[CONTRIBUTION FROM THE DIVISION OF PURE CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL OF CANADA AND THE SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH][1]

Some Speculations Concerning the Low Frequency Vibrations in the Infrared Spectra of C_{19}-Ketosteroids

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In the infrared absorption spectra of ketosteroids several bands occur below 1350 cm.$^{-1}$ that are characteristic of the position and molecular environment of the ketone group. It is postulated that these bands arise from two kinds of vibrations: (a) skeletal modes associated primarily with the system –C–C–CO–C–C– and (b) C–H deformation modes associated with the α-methylene groups. These types of vibrations can be distinguished by the fact that the former are comparatively insensitive to the replacement of hydrogen by deuterium in the α-methylene groups whereas the latter are lost by this procedure. The principal absorption bands in the spectra of 3- and 17-monoketosteroids, and 3,17-diketosteroids in both the 5α- and 5β-series, have been compared with the spectra of the appropriate deuterated analogs and an attempt has been made to identify the ketone-specific bands with one or the other of these types of vibrations. Comparison of these spectra with the spectra of androstane and etiocholane has also permitted a tentative assignment of several minor bands in the ketone spectra to centers of vibration that are not appreciably affected by the carbonyl group. These bands are presumed to be associated with vibrations centered in parts of the molecule remote from the carbonyl groups.

In the infrared spectra of complex organic compounds, the prominent absorption bands which occur *above* 1350 cm.$^{-1}$ are mainly of simple contour, and most of them can be identified with "group vibrations," *i.e.*, vibrations which are essentially localized in specific bonds or small atomic groups. In the region between 1350 and 700 cm.$^{-1}$ the spectra are much more complex; the experimentally observed absorption curves are envelopes formed by the overlap of large numbers of bands. When measured under high resolution even the more intense of these bands may show irregular changes of slope, which indicate that there are contributions from underlying weaker absorption. Because of this multiple absorption the spectra in this range are highly specific for individual compounds and hence their common designation as "finger-print spectra."

In compounds that contain carbon, hydrogen and oxygen only, the bands in this region of the spectrum are associated with stretching motions of C–C and C–O bonds and bending motions of C–H and O–H bonds. Vibrational theory indicates that these vibrations will be coupled, and indeed this coupling could be extensive enough to embrace the whole molecule. If it should be generally true that these low frequency absorption bands are associated with vibrations that appreciably involve the participation of all the atoms in a complex molecule, it would be pointless to attempt to identify the bands with more localized molecular structure. We do, however, have several examples of "group vibrations" that occur below 1350 cm.$^{-1}$ and we may cite as examples the band at 968 cm.$^{-1}$ associated with the out-of-plane in-phase C–H bending vibration of *trans*-1,2-disubstituted ethylenes, and the band near 1240 cm.$^{-1}$ associated with the acetate group.

Such well-defined low frequency group vibrations may be exceptional, but it would seem probable that much of the "finger-print" absorption in the spectra of complex molecules is associated predominantly with restricted zones in the molecule. If so, it ought to be possible to map out such zones by comparative studies of the spectra of suitably selected compounds.

Spectra of Ketosteroids

It has been shown in recent publications[4-6] that many of the low frequency absorption bands in the infrared spectra of ketosteroids and acetoxysteroids are dependent on the position of the oxygen containing functional group, and on the degree of unsaturation in its immediate environment. These bands show considerable group specificity and can often be identified in the spectra of diketones, keto-acetates and diacetates, provided the two functional groups are sufficiently well separated to keep their mutual perturbation small. The initial recognition of these group specific ketone and acetate vibrations was based solely on empirical comparisons among large numbers of curves. In this paper the ketone group frequencies of 3- and 17-ketosteroids will be examined from a more theoretical point of view, and, in accordance with the generalizations outlined in the preceding paragraph, an attempt will be made to relate them to motions of the atoms in the neighborhood of the carbonyl groups. Comparison of the ketone spectra with the spectra of androstane and etiocholane also allows of the identification of other bands in the ketone spectra that probably arise from parts of the molecule remote from the ketone groups.

Band Intensity Considerations.—In the spectra of alkyl and alicyclic hydrocarbons, the absorption below 1350 cm.$^{-1}$ is usually weak, the maximal molecular extinction coefficients are usually less than 15, and seldom exceed 30 units. On the introduction of oxygen containing substituents, stronger bands appear with extinction coefficients ranging up to 100 in ketones and 850 in acetates. This is illustrated by comparison of the spectra of androstane and etiocholane (Fig. 1A, 1B) with the ketosteroid spectra in Figs. 2–9.

The low intensity of the absorption in the spectra of the saturated hydrocarbons can be attributed to the weak electric moments of the C–H and C–C bonds that participate in the vibrations. The high

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[2] National Research Council Post-doctorate Fellow.

[3] The Sloan-Kettering Institute for Cancer Research, New York, N. Y.

[4] A. R. H. Cole, R. N. Jones and K. Dobriner, THIS JOURNAL, **74**, 5571 (1952).

[5] R. N. Jones, F. Herling and E. Katzenellenbogen, *ibid.*, **77**, 651 (1955).

[6] R. N. Jones and F. Herling, *ibid.*, in press.

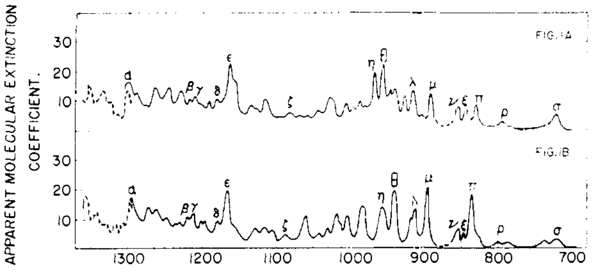


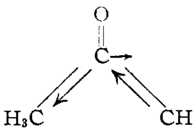
Fig. 1.—Infrared spectra of steroid hydrocarbons: A, androstane; B, etiocholane (-----, CCl_4 soln.; ——, CS_2 soln.). (α – σ designate bands identified as common to both spectra.)

intensity bands in the spectra of the oxygen containing compounds come primarily from vibrations in which the more polar C=O and C–O linkages play a dominant role. There will also be an enhancement in the intensity of bands in which C–H and C–C bonds vicinal to the oxygen atoms participate extensively, since the dipole moments of these bonds will be increased by mesomeric, inductive and field effects from the neighboring C–O, C=O and O–H bonds.

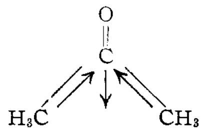
At present we are unable to calculate the manner and extent to which these changes in bond moment will influence the polarization changes associated with the normal modes of vibration of complex molecules, but, as a basis of discussion, it will be assumed here that these effects will be significant on the carbon atoms α and β to a carbonyl group, and negligible at more remote positions.

Vibrations of Ketones.—The foregoing hypothesis leads to the conclusion that the strong ketone-specific bands of ketosteroids primarily involve the system $-C_\beta-C_\alpha-CO-C_\alpha-C_\beta-$ and it is relevant next to examine the vibrations of this system in simple linear and cyclic ketones,

The normal modes of vibration of the generalized structure X–CO–X have been evaluated by Burkard[7] for mass values of X from one to infinity. These calculations suggest that for acetone (X = 15) there is a normal vibration I, which Kohlrausch[8] has identified with a Raman band at 1200 cm.$^{-1}$ and Francis[9] with an infrared band at 1218 cm.$^{-1}$. There is also a symmetrical vibration II associated with a Raman band at 787 cm.$^{-1}$. Lecomte[10] has also identified these vibrations with infrared bands in the spectrum of liquid acetone at 1204 and 790 cm.$^{-1}$, respectively.



I

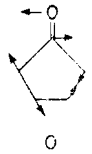
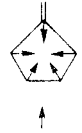
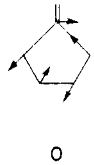
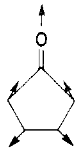
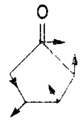
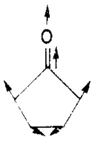
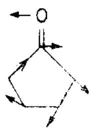
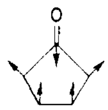


II

The normal vibrations of cyclopentanone have been discussed by Reitz[11] and by Lecomte,[12] and the in-plane skeletal modes assigned by Reitz as shown in Table I. Of these ω_2, ω_4, ω_6 and ω_8 can be regarded as derived from the simple ketone vibration I by coupling with stretching motions of the $C_\alpha-C_\beta$ bonds, and the vibrations ω_1, ω_3, ω_5, ω_7 are similarly derived from II.

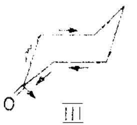
TABLE I

IN PLANE SKELETAL VIBRATIONS OF CYCLOPENTANONE[a]

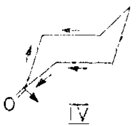
	Vibrations derived from I	Raman freq., cm.$^{-1}$		Vibrations derived from II	Raman freq., cm.$^{-1}$
ω_2		1195	ω_1		888
ω_4		1267	ω_3		1022
ω_6		956	ω_5		1149
ω_8		467	ω_7		706

[a] From the data of A. W. Reitz (ref. 11).

The skeletal modes of vibration of the chair form of cyclohexanone are more complex since the ring is less planar. Sets of vibrations can be postulated as arising from the coupling of the basic ketone in-plane skeletal motions I and II with stretching motions of the $C_\alpha-C_\beta$ bonds in various phase relationships. These may be indicated formally by the structures III–X, but these should not be identified with normal modes of vibration, since the latter may involve resultant motions that are not necessarily directed along the bond axes and that cannot readily be predicted for such asymmetrical structures. In the spectra of 3- and 17-ketosteroids, the analogous vibrations will be further com-



III



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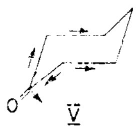

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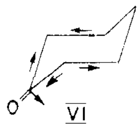

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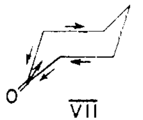

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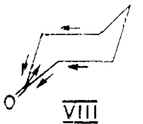
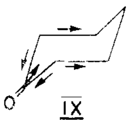
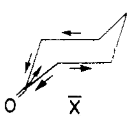


VIII



IX



X

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(7) O. Burkard, *Proc. Indian Acad. Sci.*, **8A**, 365 (1938).

(8) K. W. F. Kohlrausch, "Ramanspektren," Akademische Verlagsgesellschaft, Becker and Erler Kom.-Ges., Leipzig, 1943; J. W. Edwards, Ann Arbor, Mich., 1945, pp. 99–104.

(9) S. A. Francis, *J. Chem. Phys.*, **19**, 942 (1951).

(10) J. Lecomte, *J. phys. radium*, **6**, 127 (1945).

(11) A. W. Reitz, *Z. physik. Chem.*, **B33**, 179 (1936); **B35**, 363 (1937); **B38**, 381 (1938).

(12) J. Lecomte, *J. phys. radium*, [viii] **6**, 257 (1945).

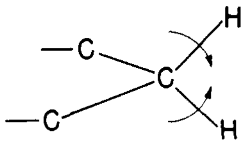
plicated by several factors, including (a) increased asymmetry in the rings, (b) additional coupling effects with more remote atoms, and (c) diminished planarity of the 5-membered ring.

The vibrations of the C–H bonds have been neglected in the above analysis, and the $-CH_2-$ and $-CH_3$ groups have been treated as point masses. If the methylene groups vicinal to carbonyl are selectively replaced by $-CD_2-$ or $-CD_3$ groups there will be some displacement of the skeletal vibration frequencies as a result of the mass change, but the effects will be comparatively small. The band intensities also should not be greatly affected since replacement of C–H by C–D should not appreciably disturb the charge on the carbon atom. It should therefore be possible to identify these skeletal vibrations by the fact that they persist with only minor changes of position and intensity on deuteration of the α-methylene groups.

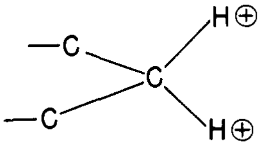
The differentiation between vibrations derived from the asymmetrical motion I and the symmetrical motion II is not difficult in the basic structures I and II since the symmetry of the latter makes it strong in the Raman spectrum and weak in the infrared. In the more complex structures the differences in the degree of symmetry between vibrations derived, respectively, from I and II will be less. Nevertheless, one might expect that vibrations of type I will tend to be stronger than those of type II in the infrared spectrum and occur at somewhat higher frequencies.

C–H Deformation Vibrations of α-Methylene Groups.—The C–H scissoring vibrations of methylene groups (XI) occur between 1460 and 1450 cm.$^{-1}$ for the unperturbed $-CH_2-$ groups in five-membered and six-membered rings, but in the structure $-CO-CH_2-$ these bands are displaced to 1435–1408 cm.$^{-1}$ and enhanced in intensity. Consequently they serve indirectly to characterize the carbonyl group.[13]

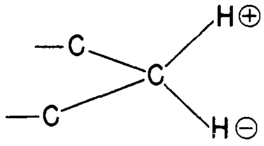
Below 1350 cm.$^{-1}$ wagging XII, twisting XIII and rocking motions XIV of the methylene groups occur, and the possibility exists that these also may be perturbed for methylene groups vicinal to carbonyl. These vibrations have been studied most extensively in the spectra of *n*-paraffin hydrocarbons[14] where the wagging bands occur between 1375 and 1200 cm.$^{-1}$ and the twisting bands (weaker in the infrared spectra) between 1300 and 1175 cm.$^{-1}$. The methylene rocking bands are well defined at 720 cm.$^{-1}$ in long polymethylene chains and at somehwat higher frequencies for $-CH_2-$, $-(CH_2)_2-$ and $-(CH_2)_3-$ groups.



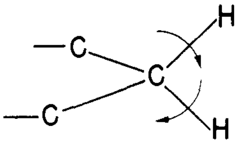
XI



XII



XIII



XIV

The C–H deformation vibrations of cyclohexane have been studied by Burket and Badger.[15] Taking into account the phase relationships between the several methylene groups, these authors have assigned four frequencies to each type of vibration. These fall in the ranges 1456–1443, 1375–1308, 1266–1176 and 1155–802 cm^{-1}, respectively, for the scissoring, wagging, twisting and rocking motions.

By analogy, bands associated with the wagging and twisting motions of α-methylene groups in ketosteroids might be expected to occur somewhere above 1000 cm.$^{-1}$ and rocking bands below 1000 cm.$^{-1}$. On selective deuteration in the α-methylene group these bands should disappear to be replaced by the analogous $-CD_2-$ vibrations at lower frequencies. This should serve to distinguish these bands from those associated with the skeletal motions discussed above.

Deuteration of the α-methylene group will also displace the scissoring vibration from 1435–1407 cm.$^{-1}$ by a factor of approximately $1/\sqrt{2}$ so that the spectra may be complicated by CD_2 scissoring vibrations in the neighborhood of 1000 cm.$^{-1}$.[15a]

17-Ketosteroids.—Consideration of the spectra of androstan-17-one (XV) and etiocholan-17-one (XVII) in terms of the above arguments suggests that the following bands might be predicted.

(a) Four bands of moderate to strong intensity associated with asymmetrical skeletal vibrations in ring D (analogs of I).[16] These would be comparatively insensitive to deuteration in the C_{16}-methylene group.

(b) Four bands of weaker intensity associated with pseudo-symmetrical skeletal vibrations in ring D (analogs of II)[16]; these also would be comparatively insensitive to C_{16} deuteration.

(c) Two bands associated with wagging and twisting vibrations of the C_{16}-methylene group. These should occur between 1350 and 1000 cm.$^{-1}$. The wagging will probably be the more intense and both bands will disappear on C_{16} deuteration.

(d) One band of weak or moderated intensity associated with the rocking vibration of the C_{16}-methylene group. This should occur below 1000 cm.$^{-1}$ and should disappear on C_{16}-deuteration.

These arguments provide for eleven bands below 1350 cm.$^{-1}$ associated with the 17-ketosteroid structure. They may be compared with the thirteen bands recognized empirically as characteristic of the 17-ketosteroids of the 5α-series (Bands a-m in Fig. 2A) and the eleven bands similarly identified

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(13) R. N. Jones and A. R. H. Cole, THIS JOURNAL, **74**, 5648 (1952).

(14) J. K. Brown, N. Sheppard and D. M. Simpson, *Phil. Trans. Roy. Soc.* (*London*), **247A**, 35 (1954).

(15) S. C. Burket and R. M. Badger, THIS JOURNAL, **72**, 4397 (1950).

(15a) It is to be noted that the displacement factor of $1/\sqrt{2}$ is normally a maximum; if the C–H deformation vibration is appreciably coupled with other modes the shift will generally be less, but it can be slightly greater than $1/\sqrt{2}$ if Fermi resonance is also involved.

(16) C_{12} and C_{18} are also β to the C_{17} carbonyl group and should rightly be included in the zone associated with the high intensity skeletal vibrations. The term "D-ring skeletal vibration" must be used with this reservation in mind.

for 17-ketosteroids of the 5β-series (Bands a′–k′ in Fig. 3A).[17]

The spectra of androstan-17-one-16-d_2 (XVI) and etiocholan-17-one-16-d_2 (XVIII) are shown in Fig. 2B and 3B, respectively, and comparison with the bands in the appropriate non-deuterated steroids make possible the following band identifications.

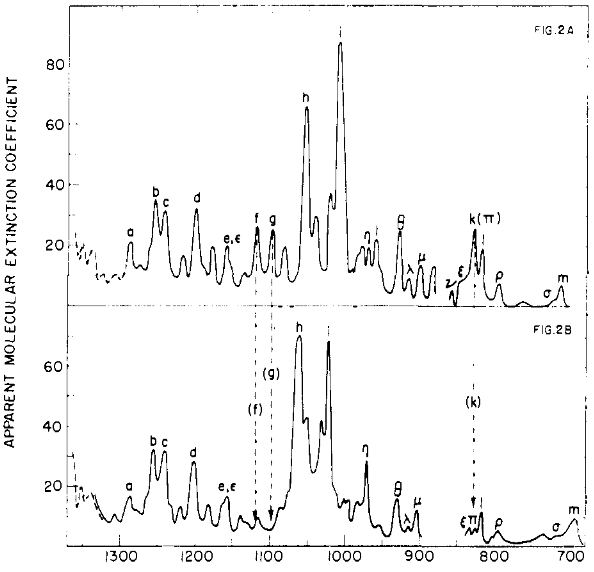
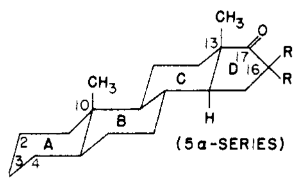


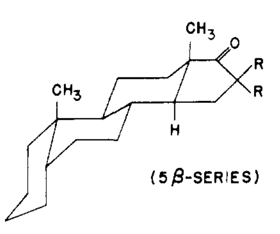
Fig. 2.—Infrared spectra of 17-keto-5α-steroids: (A), androstan-17-one; B, androstan-17-one-16-d_2 (-----, CCl_4 soln.; ——, CS_2 soln.).

Androstan-17-one: deuterium invariant bands a, b, c, d, e, h, i, l, m; deuterium sensitive bands f, g, (j?) k.

The disappearance of f, g and k is quite definite and our arguments suggest that these are to be assigned to C_{16} deformation modes. Band k would then be attributed to the rocking motion XIV; the assignments of f and g will be considered in more detail below. Band j may also be lost on deuteration but might alternatively be regarded as displaced to higher frequency and superimposed on η which is more intense in the deuterium derivative. Bands a, b, c, d, e, h, i, l, m, are clearly recognizable in both spectra and are accordingly assigned to D-ring skeletal modes.



XV R=H
XVI R=D



XVII R=H
XVIII R=D

A similar comparison of the spectra of etiocholan-17-one (XVII) with that of etiocholan-17-one-16-d_2 (XVIII) (Fig. 3A, 3B) gives the following band identifications:

Etiocholan-17-one: deuterium invariant bands a′, b′, c′, d′, f′, g′, h′, j′, k′; deuterium sensitive bands e′, i′.

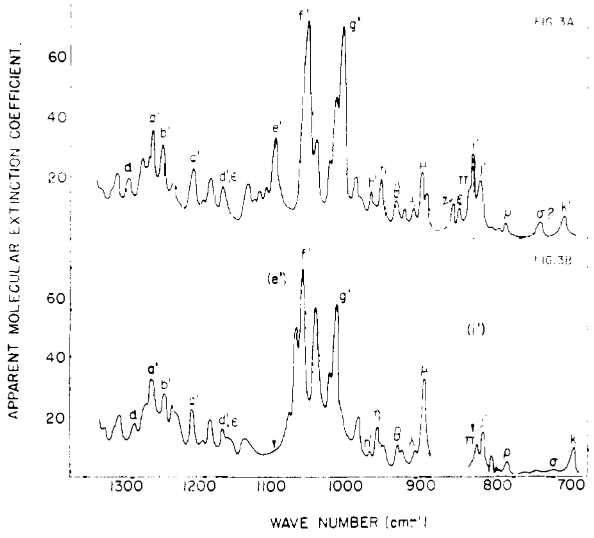


Fig. 3.—Infrared spectra of 17-keto-5β-steroids: A, etiocholan-17-one; B, etiocholan-17-one-16-d_2 (CS_2 soln.).

As in androstan-17-one, there is a series of deuterium invariant bands observed between 1260 and 1000 cm.$^{-1}$ and two additional weaker ones (j′ and k′) at lower frequencies. The deuterium sensitive band i′ at 830 cm.$^{-1}$ can be assigned to the C_{16}-methylene rocking motion (*cf.* band k at 829 cm.$^{-1}$ in androstan-17-one). In the 1150–1050 cm.$^{-1}$ region etiocholan-17-one has only one clearly recognizable deuterium sensitive band (e′) in comparison with the f, g doublet of androstan-17-one. The similarity in intensity of f and g suggests that these bands may arise from a Fermi resonance splitting of a single C_{16} deformation (wagging?) vibration rather than from the separate wagging and twisting modes, which our analysis might lead us to expect. If this be so, the failure to observe a C_{16} twisting vibration would be in accord with the weakness of this band in *n*-paraffin hydrocarbon infrared spectra.[14]

The strong pairs of deuterium insensitive bands h, i, and f′ and g′ which dominate the spectra of both types of 17-ketosteroids also suggest a Fermi resonance splitting of a single normal vibration, and the sensitivity of these bands to perturbations is consistent with this explanation. In the spectrum of etiocholan-17-one-16-d_2 there is a prominent band at 1040 cm.$^{-1}$, ($\epsilon^{(a)} = 64$) which might be assigned to the CD_2 scissoring vibration displaced from 1408 ($\epsilon^{(a)} = 50$) in the C_{16}-hydrogen compound. No comparable band is seen in the spectrum of androstan-17-one-16-d_2, but band h is broadened and intensified in comparison with the C_{16}-hydrogen compound and the CD_2-scissoring band may be overlapped by it.

The bands α-σ in these and other spectra are attributed to other parts of the molecule and are discussed separately in a later section of this paper.

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(17) The letters used to designate bands of the ketosteroids of the 5α-series are the same as were employed in reference 5; the lettering systems of the 5β-ketosteroids have been altered to avoid ambiguities in discussion.

3-Ketosteroids.—The spectra of androstan-3-one (XIX) and androstan-3-one-2,4-d_4 (XX) are shown in Fig. 4A and 4B, and the ketone-specific bands are indicated by A-J.[17] Comparison of these curves suggests that bands C, D, E, G and H are probably identifiable in both spectra. A, B, I and J are lost on deuteration; of these, I and J can be assigned to the rocking motions of the C_2 and C_4 methylene groups. The observation of two such bands is consistent with the fact that 3-ketones show two α-methylene scissoring vibrations (Fig. 11C), indicative of differing degrees of perturbation in the C_2- and C_4-positions.

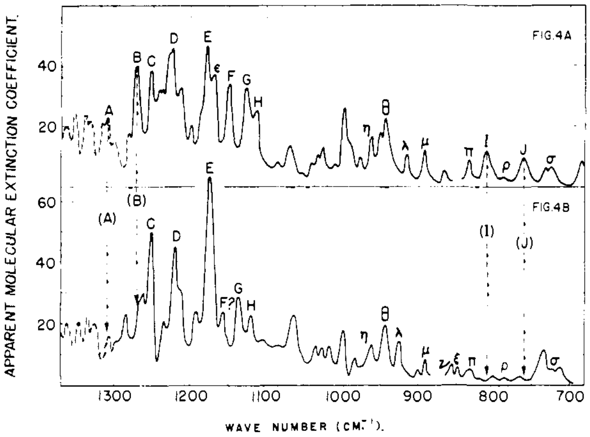
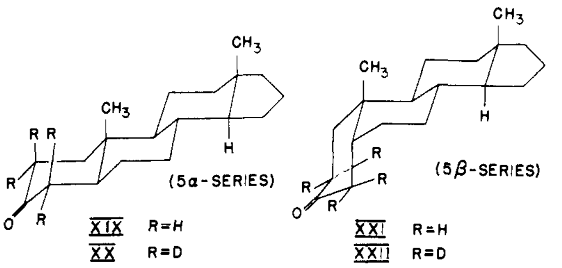


Fig. 4.—Infrared spectra of 3-keto-5α-steroids: A, androstan-3-one; B, androstan-3-one-2,4-d_4 (----, CCl_4 soln.; ——, CS_2 soln.).

Bands A and B may likewise be identified tentatively with C_2 and C_4 wagging motions, the twisting bands being assumed forbidden in the infrared. The identification of band F with F? at 1154 cm.$^{-1}$ is questionable on intensity grounds.

The spectra of etiocholan-3-one (XXI) and etiocholan-3-one-2,4-d_4 (XXII) are compared in Figs. 5A and 5B, and the changes on deuteration appear to be somewhat more extensive than in the 5α-series. Bands F′, H′, and I′ can be recognized unequivocally as deuterium invariant; C′ may also be considered as deuterium invariant, though more dubiously. The deuterium sensitive bands, D′ and E′ suggest analogies with A and B of androstan-3-one (C_2 and C_4 wagging bands?). Bands A′, B′, G′ and J′ also go on deuteration but these have no recognizable analogs in the 5α-series. At the low frequency end of the spectrum band K′ and L′ at 824 and 765 cm.$^{-1}$ are lost on deuteration and these show a parallelism with I and J at 810 and 760 cm.$^{-1}$ in androstan-3-one (C_2 and C_4 rocking modes).[18]



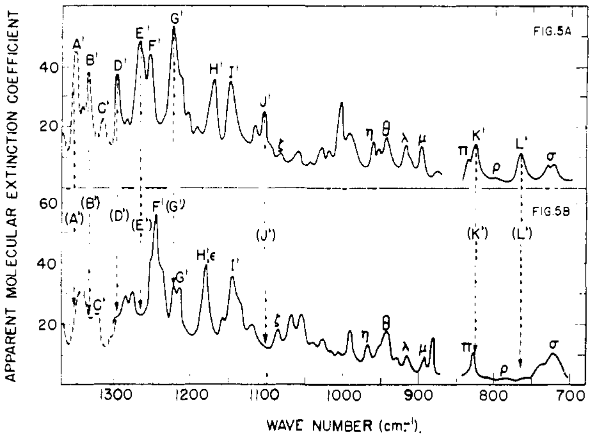


Fig. 5.—Infrared spectra of 3-keto-5β-steroids: A, etiocholan-3-one; B, etiocholan-3-one-2,4-d_4.

Summary Discussion of Monoketones.—It will be evident from the foregoing discussion that an analysis of the finger-print absorption of ketosteroids in these terms is at least partially successful. In all the spectra it is possible to identify some of the ketone-specific bands that are clearly related in the spectra of the deuterated and non-deuterated ketones; likewise, a number of the ketone-specific bands clearly disappear on α-methylene deuteration; some parallelism also holds between bands in the same regions of the spectra of ketones of the 5α- and 5β-series. In addition, there are some ketone-specific bands that do not fall into either of these two well defined categories, and these cannot be considered further at present. If a skeletal band should shift by 10–20 cm.$^{-1}$ in consequence of the mass effect on deuteration, its identification in the deuterated compound becomes uncertain, and if, in addition, it should be perturbed by Fermi resonance, a shift of this order may induce a redistribution of intensity which makes any attempt at the "identification" of the band a very questionable procedure.

There is an inconsistency between hypothesis and observation in the failure to identify all the α-methylene CD_2 deformation modes. If bands f, g, e′, A, B, D′ and E′ are correctly assigned to CH_2 wagging and twisting vibrations, it would be anticipated that the deuterated ketones should show analogous absorption between 1000 and 775 cm.$^{-1}$, and this is not the case. In the deuterated 3-ketones we are also unable to identify the C_2 and C_4 CD_2 scissoring vibrations, although the assignments of the analogous CH_2 bands (Fig. 11, bands A and B) are reasonably well substantiated on other grounds.[18] It is evident that these α-methylene CD_2 deformation vibrations must be studied in simpler compounds before this problem can be resolved.

3,17-Diketosteroids.—The majority of the ketone-specific bands are observed also in diketo-

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[18] It has been pointed out in reference 5 that the displacement of I and J in relation to K′ and L′ offer the best prospect of differentiating between 3-ketosteroids of the 5α- and 5β-series. If the assignment of these bands to C_2 and C_4 rocking modes is correct their sensitivity to the stereochemistry of the A-ring is readily explained.

steroids, and in the spectrum of androstane-3,17-dione (XXIII) (Fig. 7A) the 3-ketone bands are designated as A-J and the 17-ketone bands as a-m. For etiocholane-3,17-dione (XXIII) (Fig. 9A) the 3- and 17-ketone bands are designated A′-L′ and a′-k′, respectively, the letters correspond with those used for the appropriate monoketone spectra.

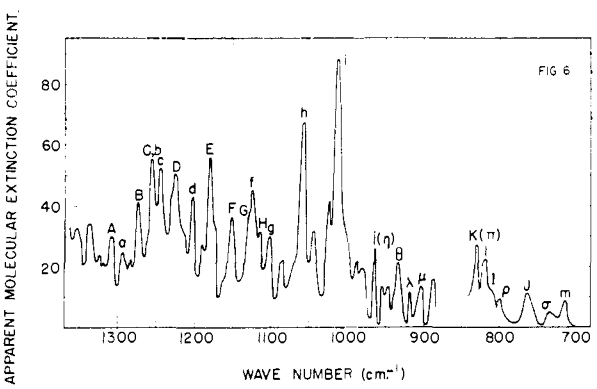


Fig. 6.—Summation curve: androstan-17-one + androstan-3-one − androstane.

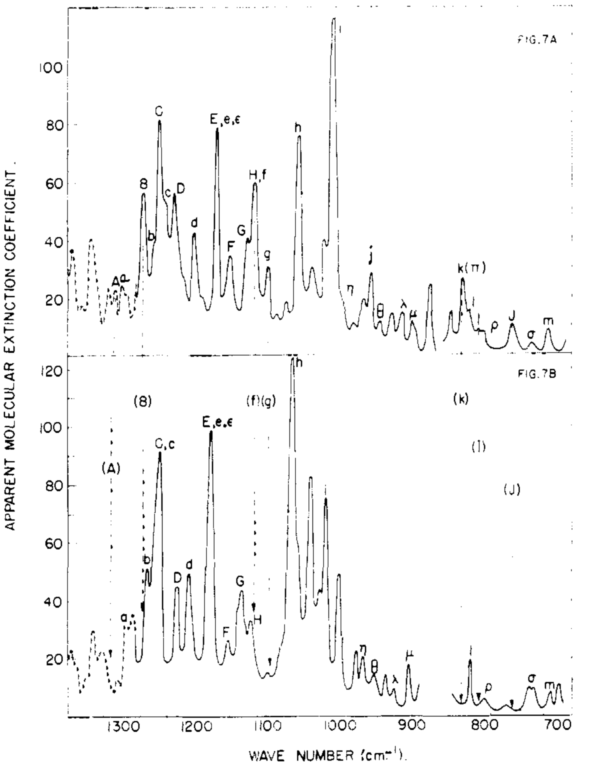


Fig. 7.—Infrared spectra of 3,17-diketo-5α-steroids: A, androstane-3,17-dione; B, androstane-3,17-dione-2,4,16-d_6 (----, CCl$_4$ soln.; ——, CS$_2$ soln.).

If these group specific bands do arise from vibrations which are truly localized within the A and D ring systems, there should be negligible cross-coupling effects, and it should be possible to simulate the spectrum of androstane-3,17-dione by an algebraic intensity summation androstan-3-one + androstan-17-one − androstane; in which the subtraction of the androstane spectrum is necessary to correct for the doubling of the contributions from the non-ketonic group absorptions that would otherwise occur.

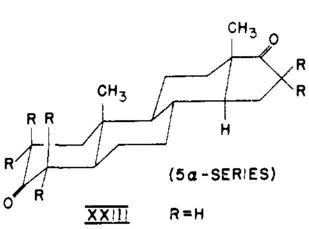
The curve obtained in this manner, by adding intensities at 2 cm.$^{-1}$ intervals across the spectrum, is shown in Fig. 6, and the parallel computation for the system etiocholan-3-one + etiocholan-17-one − etiocholane is shown in Fig. 8.

Comparison of Fig. 6 with the observed spectrum of androstane-3,17-dione (Fig. 7A) shows that practically all of the group specific bands are recognizable, although there are changes in the relative intensities of several of the bands, and an appreciable over-all enhancement of intensity in the observed spectrum. Some frequency shifts (of the order of 10 cm.$^{-1}$) occur, particularly in the 1260–1210 cm.$^{-1}$ region associated with the skeletal modes (bands b, C, c, D); band f is also displaced by about the same amount and appears to be superimposed on H. Otherwise the contours and positions of the bands agree reasonably well.

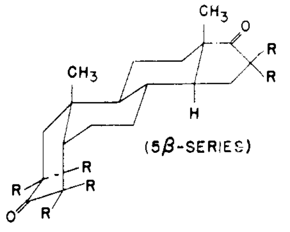
In the 5β-series there is also moderate agreement between the 3,17-diketone spectrum and the computed curve (Figs. 8, 9A); some small frequency shifts and a redistribution of intensities are noted, particularly in the 1260–1150 cm.$^{-1}$ region (bands a′, F′, b′, G′ and c′), and a very marked change in the appearance of an additional strong band at 1015 cm.$^{-1}$. This suggests a Fermi resonance splitting of g′ into a doublet (g′$_1$ and g′$_2$).[19]

Deuteration Studies on 3,17-Diketosteroids.—The spectra of androstan-3,17-dione (XXIII) and androstan-3,17-dione-2,4,16-d_6 (XXIV) are compared in Fig. 7A and 7B. The analyses of the deuterated monoketone spectra would suggest that bands A, B, I and J, which have been assigned to vibrations in the C$_2$ and C$_4$ methylene groups, should be lost on deuteration, as also should f, g and k associated with the methylene group at C$_{16}$. An examination of Fig. 7A and 7B shows that this is substantiated experimentally.

Of the bands assigned to skeletal vibrations in ring A (bands C, D, E, F, G, and H), all are present in Fig. 7B, with H diminished in intensity by the elimination of the C$_{16}$-methylene band (f), which overlaps it in the spectrum of the non-deuterated diketone.



XXIII R=H
XXIV R=D



XXV R=H
XXVI R=D

Of the D ring skeletal vibrations, bands a, b, d, h, i, l and m can be identified in Fig. 7B. There remains some doubt about the deuterium invariant

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[19] It has been suggested in a previous paragraph that f′ and g′ may themselves be products of a Fermi resonance splitting of a primary skeletal vibration and there is ambiguity in the interpretation here. Band g′2 shows some resemblance to the band in etiocholan-17-one-16-d_2 which was assigned to the CD$_2$-scissoring vibration. It is evident that this region could profitably be investigated in similar monocyclic or bicyclic model compounds.

band c, which may be overlapped in Fig. 7B by C. It must also be assumed that e is overlapped by E in both the deuterated and non-deuterated spectra. The band at 1038 cm.$^{-1}$ in Fig. 7B can be assigned to the CD_2 scissoring vibration at C_{16} (see however footnote[19]).

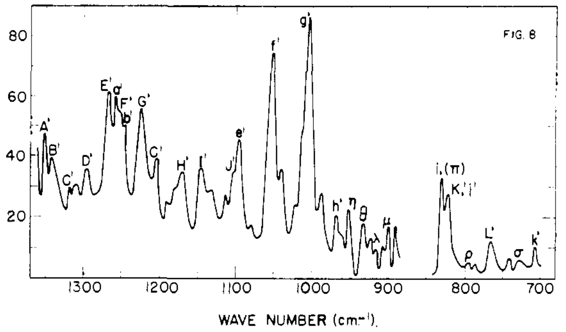


Fig. 8.—Summation curve: etiocholan-17-one + etiocholan-3-one − etiocholane.

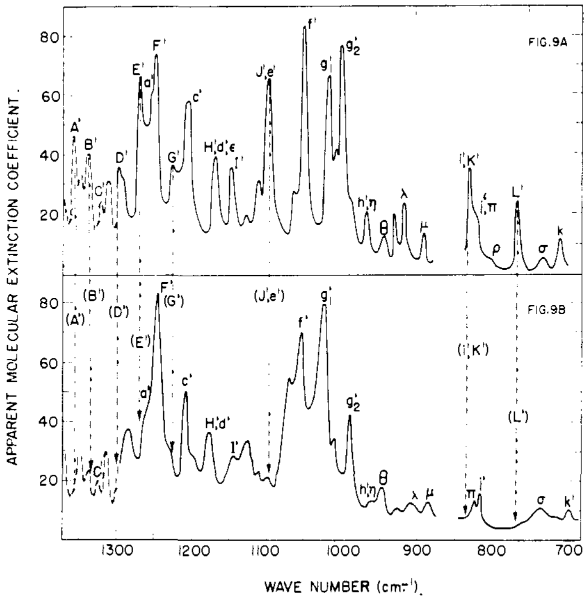


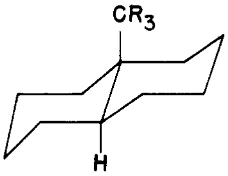
Fig. 9.—Infrared spectra of 3,17-diketo-5β-steroids: A, etiocholane-3,17-dione; B, etiocholane-3,17-dione-2,4,16-d_6 (-----, CCl_4 soln.; ——, CS_2 soln.).

The spectra of etiocholane-3,17-dione (XXV) and etiocholane-3,17-dione-2,4,16-d_6 (XXVI) are compared in Figs. 9A and 9B. From the monoketone spectra it would be expected that bands A', B', D', E', G', J', K' and L', associated with methylene groups at C_2 and C_4 should disappear, as also should e' and i' assigned to the methylene group at C_{16}. Comparison of the diketone curves shows that this holds true for E', J', K', L', e' and i', and probably also for the other bands (A', D', G') although the identifications are not as clear (thus D' could be identified with the band at 1285 cm.$^{-1}$ in Fig. 9B). The bands identified as insensitive to deuterium substitution in the monoketone spectra are C', a', F', b', c', H', d', I', L', g', h', i', k'.

Comparison of Figs. 9A and 9B indicates that a', F', c', H', I', f', j' and k' persist in the deuterated diketone. The anomalous g'_1, g'_2 doublet of etiocholane-3,17-dione appears also in the hexadeutero derivative with some change in relative intensity, and a displacement of g'_2 by 9 cm.$^{-1}$ to lower frequency. There is also a broadening of f' and g_1' and a raising of the intermediate minimum which may indicate contribution from the postulated scissoring vibration of the CD_2 at C_{16} (*cf.* androstan-17-one).

Vibrations Characteristic of the Unperturbed Steroid Ring System.—It has always been disconcerting that the extensive empirical comparisons of steroid spectra have failed to establish any group frequencies characteristic of the steroid ring system *per se*, and it has not been possible from the 1350–650 cm.$^{-1}$ region of the infrared spectrum alone to distinguish steroids from related families of organic compounds, such as triterpenoid sapogenins. The band intensity considerations discussed in a preceding section of this paper offer a rational explanation of this fact. If the strong bands are primarily associated with oxygen containing functional groups, they will vary with the nature and position of the substituents. Vibrations common to many kinds of steroids must therefore be sought among the weaker bands ($\epsilon^{(a)} < 25$) and must arise from centers of vibrations that are remote from the common positions of substitution. Vibrations primarily centered about C_{10} and C_{13} and the angular methyl groups might best meet these criteria.

In the curves of androstane and etiocholane (Fig. IA, Ib), bands which are most clearly recognizable as common to both spectra are indicated by Greek letters. The more prominent of these are ϵ, near 1160 cm.$^{-1}$ and the η–μ group between 980 and 880 cm.$^{-1}$. Band ϵ may tentatively be associated with a rocking vibration of one of the angular methyl groups, since this type of vibration has been assigned to prominent bands near 1160 cm.$^{-1}$ in the spectra of branched chain hydrocarbons.[20] An absorption band at 1170 cm.$^{-1}$, rather similar to ϵ, is also observed in the spectrum of *trans*-9-methyldecalin (XXVII) but disappears on deuteration of the angular methyl group (XXVIII) (Fig. 10A, 10B). The η–μ group of bands may also involve



XXVII R=H
XXVIII R=D

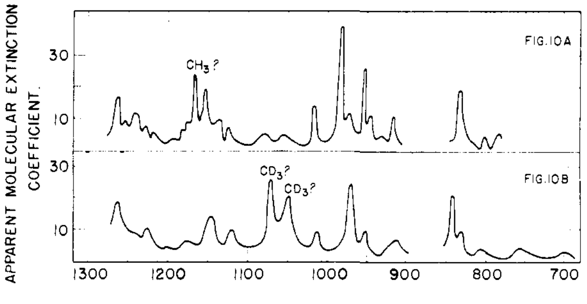


Fig. 10.—Infrared spectra. A, *trans*-9-methyldecalin; B, *trans*-9-(methyl-d_3)-decalin (CS_2 soln.).

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[20] N. Sheppard and D. M. Simpson, *Quart. Revs. London*, **7**, 19 (1953).

Table II

Bands below 1000 Cm.$^{-1}$ Tentatively Assigned to Vibrations of the Steroid Ring Systems[a]

(Carbon disulfide solution)

Compound	Band position, cm.$^{-1}$						
	η	θ	λ	μ	π	ρ	σ
			5α-Series				
Androstane	967	954	915	891	830	795	722
Androstan-17-one	971	930	915	901	830[b]	790	722[d]
Androstan-17-one-16-d_2	971	930	916	904	826	795	718
Androstan-3-one	963	944	914	892	832	789	725
Androstan-3-one-2,4-d_4	962	942	924	891	832	785	725
Androstane-3,17-dione	965	942	913	898	..	802	732
Androstane-3,17-dione-2,4,16-d_6	965	951	922	902	..	800	732
			5β-Series				
Etiocholane	956	942	912	895	836	801	720
Etiocholan-17-one	953	935	912	898	836[d]	790	742(?)
Etiocholan-17-one-16-d_2	957	932	909	896	826	788	722
Etiocholan-3-one	958	942	917	896	834	798	725
Etiocholan-3-one-2,4-d_4	967	942	916	894	829	785	722
Etiocholan-3,17-dione	966	945	916	892	820[c,d]	800[d]?	733
Etiocholan-3,17-dione-2,4,16-d_6	968	945	910	886	824	..	734

[a] Band η may be identical with j in the 5α-series and with h′ in the 5β-series, and there is some suggestion of an additional characteristic band between θ and λ. Bands ρ and σ are too weak for accurate determination of the positions at the concentrations employed, which were limited by solubility. [b] Overlapped by k. [c] Overlapped by j′. [d] Inflection.

the methyl groups although the evidence for this is not so well substantiated.[20]

An examination of the spectra of the ketosteroids discussed above shows that several of the α-σ bands are tentatively recognizable; they are indicated on the curves in Figs. 2–9, and their frequency ranges are summarized in Table II. As might be anticipated, these show up better at the lower frequencies where there is less overlap with the stronger ketone-specific bands. Band ε, however, at 1170 cm.$^{-1}$ might be identifiable with e in androstan-17-one and d′ in etiocholan-17-one. Although of theoretical interest, it is doubtful whether these weak bands would prove sufficiently characteristic to distinguish steroids from other terpenoid systems containing condensed cycloparaffin ring systems and methyl groups.

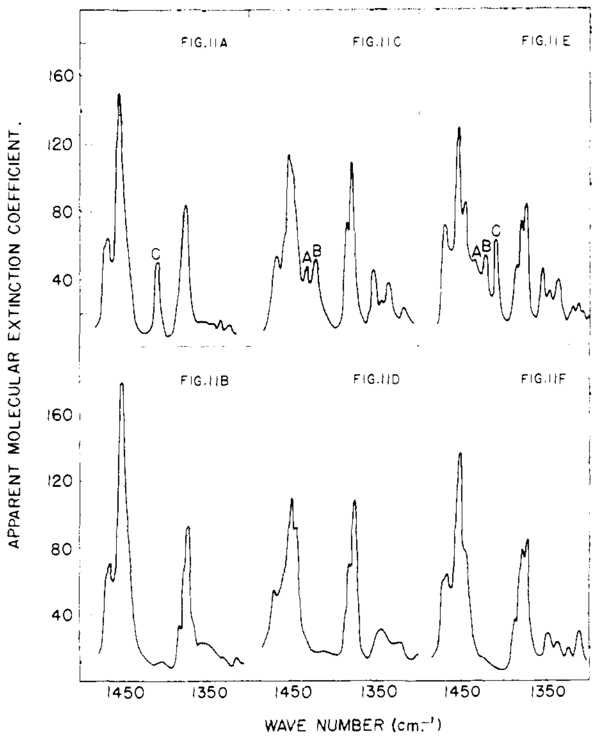

Fig. 11.—Infrared spectra in region of CH_2-scissoring vibrations (CCl_4 soln.): A, etiocholan-17-one (band C due to C_{16} methylene group); B, etiocholan-17-one-16-d_2; C, etiocholan-3-one (bands A and B due to C_2 and C_4 methylene groups); D, etiocholan-3-one-2,4-d_4; E, etiocholane-3,17-dione; F, etiocholane-3,17-dione-2,4,16-d_6.

Experimental

The preparation and characterization of androstan-17-one-16-d_2 and androstan-3-one-2,4-d_4 have been described previously.[21] The other deuterated ketones were prepared similarly by repeated exchange of the light ketone with methanol-*d* in the presence of anhydrous sodium carbonate. Deuterium analysis on androstan-3,17-dione-2,4,16-d_6 by mass spectrometry gave 5.46 atoms of deuterium per molecule. The ketones of the 5β-series were not assayed for deuterium, but the treatments with methanol-*d* were repeated until no further change in the infrared spectrum occurred, and the products showed no residual α-methylene scissoring absorption bands between 1430 and 1400 cm.$^{-1}$ (Fig. 11).

The infrared spectra were measured on a Perkin-Elmer model 112 single-beam double-pass spectrometer in carbon disulfide and carbon tetrachloride solutions at 1-mm. path length; the intensities were averaged from duplicate determinations. At the computed spectral slit widths employed (1.5–2.0 cm.$^{-1}$) errors in intensity attributable to the finite slit width are considered to be negligible, but other experimental errors affecting the intensity measurements are present, and it is estimated that these may account for uncertainties of about ±5% in the reported extinction coefficients.[22] Measurements between 875–845 cm.$^{-1}$ are subject to solvent absorption; if the compound is sufficiently soluble in carbon disulfide the bands in this region can be observed, but the intensities are subject to larger errors.

Conclusion

The results of this analysis, which are summarized in Table III, suggest that most of the absorp-

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(21) B. Nolin and R. N. Jones, *Can. J. Chem.*, **30**, 727 (1952).

(22) For precise definitions of *computed spectral slit width* and *apparent molecular extinction coefficient*, as used here, and further discussion of the errors in intensity measurements, see R. N. Jones and C. Sandorfy, "Technique of Organic Chemistry," Vol. IX, Chapter IV, edited by A. Weissberger, Interscience Pub. Inc., New York, N. Y., in press.

TABLE III

TENTATIVE ASSIGNMENTS OF THE KETONE-SPECIFIC BANDS IN THE INFRARED SPECTRA OF C_{19}-KETOSTEROIDS

(Solutions in carbon disulfide)

Band	ν_{max}	$\epsilon^{(a)}_{max}$	Characteristics and assignment[a]	Identifying letter in ref. 5
			Androstan-17-one	
a	1288	22	Deut. invar., D-ring skel. vibr.	a
b	1256	36	Deut. invar., D-ring skel. vibr.	b
c	1242	32	Deut. invar., D-ring skel. vibr.	c
d	1202	32	Deut. invar., D-ring skel. vibr.	d
e	1159	20	Deut. invar., D-ring skel. vibr., or angular methyl group vibr. (*cf.* ϵ in androstane)	e
f	1121	27	Deut. sens., C_{16}-methylene wag (Fermi resonance doublet with g ?)	f
g	1099	26	Deut. sens., C_{16}-methylene wag (see f above)	g
h	1057	67	Deut. invar., D-ring skel. vibr. (Fermi resonance doublet with i ?)	h
i	1011	88	Deut. invar., D-ring skel. vibr. (see h above)	i
j	960	22	Deut. sens. (?), or displaced to 969 cm.$^{-1}$ in C_{16}-d_2 der. and superimposed on η?	j
k	828	26	Deut. sens., C_{16}-methylene rock. The weaker steroid ring system vibration π may also be present, overlapped by k. (*cf.* C_{16}-d_2 deriv.)	k
l	818	20	Deut. invar., D-ring skel. vibr.	l
m	709	8	Deut. invar. ?. Identified with band at 698 cm.$^{-1}$ in C_{16}-d_2 der.	m
			Etiocholan-17-one	
a'	1258	35	Deut. invar., D-ring skel. vibr.	A
b'	1244	31	Deut. invar., D-ring skel. vibr.	B
c'	1204	22	Deut. invar., D-ring skel. vibr.	C
d'	1167	17	Deut. invar., D-ring skel. vibr. or angular methyl group vibration (*cf.* ϵ in etiocholane)	D
e'	1094	33	Deut. sens., C_{16}-methylene wag	E
f'	1050	72	Deut. invar., D-ring skel. vibr. (Fermi resonance doublet with g' ?)	F
g'	1005	71	Deut. invar., D-ring skel. vibr. (see f' above)	G
h'	967	15	Deut. invar.	H
i'	830	28	Deut. sens., C_{16}-methylene rock	I
j'	822	19	Deut. invar., D-ring skel. vibr.	J
k'	710	7	Deut. invar. Identified with band at 699 cm.$^{-1}$ in C_{16}-d_2 der. D-ring skel. vibr.	K
			Androstan-3-one	
A	1310^b	23	Deut. sens., C_2 or C_4-methylene wag (or twist)	A
B	1270	40	Deut. sens., C_2 or C_4-methylene wag (or twist)	B
C	1252	39	Deut. invar., A-ring skel. vibr.	C
D	1222	46	Deut. invar., A-ring skel. vibr	D
E	1176	47	Deut. invar., A-ring skel. vibr.	E
F	1149	34	Deut. invar.? Tentatively identified with weaker band ($\epsilon^{(a)} = 24$) at 1155 cm.$^{-1}$ in $C_{2,4}$-d_4 deriv., A-ring skel. vibr.	F
G	1126	33	Deut. invar., A-ring skel. vibr.	G
H	1112	26	Deut. invar., A-ring skel. vibr.	H
I	808	12	Deut. sens., C_2 or C_4-methylene rock	I
J	760	9	Deut. sens., C_2 or C_4-methylene rock	J
			Etiocholan-3-one	
A'	1352^b	46	Deut. sens., C_2 or C_4-methylene wag (or twist)	A
B'	1336^b	38	Deut. sens., C_2 or C_4-methylene wag (or twist ?)	B
C'	1319^b	30	Deut. invar., A-ring skel. vibr.	C
D'	1295	38	Deut. sens., C_2 or C_4-methylene wag (or twist)	D
E'	1266	49	Deut. sens., C_2 or C_4-methylene wag (or twist)	E
F'	1250	48	Deut. invar., A-ring skel. vibr.	F
G'	1221	53	Probably deut. sens. but might be identified with weaker band ($\epsilon^{(a)} =$ 32) at 1222 cm.$^{-1}$ in $C_{2,4}$-d_4 der.	G
H'	1169	36	Deut. invar., A-ring skel. vibr., or angular methyl group vibration (*cf.* ϵ in etiocholane)	H
I'	1147	35	Deut. invar., A-ring skel. vibr.	I
J'	1102	25	Deut. sens. C_2 or C_4-methylene twist ?	J
K'	825	14	Deut. sens. C_2 or C_4-methylene rock	K
L'	765	11	Deut. sens. C_2 or C_4-methylene rock	L
			Androstane-3,17-dione	
A	1306^b	22	Deut. sens. C_2 or C_4-methylene wag (or twist)	A
a	1290^b	21	Deut. invar., D-ring skel. vibr.	*a*
B	1268	56	Deut. sens., C_2 or C_4-methylene wag (or twist)	B
b	1254^d	38	Deut. invar. D-ring skel. vibr.	b
C	1246	81	Deut. invar., A-ring skel. vibr.	C
c	1238^d	53	By analogy with androstan-17-one should be deut. invar. Not obsd. in the $C_{2,4,16}$-d_6 der., but may be overlapped by C	c
D	1225	56	Deut. invar. Identified with band at 1220 cm.$^{-1}$ in the $C_{2,4,16}$-d_6 der., A-ring skel. vibr.	D
d	1203	49	Deut. invar., D-ring skel. vibr.	d
E,e	1165	79	Intense deut. invar. narrow band. This takes the place of E (1176 cm.$^{-1}$) and ϵ (1168 cm.$^{-1}$) in androstan-3-one and of e (1159 cm.$^{-1}$) in androstan-17-one. May be a rocking vibration of an angular methyl group analogous to ϵ in androstane	E,e
F	1149	34	Deut. invar. (Note F in the $C_{2,4,16}$-d_6 der. ($\epsilon^{(a)} = 26$) is weaker (*cf.* androstan-3-one). A-ring skel. vibr.	F
G	1126	40	Deut. invar., A-ring skel. vibr.	G
H,f	1115	59	Overlap of deut. invar. band H ascribed to A-ring skel. vibr. with deut. sens. band f, ascribed to C_{16}-methylene wag (Fermi resonance doublet with g ?). Note that in the $C_{2,4,16}$-d_6 der. the intensity falls to $\epsilon^{(a)} = 33$	H,f
g	1097	30	Deut. sens., C_{16}-methylene wag (see f above)	g
h	1054	76	Deut. invar., D-ring skel. vibr.	h
i	1007	116	Deut. invar., D-ring skel. vibr.	i
j	957	28	Deut. sens. (?)	j^e
k	830	26	Deut. sens. C_{16}-methylene rock. (May overlap π)	k
l	821	15	Deut. invar., D-ring skel. vibr.	l
l	808	9	Deut. sens., C_2 or C_4-methylene rock	I
J	760	11	Deut. sens., C_2 or C_4-methylene rock	J
m	712	9	Deut. invar., D-ring skel. vibr.	m
			Etiocholane-3,17-dione	
A'	1355	46	Deut. sens., C_2 or C_4-methylene wag (or twist)	A
B'	1335	39	By analogy with etiocholan-3-one should be deut. sens. and assigned to C_2 or C_4-methylene wag or twist. The $C_{2,4,16}$-d_6 der. however contains a weaker band at this position ($\epsilon^{(a)} = 23$)	**B'**
C'	1318	24	Deut. invar., A-ring skel. vibr.	C
D'	1296	36	By analogy with etiocholan-3-one should be deut. sens. and assigned to C_2 or C_4-methylene wag or twist. The $C_{2,4,16}$-d_6 der. contains no band at this position but does contain a band at 1285 cm.$^{-1}$ of similar intensity ($\epsilon^{(a)} = 37$)	D
E'	1267	66	Deut. sens., C_2 or C_4-methylene wag (or twist)	E
a'	1253^d	61	Deut. invar., D-ring skel. vibr.	A
F'	1246	74	Deut. invar., A-ring skel. vibr.	F
G'	1223	35	Probably deut. sens. but might be identified with inflection in $C_{2,4,16}$-d_6 deriv. (*cf.* analogous behavior of etiocholan-3-one)	G

TABLE III (*Continued*)

Band	ν_{max}	$\epsilon^{(a)}_{max}$	Characteristics and assignment[a]	Identifying letter in ref. 5
c′	1204	58	Deut. invar., D-ring skel. vibr. (Intensified in comparison with etiocholan-17-one)	C
H′,d′	1167	36	Deut. invar. Identified with H′ in etiocholan-3-one and d′ in etiocholan-17-one. May be a rocking vibration of an angular methyl group analogous to ϵ in etiocholane	H,D
I′	1146	35	Deut. invar., A-ring skel. vibr.	I
J′,e′	1095	65	Deut. sens. Overlap of J′, assigned to C_2 or C_4-methylene twist with e′ assigned to C_{16}-methylene wag or twist	J,E
f′	1049	83	Deut. invar. D-ring skel. vibr.	F
g_1'	1017	66	Anomalous doublet possibly attributable to Fermi resonance split of g′ at 1005 cm.$^{-1}$ ($\epsilon^{(a)} = 71$) in etiocholan-17-one. D-ring skel. vibr.	G
g_2'	998	77		
h′	968	21	Deut. invar.	H
i′,K′	830	35	Deut. sens. Assumed to be overlapping pair. i′ assigned to C_{16}-methylene rock and K′ to C_2 or C_4-methylene rock	I,K
j′,π	820[d]	19	Assumed to be overlapping deut. invar. pair. j′ assigned to A-ring skel. vibr. and π to a steroid ring system vibr. Note that in the $C_{2,4,16}$-d_6 deriv., where the i′, K′ pair is absent, two bands are obsd. at 823 and 818 cm.$^{-1}$ which might be separately identified as π and j′, resp.	—J
L′	765	24	Deut. sens., C_2 or C_4-methylene rock	L
k′	710	11	Deut. invar. D-ring skel. vibr.	K

[a] "Deuterium invariant" implies no significant displacement on substitution of deuterium into the methylene groups α to carbonyl. "D-ring skeletal vibration" may include C_{12} and C_{18} (see footnote 16 of text). [b] Carbon tetrachloride solution. [c] In ref. 5, j is identified with band at 965 [η]. [d] Inflection.

tion bands in these ketosteroid spectra can be tentatively assigned to vibrations that are localized in particular regions of the molecule. Such "assignments" may not carry the precise connotation which the molecular spectroscopist associates with that word, nor are they all "group frequencies" in the sense that the organic spectroscopist employs that term when using spectra for structural identification purposes. Nevertheless, this more nebulous concept of vibrations localized within somewhat ill-defined boundaries may be helpful in sorting out such complex spectra, and, in course of time, it may be possible to define more precisely the effective zones associated with these vibrations.

Two other lines of approach to this problem suggest themselves. The hypotheses on which we have based our arguments allow predictions to be made concerning the directions of the electric moments of some of the bands with respect to the molecular axes, and it may be possible to check some of the proposed assignments, particularly in regard to the methylene deformations, by analyses of the polarized infrared spectra of suitably oriented crystals.

A second approach could be made from the intensities of the Raman spectra. It is well established that in simple hydrocarbons, the various methylene C–H deformation vibrations exhibit different intensity relations in infrared and Raman spectra. Thus the unperturbed methylene rock near 720 cm.$^{-1}$ is virtually absent from the Raman spectra of *n*-paraffin hydrocarbons, but the methylene wagging and twisting bands are stronger.[21]

Although these intensity effects could be disturbed by the vicinal ketone group, it might be anticipated that if the assignments made in this paper are correct, bands g and h in the spectrum of androstan-17-one should be relatively more intense in the Raman spectrum, and band k weaker. Bands A and B should likewise be intensified and I and J weakened in the Raman spectrum of androstan-3-one.

When two or more functional groups are present, the technique of adding or subtracting appropriate combinations of the spectra of monofunctional compounds helps in unscrambling these complex spectra and identifying localized absorptions. At the same time it helps to focus attention on those regions of the spectra in which serious departures from such additivity occur. It would be naive to expect that such simple summation methods will hold precisely, and the failure to predict the g_1' band in etiocholan-3,17-dione is a case in point. This technique has also been used effectively to establish that the absorption associated with the side chains of C_{27}-steroids and of bile acid esters can be sorted out from the ring absorption as also can the acetoxy and ketone absorption of steroid keto-acetates substituted in the 3- and 17-positions. These problems will be discussed in more detail elsewhere.

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