Stereochemistry of Some Tricyclo[5.4.0.0^{3,5}]undecane and Related Isopropyldecalin Derivatives †

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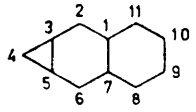
Compounds previously formulated as derivatives of tricyclo[5.4.0.0^{3,5}]undecane (i), with a *trans*-configuration at the junction of the two six-membered rings, are now shown to have the *cis*-configuration, on the basis of chemical and spectroscopic evidence (n.m.r., c.d., and i.r.). Cleavage of the cyclopropyl ring of the tricycloundecane system leads to isopropyl-*cis*-decalin derivatives, although these may subsequently undergo isomerisation to isopropyl-*trans*-decalin derivatives, given a suitable reaction path. One series of isopropyl-*cis*-decalins (26) is shown to have undergone a novel inversion of the configuration of the isopropyl group during the cyclopropyl-opening process. The configurations and preferred conformations of most of the compounds in this series are dominated by non-bonded interactions, which strongly destabilize the *trans*-tricycloundecane skeleton, and particular conformers of some of the *cis*-decalin derivatives.

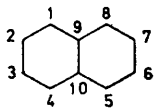
In a recent series of papers,[1-5] two of us (F. F. and A. T.) have described the preparation of a novel series of tricyclic compounds based upon the trimethyltricycloundecane skeleton (A),‡ and its 6α-methyl ‡ derivative (B) (Scheme 1). The compounds were prepared by the well-known Robinson annulation procedure from (−)-*cis*-caran-3-one (C), using either but-1-en-3-one or pent-1-en-3-one, which gave the tricyclic enones (D) and (E), respectively.[1] Cleavage of the cyclopropane ring in either of these enones with HBr–acetic acid, followed by dehydrobromination, gave known compounds of the eudesmane series, including (−)-nor-α-cyperone (F) and (−)-α-cyperone (G), respectively.[2] All formulae in these papers [1-5] were drawn with the opposite *absolute* configurations; the present paper depicts the correct absolute configurations, which correlate with those of (−)-*cis*-caran-3-one and (−)-α-cyperone, as well as with chiroptical data, discussed below.

† This paper is Part LXXXIII of the series ' Optical Rotatory Dispersion and Circular Dichroism ' (Westfield); Part LXXXII, D. N. Kirk and W. Klyne, preceding paper.

‡ The I.U.P.A.C. rules for nomenclature require different numbering systems for tricyclo[5.4.0.0^{3,5}]undecanes (i) and decalins (ii). To avoid confusion, and facilitate reference to



(i)



(ii)

steroid models in the discussion of n.m.r., c.d., and other data, we have adopted steroid-like numbering and stereochemical conventions for all bicyclic and tricyclic compounds discussed in this paper. The decalin components of both series of compounds are numbered as if they are rings A and B of a steroid. The numbering (i) of the tricycloundecane, for example, is replaced by the steroid-like numbering of formula (A) above.

Subsequent papers [3-5] described the preparation of several novel compounds from each of the tricyclic enones (D) and (E), and from the bicyclic enones (H) and (J), which are the dihydro-derivatives corresponding to (F) and (G). The key step in the further transformations of the conjugated enones was the selective reduction of the olefinic bond with lithium–liquid ammonia, and the resulting saturated ketones were accordingly assigned the 5α-configuration [*trans*-decalone structure; (K) and (L)] [4] by reference to well-established precedent.[6] The *trans*-decalin configuration was assumed to persist through subsequent transformations leading to a variety of ketones, alcohols (and their acetates), olefins, and the saturated hydrocarbons of both the tricyclic and the bicyclic series.[3-5,7]

The 6-oxo-tricyclic compound, assumed to have the 5α-configuration (M), was converted by standard methods into the known *trans*-bicyclic ketone (N).[3] This observation alone did not, however, preclude a 5β (*cis*) configuration (P) for the tricyclic ketone, for isomerisation was possible at C-5 under the acidic conditions. The 7-hydroxy tricyclic compound formulated as (Q) was therefore converted into the bicyclic alcohol

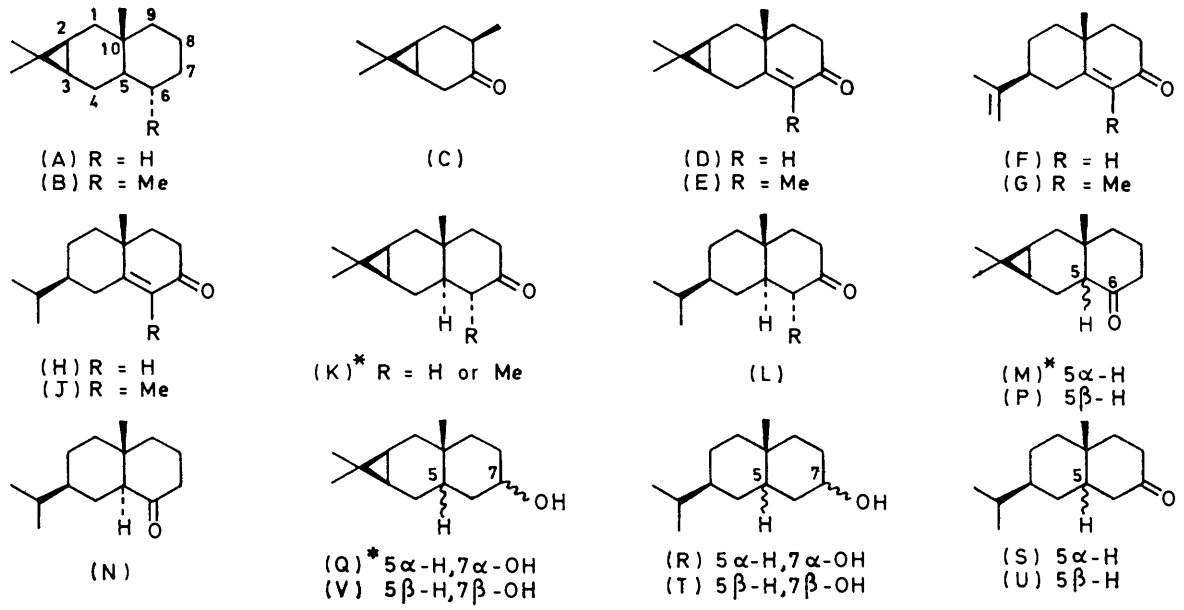
[1] F. Fringuelli, A. Taticchi, and G. De Giuli, *Gazzetta*, 1969, **99**, 219.
[2] F. Fringuelli, A. Taticchi, and G. Traverso, *Gazzetta*, 1969, **99**, 231.
[3] F. Fringuelli, A. Taticchi, and G. Traverso, *Gazzetta*, 1969, **99**, 247.
[4] F. Fringuelli and A. Taticchi, *J. Chem. Soc.* (*C*), 1971, 756.
[5] F. Fringuelli and A. Taticchi, *J. Chem. Soc.* (*C*), 1971, 1809.
[6] D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 1954, 3045; C. Djerassi and G. H. Thomas, *J. Amer. Chem. Soc.*, 1957, **79**, 3835; G. Stork and S. D. Darling, *ibid.*, 1960, **82**, 1512; 1964, **86**, 1761.
[7] F. Fringuelli, A. Taticchi, F. Fernandez, D. N. Kirk, and P. M. Scopes, *J.C.S. Chem. Comm.*, 1972, 191.

and the derived ketone, which exhibited g.l.c. and t.l.c. behaviour indistinguishable from those of the alcohol (R) and the ketone (S), obtained by an alternative route.[5] The *trans*-configurations of the alcohol (Q), and consequently of all the compounds in this series, were therefore regarded as established.

Nevertheless, subsequent studies of the circular dichroism (F. Fernandez, D. N. K., P. M. S.) and on the data for all key compounds [the n.m.r. and c.d. data are listed in Supplementary Publication No. SUP 20964 (10 pp.),* and the i.r. data are in Table 2].

DISCUSSION

6-Demethyl Series (Scheme 2).—The 6-oxo-tricyclic compound (4) shows a strongly negative Cotton effect ($n \longrightarrow \pi^*$) (SUP 20964*). The sign is consistent with a



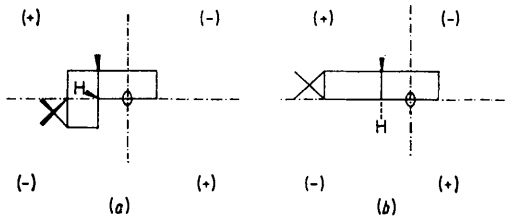
SCHEME 1 Some key compounds of the tricyclic and bicyclic series as originally formulated but with absolute configurations reversed; * indicates a compound which was assigned an incorrect *relative* configuration (refs. 1—5)

stereochemistry of the reduction (F. Fringuelli, A. T.) of ketones in both the tricyclic and the bicyclic series revealed some apparent abnormalities, and led to a re-examination of the configurations of the tricyclic compounds. We now report c.d. and n.m.r. data, together with new chemical evidence, which show conclusively that all the reduced *tricyclic* compounds must be reformulated as *cis*-decalin derivatives (5β-configuration). The supposed correlation of the tricyclic alcohol, which had been given formula (Q), with the bicyclic compounds (R) and (S) resulted from fortuitous identity, in t.l.c. and g.l.c. behaviour, of the *trans*-bicyclic alcohol (R) and the *cis*-bicyclic alcohol (T), and also of the *trans* (S) and *cis* (U) ketones. I.r. and n.m.r. spectra clearly revealed that these pairs of compounds do not correspond in structure. The tricyclic alcohol originally formulated as the *trans*-decalol (Q) actually has the *cis*-decalol structure (V).

Schemes 2 and 3 cover the important reactions of the tricyclic and bicyclic compounds, illustrated in their correct absolute and relative configurations. This account extends the chemistry of compounds of the 6α-methyl series beyond the material in earlier papers. The new schemes are supported by appropriate physical

* For details of Supplementary Publications, see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1972, Index Issue.

cis-1-decalone structure, but not with the *trans*-1-decalone (Figure). The 7-oxo compound (6) likewise exhibited c.d. behaviour ($\Delta\varepsilon$ −0·02) which was inconsistent with a *trans*-2-decalone structure, where a larger negative $\Delta\varepsilon$ value (*ca.* −1) would be expected by analogy



Octant projections: (a) 6-oxo-tricyclic compound (4), with *cis*-decalone configuration; (b) the alternative *trans*-decalone configuration

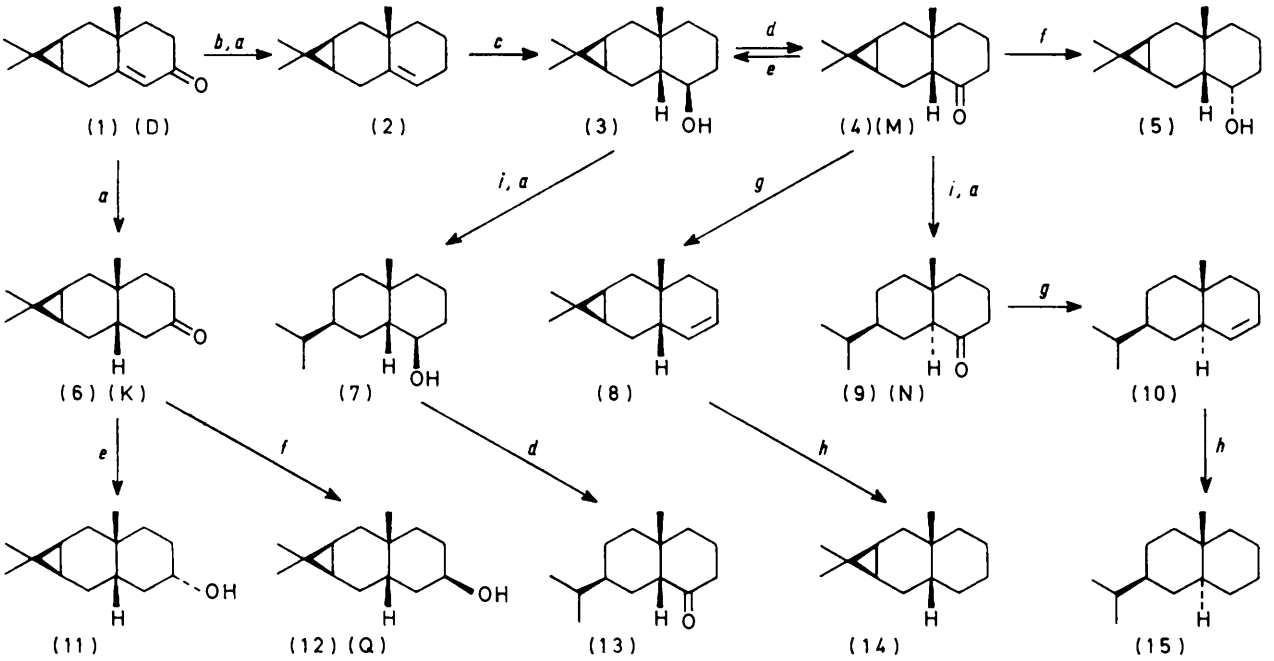
with (enantiomeric) 3-oxo-5α-steroids:[8] a very small Cotton effect could be compatible, however, with the *cis*-2-decalone formulation.[8,9]

These observations suggested that the reactions involving saturation of the olefinic bond in the enone (1) (Li–NH_3) and in the olefin (2) (hydroboronation) were both unusual in being highly stereoselective in favour of

[8] (*a*) W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4103; (*b*) C. Djerassi and W. Klyne, *J. Chem. Soc.*, 1962, 4929.

[9] D. N. Kirk and W. Klyne, preceding paper.

β-face attack. Inspection of molecular models revealed the reason, for the mutual repulsion of the 10β-methyl group and the *endo*-methyl substituent on the cyclopropane ring must cause very considerable deformation of the cyclohexane ring which carries the cyclopropyl group (16). The consequence is a marked concavity that the normal stereoelectronic preference resulting in formation of a *trans*-decalone analogue by metal–ammonia reduction of the enone [6] is overcome. The resulting *cis*-decalin analogues, with the conformation (18), are free from the unacceptable methyl–methyl interaction. The suspected 5β-configuration of all the



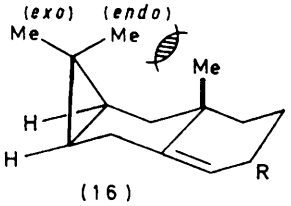
SCHEME 2 The main series of transformations of compounds of the 6-demethyl series

Reagents: (*a*) Li–NH_3; (*b*) $(CH_2SH)_2$–BF_3; (*c*) B_2H_6, followed by HO_2^-; (*d*) Jones reagent; (*e*) $LiAlH_4$–$AlCl_3$; (*f*) Na–EtOH; (*g*) $TsNHNH_2$–BuLi; (*h*) H_2–Pd/C; (*i*) HBr–HOAc; (*j*) CrO_3– HOAc

Notes: Letters in parentheses are cross-references to Scheme 1, where earlier formulae are reproduced, some of them now known to be incorrect.

To assist the reader in locating details of the method of preparation and physical data of compounds illustrated here, cross-references are as follows (asterisk indicates incorrect *relative* configuration: all compounds were originally drawn with wrong *absolute* configurations): (1) ≡ (IV) in ref. 1; (2) ≡ (VI) in ref.3; (3) ≡ (VII) * in ref. 3; (4) ≡ IV) * in ref. 3; (5) ≡ (VIII) * in ref. 3; (6 ≡ (V) * in ref. 4; (7) ≡ (XVII) in ref. 3; (8) ≡ (XIII) * in ref. 4; (9) ≡ (XI) in ref. 3; (10) ≡ (XV) in ref. 5; (11)≡ (VI) * in ref. 5; (12) ≡ (V) * in ref. 5; (13) ≡ (XIX) in ref. 3.

of the α-face of the molecule, making the α-side of the olefinic bond relatively inaccessible to hydroboronation,



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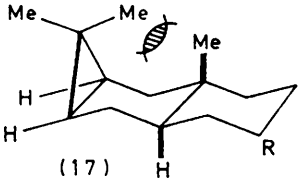

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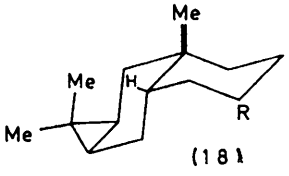


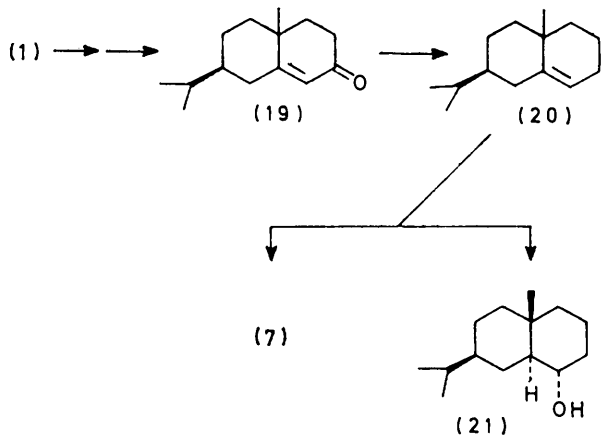
(18)

in contrast to the earlier conclusion.[10] Moreover the methyl–methyl repulsion would be accentuated by the establishment of a *trans*-fused decalin system (17), so compounds in the tricyclic series was confirmed both by a new chemical correlation with the bicyclic series, and by study of collected physical data for compounds of both the bicyclic and the tricyclic series.

Chemical correlation. The 6-hydroxy-tricyclic compound (3), the main product from hydroboronation–oxidation of the olefin (2), was subjected to the usual conditions for opening of the cyclopropyl ring to give the 3β-isopropyl compound (7) (HBr–HOAc, followed by Li–NH_3). The product (7) was identical with the *cis*-fused 6β-alcohol which had been obtained earlier by an unambiguous route [(1) ⟶ (19) ⟶ (20) ⟶ (7) + (21)].[3] The *cis*-configuration of (7) has been established by the ready conversion of the derived ketone (13) under enolising conditions into a mixture rich in the *trans*-isomer (9). Such behaviour is typical of 1-decalones, including polycyclic analogues of the steroid type.[11]

[10] C. Fringuelli and A. Taticchi, *J. Chem. Soc.* (*C*), 1971, 2011.
[11] D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, p. 15.

The only exceptions arise when the assumption of the strained *cis*-configuration permits relief of even greater strain elsewhere, as has recently been noted in the



isomerisation of 2β,3α(diaxially)-substituted 6-oxo-5α-steroids into the 5β-configuration.[12] Clearly the 3β-isopropyl group in the present series of decalones would strongly favour the more usual *trans*-decalone, with the 5α-configuration.

The preference of the tricyclic ketone (4) for the 5β-(*cis*) configuration, even under equilibrating conditions, can now be seen as a further example of the avoidance of excessive strain due to methyl–methyl compression, which would destabilise the 5α-isomer.

The stereochemistry of reduction of the tricyclic 7-oxo-compound (6) provides further evidence supporting the *cis*-decalone structure (Table 1). It had previously been observed[5] that the ketone (6) is reduced with different stereochemical results according to the reagent used. Sodium–ethanol gives the equatorial 7β-alcohol (12), whereas $LiAlH_4$–$AlCl_3$ gives the axial 7α-alcohol (11) (new assignments: see discussion of n.m.r. data below). This behaviour is normal for a cyclohexanone hindered by a ' β-axial ' substituent,[13] in the present case the C-4 group of the *cis*-decalone fragment in the ' steroid-like ' conformation (18; R = O). The hydride donor is forced to approach the less-hindered β-face of the carbonyl group to give the 7α-alcohol (11). N.m.r. data (below) show that this alcohol subsequently adopts the ' non-steroid ' conformation to minimise strain.

6-Methyl Series (Scheme 3).—The presence of the 6-methyl substituent precluded a decisive chemical correlation with the bicyclic series by the 5β ⟶ 5α isomerisation of a 6-oxo-derivative, but spectroscopic evidence strongly supports the *cis*-configuration. Moreover, the reduction of the 7-oxo-tricyclic compound (23) by either sodium–ethanol or $LiAlH_4$–$AlCl_3$ gave predominantly equatorial or axial alcohols, (25) and (24) respectively (Table 1), showing the same stereochemical control of reduction as in the demethyl analogue.

Scheme 3 illustrates all compounds of the 6-methyl tricyclic series as having the *cis*-decalone configuration, which is fully consistent with all available chemical and spectroscopic data, but an unexpected complication arose in assigning structures to the decalin derivatives obtained by opening the cyclopropyl ring of the tricyclic

TABLE 1

Alcohols formed from the reduction of ketones

	Method of reduction			
	Na–EtOH [a,b]		$LiAlH_4$–$AlCl_3$ [a,c]	
Ketone	β-Alcohol (%)	α-Alcohol (%)	β-Alcohol (%)	α-Alcohol (%)
6-Oxo-*trans*-bicyclic (9)	(52) 15	(21) 85	(52) 98	(21) 2
7-Oxo-*trans*-bicyclic (51)	(53) 96	(54) 4	(53) 81	(54) 19
6-Oxo-tricyclic (4)	(3) 7	(5) 93	(3) 92	(5) 8
7-Oxo-tricyclic (6)	(12) 94	(11) 6	(12) 35	(11) 65
6α-Me-7-oxo-tricyclic (23)	(25) 97	(24) 3	(25) 5	(24) 95
6α-Me-8-oxo-tricyclic (28)	(34) 4	(35) 96	(34) 88	(35) 12

[a] Analysis by g.l.c. [b] Figures give the ratio of the two epimers, ignoring small amounts of unchanged ketone. [c] Under conditions of kinetic control (E. L. Eliel and N. M. Rerik, *J. Amer. Chem. Soc.*, 1960, **82**, 1367; U. E. Diner, H. A. Davis, and R. K. Brown, *Canad. J. Chem.*, 1967, **45**, 207).

7β-(equatorial) alcohol (25).* The 3α-isopropyl *cis*-decalin configuration (26) and (31) is assigned to these products on the following evidence. (i) The structure and absolute stereochemistry of the tricyclic enone (22) are beyond doubt, having been confirmed by ring opening with HBr, and dehydrobromination, to give (−)-α-cyperone (G), identical with an authentic sample.† Reduction of (−)-α-cyperone by published procedures[14,15] gave the known 6β-methyl (equatorial) *cis*-decalone (37) and the known 6α-methyl (equatorial) *trans*-decalone (38). (ii) The ketone (31), obtained from the alcohol (26) by Jones oxidation, differed from the foregoing isomers (37) and (38), although all three ketones were stable to equilibration with base. Moreover, the properties of the ketone (31), and of two crystalline derivatives, were very similar to those reported[14] for the enantiomer of (31) (see Experimental section), the

* Since the completion of our work, the structure of this alcohol (25) has been confirmed by an *X*-ray crystallographic analysis of the *p*-bromobenzoate, kindly carried out by Professor D. Rogers and Dr. A. Quick, Imperial College, London (details to be published).

† Kindly provided by Dr. E. Piers, University of British Columbia, Canada.

[12] H. Velgová, V. Černý, F. Šorm, and K. Sláma, *Coll. Czech. Chem. Comm.*, 1969, **34**, 3354.

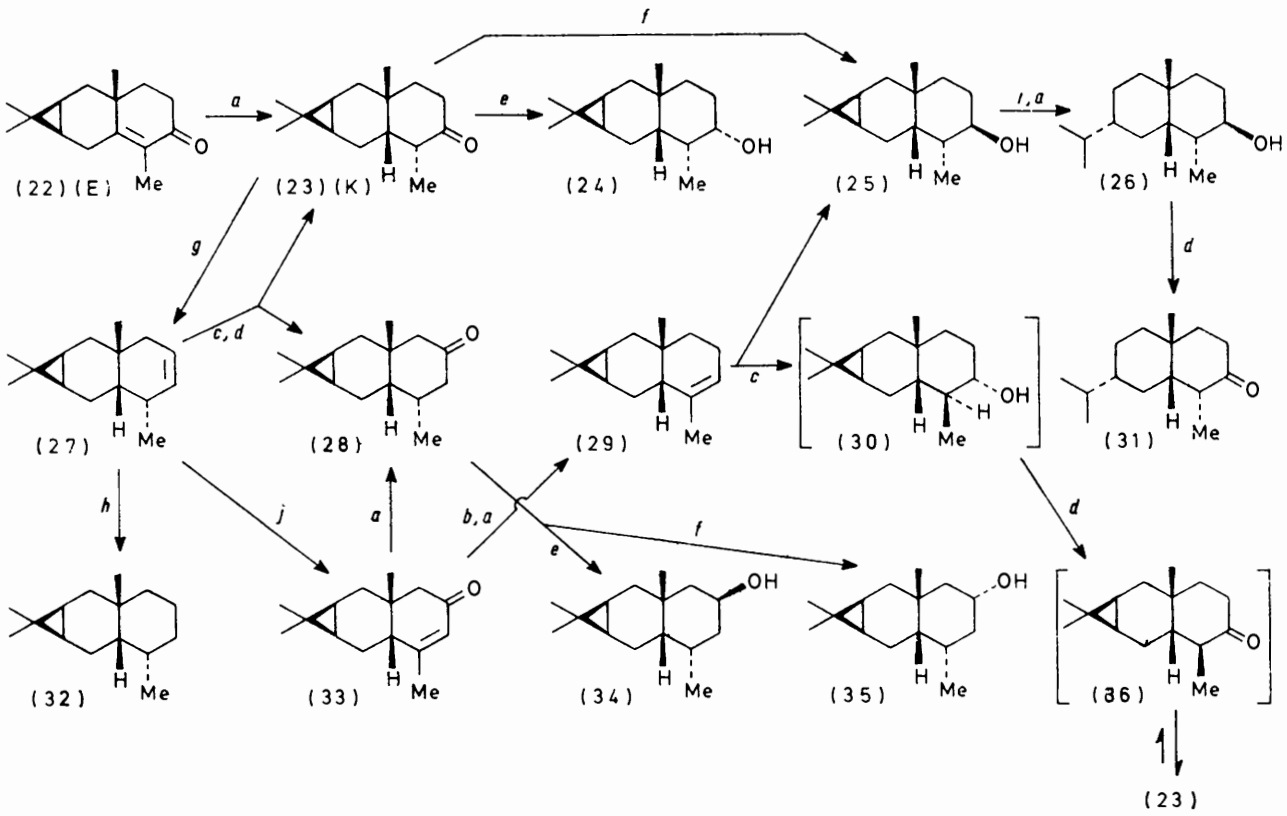
[13] Ref. 11, p. 136.

[14] R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 1958, 1194.

[15] G. L. Chetty, G. S. Krishna Rao, S. Dev, and D. K. Banerjee, *Tetrahedron*, 1966, **22**, 2311.

chiroptical properties differing in sign but not greatly in magnitude.

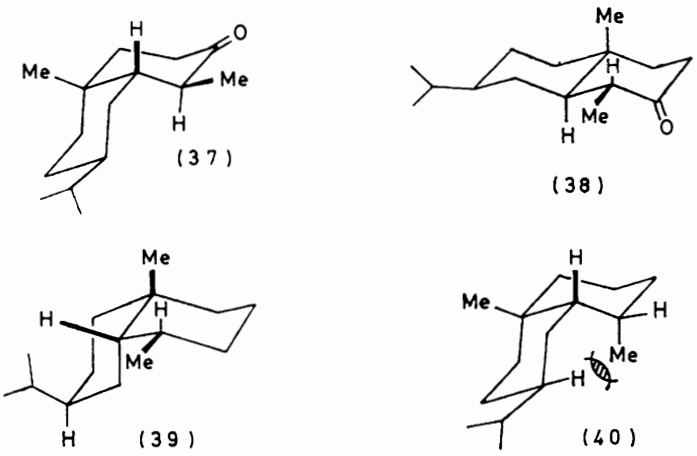
We explain the epimerisation at C-3 during cyclopropyl cleavage as a consequence of the conformational rigidity imposed upon the *cis*-decalin derivatives in this series by the spatial requirements of the 6α-methyl group. Two conformations have to be considered for each *cis*-decalin derivative, assuming the rings to be in the chair form. A 6α-methyl group must impose a strong preference for the ' steroid-like ' conformation (39), where the 6α-methyl is equatorial, rather than the ' non-steroid ' conformation (40), where the 6α-methyl group would be axial and subject to very severe compression by the adjoining ring. However, a 3β-isopropyl group would be forced by the steroid-like conformation into its less stable axial position. When the cyclopropyl ring in the 7β-alcohol (25) is opened with HBr, the resulting 3β-bromopropyl group, being equivalent in size to a



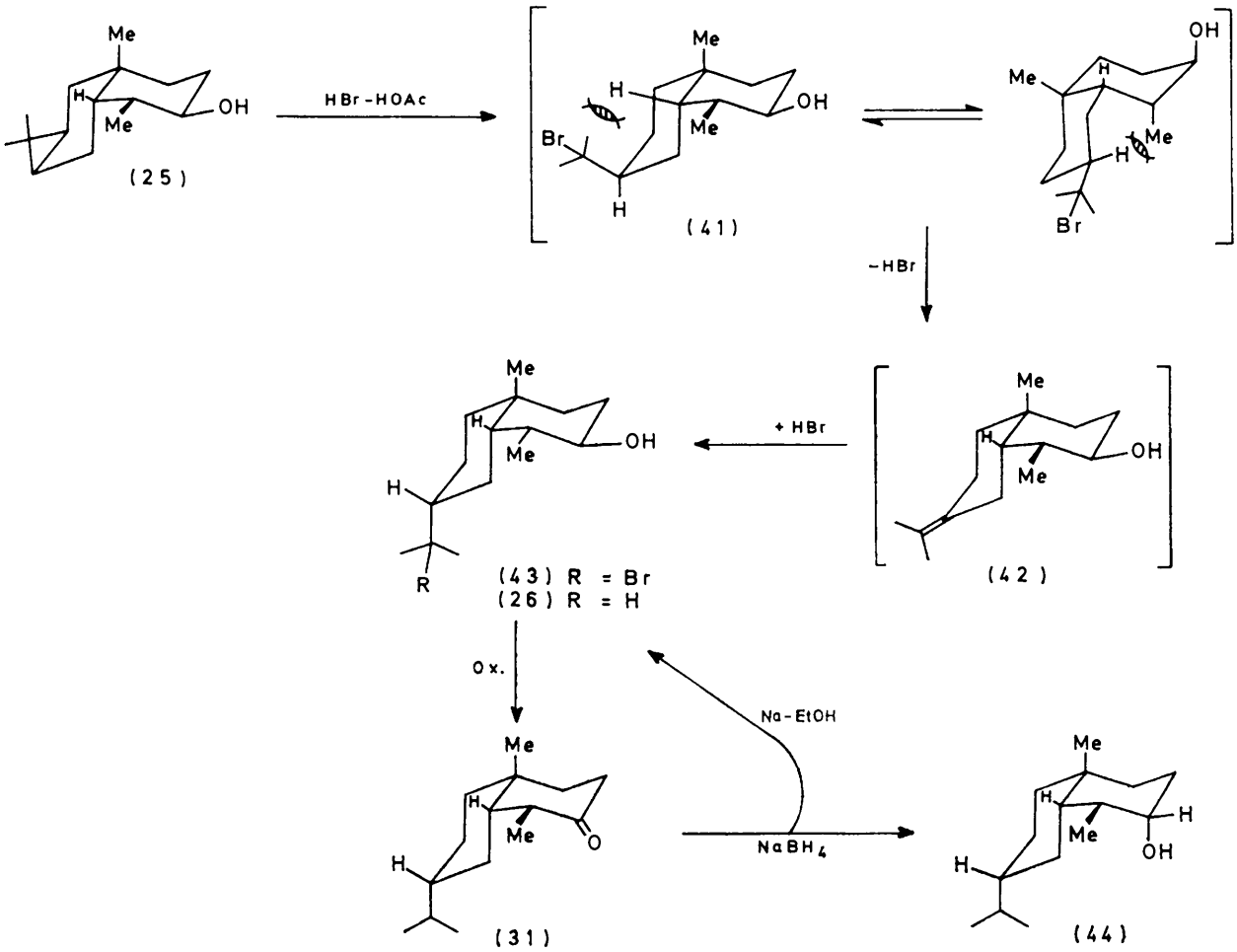
SCHEME 3 The main series of transformation of compounds of the 6-methyl series

For reagents, see Scheme 2.

Cross-references (see Scheme 2 for explanation): (22) ≡ (XXIV) in ref. 1; (23) ≡ (IV) * in ref. 4; (27) ≡ (VI) * in ref. 4; (28) ≡ (VII) * in ref. 4; (29) ≡ (XII) * in ref. 4; (33) ≡ (X) in ref. 4.



t-butyl substituent, will be even more strained in an axial conformation, so that the intermediate product (41) cannot avoid drastic deformation. The experimental conditions (HBr–HOAc) seem likely, however, to allow a hitherto unsuspected reversible elimination–addition of HBr, *via* a tertiary carbonium ion and the 3-isopropylidene derivative (42), permitting inversion of the intermediate bromopropyl derivative at C-3 to give the much more stable 3α-(equatorial)-isomer (43). Reductive debromination then gives the alcohol (26) in which all conformational strains except that inherent in a *cis*-decalin are minimised. In agreement with the conformation (26), the derived ketone (31) was reduced by sodium borohydride from the less-hindered β-direction to give the axial 7α-alcohol (44) as major product (characterised only by its g.l.c. behaviour, since material was severely limited), or by sodium–ethanol to regenerate the stable equatorial 7β-alcohol (26).



*N.m.r. Data.**—The saturated hydrocarbons (14), (15), and (32) provide reference data for evaluating substituent effects. The *trans*-decalin (15) gives a 10β-methyl resonance (τ 9·24) close to that of 5α-androstane (τ 9·21),[16] whereas the 5β-tricyclic hydrocarbons (14) and (32) show the 10β-methyl signal at τ 9·10 and 9·04, respectively (*cf.* 5β-androstane, τ 9·075 [16]). The cyclopropyl ring therefore has no significant effect on the 10β-methyl resonance, although the 6α-methyl group in (32) is responsible for a small shift (—0·06 p.p.m.) to lower field. Unsaturation causes shifts in the 10β-methyl signal consistent with data for similarly unsaturated steroids.[16] The same is true for the enones and most of the saturated ketones in the series, the 6-oxo- and 7-oxo-substituents being strictly analogous to the corresponding functionalities in steroids.[16] The only ketone in the present series which shows a serious disagreement (deviation Δτ 0·05 p.p.m.) between 'calculated' [16] (τ 9·125) and observed (τ 8·85) 10β-methyl resonances is the (bicyclic) 6-oxo-*cis*-decalone (13). Inspection of a Dreiding model suggests that this ketone would adopt the 'non-steroid' conformation (45), to allow its 3β-isopropyl group to be equatorial. Comparison with a 6-oxo-5β-steroid is therefore invalid in this case.

The most significant n.m.r. data are those for the

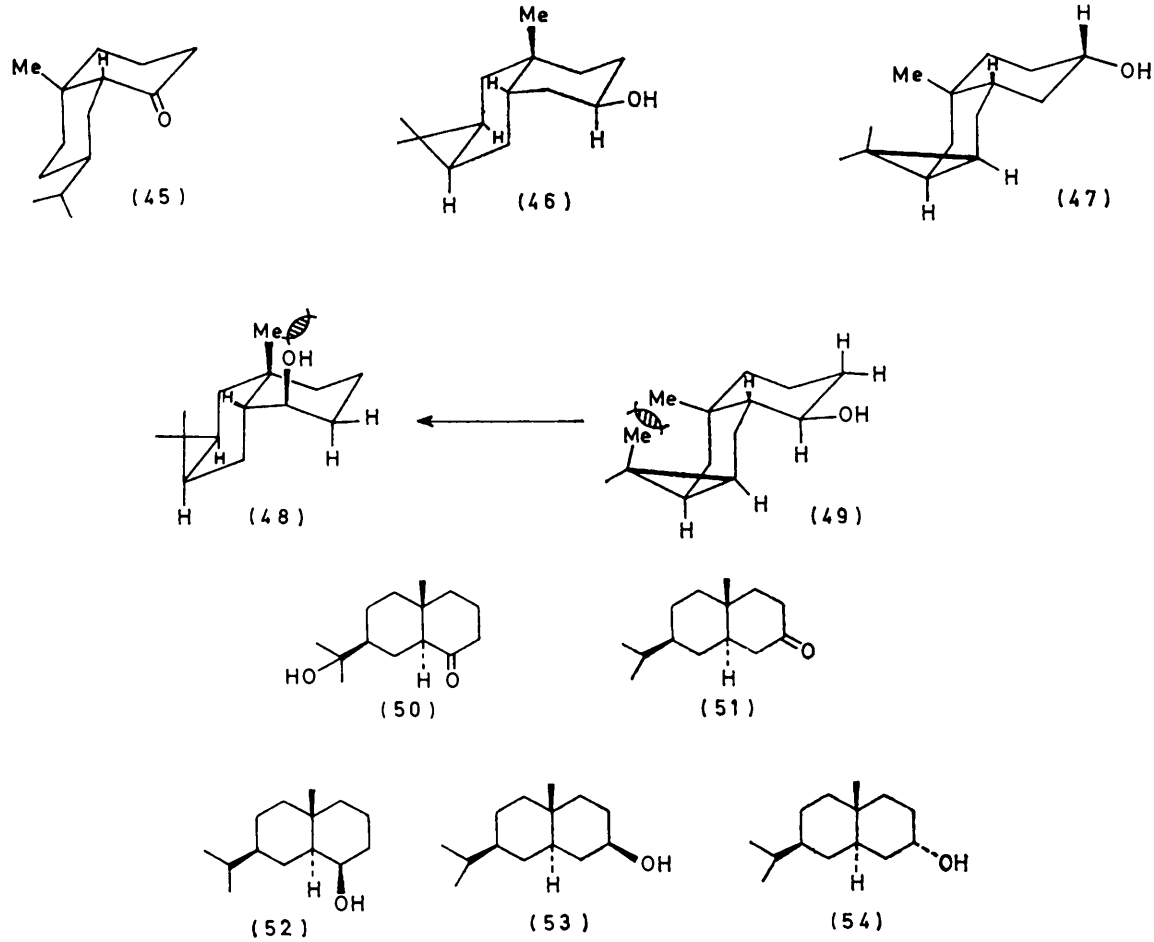
* Listed in Supplementary Publication No. SUP 20964 (10 pp.).

[16] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 19.

alcohols and acetates in the tricyclic series. The width of the signal due to the methine proton of a system C*H*OR in a cyclohexane is characteristic of the conformation of this proton.[17] The broadest signals (width 15—30 Hz) are found for axial methine protons vicinal to one or two other axial protons, the hydroxy-group then being equatorial. Narrow methine signals (5—10 Hz) generally indicate axial hydroxy-groups.

By this criterion the two isomeric alcohols (11) (*W* 25 Hz) and (12) (*W* 30 Hz) obtained by reduction of the tricyclic 7-oxo-compound (6) *both have the hydroxy-group predominantly in the equatorial conformation.* Their acetates are similar. I.r. data, reported earlier for the 6α-methyl group should remain equatorial [as in (39)], rather than become axial and acutely compressed (40), causes both isomeric C-7 alcohols in the 6α-methyl series to exist in the ' steroid ' conformation. The n.m.r. data (also i.r. data—see below) clearly show that the 7β-alcohol (25) (*W* 30 Hz) and its acetate (*W* 35 Hz) have equatorial oxygen functions, and the 7α-isomer (24) (*W* 9 Hz) axial.

The n.m.r. spectra of the 6β-hydroxy-tricyclic compound (3) and its acetate are somewhat unusual, the width of the methine proton signals (13—16 Hz) being only marginally less than for the 6α-alcohol (5) and its acetate (16—20 Hz), which are undoubtedly equatorial. The signal due to the 10β-methyl group in the 6β-alcohol



alcohols[5] and discussed further below, confirm this conclusion. Since there is no reason to suspect non-chair conformations of the ring carrying the oxygen substituent, the conformational similarity at C-7 can best be explained on the basis of a *cis*-decalol configuration, the 7β-alcohol (12) and its acetate having the ' steroid-like ' conformation (46), and the 7α-compounds (11) being predominantly in the ' non-steroid ' conformation (47), in order to avoid 1,3-diaxial compression of the 7α-OH and C-4 groups.

A different situation exists in the 6α-methyl series [compounds (24) and (25)], for the requirement that the shows quite a large solvent shift to lower field ($\Delta\tau$ −0·2 p.p.m.) in either deuteriobenzene or deuteriopyridine,[18] implying proximity of the 6β-OH and 10β-methyl groups, in contrast to the 6α-alcohol where no solvent shift was observed. [The axial 8β-alcohol (34) also shows the expected solvent shift.] These findings require a predominantly steroid-like conformation (48) for the 6β-alcohol, but with the probability of a small population

[17] Ref. 16, p. 79.

[18] Ref. 16, p. 163; S. Ricca, B. Rindone, and C. Scolastico, *Gazzetta*, 1969, **99**, 1284; for a summary see ' Terpenoids and Steroids,' ed. K. H. Overton, Specialist Periodical Reports, The Chemical Society, London, 1970, vol. 1, p. 270.

of the 'non-steroid' conformation (49), where the 6β–10β interaction is relieved, but the less acceptable 10β-Me–*endo*-Me interaction must be present. A small contribution from the non-steroid conformation, with two axial protons vicinal to the 6α-(methine) proton, would explain the unusual broadening of the signal due to the methine proton. The i.r. spectrum (see below) is consistent with this conclusion.

N.m.r. data for the other alcohols and their acetates are unexceptional.

In addition to the n.m.r. data reported in Supplementary Publication No. SUP 20964, the spectra of four compounds [(4), (2), (28), and (31)] were examined with the addition of the shift reagent $Eu(dpm)_3$.[19] The additional chemical shifts induced by the lanthanide complex were determined for each of the various methyl group signals, and the relative magnitudes of the induced shifts in each compound were compared with estimates based upon the McConnell–Robertson equation for pseudo-contact shifts $\delta = K(3\cos^2\theta - 1)/r^3$. The parameters r and θ were estimated from Dreiding models, although the time-averaged location of the europium atom is not known with certainty. For each of the four compounds examined, the *cis*-decalone configuration, in its preferred conformation, gave a correlation with observed shifts which was closer than the best possible on the basis of a *trans*-decalone model.

C.d. Data.†—*Ketones* ($n \longrightarrow \pi^*$). The 6-oxo-tricyclic compound (4) exhibits a strongly negative Cotton effect ($\Delta\varepsilon$ −2·7, hexane), consistent with the *cis*-decalone formulation [Figure, (*a*)]. The two six-membered rings are conformationally similar to rings A and B in a 6-oxo-5β-steroid, where an even larger negative Cotton effect ($\Delta\varepsilon$ *ca.* −4) results from the location of rings C and D, also in a negative octant. The bicyclic 6-ketone (9), obtained by degradation of (4), has a positive Cotton effect ($\Delta\varepsilon$ +1·1, hexane), and clearly belongs to the *trans*-decalone series [Figure, (*b*)]. Inversion of configuration occurs at C-5 during the acid-catalysed cleavage of the cyclopropane ring, since this change removes the exceptional strain favouring structure (4).

The 7-oxo-bicyclic compound (51) has the $\Delta\varepsilon$ value (−1·27) expected for a *trans*-2-decalone analogue, but the tricyclic 7-ketone exhibited almost no dichroism [$\Delta\varepsilon$ −0·06 at 294 nm (hexane)], consistent only with the *cis*-formulation (6).[9]

The 8-oxo-compound (28), in the 6α-methyl tricyclic series, had the expected negative c.d. ($\Delta\varepsilon$ −1·79), although the magnitude gives no clear indication of configuration at C-5.

$n \longrightarrow \sigma^*$ *Transition* (ca. 195 *nm*).[20] The very strongly negative c.d. [$\Delta\varepsilon$ −18·9 at 203 nm (hexane)] for ketone (6) in the tricyclic series is consistent with the 5β-formulation, for the main perturbing feature is the axial C(5)–C(4) bond on the cyclohexanone ring: we have recently demonstrated a quadrant rule for this transition,[20b] with signs corresponding to those in rear octants of the familiar octant rule. C.d. bands in this region for other tricyclic compounds are complicated by the negative Cotton effect due to the cyclopropyl system,[7] so that no further conclusions could safely be drawn.

Acetates, Alcohols, and Hydrocarbons.—The four *trans*-bicyclic alcohols (21) and (52)—(54) give only plain o.r.d. curves, and their c.d. curves provide little further information.[21] Small Cotton effects were detected, however, for the corresponding acetates. The compounds epimeric at C-7 are enantiomeric in type to 3α- and 3β-acetoxy-5α-steroids, and like the steroidal analogues [22] give negligible Cotton effects ($\Delta\varepsilon$ <0·1). The 6α- and 6β-acetates give small negative and positive Cotton effects respectively, matching in signs the corresponding 6-acetoxy-5α-steroids,[22] and enantiomeric to those shown by 4α- and 4β-acetoxy steroids.[22]

The c.d. curves for the eight tricyclic alcohols and their acetates are all dominated in the region below 200 nm by the very strong negative maximum due to a transition of the tetra-substituted cyclopropane ring. This Cotton effect has been discussed previously,[7] but the evidence presented here necessitates a revision of formula (I) in that paper to (14), *i.e.* from a *trans*- to *cis*-fusion of the decalin system. It may be significant that the sense of twist of ring A, to which the cyclopropyl group is fused at the 2,3-positions, is such that an olefinic bond at the same positions (Δ^2) would be expected to exhibit a lowest-energy c.d. band of the same sign.[23] This correlation may provide the basis of a symmetry rule for predicting the sign of c.d. associated with a dissymmetrically perturbed cyclopropane ring.

I.r. Spectra of Alcohols (*Table* 2).—According to the theory of conformational heterogeneity [24] in saturated alcohols, asymmetrical O–H stretching absorption bands result from the superposition of two or more symmetrical bands, each due to a rotamer present at equilibrium. The O–H stretching frequency is assumed to be determined primarily by the rotamer type, which decides the immediate environment of the OH group, rather than by other structural features of the molecule. The asymmetry of the absorption band is expressed as the ratio $\alpha : \beta$ (α and β are the widths at half-height of those parts of the composite and generally unsymmetrical absorption band which are on the high and low frequency sides, respectively, of $\nu_{max.}$). Axial alcohols give nearly symmetrical bands ($\alpha : \beta \approx 1$), but equatorial alcohols usually give $\alpha : \beta$ ratios significantly less than unity (0·5—0·8). Absorption maxima at the C–OH stretching frequency (940—1070 cm^{-1}) also show conformational

† Same note as on page 1108.

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

[20] (*a*) D. N. Kirk, W. Klyne, W. P. Mose, and E. Otto, *J.C.S. Chem. Comm.*, 1972, 35; (*b*) D. N. Kirk, W. Klyne, and W. P. Mose, *Tetrahedon Letters*, 1972, 1315.

[21] D. N. Kirk, W. P. Mose, and P. M. Scopes, *J.C.S. Chem. Comm.*, 1972, 81.

[22] J. P. Jennings, W. P. Mose, and P. M. Scopes, *J. Chem. Soc.* (*C*), 1967, 1102; L. Bartlett, D. N. Kirk, and P. M. Scopes, in preparation.

[23] A. I. Scott and A. D. Wrixon, *Tetrahedron*, 1970, **26**, 3695.

[24] L. Joris, P. von R. Schleyer, and E. Osawa, *Tetrahedron*, 1968, **25**, 4758.

differences (*eq.*-OH, 1020—1070; *ax.*-OH, 940—985 cm^{-1}).[25] The data presented in Table 2 support the configurations and conformations assigned above to all the alcohols in this series, including the equatorial character of both tricyclic C-7 alcohols (11) and (12). The only compound requiring further comment is the tricyclic 6β-alcohol (3). Here the α : β value is indecisive, and the C–OH stretching frequency (1011 cm^{-1}) lies between the two ranges associated with distinct conformational character. The explanation could lie in ring B adopting a partially flattened conformation, but for reasons discussed under n.m.r. spectra we prefer a conformational equilibrium involving 'steroidal' and 'non-steroidal' forms. The double absorption band observed in the C–OH stretching region for three of the alcohols is similar to that found in some decalols and 3-methylcyclohexanols.[26]

TABLE 2

I.r. spectra and other physical constants for alcohols

Compound	B.p. (°) (mmHg) or m.p. (°)	$[\alpha]_D$ (°) [a]	ν_{O-H} (cm^{-1}) [b]	α : β [c]	ν_{C-OH} (cm^{-1}) [d]	C–O Bond conformation
6β-OH-tricyclic (3)	90—95 (0·15)	−22·13 (2·62)	3628s, 3622, 3604s	0·84	1011	Mainly *ax.*
6α-OH-tricyclic (5)	125—126	−7·6 (3·95)	3628s, 3620	0·73	1050, 1038	*eq.*
7β-OH-tricyclic (12)	86—87	+23·3 (4·08)	3628s, 3619	0·43	1050	*eq.*
7α-OH-tricyclic (11)	106—108 (0·7)	−63·3 (4·07)	3628s, 3620	0·50	1046	*eq.*
6α-OH-*trans*-bicyclic (21)	78—79	+31·5 (2·59)	3629, 3624s, 3603	0·33	1048, 1034	*eq.*
6β-OH-*trans*-bicyclic (52)	148—150 (14)	−18·5 (4·31)	3628	0·90	983, 935	*ax.*
7α-OH-*trans*-bicyclic (54)	108—109	−3·5 (4·21)	3622	1·00	993	*ax.*
7β-OH-*trans*-bicyclic (53)	74—76	−6·25 (2·36)	3628s, 3620	0·57	1031	*eq.*
7β-OH-6α-Me-tricyclic (25)	123—125	−35·65 (3·30)	3603, 3627, 3642s	0·42	1038	*eq.*
7α-OH-6α-Me-tricyclic (24)	100 (0·2)	10·51 (3·1)	3640s, 3627	0·77	978	*ax.*
8α-OH-6α-Me-tricyclic (35)		3·07 (2·46)	3637s, 3626s, 3618	0·57	1034	*eq.*
8β-OH-6α-Me-tricyclic (34)	142—143	−17·91 (3·07)	3622	1·02	996	*ax.*

[a] In $CHCl_3$ (concentration in parentheses). [b] In CCl_4 (*ca.* 0·02M); s = shoulder. [c] Asymmetry of the spectral band corresponding to the OH stretching (see text). [d] In CS_2 (*ca.* 0·02M).

EXPERIMENTAL

All i.r. spectra were measured on a Perkin-Elmer 521 spectrometer. Reagent grade carbon tetrachloride and carbon disulphide were purified before use. Concentrations of alcohols were *ca.* 0·02M to prevent intermolecular association. Optical rotations were measured in chloroform on a POLAX Polarimeter. Analytical g.l.c. was carried out on a 10% Carbowax column with a Carlo Erba G.I. apparatus. C.d. curves were determined on a Cary 60 spectropolarimeter with 6001 c.d. attachment. N.m.r. spectra were recorded on a Varian A60A spectrometer, with Me_4Si as internal standard. Light petroleum refers to the fraction of b.p. 30—60°, and ligroin to the fraction of b.p. 80—120°. SILAL 13 was used for column chromatography.

Treatment of the Bicyclic Alcohols (21), (54), *and* (7) *with HBr.*—Each of the bicyclic alcohols (21), (54), and (7) (0·2 g) was treated separately with a solution of hydrogen bromide (0·1 g) in acetic acid (5 ml) for 15—20 min at 15°. The alcohols were unchanged (g.l.c., t.l.c., i.r.).

Cyclopropane Ring Opening of the Tricyclic 6β-*Alcohol* (3).—A solution of hydrogen bromide (0·25 g) in acetic acid (4 ml) was added dropwise to a solution of alcohol (3) (0·6 g) in acetic acid (10 ml) at 15°. The bulk of the solvent was removed under reduced pressure, and the residue was worked up as usual.[2,5] The residual oil in dry ether (10 ml) was added to a solution of lithium (0·075 g) in liquid ammonia (150 ml). After 5 min the mixture was quenched (NH_4Cl) and worked up. G.l.c. analysis of the crude product showed the presence of four products [A (64%), B (16%), C (16%), and D (4%)], and the i.r. spectrum revealed the presence of a methylene group (890 cm^{-1}). Catalytic hydrogenation of the crude mixture (0·45 g) over 10% Pd–charcoal (0·1 g) in ethanol (15 ml) gave a mixture containing only products A (80%) and B (20%). Product A, purified by crystallisation (petroleum) was identical (m.p., mixed m.p., g.l.c., i.r. spectrum) with the *cis*-bicyclic 6β-alcohol (7) previously described.[3] Product B has not been identified.

Preparation of the 3α-cis-*Bicyclic* 6α-*Methyl*-7β-*alcohol* (26) (7α-*Isopropyl*-1α,10β-*dimethyl*-cis-*decal*-2β-*ol*).—Cyclopropane ring opening of the alcohol (25) (5 g) with hydrogen bromide in acetic acid, and subsequent reaction with lithium–ammonia, followed by hydrogenation according to the procedure for (3) above, afforded a mixture (g.l.c.) (4·8 g) of the alcohol (26) (75%) and a second unidentified compound (25%). Column chromatography of the mixture, and elution with petroleum–ether (85 : 15), afforded the pure *alcohol* (26) (2·8 g), m.p. 98—99° (from n-hexane), τ (CCl_4) 9·03 (10β-Me), 9·16 (d, *J* 5 Hz, 6α-Me), and 6·77 (m, $W_{\frac{1}{2}}$ 26 Hz, C*H*OH) (Found: C, 80·75; H, 12·2. $C_{15}H_{28}O$ requires C, 80·3; H, 12·1%).

Preparation of the 3α-cis-*Bicyclic* 6α-*Methyl*-7-*ketone* (31) (7α-*Isopropyl*-1α,10β-*dimethyl*-cis-*decal*-2-*one*).—The foregoing alcohol (26) (1 g) was oxidised by Jones reagent, to give the *ketone* (31) (0·9 g), m.p. 106—107° (from petroleum), $[\alpha]_D$ −22·3° (*c* 2·5), τ (CCl_4) 8·75 (10β-Me) and 9·15 (d, *J* 6 Hz, 6α-Me) (Found: C, 81·5; H, 11·4. $C_{15}H_{26}O$ requires C, 81·4; H, 11·4%): 2,4-dinitrophenylhydrazone, m.p. 123° (from ethanol); semicarbazone, m.p. 217—218° (decomp.) (from ethanol), $[\alpha]_D$ +25° (*c* 0·9) (for the enantiomeric ketone: lit.,[14] m.p. 108°, $[\alpha]_D$ +24°; 2,4-dinitrophenylhydrazone, m.p. 123°; semicarbazone, m.p. 213°, $[\alpha]_D$ −16°). The ketone (31) was recovered unchanged after treatment with sodium ethoxide in ethanol.

Hydroboronation of the Tricyclic Δ^6-*olefin* (8).—The reactions with diborane followed by alkaline hydrogen peroxide were carried out essentially as described previously,[4] to give a crude alcoholic mixture (5 g) which was oxidised with Jones reagent to give a mixture of the 6- and 7-ketones, (4) (51%) and (6) (49%), respectively. Column chromatography with light petroleum–ether (49 : 1) as eluant gave pure (4) (b.p. 80—85° at 0·4 mmHg) and (6) (m.p. 76—78°) which were identical with the samples previously described.[3,4]

[25] See, for example: (*a*) M. Hanack, 'Conformational Theory,' Academic Press, New York and London, 1965; (*b*) A. Casadevall, E. Casadevall, and M. Lasperas, *Bull. Soc. chim. France*, 1968, 4506.

[26] W. Hückel, *Bull. Soc. chim. France* 1963, 1.

Hydroboronation of the Tricyclic 6-Methyl-Δ⁶-olefin (29).—The olefin (29) (0·7 g) was hydroboronated and oxidised as above, to give a mixture (0·7 g) of the 6α-methyl-7β-alcohol (25) (20%) and the 6β-methyl-7α-alcohol (30) (80%). The mixture was oxidised by Jones reagent to give a mixture (0·6 g) of the ketones (23) (20%) and (36) (80%), as shown by g.l.c. analysis. The ketonic mixture was then treated with a solution of sodium methoxide [from sodium (3 g) and absolute methanol (100 ml)] for 40 h at room temperature. The resulting oil was an equilibrated mixture of the 6α-methyl- (23) (90%) and 6β-methyl-ketones (36) (10%). The 6α-methyl-ketone (23) (m.p. 43—44°) was separated from the mixture by column chromatography (light petroleum–ether, 49 : 1, as eluant) and was identical with the sample previously described.[4]

Epimerisation of the cis-*Bicyclic 6-Ketone* (13) *with HBr*.—A solution of the ketone (13) (0·3 g) in acetic acid (5 ml) was treated with hydrogen bromide (0·12 g) in acetic acid (2 ml). After 10 min the mixture was diluted with ice-cold water and extracted with ether. G.l.c. analysis of the products showed the presence of the *cis*- and *trans*-bicyclic 6-ketones (13) and (9) in the equilibrated ratio of 15 : 85, respectively.

Preparation of Alcohols of the Tricyclic and Bicyclic Series.—The alcohols were prepared by reducing the corresponding ketones with either sodium and ethanol, or lithium aluminium hydride–aluminium chloride, as described previously.[5] Purification was carried out by crystallisation (light petroleum) or distillation under reduced pressure. The physical properties of the alcohols are collected in Table 2. Microanalyses have already been reported for the alcohols of the 6-de-methyl series. Other microanalyses are as follows:

	C (%)	H (%)
7β-OH-6α-Me tricyclic (25)	81·2	11·75
7α-OH-6α-Me tricyclic (24)	80·9	11·8
8α-OH-6α-Me tricyclic (35)	81·3	11·8
8β-OH-6α-Me tricyclic (34)	81·05	11·8
Required for $C_{15}H_{26}O$	81·0	11·8

Preparation of Acetates of the Alcohols.—A pure sample of each alcohol (0·5 g) was treated with acetic anhydride (3 ml) in pyridine (10—15 ml) and the solution was left at room temperature for 20 h. The acetates were purified either by crystallisation (light petroleum) or distillation under reduced pressure. All gave satisfactory microanalyses (data in Supplementary Publication No. SUP 20964).

Catalytic Hydrogenation of Olefins (8), (10), *and* (27).—Each olefin (0·5 g) in dry ethanol (20 ml) was separately hydrogenated in the presence of PtO_2 (0·15 g). The resulting oily products were purified from unchanged olefin by treatment with diborane and subsequent oxidation of the organoborane intermediate with hydrogen peroxide. Column chromatography (light petroleum as eluant) then gave the corresponding saturated hydrocarbons (14), (15), and (32) as oils, which were further purified by distillation at 15 mmHg pressure. G.l.c. analysis indicated that the samples were 97—98% pure.

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