471. *An Approach to the Total Synthesis of Triterpenes. Part I.*

By T. G. Halsall and D. B. Thomas.

An approach to the total synthesis of δ-amyrin is discussed and the accomplishment of the first stages described, in particular the synthesis of the 1-2′-hydroxyethyl-7 : 7 : 10-trimethyl-*trans*-octal-2-one (XXVII). An account is given of one of the factors influencing the comparative stability of the two conformations of *cis*-decalones.

In recent years much effort has been devoted to the total synthesis of steroids, but little has so far been published concerning the synthesis of triterpenes and more especially those of the pentacyclic group. The only, but important, synthesis of a tetra- or penta-cyclic triterpene which has been described is that by Woodward, Patchett, Barton, Ives, and Kelly[1] of lanostenol (I) from cholesterol (II), a steroid which had already been synthesised.[2,3,4]

The largest group of triterpenes is that related to β-amyrin (III)[5] with the oleanane skeleton (IV), the complete stereochemistry of which is known.[6,7] The object of the work which will be described in this and, it is hoped, subsequent papers is the synthesis of a compound of the oleanane group which has been directly related to β-amyrin.

A systematic building of successive rings of the oleanane structure, *e.g.*, starting from ring A, appeared to involve great difficulties and a very low overall yield. A more attractive approach was the synthesis of two bicyclic intermediates, which ultimately would become systems A/B and D/E of the oleanane skeleton, and then their coupling and cyclisation to the pentacyclic structure. Such a scheme can be derived from a consideration of the nature and properties of soyasapogenol-D. This has four carbocyclic rings, with a fifth ring closed by an ether linkage, and structure (V) has been suggested for it.[8] Treatment of its diacetate with acetic anhydride and the boron trifluoride–ether complex gives the triacetate of a pentacyclic compound. This triacetate had been provisionally formulated as (VI).[8]

Consideration of this reaction suggested that treatment of a compound such as (VII) with acidic reagents, *e.g.*, boron trifluoride–ether, would lead to cyclisation to δ-amyrin acetate (VIII) with the *trans-anti-trans-anti*-arrangement of rings A, B, C, and D. The recent work of Barton and Overton,[9] who have shown that the diacetate of the tetracyclic triterpene α-onocerin (IX) undergoes a similar cyclisation to give (X), has provided additional support for our initial idea.

The synthetic precursor of the compound (VII) could be the ketone (XI), synthesis of which would require two basic units (XII) and (XIII), with the starred position of (XII) activated in such a manner that the second component (XII) could be attached at this point with nucleophilic displacement of the group X.

The synthetic route discussed should not involve any great stereochemical difficulties. For the decalone (XII) the key step is the formation of the *trans*-fused ring system. With the component (XIII) it is simply a problem of obtaining the *cis*- or *trans*-isomer. If the racemic mixture (XII) is coupled with that of, say, the *trans*-form of (XIII), stereochemical control at C* in (XII) is provided by the α-carbonyl group which will permit the entering group from (XIII) to take up the more stable equatorial conformation. Two racemates only should result, one being (XI; 18α-H) and its enantiomer, and the other (XIV) and its enantiomer. Conversion of the ketone (XI) into the alcohol (VII) does not involve any stereochemical problem as the additional asymmetry introduced at $C_{(8)}$ will be destroyed

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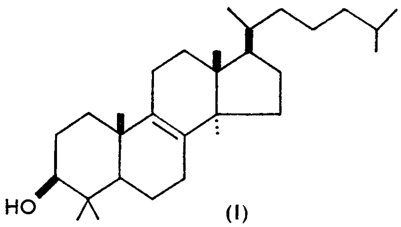
[1] Woodward, Patchett, Barton, Ives, and Kelly, *J. Amer. Chem. Soc.*, 1954, **76**, 2852.
[2] Woodward, Sondheimer, and Taub, *ibid.*, 1951, **73**, 3548.
[3] Woodward, Sondheimer, Taub, Heusler, and McLamore, *ibid.*, 1952, **74**, 4223.
[4] Cardwell, Cornforth, Duff, Holterman, and Robinson, *J.*, 1953, 361.
[5] Jeger, *Fortschr. Chem. org. Naturstoffe*, 1950, **7**, 17.
[6] Barton and Holness, *J.*, 1952, 78.
[7] Abd El Rahim and Carlisle, *Chem. and Ind.*, 1954, 279.
[8] Meyer, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 687.
[9] Barton and Overton, *J.*, 1955, 2639.



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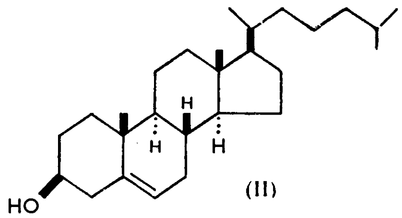

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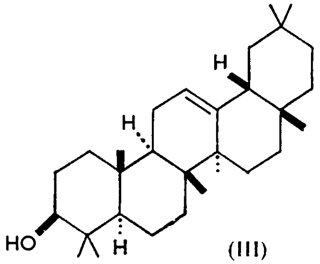

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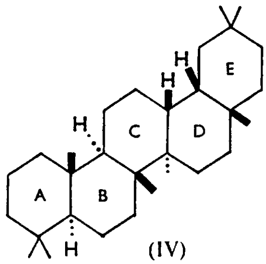

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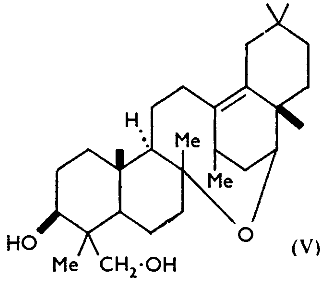

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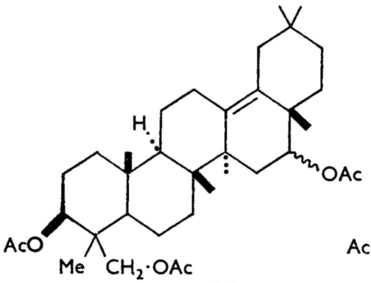

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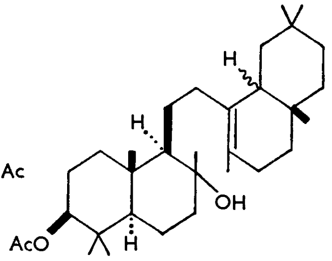

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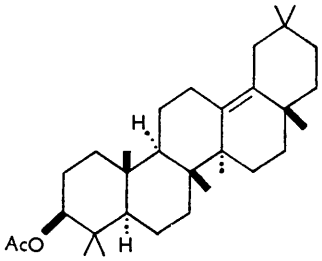

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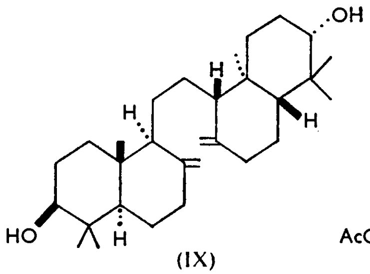

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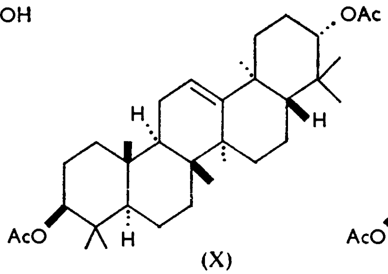

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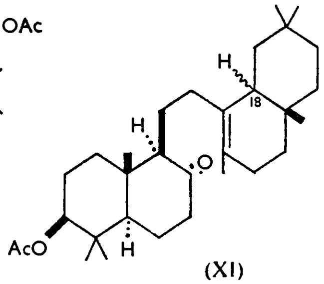
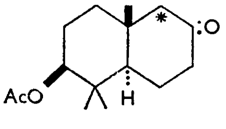


(XI)



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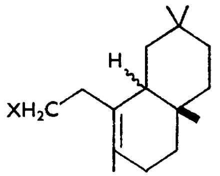

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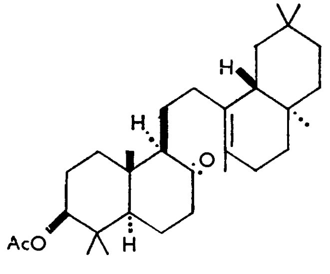

(XIV)

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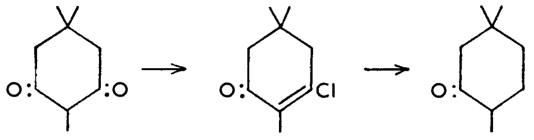
† This and subsequent formulæ imply, when the context requires it, the presence of the enantiomer.

when the carbonium ion involved in the cyclisation is formed. Finally the work of Barton and Overton [9] shows that the cyclisation step will lead to the required stereochemical arrangement of rings B, C, and D.

In this paper our concern will be with some aspects of the problem of synthesising the octalylethyl compound (XIII). The first compound made was 2 : 5 : 5-trimethyl*cyclo*hexanone (XV). To this end dimedone was methylated to give 2 : 5 : 5-trimethyl*cyclo*hexane-1 : 3-dione (XVI).[10, 11, 12] Hydrogenation in presence of Raney nickel then gave a mixture of 2 : 5 : 5-trimethyl*cyclo*hexanol and the 1 : 3-diol. The former was oxidised in good yield with chromic acid to 2 : 5 : 5-trimethyl*cyclo*hexanone. The yields on hydrogenation, however, varied since the activity of the catalyst and the efficiency of stirring were difficult to reproduce, and a better method for the conversion of the dione (XVI) into the *cyclo*hexanone (XV) was sought. The dione (XVI) with phosphorus trichloride gave the chloride (XVII) from the monoenol. Favre and Schinz [13] report that hydrogenation of the chloride similarly derived from the diketone (XVIII), under appropriate conditions, gave the keto-ester (XIX). Under similar conditions the chloride (XVII) did not absorb hydrogen and starting material was recovered. The chloride from dimedone, however, gave 3 : 3-dimethyl*cyclo*hexanone. Reduction of the chloride (XVII) with lithium in ammonia–ethanol, followed by oxidation with chromic acid, gave the required 2 : 5 : 5-trimethyl*cyclo*hexanone (XV) in better yield and more conveniently than the method involving Raney nickel.

The trimethyl*cyclo*hexanone (XV) was condensed, according to method of du Feu, McQuillin, and Robinson,[14, 15] with methyl vinyl ketone formed *in situ* from 1-diethylaminobutan-3-one methiodide,[16] the octalone (XX) being formed. Sodamide was the condensing agent. No uncyclised product was obtained. The octalone showed maximum absorption at 2430 Å, characteristic of the chromophore found in (XX). Whilst one would expect by analogy with other condensations (cf. refs. 14, 15) to obtain this ketone (XX) from the trimethyl*cyclo*hexanone (XV) and methyl vinyl ketone, with addition taking place at the more substituted α-carbon of (XV), it was desirable to be sure that the isomer



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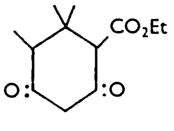

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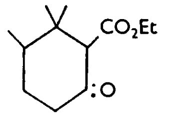

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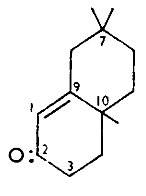

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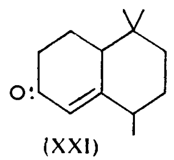
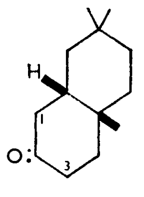
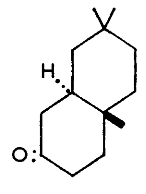


(XXI)



(XXII)



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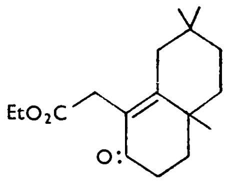

(XXIV)

$Cl{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}[CH_2]_3{\cdot}CO_2Et$

(XXV)

$Cl{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2Et$

(XXVI)

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[10] Desai, *J.*, 1932, 1079.

[11] Hirsjarvi, *Ann. Acad. Sci. Fennicae*, 1946, Ser. A II, No. 23; *Chem. Abs.*, 1948, **42**, 2936.

[12] Meek, Turnbull, and Wilson, *J.*, 1953, 811.

[13] Favre and Schinz, *Helv. Chim. Acta*, 1952, **35**, 2389.

[14] Du Feu, McQuillin, and Robinson, *J.*, 1937, 53.

[15] McQuillin, *J.*, 1955, 528.

[16] Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 471.

(XXI) was not formed, by reaction at the less substituted α-carbon atom. The product was therefore dehydrogenated with selenium and gave in low yield the expected 7-methyl-2-naphthol.[17] 5 : 8-Dimethyl-2-naphthol, which has so far not been described, would have been obtained from the isomer (XXI).

Hydrogenation of the octalone (XX) with platinum in ethanol gave a crystalline saturated ketone as the only isolable product, whilst hydrogenation in acetic acid gave a mixture of ketones. By analogy with the hydrogenation in ethanol of 10-methyl-$\Delta^{1(9)}$-octal-2-one to predominantly 10-methyl-*cis*-decal-2-one,[14, 3] it appeared likely that the crystalline saturated ketone was the *cis*-decalone (XXII) and that the product from the hydrogenation in acetic acid was a mixture of the *cis*- and the *trans*-decalone. Care, however, is necessary in drawing analogies (cf. refs. 18, 19). The octalone (XX) was therefore reduced with lithium in ammonia. The decalone obtained was not identical with that from the hydrogenation in ethanol. Reduction with lithium in ammonia is known to give the compound with the more thermodynamically stable ring junction [20] which in this case will be the *trans*-decalone (XXIII). The product from hydrogenation in ethanol is therefore the *cis*-compound (XXII).

By analogy with the 3-oxo-steroids with a *cis*-A/B ring fusion, *e.g.*, coprostanone, it was at first thought that enolisation of the *cis*-decalone (XXII) would be towards $C_{(1)}$ and that alkylation would occur at $C_{(1)}$; in preliminary attempts to introduce a side-chain at $C_{(1)}$ the enolate ion was treated with allyl iodide, to give a monoallyl derivative, and with ethyl oxalate to give a product which, on loss of carbon monoxide, gave an ethoxycarbonyl derivative. However, it became clear, for reasons discussed later, that alkylation would probably occur at $C_{(3)}$.

Since this meant that $C_{(3)}$ of the decalones (XXII) and (XXIII) would have to be blocked before introduction of a side-chain, attention was turned to a direct synthesis, from the trimethyl*cyclo*hexanone (XV), of an octal-2-one having a substituent at $C_{(1)}$ (cf. XXIV). For this purpose a suitably substituted methyl vinyl ketone or its equivalent is required. Du Feu *et al.*,[14] during their preliminary development of the reaction of an αβ-unsaturated ketone with the sodio-enolate of a ketone, tried unsuccessfully to use 2-chloroalkyl methyl ketones as precursors of the αβ-unsaturated ketones, but later they used 2-chloroethyl methyl ketone in a reaction with 2-methyl*cyclo*hexanone to give 10-methyl-$\Delta^{1(9)}$-octal-2-one in 15—20% yield. Wieland, Ueberwasser, Anner, and Miescher [21] successfully used the chloro-ester (XXV) in a similar reaction with 2-methyl*cyclo*hexane-1 : 3-dione. For the synthesis of the octalone (XXIV), ethyl 6-chloro-4-oxohexanoate (XXVI) appeared to be suitable starting material. In an attempt to prepare it the acid chloride from ethyl hydrogen succinate was treated with ethylene and aluminium chloride. Condensation occurred but the required product could not be isolated owing to the rapid loss of hydrogen chloride followed by immediate polymerisation during working up.

The next possibility examined was synthesis of the octalylethanol (XXVII) by reaction of the trimethyl*cyclo*hexanone (XV) with the vinyl ketone (XXVIII) or a precursor such as the methiodide of the tertiary base (XXIX). One route to the base (XXIX) might be by a Mannich condensation on 4-oxopentan-1-ol (XXX). Since, however, condensation could take place on either of the carbon atoms adjacent to the keto-group it would have been necessary to prove the structure of the condensation product. In the method actually used pent-4-yn-1-ol [22] (XXXI) was the starting material: the acetylenic grouping can take part in a Mannich reaction, and 6-diethylaminohex-4-yn-1-ol (XXXII) was obtained in good yield. The acetylenic bond in this base is polarised in acid (cf. XXXIII), and hydration will give the enol (XXXIV) of the required tertiary base (XXIX). This route *via* an acetylenic compound to a precursor of a vinyl ketone has already been very successfully used by Islam and Raphael.[23] Hydration of the acetylenic base (XXXII) gave a

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[17] Halsall and Thomas, *J.*, 1956, 2564.

[18] Dauben, Tweit, and MacLean, *J. Amer. Chem. Soc.*, 1955, **77**, 48.

[19] Dreiding and Tomasewski, *ibid.*, p. 168.

[20] Barton and Robinson, *J.*, 1954, 3045.

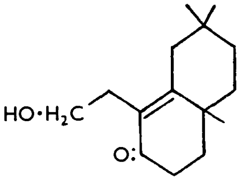
[21] Wieland, Ueberwasser, Anner, and Miescher, *Helv. Chim. Acta*, 1953, **36**, 376.

[22] Eglinton, Jones, and Whiting, *J.*, 1952, 2873.

[23] Islam and Raphael, *J.*, 1953, 2247.

product which was unstable but when treated with methyl iodide immediately after isolation gave a methiodide which could be used in reaction with 2 : 5 : 5-trimethyl*cyclo*hexanone (XV). This gave 1-2′-hydroxyethyl-7 : 7 : 10-trimethyl-$\Delta^{1(9)}$-octal-2-one (XXVII) in moderate yield. This was a viscous liquid, which showed maximum absorption at 2530 Å (ε 17,000) and was characterised as its 2 : 4-dinitrophenylhydrazone.

Although the trimethyloctalone (XXVII) has not yet been converted into a tetramethyl compound of type (XIII), some of its reactions have been studied. Hydrogenation of the double bond proved much more complicated than that of the parent ketone (XX). After one mole of hydrogen had been taken up in presence of platinum in ethanol, the product contained unchanged starting material and some diol, besides a saturated ketone, and could not be resolved by chromatography. Hydrogenation in acid solution gave similar results. The unsaturated ketone (XXVII) formed a lithium complex in liquid ammonia and ether, but decomposition with ammonium chloride produced no reduction : it is unlikely that this failure was due to the hindered position of the double bond, since the steric requirements of this reaction are small; insolubility of one of the intermediates may have been a factor but addition of dioxan in varying amounts did not lead to reduction, nor did use of larger amounts of lithium; the most likely explanation is that the anion (XXXV) is formed initially and is not reduced. When the lithium complex was decomposed with ethanol, reduction did take place, giving some of the saturated ketone, which can be formulated as the most stable isomer (XXXVI) with the *trans*-ring junction and the equatorial side chain. A diol was also formed, sometimes as the main product, and can be formulated as the most stable isomer (XXXVII) with both the side chain and the hydroxyl group attached equatorially to the ring.



(XXVII)

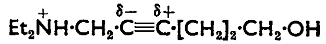
$CH_2{=}CH{\cdot}CO{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH$ (XXVIII)

$Et_2N{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH$ (XXIX)

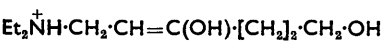
$CH_3{\cdot}CO{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH$ (XXX)

$HC{\equiv}C{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH \longrightarrow Et_2N{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH \longrightarrow$ (XXIX)

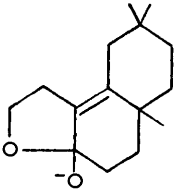
(XXXI) (XXXII)


$Et_2\overset{+}{N}H{\cdot}CH_2{\cdot}\overset{\delta-}{C}{\equiv}\overset{\delta+}{C}{\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH$

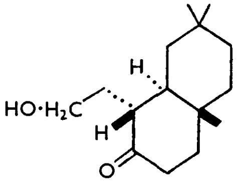
(XXXIII)


$Et_2\overset{+}{N}H{\cdot}CH_2{\cdot}CH{=}C(OH){\cdot}[CH_2]_2{\cdot}CH_2{\cdot}OH$

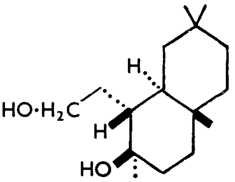
(XXXIV)



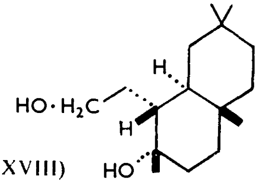
(XXXV)



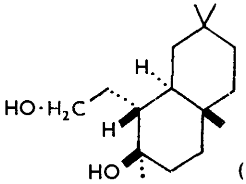
(XXXVI)



(XXXVII)



(XXXVIII)



(XXXIX)

Further work, designed to overcome the unpredictability of the lithium–ammonia–ethanol reduction technique, is in progress on the lithium–ammonia reduction of the tetrahydropyranyl ether of the alcohol (XXVII), which will not be able to form an anion such as (XXXV), and on the synthesis of an intermediate related to the decalone (XII). A preliminary reaction of the ketone (XXXVI) with methylmagnesium iodide has given two diols, (XXXVIII) and (XXXIX). Although their chemistry has not yet been studied, it seems possible that these may be convertible into a compound of type (XIII; *e.g.*, X = Br).

During our preliminary study of the alkylation of the trimethyldecalone (XXII), Dreiding[24] pointed out, in connexion with their bromination, that *cis*-decal-2-ones might exist in two conformations (*e.g.*, XL and XLI). He argued that in only one form (XL) would enolisation towards $C_{(1)}$ be favoured and that only in this case would one expect the initial product of halogenation to be substituted at $C_{(1)}$. In the case of the A/B-*cis*-3-oxo-steroids, rings A and B are restricted to the conformation corresponding to (XL) by the rigidity imposed by the B/C ring junction. With these compounds bromination should occur at the carbon atom between the keto-group and the ring junction, as is the case. No such restriction applies with the *cis*-decal-2-ones and the question arises which conformation (XL or XLI) is preferred. Very little evidence on this point is available. Dreiding[24] has discussed evidence which indicates that enolisation of some simple *cis*-decal-2-ones occurs towards $C_{(3)}$. This could indicate conformation (XLI) as slightly more stable than (XL) in these cases, and Dreiding has put forward one possible explanation for this. He points out that in (XLI) the trigonal carbon atom participates in one more skew interaction than in (XL).

Corey and Sneen[25] have calculated the geometry of some simple carbocyclic systems, including *cyclo*hexanone. They have shown that this may exist in a strain-free structure if a value of 120° is assumed for the trigonal bond angle. Axial substituents situated α and γ to the carbonyl group are brought nearer together, being only 2·37 Å apart in the case of hydrogen atoms, whilst the distance between the α- and α'-axial hydrogen atoms is 3·04 Å. These distances are to be contrasted with the normal *meta-cis*-axial hydrogen distance of 2·53 Å in *cyclo*hexane itself.

In comparing the two conformations (XL) and (XLI) one should consider, besides the above mentioned skew interaction, non-bonded interactions between the axial substituents at $C_{(1)}$, $C_{(3)}$, and $C_{(10)}$. In a decalone (XL; R = H) the axial substituents are the two hydrogen atoms at $C_{(1)}$ and $C_{(3)}$ and the methylene ($C_{(5)}$) group attached to $C_{(10)}$. In the form (XLI; R = H) the axial hydrogen atom on the α-carbon atoms $C_{(1)}$ and $C_{(3)}$ interact only with an axial hydrogen substituent at $C_{(10)}$. This difference in non-bonded interactions, together with the factor discussed by Dreiding,[24] makes it appear likely that form (XLI; R = H) will be more stable than form (XL; R = H). Turning to 10-methyl-*cis*-decal-2-one, in the conformation (XL; R = Me) the interactions are the same as in the analogue (XL; R = H), namely, two interactions between a hydrogen atom and a methylene group. In the conformation (XLI; R = Me) the interactions are now between the two α-axial hydrogen atoms and the methyl group on the γ-carbon atom $C_{(10)}$ and should be of a similar order to those in (XL; R = Me). In this case the two conformations will not differ as much as those of *cis*-decal-2-one.

When this analysis is applied to 7 : 7 : 10-trimethyl-*cis*-decal-2-one (XXII) a much more significant non-bonded interaction appears in one conformation. In the conformation corresponding to (XL), *i.e.*, in (XLII), there is a large non-bonded interaction between $C_{(1)}$ and the axial methyl group attached to $C_{(7)}$. This is equivalent to a 1 : 3-diaxial dimethyl interaction in 1 : 3-dimethyl*cyclo*hexane. This interaction is absent in the conformation corresponding to (XLI), *i.e.*, in (XLIII), and it is clear that the decalone (XXII) will exist almost completely in conformation (XLIII). Since conformation (XLIII) corresponds to (XLI), 7 : 7 : 10-trimethyl-*cis*-decal-2-one (XXII) should enolise towards $C_{(3)}$ and the allyl and ethoxycarbonyl derivatives described earlier are probably (XLIV) and (XLV), substitution having occurred at $C_{(3)}$.

To test these conclusions 7 : 7 : 10-trimethyl-*cis*-decal-2-one (XXII) was brominated in acetic acid containing a little hydrogen bromide. The bromo-derivative was obtained

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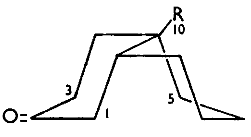
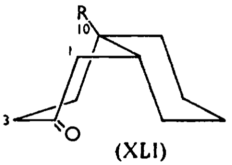
[24] Dreiding, *Chem. and Ind.*, 1954, 1419.

[25] Corey and Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.

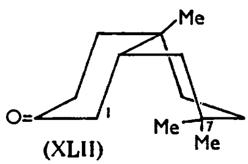
as an oil, which was not completely pure as its ultraviolet absorption indicated the presence of a small amount of an αβ-unsaturated ketone. The oil was treated with 2 : 4-dinitrophenylhydrazine in acetic acid to bring about the formation of the 2 : 4-dinitrophenylhydrazone of the corresponding αβ-unsaturated ketone. If bromination had occurred at $C_{(1)}$ the dehydrobromination product should be the octalone (XX). It was not, and must therefore be the isomer (XLVI) formed from a 3-bromo-derivative. The ultraviolet absorption spectrum of the 2 : 4-dinitrophenylhydrazone showed maximum absorption at 3790 Å (ε 26,500), *i.e.*, at shorter wavelength than that of the 2 : 4-dinitrophenylhydrazone of the $\Delta^{1(9)}$-ketone (XX) ($\lambda_{max.}$ 3910—3930 Å; ε 22,250). These figures are consistent with the formulation of the dehydrobromination product as (XLVI) and agree with the wavelength of the maximum absorption of the 2 : 4-dinitrophenylhydrazone [26] of the analogous ketone (XLVII) ($\lambda_{max.}$ 3830 Å; ε 29,000).



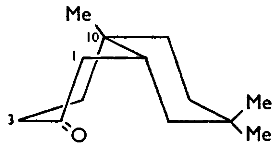
(XL)



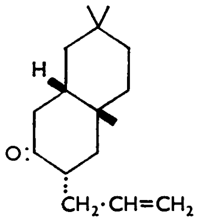
(XLI)



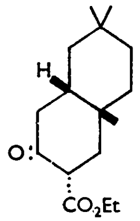
(XLII)



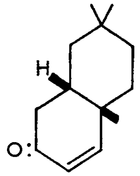
(XLIII)



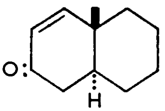
(XLIV)



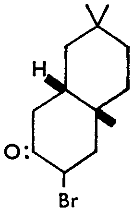
(XLV)



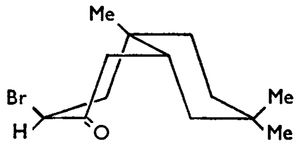
(XLVI)



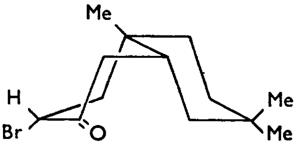
(XLVII)



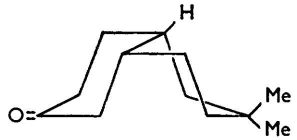
(XLVIII)



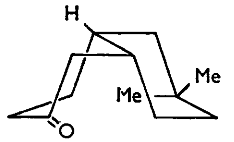
(XLIX)



(L)



(LI)



(LII)

There are several examples in the literature of the isomerisation of α-bromo-ketones to α′-bromo-ketones.[27] It can be brought about by hydrobromic acid: [28] this acid may indeed be a specific catalyst: Cookson and Dandegaonker [29] have shown that while 3β : 5α-diacetoxy-7α-bromocholestan-6-one is stable to perchloric acid in acetic acid it is isomerised

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[26] Rinika, Kalvoda, Arigoni, Fürst, Jeger, Gold, and Woodward, *ibid.*, 1954, **76**, 313.

[27] Cf. Fieser and Fieser, " Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 1949, pp. 262, 264.

[28] Smith, Wilson, and Woodger, *Chem. and Ind.*, 1954, 309.

[29] Cookson and Dandegaonker, *J.*, 1955, 352.

by hydrobromic acid to the 7β-bromide. They suggest that the isomerisation involves reduction by hydrobromic acid followed by rebromination. It is possible that a similar reduction and rebromination is involved in the migration of bromine from the α- to the α′-position in bromo-ketones.

In view of these considerations it was possible that the 3-bromodecalone derivative described above was not the primary bromination product. The *cis*-decalone (XXII) was accordingly brominated in acetic acid in the presence of excess of sodium acetate to remove any hydrogen bromide. The reaction, which was much slower than in the presence of hydrogen bromide, gave a crystalline monobromo-ketone. This yielded the same 2 : 4-dinitrophenylhydrazone after dehydrobromination as the acid-catalysed bromination product. Bromination of the decalone (XXII) therefore gives the 3-bromo-ketone (XLVIII), and the analogy with the 3-oxo-steroids with the A/B-*cis* ring fusion is not valid. The infrared spectrum of the monobromo-ketone had a band at 1731 cm.$^{-1}$, as compared with one at 1705 cm.$^{-1}$ for the ketone (XXII) itself. This shift shows that the bromine atom has the equatorial conformation,[30] as in (L). Corey [31] has shown that on bromination of a cyclic ketone the epimer which is formed faster is that in which bromine is axial. If the 7 : 7 : 10-trimethyl-*cis*-decalone reacts at $C_{(3)}$ in the conformation (XLIII), then the kinetically controlled product will be (XLIX). Because of the interaction of the bromine in (XLIX) with the axial angular methyl group this will not be the thermodynamically stable product [32] and should isomerise, by enolisation, to (L) with the bromine equatorial, as is found.

A *cis*-decalone such as 6 : 6-dimethyl-*cis*-decalone should exist in the conformation (LI), corresponding to that of rings A and B of the 3-oxo-steroids with the A/B-*cis* ring junction, because of the non-bonded interaction between the axial 6-methyl group and the $C_{(4)}$-methylene group in conformation (LII). We propose to study further the bromination of *cis*-decalones which should exist predominantly in one conformation.

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Infrared spectra were determined on liquid films unless otherwise stated. The alumina used for chromatography was of activity I—II. Light petroleum refers to the fraction with b. p. 60—80°.

Methylation of Dimedone.—Dimedone (100 g.) was shaken with methanol (320 c.c.) containing sodium (16·6 g.) until dissolution occurred. Methyl iodide (155 g.) was then added dropwise to the stirred solution which was cooled occasionally to keep the temperature below 5°. The mixture was allowed to come to 20° and was then heated under reflux for 3½ hr. The solvent was next removed and the residue extracted with ether. The ethereal solution was extracted with 10% aqueous sodium carbonate, and the resulting aqueous layer acidified with hydrochloric acid. The resulting precipitate gave 2 : 5 : 5-trimethyl*cyclo*hexane-1 : 3-dione as white needles (63 g., 58%) (from ethyl acetate), m. p. 158—159° (decomp.) with preliminary sublimation at 130—140°. The sublimation temperature and m. p. are to some extent dependent on the rate of heating. This is probably because 2 : 5 : 5-trimethyl*cyclo*hexane-1 : 3-dione very easily forms a hydrate (cf. Desai [10]). Light absorption in alkaline EtOH : Max. 2950 Å (ε = 24,500). A dioxime, made in the usual way, gave crystals (from benzene), m. p. 188—190°; Hirsjarvi [11] gives m. p. 186—188°.

From the extracted ether solution 2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-dione (16·8 g.) was isolated as plates (from light petroleum), m. p. 98°.

When kept in air at 20° for 10 days, or overnight at 100°, the 2 : 5 : 5-trimethyl*cyclo*hexandione became a viscous oil with a smell resembling that of lævulic acid (cf. ref. 12).

*2 : 5 : 5-Trimethyl*cyclo*hexanone* (XV).—2 : 5 : 5-Trimethyl*cyclo*hexane-1 : 3-dione (26 g.) in ethanol (200 c.c.) was hydrogenated, with Raney nickel (5 g.), at 190°/80—120 atm. for 6·5 hr. After removal of the catalyst and solvent, distillation of the residue under reduced pressure gave a liquid (15 g.), b. p. 68—98°/18 mm. This was dissolved in acetone (15 c.c.) and oxidised with chromic acid solution (8N; 22·5 c.c.) which was added dropwise to the ice-cooled mixture. After 30 min. the solution was diluted with water and extracted with ether. Distillation of the

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[30] Jones, Ramsey, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[31] Corey, *ibid.*, 1954, **76**, 175.
[32] *Idem*, *ibid.*, 1953, **75**, 2301.

extract under reduced pressure gave 2 : 5 : 5-trimethyl*cyclo*hexanone (11·2 g.), b. p. 63—65°/10 mm., $n_D^{19.5}$ 1·4450. Blanc [33] gives b. p. 185°. The semicarbazone, prepared in the usual way, crystallised from methanol as needles, m. p. 173—177°. Blanc [33] records m. p. 170°. The 2 : 4-*dinitrophenylhydrazone*, prepared in the usual manner, crystallised from methanol as plates, m. p. 117—119° (Found : C, 56·15; H, 6·2; N, 17·15. $C_{15}H_{20}O_4N_4$ requires C, 56·25; H, 6·3; N, 17·5%).

3-*Chloro*-2 : 5 : 5-*trimethyl*cyclo*hex*-2-*en*-1-*one* (XVII).—Anhydrous 2 : 5 : 5-trimethyl*cyclo*hexane-1 : 3-dione (17·3 g.), phosphorus trichloride (5·8 c.c.), and anhydrous chloroform (100 c.c.) were heated under reflux for 3 hr. After removal of the chloroform and addition of ice, ethereal extraction yielded an oil which was distilled under reduced pressure, to give 3-*chloro*-2 : 5 : 5-*trimethyl*cyclo*hex*-2-*en*-1-*one* (11 g.), b. p. 76—78°/4·8 mm., n_D^{20} 1·4962 (Found : C, 62·75; H, 7·65; Cl, 20·2. $C_9H_{13}OCl$ requires C, 62·6; H, 7·55; Cl, 20·55%). Light absorption in EtOH : Max. 2444 Å (ε 13,000). The *semicarbazone*, prepared in the usual manner, gave crystals (from aqueous methanol), m. p. 169° (Found : N, 18·35. $C_{10}H_{16}ON_3Cl$ requires N, 18·3%). Light absorption in EtOH : Max. 2700 Å (ε 23,800).

Attempted Hydrogenation of 3-*Chloro*-2 : 5 : 5-*trimethyl*cyclo*hex*-2-*en*-1-*one*.—The chloride (XVII) (1·88 g.) in ethanol (20 c.c.) containing pyridine (1 c.c.) was shaken with hydrogen in the presence of 2% or 8% palladium–calcium carbonate (500 mg.). No absorption of hydrogen was observed in 4 hr.

Lithium–Ammonia Reduction of 3-*Chloro*-2 : 5 : 5-*trimethyl*cyclo*hex*-2-*en*-1-*one* (XVII).—The chloride (50 g.) in dry ether (150 c.c.) was added during 45 min., with vigorous stirring, to lithium (10 g.) in liquid ammonia (1 l.). After a further 25 minutes' stirring the lithium complex was decomposed by ethanol. After 20 min. the blue colour had disappeared. The ammonia was slowly evaporated, water was added, and the product was isolated by continuous ether-extraction. It was obtained as an oil and dissolved in acetone (50 c.c.) at 0°. Chromic acid solution (8N) was added dropwise until an orange colour persisted. Dilution with water and extraction with ether gave a product which was distilled under reduced pressure, to give 2 : 5 : 5-trimethyl*cyclo*hexanone (27 g.), b. p. 71—73°/12 mm., n_D^{20} 1·4460. The 2 : 4-dinitrophenylhydrazone, prepared in the usual manner, was obtained as plates (from aqueous methanol), m. p. 115—118°, undepressed on admixture with a sample prepared from the 2 : 5 : 5-trimethyl*cyclo*hexanone obtained by hydrogenation of 2 : 5 : 5-trimethyl*cyclo*hexan-1 : 3-dione.

4-*Diethylaminobutan*-2-*one*.[16]—Ethanol (11 c.c.), paraformaldehyde (8·4 g.), diethylamine hydrochloride (21 g.), and acetone (30 c.c.) were heated under reflux for 9 hr. The solution was then made alkaline with sodium hydroxide solution (10% ; 80—90 c.c.) and the product isolated by ether-extraction. Removal of the solvent and distillation under reduced pressure gave 4-diethylaminobutan-2-one (11·5 g.), b. p. 71—74·5°/14 mm., n_D^{20} 1·4300. Wilds and Shunk [16] give n_D^{24} 1·4318. The methiodide was obtained by adding an equal weight of methyl iodide to the base cooled with ice. It was obtained as a viscous oil which crystallised from ethyl methyl ketone and benzene, then having m. p. 301—302° (decomp.).

7 : 7 : 10-*Trimethyl*-$\Delta^{1(9)}$-*octal*-2-*one* (XX).—Sodamide was prepared by adding sodium (0·7 g.) to liquid ammonia (25 c.c.) containing a small crystal of ferric nitrate. After the initial blue colour had changed to grey the ammonia was evaporated, the final traces being removed by a stream of purified nitrogen. Ether (20 c.c.) was then added, followed by 2 : 5 : 5-trimethyl*cyclo*hexanone (6·75 g.). The resulting solution was then treated under nitrogen with 4-diethylaminobutan-2-one methiodide (7 g.) in ethanol (10 c.c.). After being stirred at 20° overnight the mixture was heated under reflux for 1 hr. After acidification with hydrochloric acid, extraction with ether yielded unchanged 2 : 5 : 5-trimethyl*cyclo*hexanone (2·5 g.), b. p. 62°/12 mm., and 7 : 7 : 10-*trimethyl*-$\Delta^{1(9)}$-*octal*-2-*one* (1·7 g.), b. p. 110—115° (bath)/0·5 mm., n_D^{20} 1·5070 (Found : C, 80·95; H, 10·4. $C_{13}H_{20}O$ requires C, 81·2; H, 10·5%). Light absorption in EtOH : Max. 2430 Å (ε 17,000). The 2 : 4-*dinitrophenylhydrazone* was obtained as bright scarlet plates (from methanol and ethyl acetate), m. p. 148·5—150° (Found : C, 61·0; H, 6·65; N, 15·05. $C_{19}H_{24}O_4N_4$ requires C, 61·25; H, 6·5; N, 15·05%). Light absorption in $CHCl_3$–EtOH (1 : 1) : Max. 3910—3930 Å (ε 22,250).

Dehydrogenation of 7 : 7 : 10 *Trimethyl*-$\Delta^{1(9)}$-*octal*-2-*one* (XX).—The octalone (1·65 g.) and selenium powder (6·0 g.) were heated in a Wood's metal bath to 300—345° (internal temperature) for 30 hr. The residue was extracted with ether in a Soxhlet-type apparatus. The ether solution was extracted with sodium hydroxide solution which was then acidified, 7-methyl-2-naphthol, m. p. 112—116°, being precipitated. Sublimation of the product at 0·01 mm. gave

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[33] Blanc, *Bull. Soc. chim. France*, 1908, **3**, 786.

a solid, m. p. 118—120°, undepressed on admixture with 7-methyl-2-naphthol[17] (Found: C, 83·3; H, 6·4. Calc. for $C_{11}H_{10}O$: C, 83·5; H, 6·35%).

7 : 7 : 10-*Trimethyl*-cis-*decal*-2-*one* (XXII).—7 : 7 : 10-Trimethyl-$\Delta^{1(9)}$-octal-2-one (180 mg.) was hydrogenated with a platinum catalyst (30 mg.) in ethyl acetate (25 c.c.). One mol. of hydrogen was absorbed in 10—15 min., after which absorption became very slow. The hydrogenation was stopped after the uptake of 1·04 mol. of hydrogen. Removal of the catalyst and solvent gave 7 : 7 : 10-*trimethyl*-cis-*decal*-2-*one* (150 mg.), m. p. 67·5—68° (needles from aqueous methanol) (Found: C, 80·1; H, 11·35. $C_{13}H_{22}O$ requires C, 80·35; H, 11·4%). Light absorption in EtOH: Max. 2850 Å (ε 20). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol-ethyl acetate as orange-golden plates, m. p. 187—189° (Found: C, 60·65; H, 7·1; N, 14·85. $C_{19}H_{26}O_4N_4$ requires C, 60·95; H, 7·0; N, 14·95%). The *semicarbazone* crystallised from methanol–water as needles, m. p. 225—227° (Found: C, 66·15; H, 9·8; N, 16·5. $C_{14}H_{25}ON_3$ requires C, 66·9; H, 10·05; N, 16·7%).

Hydrogenation of 7 : 7 : 10-*Trimethyl*-$\Delta^{1(9)}$-*octal*-2-*one* (XX) *in Acetic Acid Solution.*—7 : 7 : 10-Trimethyl-$\Delta^{1(9)}$-octal-2-one (105 mg.) in acetic acid (10 c.c.) was hydrogenated with a platinum catalyst in the usual way. (Uptake of hydrogen after 10 min., 1·06 mol.) Removal of the catalyst and solvent gave a viscous liquid. The 2 : 4-dinitrophenylhydrazone crystallised from methanol–ethyl acetate as orange-red plates, m. p. 178—190°.

7 : 7 : 10-*Trimethyl*-trans-*decal*-2-*one* (XXIII).—7 : 7 : 10-Trimethyl-$\Delta^{1(9)}$-octal-2-one (500 mg.) in dry ether (30 c.c.) was added dropwise, with stirring, to lithium (750 mg.) in liquid ammonia (100 c.c.), and stirred for a further 30 min. An excess of ammonium chloride was added and the ammonia was allowed to evaporate. Addition of water followed by ethereal extraction and distillation of the product under reduced pressure gave 7 : 7 : 10-trimethyl-*trans*-decal-2-one (370 mg.), b. p. (bath) 115—125°/0·05 mm. Its infrared absorption spectrum had a band at 1703 cm.$^{-1}$. The *semicarbazone* crystallised from aqueous methanol as plates, m. p. 210—214°, depressed (m. p. 202—207°) on admixture with the semicarbazone of the corresponding *cis*-decalone (Found: C, 66·6; H, 9·9; N, 16·5%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol–ethyl acetate as plates, m. p. 191°, depressed (m. p. 168—175°) on admixture with the 2 : 4-dinitrophenylhydrazone of the corresponding *cis*-decalone (Found: C, 60·7; H, 7·15; N, 15·1%).

3?-*Allyl*-7 : 7 : 10-*trimethyl*-cis-*decal*-2-*one* (XLIV).—7 : 7 : 10-Trimethyl-*cis*-decal-2-one (0·97 g., 0·005 mole) in tetrahydrofuran (14 c.c.) was treated with potassium *tert.*-butoxide (0·006 mole) in *tert.*-butyl alcohol (7 c.c.). Allyl iodide (1·8 c.c.) in tetrahydrofuran (8 c.c.) was then added dropwise with stirring. The solution became warm and potassium iodide was immediately precipitated. After the whole had been kept for 1 hr. at 20°, dilution with water and extraction with ether yielded a liquid product which was chromatographed on alumina (80 g.). Elution with benzene–light petroleum (1 : 1; 300 c.c.) gave 3?-allyl-7 : 7 : 10-trimethyl-*cis*-decal-2-one (480 mg.) as an oil which was characterised as its 2 : 4-*dinitrophenylhydrazone*, m. p. 203·5—205° (needles from ethanol–ethyl acetate) (Found: C, 63·9; H, 7·3; N, 13·3. $C_{22}H_{30}O_4N_4$ requires C, 63·75; H, 7·3; N, 13·5%).

Ethyl 7 : 7 : 10-*Trimethyl*-2-*oxo*-cis-*decalin*-?3-*carboxylate* (XLV).—Sodium ethoxide (from 0·46 g. of sodium in ethanol) was freed from traces of ethanol on a steam-bath at 0·05 mm. Dry benzene (10 c.c.) and ethyl oxalate (2·92 g.) were added and then, with stirring, 7 : 7 : 10-trimethyl-*cis*-decal-2-one (1·94 g.) in dry benzene (15 c.c.). After the mixture had been kept under nitrogen for 4 hr. at 20°, ice-cold sodium hydroxide solution (2%; 50 c.c.) and ether were added and the two phases were separated. Acidification of the alkaline phase followed by ether extraction yielded a viscous orange oil. This was mixed with powdered soda-glass (approx. 1 g.) and heated at atmospheric pressure. Carbon monoxide began to be evolved at about 140°. Pyrolysis was continued at 160—180° (bath), evolution of gas stopping after 15 min. Distillation under reduced pressure gave the ester (? XLV) (1·6 g.), b. p. (bath) 145—160°/0·05 mm., which was characterised as its 2 : 4-*dinitrophenylhydrazone*, m. p. 158—161° (needles from methanol) (Found: C, 59·35; H, 7·0. $C_{22}H_{30}O_6N_4$ requires C, 59·2; H, 6·75%).

Bromination of 7 : 7 : 10-*Trimethyl*-cis-*decal*-2-*one* (XXII).—(i) *With hydrogen bromide–acetic acid.* The ketone (810 mg.) was dissolved in acetic acid (2 c.c.), and one drop of hydrobromic acid solution (50% w/v in acetic acid) was added followed by a 1·05N-solution of bromine in acetic acid (4·4 c.c.). The mixture was kept overnight, diluted with water, and extracted with ether; the product was distilled under reduced pressure, to give an oil (0·60 g.), b. p. (bath) 145—150°/0·05 mm., n_D^{18} 1·5168. Light absorption in EtOH: Max. 2360—2380 Å (ε 1000). The 2 : 4-dinitrophenylhydrazone of the dehydrobromination product was made as follows. The oil (75 mg.) in acetic acid (2 c.c.) was treated with 2 : 4-dinitrophenylhydrazine

(66 mg.) under nitrogen at 90° for 5 min. On cooling, the product separated. It crystallised from chloroform–methanol, to give 7 : 7 : 10-*trimethyl*-cis-Δ^3-*octal*-2-*one* 2 : 4-*dinitrophenylhydrazone* as orange-red plates, m. p. 207—209·5° (Found : C, 61·5; H, 6·8; N, 14·7. $C_{19}H_{24}O_4N_4$ requires C, 61·3; H, 6·5; N, 15·05%). Light absorption in $CHCl_3$–EtOH (1 : 1) : Max. 3790 Å (ε 26,500).

(ii) *With sodium acetate–acetic acid.*—7 : 7 : 10-Trimethyl-*cis*-decal-2-one (1 g.), water (3 c.c.), acetic acid (15 c.c.), and hydrated sodium acetate (1 g.) were treated with bromine in acetic acid (5·9 c.c.; 1·05N) at 20° for 3 hr. Most of the solvent was then removed under reduced pressure. The residue was dissolved in ether, and the ether solution washed with saturated sodium hydrogen carbonate solution and then water. Removal of solvent and distillation under reduced pressure gave two fractions. The first was unchanged starting material (500 mg.), b. p. (bath) 115—120°/0·1 mm. The second fraction (350 mg.) was obtained at 135—150° (bath)/0·1 mm. and solidified. Crystallisation from methanol–water gave a *monobromo-compound* as cubes, m. p. 118—124°, which on two further recrystallisations from methanol–water became needles, m. p. 73—77° (Found : C, 57·0; H, 7·7. $C_{13}H_{21}OBr$ requires C, 57·15; H, 7·7%). Infrared absorption in CS_2 : 1731 cm.$^{-1}$.

The 2 : 4-dinitrophenylhydrazone of the dehydrobromination product was prepared as described above. Recrystallised from chloroform–ethanol it gave 7 : 7 : 10-trimethyl-*cis*-Δ^3-octal-2-one 2 : 4-dinitrophenylhydrazone as orange-red plates, m. p. 205—209°, undepressed on admixture with the 2 : 4-dinitrophenylhydrazone prepared by method (i).

6-*Diethylaminohex*-4-*yn*-1-*ol* (XXXII).—Water (20 c.c.), 30% formaldehyde solution (21 g.), cuprous chloride (0·5 g.), diethylamine (15 g.), acetic acid (11 g.), and pent-4-yn-1-ol (17 g.) (prepared by the method of Eglinton, Jones, and Whiting [22]) were stirred under nitrogen at 38—40°. The product was isolated by continuous extraction with ether and dried by dissolution in benzene, followed by azeotropic distillation. After removal of the benzene, distillation under reduced pressure gave 6-diethylaminohex-4-yn-1-ol (19·2 g.), b. p. 78—82/0·01 mm., $n_D^{24.5}$ 1·4735. Paul and Tchelitcheff [34] record b. p. 117—119°/3 mm. The alcohol (14·5 g.) with acetic anhydride–pyridine gave 6-*diethylaminohex*-4-*yn*-1-*yl acetate* (14·7 g.), b. p. 82—84°/0·01 mm., n_D^{22} 1·4570 (Found : C, 68·15; H, 10·0; N, 6·7. $C_{12}H_{21}O_2N$ requires C, 68·2; H, 10·0; N, 6·6%), having an infrared absorption band at 1735 cm.$^{-1}$.

Hydration of 6-*Diethylaminohex*-4-*yn*-1-*yl Acetate.*—Water (15 c.c.), mercuric sulphate (0·25 g.), concentrated sulphuric acid (1·4 c.c.), and the acetate (4 g.) were kept at 60—70° under nitrogen for 1 hr. Excess of sodium hydroxide solution was then added and the mixture extracted with ether (3 × 100 c.c.). The ether solution was washed twice with saturated salt solution and evaporated; distillation under reduced pressure then gave an oil (2·2 g.), b. p. (bath) 110—115°/0·01 mm., which was collected in three fractions having n_D^{22} (i) 1·4630, (ii) 1·4623 (0·8 g.), (iii) 1·4610 (0·4 g.). These were the hydration product (6-diethylamino-4-oxohexyl acetate) but they were not stable and it was not possible to obtain satisfactory analytical figures. After 4 days the refractive indices (n_D^{21}) of the fractions had become (i) 1·4805, (ii) 1·4705, (iii) 1·4680. Recombination and redistillation of the fractions gave further fractions, n_D^{22} (i) 1·4615, (ii) 1·4613, (iii) 1·4605.

To obtain the methiodide of the Mannich base for the condensation 6-diethylaminohex-4-yn-1-ol was hydrated as described above and the distilled product was immediately treated with excess of methyl iodide. The methiodide was washed with dry ether, and the last trace of solvent was removed at 0·01 mm., to give a viscous gum which was immediately used for the preparations described below.

1-2′-*Hydroxyethyl*-10-*methyl*-$\Delta^{1(9)}$-*octal*-2-*one*.—Sodium ethoxide (from 0·5 g. of sodium) in dry ethanol (15 c.c.) was treated with 2-methyl*cyclo*hexanone (2 g.) and stirred under purified nitrogen for 2 hr. 6-Diethylamino-4-oxohexan-1-ol methiodide (6 g.; from 3·55 g. of the base) in dry ethanol (30 c.c.) was added dropwise with stirring, followed by dioxan (10 c.c.). A clear pale yellow solution resulted. After 23 hr. the solution was acidified with dilute hydrochloric acid, and the ethanol removed under reduced pressure through a small fractionating column. Water (10 c.c.) was then added and the product extracted with ether (3 × 30 c.c.). Polymeric material insoluble in water or ether was removed by filtration. After the ethereal solution had been dried ($MgSO_4$), removal of the ether and distillation under reduced pressure gave 1-2′-hydroxyethyl-10-methyl-$\Delta^{1(9)}$-octal-2-one (350 mg.) as a pale yellow oil, b. p. (bath) 160—165°/0·01 mm., $n_D^{22.5}$ 1·5332. Light absorption in EtOH : Max. 2520 Å (ε 12,300). The 2 : 4-*dinitrophenylhydrazone* formed plates (from methanol), m. p. 165·5—167° (Found : N, 14·3. $C_{19}H_{24}O_5N_4$ requires N, 14·45%). Light absorption in $CHCl_3$: Max. 3880 Å (ε 28,700).

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[34] Paul and Tchelitcheff, *Compt. rend.*, 1950, **230**, 1872.

1-2'-Hydroxyethyl-7 : 7 : 10-trimethyl-$\Delta^{1(9)}$-octal-2-one (XXVII).—2 : 5 : 5-Trimethyl*cyclo*hexanone (3 g.) was added to sodium ethoxide (from 0·6 g. of sodium) in dry ethanol (30 c.c.) under nitrogen. 1-Diethylamino-6-hydroxyhexan-3-one methiodide (9 g.) in dry ethanol was added to the stirred solution. After 3 days (working up after 1 day gave lower yields) the ethanol was removed, water was added, and the product isolated by ethereal extraction. Distillation of it under reduced pressure gave *1-2'-hydroxyethyl-7 : 7 : 10-trimethyl-$\Delta^{1(9)}$-octal-2-one* (1·9 g.), b. p. 125—130°/0·01 mm., $n_D^{20.5}$ 1·5309 (Found : C, 76·5; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%). Light absorption in EtOH : Max. 2520 Å (ε 17,000). Infrared absorption bands at 1663 cm.$^{-1}$ (αβ-unsaturated ketone), 3400 cm.$^{-1}$ ($^-$OH), 1385 cm.$^{-1}$ (*gem*-dimethyl), 1375 cm.$^{-1}$ (angular methyl), 1362 cm.$^{-1}$ (*gem*-dimethyl). The *2 : 4-dinitrophenylhydrazone* was obtained as prisms (from ethyl acetate–methanol), m. p. 228—231° (Found : C, 60·35; H, 6·75; N, 13·6. $C_{21}H_{28}O_5N_4$ requires C, 60·6; H, 6·75; N, 13·45%). Acetylation (acetic anhydride–pyridine) afforded *1-2'-acetoxyethyl-7 : 7 : 10-trimethyl-$\Delta^{1(9)}$-octal-2-one*, b. p. (bath) 100—115°/0·05 mm., $n_D^{21.5}$ 1·5184 (Found : C, 73·5; H, 9·55. $C_{17}H_{26}O_3$ requires C, 73·35; H, 9·4%).

Hydrogenation of 1-2'-Hydroxyethyl-7 : 7 : 10-$\Delta^{1(9)}$-octal-2-one (XXVII).—The keto-alcohol (930 mg.) was hydrogenated in ethanol (50 c.c.) with a previously hydrogenated palladium–charcoal catalyst (360 mg.; approx. 8% of Pd). The hydrogenation was stopped after 13 min. during which 1·11 mol. of hydrogen had been absorbed. After removal of the catalyst and solvent the residue was distilled under reduced pressure, giving an oil (875 mg.), b. p. (bath) 150—170°/0·01 mm., n_D^{20} 1·4970—1·5008 (various fractions). The infrared absorption of an intermediate fraction (n_D^{20} 1·5000) indicated that there was a mixture of unsaturated ketone and saturated ketone in the ratio 5 : 4. The mixture could not be resolved by chromatography.

Lithium–Ammonia Reduction of 1-2'-Hydroxyethyl-7 : 7 : 10-trimethyl-$\Delta^{1(9)}$-octal-2-one (XXVII).—(*a*) The keto-alcohol (350 mg.) in dry ether (10 c.c.) was added dropwise to a solution of lithium (400 mg.) in liquid ammonia (80 c.c.). After 16 minutes' stirring ammonium chloride was added until the blue colour no longer remained. After evaporation of most of the ammonia the mixture was poured into water. Extraction with ether gave an oil, n_D^{24} 1·5283, the light absorption of which in ethanol (Max. 2530 Å; ε 17,000) indicated that no reduction of the αβ-unsaturated ketone system had occurred.

(*b*) The keto-alcohol (3·25 g.) was dissolved in liquid ammonia (200 c.c.) and ether (50 c.c.). Lithium (2·5 g.) was added in small pieces and the mixture was stirred for 45 min. Dry ethanol was then added dropwise until the initial blue colour no longer remained. After evaporation of most of the ammonia the mixture was poured into water. Ethereal extraction gave a solid residue which was crystallised from ethanol–water, to give *1-2'-hydroxyethyl-7 : 7 : 10-trimethyl-*trans*-decal-2-one* (XXXVI) as rods (1·8 g.), m. p. 142—146° (Found: C, 75·55; H, 10·8. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%). Infrared absorption (melt) : bands at 1707 and 3450 cm.$^{-1}$.

Repetition of the above experiment on three times the scale afforded an oil which was chromatographed on alumina which had been deactivated with 5% (by weight) of dilute acetic acid (10% in water). The only crystalline product isolated was eluted with ether and crystallised from light petroleum, to give *1-2'-hydroxyethyl-7 : 7 : 10-trimethyl-*trans*-decal-2-ol* (XXXVII) (2·8 g.) as plates, m. p. 98—100° (Found : C, 75·35; H, 11·8. $C_{15}H_{28}O_2$ requires C, 75·0; H, 11·75%). Infrared absorption (melt) : bands at 3300(*s*) and 1035 cm.$^{-1}$; no bands between 1650 and 1750 cm.$^{-1}$.

*Reaction of 1-2'-Hydroxyethyl-7 : 7 : 10-trimethyl-*trans*-decal-2-one with Methylmagnesium Iodide.*—The keto-alcohol (1·15 g.) was added to a solution of methylmagnesium iodide [from magnesium (1 g.) and methyl iodide (4 c.c.)] in ether (25 c.c.), and the resulting solution was heated under reflux for 90 min. Solid ammonium chloride was then added, followed by dilute hydrochloric acid. Extraction with ether gave an oil which was chromatographed on alumina (110 g.) which had been deactivated as above. Benzene–ether (300 c.c.; 7 : 3) eluted an oil (450 mg.) which solidified on trituration with light petroleum and recrystallised from the same solvent, to give 1-2'-hydroxyethyl-2 : 7 : 7 : 10-tetramethyl-*trans*-decal-2(ax)-ol (XXXVIII) as plates, m. p. 117—119°. The diol was characterised as the *monophenylurethane* which was obtained as plates (from light petroleum), m. p. 144·5—146° (Found : C, 74·05; H, 9·5; N, 3·95. $C_{23}H_{35}O_3N$ requires C, 73·95; H, 9·45; N, 3·75%). Further elution of the alumina with benzene–ether (500 c.c.; 1 : 1) gave a solid (485 mg.) which crystallised from light petroleum to give *1-2'-hydroxyethyl-2 : 7 : 7 : 10-tetramethyl-*trans*-decal-2(e)-ol* (XXXIX) as plates, m. p. 116—119°, depressed to 85—90° on admixture with the less polar diol (Found : C, 75·5; H, 12·1. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%).

The authors thank Professor E. R. H. Jones, F.R.S., for his interest and advice. One of them (D. B. T.) thanks the Department of Scientific and Industrial Research for a maintenance grant. Thanks are also offered to Mr. E. S. Morton for the microanalyses.

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[*Received, February* 6*th*, 1956.]