CRYSTAL STRUCTURE AND CONFORMATION OF RING A OF 2β-BROMO-19β,28-EPOXY-18α-OLEANAN-3-ONE*

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Dedicated to Professor Otto Wichterle on the occasion of his 80th birthday.

The crystal structure of 2β-bromo-19β,28-epoxy-18α-oleanan-3-one was elucidated. The crystal is orthorhombic, $P2_12_12_1$, a = 9.686(1), b = 14.355(2), c = 19.687(4) Å, Z = 4, R = 0.042 for 2 410 observed reflections. Rings B, C, D and E adopt the chair conformation, the five-membered ether cycle in ring E occurs in the envelope form. Ring A takes the twist-boat conformation turned towards the classical boat with C2 and C5 in the stem-stern positions, in contrast to the conformation in solution, which is turned in the opposite direction towards the classical boat with C3 and C10 in the stem-stern positions.

The conformation of ring A in 3-oxotriterpenoids and related ketones possessing 4α, 4β, 8β and 10β methyl groups with the usual trans-transoid-trans annellation of the rings A, B and C has been extensively studied recently, both in solutions and in the crystal state (refs[1-4] and references therein). While the chair and boat conformations of ring A are in an equilibrium in a ratio about 3 : 2 (refs[1,2]) if the substance is dissolved, the ketones in crystals all adopt a single conformation, which exhibits a high variability of the ring A geometry: in some ketones such as 20(29)-lupen-3-one[5,6], 6β-hydroxy-20(29)-lupen-3-one[7], 12α-hydroxy-3-oxo-oleanan-28,13β-olide[8], 3,21-dioxo-11,13(18)- oleanadien-28-oic acid[9], methyl 3-oxo-12-ursen-28-oate[10], ring A occurs in the chair conformation; in 3-oxolupane-28-nitrile it occurs in the sofa conformation[3], whereas various distorted or twisted boat conformations exist in a number of other ketones such

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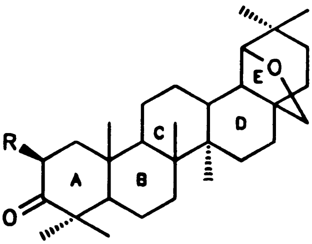
as methyl 20-hydroxy-3-oxolupan-28-oate[11], 19β,28-epoxy-18α-oleanan-3-one[1], (24*R*)-20,24-epoxy-11α-hydroxy-24-methyldammaran-3-one[12], 14-serratene-3,21-dione[13] and 8αH,14βH-onocerane-3,21-dione[14].

Of 3-ketones substituted in position 2β, only 2β-methyl-3-oxolupane-28 nitrile[15] and 2,2-dibromo-3,11-dioxo-12-oleanen-30,18β-olide[16] (echinolactone B) have been so far examined with respect to their crystal structure. In both substances, ring A adopts the boat conformation. The present paper is concerned with the crystal structure of another 2β-substituted 3-ketone, viz. 2β-bromo-19β,28-epoxy-18α-oleanan-3-one (*I*); the geometry of ring A is compared with that of the substance in solution (boat conformation[2,17]) and also with that found in the unsubstituted ketone (*II*) (ref.[1]) and in similar ketones in the crystal state.



I, R = Br
II, R = H

EXPERIMENTAL

Prismatic single crystals of bromoketone *I* (for preparation see ref.[18]) were grown from benzene–heptane by slow evaporation at room temperature. The density was determined by flotation in aqueous $ZnBr_2$ solution.

Crystal data: $C_{30}H_{47}BrO_2$, $M_R = 519.6$, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 9.686(1)$, $b = 14.355(2)$, $c = 19.687(4)$ Å (based on the least-squares refinement of 22 precisely centered reflections within the 16 – 20 θ range), $V = 2\,737.3(8)$ Å^3, $Z = 4$, $D_{calc} = 1.261$ g cm^{-3}, $D_{obs} = 1.265(3)$ g cm^{-3}, $\mu = 15.08$ cm^{-1}, $F(000) = 1\,112$.

Measurement: A crystal 0.28 × 0.21 × 0.07 mm in size was measured on a CAD4 diffractometer (MoK_α radiation, $\lambda = 0.71069$ Å). From a total of 10 568 reflections up to $2\theta = 50°$ within the *h*, *k*, *l* range of −11,11; −17,17; −23,23, respectively, 2 410 were regarded as "observed" according to the $I > 3\sigma(I)$ criterion. Three standard reflections, which were monitored every 90 min, showed no significant fluctuations (< 1.5%). Absorption correction was applied based on the crystal shape (program CRYSTL (ref.[19])).

Structure solution and refinement: direct methods (SHELXS86 (ref.[20])), full-matrix least-squares refinement (SDP program package[19]), anisotropic refinement of all non-hydrogen atoms, hydrogen atoms fixed in calculated positions. Function minimized: $\sum w(F_o^2 - F_c^2)^2$ with $w = 4F^2/[\sigma(F_o^2)]^2$, final

$R = 0.042$, $R_w = 0.046$, $R_{int} = 0.028$, $S = 1.198$, $|(\Delta/\sigma)_{max}| = 0.24$. The final difference electron density map was featureless, with extremal values of 0.55; –0.45 e Å^{-3} near the Br atom. Program PARST88 (ref.[21]) was used to calculate the molecular parameters.

RESULTS AND DISCUSSION

The final coordinates of the non-hydrogen atoms in bromoketone *I* are given in Table I, the bond distances and angles are given in Table II. The anisotropic displacement parameters, hydrogen atom coordinates and structure factors are available from the authors on request. A perspective view of molecule *I*, along with the atom numbering, is shown in Fig. 1, whereas the packing of the molecules in the unit cell is shown in Fig. 2. The

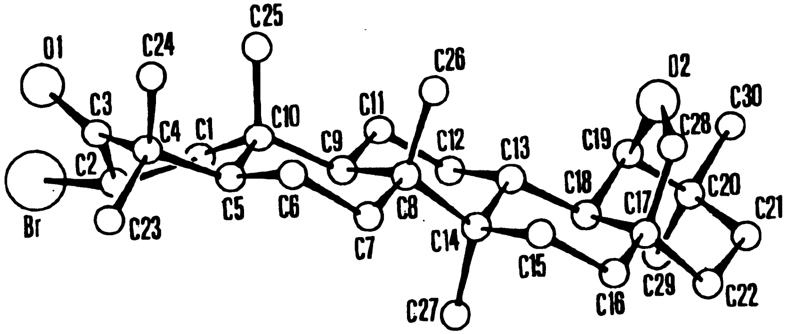


FIG. 1
Perspective view of molecule *I* with atom numbering

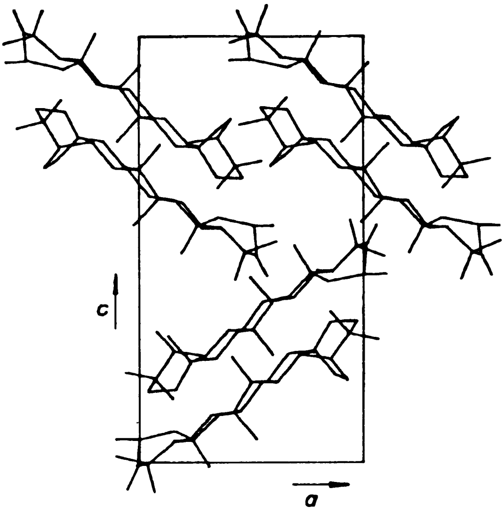


FIG. 2
Unit cell content

Table I

Fractional coordinates (. 10^4) of non-hydrogen atoms in substance *I*; standard deviation estimates are given in parentheses. $B_{eq} = (4/3)(a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33})$

Atom	*x*/*a*	*y*/*b*	*z*/*c*	B_{eq}, Å^2
Br	-960.3(9)	7134.1(6)	9436.4(5)	8.27(2)
O1	-570(5)	5785(3)	10634(3)	6.3(1)
O2	9193(4)	4630(3)	8069(2)	3.6(1)
C1	1545(6)	6074(4)	9245(3)	3.6(1)
C2	-9(6)	5956(4)	9454(4)	4.6(1)
C3	-143(7)	5451(5)	10110(4)	3.9(1)
C4	289(6)	4433(4)	10056(3)	3.3(1)
C5	1410(6)	4351(4)	9479(3)	2.8(1)
C6	2167(6)	3411(4)	9522(3)	3.4(1)
C7	3099(6)	3293(4)	8890(3)	3.3(1)
C8	4194(6)	4056(4)	8816(3)	3.1(1)
C9	3454(6)	5029(4)	8843(3)	2.7(1)
C10	2411(5)	5193(4)	9444(3)	2.6(1)
C11	4529(6)	5827(4)	8770(3)	3.4(1)
C12	5422(7)	5726(4)	8130(3)	3.7(1)
C13	6111(6)	4756(4)	8096(3)	2.7(1)
C14	4978(6)	3964(4)	8115(3)	2.7(1)
C15	5711(6)	3018(4)	8054(3)	3.4(1)
C16	6627(6)	2918(5)	7433(3)	3.7(1)
C17	7702(6)	3700(4)	7372(3)	3.0(1)
C18	7097(6)	4671(4)	7479(3)	3.0(1)
C19	8437(6)	5219(4)	7603(3)	2.7(1)
C20	9269(7)	5352(4)	6951(3)	3.6(1)
C21	9626(7)	4396(5)	6650(3)	4.5(1)
C22	8417(7)	3687(5)	6686(3)	4.3(1)
C23	-1032(6)	3910(5)	9825(3)	4.4(1)
C24	715(6)	4053(5)	10748(3)	3.9(1)
C25	3102(6)	5403(5)	10121(3)	3.7(1)
C26	5217(6)	3926(4)	9423(3)	3.4(1)
C27	4019(7)	4037(5)	7500(3)	3.8(1)
C28	8772(6)	3667(4)	7942(3)	3.3(1)
C29	8460(9)	5943(6)	6435(4)	6.4(1)
C30	10616(7)	5876(5)	7130(4)	4.8(1)

endocyclic torsion angles are presented in Fig. 3. All bond distances and angles are normal and do not require any comment.

The geometry of the skeleton, in the area of rings B, C, D and E, approaches closely that found for the unsubstituted ketone *II* (ref.[1]). The rings adopt the chair conformation. The ether bridge affects ring E, viz. by reducing the C17–C18–C19 bond angle (99.5(4)°) and by flattening at C21 and puckering at C18, as the torsion angles demonstrate. The five-membered ether ring occurs in the virtually ideal envelope form, the symmetry plane passing through C18 (asymmetry parameter $\Delta C_s(18) = 1.3°$), the C17, C19, C28 and O2 atoms lie in a plane ($\chi^2 = 0.4$), C18 being 0.70(6) Å from that plane.

Ring A adopts the boat conformation. The signs and endocyclic torsion angle values indicate that the ring geometry approaches the twist form T_1 but exhibits a marked departure from the symmetry of the ideal T_1 form* ($\Delta C_2(1) = 8.4°$, $\Delta C_2(2\text{-}3) = 10.0°$). The torsion angles (e.g. $\phi(1,2) = 36.8(7)°$) suggest that the twist form is turned towards the classical boat B_2. This $T_1(B_2)$ conformation is, according to ref.[4], energetically disadvantageous and has been never before observed for triterpenoid or 4,4-dimethylsteroid 3-ketones. For the majority of 3-oxo-derivatives whose A rings adopt the boat conformation in the crystal state, the ring geometry is closer to the classical boat B^3 and the $\phi(1,2)$ angle is smaller than 30°. In fact, this angle is about 0° in the unsubstituted ketone *II* (ref.[1]) and in 2,2-dibromo-3,11-dioxo-12-oleanen-30,18β-olide (ref.[16]) and between 10° and 23° in a number of other ketones[4,12 – 14,22], as corresponds to the $T_1(B^3)$ conformation. 2β-Methyl-3-oxolupane-28-nitrile (ref.[15]) is a limiting case, having ring A in the ideal T_1 conformation ($\phi(1,2) = 30°$). The ^{1}H NMR spectrum indicates that the conformation of ring A in the bromoketone *I* in solution approaches more the boat B^3. Based on the vicinal coupling constants of the protons in positions 1 and 2, the $\phi(1,2)$ angle has been estimated[17] to be about 20°. The NMR spectra of the analogous 2β-bromoketone in the lanostane series[23] and of the 2β-methyl-3-oxo derivatives[2] give the same value. Apparently, the $T_1(B^3)$ conformation corresponds to the energy minimum of the pseudorotation between the B_2 and B^3 boats.

Comparison of the crystal structure of the bromoketone *I* and of additional 13 structures given in refs[1,3,4,12 – 16,22] demonstrates that the geometry of the non-chair conformations of ring A in the various triterpenoid, 4,4-dimethylsteroid and related 3-ketones (both unsubstituted and 2-substituted) are appreciably different. The differences are

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* Notation according to Tsuda and Kiuchi[4] is used in the discussion of the boat form geometry: symbol B^3 refers to the classical boat with C3 and C10 in the stem-stern positions, which is characterized, among other things, by endocyclic torsion angle of the C1–C2 bond ($\phi(1,2)$) about 0°; symbol B_2 refers to the classical boat with C2 and C5 in the stem-stern positions with $\phi(1,2)$ about 60°. The twist form, which represents an intermediate form in the pseudorotation between the two classical boats, is designated T_1. The ideal T_1 twist conformation possesses two two-fold axes of symmetry, $C_2(1)$ and $C_2(2\text{-}3)$, and the $\phi(1,2)$ angle is about 30°.

TABLE II
Bond distances and angles in substance *I*; standard deviation estimates are given in parentheses

Atoms	Distances, Å	Atoms	Angles, °	Atoms	Angles, °
Br–C2	1.926(6)	C28–O2–C19	107.6(4)	C18–C13–C14	112.9(4)
O1–C3	1.210(9)	C10–C1–C2	111.1(4)	C13–C14–C8	107.1(4)
O2–C19	1.447(7)	C1–C2–Br	111.1(3)	C15–C14–C8	111.3(4)
O2–C28	1.463(7)	C3–C2–Br	113.7(4)	C27–C14–C8	113.2(4)
C1–C2	1.570(8)	C3–C2–C1	111.3(5)	C15–C14–C13	108.2(4)
C1–C10	1.567(8)	C2–C3–O1	125.2(6)	C27–C14–C13	110.7(5)
C2–C3	1.49(1)	C4–C3–O1	122.2(6)	C27–C14–C15	106.2(5)
C3–C4	1.524(9)	C4–C3–C2	112.5(5)	C16–C15–C14	114.6(5)
C4–C5	1.576(8)	C5–C4–C3	108.1(5)	C17–C16–C15	113.0(5)
C4–C23	1.552(8)	C23–C4–C3	105.0(5)	C18–C17–C16	113.3(4)
C4–C24	1.524(8)	C24–C4–C3	110.8(5)	C22–C17–C16	111.7(5)
C5–C6	1.538(8)	C23–C4–C5	108.7(4)	C28–C17–C16	112.3(4)
C5–C10	1.551(8)	C24–C4–C5	115.5(4)	C22–C17–C18	108.0(5)
C6–C7	1.546(8)	C24–C4–C23	108.2(5)	C28–C17–C18	100.8(4)
C7–C8	1.532(8)	C6–C5–C4	110.8(4)	C28–C17–C22	110.1(5)
C8–C9	1.571(8)	C10–C5–C4	113.9(4)	C17–C18–C13	114.6(4)
C8–C14	1.581(8)	C10–C5–C6	112.8(4)	C19–C18–C13	110.8(4)
C8–C26	1.563(8)	C7–C6–C5	109.3(4)	C19–C18–C17	99.5(4)
C9–C10	1.573(8)	C8–C7–C6	113.7(4)	C18–C19–O2	103.2(4)
C9–C11	1.555(8)	C9–C8–C7	108.5(4)	C20–C19–O2	109.8(4)
C10–C25	1.521(8)	C14–C8–C7	110.9(4)	C20–C19–C18	112.1(4)
C11–C12	1.535(9)	C26–C8–C7	106.3(4)	C21–C20–C19	109.4(4)
C12–C13	1.545(8)	C14–C8–C9	108.8(4)	C29–C20–C19	110.8(5)
C13–C14	1.581(8)	C26–C8–C9	111.7(4)	C30–C20–C19	108.3(5)
C13–C18	1.550(8)	C26–C8–C14	110.7(4)	C29–C20–C21	110.7(5)
C14–C15	1.537(8)	C10–C9–C8	116.8(4)	C30–C20–C21	109.4(5)
C14–C27	1.530(9)	C11–C9–C8	110.3(4)	C30–C20–C29	108.2(5)
C15–C16	1.517(8)	C11–C9–C10	112.9(4)	C22–C21–C20	113.5(5)
C16–C17	1.536(9)	C5–C10–C1	107.8(4)	C21–C22–C17	112.1(5)
C17–C18	1.527(8)	C9–C10–C1	106.0(4)	C17–C28–O2	106.6(4)
C17–C22	1.518(8)	C25–C10–C1	107.1(5)		
C17–C28	1.528(8)	C9–C10–C5	108.6(4)		
C18–C19	1.537(8)	C25–C10–C5	113.0(4)		
C19–C20	1.527(9)	C25–C10–C9	113.9(4)		
C20–C21	1.534(9)	C12–C11–C9	112.6(4)		
C20–C29	1.54(1)	C13–C12–C11	111.3(4)		
C20–C30	1.55(1)	C14–C13–C12	110.3(4)		
C21–C22	1.55(1)	C18–C13–C12	111.8(4)		

highest in the region of the C1 and C2 atoms: the endocyclic torsion angles φ(1,2) lie within the range of –35° to +37°, the φ(2,3) angle ranges from –69° to +4°, and the φ(1,10) angle takes values from +18° to +60°. Such differences, as well as the differences between the ring A geometries in solution and in the crystal state, are apparently due to the crystal packing effect (see also refs[1,3]).

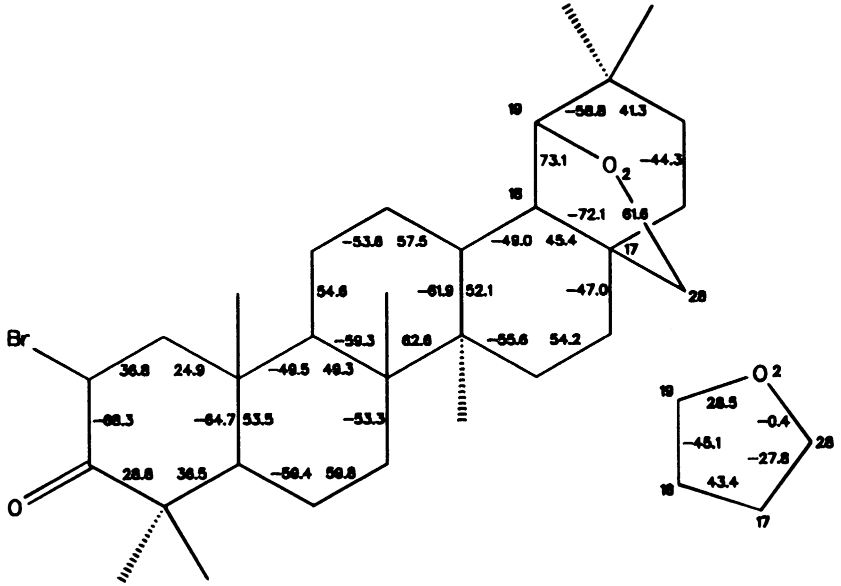

FIG. 3

Endocyclic torsion angles (deg) in substance *I* (estimated standard deviations 0.5° to 0.7°)

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