[CONTRIBUTION FROM THE DIVISION OF PURE CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL OF CANADA]

The Characterization of Methyl and Methylene Groups in Steroids by Infrared Spectrometry. II. Methyl and Methylene Bending Frequencies in Steroids Labeled with Deuterium[1]

BY R. NORMAN JONES, A. R. H. COLE[2] AND B. NOLIN[2]

RECEIVED APRIL 11, 1952

It has been shown previously that the major absorption bands between 1350 and 1500 cm.$^{-1}$ in the infrared spectra of steroids can be associated with the presence of specific methyl and methylene groups in the molecule. Steroids have been prepared in which CH_2 and CH_3 groups at selected positions have been replaced by CD_2 and CD_3 groups. It is observed that the absorption bands which have been assigned to specific methyl and methylene groups disappear when these groups are deuterized but there are no other significant changes produced in this region of the spectrum. These effects are interpreted as confirming the assignment of these bands to C–H bending vibrations which are localized in the methyl and methylene groups in question and which exhibit negligible coupling with methyl and methylene groups at neighboring positions, or with the skeletal vibrations of the ring system. The effects of introducing deuterium on the absorption of steroids in other regions of the infrared spectrum are also noted.

From a normal coördinate vibration analysis of *trans-n*-butane and other simple aliphatic hydrocarbons it has been established[3] that the C–H bending vibrations of methyl and methylene groups occur between 1350 and 1475 cm.$^{-1}$. In the preceding paper[4] *all* the prominent absorption bands in this region of the spectra of steroids have been attributed to such methyl and methylene group vibrations, and it has been assumed tacitly that the bending vibrations of each methyl and methylene group in the steroid molecule is independent of the bending vibrations of similar neighboring groups.

This hypothesis appears to fit the experimental facts well, but such absence of coupling between the C–H vibrations of adjacent groups was hardly to be anticipated on the basis of molecular vibrational theory. It was therefore considered advisable to attempt to obtain more direct experimental evidence for the localization of these vibrations in specific groups. This has been done by study of the spectra of steroids in which the CH_2 and CH_3 groups postulated to give rise to specific absorption bands have been selectively deuterized.

Previous investigators have prepared steroids enriched in deuterium by catalytic exchange,[5–7] by direct reduction with deuterium on a platinum catalyst[8–10] and by reduction of bromosteroids and steroid ethylene mercaptols with deuterized Raney nickel.[11] These reactions were undertaken with the object of introducing deuterium into tightly bound positions to serve as labels in studies of steroid metabolism.

In the work to be described in this paper deuterium atoms were introduced, for the most part, at relatively labile positions either by specific chemical reactions or by enolization in alkaline solution. When the spectra of the normal and deuterized steroids were compared it was observed that certain bands present in the spectra of the normal steroids disappeared on deuteration. In all cases the bands which disappeared were those which had been assigned to vibrations localized in the methyl or methylene groups which had been specifically deuterized.

Experimental

The spectra were measured under conditions identical with those described in the preceding publication.[4] The methods employed for the preparation of the deuterized compounds will be briefly noted in the course of the discussion. Details of their preparation, and evidence of structure will be published elsewhere.[12]

Results and Discussion

Steroid Acetates.—The effect of introducing deuterium into the acetoxy group of steroid acetates was selected for a preliminary study, in view of the ease with which such compounds can be prepared by acetylation of the steroid alcohol with acetic anhydride-d_6.

In the normal acetates[13] the two strong bands which occur near 1375 and 1365 cm.$^{-1}$ (bands L and N)[13] have been attributed to vibrations of the acetoxy methyl group. In Figs. 1 and 2 the spectra of the normal and trideuteroacetates of cyclohexanol, androstanol-3α, androstanol-17β and pregnanol-20α are shown. In each case the spectrum of the trideuteroacetate lacks the strong bands near 1365 and 1375 cm.$^{-1}$ but otherwise resembles the spectrum of the normal acetate very closely. In Figs. 1D and 2B the absorption bands assigned to the two angular methyl groups (bands I and K) are clearly observed in the spectra of the trideuteroacetates and may be compared with the spectrum of androstane in Fig. 1C of the preceding paper.

In the case of pregnanol-20α (Fig. 2C,D) the angular methyl absorption bands are not resolved

---

(1) Presented, in part, at a Symposium on the Infrared Spectroscopy of Large Molecules, Division of Physical and Inorganic Chemistry, American Chemical Society, Boston, Mass., April 3rd, 1951. Published as Contribution No. 2858 from the Laboratories of The National Research Council of Canada.

(2) National Research Council Postdoctorate Fellow.

(3) For a review and discussion of this subject see J. K. Brown, N. Sheppard and D. M. Simpson, *Discussions of the Faraday Soc.*, **9**, 261 (1950).

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

(5) K. Bloch and D. Rittenberg, *J. Biol. Chem.*, **149**, 505 (1943).

(6) H. S. Anker and K. Bloch, THIS JOURNAL, **66**, 1752 (1944).

(7) D. K. Fukushima and T. F. Gallagher, *J. Biol. Chem.*, in press.

(8) W. H. Pearlman, M. R. J. Pearlman and S. Elsey, THIS JOURNAL, **71**, 4126 (1949).

(9) W. H. Pearlman and M. R. J. Pearlman, *ibid.*, **72**, 5781 (1950).

(10) B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, *J. Biol. Chem.*, **184**, 393 (1950).

(11) D. K. Fukushima, S. Lieberman and B. Praetz, THIS JOURNAL, **72**, 5205 (1950).

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

(13) In this paper bands characteristic of specific methylene and methyl groups will be designated by the letters A-O in accordance with Table II of the preceding paper. The word "normal" designates steroids not enriched in deuterium and has no stereochemical implication.

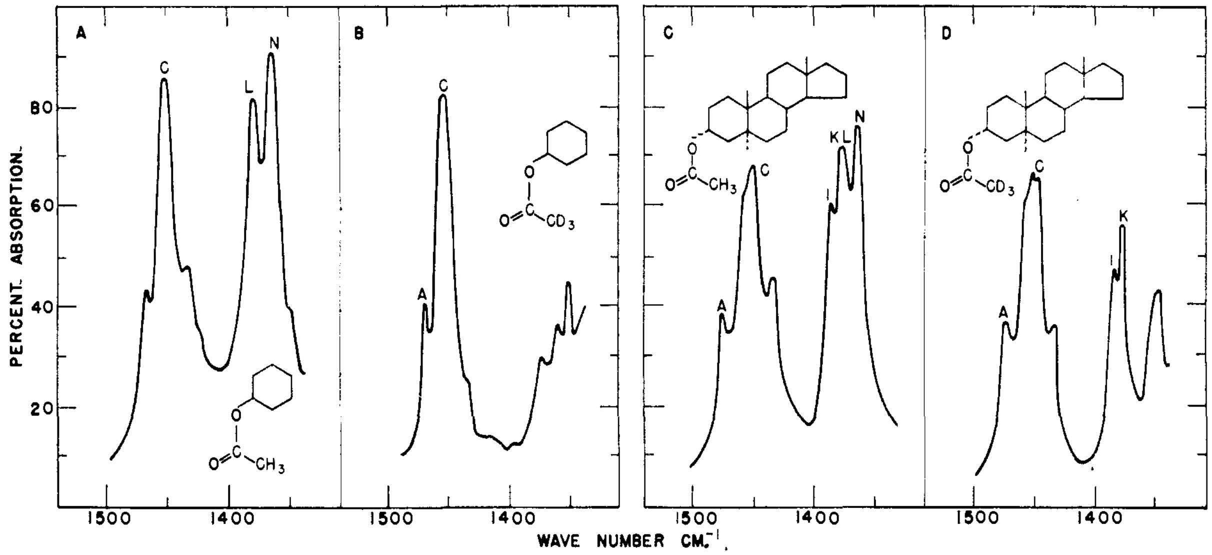

Fig. 1.—Infrared curves illustrating disappearance of bands L and N from the spectra of trideuteroacetates: A, cyclohexanol acetate; B, cyclohexanol acetate-d_3; C, androstanol-3α acetate; D, androstanol-3α acetate-d_3.

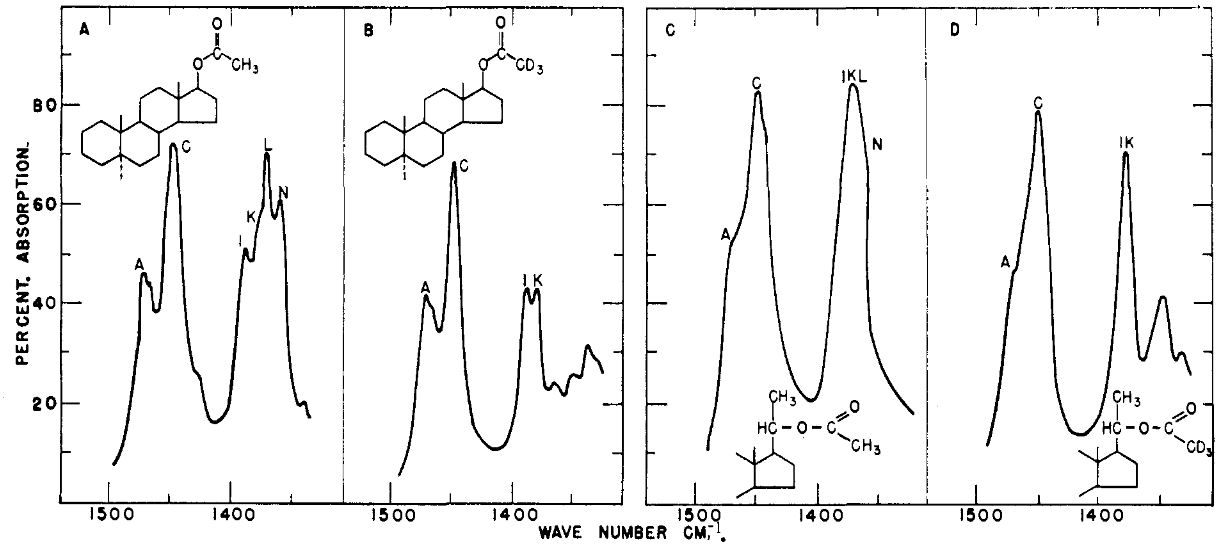

Fig. 2.—Subject as Fig. 1: A, androstanol-17β acetate; B, androstanol-17β acetate-d_3; C, pregnanol-20α acetate; D, pregnanol-20α acetate-d_3.

in the spectrum of the trideuteroacetate since the C_{21} methyl group is most probably contributing to this absorption also, paralleling the behavior of compounds containing the $-CH_2-CH_3$ and $-CH(OH)-CH_3$ side chains.[4]

The spectra of the normal and trideuteroacetates of several other steroid alcohols have also been compared with similar results (Table I).

The Pregnanone-20 Side Chain.—In the spectra of C_{21}-steroids containing a $-CO-CH_3$ side chain there is a strong band at 1357 cm.$^{-1}$ (band O), which has been assigned to the symmetrical bending vibration of the C_{21}-methyl group, adjacent to the carbonyl group.

This assignment has been confirmed by a comparison of the spectrum of Δ^5-pregnenol-3β-one-20 (I) and its normal acetate (II) with the spectra of the deuterized derivatives III–VI.[14]

The spectra of compounds I–VI are shown in Figs. 3A–4B, and the position of the band maxima are analyzed in section C of Table I. A study of the curves and table shows that the assignment of band 0 to the CH_3 group at C_{21} is substantiated, since it disappears in the derivatives in which this group is deuterized (III, IV, VI). Bands L and N are absent in the derivatives containing the trideuteroacetate group at C_3 (V, VI) and the only methyl absorption remaining in III and VI is the band at 1387 cm.$^{-1}$ assigned to the absorption of the angular methyl groups. In all the spectra the methylene absorption bands above 1400 cm.$^{-1}$ are not significantly affected by deuterium enrichment.

These curves illustrate very effectively how, in

---

(14) The C_{21}-d_3 group was introduced by exchange of I with CH_3OD and NaOD in D_2O and also by synthesis from Δ^5-3β-acetoxyetiocholenic acid chloride and dimethylcadmium-d_6. In III and VI the C_{17}-hydrogen atom is also unavoidably deuterized in the course of the hydrolysis of the 3-acetate group but this has no effect on the infrared absorption in the methyl-methylene bending region.

TABLE I

COMPARISON OF INFRARED SPECTRA OF NORMAL AND DEUTERIUM ENRICHED STEROIDS BETWEEN 1350 AND 1500 CM.$^{-1}$

A. Acetates

Compound^{a}	Bands^{b}											
	A	B	C,C'	E	H	I	J	K	L	M	N	Other bands
Cyclohexanol acetate	1467	..	1452	..	.	.	..	..	1378		1365	1434^{e}
Cyclohexanol acetate-d_3	1467	.	1452	..			..	..	*Abs.*	.	*Abs.*	1434^{e}
Androstanol-3α acetate	1474	..	*1454*, 1448	..	.	1385	.	1376	1376	..	1362	1434^{c}
Androstanol-3α acetate-d_3	1474	..	*1454*, 1448	..	..	1385	..	1379	*Abs.*	..	*Abs.*	1434^{c}
Androstanol-3β acetate	1474	..	1452	..	.	*1387*	..	1378	1378	..	1366	...
Androstanol-3β acetate-d_3	1474	..	1452	..	..	1387	..	1378	..	..	*Abs.*	...
Androstanol-17β acetate	1474, *1469*	..	*1452*, 1449	..	..	1388	..	*1380*	1372	..	1360	...
Androstanol-17β acetate-d_3	1474, *1469*	..	*1452*, 1449	..	..	1388	.	1380	*Abs.*	..	*Abs.*	...
Δ^{5}-Cholestenol-3β-acetate	..	1468	*1453*	1441	..	*1383*	1375	1375	1375	1366	1366	*1436*^{c}
Δ^{5}-Cholestenol-3β acetate-d_3	..	1468	*1453*	1441	..	1383	1378	1378	..	1368	..	1358^{w}
$\Delta^{6,8}$-Cholestadienol-3β acetate	..	1470	1454	1447	..	1379	1379	1379	1369	1369	1361	1428^{d}
$\Delta^{6,8}$-Cholestadienol-3β acetate-d_3	..	1470	1454	1447	..	1379	1379	1379	..	1366	..	1428^{d}
Ergostanol-3β acetate	..	1466	1453, 1448	..	..	*1386*	1378	1378	1378	1368	1362	....
Ergostanol-3β acetate-d_3	.	1466	1453, 1448	..	..	1387	*1387*	1376	..	1367	*Abs.*	...
Δ^{22}-5-Isoergostenol-3α acetate	*1465*	.	1455, *1450*	..	..	*1384*	1379	1379	1379	1372	1363	...
Δ^{22}-5-Isoergostenol-3α acetate-d_3	*1465*	..	1455, *1450*	..	.	1384	1379	1379	.	1372	*Abs.*	....
Estrone acetate	1475, 1468	.	1456	1437	1408	..	.	*1376*		.	1368^{e}	1495,^{f}, 1422
Estrone acetate-d_3	1475, 1468	..	1456	1437	1408	..	..	1377		..	*Abs.*	1495,^{f} 1422
$\Delta^{5,7,9}$-Estratrienol-17β acetate	1474	..	1450	1437	..	.	.	1387	1372	..	1360	1485,^{f} 1461, 1417, *1352*
$\Delta^{5,7,9}$-Estratrienol-17β acetate-d_3	1474	..	1450	1437	..	.	.	1387	*Abs.*		*Abs.*	1485,^{f} 1461, 1417, 1352

B. Ketones

	Bands											
	A	B	C,C'	E	F	G	H	I	J	K	M	O	Other bands
Androstanone-3	1472	..	1452, 1448		..	*1425*, 1418	..	1386	..	1379	..	..	1364,^{w} 1353^{w}
Androstanone-3-d_4-2,4	1472	..	1452, 1448		..	*Abs.* *Abs.*	..	1388	..	1379	..	..	1364,^{w} 1347^{w}
Cholestanone-3	.	1469	1448		.	*1425*, 1419	..	1385	1377	1377	1368	..	1352^{w}
Cholestanone-3-d_4-2,4	..	1469	1446		..	*Abs.* *Abs.*	..	1385	1377	1377	1368	..	1348^{w}
$\Delta^{8:14}$-Ergostenone-3	..	1464	1455	1437	..	*1424*, 1420	..	1380	1380	1380	1369	..	.
$\Delta^{8:14}$-Ergostenone-3-d_4-2,4	..	1464	1455	1438	..	*Abs.* *Abs.*	..	1382	1382	1382	1370	..	...
Cholestanone-7	..	1469	1450	..	1433	..	..	1384	1384	1377	1368	..	1356^{w}
Cholestanone-7-d_2-6(?)^{g}		1469	1450	..	*Abs.*	.	..	1384	1384	1378	1368	..	1356^{w}
Androstanone-17	1470	..	1455, 1448	..	..	..	1410	*1380*	..	1374	..	..	1354^{w}
Androstanone-17-d_2-16	1470	..	1455, 1448	..	..	..	*Abs.*	1389	..	1374	..	..	1354^{w}

C. Δ^{5}-Pregnenolone Derivatives

	Bands								
	A	C,C'	E	I	K	L	N	O	Other bands
Δ^{5}-Pregnenol-3β-one-20 (I)	1475	1464, 1452	1437	1387	1387		..	1356	...
Δ^{5}-Pregnenol-3β-one-20-d_4-17,21 (III)	1475	1464, 1452	1437	1385	1385	..	..	*Abs.*	...
Δ^{5}-Pregnenol-3β-one-20 acetate (II)	1475, 1469	1453	1441	1387	1387	1376	1359	1359	1435^{c}
Δ^{5}-Pregnenol-3β-one-20 acetate-d_3 (V)	1475, 1468	1453	1440	1387	1387	*Abs.*	*Abs.*	1359	1435,^{c} 1371^{w}
Δ^{5}-Pregnenol-3β-one-20-d_4-17,21 acetate (IV)	*1472*, 1469	1451	1441	1387	1387	1375	1367	*Abs.*	1436^{c}
Δ^{5}-Pregnenol-3β-one-20-d_4-17,21 acetate-d_3 (VI)	1472, 1469	1453	1441	1387	1387	*Abs.*	*Abs.*	*Abs.*	1436,^{c} 1370^{w}

[a] For sources of compounds see Table I of preceding paper (reference 4). [b] For band assignments see Table II of preceding paper (reference 4); points of inflection are indicated in italics. [c] Probably acetate group vibration. [d] $\Delta^{4,6}$-Diene group vibration. [e] Phenolic acetate methyl group vibration. [f] Aromatic ring vibration. [g] May contain some deuterium also at C_8. [w] Weak band.

the spectrum of II the four methyl groups at C_{10}, C_{13}, C_{21} and in the acetoxy radical all undergo characteristic bending vibrations in a narrow range of frequency without exhibiting any effects of mutual interaction (Fig. 4b).

3-Ketones and 7-Ketones.—The presence of a ketone group at C_3 is associated with absorption near 1420 cm.$^{-1}$ in steroids in which there is methylene group at C_2 or C_4, and this peak (band G) has been attributed to the bending vibration of the α-methylene groups perturbed from 1450 cm.$^{-1}$, the normal position in a six-membered ring, by the effect of the carbonyl group.

The spectra of cholestanone-3 and androstanone-3 are compared in Figs. 4CD and 6 with the curves of the compounds deuterized at C_2 and C_4 by exchange with CH_3OD and D_2O in alkaline solution. Both deuterized compounds lack the band at 1420 cm.$^{-1}$ and a similar result has been observed also for $\Delta^{8:14}$-ergostenone-3 (Table I).(15)

In 7-ketones there is a peak at 1433 cm.$^{-1}$ (band F) which disappears in the spectrum of cholestanone-7 after exchange with CH_3OD and

(15) It has been observed in the preceding communication that the 1420 cm.$^{-1}$ band in 3-ketones exhibits an asymmetry on the high frequency side, and this has been tentatively attributed to a difference between the frequencies of the bending vibrations of the methylene groups at C_2 and C_4. Since these deuterized C_3-ketones contained 3.5–3.8 deuterium atoms per mole (see reference 7) both methylene groups must be exchanged and the *complete* disappearance of this band is in accord with this interpretation

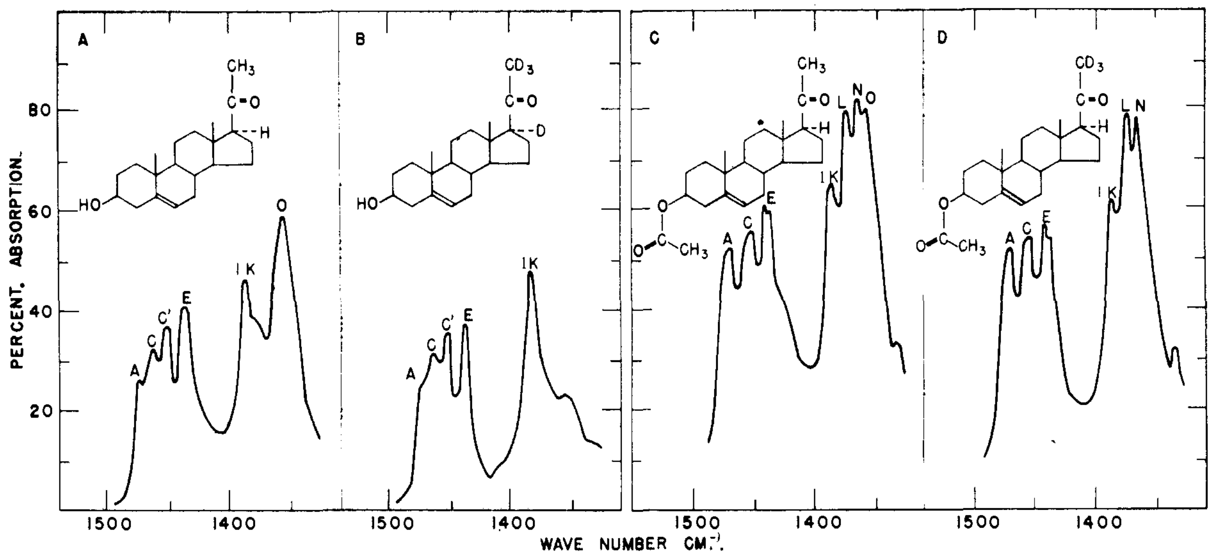

Fig. 3A.—Δ^5-pregnenol-3β-one-20; B, Δ^5-pregnenol-3β-one-20-d_4-17,21; C, Δ^5-pregnenol-3β-one-20 acetate; D, Δ^5-pregnenol-3β-one-20-d_3-21 acetate. Curves B and D illustrate disappearance of band O on introduction of C_{21}-d_3 group.

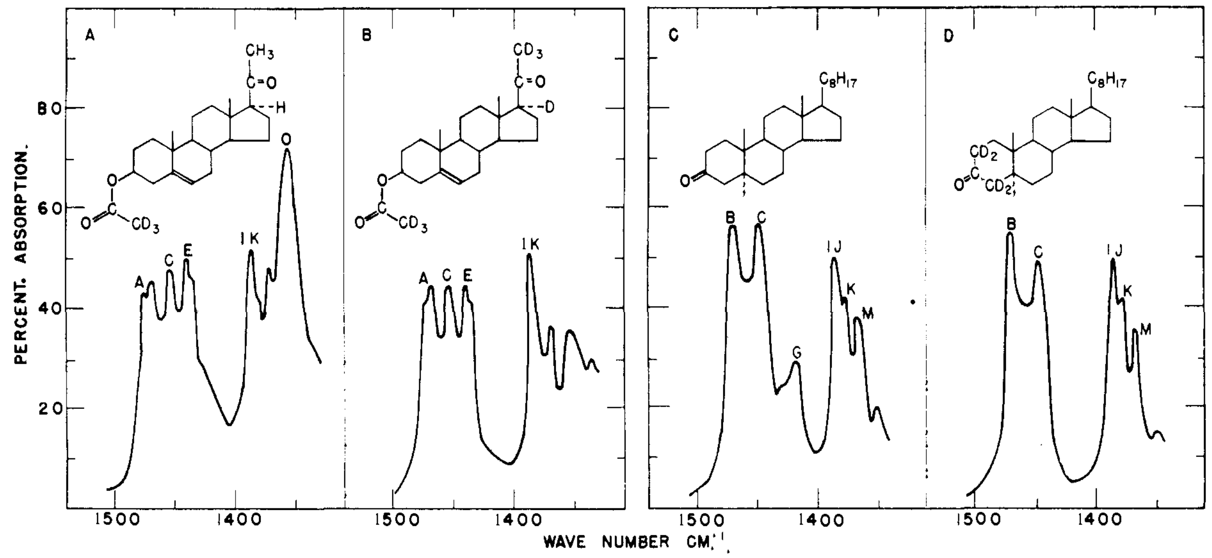

Fig. 4.—A, Δ^5-Pregnenol-3β-one-20 acetate-d_3; B, Δ^5-pregnenol-3β-one-20-d_4-17,21 acetate-d_3. Figures 4A and 4B illustrate disappearance of bands L, N and O on deuteration simultaneously at C_{21} and in the acetate group: C, cholestanone-3; D, cholestanone-3-d_4-2,4, illustrating disappearance of band G on deuteration at C_2 and C_4.

D_2O in alkaline solution (Fig. 5AB), in accord with the assignment of this band to a bending vibration of the C_6-methylene group.

17-Ketones.—The 17-ketone provides perhaps the most striking example of the effect of deuterium exchange in alkaline solution on the infrared spectra of ketosteroids. In the normal compounds the peak at 1410 cm.$^{-1}$ (band H) is assigned to the C_{16}-methylene group. The spectrum of androstanone-17-d_2-16 lacks this band completely, although, as shown in Fig. 5CD, the remainder of the spectrum in the methyl–methylene bending region is superimposable on that of the normal compound.

Effects of Deuteration on Other Regions of the Spectrum

The infrared spectra of the deuterized steroids discussed in this paper have been measured over the whole frequency range from 3700 to 650 cm.$^{-1}$. A detailed discussion of these spectra will be deferred but certain features of interest may be noted.

C–D Stretching Bands.—Absorption associated with the C–D stretching vibrations occurs between 2100 and 2300 cm.$^{-1}$ and this region of the spectrum has been used to identify metabolites of deuterium labeled steroids.[16] The positions of the absorption bands are given in Table II, and a typical example (androstanone-3-d_4-2,4) is shown in Fig. 6. The apparent molecular extinction coefficients[17] are only approximate values, but serve to indicate the order of the intensity of these

---

(16) K. Dobriner, T. H. Kritchevsky, D. F. Fukushima, S. Lieberman, T. F. Gallagher, J. D. Hardy, R. N. Jones and G. Cilento, *Science*, **109**, 260 (1949).

(17) R. N. Jones, D. A. Ramsay, D. S. Keir and K. Dobriner, This Journal, **74**, 80 (1952).

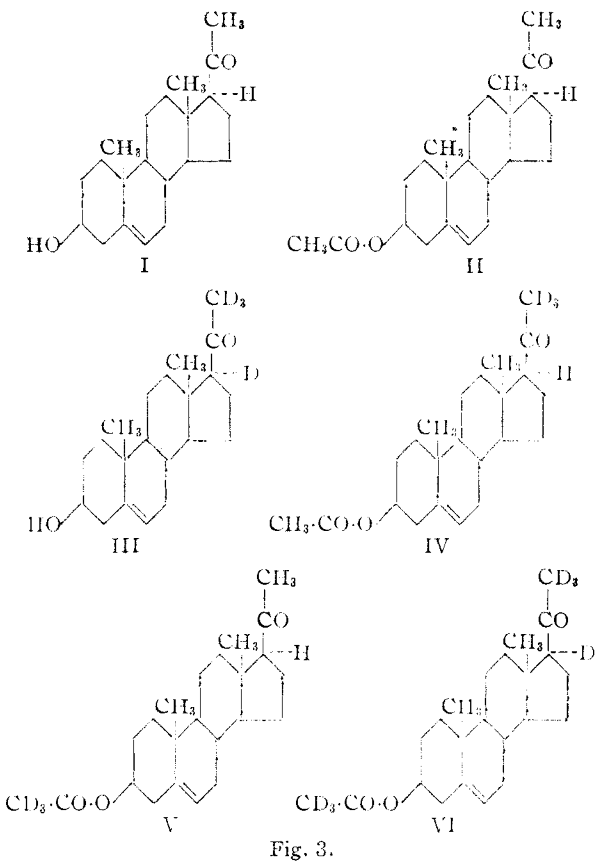

Fig. 3.

Table II

C–D Stretching Vibrations in Deuterium Enriched Steroids

Compound[a]	Bands Position cm.$^{-1}$	Bands App. molec.[c] extinc. coeff.
Androstanone-3-d_4-2,4	2215	14.5
	2145	8.5
	2105	8.5
Cholestanone-3-d_4-2,4	2215	15.0
	2145	9.0
	2105	9.0
$\Delta^{8:14}$-Ergostenone-3-d_4-2,4	2215	13.0
	2145	7.5
	2105	7.5
Cholestanone-7-d_2-6	2220	. .
	2120	. .
Androstanone-17-d_2-16	2215	4.0
	2140	3.1
Δ^5-Pregnanol-3β-one-20 acetate	2260[b]	1.5
	2145[b]	3.0
Δ^5-Pregnanol-3β-one-20 acetate-d_3	2275	4.0
	2235	3.5
	2145[b]	3.0
Δ^5-Pregnanol-3β-one-20-d_3-21 acetate	2255	9.0
	2220	5.5
Δ^5-Pregnanol-3β-one-20-d_4-17,21 acetate-d_3	2255	9.5
	2220	6.0

[a] All measurements in carbon tetrachloride solution. [b] Attributed to acetate overtone vibration. [c] See reference 17.

bands. The data suggest that bands at 2215 and 2140 cm.$^{-1}$ are associated with CD_2 groups adjacent to carbonyl groups at C_3 or C_{17}, and bands at 2255 and 2220 cm.$^{-1}$ to the C_{21}–CD_3 group next to the C_{20}-ketone. The C_3-ketones possess an additional band at 2105 cm.$^{-1}$. In these compounds the deuterium enrichment corresponds to about 90% of the theoretical, based on the proposed structures[12] and the possibility that some of the absorption in this region is due to C–D stretching vibrations in CHD groups cannot be entirely discounted.

In the acetoxy-d_3 group the C–D stretching bands are exceptionally weak, with apparent molecular extinction coefficients of between 3 and 4. Acetates show overtone absorption bands in this region with apparent extinction coefficients of about 2 and when superimposed on this absorption the CD_3 stretching bands are hardly to be distinguished.

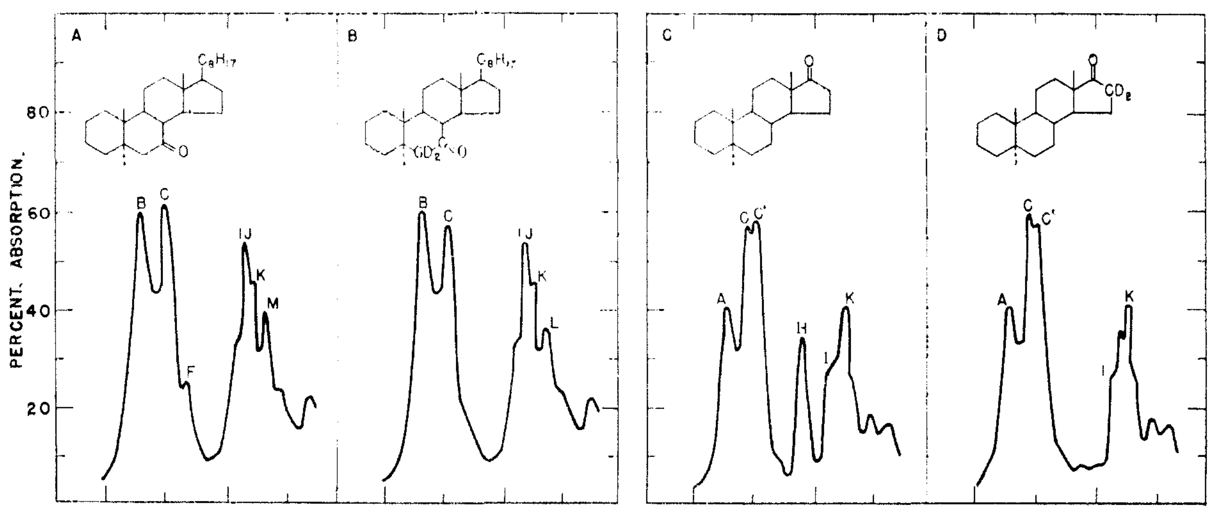

Fig. 5.—Curves illustrating disappearance of band F on deuteration of 7-ketosteroid at C_6 and disappearance of band H on deuteration of 17-ketosteroid at C_{16}: A, cholestanone-7; B, cholestanone-7-d_2-6; C, androstanone-17; D, androstanone-17-d_2-16.

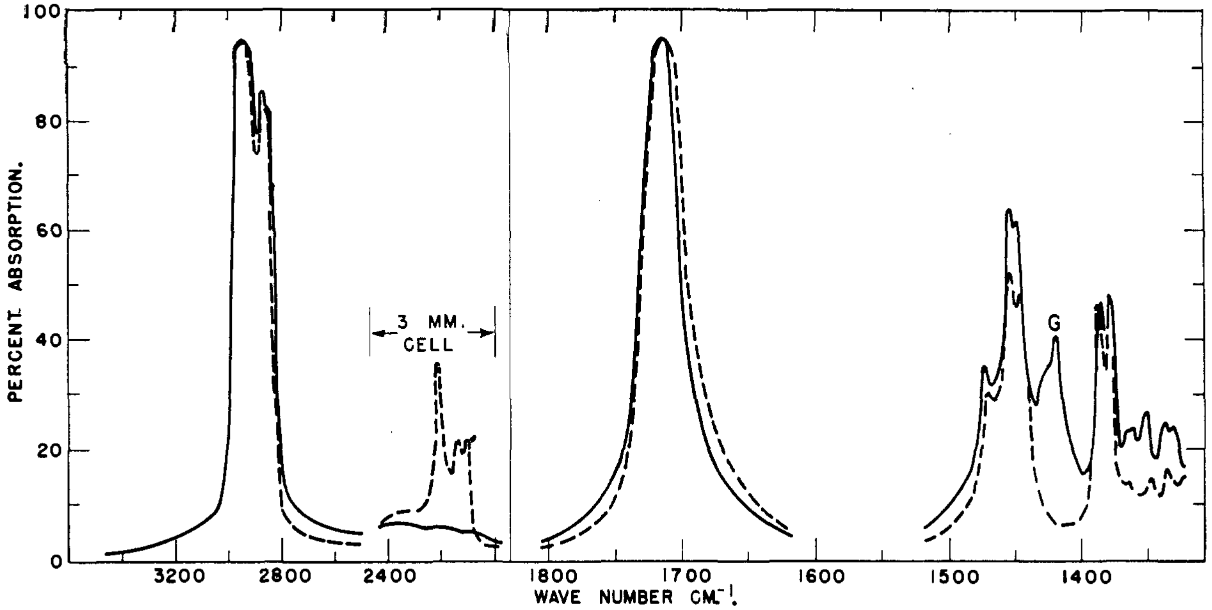

Fig. 6.—Spectra of androstanone-3 (—) and androstanone-3-d_4-2,4 (-----) between 1300 and 3400 cm.$^{-1}$. CaF_2 prism; carbon tetrachloride solution; 1 mm. cell.

Francis,[18] in a systematic study of the intensities of C–H stretching vibrations has noted the weakness of the acetoxy CH_3 group, and this observation is in agreement with the above results for the deuterized acetoxy group.

C=O Stretching Bands.—As might be anticipated, with the increase in mass resulting from deuteration of the α-methylene or methyl group, small changes can be detected in the position of the maximum of the carbonyl stretching band (Table III).

TABLE III

C=O STRETCHING VIBRATIONS IN DEUTERIUM ENRICHED STEROIDS

All measurements in carbon tetrachloride solution

Compound	C=O band positions, cm.$^{-1}$	C=O band positions in corresponding normal steroid, cm.$^{-1}$
Androstanone-3-d_4-2,4	1711	1714
Cholestanone-3-d_4-2,4	1712	1715
$\Delta^{8:14}$-Ergostenone-3-d_4-2,4	1714	1716
Cholestanone-7-d_2-6	1707	1709
Androstanone-17-d_2-16	1741	1743
Δ^5-Pregnanol-3β-one-20-d_4-17,21	1701	1705
Δ^5-Pregnenol-3β-one-20 acetate-d_3	1730, 1706	1734, 1706
Δ^5-Pregnenol-3β-one-20-d_4-17,21 acetate	1732, 1702	1734, 1706
Δ^5-Pregnenol-3β-one-20-d_4-17,21 acetate-d_3	1732, 1702	1734, 1706
Cyclohexanol acetate	1728	1732
Androstanol-3α acetate-d_3	1731	1734
Androstanol-3β acetate-d_3	1727	1732
Androstanol-17β acetate-d_3	1732	1734
Δ^5-Cholestenol-3β acetate-d_3	1729	1732
$\Delta^{6,8}$-Cholestadienol-3β acetate-d_3	1734	1735
Ergostanol-3β acetate-d_3	1730	1733
Δ^{22}-5-Isoergostenol-3β acetate-d_3	1732	1735
$\Delta^{5,7,9}$-Estratrienol-17β acetate-d_3	1735	1738
Estrone acetate-d_3	1764, 1745	1768, 1745

In both the deuterized ketones and the trideuteroacetates the C=O band is displaced to lower frequency by 1–5 cm.$^{-1}$. Although small, such displacements are quite significant since the peak frequencies can be measured with a reproducibility of better than 1 cm.$^{-1}$ with a calcium fluoride prism.

Absorption Below 1350 cm.$^{-1}$.—At lower frequencies the steroid spectra are changed very considerably by the introduction of deuterium. This region is at present being subject to a systematic study; the curve of androstanone-3, shown in Fig. 7, serves to illustrate the complexity of the effects produced. In the trideuteroacetates the strong band near 1250 cm.$^{-1}$, attributed to a C–O stretching vibration, is displaced by about 12 cm.$^{-1}$ to higher frequency. This is in line with the general observation that factors which displace the C=O stretching bands of acetates to lower frequencies tend to displace the C–O band in the opposite direction.

Methyl and Methylene Group Frequencies in Other Types of Organic Compounds

In view of their great variety, the steroids provide an exceptionally favorable group of compounds with which to evaluate the factors limiting the specificity of group vibrations, but it is self-evident that such correlations must, under appropriate circumstances be capable of generalization to other classes of organic compounds. Insofar as the methyl–methylene region is concerned this is clearly demonstrated by the work of other investigators, particularly by qualitative[19] and quantitative[18] studies of the spectra of simple esters and ketones. The manner in which the spectra of 8-methylhydrindanone-1 and 9-methyldecalone-1 tie in with the steroid correlations may also be noted.[4]

---

[18] S. A. Francis, *J. Chem. Phys.*, **19**, 942 (1951).

[19] H. W. Thompson and P. Torkington, *J. Chem. Soc.*, 640 (1945).

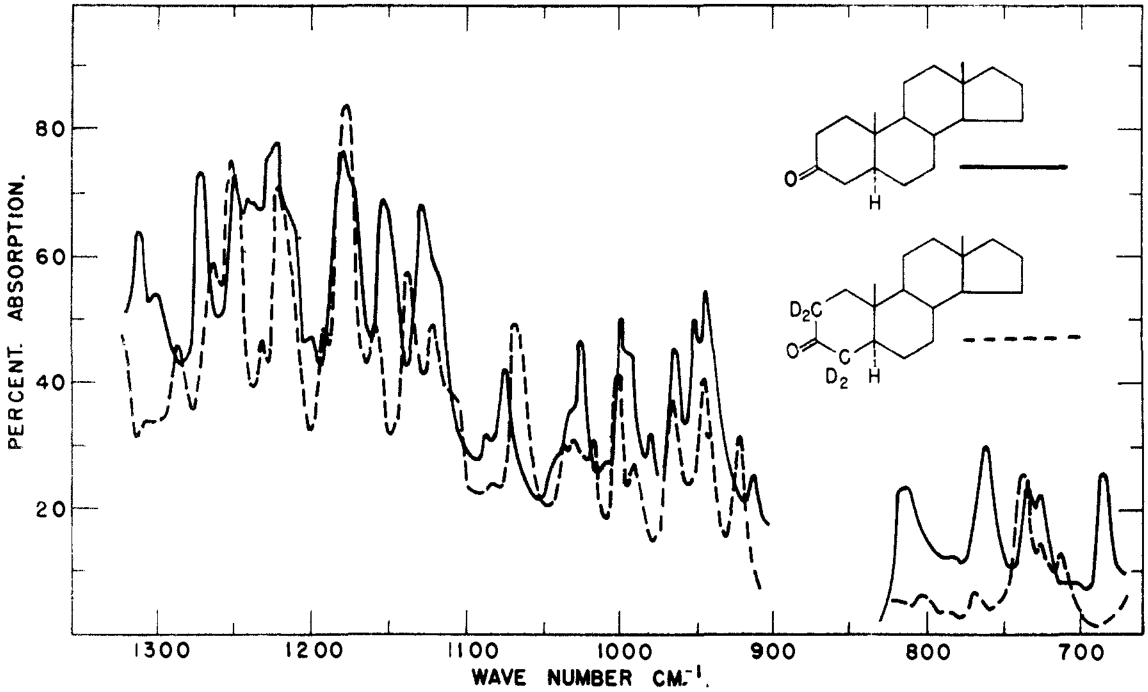

Fig. 7.—Spectra of androstanone-3 and androstanone-3-d_4-2,4 between 650 and 1300 cm.$^{-1}$: NaCl prism; carbon disulfide solution; 1 mm. cell.

The use of the deuterium labeling technique for distinguishing methyl and methylene group vibrations is being extended to simpler compounds. From a study of the spectra of selectively deuterized diethyl ketones (VII–X) it has been possible to identify absorption at 1415 cm.$^{-1}$ with the α-methylene group, and absorption at 1380 cm.$^{-1}$

VII, $CH_3 \cdot CH_2 \cdot CO \cdot CH_2 \cdot CH_3$
VIII, $CH_3 \cdot CD_2 \cdot CO \cdot CD_2 \cdot CH_3$
IX, $CD_3 \cdot CH_2 \cdot CO \cdot CH_2 \cdot CD_3$
X, $CD_3 \cdot CD_2 \cdot CO \cdot CD_2 \cdot CD_3$

with the methyl group, paralleling exactly the behavior of similarly located groups in steroids. In diethyl ketone, however, there is a band at 1462 cm.$^{-1}$ identified with the *methyl* groups, and a band at 1357 cm.$^{-1}$ identified with the *methylene* group. It must therefore be emphasized that although there may be good reasons to anticipate that characteristic group frequencies of general application may ultimately be established for this region of the spectrum, circumspection must be exercised in extending to other classes of compounds the correlations established in these papers for steroids; particularly must this be so where widely different ratios of methyl to methylene groups in the molecule are encountered, and where elements other than oxygen, hydrogen and carbon are present.

In more recent studies of the spectra of both steroids and simpler compounds greater attention is being given to the accurate control of sample concentration, cell thickness and effective slit width, so that the curves may be computed as apparent molecular extinction coefficients. This makes possible a more rigorous interpretation of the absorption, especially in regions such as the A, B, C, C′ and I, J, K, band groups where, because of overlapping absorption, the assignment of bands to individual methyl and methylene groups must be somewhat arbitrary when based solely on the positions of the maxima and a rough comparison of relative band intensities.

Lord[20] has observed that caution must be exercized in the comparison of the infrared spectra of normal and deuterized organic compounds, as the lowering of the C–H stretching and bending frequencies which occur on deuterations may cause changes in coupling with skeletal and other vibrations, leading to changes in the spectra which cannot be related in a simple fashion to the C–H bond directly involved.

In the work discussed in this paper complications of this kind are improbable, since the interpretations are based solely on the *disappearance* of C–H vibrations and not on the assignment of new bands in the deuterized compounds to CD_2 or CD_3 groups. Furthermore, it is unlikely that any fundamental C–C skeletal vibrations occur at frequencies sufficiently high to interfere in this region of the spectrum.

Acknowledgments.—We are grateful to the late Dr. Konrad Dobriner of the Sloan–Kettering Institute for helpful discussion and encouragement during the course of these investigations. We also wish to thank Dr. L. C. Leitch of the National Research Council and Drs. T. F. Gallagher and D. K. Fukushima of the Sloan–Kettering Institute for advice in the preparation of the deuterized compounds, and Drs. F. Lossing and R. Jailer for mass spectrometry analyses. Gifts of compounds from Dr. E. B. Hershberg of the Schering Corporation and Dr. C. R. Scholz of Ciba Pharmaceutical Products, Inc., are also gratefully acknowledged.

OTTAWA, CANADA

---

(20) R. C. Lord, Abstracts of Papers, 119th Meeting of American Chemical Society, Boston, Mass., p. 3p (1950).