h; methyl iodide (0.92 g) was then added, and heating was continued for a further 0.5 h. The cooled mixture was poured into water (100 cm^3) and extracted with ether; evaporation gave an oil (209 mg), $\nu_{max.}$ (film) 1 060s and 1 240s cm^{-1}, which did not separate on t.l.c. (5% ethyl acetate in benzene). This oil (206 mg) in dry toluene (6 cm^3) was added during 1 h to a solution of tri-n-butyltin hydride (313 mg) in boiling toluene (2 cm^3) under dry nitrogen, and heating was continued for 21 h. The solution was then evaporated under reduced pressure, and the oily residue was kept at 21 °C for 5 min with ethanolic N-hydrogen chloride (6 cm^3), and then poured into dilute aqueous sodium hydrogen carbonate (60 cm^3). Isolation with ether, and chromatography on silica gel (20 g), first with benzene (eluate discarded), and then with 10% ethyl acetate in benzene, gave the hexahydroindenylpropanols *rac*-(18) as an oil (54 mg), $\nu_{max.}$ (film) 1 060s and 3 330s cm^{-1}, τ 4.38 (2 H, s, =CH), 6.10—6.50 (2 H, m, CH_2·O), and 9.24s and 9.38s (3 H, Me). The mixed 3,5-dinitrobenzoates (64 mg) separated from ethanol, m.p. 87—89°; further crystallisations from the same solvent gave the 3,5-*dinitrobenzoate* of (±)-1β-(2-*hydroxyethyl*)-3aα,6,7,7aβ-*tetrahydro*-7aβ-*methylindane* as the bis-ethanol solvate, m.p. 92—98°, $\nu_{max.}$ 1 165s, 1 278s, 1 345s, 1 548s, 1 712s, 1 732s, and 3 100w cm^{-1}, τ 0.82 (3 H, m, ArH), 4.38 (2 H, s, =CH), 5.53 (2 H, s, CH_2·O), 6.30 (4 H, q, *J* 7 Hz, 2 $MeCH_2$·O), 8.78 (6 H, t, *J* 7 Hz, 2 $MeCH_2$), and 9.33 (3 H, s, MeC) (Found: C, 59.1; H, 7.15; N, 6.3. $C_{19}H_{22}N_2O_6$,2EtOH requires C, 59.2; H, 7.35; N, 6.0%).

(S)-3-*Methylbutan*-4-*olide* (21).—(+)-Methyl hydrogen 3-methylglutarate (10 g) and dry lead tetra-acetate (31 g) were stirred and heated together under reflux under dry nitrogen in dry carbon tetrachloride (400 cm³). The mixture was irradiated with two 150 W tungsten bulbs for 10 min, and irradiation was continued while iodine (23.1 g) was added in portions during 45 min. The mixture was filtered, and the filtrate was washed with aqueous sodium thiosulphate, aqueous sodium carbonate, and water, and was then dried and evaporated. The oily iodo-ester (14.1 g) (Found: M^+, 241.981 14. Calc. for $C_6H_{11}IO_2$: M, 241.980 56) was *ca.* 92% pure by g.l.c. (5% SE 30; 5 ft column at 98 °C; retention time 3.2 min) and had $\nu_{max.}$ (film) 1 735s cm^{-1}, τ 6.27 (3 H, s, CO_2Me), 6.70 (2 H, d, J 5 Hz, CH_2I), and 8.94 (3 H, d, J 6.5 Hz, CH_3).

Freshly prepared silver acetate (18.4 g), glacial acetic acid (82 cm³), and acetic anhydride (24 g) were heated together at 120 °C for 1 h. The above iodo-ester (19.1 g) was then added, and heating was continued for 2 h, after which the mixture was kept at 20 °C for 15 h. Ether (300 cm³) was added, and after filtration the solution was washed with water and with aqueous sodium carbonate, and then dried and evaporated. The aqueous washings were continuously extracted with ether, and the residue from evaporation of the extracts was united with the foregoing material to give an oil (8.12 g) composed (i.r.) of a mixture of acetate-ester and the required γ-lactone; it had $\nu_{max.}$ (film) 1 240s, 1 740s, and 1 780s cm^{-1}. This mixture was kept at 20 °C for 21 h with ethanol (10 cm³) and aqueous 2N-sodium hydroxide (70 cm³), and was then diluted with water (50 cm³) and extracted with ether, the extract being discarded. Acidification of the aqueous phase with 6N-hydrochloric acid (150 cm³), continuous extraction with ether, and distillation of the product under reduced pressure gave (−)-(S)-3-*methylbutan*-4-*olide* (21) (4.37 g), b.p. 102—105° at 34 mmHg, $[\alpha]_D^{21}$ −26.1° (*c* 5.35). G.l.c. (5% Carbowax; 5 ft column at 106 °C) showed 98% purity (retention time 3.7 min). The lactone had $\nu_{max.}$ (film) 1 775s cm^{-1}, τ 5.58 (1 H, dd, J_{gem} 9, J_{vic} 7 Hz, CH·O), 6.15 (1 H, dd, J_{gem} 9, J_{vic} 7 Hz, CH·O), and 8.84 (3 H, d, J 6.5 Hz, Me) (Found: M^+, 100.052 75. $C_5H_8O_2$ requires M, 100.052 243).

The Benzyloxy-phenylethylamide (22).—The lactone (21) (0.31 g), benzyl chloride (4.0 g), and powdered potassium hydroxide (2.1 g) were heated together under reflux in toluene (40 cm³) with vigorous stirring and removal of water as formed. After 19 h water (180 cm³) was added, the mixture was extracted with ether, and the extracts were discarded. The aqueous phase was acidified with hydrochloric acid; isolation with ether gave (S)-4-*benzyloxy*-3-*methylbutanoic acid* as an oil (0.62 g), $\nu_{max.}$ (film) 695s, 732s, 1 095s, 1 710s, and 2 500—3 500s cm^{-1}, τ 2.68 (5 H, s, ArH), 5.49 (2 H, s, O·CH_2Ph), 6.63 (2 H, m, CH_2·O·CH_2Ph), and 8.98 (3 H, d, J 6.5 Hz, Me) (Found: M^+, 208.109 452. $C_{12}H_{16}O_3$ requires M, 208.109 937).

The above acid (3.0 g), (+)-α-phenylethylamine (1.75 g) and *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (3.74 g) were stirred together at 50 °C in anhydrous benzene (75 cm³) for 18 h. The cooled mixture was diluted with ether and washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried and evaporated to give an oil (4.37 g), homogeneous by t.l.c. (20% ethyl acetate in benzene). Crystallisation of a sample from ether–light petroleum gave (S)-4-*benzyloxy*-3-*methyl*-N-[(R)-α-*phenylethyl*]*butyramide* (22) as needles, m.p. 60—62°, $[\alpha]_D^{21}$ +65.9° (*c* 1.4 in MeOH), $\nu_{max.}$ ($CHCl_3$) 1 500s, 1 660s, and 3 450s cm^{-1}, τ 2.73 (10 H, s with fine splitting, ArH), 3.76br (1 H, d, J 8 Hz, NH), 4.90 (1 H, m, CO·NH·CH), 5.56 (2 H, s, O·CH_2Ph), 6.68 (2 H, m, CH_2·O·CH_2Ph), 8.60 (3 H, d, J 7 Hz, N·CHPh·CH_3), and 9.06 (3 H, d, J 6.5 Hz, *Me*CH) (Found: C, 77.35; H, 7.9; N, 4.55. $C_{20}H_{25}NO_2$ requires C, 77.15; H, 8.1; N, 4.5%).

An equimolar mixture of (*R*)-α-phenylethylamides, prepared as for (22), but from racemic 3-methyl-γ-butyrolactone, showed the same n.m.r. spectrum as (22) except that (i) two signals of equal intensity, at τ 5.56 and 5.61, replaced the single signal at τ 5.56, and (ii) two signals of equal intensity, at τ 9.04 and 9.06, replaced the single signal at τ 9.06.

The Hydroxy-phenylethylamide (23).—Hydrogenolysis of the phenylethylamide (22) (4.22 g) in ethanol (120 cm³) containing concentrated hydrochloric acid (20 mg) over 5% palladised charcoal, followed by removal of catalyst and solvent, gave a white solid (3.17 g). Two crystallisations from ethyl acetate–ether gave (S)-4-*hydroxy*-3-*methyl*-N-[(R)-α-*phenylethyl*]*butyramide* (1.74 g), m.p. 85—86°, $[\alpha]_D^{24}$ +97.3° (*c* 1.2 in MeOH) (unchanged by repeated recrystallisation from the same solvent), $\nu_{max.}$ 700s, 760s, 1 535s, 1 645s, and 3 320s cm^{-1}, τ 2.73 (5 H, s, ArH), 3.18br (1 H, d, J 8 Hz, NH), 4.95 (1 H, m, N·CHMePh), 6.55 (2 H, m, CH_2·O), 8.59 (3 H, d, J 7 Hz, N·CHPh*Me*), and 9.11 (3 H, d, J 6.5 Hz, *Me*CH) (Found: C, 70.7; H, 8.75; N, 6.5. $C_{13}H_{19}NO_2$ requires C, 70.55; H, 8.65; N, 6.35%).

The phenylethylamide (1.7 g) was heated under reflux for 20 h with potassium hydroxide (9.0 g) in water (45 cm³) and ethanol (5 cm³). Saturated aqueous sodium chloride was added, and the mixture was extracted with ether, the extract being discarded. The aqueous layer was acidified with 6N-hydrochloric acid, and the product was isolated by continuous extraction with ether, and distillation under reduced pressure. The pure lactone (0.71 g) had $[\alpha]_D^{23}$ −26.4° (*c* 4.5).

(S)-2,2-*Diethoxy*-4-*methyltetrahydrofuran* (24).—The γ-lactone (21) (15.22 g) and triethyloxonium tetrafluoroborate (41.0 g) were kept together at 20 °C under nitrogen for 5 days. The upper layer was removed, and the lower layer, after being washed with ether, was dissolved in dichloromethane and added during 1 h to a well stirred solution of sodium ethoxide [from sodium (5.65 g)] in ethanol (138 cm³) at 0 °C. The mixture was stirred at 20 °C for 16 h and then treated with aqueous sodium carbonate and extracted with ether. Evaporation of the washed and dried extract, and distillation under reduced pressure, gave (S)-2,2-*diethoxy*-4-*methyltetrahydrofuran* (24) (20.8 g), b.p. 87—90° at 26 mmHg, $[\alpha]_D^{24}$ −18.7° (*c* 5.1), $\nu_{max.}$ (film) 1 050s cm^{-1}, τ 5.95 (1 H, apparent t, J 8 Hz, CH·O), 6.2—6.6 (5 H, m, CH·O and 2 × CH_2·O), and 8.60—9.00 (9 H, m, 3 Me) (Found: C, 62.05; H, 10.55. $C_9H_{18}O_3$ requires C, 62.05; H, 10.4%).

The Benzoate–Lactone (25).—The monobenzoate (7) (150 mg), the orthoester (24) (350 mg), and propionic acid (10 mg) were heated together under reflux in dry xylene (10 cm³) under nitrogen for 23 h; more propionic acid (20 mg) was added after 21 h. Solvent and the excess of orthoester were removed under reduced pressure, and the residue was chromatographed on silica gel (20 g). Elution with 5% ether in benzene gave (2R,3R)-2-[(1S,4S)-4-*benzoyloxy*-1-*methylcyclohex*-2-*enyl*]-3-*methylbutan*-4-*olide* (25) (139 mg), which separated from chloroform–light petroleum as needles (113 mg), m.p. 92—93°, $[\alpha]_D^{24}$ −129° (*c* 0.95),

$\nu_{max.}$ ($CHCl_3$) 708s, 1 270s, 1 712s, and 1 763s cm^{-1}, τ 1.95 (2 H, m, ArH), 2.53 (3 H, m, ArH), 4.04 (1 H, d, J 10 Hz, =CH), 4.24 (1 H, dd, J 10 and 1.5 Hz, =CH), 4.48 (1 H, m, CH·OBz), 5.64 (1 H, apparent t, J 9.5 Hz, CH·O), 6.25 (1 H, dd, J_{gem} 9.5, J_{vic} 6 Hz, CH·O), 8.70 (3 H, s, Me), and 8.81 (3 H, d, J 7 Hz, CH*Me*) (Found: C, 72.65; H, 7.25. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.05%). Further elution gave the monobenzoate (7) (18 mg).

The Hydroxy-lactone (26).—The benzoate (25) (2.067 g) was debenzoylated by the Zemplén method, as described for the preparation of *rac*-(13), giving (2R,3R)-2-[(1S,4S)-4-*hydroxy*-1-*methylcyclohex*-2-*enyl*]-3-*methylbutan*-4-*olide* (26) (1.359 g), m.p. 80—82°. Recrystallisation of a portion from ether–light petroleum gave material, m.p. 83—83.5°, $[\alpha]_D^{23}$ −57.4° (*c* 1.75), $\nu_{max.}$ ($CHCl_3$) 1 760s, 3 450s, and 3 600s cm^{-1}, τ 4.28 (2 H, s, =CH), 5.66 (1 H, apparent t, J 9 Hz, CH·O·CO), 5.82 (1 H, m, C*H*·OH), 6.27 (1 H, dd, J_{gem} 9, J_{vic} 7 Hz, CH·O·CO), 8.76 (3 H, s, Me), and 8.82 (3 H, d, J 7 Hz, CH*Me*) (Found: C, 68.5; H, 8.75. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.65%). Re-benzoylation of a portion (50 mg) of this material gave the monobenzoate (25) (68 mg), which separated from chloroform–light petroleum as needles, m.p. 92—93°, $[\alpha]_D^{22}$ −130°.

The Lactonic Ester (28).—The hydroxy-lactone (26) (1.154 g) and 1-dimethylamino-1-methoxyethylene (2.94 g) were heated together under reflux in dry xylene (40 cm^3) under nitrogen for 21 h. Solvent and excess of reagent were removed under reduced pressure, and the residue was chromatographed on silica gel (150 g). Elution with ethyl acetate gave (1S,6S)-6,NN-*trimethyl*-6-[(3R,4R)-4-*methyl*-2-*oxotetrahydrofuran*-3-*yl*]*cyclohex*-2-*enylacetamide* (27) (1.384 g), which separated from chloroform–light petroleum as needles (1.212 g), m.p. 116—117°, $[\alpha]_D^{22}$ +59.1° (*c* 1.1), $\nu_{max.}$ ($CHCl_3$) 1 635s and 1 752s cm^{-1}, τ 4.29br (1 H, d, J 12 Hz, =CH), 4.47br (1 H, d, J 12 Hz, =CH), 5.66 (1 H, dd, J_{gem} 9, J_{vic} 7.5 Hz, CH·O), 6.19 (1 H, dd, J_{gem} 9, J_{vic} 5 Hz, CH·O), 6.94s and 7.01s (6 H, CO·NMe_2), 8.78 (3 H, d, J 7 Hz, CH*Me*), and 8.89 (3 H, s, Me) (Found: C, 69.0; H, 8.95; N, 5.25. $C_{16}H_{25}NO_3$ requires C, 68.8; H, 9.0; N, 5.0%).

The amide-lactone (27) (1.94 g) was heated under reflux with potassium hydroxide (25 g) in ethanol (10 cm^3) and water (30 cm^3) for 19 h. The ethanol was distilled off, and the aqueous solution was treated for 2 h at 20 °C with 6N-hydrochloric acid (180 cm^3). The product was then isolated with ether, and methylated with an excess of ethereal diazomethane; chromatography on silica gel (25% ethyl acetate in benzene) gave the lactonic ester (28) as a solid (1.40 g). Crystallisation from ether–light petroleum gave *methyl* (1S,6S)-6-*methyl*-6-[(3R,4R)-4-*methyl*-2-*oxotetrahydrofuran*-3-*yl*]*cyclohex*-2-*enylacetate* as prisms, m.p. 69—70°, $[\alpha]_D^{23}$ +56.8° (*c* 1.32), $\nu_{max.}$ ($CHCl_3$) 1 175s, 1 735s, and 1 755s cm^{-1}, τ 4.26br (1 H, d, J 12 Hz, =CH), 4.53br (1 H, d, J 12 Hz, =CH), 5.68 (1 H, dd, J_{gem} 9, J_{vic} 7.5 Hz, CH·O), 6.21 (1 H, dd, J_{gem} 9, J_{vic} 5 Hz, CH·O), 6.30 (3 H, s, CO_2Me), 8.78 (3 H, d, J 7 Hz, CH*Me*), and 8.94 (3 H, s, Me) (Found: C, 67.9; H, 8.05. $C_{15}H_{22}O_4$ requires C, 67.65; H, 8.35%).

The Hydroxy-ketone (29).—The lactonic ester (28) (276 mg) was cyclised as described for the analogue (15) with potassium t-butoxide (3.36 g) in benzene (30 cm^3), and the resulting β-oxo-ester was heated under reflux for 2 h with toluene-*p*-sulphonic acid (0.8 g) in acetic acid (8 cm^3) and water (2 cm^3). The solution was neutralised with aqueous sodium carbonate and the product, after isolation with ether, was hydrolysed with potassium hydroxide (72 mg) in ethanol (5 cm^3) for 16 h at 20 °C. Normal work-up gave the hydroxy-ketone (29) as a semi-solid (133 mg), m.p. 34—54°, $\nu_{max.}$ (film) 1 738 and 3 390 cm^{-1}; it showed two singlet signals (=CH) at τ 4.34 and 4.42, and two (tert. Me) at 9.13 and 9.19. Esterification with *p*-nitrobenzoyl chloride and crystallisation from chloroform–light petroleum gave the p-*nitrobenzoate* of 1β-[(R)-2-*hydroxy*-1-*methylethyl*]-3aα,6,7aβ-*tetrahydro*-7aβ-*methylindan*-2-*one* as needles, m.p. 104—105°, $[\alpha]_D^{22}$ −71.9° (*c* 0.44), $\nu_{max.}$ ($CHCl_3$) 1 280s, 1 530s, and 1 734s cm^{-1}, τ 1.76 (4 H, m, ArH), 4.32 (2 H, s, =CH), 5.26 (1 H, dd, J_{gem} 11, J_{vic} 4 Hz, CH·O), 5.47 (1 H, dd, J_{gem} 11, J_{vic} 7 Hz, CH·O), 8.82 (3 H, d, J 7 Hz, CH*Me*), and 9.09 (3 H, s, Me) (Found: C, 67.4; H, 6.5; N, 3.8. $C_{20}H_{23}NO_5$ requires C, 67.2; H, 6.5; N, 3.9%). Hydrolysis of this material gave hydroxy-ketone with properties identical with those described above.

The Bicyclic Alcohol (31).—The hydroxy-ketone (29) (96 mg) was converted into its tetrahydropyranyl ether in the usual way. Reduction with lithium aluminium hydride (19 mg) in ether (4 cm^3) at 21 °C for 1 h, work-up by use of aqueous sodium potassium tartrate, and chromatography on neutral alumina (benzene) gave the hydroxy-tetrahydropyranyl ether (30) as an oil (80 mg), $\nu_{max.}$ 3 490 cm^{-1}, τ 4.41 (2 H, s, =CH), 8.97 (3 H, d, J 7 Hz, CH*Me*), 9.07 (3 H, s, Me) (Found: M^+, 294.218 11. Calc. for $C_{18}H_{30}O_3$: *M*, 294.219 48).

The hydroxy-compound (30) (95 mg) was converted into its *S*-methyl dithiocarbonate, essentially as described for the analogue *rac*-(17); chromatography of the crude product on neutral alumina gave (light petroleum) the oily *S*-methyl dithiocarbonate (61 mg), $\nu_{max.}$ 1 065s and 1 220s cm^{-1}, and also (5% benzene–light petroleum) unchanged hydroxy-tetrahydropyranyl ether (32 mg). Reaction of the *S*-methyl dithiocarbonate (61 mg) with tri-n-butyltin hydride, as described for the preparation of *rac*-(18), gave a crude product which, after chromatography on neutral alumina, gave the hexahydroindenylpropanol (31) as an oil (38 mg), $\nu_{max.}$ (film) 3 340s cm^{-1}, homogeneous to t.l.c. The 3,5-*dinitrobenzoate* (33) of 1β-[(R)-2-*hydroxy*-1-*methylethyl*]-3aα,6,7,7aβ-*tetrahydro*-7aβ-*methylindane* separated from chloroform–light petroleum as fine needles (45 mg), m.p. 79—80°, $[\alpha]_D^{23}$ +47.5° (*c* 0.64), $\nu_{max.}$ ($CHCl_3$) 1 168s, 1 280s, 1 345s, 1 731s, and 3 100s cm^{-1}, τ 0.82 (3 H, m, ArH), 4.41 (2 H, s, =CH), 5.52 (1 H, dd, J_{gem} 11, J_{vic} 4 Hz, CH·O), 5.82 (1 H, dd, J_{gem} 11, J_{vic} 7 Hz, CH·O), 8.84 (3 H, d, J 7 Hz, CH*Me*), and 9.24 (3 H, s, Me) (Found: C, 61.75; H, 6.2; N, 7.4. $C_{20}H_{24}N_2O_6$ requires C, 61.85; H, 6.25; N, 7.2%).

Degradation of Vitamin D_2 to the Hexahydroindenylpropanol (31).—The diol (35) (0.5 g) obtained by ozonolysis of vitamin D_2 and reduction of the ozonide with lithium aluminium hydride was kept at 20 °C for 15 h with benzoyl chloride (1 g) in dry pyridine (8 cm^3), and the mixture was worked up in the usual way. The *dibenzoate* (36) (1.03 g) separated from light petroleum (b.p. 40—60 °C) as prisms, m.p. 91—92°, $[\alpha]_D^{23}$ +64.4° (*c* 2.2), $\nu_{max.}$ ($CHCl_3$) 705m, 1 275s, and 1 710s cm^{-1}, τ 1.91 (4 H, m, ArH), 2.52 (6 H, m, ArH), 4.55 (1 H, m, $W_{\frac{1}{2}}$ 7 Hz, CH·O), 5.64 (1 H, dd, J_{gem} 11, J_{vic} 4 Hz, CH·O), 5.92 (1 H, dd, J_{gem} 11, J_{vic} 7 Hz, CH·O), 8.83 (3 H, d, J 7 Hz, CH*Me*), and 8.87 (3 H, s, Me) (Found: C, 77.05; H, 7.35. $C_{27}H_{32}O_4$ requires C, 77.1; H, 7.65%). The dibenzoate (0.7 g) was heated to 400 ± 5 °C under nitrogen in a bulb-to-bulb distillation tube; after 1.5 min all had distilled over. The product

in ether (50 cm^3) was washed with aqueous sodium hydrogen carbonate, and water, and was dried and evaporated. The residual oil (499 mg) was shown by t.l.c. (50% benzene–light petroleum) and n.m.r. to contain *ca.* 5% of dienes; in the mono-ene fraction the ratio of $\Delta^{8(9)}$-isomer to $\Delta^{8(14)}$-isomer was *ca.* 3 : 1. The mixture of isomeric monobenzoates (459 mg) was hydrolysed with ethanolic sodium hydroxide to give the isomeric hexahydroindenylpropanols as an oil (296 mg). This material (403 mg) was converted in the usual way into the mixed 3,5-dinitrobenzoates which formed a solid (805 mg). The mixture was chromatographed on Kieselgel G (90 g) coated with 15% (w/w) silver nitrate. Elution of the less strongly adsorbed component with 25% light petroleum–benzene, and crystallisation from chloroform–light petroleum, gave the 3,5-*dinitrobenzoate* (34) (99 mg) of 1β-[(R)-2-*hydroxy*-1-*methylethyl*]-5,6,7,7aβ-*tetrahydro*-7aβ-*methylindane*, m.p. 105—106°, $[\alpha]_D^{22}$ +54.0° (*c* 1.7), $\nu_{max.}$ ($CHCl_3$) 1 170s, 1 348s, 1 550s, 1 732s, and 3 110w cm^{-1}, τ 0.81 (3 H, m, ArH), 4.69br (1 H, s, $W_{\frac{1}{2}}$ 8 Hz, =CH), 5.47 (1 H, dd, J_{gem} 11, J_{vic} 4 Hz, CH·O), 5.74 (1 H, dd, J_{gem} 11, J_{vic} 7 Hz, CH·O), 8.81 (3 H, d, *J* 7 Hz, CH*Me*), and 9.01 (3 H, s, Me) (Found: C, 61.75; H, 6.2; N, 7.45. $C_{20}H_{24}N_2O_6$ requires C, 61.85; H, 6.25; N, 7.2%).

Further elution with the same solvent gave mixed fractions (37 mg) and then the $\Delta^{8(9)}$-isomer (33) (362 mg), m.p. 78—80° (not depressed on admixture with the synthetic material); $[\alpha]_D^{21}$ +47.3° (*c* 1.6). Its i.r. and n.m.r. spectra were identical with those of the synthetic material.

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