Condensed Cyclic and Bridged-ring Systems. Part III.[1] Regioselectivity and Stereoselectivity in the Acid-catalysed Cyclisations of Substituted Benzylcyclohexanols. Stereocontrolled Synthesis of Some *gem*-Carboxy–methyl-substituted Hexahydrofluorene and Hexahydro-5,9-methanobenzocyclo-octene Derivatives

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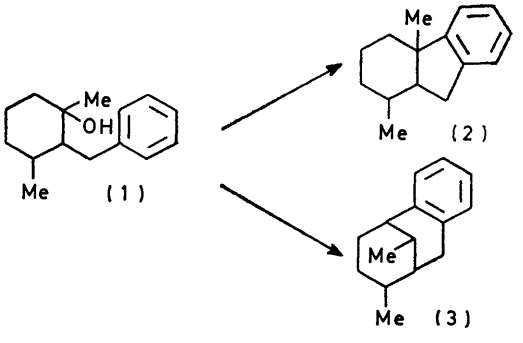
Treatment of ethyl 2-benzyl-2-hydroxy-1,3-dimethylcyclohexanecarboxylate (8) with polyphosphoric acid produced either (±)-*c*-2-benzyl-1,3-dimethylcyclohexane-*r*-1,*c*-3-carbolactone (6) or a mixture from which (1*RS*,4a*RS*,9a*RS*)2,3,4,4a,9,9a-hexahydro-1,4a-dimethyl-1*H*-fluorene-1-carboxylic acid (5a) was isolated in a moderate yield, depending upon the reaction temperature. Whereas aluminium chloride-catalysed cyclisation of the lactone (6) resulted in the stereospecific formation of (5*SR*,8*RS*,9*SR*,11*RS*)-5,6,7,8,9,10-hexahydro-8,11-dimethyl-5,9-methanobenzocyclo-octene-8-carboxylic acid (9), the epimeric *t*-2-benzyl lactone (7) produced a mixture of the hexahydrofluorene acid (5a) and the epimeric (8*SR*)-hexahydromethanobenzocyclo-octene acid (12), in high yields. By a similar process (±)-methyl *t*-2-benzyl-*t*-3-hydroxy-1,3-dimethylcyclohexane-*r*-1-carboxylate (4) gave the acid (9) and a mixture of hexahydrofluorene ester (5b) and (8*SR*)-hexahydromethanobenzocyclo-octene (13). Structures and configurations of the bridged-ring compounds were determined from chemical and n.m.r. spectral studies. Ready alkaline hydrolysis of the tertiary ester group in (5*SR*,8*RS*,9*SR*,11*SR*)-methyl 5,6,7,8,9,10-hexahydro-8,11-dimethyl-10-oxo-5,9-methanobenzocyclo-octene-8-carboxylate (11), through intramolecular oxo-group participation, revealed the stereochemistry of the ester group. The observed differences in the nature of products in polyphosphoric acid-catalysed cyclisation of (8) and the behavioural differences shown by the diastereoisomeric lactones (6) and (7) and the hydroxy-ester (4) in aluminium chloride-induced cyclisations are rationalised on the basis of steric and stereoelectronic factors in the intermediate cations as well as the thermodynamic stability of the products under reversible reaction conditions.

Our preliminary studies [1b] demonstrated that by appropriate choice of the cyclisation reagent it is possible to bring about regioselective cyclisation of the carbocations generated from 2-benzyl-1,3-dimethylcyclohexanol (1) to give the hexahydrofluorene (2) or the hexahydromethanobenzocyclo-octene (3). We have previously described [2] the polyphosphoric acid (PPA)-catalysed cyclisation of the hydroxy-ester (4) † leading to a hexahydrofluorene acid (5a) as a single stereoisomer in good yield. In contrast, the diastereoisomeric lactones (6) and (7), although they were largely unchanged on treatment with PPA under the usual conditions (80—85 °C), produced a complex mixture of hydrocarbons at *ca.* 120—125 °C containing products arising from a regioselective cyclisation to hexahydrofluorene systems. We now report in detail the results of PPA-induced cyclisations of the diastereoisomeric mixture of hydroxy-esters (8), and alu-

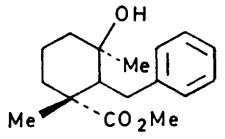


† Compounds described in this paper are all racemates.

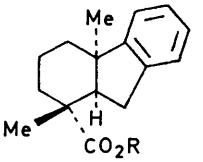
[1] (*a*) Part II, J. Chakravarty and U. R. Ghatak, *Indian J. Chem.*, 1969, **7**, 215; (*b*) U. R. Ghatak and J. Chakravarty, *Tetrahedron Letters*, 1966, 2449.

[2] U. R. Ghatak, J. Chakravarty, and A. K. Banerjee, *Tetrahedron*, 1968, **24**, 1577.

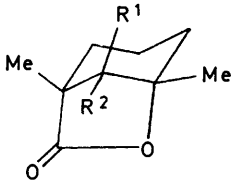
minium chloride-catalysed reactions [1b] of the lactones (6) and (7) and the hydroxy-ester (4). These investigations revealed new evidence relating to the stereochemistry and mechanism of cyclialkylation processes [3] in addition to providing simple stereocontrolled synthetic routes to (5) and the diastereoisomeric methanobenzocyclo-octene acids (9) and (12), two interesting rigid models for structure–reactivity relationship [4] and spectroscopic studies.[5]



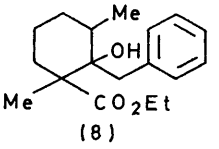
(4)



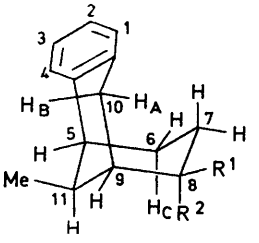
(5) a; R = H
b; R = Me



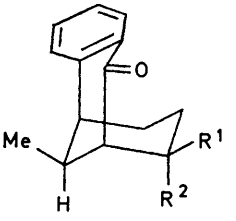
(6) R^1 = H, R^2 = CH_2Ph
(7) R^1 = CH_2Ph, R^2 = H



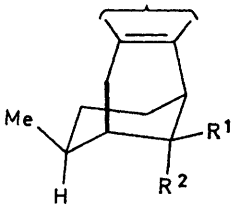
(8)



(9) R^1 = CO_2H, R^2 = Me
(12) R^1 = Me, R^2 = CO_2H
(10) R^1 = CO_2Me, R^2 = Me
(13) R^1 = Me, R^2 = CO_2Me



(11) R^1 = CO_2Me, R^2 = Me
(14) R^1 = Me, R^2 = CO_2Me
(17) R^1 = CO_2H, R^2 = Me



(19) R^1 = CO_2Me or Me
R^2 = Me or CO_2Me

The diastereoisomeric mixture of hydroxy-esters (8) was prepared through condensation of benzylmagnesium chloride with ethyl 1,3-dimethyl-2-oxocyclohexanecarboxylate [6] and characterised by spectral data. This material was used for the cyclisation studies without additional purification. On treatment with PPA at 25—30 °C the hydroxy-esters (8) gave only the lactone (6), in 90—95% yield. Repeating the reaction at 80—85 °C produced a mixture of products from which (6) and the hexahydrofluorene acid (5a) were isolated in 12 and 30% yield, respectively, through controlled alkaline hydrolyses. The n.m.r. spectrum of the hydrocarbon mixture (33%) also obtained from the reaction products contained no olefinic proton signal and showed broad methyl singlets and doublets. On dehydrogenation this afforded 1-methylfluorene, thereby indicating the presence of hydrocarbons of type (2) in the mixture.*

The stereochemistry of the acid (5a) has been conclusively established [2] through direct i.r. and g.l.c. comparisons of the corresponding methyl ester with an optically active sample of known stereochemistry, prepared by Tahara *et al.*[7] from (—)-abietic acid.

The aluminium chloride-catalysed cyclisations of the diastereoisomeric lactones (6) and (7) and the hydroxy-ester (4) led to entirely different results.[8] Treatment of (6) with aluminium chloride in the presence of hydrogen chloride in boiling benzene gave the acid (9) as a single diastereoisomer in 80% yield † as the only isolable crystalline product. However, under similar conditions the epimeric lactone (7) afforded in high yield a mixture, difficult to separate, of the acids (5) and (12) in the ratio *ca.* 1 : 1 as revealed by the g.l.c. analysis of the crude methyl ester mixture.‡

The proportions of these products varied considerably with even a slight variation of the experimental procedure. The aluminium chloride-induced cyclisation of the hydroxy-ester (4) yielded directly the acid (9) in 30% yield, along with a neutral fraction from which the acid (5a) and the ester (13) were isolated in *ca.* 20 and 15% yield, respectively, after saponification. The preliminary assignments [1a] of the bridged structures to the acids (9) and (12) were based upon dehydrogenation experiments, and also upon i.r. spectral studies of the corresponding 10-oxo-esters (11) and (14), prepared in good yield by oxidation of the methyl esters (10) and (13), respectively, with chromic acid. The stereochemistry of the diastereoisomeric methanobenzocyclo-octene derivatives was revealed [1b] by the relative saponification speeds of the methyl esters (10) and (13) and also by the intra-

* The hydrocarbon mixture resulting from the PPA-induced cyclisation of (4) at 80—85 °C showed a similar n.m.r. spectrum, indicating that a structure of type (2) should replace the olefinic structures proposed in our earlier paper.[2]

† The yield has been considerably improved since our preliminary report.[1b]

‡ In the preliminary communication [1b] the proportions of the acids (12) and (5a) were represented as 3 : 1, based upon isolation of the pure compounds.

[3] For a discussion see K. E. Harding, *Bio-organic Chemistry*, 1973, **2**, 248.

[4] U. R. Ghatak and S. Chakrabarty, *J. Amer. Chem. Soc.*, 1972, **94**, 4756.

[5] I. Lengyel and U. R. Ghatak, *Adv. Mass Spectrometry*, 1974, **6**, 47.

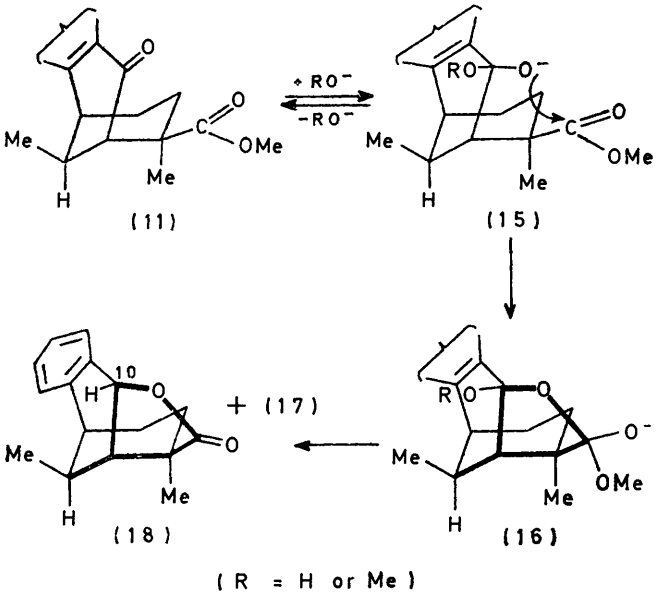
[6] K. Mori and M. Matsui, *Tetrahedron*, 1966, **22**, 879.

[7] A. Tahara, O. Hoshino, and T. Ohsawa, *Chem. and Pharm. Bull*, (*Japan*), 1969, **17**, 68; we thank (the late) Dr. Tahara for these comparisons.

[8] *Inter alia*, U. R. Ghatak, A. K. Banerjee, N. R. Chatterjee, and J. Chakravarty, *Tetrahedron Letters*, 1967, 247; C. E. Low and R. M. Roberts, *J. Org. Chem.*, 1973, **38**, 1909.

molecular participation [9] by the oxo-group in the ready alkaline hydrolysis of the oxo-ester (11) relative to (14).

The qualitative comparative saponification data [1b] of the esters (10) and (13) were unexceptional [10] in revealing the respective equatorial and axial orientation of the methoxycarbonyl group. However, the oxo-ester (11) was hydrolysed [9] under unusually mild conditions with methanolic potassium hydroxide or sodium methoxide. In the latter case, besides the high yield of the oxo-acid (17), a crystalline neutral product was obtained in 8—13% yield. This was identified as the γ-lactone (18) on the basis of i.r. ($\nu_{max.}$ 1 765 cm^{-1}) and n.m.r. spectral data [δ 5.47 (d, *J* 7 Hz, H-10)]. The γ-lactone (18) evidently arises from base-catalysed reduction of the oxo-group as observed in analogous systems.[11] The epimeric oxo-ester (14), however, was almost unaffected under these or relatively drastic hydrolysis conditions. The ready hydrolysis of the hindered tertiary ester group in the rigid oxo-ester (11) not only established the stereochemistry of the methoxycarbonyl group but also provided a notable example of neighbouring carbonyl group participation.[12] This can be interpreted by the mechanistic sequence shown in Scheme 1. Steric hindrance by the



SCHEME 1

11-methyl group to attack of hydroxide or methoxide ion on the ketone function in (11) is compensated by the release of strain [13] involved in changing the hybridisation of the carbonyl carbon atom from sp^2 to sp^3. Intramolecular attack by the negatively charged oxygen atom on the ester carbonyl group in (15) is facilitated both by the geometry of the reacting centres and by the relief of strain in going from (15) to (16). It has been shown [14] that abnormally low activation energies are involved in carbonyl-group-accelerated hydrolysis even in conformationally flexible simple γ-oxo-esters.

The stereochemistry of the 11-methyl group in the epimeric esters (10) and (13), and in the corresponding oxo-esters (11) and (14), was revealed by its identical chemical shift in both series (see Experimental section). That the orientation of the methoxycarbonyl group has no influence on this chemical shift in the two epimeric series justifies this assignment. The possibility that either of or both the esters (10) and (13) (or the corresponding acids) had structures such as (19), however, could not be excluded by the foregoing evidence. However the structural and stereochemical assignments were finally established from a 220 MHz ^1H n.m.r. study of the methyl esters (10) and (13) by use of the shift reagent trisdipivaloylmethanatoeuropium(III) [Eu(dpm)$_3$],[15] details of which we have reported [16] separately.* Thus in the spectrum (in $CDCl_3$) of the ester (10), signals from two protons on C-10 were revealed as a doublet at δ 2.34 and a pair of doublets at δ 3.00, with J_{gem} 19 Hz. A Dreiding model shows that the torsion angle between C(10)–H_A and C(9)–H is *ca.* 90°, in accord with the lack of observed coupling between these two protons. A doublet at δ 2.06 (*J* 7 Hz) can be assigned to H-9, since it showed splitting equal to that in the pair of doublets from H_B and a tilt towards the H_B signal. Finally, the C-5 benzylic proton exhibited a broad multiplet centred at δ 2.70. The low-field shifts of the H_A and H-9 signals are in accord with the assigned structure (10) with the methoxycarbonyl group being the site of complexation with the shift reagent. Since the observed H-5 shift is extremely small in comparison to that of H-9, an alternative structure such as (19) is ruled out for this epimer. The ^1H n.m.r. spectum (220 MHz; $CDCl_3$) of the epimer (13) again showed the H-10 signals as a doublet at δ 2.78 and a pair of doublets at δ 2.96, with J_{gem} 19 Hz. The benzylic proton at C-5 exhibited a broad peak at δ 2.68. The C-9 proton signal appeared as a doublet at δ 2.30 (*J* 7 Hz) whereas H_C at C-6 is assigned to the triplet of triplets centred at δ 1.91, a part of which overlapped with other signals on the high-field side. The addition of Eu(dpm)$_3$ in this case showed largest shifts of signals due to H-9 and H_C. The shift for H-9 is of the same order in both epimers, as expected owing to the nearly equal distances between the methoxycarbonyl group and this proton in (10) and (13). The benzylic C-5 proton again showed only a small paramag-

* In the light of this study the tentative assignment of stereochemistry at C-11 in these compounds reported in the preliminary communications [1b,9] had to be reversed.

[9] Preliminary communication, U. R. Ghatak and J. Chakravarty, *Chem. Comm.*, 1966, 184.

[10] *Cf.* U. R. Ghatak, N. R. Chatterjee, A. K. Banerjee, J. Chakravarty, and R. E. Moore, *J. Org. Chem.*, 1969, **34**, 3739.

[11] G. L. Buchanan, A. McKillop, and R. A. Raphael, *J. Chem. Soc.*, 1965, 833; R. D. Sands, *J. Org. Chem.*, 1969, **34**, 2794.

[12] M. S. Newman and A. L. Leegwater, *J. Amer. Chem. Soc.*, 1968, **90**, 4410; K. Bowden and G. R. Taylor, *Chem. Comm.*, 1967, 1112; M. L. Bender, J. A. Reinstein, M. S. Silver, and R. Mikulak, *J. Amer. Chem. Soc.*, 1965, **87**, 4545.

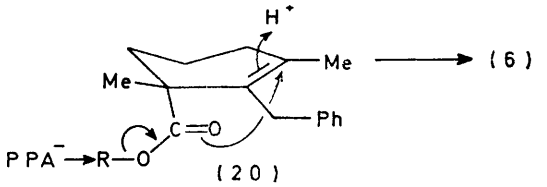
[13] G. L. Buchanan, *Topics Carbocyclic Chem.*, 1969, **1**, 199.

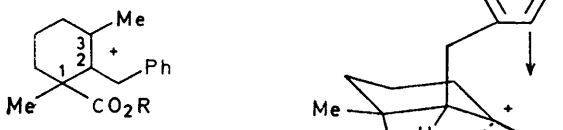
[14] K. C. Kemp and M. L. Mieth, *Chem. Comm.*, 1969, 1260.

[15] J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 641.

[16] L. F. Johnson, J. Chakravarty, R. Dasgupta, and U. R. Ghatak, *Tetrahedron Letters*, 1971, 1703.

netic shift, thereby ruling out a structure such as (19). However, H_Q showed a large shift whereas H_A showed only a small shift, in agreement with the assigned configuration of the methoxycarbonyl group in (13). Finally, the C-11

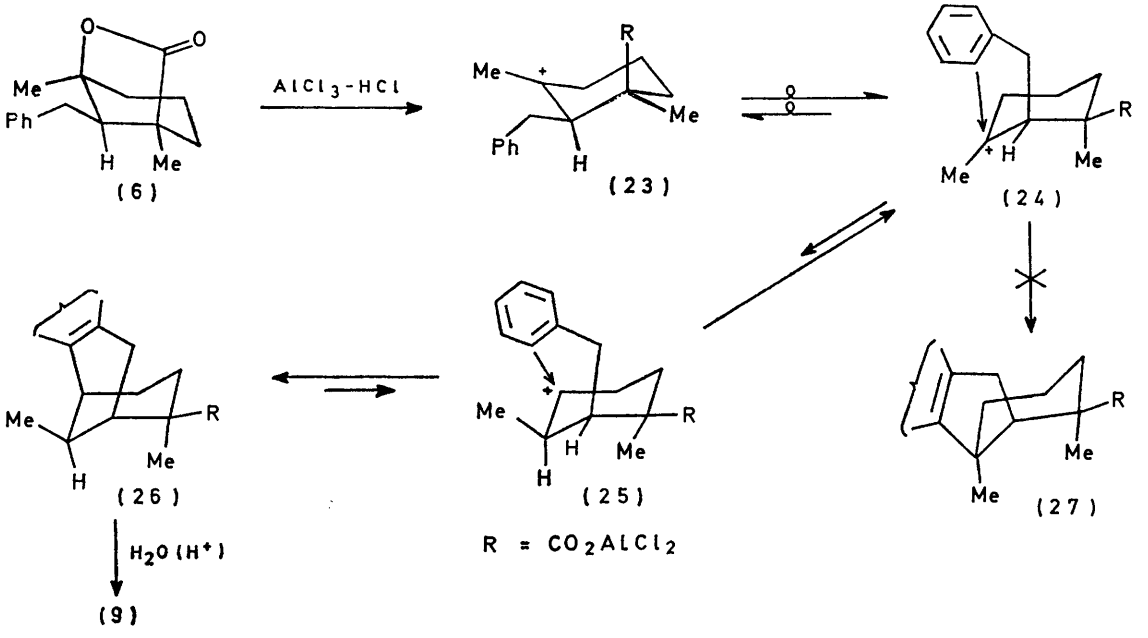




(21) a; charge at C-2
b; charge at C-3

(22)

methyl signal for both epimeric esters showed only a small paramagnetic shift, confirming the assigned configuration for this in both epimeric series. The stereochemical assignments of the diastereoisomeric temperature with PPA may involve a cyclohexene intermediate which readily undergoes concerted protonation–lactonisation [17] [(20) ⟶ (6)]. At elevated temperatures, the cyclohexyl cations (21a and b) possibly generated through protonation of olefinic intermediates could give rise to the products *via* higher energy reaction paths. Formation of the hexahydrofluorene ester (5; R = Et) as a single epimer in *ca.* 30% yield indicates that only the cyclohexyl cation with an axial orientation of the benzyl group, which can attain the transition state (22) having an axial alkoxycarbonyl group to minimise the energy [2,18] by stabilising the developing positive charge at C-3 through π-bonding, is involved in the cyclisation. Experimental evidence in support of this mechanism comes from our earlier observation [2] that the hydroxy-ester (4), which can generate the cyclohexyl cation (22) directly, produces the hexahydrofluorene ester (5b) in much higher yield (*ca.* 60%). The decarboxylated cyclised hydrocarbons (2) from this reaction arise through the cation (21a), possibly by elimination of carbon dioxide *via* a β-lactone [19] or through direct decarboxylation by other processes. At high temperature (120—125 °C) in the PPA cyclisation of the hydroxy-esters (4) and (8) and the lactones (6) and (7), this probably becomes the



SCHEME 2

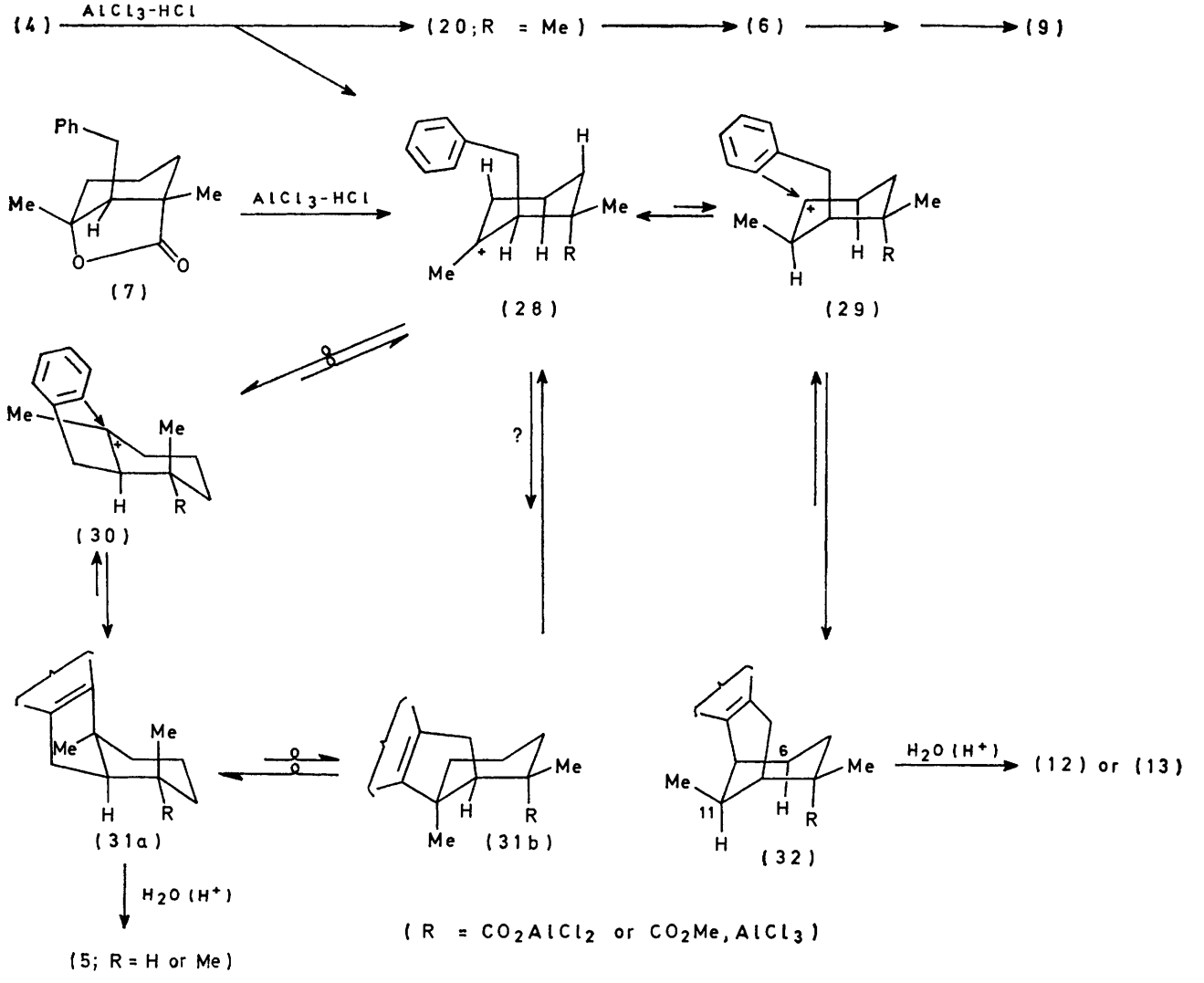
pairs (9)—(14) have been further confirmed by their stereoselective mass spectral fragmentations.[5]

Mechanism of the Cyclisation Reactions.—The observed differences in the nature of products of the PPA-catalysed cyclisation reactions of (8) at different temperatures raised some interesting mechanistic possibilities. Formation of the lactone (6) as a single diastereoisomer, in high yield, from (8) at a relatively low major path of the reaction, accompanied by other processes such as aromatisation and rearrangement.[20]

The foregoing arguments explain the high regio- and stereo-selectivity [2] in the PPA-induced cyclisations of (4) and (8), and also indicate the influence of structure and stereochemistry of the open-chain substrates on the nature of this cyclialkylation.

[17] M. F. Ansell and M. H. Palmer, *Quart. Rev.*, 1964, **18**, 211.
[18] R. E. Ireland, S. W. Baldwin, and S. C. Welch, *J. Amer. Chem. Soc.*, 1972, **94**, 2056.
[19] T. K. Sarkar, *J.C.S. Perkin I*, 1973, 2454.
[20] F. D. Popp and W. E. McEwen, *Chem. Rev.*, 1958, **58**, 321; F. Uhlig and H. R. Snyder, *Adv. Org. Chem.*, 1960, **1**, 35; J. W. Huffman and J. J. Gibbs, *J. Org. Chem.*, 1973, **38**, 2732.

Mechanistically, the formation of the products in the $AlCl_3$–HCl-catalysed cyclisation of compounds (6), (7), and (4) can be explained by considering the conformational preferences of the products and the possible intermediate stages as depicted in Schemes 2 and 3. In the cyclisation of (6), a tertiary cyclohexyl cation (23) is



SCHEME 3

astereoisomeric lactone (7), in producing both (5) and (12), can be explained in terms of Scheme 3. The highly unfavourable steric interactions of the bulky axial groups in the preponderant tertiary cation (28) and the less abundant secondary cation (29) are considerably reduced by cyclisation leading to the bridged-ring system (32) in the latter, and by a conformational inversion in the former [to give (30)] followed by cyclisation to the hexahydrofluorene system (31a). An alternative path involving direct cyclisation of the tertiary cation (28) leading to (31b) is highly unfavourable owing to the strong 1,3-diaxial repulsion it would set up. In this case both the bridged-ring (32) and the hexahydrofluorene (31a) intermediates set up comparable unfavour-

generated in which the bulky aluminium chloride-complexed carboxy-group [21] is placed axially. As cyclisation of the cation (23) is highly unfavourable,[22] this can release strain by conformational inversion to give (24), in equilibrium with less stable secondary cation (25) to a sufficient extent,[23] in the strong Lewis acid medium, to produce the thermodynamically preferred product (26) rather than the regioisomer (27). This cyclisation is highly regio- and stereo-selective.

The low regioselectivity in the cyclisation of the di-

[21] N. N. Greenwood and K. Wade in 'Friedel–Crafts and Related Reactions,' ed. G. A. Olah, Interscience, New York, vol. I, p. 586.

[22] *Inter alia*, E. Wenkert and B. G. Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211; E. Wenkert and J. W. Chamberlin, *ibid.*, 1959, **81**, 688.

[23] R. M. Roberts, K. H. Bantel, and C. E. Low, *J. Org. Chem.*, 1973, **38**, 1903.

able interactions such as 1,3-repulsions of the bulky aluminium chloride-complexed carboxy-group with C-6 and C-11 axial hydrogen atoms in the former and a 1,3-methyl–aryl interaction along with the bond deformation in the latter.

Evidence that both kinetic and thermodynamic factors operate in this cyclisation has been obtained from equilibration experiments with the acids (5a) and (12). Treatment of the acid (5a) with an excess of aluminium chloride in boiling benzene in the presence of hydrogen chloride for 4 h produced a mixture of the acids (5a) and (12) in the ratio *ca.* 30 : 70 (g.l.c. analysis of methyl ester mixture). The acid (12), under similar conditions, was transformed into a mixture containing only 5—10% of the hexahydrofluorene acid (5a), thereby indicating the relative stabilities of these acids under the reaction conditions. These results indicate that although aluminium chloride-catalysed cyclisation of (7) is a reversible reaction,[18,23] the product distribution at a shorter reaction time does not reflect the true equilibrium position. The energetically less favoured product (31a and b) in this reaction, produced in appreciable quantity in the earlier stages, is slowly transformed into the more stable product (32).

The acid (9) formed in the aluminium chloride-induced cyclisation of the hydroxy-ester (4) originates from the lactone (6), which may be generated through a cyclohexene intermediate. In this case again, the formation of both the hexahydrofluorene (5b) and the bridged-ring ester (13) can be rationalised in terms of intermediate cyclohexyl cations containing bulky aluminium chloride-complexed methoxycarbonyl groups,[22,24] as postulated in the cyclisation of the lactone (7) (Scheme 3).

The foregoing results demonstrate that in these cyclisations the stereochemistry and structures of the substrates, reflected in intrinsic steric and stereoelectronic factors in the intermediate cations, have a dominant role in controlling regio- and stereo-selectivity.

EXPERIMENTAL

The compounds described are all racemic forms. M.p.s were taken for samples in open capillaries in a sulphuric acid-bath. The homogeneity of all compounds was checked by t.l.c. on silica gel (Merck; *ca.* 0.2 mm), with benzene–methanol and benzene–ethyl acetate as solvent systems. Spots were located by exposing the dried plates to iodine vapour. U.v. spectra were determined for solutions in 95% ethanol with a Beckmann DU spectrometer and i.r. spectra for solutions in chloroform with a Perkin-Elmer 21 spectrometer. N.m.r. spectra were recorded on Varian HA-60 and T-60 instruments. G.l.c. analyses were carried out by Drs. S. N. Balasubrahmanyan and M. Balasubramanian, Indian Institute of Science, Bangalore, with a Willy Giede 18.3 gas chromatograph (2 m column packed with 10% Carbowax on HMDS celite; N_2 as carrier gas; 185—210 °C). Microanalyses were performed by Mrs. C. Dutta of this laboratory. Light petroleum and petroleum refer to the fractions of b.p. 40—60 and 60—80°, respectively.

Ethyl 2-Benzyl-2-hydroxy-1,3-dimethylcyclohexanecarboxylate (8).—To a stirred ice-cold solution of ethyl 1,3-dimethyl-2-oxocyclohexanecarboxylate [6] (30 g, 0.15 mol) in dry ether (50 ml), a solution of benzylmagnesium chloride [from magnesium turnings (3.6 g, 0.15 g atom)] was added dropwise. The mixture was stirred in the cold for 40 min followed by 1 h at room temperature and finally refluxed for 2 h. The cooled Grignard complex was decomposed with saturated aqueous ammonium chloride and worked up in the usual way to afford a liquid which on fractional distillation gave a viscous liquid (8) (24.5 g, 66%), b.p. 150—155° at 0.3 mmHg; $\nu_{max.}$ (film) 3 540br and 1 725s cm^{-1}; $\lambda_{max.}$ 255 nm (log ε 2.46); δ (CCl_4) 0.94 (d), two unresolved methyl singlets overlapped by the $OCH_2{\cdot}CH_3$ triplets at 1.17 (*J* 7 Hz), complex multiplets between 0.67 and 2.5, benzylic protons at 2.6—3.13, overlapping peaks at 4.06 (q, *J* 7 Hz), OH signal at 4.5 (br, s, exchangeable with D_2O), and 7.0—7.3 (m). An analytically pure sample could not be prepared.

PPA-catalysed Cyclisation of the Hydroxy-ester (8).—(i) *At* 25—30 °C. To PPA [from phosphorus pentaoxide (20 g) and orthophosphoric acid (85%; 13 ml)] at room temperature, the hydroxy-ester (8) (4 g) in dry ether (25 ml) was added and the mixture was stirred for 1 h. The solid isolated after decomposition with iced water and extraction with ether, on recrystallisation from petroleum, afforded *c*-2-benzyl-1,3-dimethylcyclohexane-*r*-1,*c*-3-carbolactone (6) (3.5 g, 95%), m.p. and mixed m.p.[2] 106°.

(ii) *At* 80—85 °C. Treatment of the hydroxy-ester (8) (3.2 g) with PPA [from phosphorus pentaoxide (12 g) and orthophosphoric acid (5 ml)] at 80—85 °C for 1 h afforded a liquid neutral fraction (2.9 g), b.p. 140—170° at 0.3 mmHg; $\nu_{max.}$ 1 765s and 1 725s cm^{-1}. A small amount of an acidic product was obtained which could not be characterised further. The neutral material was partially saponified by refluxing for 30 min under nitrogen with potassium hydroxide (1.5 g) in water (3 ml) and methanol (27 ml). The solution was diluted with water (45 ml) and extracted repeatedly with ether; the extracts were washed with water, dried (Na_2SO_4), and evaporated to leave an oil (2.4 g), which still showed γ-lactone i.r. absorption. The cooled aqueous alkaline layer on acidification with 6N-hydrochloric acid and warming for a few minutes on a steam-bath afforded the lactone (6) (320 mg, 12%), m.p. and mixed m.p. 106°, after the usual isolation and recrystallisation.

The unhydrolysed material was refluxed for 5 h under nitrogen with potassium hydroxide (2.5 g) in water (2 ml) and ethylene glycol (23 ml). The neutral fraction isolated from the hydrolysis after dilution with water and extraction with ether showed a weak ester band in its i.r. spectrum. It was chromatographed over activated neutral alumina and the liquid hydrocarbon fraction (730 mg, 33%) was eluted with petroleum; $\nu_{max.}$ 1 600 cm^{-1}; $\lambda_{max.}$ 260 (log ε 2.4), 267 (3.52), and 274 nm (3.48); δ (CCl_4) 0.8—1.1 (br singlets and doublets under complex multiplets), benzylic protons at 2.6—3.2, no olefinic proton, aromatic protons 7.0—7.3 (m).

Dehydrogenation [2] of the hydrocarbon mixture (100 mg) over palladium–charcoal gave 1-methylfluorene (35 mg), m.p. and mixed m.p. 85°.

The basic aqueous phase from the hydrolysis, on acidification with 6N-hydrochloric acid and extraction with ether, afforded a solid which was recrystallised twice from ethyl acetate to yield the pure hexahydrofluorene acid (5a) (845 mg, 29%), m.p. 170—171°, identical (mixed m.p. and i.r. spectra in $CHCl_3$ solution) with authentic material.[2]

Cyclisation of the Lactone (6) *with Aluminium Chloride:*

[24] M. F. Lappert, *J. Chem. Soc.*, 1961, 817.

(5SR,8RS,9SR,11RS)-5,6,7,8,9,10-*Hexahydro*-8,11-*dimethyl*-5,9-*methanobenzocyclo-octene*-8-*carboxylic Acid* (9).—A solution of the lactone (6) (3.2 g) in dry benzene (60 ml) was added slowly to a stirred refluxing suspension of powdered, sublimed anhydrous aluminium chloride (8 g) in dry benzene (50 ml), into which dry hydrogen chloride gas was passed (*ca.* 3 bubbles per second). After the addition was complete (*ca.* 1 h), stirring and refluxing, with constant flow of hydrogen chloride, were continued for a further 1½ h, and the mixture was finally allowed to attain room temperature. It was poured on ice–concentrated hydrochloric acid, the benzene layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water, and thoroughly extracted with 5% sodium carbonate solution. The regenerated acidic product, obtained on acidification of the combined alkaline washings, was taken up in ether, washed with water, and dried (Na_2SO_4). Evaporation yielded a light red solid, which on sublimation at 160—165 °C (bath temperature) and 0.2 mmHg yielded a colourless solid (2.55 g; 80%), m.p. 178—180°. Recrystallisation from ether–light petroleum gave the *acid* (9) as needles, m.p. 180—181°; $\nu_{max.}$ 1 700 cm^{-1}; $\lambda_{max.}$ 266 (log ε 2.84) and 274 nm (2.86); δ [$(CD_3)_2SO$] 0.89 (3 H, d, *J* 7 Hz), and 1.25br (m) masked under 1.35 (3 H + 1 H, s) (Found: C, 78.55; H, 8.0. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%). Dehydrogenation of (9) (100 mg) with palladium–charcoal (10%; 50 mg) at 320—330 °C for 20 h and chromatography of the crude product gave a liquid (*ca.* 30 mg) which showed a weak band in the u.v. at 254 nm.

The acid (9) (225 mg) was esterified with ethereal diazomethane to afford the *methyl ester* (10) (225 mg, 100%), m.p. 90—91°, which on recrystallisation twice from light petroleum gave thick plates, m.p. 95—96°; $\nu_{max.}$ 1720 cm^{-1}; δ ($CDCl_3$; 220 MHz) 0.87 (3 H, d, *J* 7 Hz), 1.31 (3 H, s), and 3.69 (3 H, s) (Found: C, 78.75; H, 8.3. $C_{17}H_{22}O_2$ requires C, 79.05; H, 8.6%).

(5SR,8RS,9SR,11SR)-*Methyl* 5,6,7,8,9,10-*Hexahydro*-8,11-*dimethyl*-10-*oxo*-5,9-*methanobenzocyclo-octene*-8-*carboxylate* (11).—The methyl ester (10) (230 mg) in acetic acid (2.5 ml) was mixed with a solution of chromic acid (350 mg) in water (1.5 ml) and acetic acid (6 ml) at room temperature and left for 18 h. The mixture was finally heated at 80—85 °C for 1 h, diluted with water, and extracted with ether after saturation with sodium chloride. The extract was washed with cold 2% sodium hydroxide solution until alkaline, and with water, and dried (Na_2SO_4). Evaporation gave a solid which was recrystallised once from light petroleum to afford the *oxo-ester* (11) as needles (205 mg, 82%), m.p. 89—90°; $\nu_{max.}$ 1 722s and 1 768s cm^{-1}; $\lambda_{max.}$ 254 nm (log ε 3.91); δ ($CDCl_3$) 0.94 (3 H, d, *J* 7 Hz), 1.44 (3 H, s), and 3.70 (3 H, s) (Found: C, 75.0; H, 7.2. $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.4%).

Cyclisation of the Lactone (7) *with Aluminium Chloride.*—The lactone (7) [2] (2.2 g) in dry benzene (25 ml) was treated with sublimed anhydrous aluminium chloride (6 g) in dry benzene (30 ml) in the presence of dry hydrogen chloride as described above. The crude solid acidic product was sublimed at 160—165 °C (bath temperature) and 0.2 mmHg to yield material (1.65 g, 75%), m.p. 140—150°. A sample of this mixture was esterified with ethereal diazomethane; g.l.c. analysis of the ester mixture showed the presence of only (5b) and (13), in the ratio *ca.* 1 : 1. Repeated fractional crystallisation of the acid mixture from ethyl acetate–light petroleum afforded (5SR,8SR,9SR,11RS)-5,6,7,8,9,10-*hexahydro*-8,11-*dimethyl*-5,9-*methanobenzocyclo-octene*-8-*carboxylic acid* (12) (*ca.* 200 mg, 10%), m.p. 210°; $\nu_{max.}$ 1 699s cm^{-1}; $\lambda_{max.}$ 260 (log ε 2.76), (2.89), and 274 nm (2.88); δ ($CDCl_3$) 0.94 (3 H, d, *J* 7 Hz) and 1.21br under 1.30 (3 H + 1 H, s) (Found: C, 78.4; H, 8.2. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%).

The acid (12) (150 mg) was esterified with diazomethane; recrystallisation from light petroleum gave the *methyl ester* (13) (140 mg), m.p. 98—99°, as needles; $\nu_{max.}$ 1 722 cm^{-1}; $\lambda_{max.}$ 260 (log ε 2.61), 266 (3.09), and 274 nm (3.11); δ ($CDCl_3$; 220 MHz) 0.88 (3 H, d, *J* 7 Hz), 1.17 (3 H, s), and 3.71 (3 H, s) (Found: C, 78.9; H, 8.5. $C_{17}H_{22}O_2$ requires C, 79.05; H, 8.6%).

The mother liquors from the fractional crystallisation of the aforementioned acid mixture were combined and esterified with diazomethane in ether. The crude methyl ester (1.35 g) was refluxed with potassium hydroxide (2 g) in water (12.5 ml) and 95% ethanol (12.5 ml) for 5 h under nitrogen. The usual work up gave the unhydrolysed ester fraction (660 mg, 30%) which solidified. On crystallisation twice from light petroleum it afforded the pure ester (13), m.p. and mixed m.p. 98—99°.

The acidic fraction gave a solid product (305 mg, 14%), m.p. 165—168°. Recrystallisation three times from ethyl acetate–petroleum afforded the pure acid (5a), and m.p. and mixed m.p.[2] 170—171°, further characterised through as the methyl ester (5b), m.p. and mixed m.p. 47°.

(5SR,8SR,9SR,11SR)-*Methyl* 5,6,7,8,9,10-*Hexahydro*-8,11-*dimethyl*-10-*oxo*-5,9-*methanobenzocyclo-octene*-8-*carboxylate* (14).—The methyl ester (13) (1.3 g) was dissolved in acetic acid (13 ml) and oxidised with chromic acid (1.75 g) in water (8 ml) and acetic acid (30 ml), by the procedure mentioned above, to yield the *oxo-ester* (14) (960 mg, 71%), m.p. 95—96°, as needles (from light petroleum); $\nu_{max.}$ 1 728s and 1 678s cm^{-1}; $\lambda_{max.}$ 255 nm (log ε 4.16); δ ($CDCl_3$) 0.94 (3 H, d, *J* 7 Hz), 1.15 (3 H, s), and 3.75 (3 H, s) (Found: C, 75.1; H, 7.6. $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.4%).

Cyclisation of the Hydroxy-ester (4) *with Aluminium Chloride*—The hydroxy-ester (4)[2] (5 g) in benzene (70 ml) was cyclised with aluminium chloride (12.5 g) in benzene (80 ml) in the presence of hydrogen chloride gas under the same conditions as described for the lactone (6). The solid acidic fraction was purified by sublimation to afford the acid (9) as a solid (1.3 g, 30%), m.p. 179—180°. After recrystallisation from ether–light petroleum it had m.p. and mixed m.p. 180—181°.

The liquid neutral fraction was fractionated to afford (i) material (0.75 g), b.p. 70—100° at 0.3 mmHg and (ii) material (2.6 g), b.p. 135—145° at 0.3 mmHg. G.l.c. analysis of the material (ii) showed the presence of the esters (5b) and (13) as the major components, and several minor components. This was subjected to partial alkaline hydrolysis with potassium hydroxide (1.85 g) in water (13 ml) and 95% ethanol (13 ml), as described above. The unhydrolysed neutral fraction (1.4 g) on chromatography over activated acid-washed alumina (40 g) and elution with benzene–petroleum (1 : 1 to 2 : 1) afforded the ester (13) (670 mg, 15%), m.p. and mixed m.p. 98—99° (from light petroleum). The liquid fractions were not characterised.

The acidic fraction from the hydrolysis was repeatedly recrystallised from aqueous methanol and ethyl acetate–petroleum to afford the pure acid (5a) (880 mg. 20%), m.p. and mixed m.p. 170—171°.

Rearrangements of the Acids (5a) *and* (12) *with Aluminium Chloride.*—(i) *The acid* (5a). A stirred solution of the acid (5a) (500 mg) in dry benzene was refluxed for 4 h with anhy-

drous sublimed aluminium chloride (1.5 g) in the presence of dry hydrogen chloride. The dark red acidic product on sublimation and trituration with ether gave a mixture of acids (5a) and (12) (310 mg), m.p. 150—160°. A portion of this was esterified with diazomethane in ether; g.l.c. analysis then showed the presence of the methyl esters (5b) and (13) in the ratio *ca.* 30 : 70.

(ii) *The acid* (12). The acid (12) (500 mg) under similar conditions gave an acidic product (410 mg), m.p. 195—200°, containing mostly unchanged acid (12). G.l.c. analysis of the crude methyl ester showed the presence of only 5—10% of the ester (5b).

Hydrolysis of the Oxo-esters (11) *and* (14).—(i) A solution of the oxo-ester (11) (100 mg) in methanolic sodium methoxide [from sodium (25 mg) and methanol (20 ml)] was refluxed for 4 h. The solvent was removed *in vacuo* and the residue was diluted with water, acidified, and extracted with ether. The acidic product was re-extracted by thorough washing with 5% sodium carbonate solution, followed by water. The dried (Na_2SO_4) ethereal layer on evaporation left a white crystalline solid (*ca.* 15 mg), m.p. 112°, which on recrystallisation from light petroleum afforded (5SR,8RS,9SR,10RS,11SR)-5,6,7,8,9,10-*hexahydro*-8,11-*dimethyl*-5,9-*methanobenzocyclo-octene*-8,10-*carbolactone* (18), m.p. 113°; $\nu_{max.}$ 1 765 cm^{-1}; $\lambda_{max.}$ 258 nm (log ε 3.4); δ ($CDCl_3$) 0.93 (3 H, d, *J* 7 Hz), 1.27 (3 H, s), and 5.47 (1 H, d, *J* 7 Hz) (Found: C, 79.1; H, 7.6. $C_{16}H_{18}O_2$ requires C, 79.35; H, 7.85%).

The basic aqueous extracts on acidification and extraction with ether gave the acid (17) (75 mg), m.p. 174—175°, which on recrystallisation from ether–light petroleum afforded hexagonal prisms, m.p. 175—176°; $\nu_{max.}$ 1 680s and 1 725s cm^{-1}; $\lambda_{max.}$ 250 (log ε 4.19), 255 (4.20), and 294 nm (3.24) (Found: C, 74.25; H, 7.2. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%).

(ii) The oxo-ester (11) (100 mg) on refluxing with potassium hydroxide (100 mg) in water (1 mg) and methanol (9 ml) for 15 min afforded the acid (17) (95 mg), m.p. and mixed m.p. 174—175°.

(iii) The diastereoisomeric oxo-ester (14) (100 mg), on refluxing for 4 h with sodium methoxide in methanol (20 ml) [from sodium (25 mg)] gave only the unchanged compound (14) (90 mg), identified by mixed m.p. and i.r. spectrum. An almost identical result was obtained on attempted hydrolysis of (14) (100 mg) with aqueous methanolic 5% potassium hydroxide (20 ml) at reflux temperature for 30 min.

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