CONFORMATION OF RING A IN TRITERPENOID KETONES. CARBON-13 CHEMICAL SHIFTS AND SPIN–LATTICE RELAXATION TIMES OF LUPANE AND 18α-OLEANANE DERIVATIVES*

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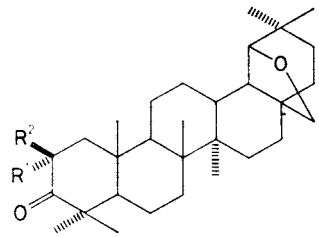
Received September 19, 1988
Accepted October 4, 1988

^{13}C NMR spectra of sixteen lupane and 19β,28-epoxy-18α-oleanane triterpenoids *I*—*XVI* were measured and a complete structural assignment of chemical shifts was made. For most compounds also the carbon spin-lattice relaxation times T_1 were obtained. Characteristic differences in chemical shifts of some carbon atom signals were found between 2α-methyl-3-oxo and 2α-methyl-1-oxo derivatives *II*, *V* and *VIII* with chair conformation of the ring A on the one hand and their 2β-isomers *III*, *VI* and *IX* (boat form) on the other. Using these 2-methyl ketones as models, the chair–boat population in allobetulone (*I*), 3-oxo-28-lupanenitrile (*IV*) and 1-oxo derivative *VII* was determined. The results agree well with the data obtained by other physical methods.

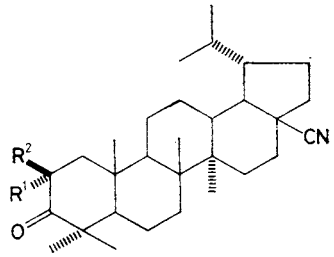
Within the framework of our investigation on conformation of ring A in triterpenoid and 4,4-dimethylsteroid compounds we have shown previously[1-3] that 3-oxo derivatives of pentacyclic triterpenoids with 4α,4β,8β and 10β-methyl groups (e.g. *I*, *IV*, *XVI* etc.) exist as an equilibrium mixture of chair and boat conformations of the ring A. The same conclusion was obtained by Tsuda and coworkers[4,5] on the basis of CD spectra. The most convincing evidence for this conformational equilibrium has come from IR spectra of 2α- and 2β-deutero derivatives of allobetulone (*I*) in the carbon–deuterium stretching vibration region[1]. The population of the boat form has been estimated to be about 40 ± 10% from ^{1}H NMR spectra (vicinal coupling constants of protons in positions 1 and 2; see ref.[2]), dipole moments[3], CD spectra[3] and simulation of conformational equilibrium by isomerization of 2α- and 2β-substituted 3-ketones[3]. On the other hand, the vicinal coupling constants of protons in positions 2 and 3 in the 1-ketone *VII* (ref.[2]), as well as isomerisation of its 2α- and 2β-substituted derivatives[6] led to the conclusion that in 1-oxo derivatives the ring A exists predominantly in the chair form. The mentioned results are based on

* Part XCI in the series Triterpenes; Part XC: Collect. Czech. Chem. Commun. *54*, 1036 (1989).

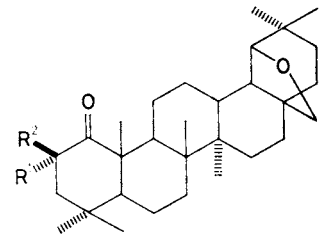
using 2α-methyl ketones *II*, *V* and *VIII* as models for the chair form and 2β-methyl ketones *III*, *VI* and *IX* for the boat form.



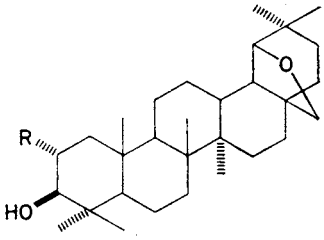
I, $R^1 = R^2 = H$
II, $R^1 = CH_3$; $R^2 = H$
III, $R^1 = H$; $R^2 = CH_3$



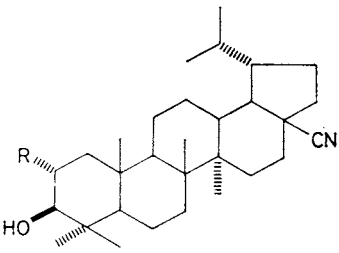
IV, $R^1 = R^2 = H$
V, $R^1 = CH_3$; $R^2 = H$
VI, $R^1 = H$; $R^2 = CH_3$



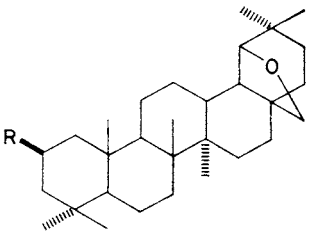
VII, $R^1 = R^2 = H$
VIII, $R^1 = CH_2$; $R^2 = H$
IX, $R^1 = H$; $R^2 = CH_3$



X, R = H
XI, $R = CH_3$



XII, R = H
XIII, $R = CH_3$



XIV, R = H
XV, $R = CH_3$

Since ^{13}C NMR spectra are very sensitive to conformational effects[7], it was of interest to study how the conformation of ring A is reflected in the chemical shifts of carbon atoms and whether these shifts could be used for estimation of conformer

population in chair–boat equilibria. Our present communication concerns the results obtained from the ^{13}C NMR spectra of ketones *I*–*IX* and *XVI*, derived from 19β,28-epoxy-18α-oleanane (*XIV*), 28-lupanenitrile and lupane (*XVII*). For comparison and easier assignment of carbon signals we also measured ^{13}C NMR spectra of several other compounds (*X*–*XV*) and determined the spin–lattice relaxation times T_1 for most compounds.

EXPERIMENTAL

The preparation of all studied compounds was already described: *I* and *X* in ref.[8], *II*, *III*, *XI* and *XV* in ref.[9], *IV*–*VI*, *XII* and *XIII* in ref.[10], *VII* in ref.[11], *VIII* and *IX* in ref.[6], *XIV* in ref.[12] and *XVI* in ref.[13].

The ^{13}C NMR spectra were measured on a Varian XL-200 FT NMR spectrometer at 50·3 MHz in $CDCl_3$ solutions (about 50 mg of compound in 0·4 ml of $CDCl_3$) with tetramethylsilane as internal standard. Chemical shifts were determined from proton noise-decoupled spectra (typical experimental conditions: spectral width 12 kHz, acquisition time 1·333 s, data points 32 k, pulse width 5 μs (flip angle 50°), repetition time 2 s, c. 200 transients, exponential multiplication of FID's with line broadening factor 1 Hz). For signal assignment the attached proton test spectra (APT)[14] were measured under similar conditions (*J*-modulation delay time 7 ms). ^{13}C relaxation times T_1 were measured at 23°C using the inversion recovery technique (pulse sequence $(180° - t - 90° - A_t - T)_n$; exp. conditions: spectral width 4·4 kHz, acquisition time A_t 0·92 s, zero filling to 8 k data points, variable relaxation delay time t — seven values between 0·05 s and 40 s, equilibrium delay time T — 40 s, 32 transients for each t value, processing with line broadening factor 1 Hz); the automatic numerical evaluation was done using the AUTOT1 program (standard part of Varian XL-200 software version H1Z). For the measurements of T_1's we used the same solutions as for the above-mentioned NMR experiments; prior to the measurements oxygen was removed from the solution by passage of nitrogen for 2 minutes.

RESULTS AND DISCUSSION

The chemical shifts and relaxation times T_1 of carbon atoms in compounds *I*–*XVI* are summarized in Table I. In assigning the signals we considered the conformation of ring A in the individual compounds, which was either known or followed from the rules for substituent effects on the ring A conformation[9,15]. The chair form in the unsubstituted derivative *XIV* and in the 3β-hydroxy derivatives *X*–*XIII* is obvious[4], in the 2α-methyl-3β-ols *XI* and *XIII* it has been confirmed by ^{1}H NMR spectra[9,10]. The evidence of the chair–boat equilibrium in 3-ketones *I*, *IV* and *XVI* and of predominating chair form in the 1-ketone *VII* has already been mentioned above. The presence of 2α-methyl ketones *II*, *V* and *VIII* in the chair and 2β-methyl ketones *III*, *VI* and *IX* in the boat form was derived from vicinal coupling constants of the ring A protons[2]. In the 2β-methyl derivative *XV* the boat form should highly predominate because in analogous 2β-hydroxy and 2β-acetoxy derivatives the ratio of the chair and the boat conformers is about 1 : 1 (ref.[15]) and because a 2β-methyl group destabilises the chair form much more than does a hydroxy or acetoxy group[9].

TABLE I

Carbon-13 chemical shifts (δ) and spin-lattice relaxation times T_1 (s; in parentheses)

Carbon	*I*	*II*	*III*	*IV*	*V*	*VI*	*VII*	*VIII*
C-1	39·78 (0·5)	49·89 (0·4)	51·10 (0·5)	39·57 (0·6)	49·52 (0·4)	50·90 (0·4)	217·35 (—[a])	218·63 (—[a])
C-2	34·05 (0·8)	36·48 (0·9)	35·79 (1·0)	34·09 (1·0)	36·44 (0·8)	35·77 (1·0)	35·39 (0·6)	35·81 (0·9)
C-3	218·04 (—[a])	218·00 (—[a])	220·77 (—[a])	217·74 (—[a])	217·95 (—[a])	220·62 (—[a])	42·96 (0·5)	54·27 (0·4)
C-4	47·26 (9·3)	48·11 (7·7)	46·39 (9·4)	47·30 (6·8)	48·11 (7·9)	46·42 (7·1)	33·26 (1·2)[b]	33·97 (5·5)
C-5	54·92 (1·0)	57·37 (0·9)	52·46 (0·8)	54·92 (0·8)	57·22 (0·7)	52·31 (0·5)	57·68 (1·1)	59·56 (1·0)
C-6	19·59 (0·8)	19·26 (0·4)	20·06 (0·3)	19·59 (0·5)	19·30 (0·3)	20·06 (0·4)	19·14 (0·5)	19·18 (0·7)
C-7	33·13 (0·6)	33·65 (0·4)	32·59 (0·4)	33·76 (0·5)	34·24 (0·4)	33·19 (0·4)	33·33 (1·2)[b]	33·33 (0·4)
C-8	40·49 (6·5)	40·63 (5·9)	40·49 (6·5)	40·56 (5·9)	40·66 (5·4)	40·59 (5·4)	40·62 (10·2)	40·54 (9·7)
C-9	50·36 (1·0)	50·57 (0·7)	50·49 (0·9)	49·47 (1·1)	49·66 (0·5)	49·62 (1·7)[b]	42·18 (1·1)	42·27 (1·1)
C-10	36·92 (7·9)	37·50 (7·2)	36·84 (5·2)	36·86 (6·9)	37·42 (4·6)	36·73 (5·2)	52·58 (11·4)	53·22 (9·3)
C-11	21·48 (0·4)	21·19 (0·4)	22·01 (0·4)	21·19 (0·4)	20·88 (0·4)	21·78 (0·4)	23·94 (0·7)	24·03 (0·4)
C-12	26·39 (0·4)[b]	26·32 (0·4)[b]	26·52 (0·4)	26·35 (0·4)	26·26 (0·4)	26·53 (0·5)	26·21 (0·5)[c]	26·17 (0·5)[c]
C-13	34·22 (1·2)	34·10 (0·8)	34·44 (0·5)	41·21 (0·8)	41·10 (1·0)	41·44 (1·0)	34·57 (0·9)	34·62 (1·1)
C-14	40·72 (8·1)	40·77 (8·4)	40·69 (5·7)	42·63 (8·6)	42·66 (7·1)	42·59 (5·8)	41·11 (8·4)	41·17 (7·5)
C-15	26·39 (0·4)[b]	26·37 (0·4)[b]	26·41 (0·5)	28·94 (0·4)	28·90 (0·3)	28·94 (0·4)	26·43 (0·5)[c]	26·45 (0·5)[c]
C-16	36·68 (0·6)	36·69 (0·4)	36·72 (1·1)	31·06 (0·5)	31·09 (0·4)	31·03 (0·3)	36·73 (0·6)	36·73 (0·5)
C-17	36·23 (6·3)	36·22 (5·2)	36·25 (5·4)	49·56 (3·5)	49·73 (6·2)	49·62 (1·7)[b]	36·25 (7·9)	36·24 (7·0)
C-18	46·73 (1·1)	46·76 (0·7)	46·74 (0·9)	48·77 (0·7)	48·79 (1·0)	48·75 (0·8)	46·68 (1·2)	46·69 (0·8)
C-19	87·84 (1·0)	87·85 (0·8)	87·84 (0·8)	45·13 (0·9)	45·16 (0·9)	45·11 (0·8)	87·88 (1·3)	87·89 (0·5)
C-20	41·43 (7·7)	41·40 (5·8)	41·44 (6·0)	29·29 (0·6)	29·29 (0·6)	29·30 (0·6)	41·44 (6·6)	41·45 (5·8)
C-21	32·65 (0·2)	32·66 (0·4)	32·68 (0·3)	22·21 (0·5)	22·20 (0·8)	22·21 (0·5)	32·72 (0·5)	32·72 (0·5)
C-22	26·19 (0·5)	26·21 (0·5)	26·20 (0·4)	36·26 (0·5)	36·26 (0·4)	36·27 (0·4)	26·28 (0·5)[c]	26·29 (0·3)[c]
C-23	26·71 (0·7)	25·19 (0·8)	29·41 (0·6)	26·58 (0·6)	25·20 (0·5)	29·39 (0·6)	31·90 (0·6)	32·12 (0·6)
C-24	20·96 (1·1)	21·78 (1·4)	19·51 (1·0)	21·06 (1·3)	21·81 (1·3)	19·50 (0·8)	22·66 (0·9)	22·35 (1·0)
C-25	16·31 (0·9)	16·45 (1·5)	15·50 (0·9)	15·90 (1·5)[c]	16·10 (1·9)[b]	15·44 (1·2)[b,c]	15·67 (2·9)[d]	16·02 (3·0)[d]
C-26	15·48 (4·1)	15·82 (2·5)	15·06 (1·4)	15·82 (1·6)[c]	16·10 (1·9)[b]	15·37 (1·2)[b,c]	16·44 (2·8)[d]	16·48 (3·0)[d]
C-27	13·42 (4·5)	13·40 (2·5)	13·43 (1·9)	14·67 (2·8)	14·66 (3·1)	14·68 (2·4)	13·43 (2·3)	13·45 (2·0)
C-28	71·20 (0·4)	71·20 (0·4)	71·22 (0·1)	123·62 (—[a])	123·62 (—[a])	123·61 (—[a])	71·29 (0·6)	71·28 (0·3)
C-29	24·52 (0·5)	24·51 (0·8)	24·54 (0·5)	15·00 (1·4)	14·99 (1·7)	15·01 (1·4)	24·52 (1·0)	24·52 (0·6)
C-30	28·78 (0·6)	28·78 (0·5)	28·79 (0·4)	22·68 (0·8)	22·68 (0·8)	22·67 (0·9)	28·80 (0·7)	28·79 (0·5)
C-31[f]	—	15·64 (1·3)	18·83 (0·4)	—	15·59 (1·1)	18·59 (0·4)	—	15·07 (1·2)[d]

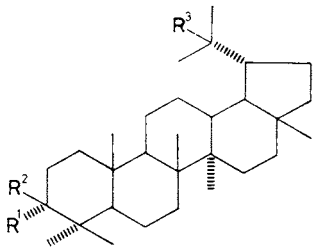
TABLE I (*Continued*)

Carbon	*IX*	*X*[a]	*XI*[a]	*XII*[a]	*XIII*[a]	*XIV*	*XV*	*XVI*
C-1	218·87 (—[a])	38·92	48·59	38·74	48·43	40·47 (0·6)	45·06 (0·4)	39·57 (0·7)
C-2	38·64 (1·2)	27·40	30·62	27·38	30·52	18·70 (0·7)	26·05 (0·5)	34·13 (1·0)
C-3	44·22 (0·5)	78·91	84·75	78·94	84·69	42·10 (0·5)	49·93 (1·0)[b]	218·01 (—[a])
C-4	31·91 (7·6)	38·87	39·04	38·86	39·00	33·29 (3·0)[b]	32·42 (6·2)	47·31 (10·7)
C-5	50·81 (1·0)	55·48	55·84	55·30	55·62	56·59 (1·2)	51·64 (1·4)[c]	54·88 (1·0)
C-6	19·24 (0·7)	18·25	18·47	18·28	18·47	18·57 (0·6)	19·78 (0·5)	19·68 (0·7)
C-7	33·40 (0·4)	33·90	33·89	34·47	34·45	33·87 (0·9)	33·16 (0·4)	33·65 (0·8)
C-8	41·39 (8·6)	40·60[c]	40·62[c]	40·63	40·62	40·80 (10·3)[c]	40·86 (9·4)[d]	40·80 (8·9)
C-9	43·28 (0·6)	51·07	51·02	50·14	50·07	51·15 (1·1)	49·98 (1·0)[b,c]	49·43 (1·1)
C-10	49·73 (8·1)	37·24	37·50	37·17	37·37	37·55 (9·9)	38·01 (5·6)	36·83 (6·1)
C-11	22·96 (0·4)	20·98	20·99	20·68	20·66	20·86 (0·7)	21·78 (0·7)	21·46 (0·6)
C-12	26·12 (0·3)[c]	26·44	26·41[d]	26·38	26·37	26·53 (0·6)	26·74 (0·4)	26·81 (0·6)
C-13	34·20 (0·9)	34·14	34·14	41·15	41·13	34·10 (1·0)	34·46 (1·3)	37·91 (1·5)
C-14	41·09 (9·9)	40·70[c]	40·72[c]	42·59	42·58	40·73 (9·1)[c]	40·73 (7·9)[d]	43·08 (8·0)[b,c]
C-15	26·41 (0·5)[c]	26·44	26·44[d]	28·97	28·92	26·38 (0·6)	26·44 (0·5)	27·31 (0·5)
C-16	36·71 (0·5)	36·74	36·74	31·14	31·12	36·77 (0·6)	36·77 (0·6)	35·46 (0·7)
C-17	36·23 (5·1)	36·25	36·25	49·59	49·55	36·25 (6·2)	36·25 (5·7)	43·13 (8·0)[b,c]
C-18	46·65 (0·9)	46·82	46·82	48·86	48·82	46·85 (1·3)	46·79 (1·2)	47·55 (1·1)
C-19	87·81 (1·1)	87·90	87·91	45·16	45·15	87·92 (1·3)	87·88 (1·2)	44·65 (1·1)
C-20	41·49 (9·2)	41·46	41·46	29·30	29·28	41·49 (6·9)	41·48 (5·3)	29·38 (0·9)
C-21	32·72 (0·5)	32·70	32·71	22·22	22·19	32·73 (0·6)	32·73 (0·6)	21·92 (0·7)
C-22	26·28 (0·5)[c]	26·26	26·26	36·32	36·28	26·30 (0·5)	26·28 (0·5)	40·37 (0·6)
C-23	31·13 (0·4)	27·98	28·36	28·01	28·38	33·36 (3·0)[b]	31·02 (0·4)	26·65 (0·6)
C-24	25·92 (0·5)	15·38	16·17	15·38	16·18	21·55 (1·1)	22·19 (1·0)	21·07 (1·4)
C-25	15·87 (1·3)[b,d]	16·48	17·28	16·10[c]	16·88	16·44 (1·4)	24·78 (1·1)[e]	15·90 (1·8)[d]
C-26	16·61 (3·4)[d]	15·70	15·71	15·99[c]	15·97	15·76 (4·0)	15·36 (2·8)	15·81 (2·9)[d]
C-27	13·25 (2·8)	13·50	13·50	14·75	14·73	13·51 (3·3)	13·45 (3·3)	14·36 (3·9)
C-28	71·27 (0·4)	71·24	71·25	123·73	123·68	71·27 (0·5)	71·28 (0·4)	18·07 (1·8)
C-29	24·50 (0·6)	24·54	24·54	15·01	14·99	24·55 (0·9)	24·55 (0·9)	15·15 (1·7)
C-20	28·77 (0·5)	28·80	28·80	22·70	22·68	28·81 (0·6)	28·81 (0·6)	22·99 (0·7)
C-31[f]	15·87 (1·3)[b,d]	—	19·41	—	19·41	—	23·25 (0·6)[e]	—

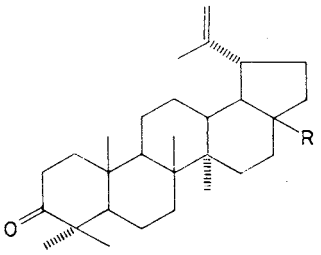
[a] Relaxation times not measured; [b] uncertain values of T_1 due to the total or partial overlap of the signals; [c,d,e] signals with the same symbol may be interchanged; [f] carbon atom of C-2 methyl group.

Structural Assignment of ^{13}C Chemical Shifts

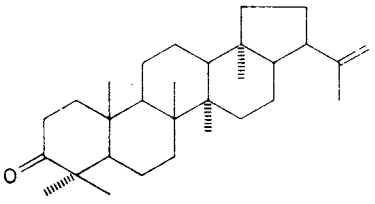
The first step toward complete assignment of the ^{13}C NMR signals was their classification according to the number of directly bonded hydrogen atoms. For this we used the attached proton test spectra[14] as well as the relaxation times T_1. Although the potentialities of using relaxation times of carbon atoms (T_1) for assignment and investigation of dynamic processes are well known, in the region of triterpenes they have been utilized only scarcely[16]. The experimental error of T_1 values given in Table I varies (for most of the proton-bearing carbon atoms the error is smaller than 10% whereas for some quaternary carbon atoms it is as high as 25%) and in some cases of carbons with very similar or identical chemical shifts it cannot be determined with certainty; however, the obtained values of T_1 afforded valuable supplementary information to the APT spectra. In all the measured compounds *I–IX*, *XIV–XVI* the quaternary carbon atoms have long relaxation times ($T_1 \geq 5$ s) enabling their safe distinction from the methylene carbon atoms (with T_1 0·3–0·8 s). The values of T_1 for methine carbon atoms are close to 1 s whereas those of methyl carbons vary considerably, depending on the position of the methyl on the triterpene skeleton (for a more detailed discussion vide infra).



XVI, $R^1 + R^2 = O$; $R^3 = H$
XVII, $R^1 = R^2 = R^3 = H$
XVIII, $R^1 = R^3 = H$; $R^2 = OH$
XIX, $R^1 + R^2 = O$; $R^3 = OH$



XX, R = CH_3
XXI, R = COOH



XXII

Our structural assignment of signals to the individual carbon atoms was based on the published data for a series of lupane derivatives[17-23], particularly for lupane[17,18] (*XVII*), 3β-lupanol[18,19] (*XVIII*), lupeol[18,20] and 20(29)-lupen-3-one[18,21-23] (*XX*). The carbon atoms in the rings D and E in derivatives of 19β,28-epoxy-18α-oleanane (*XIV*) were assigned on the basis of comparison with other compounds of this skeleton[24,25]; in 28-lupanenitrile derivatives we utilized the known effect of the cyano group[26].

In general, the signals were assigned so as to make self-consistent the differences between chemical shifts due to structural changes in the ring A on the one hand and in the ring E on the other. Three series of compounds were compared: 19β,28-epoxy--18-oleanane (*I–III*, *X*, *XI* and *XIV*), 28-lupanenitrile (*IV–VI*, *XII* and *XIII*) and lupane (*XVI–XVIII*) derivatives. In all the compared series the shifts induced by the same structural change agreed well. So, e.g. the shifts due to the 2α-methyl in two sets of 3β-hydroxy derivatives (*X*, *XI* and *XII*, *XIII*) for all carbon atoms differ less than 0·1 ppm; mean values of these shifts are given in Fig. 1. The 2α-methyl group affects only the carbon atoms of ring A and the C-6 and C-9 atoms whereas the effect on the more distant carbon atoms is negligibly small (order of magnitude of hundredths ppm, i.e. within the limits of experimental error). The carbon atoms of both axial methyl groups on the ring A (C-24 and C-25), which are placed symmetrically relative to C-2, exhibit the same downfield shift (+0·8 ppm). This value is comparable with the shift of the 10β-methyl, induced by 2α, 4α or 6α-equatorial methyl groups in 3β-hydroxy and 3-oxo steroids (0·9–1·1 ppm as follows from the data in refs[27-30]).

The assignment of C-25 and C-26 carbon atoms in the lupane compounds *IV*, *VI*, *XII* and *XVI* is difficult because their chemical shifts differ only very little (≦0·1 ppm). We prefer to ascribe the lowfield signal to carbon C-25: this leads to a better accord with analogous derivatives of the 19β,28-epoxy-18α-oleanane series (*I*, *III*, *X* and *XI*). Our chemical shifts for 3-lupanone (*XVI*) agree well with those reported by Ayer and coworkers[19], except for C-22 (δ 40·47 vs δ 39·6 in ref.[19]) and assignment of the C-2 and C-7 carbon atoms (our assignment is consistent with that for 20(29)-lupen-

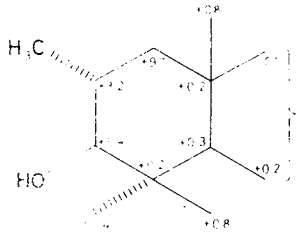


FIG. 1

Substituent effect of 2α-methyl group on ^{13}C chemical shifts in 3β-hydroxy derivatives *XI* and *XIII* (for the other carbon atoms <0·1 ppm — not shown)

-3-one (*XX*) in refs[18,21-23]). In the case of 1-oxo derivatives *VII*–*IX* and the 2-methyl derivative *XV* we had in hand only one series of compounds for which we found no analogy in the literature. Therefore, the assignment is less dependable, particularly for the atoms C-25, C-26 and C-31 (the methyl carbon on C-2) which have similar chemical shifts.

The relaxation times T_1 of the methyl carbon atoms are also worth notice. The carbon atoms of geminal methyl groups (C-29 and C-30 in the 19β,29-epoxy-18α--oleanane derivatives and C-23 and C-24 in all the studied compounds) have shorter T_1 than other skeletal methyl groups. The same effect has also been observed[16] recently for the C-29 and C-30 atoms in friedelin (D:A-friedooleanan-3-one). Of the pair of C-23, C-24 methyl carbon atoms, the C-23 carbon has invariably shorter T_1 ($\sim 0{\cdot}5$ s) than the C-24 one (~ 1 s). The longest times T_1 were observed for methyl carbon atoms in the middle of the skeleton (C-26 and C-27). In all the lupane derivatives studied, one of the methyl carbon atoms in the isopropyl group (C-30 at $\delta \sim 23$) has shorter T_1 than the other one (C-29 at $\delta \sim 15$). Interestingly, the 2-methyl carbon atom (C-31) in 2β-methyl-3-ketones *III* and *VI* shows markedly shorter T_1 (0·4 s) than in the 2α-isomers *II* and *V* ($\sim 1{\cdot}2$ s). This may indicate that the internal rotation of the equatorial methyl group on C-2 is faster in the chair (2α-isomer) than in the boat (2β-isomer).

^{13}C *Chemical Shifts and Conformation of Ring* A

Comparison of data in Table I for 2β-methyl-3-ketones *III* and *VI* (boat form of ring A) and for 2α-methyl-3-ketones *II* and *V* (chair form) shows that the conformation of ring A affects considerably chemical shifts of some carbon atoms. Not considering the atoms C-1, C-2 and C-3, where the large substituent effect of the 2-methyl group (α- and β-effects; see Fig. 1) may overbalance the effects due to conformation change of ring A, we observed significant differences for skeletal carbon atoms C-4, C-5, C-6, C-7, C-11 and methyl carbon atoms C-23, C-24 and C-26. The most pronounced is the upfield shift of C-5 (−4·9 ppm) and the downfield shift of C-23 (+4·2 ppm) in the boat form (*III*, *VI*) compared with the chair form (*II*, *V*). The differences, observed with more distant atoms, may reflect small changes in geometry of the ring B found when comparing crystal structures[31] of various 3-ketones with chair or boat form of the ring A.

In the unsubstituted 3-ketones *I* and *IV* the population of the boat form could be calculated from the ^{13}C chemical shifts (which represent time-averaged shifts of both conformers) using the relationship (*1*)

$$\%\,(\text{boat}) = 100(\delta - \delta(\text{c}))/(\delta(\text{b}) - \delta(\text{c}))\,, \qquad (1)$$

where δ is the observed shift of the given carbon atom in the ketone *I* or *IV* and δ(c) and δ(b) are the respective shifts of the same atom in the chair and boat form of these

ketones. The values of δ(c) and δ(b) can be approximated by the shifts found for the model compounds, i.e. in the chair 2α-methyl ketones *II* and *V* and the boat 2β-methyl ketones *III* and *VI*, under the assumption that the methyl group on C-2 influences neither the shift of the given carbon atom nor the geometry of the corresponding conformer (for a detailed discussion of assumptions and possible errors in using these models see refs[2,3]). Whereas the effect of the 2α-methyl on the individual carbon atoms in the chair form may be taken from the 3β-hydroxy derivatives *X*–*XIII*, no suitable compounds are available for estimation of the effect of the 2β-methyl in the boat form. Therefore, we limited our selection of carbon atoms, suitable for determination of boat population in ketones *I* and *IV*, to atoms for which the chemical shifts in 2α- and 2β-methyl ketones differ sufficiently and are little affected by the substituent effect of the 2α-methyl group (Fig. 1). The results are summarized in Table II.

The calculated populations of the boat forms differ somewhat according to the carbon atom used, depending apparently on how for a given atom the above-discussed conditions are satisfied. Since these systematic errors for individual carbon atoms are not known, no atom can be preferred. All the obtained boat populations in ketones *I* and *IV* range from 32% to 50%; within similar limits are also values obtained by other physical methods such as vicinal coupling constants *J*(H, H) in ^{1}H NMR spectra[2] (30–40%), dipole moments[3] (39–45%) or CD spectra[3] (27–32%).

As seen from Table II, the largest differences between both conformers occur in the chemical shifts of atoms C-4, C-5, C-23 and C-24 and therefore these shifts

TABLE II

^{13}C Chemical shift differences ($\Delta\delta$) between 2β- (*III*, *VI*) and 2α-methyl-3-oxo derivatives (*II* and *V*), respectively, and estimated populations of boat form (% boat) in 3-oxo derivatives *I* and *IV*

Parameter	C-4	C-5	C-6	C-7	C-11	C-23	C-24	C-26
				ketone *I*				
$\Delta\delta^a$	−1·72	−4·91	0·80	−1·06	0·82	4·22	−2·27	−0·76
% boat	49	50	41	49	35	36	36	45
				ketone *IV*				
$\Delta\delta^b$	−1·69	−4·91	0·76	−1·05	0·90	4·19	−2·31	−0·73
% boat	48	47	38	46	34	33	32	38

[a] $\Delta\delta = \delta(III) - \delta(II)$; [b] $\Delta\delta = \delta(VI) - \delta(V)$.

may also be useful in conformational studies of other 3-oxotriterpenoids which are structurally different from ketones *I* and *IV* in positions sufficiently remote from the ring A. Thus, for example, the values of ^{13}C-shifts of the mentioned atoms, published for 20-hydroxy-3-lupanone[22] (*XIX*), 20(29)-lupen-3-one[18,21-23] (*XX*), betulonic acid[21] (*XXI*) and moretenone[23] (*XXII*) agree well (±0·1 ppm) with those found for ketones *I*, *IV* and *XVI* (Table I). This accord indicates that in all the mentioned ketones the population of the boat form in the chair–boat equilibrium is approximately the same.

Also in the series of 1-oxo derivatives the carbon atoms of rings A and B in the 2β-methyl ketone *IX* (boat) have different chemical shifts than in the 2α-methyl ketone *VIII* (chair). The most marked difference appears for C-5 which exhibits an upfield shift (−8·76 ppm) in *IX* compared with *VIII*, similarly to the 2-methyl-3-oxo derivatives. The shifts of most carbon atoms in the unsubstituted 1-ketone *VII* resemble the values for the 2α-methyl ketone *VIII* rather than for the 2β-isomer *IX*, in accord with the fact that in ketone *VII* the chair form highly predominates[2,6]. The boat form content in the ketone *VII* was determined in the similar manner as in the 3-oxo derivatives (using the relationship (*1*) and 2-methyl ketones *VIII* and *IX* as models) and the results are summarized in Table III. Most of the values range from 8% to 22% of boat, in agreement with the value of 9%, derived[6] from isomerization of 1-oxo derivatives substituted in position 2 with bromine or a methyl group. The only value (31%) outside the given limits was obtained using the parameters for C-4; in this case probably the effect of the 2-methyl group on the chemical shift of C-4 is not negligible in one conformer or another.

A comparison of spectra of the 2-methyl derivative *XV* and the unsubstituted compound *XIV* shows that the differences in chemical shifts of atoms C-4 to C-7, C-11 to C-13 and C-15 are similar to those found between the 2β-methyl-3-ketones (boat) and their 2α-isomers (chair). Again the high upfield shift of C-5 in the 2-methyl derivative *XV* compared with that in *XIV* is significant. It is thus very probable that

TABLE III

^{13}C Chemical shift differences (Δδ) between 2β- and 2α-methyl ketones *IX* and *VIII*, respectively, and estimated populations of boat form (% boat) in 1-oxo derivative *VII*

Parameter	C-4	C-5	C-8	C-10	C-11	C-23	C-24
Δδ[a]	−2·06	−8·76	0·85	−3·49	−1·07	−0·99	3·57
% boat	31	21	9	18	8	22	9

[a] $\Delta\delta = \delta(IX) - \delta(VIII)$.

in *XV* the ring A exists preferably in the boat form. Surprisingly, however, the C-25 signal in compound *XV* is shifted considerably downfield (δ 24·78) which has no analogy in other compounds compared.

We may conclude, that the ^{13}C NMR shifts can be utilized for estimating the chair–boat population in the ring A of triterpenoid ketones and give results comparable with those obtained by other physical methods.

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Translated by M. Tichý.