Some Unexpected Products from the Treatment of Organoboranes from α,β-Unsaturated Ketones with Acetic Acid–Acetic Anhydride

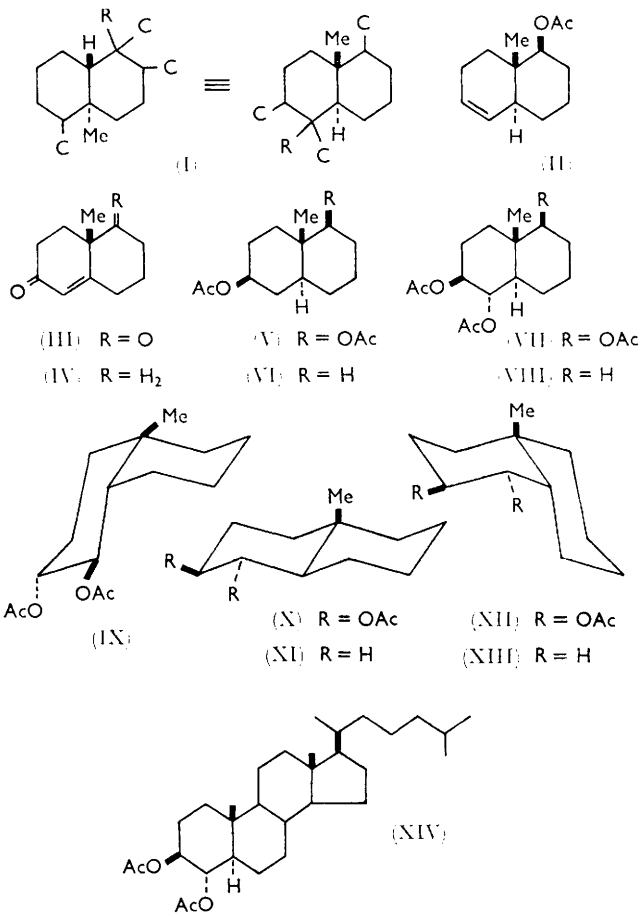
By **K. Bailey** and **T. G. Halsall,*** The Dyson Perrins Laboratory, Oxford University, Oxford

The synthesis of 1β-acetoxy-9β-methyl-Δ^5-*trans*-octalin from 9-methyl-$\Delta^{5(10)}$-octalin-1,6-dione has been carried out by treatment of the dione with a large excess of lithium aluminium hydride in ether and then boron trifluoride etherate followed by heating the resulting organoboranes with acetic acid–acetic anhydride. The yield was low (16%). Unexpectedly, a small yield of 1α,2β,5β-triacetoxy-10β-methyl-*trans*-decalin was obtained although no specific oxidising agent was used. Under similar conditions 10-methyl-$\Delta^{1(9)}$-octalin-2-one and cholest-4-en-3-one also afforded oxidation products, *viz.* 1α,2β-diacetoxy-10β-methyl-*trans*-decalin (26% yield) and 3β,4α-diacetoxy-5α-cholestane (19% yield). No evidence has yet been obtained concerning the mechanism whereby the organoboranes are oxidised.

In connection with the synthesis of diterpene structures possessing the carbon ring system (I) the synthesis of the acetoxy-octalin (II) was attempted starting from the octalindione (III) following the method of Caglioti *et al.*[1] who have reported that treatment of 3-oxo-Δ^4-steroids with an excess of diborane followed by treatment with acetic anhydride or propionic acid gives the corresponding Δ^3-5α-steroid (65% or 25% yield).

As treatment of the octalindione (III) with externally generated diborane gave only small amounts of organoboranes 'internal' hydroboration was attempted by adding lithium aluminium hydride to a solution of the olefin and boron trifluoride in ether,[2] but poor yields were again obtained. The procedure was then modified by first treating the octalindione (III) in ether with a large excess of lithium aluminium hydride under the specified conditions[3] † for reduction and then adding boron trifluoride etherate to destroy the residual reagent and to generate diborane *in situ*.[4,5] A mixture of organoboranes was then obtained in good yield. Treatment of the mixture with acetic acid–acetic anhydride gave only a small yield (16%) of the acetoxy-octalin (II) together with a diacetate (4%) formulated as (V) and a crystalline triacetate (*ca.* 10%) formulated as (VII). When the organoborane mixture was treated with acetic anhydride only, the acetoxy-octalin (II) (8%) and oily triacetate (12%), from which the crystalline triacetate (3%) was isolated, were obtained. Caglioti and Cainelli[6] have been able to obtain good yields of *trans*-diequatorial diols, *e.g.*, cholestane-3β,4α-diol, by oxidation of organoboranes from steroidal α,β-unsaturated ketones but in the experiments now described a *trans*-diequatorial diol has been obtained (as its diacetate), albeit in small yield, without any specific oxidising agent being used.

To investigate these results further a similar reaction was carried out using acetic acid–acetic anhydride on the organoboranes obtained starting from the octalinone (IV). The only fully characterised product which was isolated was the *trans*-diequatorial diacetate (VIII) (26% yield). The *trans*-diequatorial stereochemistry was indicated[7] by the protons of the acetate methyl



groups which gave rise to signals at τ 8·00 and 8·02 (in $CDCl_3$) and by the 1- and 2-protons which gave a complex signal at τ 5·0—5·5 (this signal was not resolved in

† When these conditions were followed and the product was worked up directly, none of the reported 1β,6α-diol was obtained. In one experiment chromatography furnished the 1β,6β-diol only and in another the crude product crystallised directly to give the 1β,6β-diol in 95% yield.

[1] L. Caglioti, G. Cainelli, G. Maina, and A. Selva, *Gazzetta*, 1962, **92**, 309.
[2] S. Wolfe, M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, 1959, **24**, 1034.
[3] C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 1960, 2680.
[4] I. Shapiro, H. G. Weiss, M. Schmich, S. Sckolnik, and G. B. L. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 901.
[5] E. L. Eliel, B. E. Novak, R. A. Daignault, and V. G. Badding, *J. Org. Chem.*, 1965, **30**, 2441, footnote 6.
[6] L. Caglioti and G. Cainelli, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1960, **29**, 555.
[7] Cf. A. C. Richardson and K. A. McLauchlan, *J. Chem. Soc.*, 1962, 2499.

benzene). The three structures (IX), (X), and (XII) account for the diequatorial diacetate grouping but (IX) may be excluded since the stereospecificity of the lithium aluminium hydride reduction [8] of the ketone (IV) will give rise to a 2β-substituent. The observed chemical shift of the angular methyl group in the diacetate strongly favours structure (X): the methyl signal of isomers (X) and (XII) should be shifted (using steroid data [9]) by 0·09 p.p.m. to τ 9·08 and 8·95, respectively, from the values of τ 9·17 and 9·04 in the corresponding decalins (XI) and (XIII).[10] The observed value was τ 9·06, a downfield shift of 0·11 p.p.m. In both 2α,3β-diacetoxy-5α-cholestane and 3β,4α-diacetoxy-5α-cholestane the corresponding shift from 5α-cholestane was 0·14 p.p.m.

The n.m.r. spectrum of the triacetate (VII) obtained from the octalindione had all the acetate methyl signals between τ 8·05 and 8·08, indicating that all three acetate groups were equatorial. This conclusion together with the stereochemical course of the initial lithium aluminium hydride reduction indicates that the three acetate groups of the triacetate must have the 1α-, 2β-, and 5β-configurations in agreement with the stereochemistry of the diacetate (VIII) from the octalinone (IV). The stereochemistry of the diacetate (V) and monoacetate (II) follows by analogy. That of the diacetate (VIII) and the triacetate (VII) is in accord with the recent results of Klein and Dunkelblum [11] who have shown the *trans*-directive effect of an allylic hydroxy-group in hydroboration.

The reactions described above were finally extended to cholest-4-en-3-one. 3β,4α-Diacetoxy-5α-cholestane (XIV) was obtained in 19% yield together with 5α-cholestan-3β-yl acetate (10%) and hydrocarbon material from which cholesta-3,5-diene was obtained. The diene probably arises directly from the dehydration of cholest-4-en-3-ol.

The results with the octalinone (IV) and cholest-4-en-3-one again indicate that *trans*-diol groupings may be formed in quite significant yields without the use of specific oxidising agents. So far no evidence has been obtained concerning the mechanism whereby the organoborane is oxidised under the conditions now described. One possibility is that the oxidant is atmospheric oxygen.

EXPERIMENTAL

All bicyclic compounds are racemic; the angular methyl group (designated β in the one enantiomer named) is chosen as reference point. M. p.s were determined on a Kofler block. The alumina used for chromatography was activity I—II; 5% or 10% deactivated alumina refers to alumina treated with 5% or 10% of 10% acetic acid. The silica gel used was Whatman Chromedia SG 31. I.r. spectra refer to liquid film or Nujol mulls. N.m.r. spectra were determined at 60 Mc./sec.

Hydroboration of 9-Methyl-Δ⁵(¹⁰)-octalin-1,6-dione (III).—The dione (2·5 g., 0·014 mole) in ether was added dropwise to a vigorously stirred suspension of lithium aluminium hydride (6·0 g., 0·16 mole) heated under reflux in ether (200 c.c.). The mixture was heated for 2½ hr. with stirring and then cooled. A solution of boron trifluoride etherate (35·5 g., 0·25 mole) in ether (70 c.c.) was added with stirring during 1½ hr. at such a rate as to maintain a gentle reflux. The mixture was stirred at room temperature for a further 3 hr., and then poured cautiously into a saturated solution of sodium sulphate. Ether extraction afforded the organoboranes as a milky glass.

Reactions of the Organoboranes from 9-Methyl-Δ⁵(¹⁰)-octalin-1,6-dione.—(a) *With acetic acid–acetic anhydride.* The organoboranes (from 1·25 g. of the dione) were heated under reflux with acetic acid–acetic anhydride (1 : 1, 30 c.c.) for 1 hr. The yellow solution was allowed to cool, was poured onto ice (100 g.) and was extracted with ether (3 × 100 c.c.) to afford a yellow gum which partially crystallised at 0° after 4 weeks. The crystalline material was collected (10 mg.) and recrystallised from ether to give prisms, m. p. 142—143° (Found: C, 59·25; H, 8·6. Calc. for $C_{15}H_{26}O_6$: C, 59·6; H, 8·7%). It was not investigated further.

The non-crystalline material was adsorbed from ether on alumina (10% deactivated, 70 g.). Elution with light petroleum (300 c.c.) gave 1β-*acetoxy*-9β-*methyl*-Δ⁵-*trans*-*octalin* (II) (216 mg., 16%) as a mobile oil, identical (t.l.c.) with the sample obtained below, $\nu_{max.}$ 1730 and 1245 cm.⁻¹ (Found: C, 75·7; H, 9·9. $C_{13}H_{30}O_2$ requires C, 75·0; H, 9·7%).

Elution with light petroleum–ether (10 : 1, 150 c.c.) gave an oil (170 mg., *ca.* 10%) which was bulb-distilled under reduced pressure (14 mm.) in a hot air-bath. The distillate crystallised as prisms, m. p. 122—124·5°, identical (t.l.c. and mixed m. p.) with the triacetate (VII) described below.

Further elution with light petroleum–ether (1 : 1, 150 c.c.) gave 1β,6β-*diacetoxy*-9β-*methyl*-*trans*-*decalin* (V) (70 mg., 4%) as an oil which crystallised on trituration with light petroleum–ether as prisms, m. p. 95—96·5°, $\nu_{max.}$ 1730 shoulder on 1720 (s), 1250, 1030, and 980 cm.⁻¹ (Found: C, 67·5; H, 9·15. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%).

(b) *With acetic anhydride.* The organoboranes (from 5 g. of the dione) were heated under reflux with acetic anhydride (50 c.c.) for 1 hr. The deep red solution was worked up in the usual way to give a deep red oil which was adsorbed from ether on alumina (10% deactivated, 200 g.). Elution with light petroleum (1000 c.c.) gave an oil (1·2 g., 24%) which was purified by chromatography on silica gel to give 1β-acetoxy-9β-methyl-Δ⁵-*trans*-octalin (II) as an oil (450 mg., 8%), n_D^{25} 1·4858, $\nu_{max.}$ 2950, 1730, 1375, 1245, and 1035 cm.⁻¹, n.m.r. (CCl_4): τ 9·02 (s, CH_3·CR_3), 8·05 (s, CH_3·CO·O), 5·14 (broad unresolved multiplet, $w_{\frac{1}{2}}$ *ca.* 12 Hz, HC·OAc), and 4·71 and 4·30 (2 doublets, J = 10 Hz, 2HC=) (Found: C, 75·0; H, 9·9%).

Elution with light petroleum–ether (10 : 1, 500 c.c.; 5 : 1, 200 c.c.; and 1 : 1, 700 c.c.) gave oils of saturated triacetate (12%) (Found: C, 63·2; H, 8·4. $C_{17}H_{26}O_6$ requires C, 62·6; H, 8·0%). The fraction eluted with light petroleum–ether (5 : 1) crystallised from light petroleum–ether to give 1α,2β,5β-*triacetoxy*-10β-*methyl*-trans-*decalin*

[8] H. B. Henbest and J. McEntee, *J. Chem. Soc.*, 1960, 3563.
[9] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, pp. 14 and 19.
[10] M. J. T. Robinson, *Tetrahedron Letters*, 1965, 1685.
[11] J. Klein and E. Dunkelblum, *Tetrahedron Letters*, 1966, 6047.

(VII) as needles (242 mg., 3%), m. p. 122—124·5°, $\nu_{max.}$ 1735, 1245, and 1033 cm.$^{-1}$, n.m.r. (CCl_4): τ 8·98 (s, $CH_3{\cdot}CR_3$), 8·05—8·08 (3 s, 3 $CH_3{\cdot}CO{\cdot}O$), and 5·1—5·7 (3 unresolved multiplets, 3 $HC(OAc)$); total proton count: 26 H (Found: C, 62·55; H, 8·0. $C_{17}H_{26}O_6$ requires C, 62·6; H, 8·0%).

9-Methyl-Δ^5*-trans-octalin-1-one*.— 9β-Methyl-Δ^5-*trans*-octalin-1β-ol [prepared by hydrolysis of the corresponding acetate (II) (545 mg.)] in pyridine (12 c.c.) was added dropwise to a stirred cooled solution of chromium trioxide (3·0 g.) in pyridine (60 c.c.) and the mixture was stirred at 20° for 50 hr. The crude product (320 mg.) was adsorbed from light petroleum on silica gel (activity IV, 60 g.). Elution with light petroleum–ether (20 : 1, 550 c.c.) afforded *9-methyl-*Δ^5*-trans-octalin-1-one* as an oil (170 mg., 38%), b. p. 70—80° (bath)/14 mm., n_D^{25} 1·4977, $\nu_{max.}$ 2930, 2850, 1701, 1460, 1120, 995, 960, and 930 cm.$^{-1}$, n.m.r. (CCl_4): τ 8·86 (s, $CH_3{\cdot}CR_3$) and 4·65 and 4·29 (2 doublets, J = 10 Hz, 2 $HC{=}$) (Found: C, 80·4; H, 9·9. $C_{11}H_{16}O$ requires C, 80·4; H, 9·8%). The semicarbazone of the octalinone had m. p. 190—191°.

Hydroboration of 10-Methyl-$\Delta^{1(9)}$*-octalin-2-one* (IV).— The octalinone (IV) (1·21 g., 0·0074 mole) in ether (30 c.c.) was added dropwise during 10 min. to a vigorously stirred suspension of lithium aluminium hydride (3 g., 0·079 mole) heated under reflux in ether (100 c.c.). After 2¾ hr. boron trifluoride etherate (18·4 g., 0·130 mole) in ether (35 c.c.) was added with stirring during ¾ hr. at such a rate that the ether boiled gently. The mixture was stirred overnight at 20° and then worked up in the usual manner to afford a mixture of organoboranes as a glass (1·2 g.).

Treatment of the Organoboranes from 10-Methyl-$\Delta^{1(9)}$*-octalin-2-one* (IV) *with Acetic Acid–Acetic Anhydride*.—The organoboranes obtained above were heated under reflux with acetic acid–acetic anhydride (1 : 1, 30 c.c.) for 1 hr. The brown solution was worked up in the usual manner to give an oil (1·0 g.) which was adsorbed on silica gel (activity III, 50 g.). Elution with light petroleum gave an *oil* (100 mg.), n_D^{25} 1·4743, $\nu_{max.}$ 2930, 2860, and 1460 cm.$^{-1}$, n.m.r. ($CDCl_3$): τ 9·20 (s, $CH_3{\cdot}CR_3$) and 4·55 (doublet, J = 9 Hz, $HC{=}$) (Found: C, 87·3; H, 12·85. $C_{11}H_{18}$ requires C, 87·9; H, 12·1%). The remaining material was eluted with ether as two fractions (ii) and (iii).

Fraction (ii) was further chromatographed on silica gel but only unidentified oils were obtained.

Fraction (iii) was adsorbed on silica gel (activity III, 80 g.). *1α,2β-Diacetoxy-10β-methyl-trans-decalin* (VIII) (535 mg., 26%) was eluted with light petroleum–ether (5 : 1, 350 c.c.) as a colourless glass, $\nu_{max.}$ 2950, 2870, 1730, 1450, 1365, 1240, 1230, 1055, and 1030 cm.$^{-1}$, n.m.r. ($CDCl_3$): τ 9·06 (s, $CH_3{\cdot}CR_3$), 8·02 and 8·00 (2 singlets, 2 $CH_3{\cdot}CO{\cdot}O$), and 5·0—5·5 (2 unresolved multiplets, total band width 30 Hz, 2 $HC{\cdot}OAc$) (Found: C, 67·1; H, 9·3. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%). On further chromatography and trituration at −70° with light petroleum–ether the glass afforded needles (from methanol), m. p. 74—75°.

Hydroboration of Cholest-4-en-3-one.—Cholest-4-en-3-one (5·76 g., 0·015 mole) in dry ether (50 c.c.) was added dropwise to a vigorously stirred suspension of lithium aluminium hydride (6·0 g., 0·16 mole) in boiling ether (250 c.c.). The mixture was boiled for 2½ hr. and cooled. A solution of boron trifluoride etherate (37 g., 0·26 mole) in ether (70 c.c.) was added with stirring during 1½ hr. at such a rate as to maintain a gentle reflux. The mixture was then stirred at 20° overnight and then worked up in the usual manner to give the organoboranes as a partially crystalline glass (5·7 g.).

Treatment of the Organoboranes from Cholest-4-en-3-one with Acetic Acid–Acetic Anhydride.—The organoboranes described above were heated under reflux with acetic acid (50 c.c.) and acetic anhydride (50 c.c.) for 1 hr. The solution was cooled and added to crushed ice and the product was isolated by ether extraction as a gum (5·9 g.) which was adsorbed from light petroleum on alumina (5% deactivated, 350 g.). Elution with light petroleum (550 c.c.) and light petroleum–ether (20 : 1, 750 c.c.) gave a fraction (i) (1·4 g.). Further elution with light petroleum–ether (20 : 1, 1900 c.c.) gave 3β,4α-diacetoxy-5α-cholestane (1·4 g.) as prisms (from light petroleum–ether), m. p. 158—160°, $[\alpha]_D^{20}$ +31° (*c* 1·0 in $CHCl_3$) (lit.,[6] m. p. 160°, $[\alpha]_D$ +31°) (Found: C, 76·4; H, 10·7. Calc. for $C_{31}H_{52}O_4$: C, 76·2, H, 10·7%). Hydrolysis afforded 5α-cholestane-3β,4α-diol, m. p. 235·5—236·5°, $[\alpha]_D^{20}$ +14° (*c* 1·0 in $CHCl_3$) (lit.,[12] m. p. 236—237°, $[\alpha]_D$ +19°).

Fraction (i) was adsorbed on silica gel (250 g.). Elution with light petroleum (1300 c.c.) gave crystals (0·5 g.), m. p. 50—60°, raised by recrystallisation from acetone to 77—78·5°, $[\alpha]_D^{20}$ −94° (*c* 1·0 in $CHCl_3$), $\lambda_{max.}$ (in EtOH) 2350 Å (ε 18,500) [lit.,[13,14] m. p. 78—79°, $[\alpha]_D$ −118° (*c* 1·0), $\lambda_{max.}$ 2350 Å (ε 19,000)] (Found: C, 87·5; H, 11·9. Calc. for $C_{27}H_{34}$: C, 88·0; H, 12·0%). These data indicate that the crystals are essentially of cholesta-3,5-diene but the presence of a small percentage of 5α-cholest-3-ene (lit.,[6] m. p. 78—79°, $[\alpha]_D$ +65°) cannot be excluded. Further elution with light petroleum (500 c.c.) and light petroleum–ether (50 : 1, 400 c.c.) gave 3β-acetoxy-5α-cholestane (360 mg.) as crystals (from methanol), m. p. and mixed m. p. 109—110°, $[\alpha]_D^{20}$ +14° (*c* 1·0 in $CHCl_3$).

We thank the S.R.C. for the award of a studentship to one of us (K. B.).

[7/1135 *Received, August 29th,* 1967]

[12] L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.*, 1954, **76**, 1728.

[13] W. G. Young, R. E. Ireland, T. I. Wrigley, C. W. Shoppee, B. D. Agasha, and G. H. R. Summers, *J. Amer. Chem. Soc.*, 1959, **81**, 1452.

[14] L. Dorfmann, *Chem. Rev.*, 1953, **53**, 47.