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Infrared Spectra of Steroids

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Valuable information about chemical structure obtained in the study of infrared spectra of individual compounds produces a natural increase in the interest of chemists in molecular spectroscopy.

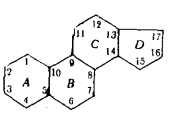
In the Russian literature there are hardly any papers dealing with the infrared spectra of steroids. Furthermore there is not one review on the infrared spectra of the steroids.

This review considers work on the infrared spectra of the steroids during the period from its inception (1939) to 1966.

I. FEATURES OF THE CHEMICAL STRUCTURE OF THE STEROIDS

The main features of the chemical structure of the steroids have now been explained quite definitely. The general principles are reliable, although there are still a greater number of compounds of the steroid series details of whose structure are either unknown or require proof.

The structure of the steroids is based on a complex polycyclic system consisting of three cyclohexane rings and one cyclopentane ring. Such a system is 10,13-dimethylcyclopentanoperhydrophenanthrene, with the accepted numbering of the atoms of the carbon skeleton (I):



(I)

The rings are denoted by the letters A, B, C, and D in accordance with the increasing numbering of the carbon atoms.

There are six asymmetric carbon atoms, so theoretically such a compound can have $2^6 = 64$ stereoisomers but only some of the steroisomeric forms are encountered in natural compounds. From this it follows that the steroid molecules have rigidly fixed spatial conformations, unlike the mobile conformations of cyclohexane.

Sometimes the ring of the steroidal skeleton (ergosterol, 7-dehydrocholesterol, ring B; oestrogen, ring A) contains a C=C double bond. This fixes still more rigidly a definite conformation of the molecule. Despite the non-planar structure of the cyclohexane rings, their combination in a

steroid molecule exhibits a compressed structure—the "thickness" of the plane of the skeleton is ~ 0.8 Å. The cyclohexane rings in the steroidal skeleton have the "chair", not the "boat", conformation.

Free five-membered rings have a non-planar structure thanks to the presence of "Pitzer strain"[1-3]. Clearly, the five-membered ring D in the steroid molecules also has a non-planar conformation, as is shown by certain stereospecific reactions which take place with participation of the functional groups of ring D.

In the sterols and most other steroids side chains of various dimensions are attached to $C_{(17)}$ of the cyclic skeleton.

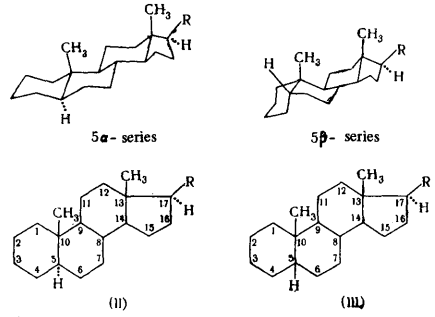
The naming of the steroids depends on the conformation of the cyclic skeleton and the length of the side chain at $C_{(17)}$.

In 1957 the Commission on [the Nomenclature of Organic Chemistry and] the Nomenclature of Biological Chemistry [of the International Union of Pure and Applied Chemistry] issued Definitive Rules for Nomenclature of Steroids.

The conformations of the steroids are distinguished by the type of junction of rings A/B because in all the steroids without exception and their synthetic analogues ring junctions B/C and C/D are the same and are *trans*-fused. Hence there are two steric series of steroids: a series with *trans*-fusion of rings A and B, and a series with *cis*-fusion of rings A and B.

Substituents above the plane of the cyclic system are denoted by the letter β, those beneath the plane by α.

It is easy to see that in the *trans*-fusion of rings A and B the hydrogen atom at $C_{(5)}$ is beneath the plane of the cyclic system, that is, in the α-position (II). With *cis*-fusion at A/B the hydrogen atom at $C_{(5)}$ is in the β-position (III). Therefore the series with A/B *trans*-fusion is termed the 5α-series, and that with A/B *cis*-fusion, the 5β-series.



It has now been shown that in all steroids the side chain at $C_{(17)}$ is in the β position. Unfortunately, investigators working in the field of steroid chemistry have not adhered to unique names for these compounds. Detailed information about the nomenclature of the steroids is given in the Fiesers' monograph[5] and Protiva's paper[6].

A review of the accepted nomenclature of the steroids taking account of the geometrical and optical isomerism has also been given in a special article by Götzky[7] devoted to this question.

II. CORRELATION OF THE INFRARED SPECTRA OF STEROIDS WITH THEIR STRUCTURE

a. C–O Bonds

The C–OH stretching vibrations appear in the infrared spectra of alcohols as an intense band in the 1000–1200 cm^{-1} range. Differences in the position of this band for primary, secondary, and tertiary alcohols were observed by Weniger[8] as long ago as 1910. These researches were continued much later by Tout and Lecomte[9], who also observed a relation between the position of the C–OH band and the structure of the molecule. The more detailed investigations of Zeiss and Tsusui[10] showed the influence of electronic effects and the symmetry of the molecule on the position of this band.

Regular investigations of the infrared spectra of the steroids and particularly the sterols, began about 1946. In one of the first works on the assignment of the bands in the infrared spectra of the sterols, Furchgott and coworkers[11] noted a series of features of the band of the C–OH stretching vibrations. In particular, they showed that the absorption band of the C–O stretching vibrations for the >C–OH group is at ~ 1250 cm^{-1}, but when the carbon atom is connected to only single bonds, the absorption takes place in the 1000–1100 cm^{-1} region. They also reported the important fact of the dependence of the position of the C–O band on the mutual arrangement of the substituents at the third and fifth carbon atoms of the steroid skeleton. Thus the 3β-*trans*-5α- and 3α-*trans*-5β-steroids exhibit a band in the 1047–1058 cm^{-1} region, but the 3α-*cis*-5α-steroids have a weaker band with a maximum at 1064 cm^{-1}. Nevertheless a molecule with two OH groups can show only a single C–O bond absorption band (androstan-3β,17α-diol). The same correlation was found by these authors in a subsequent study[12], where they investigated the infrared spectra of the steroids of the pregnane series. Substances of the pregnane series with the 3β-*trans*-5α-configuration are characterised by a band between 1047 and 1058 cm^{-1}. A hydroxyl in the 3β-position and a Δ^5-double bond always produce a band in the 1058–1064 cm^{-1} range and a $C_{(20)}$ hydroxyl, a band at 1079 cm^{-1}. In another paper by the same authors it was noted that a hydroxyl group at $C_{(21)}$ causes an intense band for the C–OH bond between 1073 and 1078 cm^{-1}. Somewhat later (1952) a coauthor of Furchgott's first three papers (Rosenkrantz) and Zabloy[14] made a more detailed examination of the infrared spectra of the steroidal $C_{(3)}/C_{(5)}$ epimers. These investigations refined the results of the first studies. Moreover the range of compounds investigated was extended. Fig. 1 gives their results for the $C_{(3)}/C_{(5)}$ epimers of androstane. Rosenkrantz and coworkers[15] obtained similar results for cholestane, cholest-2-ene, cholest-4-en-3-one, 7-ketocholesterol, and various other compounds. The corresponding infrared frequencies found by the authors[14,15] for various stereoisomeric forms are:

Coprostanol (3β, 5β)	1041 cm^{-1},
Epicoprostanol (3α, 5β)	1062 and 1040 cm^{-1},
Cholestanol (3β, 5α)	1075 and 1041 cm^{-1},
Epicholestanol (3α, 5α)	1038 and 1004 cm^{-1}.

In another study, Rosenknrantz and coworkers[16] investigated the absorption of C–OH bonds in some unsaturated sterols. They assigned the 1053 cm^{-1} band of Vitamin D_2 to the C–OH stretching vibrations and it is evidently characteristic for the opened ring B. However, this correlation cannot be considered to be completely reliable, since in this range of the Vitamin D_2 spectrum there are other bands which are no less intense[17].

At about the same time, two papers by Cole[18] and Cole and coworkers[19] appeared, the latter deserving special attention. It gave proof of the conformational sensitivity of the band of the C–OH stretching vibrations, illustrated by a rather large number of examples. The authors[19] measured the spectra of 72 different steroids and showed conclusively that the band of the C–OH stretching vibrations

is most intense in the 1000–1100 cm^{-1} range and its position is determined by the conformation of the steroid molecule. Table 1 gives the results of Cole and coworkers[19] which charaterise the dependence of the absorption in the 1000–1100 cm^{-1} range on the structural type of the molecule.

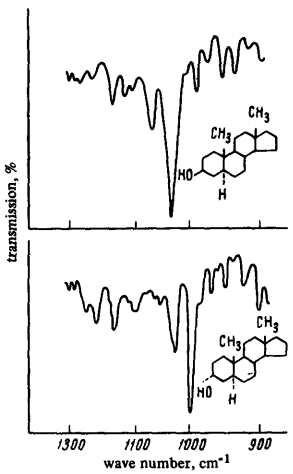


Figure 1. Infrared spectra of $C_{(3)}/C_{(5)}$-epimers of androstane in the 900–1200 cm^{-1} range (see Rosenkrantz and Zabloy[14]).

Table 1. Frequencies of the C–OH stretching vibrations at various orientations of the OH group at $C_{(3)}$ and of the hydrogen atom at $C_{(5)}$ in sterol molecules[19].

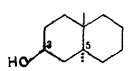
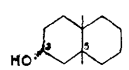
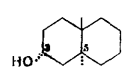
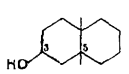
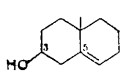
Structural type	Absorption of the most intense band in the 1000–1100 cm^{-1} range	Number of examples
	1037—1040	18
	1036—1040	25
	996—1002	9
	1032—1036	6
	1050—1056	14

Fig. 2 gives the spectra of androstan-3β-ol and coprostan-3α-ol. Both compounds have a *trans*-position for the hydroxyl groups and a hydrogen atom at $C_{(5)}$. As Fig. 2 shows, the side-chain at $C_{(17)}$ has no effect on the position of the maximum of the absorption band for the C–OH stretching vibrations (1039 cm^{-1}). In the same paper they showed[19] that the frequency of this band in hydroxy-steroids also depends on the configuration of the C–O bond itself, and not only on the α- or β-positions of the OH groups relative to the plane of the cyclic part of the molecule. The four possible configurations of the C–O bond, taking account of the αβ-epimers, are shown in Fig. 3, and the corresponding infrared frequencies of the sterols in Table 2.

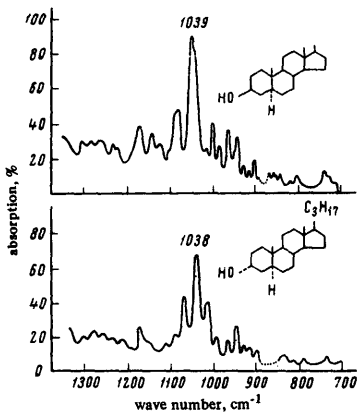


Figure 2. Infrared spectra of androstan-3β-ol and coprostan-3β-ol in the 700–1300 cm^{-1} range (see Cole and coworkers[19]).

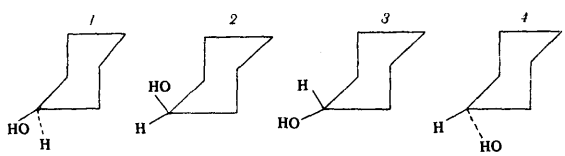
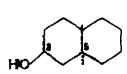
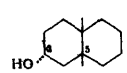
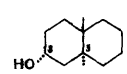
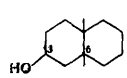
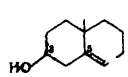


Figure 3. Four possible orientations of the C–O bond in the steroid molecules:
1) β-equatorial; *2*) β-polar; *3*) α-equatorial; *4*) α-polar.

Table 2. Frequencies of the C–OH stretching vibrations for various orientations of the OH group at $C_{(3)}$ and of the hydrogen atom at $C_{(5)}$ and various configurations of the C–O bond in sterol molecules[19].

Type of structure	A/B ring fusion	Configuration		Frequency range, cm^{-1}
		OH	C–O	
	*trans*	3β	equatorial	1037—1040
	*cis*	3α	equatorial	1037—1044
	*trans*	3α	polar	996—1002
	*cis*	3	polar	1032—1036
	Δ^5-double bond	3	equatorial	1050—1056

The frequency of the C–OH stretching vibrations is somewhat greater for the equatorial configuration. This is because an equatorial C–O bond causes some displacement of the $C_{(3)}$ atom along the C–O axis, which produces additional strain and compression of ring A, and this leads to an increase in the frequency of the C–O stretching vibrations. Nothing similar is observed for the polar configuration, since the stretching vibration of the C–O polar bond takes place mainly in the direction normal to the ring. Hence the investigation of the absorption in the range 950–1100 cm^{-1} can provide valuable information about the structure.

True, it must be mentioned that these authors[19] showed that it was possible for bands unconnected with a hydroxyl group to appear in the 1000–1100 cm^{-1} range, but their intensity is always lower. They usually appear for ketosteroids with a C=O group at the $C_{(17)}$, $C_{(7)}$, $C_{(11)}$, $C_{(12)}$, or $C_{(20)}$ carbon atom.

Yet another important work on this problem was published by Rosenkrantz and Scogstrom[20] in 1955. In it they investigated not only the most intense band in the 950–1100 cm^{-1} range but also a series of less intense and closely adjacent bands. Tetrahydrosteroids formed the subject of the investigation. The group of less intense bands situated close to the main band also seemed characteristic for the mutual arrangement of the substituents at $C_{(3)}$ and $C_{(5)}$. The authors[20] give the following results for the absorption of the C–O bond of the tetrahydrosteroids in dependence on the epimeric forms: 3α,5α 1005 cm^{-1}; 3β,5β 1035 cm^{-1}; 3α,5β 1041 cm^{-1}; 3β,5α 1044, 995, 978, and 956 cm^{-1}, depending on the structure of the rest of the molecule. The constant presence of a triplet band in the 3β,5α steroids was associated by the above authors with the possibility of the existence of three spatial orientations of the C–O bond. The possibility of using infrared spectroscopy for determining the spatial arrangement of the C–O bond of sterols was also demonstrated by Heller[21], who illustrated the determination of the polar and equatorial configurations by the example of 22 sterols. Page[22] undertook a similar study of other compounds of the sterol series.

In 1962 Rosenkrantz and coworkers[23] confirmed the earlier correlations by the example of thirteen 19-norsteroids. Unlike the previous studies the spectra of the 19-norsteroids were measured for the solid phase by the technique of the KBr disc. The authors obtained the following values for the infrared frequencies for the various isomeric forms of the 19-norsteroids: 3α,5α 998–1017 cm^{-1}, 3α,5β 1035–1060 cm^{-1}, 3β,5α 1042–1060 cm^{-1}, 3β,5β 1033–1055 cm^{-1}.

The band of the C–OH stretching vibrations is also sensitive to other structural factors. Thus, Meda[24] showed that the epoxide ring has an effect on the free OH group at $C_{(20)}$ but does not affect the absorption of an acetylated OH group in the same position. Jones and Roberts[25] studied the infrared spectrum of various hydroxysteroids. They found the frequencies of the C–O vibrations which characterise the location of the hydroxyl group in the steroid molecule. Jones and Roberts[25] obtained the following frequencies: for OH in the 3β-position and a Δ^5-double bond 1056–1047, 1025–1019, 989–978, 958–953 cm^{-1}; OH in the 17β-position 1059–1046 cm^{-1}; OH in the 20β-position 1100–1090 cm^{-1}; OH in the 20α-position 1016–1008 cm^{-1}. Both 20α,5α- and 20α,5β-steroids have a band in the 957–952 cm^{-1} range, but only the 20α, 5β-epimers are distinguished by a band between 962 and 965 cm^{-1}.

Important successes were achieved in investigating the infrared spectra of the steroidal acetates. Even in an early study of Furchgott[11] it was shown that the >C–O group gives a band for the C–O stretching vibrations close to 1250 cm^{-1}. Subsequently Jones and coworkers[26] studied the dependence of the absorption by the acetate group at $C_{(3)}$ on its *cis*- or *trans*-position in relation to a hydrogen atom at $C_{(5)}$. The decisive role in studying this subject is played by the number of bands of the acetate group (1190–1280 cm^{-1} range). An isolated band in the 1236–1247 cm^{-1} range is observed for all the compounds in which the acetate group at $C_{(3)}$ and the hydrogen at $C_{(5)}$ are in the *trans*-position and also for compounds with a Δ^5-double bond. In every instance when the acetate group occupies a 3β position *cis* to $C_{(5)}$ (3β,5β) there is a triplet band in the range 1200–1250 cm^{-1}. A less expressed triplet band is observed also for the 3α, *cis* to $C_{(5)}$ (3α,5α) configuration[26]. Each of the *trans*- and *cis*-forms has, of course, two stereoisomers, but the latter are readily distinguished by precipitation of the steroid with digitonin, which also determines the configuration at $C_{(3)}$. In another paper, Jones and Herling[27] investigated about 90 spectra of steroidal acetates, which confirmed their previous results. They suggest[26,27] that the reason for the observed differences in the absorption by the C–O bond of the *cis*- and *trans*-compounds is that the *cis*-compounds, which give three bands, can exist as mixtures of rotational isomers produced as a result of the delayed rotation of the acetate group around the C–O bond. As might be expected, when ring A is aromatic, there is a displacement of the band of the C–O stretching vibrations of the acetate group at $C_{(3)}$ to 1205 cm^{-1}.

The characteristic frequencies of the acetate group of steroids was also studied by Fürst and coworkers[28], who confirmed the presence of a triplet band for the 3α-acetoxysteriods. In addition to the 3-acetoxysteroids they investigated[28] the infrared spectra of sterols with acetate groups at $C_{(2)}$ and $C_{(4)}$. It is interesting that in this work[28] the authors ascribe the sterol band in the 1000–1100 cm^{-1} range not to the C–OH stretching vibration but to the deformation vibrations of the O–H bond. Fig. 4 shows the infrared spectra of the sterols and the corresponding acetates.

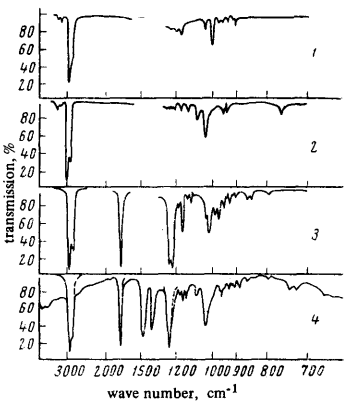


Figure 4. Infrared spectra of 3α-hydroxycholestane (1), 3β-hydroxycholestane (2), 3α-acetoxycholestane (3), and 3β-acetoxycholestane (4) in the 700–4000 cm^{-1} range (see Furst and coworkers[28]).

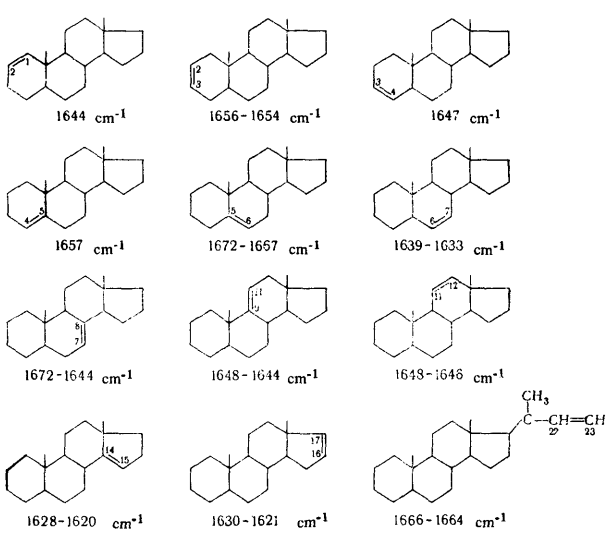
Rosenkrantz[20] obtained similar results, as later did Wotiz and coworkers[29] for 2,3,4-steroidal acetates. The same regularity of absorption was also observed for decanol acetates[30].

b. C=C Bonds

The band for the C=C stretching vibrations in the infrared spectrum is of weak intensity. Its intensity with symmetrical or pseudosymmetrical substitution is especially low. For ethylene and its symmetrical substituted derivatives this band generally does not appear, since it is forbidden by symmetry.

However, in the infrared spectra of such molecules as steroids, which have the lowest symmetry group, the band for the C=C stretching vibrations are sometimes rather sharp and can be suitable for structural conclusions.

Table 3. Frequencies of the C=C stretching vibrations as a function of the position of the C=C bond of the steroid molecule[31].



In the first studies on the infrared spectroscopy of the steroids[11-13] it was shown that the band of the C=C bond lies at 6.0 μm (1667 cm^{-1}) and the conjugation of the double bonds leads to the appearance of a band near 6.2 μm (1613 cm^{-1}). In the same studies[11-13] there were shown to be a difference in the frequencies of absorption by the C=C bond for differences in its position in the steroidal molecule: Δ^5 1671–1667 cm^{-1}, Δ^4 1610 cm^{-1}, Δ^{16} 1597 cm^{-1}, and when the Δ^4 double bond is conjugated with the carbonyl group at $C_{(3)}$ 1616 cm^{-1}.

Somewhat later Jones and coworkers[31] found a similar correlation between the frequency of the stretching vibrations of the C=C bond and its position in the molecule (Table 3).

In another investigation Jones and coworkers[32] confirm the absorption by the Δ^4-double bond of steroids in the 1612–1615 cm^{-1} range when there is a carbonyl group at $C_{(3)}$. The infrared spectra of steroids which contain Δ^5-, Δ^6-, Δ^7-, $\Delta^{5,7}$-, $\Delta^{8(14)}$-, $\Delta^{14(15)}$-double bonds were investigated by Jones and coworkers[33], who found that the compounds with Δ^5- and Δ^7-double bonds give a single weak band at 1600 cm^{-1}. The $\Delta^{5,7}$-sterols, which have two double bonds in conjugation, show two stronger bands at 1607 and 1625 cm^{-1}. Scheer and coworkers[34] found more accurately the characteristic frequencies of $\Delta^{5,7}$ conjugated bonds. They found three bands in the spectra of many steroids: 1575, 1603, and 1629–1624 cm^{-1}.

The dependence of the absorption of the C=C bond on its position in the triterpenoids was studied by Cole and Thornton[35].

The absorption of the Δ^4-double bond in 3,6-diketosteroids[36] lies between 1603 and 1609 cm^{-1}.

The paucity of results on the spectroscopic–structural correlations of the C=C bond is apparently due the the following causes: firstly, the presence and the nature of the double bond is easily found from the ultraviolet absorption spectra; secondly, when there is a hydrogen atom at an aromatic carbon atom the absorption of the stretching and out-of-plane deformation C–H vibrations of the >C–H group is more sensitive to a change in structure than the absorption of the C=C bond itself; thirdly, the weak intensity of the band of the C=C stretching vibrations often creates additional difficulties in studying infrared spectra.

In conclusion we note that the band of the C=C stretching vibrations is always active in the Raman spectra. With non-symmetrical substitution the band of the C=C bond is more intense for the *cis*-isomer than the *trans*-isomer.

c. C=O Bonds

The high intensity, the isolated position in the infrared spectrum, and localised nature of the bands of the stretching vibrations of carbonyl groups makes these bands very convenient for spectroscopic investigations of structure. For the same reason the C=O bands are convenient for theoretical investigations of the dependence of the intensity of the bands on the redistribution of the charges in the molecule during the vibration process[37,38].

The keto-steroids have for the most part been studied from the empirical standpoint. The main problem in these investigations was whether a correlation exists between the number and position of the carbonyl groups and the corresponding absorption in the infrared spectrum, on the basis of an analysis of the spectra of keto-steroids with a known structure.

Significant success was attained in this study mainly thanks to the work of Norman Jones, whose investigations into the infrared spectroscopy of steroids can justifiably be considered classical. Earlier investigations of the infrared spectra of the steroids had shown that the frequency of the C=O stretching vibrations depends on the position of the C=O group in the keto-steroid molecule[11-13,39]. The following correlations were established in these studies:

$C_{(3)}$=O of steroids of the pregnane series	1739 cm^{-1},
$C_{(3)}$=O and Δ^4 double bond	1675–1672 cm^{-1},
$C_{(20)}$=O	1704–1712 cm^{-1},
$C_{(20)}$=O and Δ^{16} double bond	1675 cm^{-1}.

(the numbers at the carbon atoms show the numbers of the atoms according to the accepted numbering of carbon atoms in steroids).

Jones and coworkers[32] obtained more detailed information:

Nature of the bond		Frequency of the stretching vibrations, cm^{-1}	Number of examples
Non-conjugated	$C_{(3)}$=O	1717–1719	11
ditto	$C_{(20)}$=O	1706–1710	21
"	$C_{(17)}$=O	1742–1745	14
Conjugated	$C_{(3)}$=O	1674–1677	17
ditto	$C_{(20)}$=O	1666–1670	5

The diketo-steroids mainly have two bands, each of which corresponds to an individual C=O group[32].

In a later investigation Jones and another group of authors[40] completely confirmed the results of the previous work and also investigated some other keto-steroids. The following information was added:

Nature of the bond	Frequency of the stretching vibrations, cm^{-1}	Number of examples
Non-conjugated $C_{(11)}$=O	1710–1716	21
$C_{(7)}$=O	1719*	3
$C_{(12)}$=O	1710	2
Simultaneous presence of $C_{(11)}$=O and $C_{(17)}$=O	1751–1754	5
21-Acetoxy-group and $C_{(20)}$=O	1756–1758	4

* Rosenkrantz[15] obtained the same result later (17121 cm^{-1}).

Finally the generalising work of Jones and coworkers[41] appeared a year later (1950). The results of the previous studies were again confirmed and perhaps only some new results need be stated:

Nature of the bond	Frequency of the stretching vibrations, cm^{-1}	Number of examples
$C_{(16)}$=O	1745	5
$C_{(7)}$=O	1713–1714	7
$C_{(20)}$= and $C_{(21)}$-acetoxy	1756–1758	12
$C_{(6)}$=O	1713–1714	3
$C_{(12)}$=O and $\Delta^{9(11)}$-double bond	1680–1684	4

Approximately the same results were obtained later by Rosenkrantz and coworkers[16,20].

The carbonyl band of an acetate group in the side-chain of a steroid[40] appears at 1742 cm^{-1}, more rarely at 1739 cm^{-1}.

Replacement of a hydrogen atom close to a C=O group by halogen leads to a drop in the frequency of the C=O band[42], by 7 cm^{-1} for 17α-bromo-3β-hydroxy-5α-androstan-16-one, and by 17 cm^{-1} for the corresponding 17β-5α-epimer.

The carbonyl absorption of the steroids of the cholestane series which contain an acetate group was investigated by Fürst and coworkers[28]. Their results[28] suggest that irrespective of the position of the acetate group the carbonyl absorption of this group is strictly localised in the 1734–1740 cm^{-1} range. However, for the 3α- and 3β-acetates of the pregnane series Jones and coworkers[43] found the absorption of C=O between 1735 and 1732 cm^{-1} that is, somewhat lower.

Other results of Jones[44] and of Josien and coworkers[45,46] confirmed the correctness of the assignment of the carbonyl frequencies of the keto-steroids.

Depending on the molecular environment it seemed possible to characterise about 130 types of carbonyl systems of steroids according to their characteristic infrared frequencies. This work was carried out by Jones and Herling[47].

Bellamy and Williams[48], in studying the infrared spectra of keto-sterols noted that the frequencies of the C=O stretching vibrations of these substances are somewhat less (by 6–15 cm^{-1}). The authors[48] explained this by the formation of an intramolecular hydrogen bond C=O....HO. However, directly contradictory results were obtained by Jones and Robertson[49] for the 16,17-ketols of steroidal origin. In this work it was found that in the presence of hydroxy- and acetoxy-groups near to a C=O group there is an increase in the frequency of the C=O stretching vibrations by approximately 10 cm^{-1}. This problem apparently requires further precision.

The number of carbonyl groups could be determined by measurement of the integral intensities. By integral intensity is usually meant the total area bounded by the absorption band. For several monoketo-steroids the integral intensities of the C=O band were found by Jones and coworkers[50]. These results are given in Table 4.

Table 4. Integral intensities of the band of the C=O stretching vibration in the infrared spectra of monoketo-steroids[50].

Type of carbonyl group	Value of the integral intensity for various compounds, 10^4 litre $mole^{-1}$ cm^{12}	Mean value
C_3=O	2.63; 2.41; 2.39; 3.62;	2.55
C_7=O	2.17; 2.15	2.16
C_{12}=O	2.27	2.27
C_{17}=O	2.52; 2.72; 2.81; 2.64; 2.54; 2.91; 2.69	2.69
C_{20}=O	1.75; 1.84	1.80
C_3=O and Δ^4-double bond	2.88; 3.04; 3.67; 4.02; 3.39; 3.51; 3.67; 3.70; 4.11	3.65
Acetate group	3.15; 3.06; 3.14; 3.27; 3.39; 3.41	3.24

Then on starting from the integral intensities of the C=O band of the monoketosteroids, the integral intensities of the C=O absorption of the di- and poly-carbonyl steroids were calculated by an additive scheme. The results of these calculations and the directly observable integral intensities of some polyketosteroids are compared in Table 5.

Dvoryantseva and Sheinker[51] carried out a more concrete study, the aim of which was to determine the number of keto-groups in steroidal ketones.

Table 5. Integral intensities of the bands of the C=O stretching vibrations in the infrared spectra of di- and poly-carbonyl steroids[50].

Number and position of the carbonyl groups of the compounds	Infrared absorption maximum, cm^{-1}	Integral intensity of absorption, 10^4 litre $mole^{-1}$ cm^{-2}	
		calculated from the results in Table 4	observed
C_3=O and C_{17}=O	1719 1745	5.24	5.19
C_3=O and C_{20}=O	1719 1710	4.34	4.45
C_3=O; C_{20}=O and C_{12}=O	1712	6.61	6.93
C_3=O; C_{20}=O and Δ^4-double bond	1708 1677	5.44	5.90
3,20-diacetate	1739	6.48	6.21
3,16,20-triacetate	1739	9.72	9.05

The absorption of the carbonyl groups having various positions in the triterpene skeleton was studied by Cole and Thornton[35]. The effect on the absorption of the conjugation of a double bond with a C=O group was noted. In two papers of Tarpley and Vitiello[52] the influence of the solvent on the position of the bands of the C=O stretching vibrations in the infrared spectra of steroids was studied. The authors[52,53] measured 56 spectra in CS_2, CCl_4, $CHCl_3$, CH_2Br_2, and $CHBr_3$ solutions.

Recently a series of papers has appeared[54–59] on a study of the isotopic shift of the C=O frequency in the infrared

spectra on replacing ^{16}O by ^{18}O. In all instances a drop in frequency by 20–40 cm^{-1} is observed. Simultaneously there is an increase in the intensity of the displaced bands by ~20%.[59] The use of isotopic replacement of oxygen in keto-steroids could give interesting results in the near future.

As regards the other types of vibrations of the C=O bond, evidently they can also appear in the infrared spectrum. Thus Weinmann[60], by measuring the spectra of twenty-three 20-keto-steroids in the 450–800 cm^{-1} range, assigned the band between 588 and 597 cm^{-1} to C=O planar deformation vibrations. For a conjugated keto-group the frequency of this band is increased to 650–655 cm^{-1} and in the presence of an acetoxy-group at $C_{(21)}$ two bands are observed: at 604–600 and 640–648 cm^{-1}. The orientation of an acetoxygroup in steroid acetates was determined from the absorption in this range[61].

d. C–H Bonds

The C–H stretching vibrations appear in the infrared spectra of all organic compounds in the 2750–3100 cm^{-1} range. The bands of the vibrations of the C–H bonds of the methyl, methylene, and ethylene groups differ in frequency and can be differentiated in the infrared spectrum. Furthermore there is a series of different types of vibrations for the same bonds. Such different types of vibrations also differ in frequency. Fox and Martin[62,63] assigned the bands to different forms of C–H vibrations and the assignment was subsequently confirmed by other investigators[64–66].

The following frequencies of the C–H stretching vibrations were found for steroids: 2985, 3080 (for the $\gtrless$C–H structure), 2941 cm^{-1}.[11,12,32,33] The C–H bonds of the aromatic carbon atoms of steroids of the cholestane series give a band for C–H stretching vibrations at 3050 cm^{-1}.[33]

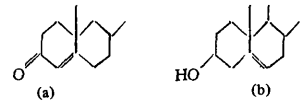
For the $\Delta^{4,6}$-3-keto steroids absorption analogous in nature is found at 3028 cm^{-1}, but for the Δ^{4}-3-keto steriods there is a weak band at 3034 cm^{-1}.

The increase in the frequency of the C–H stretching vibrations is a general phenomenon in the infrared spectra of polycyclic systems. Avram and coworkers[68] investigated this problem in detail, and in 27 polycyclic compounds found an increase in the frequency of the C–H stretching vibrations by 20–100 cm^{-1}. They thought[68] the reason for this is a change in the hybridisation of the electronic orbitals, which is expressed in the fact that the C–C bonds acquire a more and more marked p-character and the C–H bonds acquire an s-character, right up to sp^2 hybridisation.

Despite the fact that there is much information on the infrared spectra of steroids in the range of C–H stretching vibrations, these results do not give particularly valuable information about structure. However, from the absorption in the 2750–3100 cm^{-1} range methyl, methylene, and ethylene groups can be identified and by measuring the integral intensities the number of corresponding groups can be determined.

In studying the infrared spectra of steroids much more attention was and is being paid to the deformation vibrations of C–H bonds.

In even one of the first papers on the infrared spectroscopy of the steroids[7] it was shown that the ranges of the deformation vibrations of the methyl and methylene groups are respectively 1379–1389 and 1429–1481 cm^{-1}. The same investigation showed that steroids with structural formations of types (a) and (b) absorb at 870 and 840 cm^{-1} respectively (the range of the out-of-plane deformation vibrations of the ethylenic C–H bonds).



(a) (b)

Later this correlation was confirmed by other authors[15–16]. Jones and Cole specially considered[69] the problem of the absorption by methyl and methylene groups in steroid spectra. Their results are shown in Fig. 5, where the absorption by the methyl and the methylene groups of androstane are sharply differentiated. Hence their

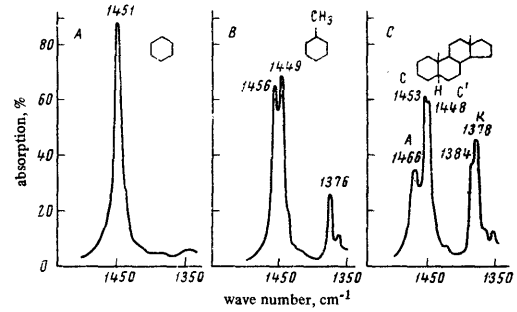


Figure 5. Infrared spectra in the range of the deformation vibrations of the methyl and methylene groups:
A) cyclohexane; *B*) methylcyclohexane; *C*) androstane[65].

results[69] show that the deformation vibrations of methylene groups give a band at ~ 1450 cm^{-1} and the angular methylene groups gives the doublet of bands at 1384 and 1378 cm^{-1} (confirmed by the spectra of many simple steroids which contain two angular methyl groups). However, their spectra of ten steroids which do not have a methyl group at $C_{(10)}$ (19-norsteroids) show a band only in the 1375–1378 cm^{-1} range. This observation allows the bands of the individual methyl groups to be identified:

CH_3 at $C_{(10)}$ 1375–1378 cm^{-1},
CH_3 at $C_{(13)}$ 1384 cm^{-1}.

We will quote some other correlations found by Jones and Cole[69]:

CH_2 group of keto-steroids	1400–1440 cm^{-1},
CH_2 group in a side-chain	1466–1469 cm^{-1},
CH_3 group in a side-chain attached to different atoms	1368 cm^{-1},
CH_3 group in a side-chain attached to a single atom	1380 cm^{-1},
CH_2 group of the cyclic part of the molecule	1448–1456 cm^{-1}.

In addition the authors investigated the region of absorption of an acetate methyl group (doublet band sensitive to the position of the acetate group in the molecule) and the effect of double bonds on the absorption of the methylene groups. Hence individual methyl and methylene groups of steroids could be identified from the infrared spectrum in the 1300–1500 cm^{-1} range. An example in this respect is the spectrum of 19-norpregn-4-en-3,20-dione (Fig. 6) which distinctly shows the absorption by different functional groups and even of the same functional groups found in different atomic environments. These results are confirmed in another paper[43] where the assignment of the bands is checked with the aid of selective deuteration. At about the same time Jones and coworkers[70] undertook the work of

assigning the bands in the infrared spectra of steroidal sapogenins. The range 1408–1435 cm^{-1} was given in a later work of Jones and coworkers[71] for absorption by the methylene group of the $CO-CH_2$ structure of $C_{(19)}$-keto-steroids.

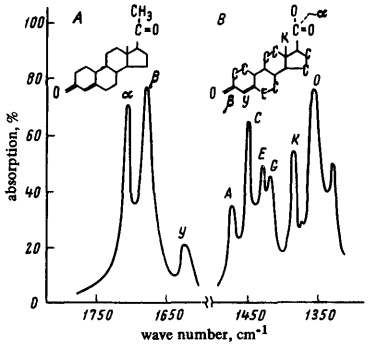


Figure 6. Infrared spectra of 19-norpregn-4-en-3,20-diol in the 1300–1800 cm^{-1} range[69]. *A*) and *C*) methylene groups of the cyclic part of the molecule at $C_{(1)}$, $C_{(7)}$, $C_{(11)}$, $C_{(12)}$ $C_{(14)}$, and $C_{(15)}$; *G*) methylene group at $C_{(2)}$ (influence of $C_{(3)}$=O); *E*) methylene group at $C_{(6)}$ (influence of Δ^4-double bond); *K*) angular methyl group at $C_{(13)}$; *O*) CH_3 at $C_{(21)}$ (characteristic frequency of the structure $H_3C-C=O$); α) and β) $C_{(3)}$=O and $C_{(20)}$=O keto-groups respectively; γ) $C_{(4)}=C_{(5)}$ double bond.

Much attention was paid to the absorption by C–H in unsaturated steroids. The deformation vibrations of the hydrogen atoms connected to aromatic carbon atoms occupy the range 650–1000 cm^{-1}, very sensitive to the molecular structure, in particular, to the location of the double bonds of the molecule. Thus for Δ^{22}-steroids which contain a double bond in the side-chain (ergosterol, vitamin D_2)[17,72], absorption in the 970–974 cm^{-1} range is characteristic. At the same time for steroids which do not have a Δ^{22}-double bond this band is absent (this is evident on comparing the spectra shown in Figs. 7–11).

The difference in the absorption of the C–H deformation vibrations for different positions of the double bond in steroids was found by Furchgott and coworkers[12,13]. Jones and coworkers[33], and then Hirschmann[73] investigated the spectra of steroids with Δ^5-, Δ^7-, or $\Delta^{5,7}$-double bonds in ring B. All the steroids with a Δ^5-double bond are characterised by a 798–803 cm^{-1} band. The $\Delta^{5,7}$-steroids have a characteristic doublet at 800 and 840 cm^{-1}. The Δ^7-steroids show only one band[33], at 835–840 cm^{-1}. Evidently the band at 800 cm^{-1} is from the $C_{(6)}$–H bond and the band at 835–840 cm^{-1} from the $C_{(7)}$–H bond.

Jonson and coworkers[33] also studied the influence on the absorption in this region of the hydroxy- and acetoxy-groups at $C_{(3)}$ and found a characteristic doublet for 3-acetoxy-Δ^4-steroids at 800 and 812–815 cm^{-1}.

The same results in assigning the bands in the infrared spectra of the steroids in the 700–1000 cm^{-1} range were obtained by authors of both earlier[74,75] and later[34,76,77] studies.

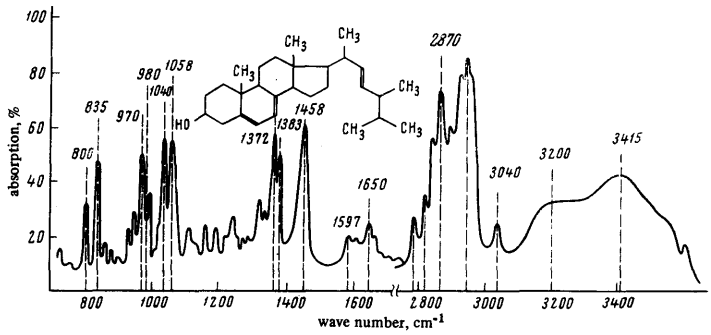


Figure 7. Infrared spectrum of the provitamin D_2 (ergosterol) in the range 700–1400 cm^{-1}.

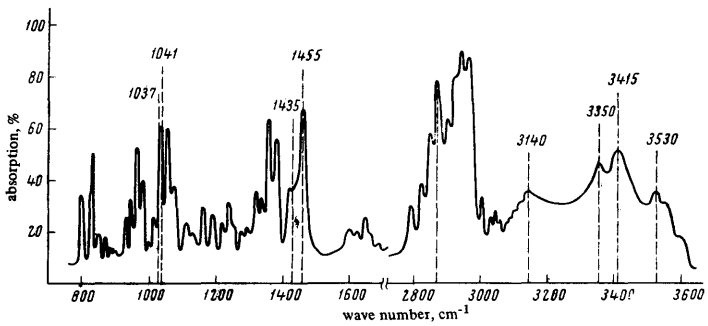


Figure 8. Infrared spectrum of ergosterol in the 700–4000 cm^{-1} range at −183°C.

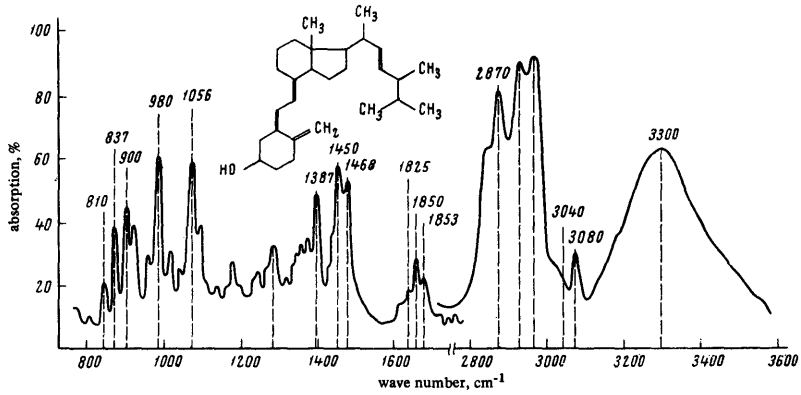


Figure 9. Infrared spectrum of vitamin D_2 in the 700–4000 cm^{-1} range.

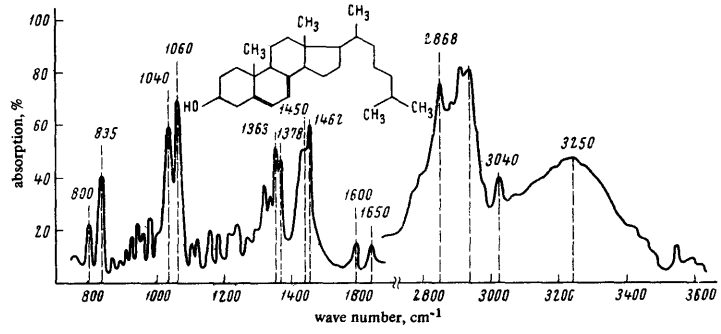


Figure 10. Infrared spectrum of the provitamin D_3 (7-dehydrocholestane) in the 700–4000 cm^{-1} range.

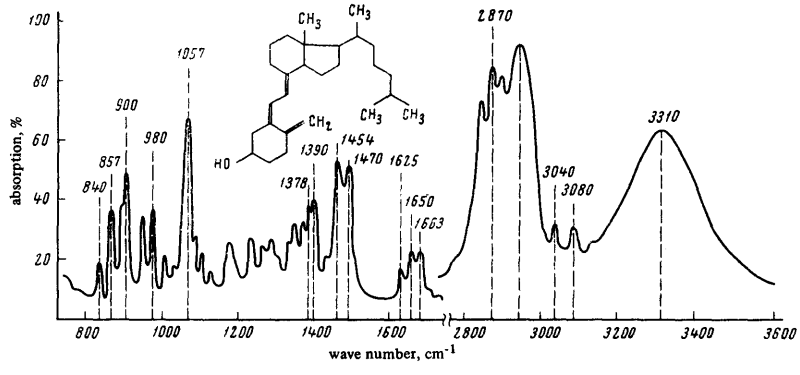


Figure 11. Infrared spectrum of vitamin D_3 in the 700–4000 cm^{-1} range.

When an ethylene bond is conjugated with a carbonyl group, the frequency of the C–H out-of-plane deformation vibrations is raised to the 867–904 cm^{-1} range[78].

Meda and coworkers[79] found a characteristic band in the 860–847 cm^{-1} range for pregn-4-en-16,17epoxy-steroids. This band can be assigned to the out-of-plane deformation vibrations of the $C_{(4)}$–H bond, but Meda and coworkers[79] evidently hold another opinion, since this band is proposed by them for the identification of the epoxy-group.

e. O–H Bonds

Free hydroxyl groups of alcohols in solutions are responsible for the appearance of a narrow absorption band in the 3610–3636 cm^{-1} range. For hydroxy-steroids the region of absorption of the O–H stretching vibrations is rather variable and depends considerably on structure and on the nature of the intermolecular interaction. Furchgott and coworkers[11] found the absorption of the O–H stretching

vibrations at 3597–3344 cm^{-1} for the steroids which they investigated. For the hydroxy-steroids of the pregnane series the same authors give a somewhat different region: 3572–3448 cm^{-1}. Rosenkrantz and Zabloy[14] found a band for O–H stretching vibrations of steroids at 3679 cm^{-1} and showed that a change in solvent can lead to a displacement of the band to 3445 cm^{-1}.

For cholestanol derivatives Jones and coworkers[33] observed the band of the free OH group at 3620 cm^{-1}.

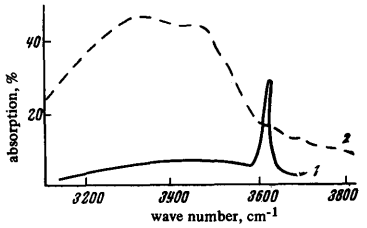


Figure 12. Infrared spectrum of ergosterol in the range of the stretching vibrations of the O–H bond: *1*) solution in CCl_4; *2*) solid phase.

In studying steroids with an aromatic ring A, Pickering and Werbin[77] found that an OH group at $C_{(3)}$ gives a band for O–H stretching vibrations at 3230–3335 cm^{-1}, and on OH group at $C_{(17)}$, one at 3415 cm^{-1}.

Dalton and coworkers[80] observed an increase in the splitting of the absorption bands of the O–H stretching vibrations from a slight shoulder for C_2H_5OH to a well differentiated band of almost equal intensity for 5α-cholestanol. It is suggested[80] that such a splitting occurs thanks to the conformational complexity of the structure of the molecule.

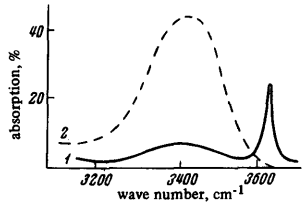


Figure 13. Infrared spectrum of 7-dehydrocholesterol in the range of the O–H stretching vibrations: *1*) solution in CCl_4; *2*) solid phase.

The influence of solvent on the frequency of the O–H stretching vibrations in the infrared spectra of the steroids was studied by Horak and Faikos[81]. The authors of the present review observed that for steroids the band of the free hydroxyl group lies at 3620 cm^{-1}. However, it can only be detected in the spectra for solutions where the molecules of the sterols are in monomeric form. In the spectra of the solid phase this band is absent, but a broad intense band appears between 3100 and 3600 cm^{-1}, due to intermolecular hydrogen bonds (Figs. 12 and 13). Hence the formation of large associates of molecules maintained by hydrogen bonds are inherent for steroids in the crystalline state. In addition to OH groups, the π-electrons of double bonds can participate in the formation of double bonds, for the spectroscopic manifestation of a hydrogen bond in the spectra of crystalline sterols which contain different numbers of C=C bonds is different. The structure of the hydrogen bond band (Fig. 8) is resolved in spectra at low temperature (–183 °C), showing that several types of intermolecular aggregation are realised simultaneously.

f. C–C Bonds and Large Fragments of Molecules

The bands of the stretching vibrations of simple carbon–carbon bonds are of low intensity and lie in the infrared spectrum below 1200 cm^{-1}. The general regularity of the absorption in this region was investigated by Brown and coworkers[82]. The possibility of the use of the band for the C–C stretching vibrations in studies of structure was investigated by McMurry and Thornton[83].

Jones and coworkers[76] found the frequency of the skeletal vibrations which characterise two different structural types of keto-steroids. Josien and coworkers assign the bands at 794 and at 811 cm^{-1} to the vibrations of the cyclopentane ring of 3,5-methylenesteroids.

The band for the deformation vibrations of the C=C bonds lies in the infrared spectrum below 600 cm^{-1} and has not yet found a use in structural spectroscopy.

III. USE OF INFRARED SPECTROSCOPY IN STEROID CHEMISTRY

In most studies of the infrared spectra of steroids carried out up to the 1950's only the nature of the absorption and the known structure of the molecule were connected.

The results on the infrared spectroscopy of steroids have been surveyed in atlases of spectra[85,86], repeatedly checked. The spectroscopic–structural correlations which have been deduced and repeatedly confirmed have enabled molecules of unknown structures to be introduced into the field of the infrared spectroscopy of steroids. Hence since the 1950's infrared spectroscopy has been widely used for revealing the most varied problems of the structure of natural steroids and their synthetic analogues. The examples cited below illustrate the great possibilities and occasionally the necessity of using infrared spectroscopy in investigating the structure and conversions of the steroids.

1. Sterols

The most diverse problems of the steroid chemistry have been solved by analysis of their infrared spectra. Information on the absorption by the hydroxyl groups of sterols has appeared in Soviet[87] and foreign[88] literature.

Specific absorption of the OH groups is observed in the spectra of the cardenolides[89] and glycosides[90]. The infrared spectra of the sterols are used both for identification and for solving structural problems[92]. Thus Fudge and coworkers[93] used the infrared spectra for finding the structure of 5-hydroxy-derivatives of cholestane[93]. The results from molecular spectroscopy were used to determine the orientation of the hydroxyl group itself in molecules of natural sterols[94] and also for investigating the structure of cerebrosterol[95], 20-ketosteroid-3,11-diols[96], lanosterol and its derivatives[97,98], β-spinasterol[99], and derivatives of ergosterol[100].

The hydroxyl groups of steroids are capable of forming both intramolecular and intermolecular hydrogen bonds. From the infrared spectroscopy results the presence of intramolecular hydrogen bonds in 7-hydroxycholesterol was established between the 3-OH and 7-OH hydroxyl groups[101] and in steroidal 3,5-*cis*-diols between the 3-OH and 5-OH hydroxyl groups[102] (there are no hydrogen bonds in the 3,5-*trans*-diols), and in cholesterol and epicholesterol between the OH groups and the π-electrons of the double bonds[103].

Bernstein and coworkers[104] used infrared spectra to study 7α-hydroxysteroids. Infrared spectroscopy has been widely used in the investigation of steroidal diols[105-109] and triols[110-112], and also new sterols[113].

Infrared spectra were used successfully to study the structure and conversions of sterols of un-natural conformation, particularly lumisterol[114-117], which is an important intermediate in the photosynthesis of the vitamins of group D.

2. Unsaturated Steroids

In studying the unsaturated steroids the infrared spectra in the ranges 700–1000 cm^{-1} ($\diagdown\!\!\diagup$C–H out-of-plane deformation vibrations) and 1550–1650 cm^{-1} (C=C stretching vibrations) are used.

The presence and position of C=C double bonds was shown by infrared spectra for derivatives of allopregn-6-ene[118], Δ^{11}-unsaturated steroids[119], and 1-dehydrosteroids[120]. Levin and coworkers[121] studied the conformation of $\Delta^{5(10)}$-unsaturated steroids. The infrared spectra found application for studying the structure and conversions of steroidal hormones[122-126], derivatives of vitamin D_2,[127] $\Delta^{5,7}$-steroids[128,129], and steroids with an aromatic ring A.[130] Elks[131], and also Henbest and Wilson[132] studied steroidal trienes. Bergman investigated the infrared spectra with the aim of identifying C=C bonds in the side-chain of 22-, 24-, and 25-dehydro-derivatives of cholesterol[133,134]. The results of molecular spectroscopy were used to study the conformation of the D rings in Δ^{14}-unsaturated steroids[135]. Absorption in the 700–1000 cm^{-1} range was used to find certain features of the structure of $\Delta^{3,5}$-steroids[136]. Information has also been obtained about the spectra of synthetic steroidal hormones[137] and their derivatives[138].

3. Steroidal Ketones

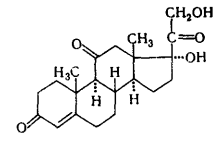
The infrared spectra of steroidal ketones have been widely used both for the identification[139-141] and for elucidating the structure[142-145] of steroids. The principal task of these spectroscopic investigations was naturally to find the presence and position of the carbonyl groups. In the chemistry of steroidal ketones infrared spectra are usually the main test of an investigation of the structure and of the mechanism of chemical reactions in which C=O groups participate.

Infrared spectra are used successfully in studying 3-keto-steroids[146-148], 7-keto-steroids[149], the conversions of 11-keto-steroids[150-152], and 15- and 20-keto-steroids of the pregnane series[153].

The results from infrared spectroscopy allowed the isomerisation of unsaturated ketones to be observed[154] and also the structure and conversions of various steroidal diketones to be investigated[155-161].

On the basis of the results of infrared spectroscopy, Baron and le Boulch[162] studied the structure of intermediate products between cholesterol and the "ketone 250" known in steroid chemistry.

Cortisone (IV) occupies a special place in the chemistry of steroidal ketones—it is the most important of the corticosteroidal hormones. After the discovery of the therapeutic action of this hormone intensive attempts to synthesise cortisone and its analogues were made.

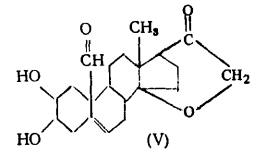


(IV)

In many of these studies the results from infrared spectroscopy of cortisone itself[163] and of its derivatives[164-167] were used fruitfully. With the aid of infrared spectra certain problems in the synthesis of cortisone were solved[168-171], and in particular the problems of the structure of intermediates in the synthesis[172,173].

4. Epoxysteroids and Lactones

In 1953 Gunthard and coworkers[174] proposed a method of distinguishing the stereoisomers of steroidal epoxides by their infrared spectra. Later with the aid of infrared spectroscopy features in the structure of steroids containing a seven-membered lactone ring were established[175]. On the basis of a study of infrared spectra, the structure of digifologenin[176] (V) together with certain other steroids having a five-membered lactone ring as ring D was established.



(V)

Many studies have employed infrared spectra to draw conclusions about the structure of other steroidal lactones[177-182] and epoxysteroids[183-188]. Infrared spectra have also been used to establish the structure of new synthesised lactones[189-191] and epoxysteroids[192]. Henbest and Wrigley[193] studied the reaction of 5,6-epoxysteroids with the complex $BF_3.Et_2O$ on the basis of the results from infrared spectroscopy. A large number of results from infrared spectroscopy was used for solving the problems of the synthesis of an important hormone of adrenal cortices—aldosterone[194-200]. Several studies were also devoted to the infrared spectra of steroidal sapogenins[201-209].

5. Methyl- and Methylene-steroids. Steroidal Acetates

Steroids which contain methyl and methylene groups as angular substituents and substituents in side-chains are conveniently investigated by the methods of molecular spectroscopy thanks to the specific absorption by these functional groups.

Certain structural aspects of this type of absorption were considered in Cole's review[210]. The problems of the structure of 3-methylcholestanol and its photo-derivatives was considered by Barton and coworkers[211]. Several authors give information about the infrared spectra of steroids which contain methyl substituents in the most varied positions in relation to the steroidal skeleton of the molecule: 6,[212,213] 7,[214] 16,[215,216] 20,[217] 9α,[218] 17α,[219,220]

17β,[221] 4α,[222] etc. There are also spectrographic results used in studying dimethyl-[223-225] and methylene-[226,227] steroids.

Since the infrared frequencies of the acetate group are sensitive to its stereochemical location in the molecule, the infrared spectra are often used in studying the structure[228-230], synthesis (acetylated derivatives of cortisone[231-233]), and conversions[234,235] of steroidal acetates and diacetates[236].

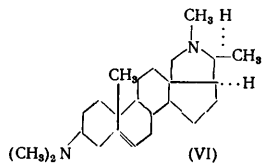
6. Halogenosteroids

The infrared spectra of the bromo-derivatives of steroids have been studied best, those of the iodo-derivatives worst. However, this is not paradoxical, the earliest information concerns iodosteroids; from an analysis of infrared spectra Djerassi and Lenk[237] proved the structure of intermediates in the synthesis of 21-iodo-Δ^{16}-20-ketosteroids. Infrared spectroscopy was used to investigate the bromination of sapogenins[238], bromosteroids of the cholane[239] and androstane[240] series, the configuration of the $C_{(17)}$ substituents in 16-ketoandrostan-6-ol[241]†, the conversion of 17α-acetoxy-16β-bromo-20-ketosteroids[242], the mechanism of bromination of keto-steroids[243-244] and certain other problems[245-247].

The infrared spectra of fluorosteroids have also been fairly well studied[248-253]. Less information is available on the infrared spectroscopy of chloro-steroids[254-256].

7. Nitrogen-Containing Steroids

Nitrogen enters into the composition of the molecule of many natural and modified steroids. It can be found in the steroids both as hetero-atoms in the rings and in the composition of various groups of angular substituents. A good example is conessine (VI), the infrared spectrum and structure of which were investigated by Phillips and Johnson[257].



(VI)

Results from infrared spectroscopy were also used in studying the synthesis of conessimine from conessine[258]. The infrared spectra of nitrogen-containing steroids were characterised by various chromophores, including nitrogen atoms: imine[259] (>C=NH–) 1638 cm^{-1} diazochromophores[260] (–$\overset{+}{N}$=N–) 2080 cm^{-1}, and the cyano- (nitrile-) chromophore[261-263] (–C≡N–) 2237 cm^{-1}.

The molecular spectra of nitrogen-containing steroids have now been reliably interpreted and are used in investigations of aza-steroids[264-267] nitro-steroids[268-270], amino-steroids[271], and hydroxyiminocholane acids[272].

8. Conversions of Steroids

Various changes in the structure of steroids are positively reflected in the infrared spectra. This disclosed the possibility of judging the converions of steroids from the changes in their infrared spectra. The results of this nature are available for steroids modified in the most diverse ways.

Thus Bladon and coworkers[273] observed a change in the infrared spectra of steroids subjected to reduction with sodium amalgam. Several studies are devoted to the infrared spectra of steroids modified by photochemical action[274-277].

Shoppee and coworkers often used infrared spectroscopy in a series of studies they made into the Walden inversion in reactions of compounds of a steroidal nature[278-280]. Infrared spectroscopy has been extensively used in studying the most varied conversions of steroids brought about by micro-organisms[281-291].

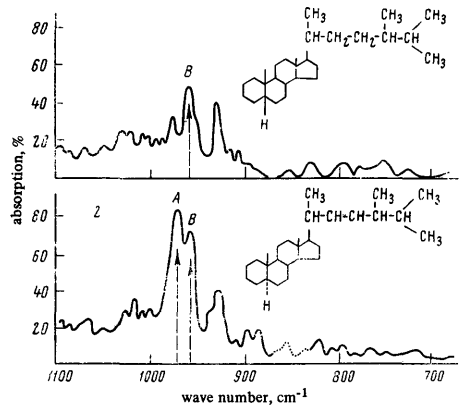


Figure 14. Infrared spectra of ergostane (1) and of ergost-22-ene (2) in the 700–1300 cm^{-1} range[168].

9. Some Particular Structural Problems

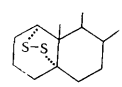
Infrared spectroscopy has been used successfully to solve some particular problems of structure, conversions, and metabolism of steroids.

The first of such studies were made by Jones as long ago as 1950.[72] In it, the absorption in the range 970–974 cm^{-1} showed that for ergost-22-ene the side-chain in $C_{(17)}$ steroids which contain a Δ^{22}-double bond has a *trans*-configuration relative to this bond (Fig. 14). For the *cis*-configuration absorption took place in the 670–800 cm^{-1} range.

Taub and coworkers[292] studied the side chain of corticosteroids from the absorption in the infrared range. Dobriner and coworkers[293] studied the metabolism of previously deuterated steroids from the band of the C–D stretching vibrations in the 2145–2165 cm^{-1}.

On the basis of infrared spectra Mateos and Chao[294] determined the form of ring D in certain steroid molecules.

Tweit and Dobson investigated the spectra of steroids with a trans-annular S–S bridge (VII) in ring A[295]:



(VII)

† This reference (241) does not mention 16-ketoandrostan-6-ol nor infrared spectroscopy! (Ed. of Translation).

Information on absorption in the infrared range of the spectrum was used in studying the structure of the most varied steroids, in particular, digacetinin[296], kitigenin[297], β-anhydrogromphogenin[298], steroidal nucleotides[299], steroidal glucosides[300-302], stereoisomers of prednizolone[303], and steroids with a butenolide ring[304,305]. An atlas of infrared spectra was recently published[306] which contains, in addition to the spectra of coumarins, flavonoids, and anthraquinones, 44 spectra of cardenolides—steroids which exhibit a butenolide ring. The infrared spectra have also found application in studying natural 24-alkyl steroids[307] and steroids isolated from marine products[308,309].

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In conclusion it should be noted that the material surveyed in the present review far from exhausts the possibilities of the infrared spectroscopy of steroids. In addition to the structural aspect and identification, infrared spectroscopy can be used for other purposes. However, the space for the present review does not permit consideration of all possible applications of the molecular spectroscopy of steroids.

In recent years the chemistry of steroids has been enriched by physical methods of investigation. Many authors employ in their investigation not only infrared spectroscopy but also the results of ultraviolet spectroscopy, optical rotatory dispersion, and circular dichroism, and electron paramagnetic and nuclear magnetic resonance. However, the value of the infrared spectra of the steroids is not diminished by this, since the combined use of all the above physical methods of studying structure gives, of course, a considerably more detailed information about steroid molecules than any method used in isolation.

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