

CONFORMATION OF RING A IN 3-OXOTRITERPENOIDS. SOFA CONFORMATION IN 3-OXOLUPANE-28-NITRILE CRYSTAL*

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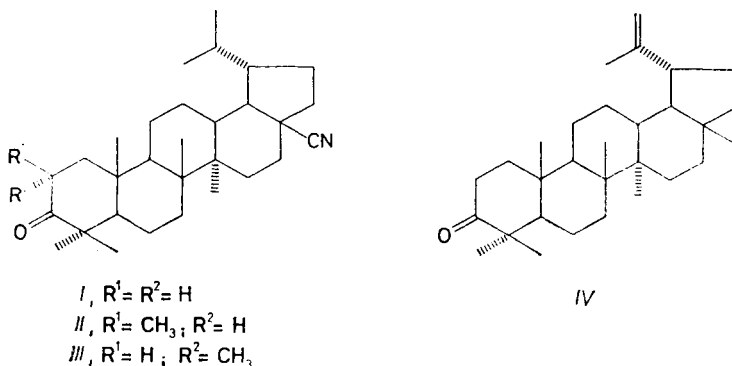
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Crystal structure of 3-oxolupane-28-nitrile (*I*) has been determined. As usual, the B, C and D rings adopt a chair, and the E ring an envelope conformation. Surprisingly enough, the A ring exists in a sofa arrangement with coplanar C(1) to C(5) and O atoms. The existence of this uncommon and energetically unfavourable conformation is explained by an intermolecular interaction of carbonyl dipoles facilitated by the particular mode of crystal packing. The comparison with crystal structure of 3-oxolupanes *II–IV* demonstrates that these compounds differ in conformation of the A and E rings whereas the rest of the skeleton remains essentially the same and is remarkably bent about the B and C rings. Differences in the effect of 8 β -methyl group on the energy of the chair and boat forms of the A ring are tentatively explained on the basis of the B ring deformation. Conformation of the A ring in solution is generally unlike that in the crystal since energy differences between the conformers tend to be effectively overbalanced by crystal packing forces.

The conformation of the ring A in triterpenoid 3-ketones with methyl groups in positions 4 α , 4 β , 8 β and 10 β and with the usual annelation of the rings A, B, C and D (*trans-transoid-trans-transoid-trans*) has been studied mainly in solutions and only in some cases in the crystalline state (see refs^{1–7} and references therein). The physical data obtained for solutions of these ketones have been interpreted in terms of either 1) chair-boat equilibrium of the ring A or 2) of a single conformation denoted as deformed (distorted) chair or half-chair^{1–4}. Our results^{2,3}, obtained by ¹H NMR and CD spectra, dipole moments and several other methods, indicate that in nonpolar solvents 3-oxolupane-28-nitrile (*I*), allobetulone (19 β ,28-epoxy-18 α -oleanan-3-one) and other ketones exist as a mixture of chair and boat forms (about 3 : 2) rather than in a single conformation. These results are based on the use of 2 β -methyl-3-ketones (e.g. *II*) and 2 α -methyl-3-ketones (e.g. *III*) as models for the boat and chair forms, respectively.

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In order to compare the conformation of the ring A in solution with that in the crystalline state, we have recently determined^{6,7} the crystal structures of the mentioned model compounds *II* and *III*. In the present paper we describe the crystal structure of unsubstituted ketone *I* and compare it with that of other 3-ketones containing the lupane skeleton⁶⁻⁸ and also with the conformation in solution.



EXPERIMENTAL

Single crystals were obtained by cooling slowly (0.5°C h^{-1}) a hot 5% solution of ketone *I* (ref.⁹) in tetrachloromethane–cyclohexane (1 : 4 (v/v)). Their density was determined by flotation in an aqueous ZnBr_2 solution.

Crystal Structure Determination

$\text{C}_{30}\text{H}_{47}\text{NO}$, orthorhombic, space group $P2_12_12_1$, $a = 6.792(1)$, $b = 29.784(4)$, $c = 12.989(1)$ Å, $V = 2627.6(6)$ Å³, $Z = 4$, $\rho_m = 1.100(8)$, $\rho_c = 1.106$ g cm⁻³, $\lambda(\text{MoK}\alpha) = 0.71069$ Å, $F(000) = 968$, $T = 298$ K. Crystal dimensions $0.25 \times 0.40 \times 0.40$ mm³, 54 reflections with θ range of $4-17^\circ$ used for lattice parameter determination, Hilger and Watts diffractometer, maximal value of $\sin \theta/\lambda = 0.64$ Å⁻¹, total of 3283 reflections measured in the range $0 \leq h \leq 8$, $0 \leq k \leq 38$, $0 \leq l \leq 16$, 2334 of them assumed as “observed” using criterion $I > 1.96\sigma(I)$. Direct methods (SHELX76, ref.¹⁰), full-matrix least-squares refinement using F -values (TLS-system, ref.¹¹); all hydrogen atoms located in the difference map; in the final refinement in three blocks, coordinates of all atoms and anisotropic thermal parameters of non-H atoms were refined simultaneously; isotropic thermal parameters of H atoms were fixed at B_{eq} values of their bonding partners; the function minimized $\sum w(|F_o| - |F_c|)^2$ where $w = (\sigma^{-2}(F_o))$ and the σ value is given by counting statistics. The refinement converged to $R = 0.091$, $wR = 0.117$ and maximal residual electron density of 0.36 e Å⁻³. The high R value is probably connected with the fact that the only single crystal available had the form of a brittle long needle; therefore, partial mechanical damage might have occurred when cutting the needle into fragments of appropriate size.

RESULTS AND DISCUSSION

Final coordinates of non-hydrogen atoms of ketone *I* are given in Table I. Tables of structure factors, anisotropic thermal parameters of non-hydrogen atoms and coordinates of hydrogen atoms are available from the authors on request. Figure 1 represents a perspective view of the molecule of *I* with atom numbering and Fig. 2 shows the packing of molecules in the unit cell. The selected bond lengths, bond angles and torsion angles, important for the conformation of rings A and E, are given in Tables II and III which, for comparison, also contain parameters of other 3-oxolupane derivatives taken or calculated from the available atomic coordinates (for *II* ref.⁶, for *III* ref.⁷, for *IV* refs^{8,12}). For the 2 β -methyl-3-ketone *II*, the asymmetric unit of the crystal⁶ contains two independent molecules differing slightly in geometry; in the Tables they are denoted as *Ila* and *Ilb* (molecule 1 and 2, respectively, in ref.⁶).

Crystal Structure of Ketone I

The bond lengths and bond angles are within the normal limits. The mean length of the C—C bond is 1.534(23) Å* and only the lengths of the C(8)—C(14) and C(17)—C(28) bonds (1.591 Å and 1.488 Å, respectively) are outside the 2 σ limit of the mean, as is usual for this type of compounds^{6,7}. The bond lengths and angles (except the values for the ring A, see Table II) exhibit trends similar to those in ketones *II* and *III*, reported in refs^{6,7}. The rings B, C and D exist in a chair conformation and the ring E assumes an envelope form with the coplanar C(18), C(19), C(21) and C(22) atoms. The deviations of these atoms from the least-squares plane are less than 0.01 Å, the distance of the C(17) atom from this plane amounts to 0.64 Å.

The geometry of the ring A in ketone *I* corresponds to a sofa conformation¹³ (also denoted¹ as the flat form): the atoms C(1), C(2), C(3), C(4), C(5) and the carbonyl oxygen lie practically in one plane, their deviation from the least-squares plane being less than 0.04 Å. The atom C(10) is 0.70 Å above this plane. Carbon atoms of the methyl groups on C(4) are placed almost symmetrically relative to the plane: the distance from the plane is 1.34 Å for C(23) and 1.20 Å for C(24). The occurrence of the sofa conformation of the ring A is quite exceptional: the hitherto studied crystalline 3-ketones of the lupane series exist either in the chair (2 α -methyl ketone *III*, ref.⁷, 20(29)-lupen-3-one (*IV*), refs^{8,12}) or in the twist-boat conformation (2 β -methyl ketone *II*, ref.⁶, methyl 3-oxo-20-hydroxylupan-28-oate, ref.¹⁴). Of other pentacyclic 3-oxotriterpenoids with similar arrangement of the skeleton and methyl groups, papyriogenin A (3,21-dioxo-11,13(18)-oleanadien-28-oic acid) exists in a chair form¹⁵ whereas allobetulone in a boat form¹⁶. Also in other similar 4,4-dimethyl ketones the ring A assumes either chair or deformed boat conformations^{1,12,17,18}.

* Estimated standard deviations (e.s.d.) of the mean are given in parentheses.

The existence of ring A in the sofa form is probably caused by intermolecular effects in the crystal (Fig. 2) in which the molecules are arranged in layers and the carbonyl group of each molecule is located between the carbonyl groups of two oppositely oriented molecules. The mutual arrangement of the carbonyl groups in

TABLE I
Atomic coordinates ($\cdot 10^4$) of non-H atoms of ketone I with estimated standard deviations in parentheses

Atom	x/a	y/b	z/c	$B_{\text{eq}}, \text{\AA}^2$ ^a
C(1)	5734(15)	1640(2)	3554(5)	5.45(21)
C(2)	5583(18)	1981(3)	4418(6)	7.16(27)
C(3)	5491(11)	2460(2)	4117(5)	5.12(20)
C(4)	5397(11)	2619(2)	2992(5)	4.66(19)
C(5)	5500(9)	2219(2)	2211(4)	3.55(16)
C(6)	4762(12)	2347(2)	1145(5)	4.50(19)
C(7)	5352(11)	1993(2)	350(4)	4.25(18)
C(8)	4516(8)	1523(2)	602(4)	2.99(15)
C(9)	5033(8)	1406(2)	1739(4)	2.79(15)
C(10)	4599(8)	1769(2)	2576(4)	3.13(16)
C(11)	4301(11)	942(2)	2009(4)	4.23(18)
C(12)	5058(12)	577(2)	1307(4)	4.36(19)
C(13)	4652(9)	683(2)	172(4)	3.34(15)
C(14)	5471(8)	1156(2)	-133(4)	3.16(15)
C(15)	4910(11)	1240(2)	-1277(4)	4.30(17)
C(16)	5520(12)	872(2)	-2019(5)	4.72(18)
C(17)	4708(9)	429(2)	-1683(4)	4.25(16)
C(18)	5383(10)	320(2)	-572(4)	3.88(16)
C(19)	4830(13)	-176(2)	-420(5)	5.40(20)
C(20)	6180(16)	-448(2)	314(6)	6.86(28)
C(21)	4782(14)	-381(3)	-1515(6)	6.29(23)
C(22)	5320(13)	4(3)	-2247(6)	5.78(20)
C(23)	7312(19)	2897(4)	2874(9)	8.96(31)
C(24)	3567(18)	2909(3)	2911(7)	7.00(27)
C(25)	2419(11)	1810(3)	2860(6)	4.70(18)
C(26)	2322(9)	1541(3)	429(5)	4.24(17)
C(27)	7732(8)	1153(2)	-57(5)	4.13(16)
C(28)	2518(10)	442(2)	-1722(5)	4.67(17)
C(29)	8341(17)	-454(3)	5(8)	8.19(30)
C(30)	5361(30)	-918(3)	498(9)	11.37(48)
O(1)	5491(11)	2727(2)	4797(4)	8.23(21)
N(1)	848(9)	450(3)	-1795(5)	6.86(19)

$$^a B_{\text{eq}} = 4(V^2(\beta_{11}\beta_{22}\beta_{33} + 2\beta_{12}\beta_{13}\beta_{23} - (\beta_{22}\beta_{13}^2 + \beta_{33}\beta_{12}^2 + \beta_{11}\beta_{23}^2)))^{1/3}.$$

three neighbouring molecules is schematically depicted in Fig. 3. The C(3)=O bonds are parallel and the intermolecular distances are: C(3)⋯O 3.72 Å, O⋯O 3.69 Å, and C(3)⋯C(3) 4.10 Å. The planes of the carbonyl groups are almost parallel, the dihedral angle between neighbouring planes being only 5°. The attraction between the oppositely oriented dipoles C=O of the neighbouring molecules, together with the repulsion between the first and third (more distant) C=O dipoles leads to an overall energy decrease of about 8 kJ mol⁻¹. Such decrease may partially compensate the higher energy of the sofa conformation caused by ring flattening (i.e. increase of the bond angles (see Table II) and torsion energy). The sofa form of the ring A seems thus to be forced out specifically by such arrangement of molecules in the crystal as found in ketone I.

Comparison of Crystal Structures of Ketones I–IV

According to the endocyclic torsion angles in the ring A and other angles, characterizing its conformation in triterpenoid ketones (Table III; see also ref.¹), the

TABLE II
Selected bond distances (Å) and angles (°) in ketones I–IV

Atoms	I	IIa	IIb	III	IV
Bond distances ^a					
C(1)—C(2)	1.517	1.545	1.543	1.519	1.527
C(2)—C(3)	1.481	1.512	1.507	1.526	1.494
C(3)—C(4)	1.537	1.515	1.532	1.537	1.493
C(4)—C(5)	1.566	1.570	1.561	1.572	1.587
C(5)—C(10)	1.549	1.552	1.554	1.559	1.556
C(10)—C(1)	1.534	1.555	1.548	1.555	1.524
Bond angles ^b					
C(10)—C(1)—C(2)	114.3	115.4	115.5	115.5	115.6
C(1)—C(2)—C(3)	116.9	110.0	110.0	110.0	110.9
C(2)—C(3)—C(4)	123.3	115.3	114.3	116.4	119.2
C(3)—C(4)—C(5)	112.3	109.4	109.5	108.3	107.7
C(4)—C(5)—C(10)	116.3	113.5	114.3	116.7	116.5
C(5)—C(10)—C(1)	105.8	107.4	108.1	106.8	105.3

^a Mean e.s.d. values: I (0.009), IIa and IIb (0.004), III (0.007), IV (unknown; coordinates excerpted from the Database^{1,2}); ^b mean e.s.d. values: I (0.5), IIa and IIb (0.2), III (0.4), IV (unknown).

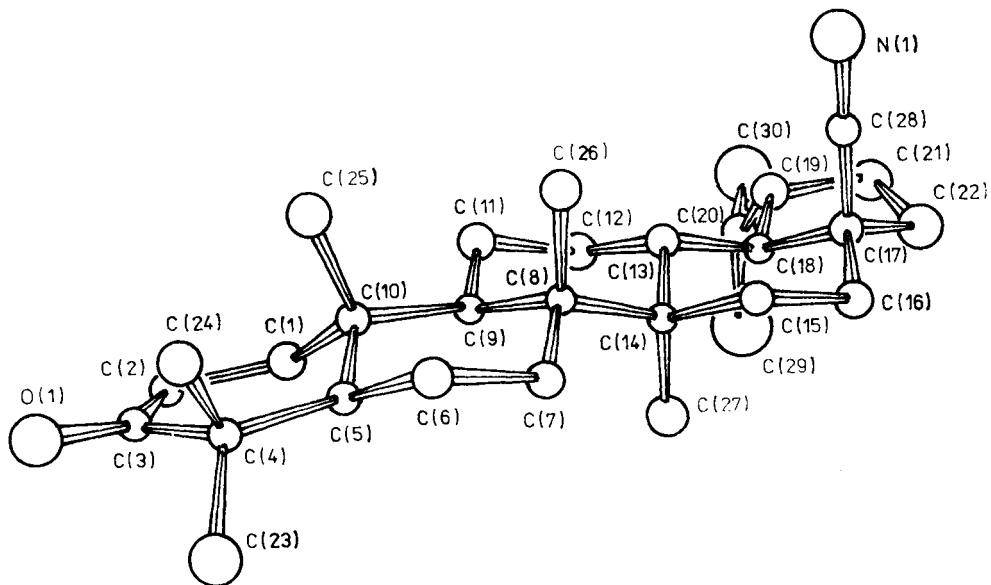


FIG. 1
Perspective view of molecule *I* with atom numbering

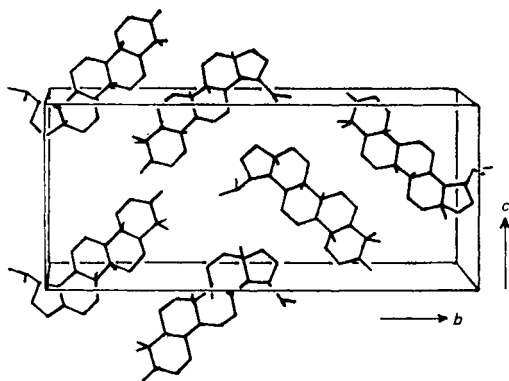


FIG. 2
Unit cell contents

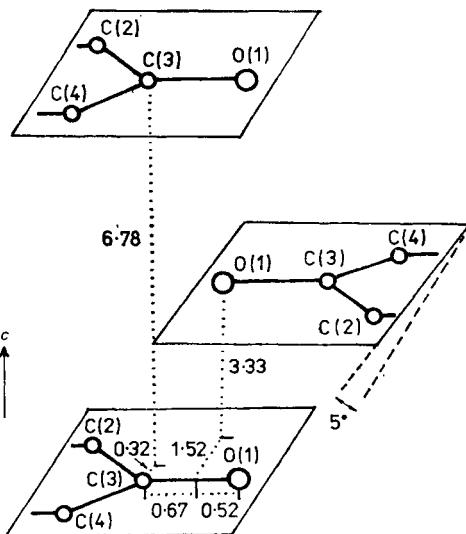


FIG. 3
Arrangement of the carbonyl groups of three adjacent molecules of ketone *I* in the crystal (not in scale; distances in Å)

molecules of *I–IV* may be divided into three groups: those which have the ring A in the chair (*III, IV*), twist-boat (*IIa, IIb*) and sofa (*I*) conformation.

The chair conformation of the ring A in the 3-ketones should have a plane of symmetry passing through the atom C(3) (see ref.¹). The chair found in ketones *III* and *IV* shows only a small deviation from the ideal chair form as illustrated by the

TABLE III
Selected torsion angles (°) in ketones *I–IV*

Atoms ^a	<i>I</i>	<i>IIa</i>	<i>IIb</i>	<i>III</i>	<i>IV</i>
Ring A					
C(10)—C(1)—C(2)—C(3)	—34.9	30.1	29.7	—53.6	—53.1
C(1)—C(2)—C(3)—C(4)	4.4	—61.9	—63.3	51.2	48.2
C(2)—C(3)—C(4)—C(5)	—2.4	28.0	31.5	—48.8	—46.0
C(3)—C(4)—C(5)—C(10)	31.2	35.0	30.9	51.2	50.5
C(4)—C(5)—C(10)—C(1)	—59.1	—63.1	—61.0	—53.0	—55.2
C(5)—C(10)—C(1)—C(2)	60.0	27.7	28.0	53.5	55.7
O(1)—C(3)—C(4)—C(23)	62.0	90.6	94.1	14.1	17.4
O(1)—C(3)—C(4)—C(24)	—55.8	—25.0	—22.0	—102.1	—101.0
C(23)—C(4)—C(5)—C(6)	—85.8	—81.3	—83.9	—60.0	—64.6
C(24)—C(4)—C(5)—C(6)	40.1	38.7	37.0	60.6	56.6
C(24)—C(4)…C(10)—C(25) ^b	—24.3	—27.2	—27.6	—3.0	—6.9
Ring B					
C(10)—C(5)—C(6)—C(7)	—61.4	—58.8	—59.6	—63.0	—63.6
C(5)—C(6)—C(7)—C(8)	59.7	59.6	58.8	56.9	57.6
C(6)—C(7)—C(8)—C(9)	—51.0	—53.3	—50.5	—47.3	—47.8
C(7)—C(8)—C(9)—C(10)	48.3	49.8	48.2	46.9	47.0
C(8)—C(9)—C(10)—C(5)	—50.1	—48.6	—49.5	—52.0	—54.5
C(9)—C(10)—C(5)—C(6)	54.6	51.1	52.7	58.5	60.0
Ring E					
C(22)—C(17)—C(18)—C(19)	—40.8	—41.2	—41.4	—44.6	—47.2
C(17)—C(18)—C(19)—C(21)	25.1	22.8	20.9	32.0	32.6
C(18)—C(19)—C(21)—C(22)	0.3	4.3	7.1	—7.5	—6.6
C(19)—C(21)—C(22)—C(17)	—26.1	—29.9	—32.9	—19.6	—21.7
C(21)—C(22)—C(17)—C(18)	41.1	43.3	45.4	39.3	42.1

^a Mean e.s.d. values: *I* (0.9), *IIa* and *IIb* (0.3), *III* (0.9), *IV* (unknown; coordinates excerpted from the Database¹²); ^b pseudo torsion angle.

low value of the asymmetry parameter* $\Delta C_s(3) = 2.0^\circ$ for both ketones. Also the conformation of the ring A in ketone I is close to an ideal sofa form with plane of symmetry passing through C(3) ($\Delta C_s(3) = 2.5^\circ$). The endocyclic bond angles at atoms C(2), C(3) and C(4) are larger than those in the twist-boat (*IIa*, *IIb*) and chair (*III*, *IV*) forms as a consequence of flattening of this part of the molecule (Table II).

In both molecules of the 2 β -methyl ketone *II* (*IIa* and *IIb*) conformation of the ring A corresponds to a twist-boat T_1 (ref.¹), the geometry of which represents an intermediate form in the pseudorotation between two classical boat forms, one with the C(3), C(10) and the other with the C(2), C(5) atoms in the stem-stern positions (conformation B^3 and B_2 , respectively, according to classification of Tsuda and Kiuchi¹). The geometry of ring A is nearer to an ideal twist-boat T_1 in the molecule *IIb* ($\Delta C_2(1) = 1.7^\circ$, $\Delta C_2(2-3) = 2.4^\circ$) than in the molecule *IIa* (the respective values are 4.3° and 5.4°). However, in both molecules the deviations from symmetry are smaller than in triterpenoid ketones without the 2 β -methyl group where the asymmetry parameters are much higher¹ ($10^\circ - 20^\circ$). This is also seen from the endocyclic torsion angles about the C(1)—C(2) bond which are 30° both in *IIa* and *IIb* whereas they are only 10° in 20,24-epoxy-11 α -hydroxy-24-methyl dammaran-3-one, 14° in 8 α H,14 β H-onocerane-3,21-dione and 18° in 14-serratene-3,21-dione (for references see^{1,2}). The higher torsion angle in 2 β -methyl ketone *II* may be caused by a non-bonding interaction of the 2 β -methyl group with H-1 β .

Comparison of the chair and boat conformations in ketones *II-IV*, which are derived from the same skeleton and differ only in positions quite distant from the rings A and B, allows now to contribute to the explanation of the so-called "8 β -methyl effect"^{2,19}. This effect consists in an increase in energy of the chair form relative to the boat one (by about $2-4 \text{ kJ mol}^{-1}$) upon introduction of a methyl group into the 8 β -position. It is generally manifested by an increase of the boat population in solutions of many derivatives (not only 3-ketones), and also in some chemical reactions by preference of the boat transition state over the chair one¹⁹. As seen from Table III, the torsion angle C(4)—C(5)—C(10)—C(1) is smaller ($\sim -54^\circ$) in the chair form (*III*, *IV*) than in the boat ($\sim -62^\circ$; *IIa*, *IIb*). The same conclusion also follows from comparison of data published¹ for a less consistent series of ketones. This effect is transferred to the chair form of the ring B in which the endocyclic torsion angles about the C(5)—C(10), C(9)—C(10), and C(5)—C(6) bonds are smaller when the ring A is a boat than when it is a chair; this indicates that the ring B is more flattened in this part. The 8 β - and 10 β -methyl groups in the boat form of ring A are more apart from each other: the angle between the C(25)—C(10) and

* For definition of the asymmetry parameters see ref.¹³. The number of the carbon atom which lies in (or the numbers of atoms whose mutual bond is bisected by) the twofold axis or the plane of symmetry in question is given in parentheses. A higher value of the asymmetry parameter indicates a larger deviation from symmetry.

C(26)—C(8) bonds is $\sim 23^\circ$ in *Ia* and *Ib* but only 20° in *III* and *IV*. This is also reflected in the interatomic distances C(25)⋯C(26) which in *Ia* and *Ib* are 3.28 Å whereas in *III* and *IV* only 3.21 Å and 3.18 Å, respectively. Therefore, the 1,3-synaxial interaction between the 8 β - and 10 β -methyl groups is larger in the chair form of ring A and destabilises more the chair than the boat form.

Comparison of the mentioned data for ketones *I—IV* with those for other 3-ketones containing 4 α -, 4 β -, 8 β - and 10 β -methyl groups^{1,16} reveals a certain characteristic feature of all the hitherto observed non-chair conformations of the ring A. Irrespective of their actual geometry (sofa, twist-boat, deformed or distorted boat), all of them have very similar arrangement about the C(4)—C(5) and C(5)—C(10) bonds. The torsion angles C(3)—C(4)—C(5)—C(10) differ only slightly: the mean value obtained from eight compared structures is $31(2)^\circ$. Similarly, there is no great difference between the torsion angles C(4)—C(5)—C(10)—C(1), their mean value being $-63(2)^\circ$. Also the mutual position of the 4 β - and 10 β -methyl groups is very similar in this series (as illustrated by the pseudotorsion angle C(24)—C(4)⋯C(10)—C(25) which amounts to $-27(3)^\circ$). The position of C(1), C(3), C(4), C(23), and C(24) relative to the ring B is about the same in all the non-chair forms and corresponds to the minimized non-bonding interactions between the 4 β - and 10 β -methyl groups on the one side and between the 4 α - and 4 β -methyl groups and the 6-methylene group on the other. The individual non-chair forms differ from each other mainly in the position of the C(2) atom relative to the other carbon atoms in the ring A. The largest differences are found in the torsion angles about the C(1)—C(2) bond (from $+30^\circ$ to -35°) and the C(2)—C(3) bond (from $+4^\circ$ to -63°). Most probably the varying geometry in this part of the ring A results from a different crystal packing.

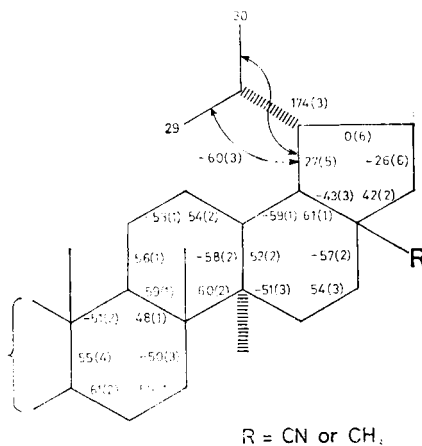


FIG. 4

Average values of selected torsion angles for molecules *I—IV* with e.s.d.'s of the mean in parentheses

Except the ring A, the overall geometry of the lupane skeleton in ketones *I–IV* is similar. The rings B, C, and D assume chair conformations and the ring E has an envelope-like geometry. The mean values of torsion angles in these molecules are given in Fig. 4. Their skeleton is markedly bent in the region of rings B and C: the mean value of the dihedral angle between the least squares planes of the atoms C(6), C(7), C(9), C(10) and atoms C(8), C(11), C(12), C(14) in the molecules of *I–IV* amounts to $11(1)^\circ$. The 10β -methyl group is bent outside the ring B as seen from the angles between the C(25)—C(10) and C(26)—C(8) bonds ($22(2)^\circ$) and the C(25)—C(10) and C(27)—C(14) bonds ($161(2)^\circ$). The twist about the length of the skeleton in this part is relatively small, as shown by the pseudotorsion angles C(25)—C(10)⋯C(8)—C(26) and C(25)—C(10)⋯C(14)—C(27), amounting to $4(2)^\circ$ and $-175(3)^\circ$, respectively.

However, the ketones *I–IV* differ in geometry of the five-membered ring E (Table III). Whereas the conformation of the ring E in ketone *I* is very close to the envelope form with the plane of symmetry passing through C(17) and bisecting the C(19)—C(21) bond ($\Delta C_s(17) = 0.7^\circ$), in both molecules of the ketone *II* the envelope form is twisted towards the half-chair conformation with $C_2(19)$ axis of symmetry ($\Delta C_s(17) = 5.2^\circ$ and 8.9° ; $\Delta C_2(19) = 15.3^\circ$ and 11.5° for *Ila* and *Iib*, respectively). In ketones *III* and *IV* the envelope form is twisted in the opposite direction towards the half-chair with $C_2(21)$ axis of symmetry ($\Delta C_s(17) = 13.5^\circ$ and 8.5° ; $\Delta C_2(21) = 10.0^\circ$ and 12.6° for *III* and *IV*, respectively). The conformational changes in the ring E can hardly be explained by a conformational transmission from the ring A and they are probably caused also by crystal packing.

In all molecules of *I–III* with isopropyl group on C(19) there is a staggered arrangement about the C(19)—C(20) bond. The methyl group of the pro-*S* configuration (C(29)H₃) is on the α -side of the skeleton between the C(18) and C(21) atoms whereas the pro-*R* methyl group (C(30)H₃) is on the β -side (see the torsion angles in Fig. 4). Evidently, this arrangement is energetically the most advantageous since other possible staggered conformers suffer from strong non-bonding interactions between one or other methyl and the 12-methylene group.

Comparison of Conformation of Ring A in Crystal and Solutions

The conformation of ring A in 3-oxolupane-28-nitrile (*I*) and its 2β -methyl and 2α -methyl derivatives *II* and *III* in solutions in nonpolar solvents was studied mainly using dipole moments³ and ¹H NMR spectra². The dipole moments give information only on the relative arrangement of the carbonyl and nitrile groups whereas the vicinal coupling constants of the protons in position 1 and 2 concern the arrangement about the C(1)—C(2) bond. Comparison of the crystal structure with the data for solutions^{2,3} allows to decide to what extent the conformation of ring A in solution differs from that in crystal.

In the 2α -methyl ketone *III*, the ring A is a chair, both in solution and in crystal. The angle between the dipoles $C=O$ and $C\equiv N$, calculated³ from the dipole moment of *III* and from the group moments of the carbonyl and nitrile groups, is 137° . A similar value (142°) has been found in crystal. In 20(29)-lupen-3-one (*IV*), which in crystal has the ring A in the chair form, the direction of the $C\equiv N$ dipole may be approximated by direction of the $C(17)-C(28)$ bond: this leads to an angle of 137° . The similarity of all these values, together with the results obtained from coupling constants², shows that the chair forms of the ring A in crystal and solution are of comparable geometry.

For the 2β -methyl ketone *II*, twist-boat conformation was found both in crystal and in solution. However, the angle between the dipoles in crystal (61° for both *IIa* and *IIb*) differs from that calculated³ from the dipole moment (80°). The endocyclic torsion angle about the $C(1)-C(2)$ bond, estimated from the coupling constants², is about 18° whereas in crystal it amounts to 30° for both molecules. Both these facts indicate that the geometry of the twist form in the two states somewhat differs.

The greatest conformational differences between the crystalline state and solution have been found for ketones *I* and *IV* which contain no substituent on $C(2)$. In the ketone *I* the angle between the dipoles $C=O$ and $C\equiv N$ in crystal (93° , sofa conformation of ring A) differs from that calculated from the dipole moment of *I* and the group moments³ (111°) under the assumption of conformational homogeneity of ring A. Neither the vicinal coupling constants² agree with the sofa conformation. This is particularly apparent in the case of the constant $J(1\beta, 2\alpha)$: in the sofa form (in crystal) the torsion angle $H(1\beta)-C(1)-C(2)-H(2\alpha)$ is 85° which should correspond (according to the Karplus equation²⁰) to an almost zero value of $J(1\beta, 2\alpha)$; the actual value is, however, 4.3 Hz. The coupling constants observed for the ketone *I*, for the saturated analogue of *IV* (3-lupanone) and for other triterpenoid 3-ketones² are at variance with the chair form observed in the crystalline ketone *IV* and also do not agree with any of the boat forms. Therefore, we assume that the observed dipole moments, coupling constants and other physical data obtained in solutions can be best explained by a chair-boat equilibrium as has already been postulated^{2,3}.

The results of the present study, together with those published in the literature^{1-3,14-18} for polycyclic 3-ketones with $4\alpha,4\beta$ - and 10β -methyl groups, may be summarized as follows: In ketones without 8β -methyl group (such as 4,4-dimethylsteroids and similar compounds) the ring A assumes chair conformation in the crystalline state. 6α -Hydroxy-4,4-dimethylandrostan-3-one represents an exception: in this compound the chair is destabilized by strong interaction of the 4α -methyl with the 6α -hydroxyl and the ring A exists in a twist-boat¹⁷. In the crystalline state, the ring A in 8β -methyl ketones exists either in the chair form or in variously deformed or twisted boat, or in a sofa conformation. The non-chair conformations differ predominantly in the position of $C(2)$ and may be best characterized by the endocyclic torsion angles about the $C(1)-C(2)$ and $C(2)-C(3)$ bonds where greatest differences

occur. The great variability of conformations of ring A in structurally very similar ketones shows that intermolecular forces in crystals, rather than conformational transmission (used for explanation of some differences¹), have the decisive influence. Ketones, differing in conformation of the ring A in crystal, have very similar physical properties in solution, which indicate approximately the same solution conformation. Generally, conformation of ring A in solution may differ considerably from that in crystal because the effect of crystal packing forces may be comparable with the energy differences between the individual conformers.

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