# INFRARED SPECTRA OF 2α-SUBSTITUTED 3-OXOTRITERPENOIDS AND CONFORMATION OF RING A*

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*Dedicated to the memory of Professor František Šorm.*

Infrared spectra of triterpenoid 19β,28-epoxy-18α-oleanane 3-ketones *I—VI* in the region of carbonyl stretching frequencies have been studied. Comparison of the spectra of crystals with those of solutions in various solvents, together with comparison of fundamental C=O frequencies with their first overtone leads to the conclusion that the doublet character of the carbonyl band in the solution of ketones *I—IV* with polar substituent in position 2α is caused by the chair-boat equilibrium of the ring A.

In connection with studies on conformation of the ring A in triterpenoid 3-ketones we observed[1] that the infrared spectrum (in carbon disulfide) of 2α-bromo-19β,28--epoxy-18α-oleanan-3-one (*I*) exhibited two bands in the carbonyl region. The strong higher-frequency band has been ascribed to the chair conformation *C* with an equatorial bromine atom whereas the weak low-frequency band to the boat form *B* in which the bromine atom has axial character. However, Lehn and Ourisson[2], who measured ¹H NMR spectra of bromo ketone *I* in solvents of various polarity, did not find any differences between the values of vicinal coupling constants that would confirm the conformational equilibrium $C \rightleftharpoons B$. According to the cited authors, the doublet in the carbonyl region is due to the Fermi resonance. Such splitting of a carbonyl band due to Fermi resonance had been observed with some simple alicyclic α-halo ketones; responsible for it is probably the first overtone of the deformation vibration of hydrogen atoms in the neighbourhood of the carbonyl group (ref.[3] and references therein).

A weak low-frequency band was observed in the spectra of bromo ketone *I* in other solvents[4] as well; it was also found in the spectra of the analogous 2α-bromo--20β,28-epoxy-18α,19βH-ursan-3-one[4] and the chloro, methoxy and ethoxy ketones *II*, *III* and *IV*, respectively[5], and it seems thus to be characteristic of 3-oxotriter-

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penoids with a polar substituent in position 2α. In the present communication we describe the results of our more detailed study of infrared spectra of 2α-substituted ketones $I-IV$ in various solvents and in the crystalline state. In addition to the
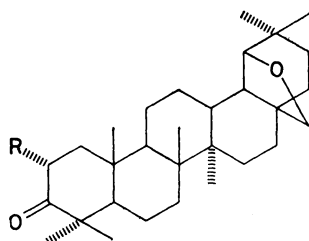


| $I$, R = Br | $IV$, R = OC$_2$H$_5$ |
| $II$, R = Cl | $V$, R = CH$_3$ |
| $III$, R = OCH$_3$ | $VI$, R = H |

$ν(C{=}O)$ fundamental vibration region, we measured in some cases also the first overtone region. For comparison, also spectra of the unsubstituted ketone $VI$ and its 2α-methyl derivative $V$ have been studied.

## EXPERIMENTAL

Ketones $I- VI$ were prepared by the already described[4−6] procedures. IR spectra were measured on a PE 684 (Perkin-Elmer) spectrometer with a Data Station Model 3500. To achieve a better signal-to-noise ratio, 10—60 spectra were accumulated. Measurements in solutions ($c$ 0·01 to 0·1 mol l$^{-1}$) were carried out in 1—2 cm infrasil cells for the region 3 300—3 600 cm$^{-1}$ and in 0·1—1 mm sodium chloride cells for the 1 600—1 800 cm$^{-1}$ region. Crystalline material was measured in Nujol mull (capillary film). The wavenumber scale of the spectrometer was calibrated by ammonia and water vapour; accuracy ±0·1 cm$^{-1}$. Slit width 2·5—3·5 cm$^{-1}$.

Mathematical separation of overlapping bands was carried out using a described program[7]; Cauchy (Lorentz) profile function was used for description of the bands and the background was approximated by a straight line. In the region 3 300—3 600 cm$^{-1}$, the parabolic background, caused by the very strong $ν(C-H)$ bands between 2 900—3 000 cm$^{-1}$, was subtracted. The accuracy of the wavenumbers of most band maxima after the separation was better than 0·5 cm$^{-1}$; in cases of strongly overlapping bands (bromo ketone $I$ in chloroform, dichloromethane and nitromethane) the error for weaker bands was higher than 1 cm$^{-1}$.

## RESULTS AND DISCUSSION

In all the solvents used, ketones $I-IV$ with polar 2α-substituent exhibit two bands in the C=O stretching vibrations region. The parameters of both bands, obtained by mathematical separation, are given in Table I: the strong higher-frequency band is denoted as the first band whereas the weak lower-frequency one as the second band. The intensities are given in per cents of the integrated absorption intensity

of the second band related to the sum of intensities of both bands $(k = 100 \cdot A_2/$ $/(A_1 + A_2))$ and in the same manner are defined the relative molar absorption coefficients of the second band $(k_\varepsilon = 100\varepsilon_2/(\varepsilon_1 + \varepsilon_2))$. Both bands are well resolved in nonpolar solvents (cyclohexane, tetrachloromethane or carbon disulfide). In more polar solvents (chloroform, dichloromethane, nitromethane) the bands of the bromo ketone *I* are resolved only partially, whereas in the spectra of the chloro ketone *II* and alkoxy ketones *III* and *IV* they are unresolved. In the latter cases the band

TABLE I

Parameters of carbonyl bands in spectra of ketones *I—IV*

| Ketone | R | Medium | 1st band | | 2nd band | | $k_\varepsilon{}^a$ | $k_A{}^a$ |
|---|---|---|---|---|---|---|---|---|
| | | | $\nu$ cm$^{-1}$ | $\Delta\nu_{1/2}$ cm$^{-1}$ | $\nu$ cm$^{-1}$ | $\Delta\nu_{1/2}$ cm$^{-1}$ | | |
| *I* | Br | $C_6H_{12}$ | 1 729·4 | 9 | 1 710·3 | 9 | 19 | 20 |
| | | $CCl_4$ | 1 726·0 | 11 | 1 706·7 | 11 | 16 | 16 |
| | | $CCl_4{}^b$ | 3 433·6 | 31 | 3 396·1 | 24 | 20 | 16 |
| | | $CS_2$ | 1 724·4 | 9 | 1 705·2 | 10 | 16 | 17 |
| | | $CHCl_3$ | 1 720·5 | 14 | $\sim$1 705 | $\sim$25 | 12 | 20 |
| | | $CH_2Cl_2$ | 1 720·3 | 12 | $\sim$1 705 | $\sim$19 | 9 | 14 |
| | | $CH_3NO_2$ | 1 719·9 | 11 | $\sim$1 705 | $\sim$27 | 10 | 21 |
| | | Nujol | 1 717·9 | 7 | — | — | — | — |
| *II* | Cl | $C_6H_{12}$ | 1 733·1 | 7 | 1 716·1 | 8 | 9 | 10 |
| | | $CCl_4$ | 1 729·7 | 10 | 1 712·8 | 9 | 8 | 8 |
| | | $CCl_4{}^b$ | 3 439·9 | 26 | 3 407·4 | 20 | 9 | 7 |
| | | $CS_2$ | 1 727·7 | 9 | 1 711·0 | 10 | 8 | 10 |
| | | Nujol | 1 722·8 | 8 | — | — | — | — |
| *III* | $OCH_3$ | $C_6H_{12}$ | 1 723·2 | 9 | 1 711·3 | 9 | 20 | 21 |
| | | $CCl_4$ | 1 720·2 | 10 | 1 707·8 | 10 | 19 | 19 |
| | | $CCl_4{}^b$ | 3 422·7 | 24 | 3 399·0 | 29 | 22 | 25 |
| | | $CS_2$ | 1 719·1 | 9 | 1 707·3 | 9 | 17 | 18 |
| | | Nujol$^c$ | 1 722·0 | 7 | — | — | — | — |
| *IV* | $OC_2H_5$ | $C_6H_{12}$ | 1 723·4 | 9 | 1 710·7 | 12 | 20 | 24 |
| | | $CCl_4$ | 1 720·8 | 12 | 1 707·0 | 10 | 17 | 14 |
| | | $CCl_4{}^b$ | 3 421·6 | 27 | 3 396·8 | 23 | 20 | 18 |
| | | $CS_2$ | 1 719·1 | 11 | 1 706·4 | 10 | 17 | 16 |
| | | Nujol | 1 715·7 | 8 | — | — | — | — |

$^a$ $k_\varepsilon = 100\varepsilon_2/(\varepsilon_1 + \varepsilon_2)$, $k_A = 100A_2/(A_1 + A_2)$, $A = \pi/2 \cdot \Delta\nu_{1/2} \cdot \varepsilon$; $^b$ first overtone; $^c$ measurement performed with a sample crystallized from heptane; ketone *III*, crystallized from chloroform–methanol, exhibited two bands at 1 722 and 1 714 cm$^{-1}$ with intensity ratio of about 1 : 1.

separation was not possible and these results are not included in Table I. Measurements in other more polar solvents were prevented by low solubility of the ketones and high absorption of the solvents. For the same reasons the first overtone region was measured only in tetrachloromethane.

The spectra of the unsubstituted ketone *VI* and the ketone with a nonpolar group in position 2α (methyl ketone *V*) exhibit only one band, the parameters of which are given in Table II. In some solvents this band is not symmetrical and its shape does not correspond entirely to the Cauchy function. This asymmetry is characterized by the ratio of the low-frequency part of the halfwidth ($\alpha$) to the high-frequency one ($\beta$).

As seen from Table I, the frequency of both bands in the spectra of ketones $I-IV$ changes within wide margin, depending on the character of the 2α-substituent R and on the solvent used: for the first band the values range from $1\,719\,\text{cm}^{-1}$ to $1\,733\,\text{cm}^{-1}$ whereas for the second from $1\,705$ to $1\,716\,\text{cm}^{-1}$; however, the shape of the spectra is very similar in all cases and the relative intensities of the bands differ only little. The frequencies of both the first and the second bands exhibit similar dependence on solvent as those of the 2α-methyl ketone *V* and unsubstituted ketone *VI* (Table II): they decrease with increasing solvent polarity. Moreover, in the first overtone region all the ketones $I-IV$ exhibit again two bands at frequencies roughly 1·99 times higher than the fundamental ones; also the intensity ratios are comparable with those in the fundamental series. On the basis of these data we can practically exclude the assumption that the carbonyl band splitting is due to Fermi resonance.

The spectra of the crystalline ketones $I-IV$ exhibit only one $\nu(\text{C=O})$ band corresponding to the chair conformation $C$ with equatorial substituent R, confirming

TABLE II
Parameters of carbonyl bands in spectra of ketones *V* and *VI*

| Solvent | Ketone *V* | | | Ketone *VI* | | |
|---|---|---|---|---|---|---|
| | $\nu$ cm$^{-1}$ | $\Delta\nu_{1/2}$ cm$^{-1}$ | $\alpha/\beta^a$ | $\nu$ cm$^{-1}$ | $\Delta\nu_{1/2}$ cm$^{-1}$ | $\alpha/\beta^a$ |
| $C_6H_{12}$ | 1 709·7 | 8 | 1·1 | 1 712·4 | 10 | 0·9 |
| $CCl_4$ | 1 705·4 | 10 | 1·1 | 1 708·0 | 13 | 1·0 |
| $CS_2$ | 1 704·0 | 9 | 1·0 | 1 706·7 | 12 | 1·0 |
| $CHCl_3$ | 1 698·7 | 18 | 1·4 | 1 698·9 | 20 | 1·1 |
| $CH_2Cl_2$ | 1 698·4 | 13 | 1·0 | 1 700·5 | 16 | 1·1 |

$^a$ Ratio of the low-frequency part of the halfwidth ($\alpha$) to the high-frequency one ($\beta$).

thus that in the crystalline state the ketones are conformationally homogeneous whereas in solution the A-ring exists as an equilibrium mixture of conformers C and B. In accord with this conclusion is a strong band of the C—O—C vibration at 1 126 cm$^{-1}$ in the spectrum of crystalline methoxy ketone III which can be assigned[5,8] to an equatorial methoxyl (conformation C). In tetrachloromethane solution the intensity of this band decreases and a weak band at 1 087 cm$^{-1}$ appears that is characteristic of an axial methoxyl[8] (conformation B). The frequency of the first carbonyl band of ketones I—IV decreases in all solvents used in the order chloroketone II, bromoketone I, alkoxy ketones III and IV, the frequency of the second band is practically the same for the bromo ketone I and alkoxy ketones III and IV whereas it is considerably higher for the chloro ketone II. These relations agree with the known effect of equatorial (first band) and axial (second band) chlorine, bromine and alkoxyl on the C=O stretching vibration in six-membered cyclic ketones[8-10] and support the assignment of the bands to conformers C and B.



$$C \qquad\qquad B$$
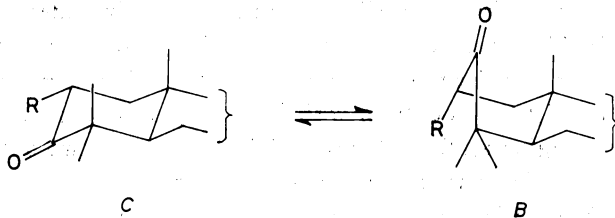
The population of the boat conformation B in the equilibrium between both forms should decrease with increasing solvent polarity which should be manifested by decrease of the $k_\varepsilon$ and $k_A$ values. Considering only the fundamental frequencies, we see from Table I that these values indeed follow the mentioned trend but the differences between the individual solvents are relatively small. The $k_A$ values for the bromo ketone I represent an exception: in polar solvents, particularly in chloroform and nitromethane, they are too high even when compared with the values of $k_\varepsilon$. This is obviously due to imperfect separation of the strongly overlapping bands; the shape of the first bands probably does not correspond to the Cauchy function, the bands are unsymmetric, similarly as found for the ketone V in chloroform (Table II); separation in this case leads to abnormally high halfwidths of the second bands and high values of $k_A$. It is worth notice that the values of $k_\varepsilon$ and $k_A$ may not correctly describe the population of the boat form B because the intrinsic intensity $(\varepsilon, A)$ of conformers C and B with equatorial and axial group R, respectively, may not be the same. It is known[9,10] that the integrated absorption intensity for the equatorial bromo ketones is about 25% lower than that for the axial ones. If we consider this relation and assume that the same relation holds also for molar absorption coefficients, we may estimate from the values of $k_\varepsilon$ and $k_A$ the population of the boat conformation B in the bromo ketone I: in the mentioned solvents it

ranges between 7% and 16%. Assuming that the same intensity relations hold also for the chloro and alkoxy ketones, we estimated the population of the boat in chloro ketone *II* to be 6−8%, in methoxy ketone *III* 14−18% and in ethoxy ketone *IV* 11−19%. Such a low content of the boat conformation can hardly be determined by other physical methods. Also the changes in coupling constants $^3J(H, H)$ with solvent polarity (see ref.[2]) would obviously not exceed the measurement error.

The content of the boat form *B* in the bromo ketone *I* is higher than in the chloro ketone *II*; this conclusion is in accord with the observation[11,12] that in cyclic α-halogeno ketones the conformation with axial halogen is more preferred in bromo ketones than in chloro ketones. In alkoxy ketones we can (according to ref.[12]) expect a lower content of the axial conformer than in the chloro and bromo ketones. However, the population of the boat in the alkoxy ketones *III* and *IV* is relatively high. In this case, probably, another effect is operating − a non-bonding interaction between the 2α-substituent R and the 4α-methyl group in the form B. It is known[5] that in a chair conformation the 1,3-*syn*-axial interactions $OCH_3/CH_3$ and $OC_2H_5/$ $/CH_3$ are smaller than the interactions $Cl/CH_3$ and $Br/CH_3$. Although the flexibility of the boat makes the interaction between the substituent R and the 4α-methyl group in the form *B* lower than the 1,3-*syn*-axial interaction in the chair conformation, we may expect that the mentioned trend will be the same. Thus, the boat form *B* in the alkoxy ketones *III* and *IV* is less destabilized than in the halogeno ketones *I* and *II*.

The assignment of the second band to the boat conformation of ring A is in accord with the general rules stating that the boat form is less populated (i) in 1,2-disubstituted derivatives than in the analogous 2,3-isomers[13], and (ii) in the derivatives without the 4β- or 10β-methyl group[14]. This follows from comparison of the spectra of the bromo ketone *I*, the analogous 1-oxo derivative (2α-bromo-19β,28-epoxy-18α-oleanan-1-one[13]) and the bromo ketone without the 4β-methyl group (2α-bromo-19β,28-epoxy-24-nor-18α-oleanan-3-one[14]); in the spectra of the latter two bromo ketones (in tetrachloromethane) the second band was not found indicating that the content of a boat form is negligibly small.

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