## 788. *Terpene Synthesis. Part V.* Benzyloxymethylation as a Route to both the* 1α- *and* 1β-*Hydroxymethyl Derivatives of* 1,4a-*Dimethyl*-$\Delta^{8,8a}$-*octal*-2-*one*

By F. J. McQuillin and R. B. Yeats

Alkylation of octalones of type (I) with benzyloxymethyl chloride has already been shown to lead to the 1β- and 1α-benzyloxymethyl derivatives, (II) and (III), respectively, as the principal product in the cases when R = $CO_2Et$ or Me. A method of reduction of the ester group in compound (II), *i.e.*, $CO_2Et \longrightarrow$ Me, has been worked out to give access to the 1β-hydroxymethyl-substituted series represented by structure (V). Observations are made on the relative stability of various bridged lactones and lactols derived from compounds (XI) and (VII) which require chair $\longrightarrow$ boat inversion of a ring.

In exploring the use of benzyloxymethyl chloride for the alkylation of octalones of the type (I) we encountered what appeared to be a steric directing effect depending on the nature of the substituent group R. In the instances where R = $CO_2Et$ or Me the principal products were the 1β- (II; R = Et) and the 1α-benzyloxymethyl derivative (III), respectively. By conversion into the lactone (IV), the orientation of the 1β-isomer (II) could be determined with certainty.[1b] In the case of the product (III), however, the steric assignment was based on acceptable, but less certain, grounds.[1a] Alkylation from the α-side is reasonably ascribed to steric repulsion exerted by the methyl substituent, R. The converse influence of the ester group (I; R = $CO_2Et$) was attributed [1b] to a preferential

* Part IV, F. J. McQuillin, W. O. Ord, and P. L. Simpson, *J.*, 1964, 5526.

[1] (*a*) C. L. Graham and F. J. McQuillin, *J.*, 1963, 4634; (*b*) F. J. McQuillin and P. L. Simpson, *J.*, 1963, 4726.

solvation effect of the ester group on the transition state leading to β-alkylation. An effect of this kind could be more widely useful. However, in a number of instances of rapid protonation,[2] of bromination,[2] and of some alkylation reactions [3] there have been indications of a preferred axial approach of the reagent, and the steric course of substitution reactions of this kind is in any case sensitive to small structural changes.[4] We were, therefore, conscious of the need to establish with certainty the orientation of the product regarded as compound (III).

The main product of alkylation of the octalone (I; R = Me), *i.e.*, (III), is accompanied by the isomer (V), which we have already characterised.[1a] We have now verified the steric configuration (V) assigned to this isomer by showing, through reduction of the ester group in compound (II), that compounds (II) and (V) belong to the same 1β-substituted series. The major alkylation product (III) therefore belongs to the 1α-series. For reduction of the ester group we employed the sequence: $CO_2R \longrightarrow CHO \longrightarrow CH_3$. In the alternative route: $CO_2R \longrightarrow CH_2OH \longrightarrow CH_3$ the intermediate alcohol would be expected to be sensitive to homoallylic rearrangement.[5] The procedure was first examined in the series: (VI) ⟶ (VII) ⟶ (VIII) ⟶ (X). This simpler model was chosen also so as to examine the stability of the lactone intermediate (VII) in comparison with the rather more heavily substituted analogue (XI) which we had already prepared.[1b] The lactone (XI) ($\nu_{CO}$ 1748 cm.$^{-1}$) by hydrolysis and esterification of the hydroxy-acid with diazomethane gave a product which chromatography indicated to be the derived ester (XII), and which, however, reverted to the lactone (XI) too rapidly for it to be isolated. Sodium borohydride reduction of compound (VI; R = Et) gave directly a lactonic product (VII) ($\nu_{CO}$ 1742 cm.$^{-1}$) of comparable stability. We were especially interested in the stability of the boat-form ring in these lactones because of the reasoning regarding conformation which we had employed [1b] in deriving the stereochemistry assigned to the ketone (III).

The lactone (XI) was found to be rather easily reduced. Sodium borohydride in warm solution, for example, gave the diol (XIII); certain sugar lactones provide a parallel.[6] By contrast, in the aldosterone series, it was found possible to limit reaction so as to effect lactone ⟶ lactol reduction using lithium aluminium hydride.[7] The alkoxy-metal hydrides [8] and certain boranes [9] are milder reagents and by careful experimental control using lithium triethoxyaluminium hydride we have been able to reduce the lactone (VII) to the lactol (VIII) in 85% yield. We have at present no indication of the orientation of the lactol hydroxyl group, but our reaction product appeared to comprise only a single isomer. By Wolff–Kishner reduction, using anhydrous hydrazine,[10] the lactol (VIII) gave in high yield the known [11] trimethyloctalol (X). This we have been able to obtain in a

[2] Cf. E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 6269.

[3] C. Djerassi, J. Burakevich, J. W. Chamberlain, D. Elad, T. Toda, and G. Stork, *J. Amer. Chem. Soc.*, 1964, **86**, 465; W. S. Johnson, *Chem. and Ind.*, 1956, 167; R. Howe and F. J. McQuillin, *J.*, 1958, 1194.

[4] Cf. Y. Mazur and F. Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 6296; F. Sondheimer, Y. Klibansky, Y. M. Y. Haddad, G. H. R. Summers, and W. Klyne, *J.*, 1961, 767; E. Wenkert and A. Tahara, *J. Amer. Chem. Soc.*, 1960, **82**, 3229; C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *ibid.*, 1961, **83**, 4433; J. H. Fried, A. N. Nutile, and G. E. Arth, *ibid.*, 1960, **82**, 5704.

[5] J. W. Rowe, A. Melera, D. Arigoni, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1957, **40**, 1; J. J. Bonet, H. Wehrli, and K. Schaffner, *ibid.*, 1962, **45**, 2615.

[6] M. L. Wolfrom and H. B. Wood, *J. Amer. Chem. Soc.*, 1951, **73**, 2933.

[7] J. von Euw, R. Neher, and T. Reichstein, *Helv. Chim. Acta*, 1955, **38**, 1423; K. Heusler and A. Wettstein, *ibid.*, 1962, **45**, 347; W. S. Johnson, J. C. Collins, R. Pappo, and M. B. Rubin, *J. Amer. Chem. Soc.*, 1958, **80**, 2585.

[8] H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, 1959, **81**, 502; G. Hesse and R. Schrödel, *Annalen*, 1957, **607**, 24; R. Grewe and H. Büttner, *Chem. Ber.*, 1958, **91**, 2452.

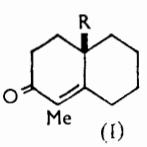
[9] H. C. Brown and D. B. Bigley, *J. Amer. Chem. Soc.*, 1961, **83**, 486; W. R. Vaughan, C. T. Geotschal, M. H. Goodrow, and C. L. Warren, *ibid.*, 1963, **85**, 2282.

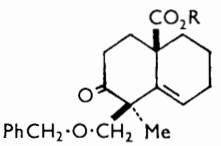
[10] D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, *J.*, 1955, 2056; D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1961, **83**, 4076.

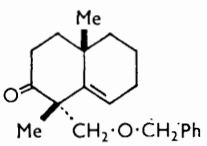
[11] P. C. Dutta and S. L. Mukherjee, *J.*, 1960, 67; W. G. Dauben and A. C. Ashcraft, *J. Amer. Chem. Soc.*, 1963, **85**, 3673.

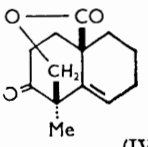
crystalline state and to characterise more fully than previously. The trimethyloctalol (X) was also produced by sodium borohydride reduction of the ketone (IX), obtained by methylation of compound (I; R = Me).

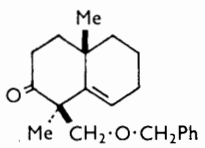
This method of reduction of the ester group in substances of the type (VI) was then applied to the benzyloxymethyl derivative (II; R = Et).

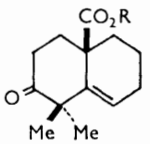

(I)

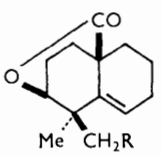

(II)

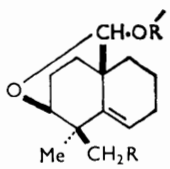

(III)

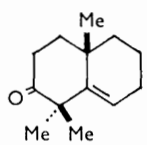

(IV)

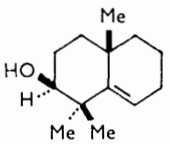

(V)

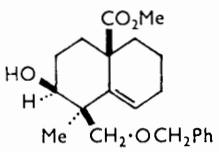

(VI)

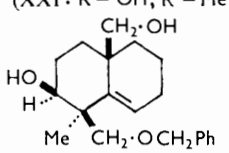

(VII: R = H)
(XI: R = O·CH$_2$Ph)
(XV: R = OH)

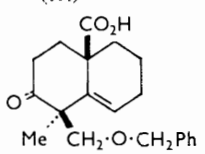

(VIII: R = R′ = H)
(XVII: R = O·CH$_2$Ph, R′ = H)
(XVIII: R = OH, R′ = H)
(XX: R = O·CH$_2$Ph, R′ = Me)
(XXI: R = OH, R′ = Me)

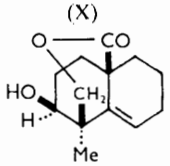

(IX)

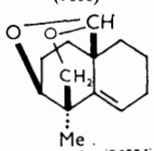

(X)

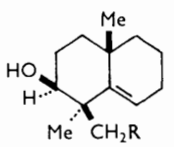

(XII)

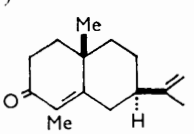

(XIII)

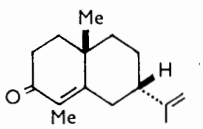

(XIV)


(XVI)


(XIX)


(XXII: R = O·CH$_2$Ph)
(XXIII: R = OH)


(XXIV)


(XXV)

In the earlier work,[1b] sodium borohydride reduction of the ester (II; R = Et) was found to give the lactone (XI) accompanied by other materials. We find sodium borohydride reduction of the keto-acid (XIV), as its sodium salt, in place of the ester (II; R = Et), a more satisfactory procedure which avoids further reduction of the lactone which is responsible for some of the by-products.

Debenzylation of the lactone (XI) gave a crystalline product, evidently (XV), with a significant change also in the lactone carbonyl absorption: $\nu_{CO}$ for (XI) 1747 cm.$^{-1}$, for (XV) 1727 cm.$^{-1}$. We were interested in comparing the stability of this product, compound (XV), with that of the isomeric lactone (XVI). By hydrolysis and relactonisation, compound (XV) gave what was clearly a mixed product with two carbonyl absorption bands: $\nu_{CO}$ 1727 and 1712 cm.$^{-1}$ of about equal intensity. From this product we have been able, so far, to reisolate in a pure condition only the lactone (XV). The second

carbonyl absorption at 1712 cm.$^{-1}$ must be attributed to the isomeric lactone (XVI) which is evidently of a closely similar order of stability.

Reduction of the lactone (XI) to the lactol (XVII) was effected using lithium triethoxyaluminium hydride under the conditions already devised for the lactone (VII). The lactol (XVII) could be debenzylated by catalytic reduction to a product (XVIII) which, like its precursor (XVII), was crystalline and evidently a single substance. The hydroxymethyl lactol (XVIII), on treatment with anhydrous copper sulphate in acetone,[12] gave an anhydro-derivative, $C_{13}H_{15}O_2$, which we have formulated as (XIX); there was no indication of an isopropylidene derivative being formed.

The lactols (XVII) and (XVIII), by means of methanol–ammonium chloride,[13] were both converted into methyl ether derivatives, (XX) and (XXI), respectively, which could be inter-related by lithium–ammonia debenzylation: (XX) ⟶ (XXI). Unlike the lactols, these methyl ether derivatives were both non-crystalline materials which on chromatography were found to contain two closely similar components; the anomeric methyl ethers may be expected to be of closely similar stability. It is of interest that compound (XXI) is formed rather than the anhydro-derivative (XIX).

Wolff–Kishner reduction of the lactol (XVII) gave an alcohol (XXII) characterised as the 3,5-dinitrobenzoate, m. p. 137°. This same product was obtained by benzyloxymethylation of the octalone (I; R = Me), removal by crystallisation of the major product (III), and reduction with sodium borohydride of the residual ketone which is mainly the 1β-isomer (V). Chromic acid oxidation of the alcohol (XXII) gave the ketone (V) which, however, decomposed rapidly and is clearly less stable than the isomer (III). The cyperones (XXIV) and (XXV) represent another isomeric pair, of which one, epi-α-cyperone (XXV), is much the more sensitive to autoxidation.[14]

These results confirm the stereochemistry of alkylation of the octalone (I; R = Me) and hence the stereo-directive influence dependent on the nature of the substituent R = Me or $CO_2Et$. The procedure for reduction of the lactone (XI) also makes available *via* benzyloxymethylation both of the isomeric hydroxymethyl derivatives corresponding to compounds (III) and (V), by appropriate choice of the substituent groups R in the parent octalone (I).

## Experimental

Thin-layer chromatography has been used throughout as a routine means of following reactions, and as a rapid method of checking the homogeneity and/or identity of fractions taken in column chromatography. As previously, we have used phosphomolybdic acid as a general detector spray, with 2,4-dinitrophenylhydrazine spray for ketones.

*8β-Benzyloxymethyl-Δ$^{1,8a}$-octahydro-7β-hydroxy-8α-methylnaphthalene-4aβ-carboxylic Acid Lactone* (XI).—The acidic product of hydrolysis of ethyl 8β-benzyloxymethyl-Δ$^{1,8a}$-octahydro-8α-methyl-7-oxonaphthalene-4*a*β-carboxylate (3 g.) with methanolic potash was isolated, redissolved in warm 10% aqueous sodium hydroxide solution (20 c.c.) and water (135 c.c.), treated with sodium borohydride (0·3 g.), and warmed for 2 hr. Careful acidification and extraction into ether gave a product which from its small $R_F$ value on silica gel in 20% ethyl acetate in benzene is regarded as the hydroxy-acid. However, the residue obtained after vacuum evaporation of the solvent without heating was in the same way found to comprise only the derived *lactone*. This, which could be isolated (2·53 g., 96%) by distillation, b. p. 205°/0·2 mm., $n_D^{20}$ 1·5500, crystallised as prisms, m. p. 54°, from pentane, $\nu_{max.}$ 3086, 3061, 3030, 1761, 734, 694 cm.$^{-1}$ (Found: C, 77·0; H, 7·7. $C_{20}H_{24}O_3$ requires C, 76·9; H, 7·7%).

Esterification of the intermediate hydroxy-acid with diazomethane and rapid removal of the solvent gave a residue which, on chromatography, was evidently neither the hydroxy-acid nor the lactone. However, attempted crystallisation of this, presumably methyl 8β-benzyloxymethyl-Δ$^{1,8a}$-octahydro-7β-hydroxy-8α-methylnaphthalene-4aβ-carboxylate, gave only the lactone.

[12] H. Ohle and I. Koller, *Ber.*, 1924, **57**, 1566.
[13] R. D. Haworth and A. Lapworth, *J.*, 1922, **121**, 76.
[14] R. Howe and F. J. McQuillin, *J.*, 1958, 1513.

*$\Delta^{1,8a}$-Octahydro-7β-hydroxy-8β-hydroxymethyl-8α-methylnaphthalene-4aβ-carboxylic Acid* 4a ⟶ *7-Lactone* (XV).—The foregoing lactone (XI) (366 mg.) in ethanol (20 c.c.) with palladised charcoal (98 mg.) absorbed hydrogen (27·5 c.c. = 1 mole) in 17 hr. to yield the *δ-lactone* (261 mg.) as hexagonal plates, m. p. 114·5°, from ether–light petroleum (Found: C, 70·3; H, 8·13. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·17), $\nu_{max.}$ 3493 (hydroxyl) and 1727 cm.$^{-1}$ (lactone).

*Hydrolysis of the δ-Lactone* (XV).—The δ-lactone (95 mg.) in methanol (6 c.c.) was heated with 10% aqueous sodium hydroxide (3 c.c.) for 2 hr., and the mixture cooled and acidified with 10% aqueous hydrochloric acid (3 c.c.). The product, recrystallised from ether–light petroleum, formed a solid, m. p. 79—80°; slow recrystallisation from ether, however, gave two distinct sets of crystals in roughly equal proportions: hexagonal plates, m. p. 114·5°, mixed m. p. with authentic $\Delta^{1,8a}$-octahydro-7β-hydroxy-8β-hydroxymethyl-8α-methylnaphthalene-4aβ-carboxylic acid 4a ⟶ 7-lactone, 114·5°, and clusters, m. p. 92—108°, evidently a mixture of the lactones (XV) and (XVI).

*4β-Benzyloxymethyl-6,7,8,8a-tetrahydro-4α-methyl-3,8a-ethanoisochroman-1-ol* (XVII).—(*a*) *Lithium aluminium triethoxyhydride.* Lithium aluminium hydride (2·77 g.) was purified by refluxing it in dry ether (60 c.c., 8 hr.), filtering the solution under nitrogen through a glass sinter, and heating the residue remaining after removal of ether, *in vacuo* for 11 hr. at 50°. The resulting lithium aluminium hydride (2·31 g.) was redissolved in dry ether (70 c.c.), again filtered, and diluted with dry ether (20 c.c.).

The addition of dry ethanol to this solution was guided by the ability of the resultant slurry of lithium aluminium triethoxyhydride to reduce the lactone (XI) to the corresponding lactol with no over-reduction to the diol. The reaction could be carried out on a very small scale and followed by chromatography.

The lithium aluminium hydride solution, at 0°, was treated with dry ethanol (10·2 c.c.) corresponding to 96% of the lithium aluminium hydride in solution.

(*b*) The lactone (XI) (4·242 g.) in dry ether (340 c.c.), stirred at 0°, was treated with portions (5 × 5 c.c.) of lithium aluminium triethoxyhydride slurry at five-minute intervals, two further portions of the hydride slurry (10 and 9 c.c., respectively) were added, with stirring, after 1¼ and 3¼ hr., respectively, and the mixture was set aside for 5½ hr. at 0°. Water followed by a saturated solution of sodium potassium tartrate was added. Extraction gave a *solid* (3·76 g., 88%), m. p. 121—122° from ether–light petroleum, $\nu_{max.}$ 3356 (hydroxyl), 3086, 3049, 3030, 1495, 1453, 754, 702 cm.$^{-1}$ (benzyl) (Found: C, 76·5; H, 8·3. $C_{20}H_{26}O_3$ requires C, 76·5; H, 8·3%).

*6,7,8,8a-Tetrahydro-4β-hydroxymethyl-4α-methyl-3,8a-ethanoisochroman-1-ol* (XVIII).—The foregoing isochromanol (XVII) (294 mg.) in methanol (15 c.c.) with palladised charcoal (84 mg.) absorbed hydrogen (22·4 c.c., 1 mole) in 17 hr. to give the *isochromanol* (0·2 g., 95%), m. p. 162°, from ether–light petroleum (Found: C, 69·5; H, 9·1. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%), $\nu_{max.}$ 3344 (hydroxyls, strong), and 3049 cm.$^{-1}$ (C=CH).

*The Isochromanol Methyl Ether* (XX).—The benzyloxymethyl-lactol (0·26 g.) with ammonium chloride (0·375 g.) in dry methanol (30 c.c.) was heated until chromatography of a sample on silica in 20% ethyl acetate–benzene showed complete reaction (2 days). The *product*, eluted from alumina with benzene, formed a colourless oil, b. p. 145°/0·01 mm., $n_D^{22}$ 1·5363 (Found: C, 76·4; H, 8·3. $C_{21}H_{28}O_3$ requires C, 76·9; H, 8·5%), $\nu_{max.}$ 3086, 3067, 3030, 1497, 1451, 733, 693 cm.$^{-1}$. Chromatography indicated in this material the presence of two (isomeric) substances but rather too close for ready separation.

*6,7,8,8a-Tetrahydro-4β-hydroxymethyl-1-methoxy-4α-methyl-3,8a-ethanoisochroman* (XXI).—(*a*) The lactol methyl ether (XX) (116 mg.) in dry ether (6 c.c.) was debenzylated by addition to a solution of lithium (103 mg.) in liquid ammonia (60 c.c.), further small pieces of lithium being added to give a persistent blue colour. The product formed an oil (86·8 mg.) in which chromatography revealed two isomers in approximately equal amounts. Chromatography on alumina (6 g.) gave the faster-running *isomer*, b. p. 115°/0·02 mm., $n_D^{22}$ 1·5165 eluted with 8% ether–benzene, $\nu_{max.}$ 3436 (hydroxyl), 3030 cm.$^{-1}$ (C=C), with increased absorption at 1464 cm.$^{-1}$ (Found: C, 70·5; H, 9·5. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·3%).

(*b*) The lactol (XVIII) (0·1 g.) with ammonium chloride (0·19 g.) in dry methanol (30 c.c.) refluxed for 48 hr. gave a product which, by chromatography, yielded material, b. p. 115°/0·02 mm., $n_D^{23}$ 1·5163, identical in infrared spectrum with that obtained in (*a*).

(*c*) Formation of the lactol methyl ether was observed on one occasion during catalytic

debenzylation of the lactol (XVII); this substance (0·657 g.), with palladised charcoal (0·17 g.) in methanol (30 c.c.), absorbed the theoretical amount of hydrogen to give a product which, on a silica plate in 20% ethyl acetate–benzene, was observed to contain the expected lactol, together with the isomeric methyl ethers noted above. Elution with 10% ether–benzene from silica (10 g.) gave an oil, b. p. 115°/0·02 mm., $n_D^{22}$ 1·5172, identical in infrared spectrum with the materials obtained in (*a*) and (*b*) above.

6,7,8,8a-*Tetrahydro*-4α-*methyl*-1,4-*epoxymethano*-3,8a-*ethanoisochroman* (XIX).—The lactol (XVIII) (51·2 mg.) was shaken with anhydrous copper sulphate in dry acetone (20 c.c.) for 1 week. The product, on benzene elution from alumina, gave an oil (23 mg.), b. p. 70°/0·02 mm., $n_D^{21}$ 1·5213, showing no hydroxyl absorption in the infrared (Found: C, 75·2; H, 8·7. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

1β-*Benzyloxymethyl*-$\Delta^{8,8a}$-*octahydro*-1α,4aβ-*dimethyl*-2-*naphthol* (XXII).—To a solution of sodium (0·28 g.) in dry freshly distilled diethylene glycol (10·3 c.c.), was added 100% hydrazine (1·2 c.c.; freshly distilled from NaOH), then 4β-benzyloxymethyl-6,7,8,8a-tetrahydro-4α-methyl-3,8a-ethanoisochroman-1-ol (1 g.). The mixture was heated under nitrogen at 140° (4¾ hr.) and then at 215° (2½ hr.). The *product* formed a pale yellow oil (0·89 g., 93%), b. p. 160°/0·07 mm., $n_D^{23}$ 1·5415; chromatography on silica with benzene elution removed a trace of yellow impurity (Found: C, 79·6; H, 9·6. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·4%), $\nu_{max.}$ 3425 (hydroxyl), 3081, 3058, 3021, 1499, 1456, 732, 694 cm.$^{-1}$ (benzyl); 3,5-*dinitrobenzoate*, m. p. 137°, from methanol (Found: C, 66·1; H, 6·5. $C_{27}H_{30}N_2O_7$ requires C, 65·7; H, 6·1%).

$\Delta^8$-*Octahydro*-1β-*hydroxymethyl*-1α,4aβ-*dimethyl*-2-*naphthol* (XXIII).—The foregoing diol (XXII) (388 mg.) in dry ether (20 c.c.) was added to a stirred solution of lithium (186 mg.) in liquid ammonia (150 c.c.). The product formed an oil which crystallised to yield the *diol* (XXIII) (0·225 g., 83%), m. p. 96·5° (from ether–pentane) (Found: C, 73·8; H, 10·5. $C_{13}H_{22}O_2$ requires C, 74·3; H, 10·5%), $\nu_{max.}$ 3410 (two hydroxyls), 3049 cm.$^{-1}$ (C=C); *dibenzoate*, m. p. 119·5°, from methanol (Found: C, 77·5; H, 7·3. $C_{27}H_{30}O_4$ requires C, 77·5; H, 7·2%).

1β-*Benzyloxymethyl*-1α,4aβ-*dimethyl*-$\Delta^8$-*octal*-2-*one*.—The hydroxy-compound (XXII) (170 mg.) in dry pyridine (2·5 c.c.) was added to a solution of chromium trioxide (234·5 mg.) in dry pyridine (3 c.c.) and kept for 36 hr. The product, isolated after removal of excess of chromic acid with sulphur dioxide, formed an oil, b. p. 135°/0·02 mm., $\nu_{max.}$ 3086, 3065, 3030, 1715 (ketone), 1497, 1456, 734, 700 cm.$^{-1}$ (benzyl), which, on thin-layer chromatography on silica in 20% ethyl acetate–benzene, showed a single spot of the same $R_F$ value as that shown by the known [1a] 1β-benzyloxymethyl-1α,4aβ-dimethyl-$\Delta^8$-octal-2-one, m. p. 69°. Attempts to obtain the semicarbazone under conditions which with the ketone of m. p. 69° readily gave the known [1a] derivative, m. p. 168°, failed; the reaction mixture became brown and gave no crystalline product.

1β-*Benzyloxymethyl*-$\Delta^8$-*octahydro*-1α,4aβ-*dimethyl*-2-*naphthyl* 3,5-*Dinitrobenzoate*.—The crude product of benzyloxymethylation of 1,4a-dimethyl-$\Delta^{1,8a}$-octal-2-one was separated into the known crystalline isomer of m. p. 69°, and a liquid residue, b. p. 135°/0·01 mm., $n_D^{21}$ 1·5335, for which the infrared spectrum; $\nu_{max.}$ 3086, 3060, 3030, 1496, 1455, 738, 700 (benzyl), 1710 cm.$^{-1}$, was very similar to that of the product obtained above by chromium trioxide oxidation of the hydroxy-compound (XXII). Chromatography on alumina (20 g.) and elution with 10% ether–benzene gave purified material (0·524 g.) which, in ethanol (15 c.c.), was reduced with sodium borohydride (102 mg.) in water (2·5 c.c.).

The reduction product, chromatographed on silica gel (11 g.), gave as a first fraction, eluted with 2% ether–benzene, a colourless oil (77 mg.), b. p. 145°/0·02 mm., which was found by thin-layer chromatography to correspond to compound (XXII) prepared as described above. Further fractions yielded an oil (280 mg.), b. p. 145°/0·02 which was evidently a mixture.

The first fraction, converted into the 3,5-dinitrobenzoate, gave a product (100 mg.) which by chromatography on silica gel (2 g.) and elution with 80% benzene–light petroleum gave a 3,5-dinitrobenzoate, m. p. 133°, from ethanol. Recrystallisation gave a product of m. p. and mixed m. p. with the 3,5-dinitrobenzoate prepared as described above, 137°.

*Ethyl* $\Delta^{1,8a}$-*Octahydro*-8,8-*dimethyl*-7-*oxonaphthalene*-4aβ-*carboxylate* (VI; R = Et).—A solution of ethyl $\Delta^{1,8a}$-octahydro-1-methyl-2-oxonaphthalene-4*a*β-carboxylate in dry dioxan (30 c.c.) was added with vigorous stirring to sodium hydride (1·43 g.) under dry dioxan (50 c.c.) in oxygen-free nitrogen. After being heated and stirred in dry nitrogen (5 hr.), the mixture was cooled in ice, methyl iodide (6·9 c.c.) in dry dioxan (30 c.c.) was added dropwise, and the mixture kept for 14 hr. The product, by careful fractional distillation, gave the *ester* (8 g.),

b. p. 90—92°/0·01 mm., $n_D^{18\cdot5}$ 1·4965 (Found: C, 71·5; H, 8·71. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%), $\nu_{max.}$ 1724 (ester and saturated ketone), 3030 cm.$^{-1}$ (C=C); 2,4-*dinitrophenylhydrazone*, orange plates, m. p. 139°, from ethanol (Found: C, 58·4; H, 6·2. $C_{21}H_{26}N_4O_6$ requires C, 58·6; H, 6·1%).

$\Delta^{1,8a}$-*Octahydro*-8,8-*dimethyl*-7-*oxonaphthalene*-4aβ-*carboxylic Acid* (VI; R = H).—The foregoing ester (1 g.) with 10% aqueous sodium hydroxide (4 c.c.) in methanol (15 c.c.) under reflux (3 hr.) gave the free *acid*, m. p. 86°, from ether (Found: C, 70·2; H, 8·3. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·2%), $\nu_{max.}$ 3311 (carboxylic hydroxyl), 3030 (C=C), 1739 (carboxylic carbonyl), 1715 cm.$^{-1}$ (ketone).

$\Delta^{1,8a}$-*Octahydro*-7β-*hydroxy*-8,8-*dimethylnaphthalene*-4aβ-*carboxylic Acid Lactone* (VII).—The ester (VI; R = Et) (4·549 g.) in ethanol (50 c.c.) was treated with stirring with a solution of sodium borohydride (433 mg.) in water (10 c.c.) at 0°. The product, isolated after 20 hr., gave the lactone. After heating *in vacuo* at 50° (¾ hr.) to complete lactonisation, chromatography on silica gel (67 g.) yielded the *lactone* (2·933 g., 78%), eluted with 5% ether–benzene, m. p. 96·5°, from ether–pentane, $\nu_{max.}$ 3021 (C=C), 1742 cm.$^{-1}$ (lactone) (Found: C, 76·2; H, 8·9. $C_{13}H_{18}O_2$ requires C, 75·8; H, 8·8%).

6,7,8,8a-*Tetrahydro*-4,4-*dimethyl*-3,8a-*ethanoisochroman*-1β-*ol* (VIII).—The lactone (VII) (819 mg.) in dry ether (40 c.c.) was treated dropwise at ice temperature with stirring, with the lithium aluminium triethoxyhydride slurry (5·5 c.c.), prepared as described above. The mixture was stirred for 2½ hr. The product, chromatographed on silica gel (16 g.) and eluted with 20% ether–benzene, gave the *isochromanol* (733 mg., 89%), $\nu_{max.}$ 3356 (hydroxyl), 3040 cm.$^{-1}$ (C=C) (Found: C, 74·9; H, 9·6. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·7%).

$\Delta^8$-*Octahydro*-1,1,4aβ-*trimethyl*-2β-*naphthol* (X).—(*a*) To the foregoing isochromanol (541·5 mg.) was added a solution of sodium (103 mg.) in dry diethylene glycol (6 c.c.) containing anhydrous hydrazine (0·43 c.c.). The mixture was heated at 145° for 4¾ hr. and at 210—216° for a further 2½ hr. The crude product (477 mg.) on chromatography showed no starting material, but some slow-running substance, probably nitrogeneous impurity. Chromatography on silica (11 g.) yielded, by elution with 5% ether–benzene, the naphthol, b. p. 90°/0·07 mm., $n_D^{22}$ 1·5180, m. p. 80° (lit.,[15] 80°), from pentane (Found: C, 79·8; H, 11·2. Calc. for $C_{13}H_{22}O$: C, 80·3; H, 11·4%). The benzoate was obtained, m. p. 88° (lit.,[15] 88°) from aqueous methanol, $\lambda_{max.}$ 227 mμ (ε 13,621), $\nu_{max.}$ 3049 (C=C), 1712 (ester), 704 cm.$^{-1}$ (ArH) (Found: C, 79·95; H, 8·6. Calc. for $C_{20}H_{26}O_2$: C, 80·4; H, 8·8%).

(*b*) Sodium borohydride reduction of the ketone (IX) yielded the naphthol, m. p. and mixed m. p. with the material formed by Wolff–Kishner reduction of the isochromanol (VIII), 80°.

The two preparations showed identical infrared spectra and gave the same benzoate, m. p. and mixed m. p. 88°.

1,1,4aβ-*Trimethyl*-$\Delta^8$-*octal*-2-*one* (IX).—1,4aβ-Dimethyl-$\Delta^{1,8a}$-octal-2-one, converted into its sodio-enolate with sodium hydride in dry dioxan was treated with methyl iodide to yield the trimethyloctalone, b. p. 58°/0·1 mm., $n_D^{18\cdot5}$ 1·5008, $\nu_{max.}$ 1715 (ketone), 3040 cm.$^{-1}$ (C=C).

We thank the D.S.I.R. for a studentship award to R. B. Y.

Department of Organic Chemistry,
The University, Newcastle upon Tyne. [*Received, October 29th*, 1964.]

[15] Ritchie, Ph.D. Thesis, Nottingham University, 1956.