904. *Terpene Synthesis. Part II.* A Stereoselective Alkylation Induced by an Ethoxycarbonyl Substituent.*

By F. J. McQuillin and P. L. Simpson.

Alkylation of the sodium enolate of ethyl 4-methyl-3-oxo-Δ^4-octalin-9-carboxylate (Ia) with benzyloxymethyl chloride leads to a highly stereoselective introduction of the benzyloxymethyl group on the same side of the molecule as the ethoxycarbonyl group. This stereoselectivity is attributed to a directive influence of the ethoxycarbonyl group which, through its dipolar nature, exerts a favourable solvolytic effect on the transition complex in alkylation with which it is associated. The chemistry of the benzyloxymethyl derivative (Va) has been examined.

In parallel with other experiments * we have examined the benzyloxymethylation of the octalone-ester (Ia). This was chosen so that the stereochemistry of alkylation could be unambiguously determined, but we had in mind also terpenes and terpenoid derivatives with other than a methyl substituent in the angular position.

The ester (Ia), which had not previously been prepared, we made by the Robinson cyclisation method.[1] The derived decalone ester (IIa) and acid (IIb), required later, were obtained by reduction with lithium in ammonia. Catalytic hydrogenation of the ester (Ia) was also examined; an analogue (Ib), lacking the methyl substituent, is hydrogenated exclusively to the *trans*-decalin.[2] The present ester (Ia) behaved similarly; an intermediate first product (III) was characterised and in contact with perchloric acid in acetic acid was isomerised to the more stable epimer (IIa).

The ester (Ia), as its sodium enolate made by the action of sodium hydride in dioxan, gave with benzyloxymethyl chloride a product showing appreciable absorption ($\lambda_{max.}$ 243 mμ, log ε 3·95), indicating the presence of the expected benzyloxymethyl ether (VI) in addition to the required *C*-alkylated material. After removal of the ether by acid hydrolysis to the parent ketone, the *C*-alkylated product, which is resistant to acid, was isolated by distillation and consisted largely of a single isomer which crystallised. This

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* Part I, *J.* 1963, 4634.

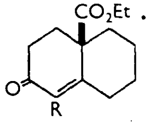
[1] Cf. Ferry and McQuillin, *J.*, 1962, 103, who give references.

[2] (*a*) Dauben, Tweit, and MacLean, *J. Amer. Chem. Soc.*, 1955, **77**, 48; (*b*) Dreiding and Tomasowski, *ibid.*, p. 411; (*c*) Idelson and Becker, *ibid.*, 1958, **80**, 908.

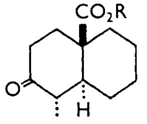
product, which shows a combined ester and ketone absorption at 1711 cm.$^{-1}$, has the structure (Va); alkaline hydrolysis to the corresponding acid (Vb), followed by catalytic debenzylation gave, in high yield, a neutral product, $C_{13}H_{18}O_3$, $\nu_{max.}$ 1730 and 1709 cm.$^{-1}$, which is clearly formed by lactonisation to give a product (VII). From the material remaining after removal of the crystalline isomer (Va), two semicarbazones were obtained, one of which corresponded with that from the ester (Va). The second semicarbazone was shown to correspond with a derivative of an isomeric ketone. From isolation of the semicarbazone the ratio of the amount of isomer (Va), corresponding to β-oriented alkylation,* to the amount of the isomeric ketone, evidently the α-benzyloxymethyl derivative (IV), was found to be *ca.* 8 : 1.

The steric course of alkylation of enolates (X) of substituted cyclohexanones will in general be the result of the balance of steric repulsions between the alkylating agent and proximate groups, *e.g.*, R, on the one hand, and the developing oxo-group on the other. Examples may be noted of a major influence [4,3d] by the substituent R leading to alkylation as in (XI), or of substitution in the converse fashion [3] leading to the stereoisomer (XII) (X = the introduced alkyl group).

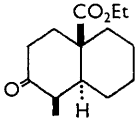
Hydrogenation of octalones of the type (VIII; R′ = H), in which R = Me or $CH_2{\cdot}OH$, give a decalone consisting mainly of the *cis*-fused isomer,[5,6] but when R = CO_2Et the pure *trans*-fused decalone is obtained.[2] The ester group is thus effectively larger than a methyl substituent in hindering absorption and hydrogenation, in this case, from the upper face of the molecule.[7] Since in the alkylation of a compound (VIII; R = R′ = Me) the major product arises from α-substitution,[8] the effect of the ester group in (Ia) in



(Ia : R = Me)
(Ib : R = H)



(IIa : R = Et)
(IIb : R = H)



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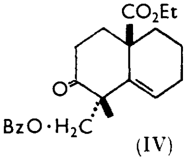

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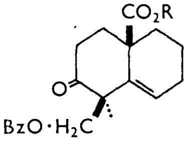
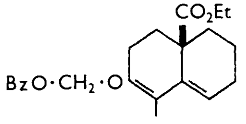


(Va : R = Et)
(Vb : R = H)



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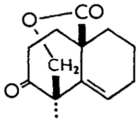

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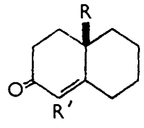
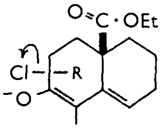


(VIII)



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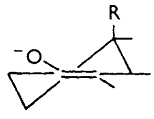
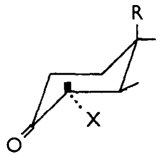
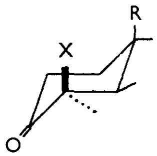


(X)



(XI)



(XII)

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* We use the steroid convention to indicate relative orientation of substituent groups, but the compounds are all racemic.

[3] (*a*) Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753; (*b*) Johnson and Allen, *J. Amer. Chem. Soc.*, 1957, **79**, 1261; (*c*) Fried, Nutile, and Arth, *ibid.*, 1960, **82**, 5704; (*d*) Howe and McQuillin, *J.*, 1958, 1194.

[4] (*a*) Sarett, Johns, Beyler, Poos, and Arth, *J. Amer. Chem. Soc.*, 1953, **75**, 2112; (*b*) Fried, Arth, and Sarett, *ibid.*, 1960, **82**, 1684; (*c*) Djerassi, Osiecki, and Eisenbraun, *ibid.*, 1961, **83**, 4433.

[5] Dauben, Rogan, and Blanz, *J. Amer. Chem. Soc.*, 1954, **76**, 6384.

[6] Minkler, Hussey, and Baker, *J. Amer. Chem. Soc.*, 1956, **78**, 1009.

[7] McQuillin and Ord, *J.*, 1959, 2902.

[8] Cf. Stork and Schulenberg, *J. Amer. Chem. Soc.*, 1962, **84**, 284; and Part I.

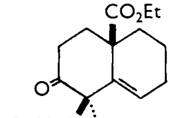
giving the 4β-isomer (Va) as main alkylation product is anomalous in relation to its bulk. This influence of the ester group we attribute to its polar nature and to its effect in stabilising the transition state leading to β-substitution.

In dioxan (dielectric constant 2·2) the sodium enolate will be present largely as an ion pair or aggregate.[9] Reaction with the alkylating agent will involve increasing polarisation of the alkylating agent in the sense, $\overset{\curvearrowright}{\mathrm{R-Cl}}$. In a transition-state complex such as (IX) the ester group, by dipole pairing, or solvation of the developing cation R^+, is suitably placed for assisting preferentially the formation of the observed product. A stereo-directive influence of this kind exerted by a proximate group has been noted by Henbest and his co-workers[10] in relation to epoxidation of olefins where the effective reagent is also an electrophile generated in the transition complex.

The benzyloxymethyl ketone (Va), on debenzylation by palladised charcoal in alcohol, gave the unstable hydroxymethyl ketone (XIII). This substance decomposed slowly in neutral solution, but rapidly in acid and more rapidly in alkaline solution to reform the parent ketone (Ia). In neutral alcohol the unstable product (XIII) was further hydrogenated, with saturation of the olefinic bond. The hydrogenation product, under the action of perchloric acid in acetic acid, gave, in a retroaldol reaction,[11] the *trans*-decalone (IIa) and it is therefore the hydroxymethyl-*trans*-decalone (XIV). Together with this hydroxy-ester, a lactone, $C_{13}H_{18}O_3$, m. p. 136°, was isolated in small amount; for reasons given below, we regard this as having structure (XV).

The unsaturated lactone (VII), by contrast with (XIII), was hydrogenated only very slowly, reduction of the oxo-group accompanying saturation of the olefinic bond. The product from absorption of two equivalents of hydrogen was a hydroxy-lactone, $C_{13}H_{20}O_3$ ($\nu_{max.}$ 3450 and 1721 cm.$^{-1}$), which was oxidised by chromic acid to a keto-lactone ($\nu_{max.}$ 1704 and 1721 cm.$^{-1}$), m. p. 128°. Both of these substances were obtained in high yield. The keto-lactone was converted by methanolic potassium hydroxide into an acid, $C_{12}H_{18}O_3$, $\nu_{max.}$ 1698 cm.$^{-1}$, by elimination of formaldehyde;[11] this differed from the reference acid (IIb) and is therefore regarded as the corresponding acid (XVI) of the *cis*-decalin series. The lactone, m. p. 128°, was also shown to be different from the lactone, m. p. 136°. These lactones are therefore represented as belonging to the *cis*- (XVII) and *trans*-series (XV), respectively.

The different steric course of hydrogenation of the olefinic bond in compounds (VII) and (XIII) appears to be related to a small change in conformation or molecular rigidity derived from formation of the lactone bridge. The major influence we associate with a resistance to conformational twisting of the molecule in the direction indicated by the arrows in (XVIII). Hydrogenation of a lactone (XVIII) would be expected to be hindered



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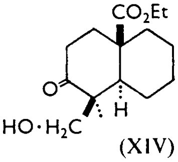
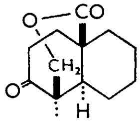


(XIV)



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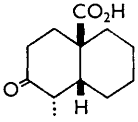

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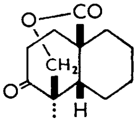
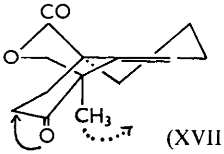
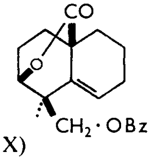


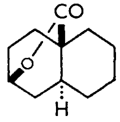
(XVII)



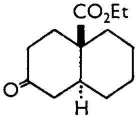
(XVIII)



(XIX)



(XX)



(XXI)

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[9] Zaugg, *J. Amer. Chem. Soc.*, 1960, **82**, 2903; Zaugg, Horron, and Borgwardt, *ibid.*, p. 2895.

[10] Cf. Henbest, Nicholls, Jackson, Wilson, Crossley, Meyers, and McElhinney, *Bull. Soc. chim. France*, 1960, 1365.

[11] Cf. Barton and de Mayo, *J.*, 1954, 887.

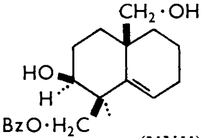
and difficult from either face of the molecule; the influences indicated in that formula are consistent with the observed preference for absorption from the upper (β) face. A further example in support of this interpretation is discussed below.

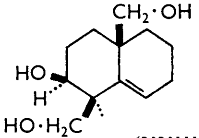
Sodium borohydride reduces the keto-carboxylic ester (Va) mainly to a lactone, $C_{20}H_{24}O_3$, $\nu_{max.}$ 1748 cm.$^{-1}$, which is evidently the bridged lactone (XIX). A similarly constituted lactone (XX) has been described as a product of hydrogenation [2a] or of Ponndorf–Meerwein [12] reduction of the keto-ester (XXI). In the latter case, however, the corresponding hydroxy-ester was isolated and acetylated; our material appeared to relactonise rather readily on acidification after hydrolysis.

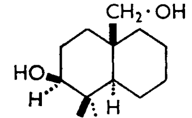
The infrared carboxyl frequencies for the lactones show what appear to be significant differences:

Lactone	(XVII)	(XV)	(VII)	(XIX)
ν(CO) (cm.$^{-1}$)	1721	1730	1730	1748

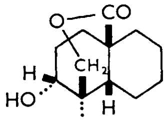
In the lactone (XV), belonging to the *trans*-decalone series, and in (VII), containing the double bond, the "strains" in the lactone rings appear to be of a similar order. The lower carbonyl stretching frequency shown by the lactone (XVII), belonging to the *cis*-decalone series, indicates a somewhat greater stability of the lactone ring than in (XV) or (VII). The value for the lactone (XIX) is still within the expected range [13] for a δ-lactone, but the rather higher frequency indicates greater compression in the boat conformation.

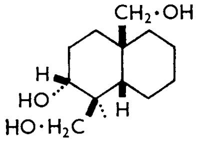

(XXII)


(XXIII)


(XXIV)

(XXV)




(XXVI)

Reduction of the carbonyl groups in the ester (Va) and the lactone (XVII) was found to lead to isomeric triols. Lithium aluminium hydride with ester (Va) gave a diol, clearly (XXII), which by debenzylation and hydrogenation gave successively the triol (XXIII) and the saturated triol (XXIV), m. p. 138°. Sodium borohydride reduced the lactone (XVII) to the same hydroxy-lactone as was obtained from (VII) by hydrogenation and from which (XVII) was derived by oxidation. Formulation of the hydroxy-lactone as the α-hydroxy-derivative (XXV) is in agreement with the course of reduction of other *cis*-decalone derivatives.[14] This lactone (XXV) was reduced by lithium aluminium hydride to a triol, m. p. 144°, which we regard as having the structure (XXVI) and differs from the isomer (XXIV), m. p. 138°. Unless isomers (XXVI) and (XXIV) differ as *cis*- and *trans*-decalin derivatives there is no reason why the reduction of their ketone precursors should lead to these different products.

We have examined also similar transformations starting from the deoxy-acid (XXVIIb), which was obtained in good yield by Wolff–Kishner reduction of the acid (Vb). The acid (XXVIIb) gave, on complete hydrogenation, a saturated lactone which on analogy with the hydrogenation of (Vb) we regard provisionally as the *cis*-decalin derivative (XXVIII). The lactone carbonyl stretching frequency was at 1724 cm.$^{-1}$. The ester (XXVIIa), on

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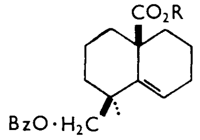
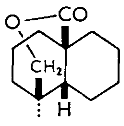
[12] Hussey, Liao, and Baker, *J. Amer. Chem. Soc.*, 1953, **75**, 4727.

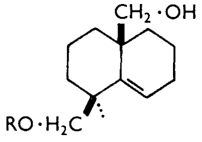
[13] Jones and Gallagher, *J. Amer. Chem. Soc.*, 1959, **81**, 5242.

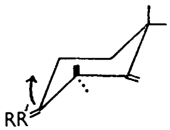
[14] Shoppee and Summers, *J.*, 1950, 687; Djerassi, Yashin, and Rosenkranz, *J. Amer. Chem. Soc.*, 1951, **73**, 4654; 1952, **74**, 422.

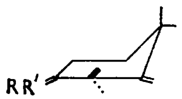
hydrogenation, gave the same lactone (XXVIII) in good yield, and by means of lithium aluminium hydride and debenzylation gave rise also to the mono- and the di-alcohols (XXIXa and b).


(XXVIIa : R = Me)
(XXVIIb : R = H)


(XXVIII)


(XXIXa : R = Ph·CH$_2$)
(XXIXb : R = H)


(XXX)


(XXXI)

In giving rise to the same hydrogenation product (XXVIII), the ester (XXVIIa) and the acid (XXVIIb) differ in behaviour from their oxo-analogues (Va) and (Vb), where the steric course of reduction of the 8,9-double bond is different with the ester (Va) and acid (Vb). There is an evident difference also in the much more ready lactonisation of the intermediate hydroxymethyl ester from (XXVIIa) than of that from (Va). These differences we ascribe to the different degree of conformational distortion possible in the two series. Twisting of the molecule in the sense (XXX) ⟶ (XXXI) will be easier[15] when RR′ = oxo than when R = R′ = H or some other group. This molecular twisting will reduce compression for hydrogenation of the molecule from the lower face[16] and will impede lactonisation by increasing the separation of the ester and the hydroxymethyl group.

EXPERIMENTAL

Ethyl 4-Methyl-3-oxo-Δ^4-octalin-9β-carboxylate (Ia).—Ethyl 2-oxohexanecarboxylate (30 g.) in dry ethanol (100 c.c.) was added with stirring to sodium (4·5 g.) dissolved in dry ethanol (100 c.c.). The sodium enolate solution was cooled in ice, and the methiodide from diethylaminopentan-3-one (25 g.) and methyl iodide (23 g.) in alcohol (100 c.c.) was added slowly with stirring. After 4 hr. at room temperature, the mixture was refluxed for 4 hr., and, after cooling, the pH was adjusted to 7 by addition of acetic acid. After distillation of much of the solvent, the residue was added to water (500 c.c.) and extracted with ether. The ethereal extract was washed with 10% sodium carbonate solution and water, dried, and distilled, to give the *ester* (Ia) (36 g., 55%), b. p. 120—124°/0·4 mm., n_D^{20} 1·5085, $\lambda_{max.}$ 248 mμ (log ε 4·10), $\nu_{max.}$ 1724 (ester), 1667 and 1616 cm.$^{-1}$ (αβ-unsaturated ketone) (Found: C, 70·8; H, 8·15. $C_{14}H_{20}O_3$ required C, 71·15; H, 8·45%). The *2,4-dinitrophenylhydrazone* formed red needles, m. p. 156°, from ethanol (Found: C, 57·7; H, 6·15. $C_{20}H_{24}N_4O_6$ requires C, 57·7; H, 5·8%).

Ethyl 4α-Methyl-3-oxo-10α-decalin-9β-carboxylate (IIa).—Ethyl 4-methyl-3-oxo-Δ^4-octalin-9β-carboxylate (0·5 g.) in ether (20 c.c.) was added to a stirred solution of lithium (1 g.) in liquid ammonia (~200 c.c.). After 20 min., ammonium chloride was added to discharge the blue colour and, after evaporation of the ammonia overnight, ether and water were added to the residue. The ethereal extract, washed with water and dried, gave the *ester* (IIa) (0·4 g., 80%), b. p. 96°/0·1 mm., n_D^{20} 1·4890, $\nu_{max.}$ 1721 (ester) and 1709 cm.$^{-1}$ (ketone) (Found: C, 71·0; H, 9·7. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·4%). The orange *2,4-dinitrophenylhydrazone* had m. p. 156°, from ethanol (Found: C, 57·3; H, 6·35. $C_{20}H_{26}N_4O_6$ requires C, 57·4; H, 6·25%). The *semicarbazone* formed needles, m. p. 172°, from ethanol (Found: C, 60·8; H, 8·5. $C_{15}H_{25}N_3O_3$ requires C, 61·0; H, 8·5%).

Ethyl 4β-Methyl-3-oxo-10α-decalin-9β-carboxylate (III).—Ethyl 4-methyl-3-oxo-$\Delta^{1,9}$-octalin-9β-carboxylate (0·745 g.) in ethanol (30 c.c.) with palladium–charcoal (0·2 g.) absorbed 77 c.c. (1 mol.) of hydrogen, to give the *decalin* (III) (0·65 g., 85%), b. p. 92°/0·1 mm., n_D^{20} 1·4870 (Found: C, 70·9; H, 9·5. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·4%); the infrared absorption [1724 (ester) and 1714 cm.$^{-1}$ (ketone)] differed in detail from that of the 4α-methyl derivative. The 2,4-dinitrophenylhydrazone, m. p. 156° (from ethanol), was identical with that from ethyl

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[15] Barton, Lewis, and McGhie, *J.*, 1957, 2907.
[16] Cf. Lewis and Shoppee, *J.*, 1955, 1365.

4α-methyl-3-oxo-10α-decalin-9β-carboxylate, but a characteristic *semicarbazone* was obtained as plates, m. p. 191° (from ethanol) (Found: C, 60·6; H, 8·7%).

This product (0·4 g.), when kept for 24 hr. in acetic acid (10 c.c.) containing 60% perchloric acid (3 drops), was isomerised to the 1α-methyl compound (0·35 g., 88%), characterised by its infrared spectrum and by formation of the semicarbazone, m. p. and mixed m. p. 172°.

4α-*Methyl*-3-*oxo*-10α-*decalin*-9β-*carboxylic Acid* (IIb).—Ethyl 4α-methyl-3-oxo-10α-decalin-9β-carboxylate (0·1 g.) was warmed with 10% aqueous sodium hydroxide (2 c.c.) and methanol (5 c.c.) for 3 hr. and, after addition of water (5 c.c.) and removal of methanol, the solution was acidified to pH 2. The product, obtained by use of sodium carbonate solution, was 4α-*methyl*-3-*oxo*-10α-*decalin*-9β-*carboxylic acid* (0·055 g., 62%), m. p. 85° (from ether–light petroleum), $\nu_{max.}$ 3159, 1724 (CO_2H) and 1709 cm.$^{-1}$ (ketone) (Found: C, 68·3; H, 8·8. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·6%).

Ethyl 4β-*Benzyloxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylate* (Va).—Sodium hydride (3·5 g.) was added to dry dioxan (60 c.c.) in a 250-c.c. round-bottomed flask carrying a condenser and soda-lime drying tube, a stirrer, and an inlet-tube for nitrogen (dry). The apparatus was placed on a water-bath at 100°, the air displaced by nitrogen, and a solution of ethyl 4-methyl-3-oxo-Δ^4-octalin-9-carboxylate (30 g.) in dry dioxan (50 c.c.) was added during 5 min. with stirring. After 5 hours' heating and stirring in dry nitrogen, the solution was cooled (ice) and benzyl chloromethyl ether (21 g.) in dry dioxan (60 c.c.) was added with stirring in ½ hr. The mixture was stirred for a further 4 hr. at room temperature. Water (600 c.c.) was then added, followed by ether. The ethereal extract was washed with 10% sodium carbonate solution and water, and dried. Distillation gave a little benzyl alcohol and unchanged material, followed by a fraction (21·8 g., 52%), b. p. 170—200°/0·1 mm., n_D^{20} 1·5370, $\lambda_{max.}$ 243—245 mμ (log ε 3·95). This material (21·8 g.) was shaken in dioxan (35 c.c.) with concentrated sulphuric acid (1 c.c.) and water (4 c.c.) at 60° for 25 min., poured into 5% sodium hydrogen carbonate solution (25 c.c.), and extracted into ether. The ethereal extract, when washed, dried, evaporated, and distilled, gave benzyl alcohol and recovered ester, and a fraction (12·3 g.), b. p. 170—180°/0·5 mm., n_D^{20} 1·5340, $\lambda_{max.}$ 243—245 mμ (log ε 3·0), which crystallised to give *ethyl* 4β-*benzyloxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylate* (8 g.), m. p. 60—61°, (from light petroleum), $\nu_{max.}$ 3079, 3046, 3030, 745, and 703 (benzyl), and 1711 cm.$^{-1}$ (ester and ketone combined) (Found: C, 74·0; H, 8·2. $C_{22}H_{28}O_4$ requires C, 74·0; H, 7·9%). The 2,4-*dinitrophenylhydrazone* formed orange-yellow plates, m. p. 102°, from ethanol (Found: C, 62·8; H, 5·9. $C_{28}H_{32}N_4O_7$ requires C, 62·6; H, 5·9%). The *semicarbazone* was obtained as plates, m. p. 142° (from ethanol), $\lambda_{max.}$ 224 mμ (ε 11,400) (Found: C, 66·5; H, 7·6. $C_{23}H_{31}N_3O_4$ requires C, 66·8; H, 7·5%). Removal of the crystalline material, m. p. 61°, left a residue which on chromatography gave further small quantities of the crystalline ketone. The remaining oil gave a mixture of semicarbazones which was separated into the above semicarbazone, m. p. 142°, as the major constituent, and an isomeric *semicarbazone*, m. p. 153°, as plates from benzene–light petroleum (Found: C, 66·9; H, 7·55%), $\lambda_{max.}$ 225 mμ (ε 11,200; *i.e.*, typical of a semicarbazone of a saturated ketone). The latter is regarded as the derivative of ethyl 4α-benzyloxymethyl-4β-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylate.

4β-*Benzyloxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylic Acid* (Vb).—Ethyl 4β-benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylate (3 g.) in methanol (15 c.c.) was warmed for 3 hr. with 10% sodium hydroxide solution (10 c.c.). The *acid* (Vb) released by acidification was extracted in 10% sodium carbonate solution (50 c.c.) and recovered by acidification; it was obtained as a powder (2·8 g., 90%), m. p. 96° (from ether–pentane), $\nu_{max.}$ 3052, 3030, 1660, 745, 697 (benzyl), 3358 (CO_2H), and 1739 cm.$^{-1}$ (CO_2H and ketone combined) (Found: C, 73·3; H, 7·3. $C_{20}H_{24}O_4$ requires C, 73·2; H, 7·3%).

Hydrogenation of Ethyl-4β-*Benzyloxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylate*.—This ester (0·424 g.) in ethanol (30 c.c.) with palladised charcoal (0·1 g.) took up 1 equiv. of hydrogen (28 c.c., 1 mol.) in 1 hr., 2 days being required for complete hydrogenation (59 c.c.). The products were *ethyl* 4β-*hydroxymethyl*-4α-*methyl*-3-*oxo*-10α-*decalin*-9β-*carboxylate* (XIV) (0·25 g., 85%), b. p. 130—133°/0·15 mm., n_D^{20} 1·5062, $\nu_{max.}$ 3490 (OH), 1724 (ester), and 1709 cm.$^{-1}$ (ketone) (Found: C, 67·5; H, 8·8. $C_{13}H_{24}O_4$ requires C, 67·2; H, 8·95%) and the corresponding *lactone* (XV) (0·01 g., 3%) as needles, m. p. 136° (from benzene–light petroleum), $\nu_{max.}$ 1730 (δ-lactone) and 1705 cm.$^{-1}$ (ketone) (Found: C, 70·1; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%).

This decalin ester (0·2 g.) was kept overnight in acetic acid (5 c.c.) containing 60% perchloric acid (5 drops), and the product recovered by adding 10% sodium carbonate solution to pH 7 and extracting the whole with ether; this gave ethyl 4α-methyl-3-oxo-10α-decalin-9β-carboxylate (0·17 g., 90%), b. p. 95°/0·1 mm., n_D^{20} 1·4900, identified by its infrared spectrum and by formation of a semicarbazone, m. p. and mixed m. p. 172°.

Stability of Ethyl 4β-*Hydroxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylate* (XIII) *under Acid and Alkaline Conditions.*—Ethyl 4β-benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylate (0·1 g.) was debenzylated by hydrogenation (uptake 6·9 c.c., 1 mol.) at room temperature in ethanol (10 c.c.) with palladised charcoal (0·05 g.), and the product was isolated carefully to avoid decomposition. The product of loss of formaldehyde, ethyl 4-methyl-3-oxo-Δ^{4}-octalin-9-carboxylate, had $\lambda_{max.}$ 248 mμ (log ε 4·10). The crude hydrogenation product had $\lambda_{max.}$ 242 mμ (log ε 3·48). This absorption was observed not to increase for an ethanol solution kept for 2 days. The effect of added acid and alkali was as follows:

2% Hydrochloric acid in ethanol.

Time (hr.)	0	0·08	0·5	2·0	12·0	30·0
$\lambda_{max.}$ (mμ)	242	242	242	243	244	245
ε	3050	3310	3810	5100	9650	11,100
Loss of CH_2O (%)	24	26	30	40	75	89

5% Sodium hydroxide in ethanol.

Time (hr.)	0	0·5	1·0	12·0
$\lambda_{max.}$ (mμ)	242	246	247	248
ε	3200	9750	9900	11,200
Loss of CH_2O (%)	25	75	76	89

The loss of formaldehyde was calculated by taking ε = 12,600 for the product.

4β-*Benzyloxymethyl*-3β-*hydroxy*-4α-*methyl*-$\Delta^{5,10}$-*octalin*-9β-*carboxylic Acid* 3,9-*Lactone* (XIX).—Ethyl 4β-benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylate (2·0 g.) in ethanol (15 c.c.) was mixed with sodium borohydride (0·4 g.) in water (2 c.c.) and kept overnight. After addition of acetic acid, followed by 10% sodium carbonate solution to pH 7, the ethanol was removed *in vacuo*. The residue, when extracted with ether, gave a product, b. p. 180°/0·05 mm., n_D^{20} 1·5352, $\nu_{max.}$ 3490 (OH) and 1751 cm.$^{-1}$ (lactone) with a shoulder at 1721 cm.$^{-1}$ (ester). This *lactone* was purified by dissolving it in sodium hydroxide solution, washing the alkaline solution with ether, and reisolating it by acidification. Distillation then gave the product (1·0 g., 65%), b. p. 170°/0·1 mm., n_D^{20} 1·5330, $\nu_{max.}$ 3050, 3023, 1658, 737, 697 (benzyl), and 1748 cm.$^{-1}$ (δ-lactone) (Found: C, 77·2; H, 7·9. $C_{20}H_{24}O_3$ requires C, 76·9; H, 7·7%).

1β-*Benzyloxymethyl*-10-*hydroxymethyl*-1α-*methyl*-$\Delta^{8,9}$-2β-*octalol* (XXII).—Ethyl 4β-benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylate (1 g.) in dry ether (50 c.c.) was mixed with lithium aluminium hydride (0·4 g.) in dry ether (50 c.c.) and after 1 hr. the mixture was heated under reflux for 5 hr. The product released into ether by careful addition of water and sodium potassium tartrate solution gave the *octalol* (XXII) (0·65 g., 68%), as plates, m. p. 106° (from ether–light petroleum), $\nu_{max.}$ 3390 (OH), 3078, 3058, 3029, 1660, 737, and 697 cm.$^{-1}$ (benzyl) (Found: C, 75·7; H, 9·1. $C_{20}H_{28}O_3$ requires C, 76·0; H, 8·8%). With boiling acetic anhydride–sodium acetate this gave a *diacetate*, b. p. 160°/0·1 mm., n_D^{20} 1·5230 (Found: C, 71·7; H, 8·3. $C_{24}H_{32}O_5$ requires C, 72·0; H, 8·0%). The *bis*-3,5-*dinitrobenzoate* formed needles, m. p. 170°, from methanol (Found: C, 57·4; H, 4·8. $C_{34}H_{34}N_4O_{13}$ requires C, 57·7; H, 4·8%).

4β-*Hydroxymethyl*-4α-*methyl*-3-*oxo*-10β-*decalin*-9β-*carboxylic Acid Lactone* (XVII).—4β-Hydroxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylic acid (3·12 g.) in ethanol (25 c.c.) with palladised charcoal (1 g.) absorbed 230 c.c. (1 mole) of hydrogen in 3—4 hr., but absorption of the second mole required 4 days. The resulting *lactone* (1·75 g., 82%) formed needles, m. p. 128° (from light petroleum), $\nu_{max.}$ 1721 (δ-lactone) and 1704 cm.$^{-1}$ (saturated ketone) (Found: C, 70·7; H, 8·4. $C_{13}H_{18}O_3$ requires C, 70·4; H, 8·1%). The 2,4-*dinitrophenylhydrazone* formed yellow plates, m. p. 220°, from ethanol–ethyl acetate (Found: C, 57·0; H, 5·6. $C_{19}H_{22}N_4O_6$ requires C, 56·7; H, 5·5%). The *semicarbazone* formed plates, m. p. 230—231°, from ethanol–chloroform (Found: C, 60·6; H, 7·9. $C_{14}H_{21}N_3O_3$ requires C, 60·2; H, 7·5%).

4α-*Methyl*-3-*oxo*-10β-*decalin*-9β-*carboxylic Acid* (XVI).—The lactone (XVII) (0·5 g.) was heated with sodium hydroxide (4 g.) in water (10 c.c.) and methanol (30 c.c.) for 5 hr. and the mixture brought to pH 7 by addition of dilute hydrochloric acid. After removal of methanol by distillation the pH was brought to 2 and the product extracted in ether. Recovery of acidic material with 10% sodium carbonate solution gave the *acid* (XVI) (0·3 g., 70%), m. p. 155° (from ethyl acetate), $\nu_{max.}$ 3159 (CO_2H) and 1698 cm.$^{-1}$ (CO_2H and ketone combined) (Found: C, 69·0; H, 8·8. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·8%).

4β-*Hydroxymethyl*-4α-*methyl*-3-*oxo*-$\Delta^{5,10}$-*octalin*-9β-*carboxylic Acid Lactone* (VII).—4β-Benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylic acid (1 g.) in ethanol (30 c.c.) with palladised charcoal (0·2 g.) absorbed 73 c.c. (1 mol.) of hydrogen in 2 hr., to give the *lactone* (VII) (0·55 g., 85%), as needles, m. p. 71° (from ether–light petroleum), $\nu_{max.}$ 3046 (C=C), 1730 (δ-lactone), and 1709 cm.$^{-1}$ (ketone) (Found: C, 70·8; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The 2,4-*dinitrophenylhydrazone* was obtained as orange-yellow plates, m. p. 222°, from ethyl acetate–chloroform (Found: C, 56·8; H, 5·0. $C_{19}H_{20}O_6N_4$ requires C, 57·0; H, 5·0%). The *semicarbazone* formed plates, m. p. 248°, from ethanol–chloroform (Found: C, 60·5; H, 6·9. $C_{14}H_{19}N_3O_3$ requires C, 60·7; H, 6·9%).

3α-*Hydroxy*-4β-*hydroxymethyl*-4α-*methyl*-10β-*decalin*-9β-*carboxylic Acid* 4,9-*Lactone* (XXV).—The lactone of 4β-hydroxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylic acid (0·3 g.) with palladised charcoal (0·2 g.) in ethanol (30 c.c.) gave, after the uptake of 31 c.c. (1 mol.) of hydrogen (3 days), a mixture showing infrared bands at 3490 (OH), 3048 (C=C), and 1715 cm.$^{-1}$ (lactone). After addition of more catalyst (0·4 g.) hydrogenation was continued for a further 3 days, to a hydrogen uptake of $\sim$2 mol. The *lactone* (XXV) was then isolated (0·18 g., 61%), as needles, m. p. 127° (from ethyl acetate containing a little light petroleum), $\nu_{max.}$ 3450 (OH) and 1721 cm.$^{-1}$ (δ-lactone) (Found: C, 69·7; H, 9·2. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%).

This material (0·334 g.) in acetic acid (20 c.c.) was mixed with chromium trioxide (0·2 g.) in water (20 c.c.) and kept for 24 hr., giving the lactone (XVII) (0·28 g., 85%), m. p. 128°, identified by m. p., mixed m. p., and infrared spectrum.

This lactone (XVII) (0·12 g.) in ethanol (30 c.c.) was mixed with sodium borohydride (0·05 g.) in water (2 c.c.) and kept overnight; it thus reformed the lactone (XXV) (0·08 g., 65%), m. p. 127°, identified by m. p., mixed m. p., and infrared spectrum.

1β,10β-*Bishydroxymethyl*-1α-*methyl*-9β-*decalin*-2α-*ol* (XXVI).—Lithium aluminium hydride (0·06 g.) in dry ether (15 c.c.) was added to the lactone (XXV) (0·1 g.) in dry ether (15 c.c.) and after 1 hr. the mixture was refluxed for 3 hr. The product, isolated by addition of water and of sodium potassium tartrate solution, gave the *triol* (XXVI) (0·061 g., 65%), plates, m. p. 144° (from ethyl acetate), with intense infrared absorption at 3350 cm.$^{-1}$ (OH) (Found: C, 69·0; H, 10·5. $C_{13}H_{24}O_3$ requires C, 68·6; H, 10·5%).

1β,10β-*Bishydroxymethyl*-1α-*methyl*-$\Delta^{8,9}$-2β-*octalol* (XXIII).—1β-Benzyloxymethyl-10-hydroxymethyl-1α-methyl-$\Delta^{8,9}$-2β-octalol (1 g.) in ether (50 c.c.) was added with stirring to lithium (0·4 g.) dissolved in liquid ammonia ($\sim$ 400 c.c.). After 20 min., ammonium chloride was added and, after evaporation of ammonia (overnight), the product was isolated by addition of water. This was the *octalol* (XXIII) (0·65 g., 87%), needles, m. p. 169° (from chloroform–light petroleum), $\nu_{max.}$ 3335 (OH), 3058, and 1621 cm.$^{-1}$ (C=C) (Found: C, 69·3; H, 9·75. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·75%).

1β,10β-*Bishydroxymethyl*-1α-*methyl*-9β-*decalin*-2β-*ol* (XXIV).—1β-Benzyloxymethyl-10-hydroxymethyl-1α-methyl-$\Delta^{8,9}$-2β-octalol (0·115 g.) with palladised charcoal (0·1 g.) in ethanol (20 c.c.) absorbed 17·5 c.c. (2 mol.) of hydrogen in 24 hr., to give the *triol* (XXIV) (0·065 g., 78%), needles, m. p. 138° (from ethyl acetate) (Found: C, 68·8; H, 10·1. $C_{13}H_{24}O_3$ requires C, 68·6; H, 10·5%). The infrared spectrum [intense absorption at 3365 cm.$^{-1}$ (OH)] differed in detail from that of 1β,10β-bishydroxymethyl-1α-methyl-9β-decalin-2α-ol. The two triols gave a mixed m. p. 115—120°, showing clearly that they are different.

Hydrogenation of 1β,10β-bishydroxymethyl-1α-methyl-$\Delta^{8,9}$-2β-octalol also gave the triol (XXIV), identified by its infrared spectrum, and m. p. and mixed m. p. 138°.

4β-*Benzyloxymethyl*-4α-*methyl*-$\Delta^{5,10}$-*octalin*-9β-*carboxylic Acid* (XXVIIb).—Sodium (1·25 g.) was dissolved in diethylene glycol (50 c.c.), and the mixture heated to 180°. Anhydrous hydrazine ($\sim$7 c.c.) was then added until the mixture refluxed. The mixture was cooled to 70°, and 4β-benzyloxymethyl-4α-methyl-3-oxo-$\Delta^{5,10}$-octalin-9β-carboxylic acid (3·4 g.) was added. After being heated for 5 hr. at 180°, followed by 3—4 hr. at 210°, the mixture was cooled, poured into water (100 c.c.), neutralised with 10% hydrochloric acid, and extracted with ether. The ethereal extracts gave the *acid* (XXVIIb) (2·5 g., 78%), plates, m. p. 108° (from light petroleum containing a few drops of ether), $\nu_{max.}$ 3061, 750, 702 (benzyl), and 1689 cm.$^{-1}$ (CO_2H) (Found: C, 76·8; H, 8·2. $C_{20}H_{26}O_3$ requires C, 76·5; H, 8·3%). The *methyl* *ester*, obtained by the use of diazomethane, formed needles, m. p. 82—83° (from ether–light petroleum), $\nu_{max.}$ 3058, 3038, 1639, 740, 649 (benzyl), and 1724 cm.$^{-1}$ (ester) (Found: C, 76·3; H, 8·5. $C_{21}H_{28}O_3$ requires C, 76·7; H, 8·5%).

1β-*Benzyloxymethyl*-10-*hydroxymethyl*-1α-*methyl*-$\Delta^{8,9}$-*octalin* (XXIXa).—The last-mentioned ester (1·5 g.) was kept overnight with lithium aluminium hydride in dry ether (100 c.c.), to give the *alcohol* (XXIXa) (1·45 g., 95%), b. p. 160°/0·3 mm., n_D^{20} 1·5442, $\nu_{max.}$ 3415 (OH), 3067, 3030, 733, 694 cm.$^{-1}$ (benzyl) (Found: C, 79·9; H, 9·6. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·3%).

4β-*Hydroxymethyl*-4α-*methyl*-10β-*decalin*-9β-*carboxylic Acid Lactone* (XXVIII).—(i) 4β-Benzyloxymethyl-4α-methyl-$\Delta^{5,10}$-octalin-9β-carboxylic acid (0·17 g.) in ethanol (30 c.c.) with palladised charcoal (0·2 g.) absorbed 13 c.c. (1 mol.) of hydrogen in 1 hr., and 26 c.c. after 2 days. The product was the *lactone* (XXVIII) (0·1 g., 88%), b. p. 110°/0·3 mm., n_D^{20} 1·5150, $\nu_{max.}$ 1724 cm.$^{-1}$ (δ-lactone) (Found: C, 74·7; H, 10·0. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·7%).

(ii) Methyl 4β-benzyloxymethyl-4α-methyl-$\Delta^{5,10}$-octalin-9β-carboxylate (0·27 g.), similarly hydrogenated, absorbed 20·5 c.c. (1 mol.) in 1 hr. and 40 c.c. (2 mol.) in 2 days. The product, on distillation, gave the lactone (XXVIII) (0·16 g., 90%), b. p. 105°/0·1 mm., n_D^{20} 1·5155, with the infrared absorption stated above.

1β,10β-*Bishydroxymethyl*-1α-*methyl*-$\Delta^{8,9}$-*octalin* (XXIXb).—1β-Benzyloxymethyl-10-hydroxymethyl-1α-methyl-$\Delta^{8,9}$-octalin (0·4 g.) in ether (30 c.c.) was added to a solution of lithium (0·3 g.) in liquid ammonia (~200 c.c.) and after 15—20 min. treated with ammonium chloride. The product, isolated by addition of water and ether, was 1β,10β-*bishydroxymethyl*-1α-*methyl*-$\Delta^{8,9}$-*octalin* (0·2 g., 66%), plates, m. p. 76° (from chloroform–light petroleum), $\nu_{max.}$ 3370 cm.$^{-1}$ (OH) (Found: C, 74·1; H, 10·5. $C_{13}H_{22}O_2$ requires C, 74·3; H, 10·5%). The *bis*-3,5-*dinitrobenzoate* formed needles, m. p. 168°, from ethanol (Found: C, 54·1; H, 4·7. $C_{27}H_{26}N_4O_{12}$ requires C, 54·1; H, 4·3%).

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