The ketonic fraction (4 g., 40%) was shown to be 2-ketobicyclo-(2,2,1)-heptane (VI) by its conversion into the 2,4-dinitrophenylhydrazone of VI; m.p. and mixed m.p. with an authentic sample was 130–131°.

The tertiary amine VII (3 g., 27% yield) was distilled; b.p. 165–180°.

Anal. Calcd. for $C_9H_{17}N$: C, 77.71; H, 12.2. Found: C, 78.21; H, 12.3.

The methiodide of this amine melted at 292° with decomposition. The identity of this product to that obtained by the reduction of III has already been noted.

The Hofmann Degradation of the Methiodide of *endo*-5-Dimethylaminobicyclo-(2,2,1)-heptene-2 (III).—A solution of the methiodide (5.4 g.) in 100 ml. of 15% potassium hydroxide was distilled in an atmosphere of nitrogen. The exhaust gases were passed through a solution of picric acid. Decomposition occurred when about 85 ml. of water had distilled; however, no trimethylamine was formed. The picrate of the product melted at 190–194° (dec.) and a mixed melting point of this picrate with an authentic sample of the picrate of *endo*-5-dimethylaminobicyclo-(2,2,1)-heptene-2 (III), m.p. 190–195° (dec.), was 190–194°.

A solution of the methiodide (21 g.) in methanol (300 ml.) was treated with silver oxide (9.25 g.), and the solution of methohydroxide was distilled at atmospheric pressure. The residue decomposed at 100–180°; however, no trimethylamine was observed. The product was III.

Methylation of *d*-dimethyl-(β-phenylisopropyl)-amine (X) with formaldehyde and formic acid gave *d*-dimethyl-(β-phenylisopropyl)-amine (XI), b.p. 68–72° (2.5 mm.), 66% yield, $[\alpha]^{25}D$ +5.11° (absolute ethanol).

Anal. Calcd. for $C_{11}H_{17}N$: C, 80.92; H, 10.50; N, 8.58. Found: C, 81.06; H, 10.59; N, 8.78.

Conversion of XI to XII was effected by reaction of XI with methyl iodide in ether. The product was recrystallized from ethanol; m.p. 196–197°, $[\alpha]^{25}D$ −4.81° (distilled H_2O).

Anal. Calcd. for $C_{12}H_{20}NI$: C, 47.2; H, 6.56. Found: C, 47.6; H, 6.98.

Methylation of *d*-(β-Phenylisopropyl)-amine with Methyl Iodide.—A mixture of 250 ml. of water, 25 g. of sodium carbonate, 11.2 g. of X and 30 g. of methyl iodide was heated at the reflux temperature for nine hours. The reaction mixture was cooled and the crystals filtered, washed with ether, and dried. The product weighed 18.2 g. (72% yield) and was the methiodide of XI. A sample of the product was recrystallized from ethanol. The m.p. and mixed m.p. with the product described in the preceding experiment was 196–197°; $[\alpha]^{25}D$ −4.83° (distilled H_2O).

The decomposition of bicyclo-(2,2,1)-2-heptene-5 acetate[7] was carried out by allowing the ester to pass (25 g./hr.) through a hot tube (580°) in an atmosphere of nitrogen. A material balance was not obtained; however, the following products were isolated: (a) acetylene (in exhaust gas), (b) acetic acid, (c) cyclopentadiene (m.p. and mixed m.p. of dibromo derivative[8] was 45–46°) and (d) vinyl acetate.

The Decomposition of the Methyl Xanthogenate of *endo*-5-Hydroxybicyclo-(2,2,1)-heptene-2 (XIIb).—The crude xanthogenate[9] (b.p. 120–126° (10 mm.)) was decomposed at 250° in an atmosphere of nitrogen. A small amount of volatile oil (*ca.* 5%) boiling at 40–70° was obtained. This product reacted with phenylazide in ether to give a crystalline product (dec. 200°) which was insoluble in ether, benzene, alcohol and chloroform. The light tan needles were washed with alcohol and ether.

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 69.08; H, 5.49. Found: C, 69.03; H, 5.81.

(7) K. Alder and H. Rickert, *ibid.*, **543**, 15 (1939).
(8) E. Farmer and W. Scott, *J. Chem. Soc.*, 177 (1929).
(9) Whitmore and Simpson, THIS JOURNAL, **55**, 3809 (1933).

MINNEAPOLIS 14, MINNESOTA

[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. I. Correlations of Bending Frequencies with Molecular Structure[1]

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

RECEIVED APRIL 11, 1952

The major absorption bands between 1350 and 1500 cm.$^{-1}$ in the spectra of steroids can be assigned to vibrations of methyl and methylene groups in the molecule. These vibrations appear to be localized in individual methyl and methylene groups, and the following correlations between molecular structure and infrared spectra have been established for this region of the spectrum. (a) The cyclic methylene groups of the steroid ring system absorb at a different frequency from the linear methylene groups in the side chain. (b) Methylene groups adjacent to carbonyl groups and to ethylenic linkages absorb at characteristic positions. In steroids containing the group $-CH_2-CO-$ the frequency of the α-methylene bending vibrations is determined by the location of the carbonyl group and serves to supplement the C=O stretching frequency for the characterization of the carbonyl position. (c) The angular methyl groups, the terminal side chain methyl groups, and the methyl group in the acetoxy radical of steroid acetates, absorb at different positions and can be distinguished. The band positions associated with these various types of methyl and methylene groups are listed in tables, and examples are given to illustrate the application of these correlations to the elucidation of molecular structure.

The infrared absorption bands of large organic molecules may be classified into three principal types; (i) a relatively small number of bands due to *stretching* vibrations of specific groups, notably O–H, C–H, C=O, and C=C in the higher frequency region (1575–3650 cm.$^{-1}$); (ii) C–H *bending* bands of methyl and methylene groups between 1350 and 1500 cm.$^{-1}$; (iii) a complicated pattern of overlapping bands due to skeletal stretching vibrations and C–H deformation vibrations below 1350 cm.$^{-1}$. The latter absorption is most sensible to small changes in molecular structure and has been aptly described as the "fingerprint" region.

An extensive study of the bands due to specific O–H, C=O and C=C stretching vibrations in steroids has enabled a set of correlations to be established between band position and molecular structure,[3-6] and these correlations have proved useful in determining the structure of newly isolated steroids.

From studies of the infrared spectra of simple ali-

(1) Presented, in part, at a Symposium on Molecular Spectroscopy held at the Ohio State University, Columbus, Ohio, June, 1950, and published as Contribution No. 2857 from the Laboratories of The National Research Council of Canada.

(2) National Research Council Postdoctorate Fellow.

(3) R. N. Jones and K. Dobriner, *Vitamins and Hormones*, **7**, 293 (1949).

(4) R. N. Jones, P. Humphries, E. Packard and K. Dobriner, THIS JOURNAL, **71**, 241 (1949).

(5) R. N. Jones, P. Humphries and K. Dobriner, *ibid.*, **72**, 956 (1950).

(6) P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch and G. W. Wood, *J. Chem. Soc.*, 2402 (1951).

TABLE I

ABSORPTION MAXIMA BETWEEN 1350 AND 1500 CM.$^{-1}$ IN THE SPECTRA OF STEROIDS AND CYCLOHEXANE ANALOGS IN CARBON TETRACHLORIDE SOLUTION

Compound[a]	Source[b]	Absorption bands (See Tabel II) A	B	C,C'	D	E	F	G	H	I	J	K	L	M	N	O	Other bands
I. Hydrocarbons																	
Cyclohexane		..	..	1451	..	..	..	..	..	..	..	..	..	..	..	..	..
Methylcyclohexane		..	..	1456, 1449	..	..	..	..	..	..	..	1376	..	..	..	..	1363[v]
Methylcyclopentane		..	..	1462, 1453	..	..	..	..	..	..	..	1376	..	..	..	..	1350[v]
Androstane	19	*1472*, 1466	..	1453, 1448	..	..	..	..	..	1384	..	1378	..	..	..	..	1354[v]
Etiocholane*	19	1466	..	1452	..	..	..	..	..	1378	..	1378	..	..	..	..	1358[v]
Allopregnane*	19	1468	..	1451	..	..	..	..	..	*1386*	..	1378	..	..	..	..	1366[v]
Pregnane	19	*1471*, 1464	..	1451	..	..	..	..	..	1377	..	1377	..	..	..	..	1357[u]
Cholestane	2	..	1469	*1454*, 1448	..	..	..	..	..	1385	*1379*	*1379*	..	1367	..	..	..
Ergostane	11	..	1466	1448	..	..	..	..	..	*1386*	*1382*	1377	..	1368	..	..	1354[v]
Cyclohexene		..	..	1449	..	1439	..	..	..	..	..	..	..	..	..	..	..
Δ^5-Cholestene	11	..	1469	1446	..	1438	..	..	..	1384	1381	1376	..	1368	..	..	1358[v]
$\Delta^{8(14)}$-Ergostene*	11	..	1469	1455	..	*1440*	..	..	..	*1385*	1378	*1375*	..	1368	..	..	..
Δ^{14}-Ergostene	11	..	1466	1457, 1449	..	*Abs.*	..	..	..	*1386*	1380	1380	..	1369	..	..	..
Δ^{22}-Ergostene	2	..	*Abs.*	1459, 1448	..	*Abs.*	..	..	..	1384	1384	1374	..	*1370*	..	..	1364[v], 1355[v]
II. Alcohols																	
Estranol-17β	3	1471, 1466	..	1455, 1448	..	..	..	..	..	*Abs.*	..	1378	..	..	..	..	1396[v]
Androstanol-3α	20	1473	..	1452, 1448	..	..	..	..	..	*1383*	..	1378	..	..	..	..	1432,[m] 1370[v]
Androstanol-3β	20	1474, 1466	..	1452	..	..	..	..	..	*1385*	..	1378	..	..	..	..	..
Pregnanol-20α	15	*1475*, 1466	..	1451	..	..	..	..	..	1378	..	1378	..	..	..	..	..
Ergostanol-3β	11	..	1466	1448	..	..	..	..	..	1386	1381	1377	..	1368	..	..	..
Δ^6-Androstenol-3β	20	..	..	1457	..	1440	..	..	..	1380	..	1380	..	..	..	..	..
Δ^5-Cholestenol-3β	7	..	1468	1448	..	1438	..	..	..	1383	1383	*1376*	..	1368	..	..	..
$\Delta^{5,7}$-Cholestadienol-3β	21	..	1469	1462, 1450	..	1434	..	..	..	*1385*	1379	1379	..	1369	..	..	..
$\Delta^{6,8}$-Cholestadienol-3β	2	..	1469	1456	..	1444	..	..	..	*1384*	1378	1378	..	1367	..	..	1428[m,c]
Δ^8-5-Methyl-19-norcholestene-diol-3β-6 (*Westphalen's diol*)	5	..	1468	1460	..	1444	..	..	..	1382	1382	1382	..	1367	..	..	1428,[v] 1360[v]
Δ^8-Ergostenol-3β	2	..	1465	1455	..	1436	..	..	..	*1385*	1378	1378	..	1368	..	..	..
$\Delta^{8(14)}$-Ergostenol-3β	2	..	1469	1454	..	1438	..	..	..	1384	1378	1378	..	1367	..	..	..
Δ^{14}-Ergostenol-3β	2	..	1466	1456, 1450	..	*Abs.*	..	..	..	1381	1381	1381	..	1369	..	..	..
Δ^{22}-5-Isoergostenol-3α	2	..	*Abs.*	1456, 1451	..	*Abs.*	..	..	..	1386	1378	1372	..	*1368*	..	..	..
β-Sitosterol (Δ^5-*Stigmastenol*)	1	..	1468	1446	..	1438	..	..	..	1385	1379	*1375*	..	1369	..	..	..
Δ^{22}-Stigmastenol-3β	2	..	1463	1452, 1448	..	*Abs.*	..	..	..	1386	*1380*	*1380*	..	1370	..	..	..
Δ^{22}-5-Isostigmastenol-3α	2	*1472*	1464	1451	..	*Abs.*	..	..	..	1385	1377	1377	..	1369	..	..	..
α-Spinasterol ($\Delta^{7,22}$-*stigmastadienol-3β*)	2	1471	1463	1455, 1447	..	*1436*	..	..	..	1383	1383	1383	..	1368	..	..	..
Fucosterol	22	..	1467	1448	..	1438	..	..	..	1381	1377	1377	..	*1365*	..	..	..
Lumisterol$_2$*	11	..	..	1460	..	*1440*	..	..	..	1382	1374	1374	..	*1368*	..	..	1422[m]
Vitamin D$_2$*	14	..	..	1462	..	1445	..	..	..	1378	1378	1378	..	*1368*	..	..	..
Vitamin D$_3$		..	1470	*1462*	..	1442	..	..	..	1378	1378	1378	..	1368	..	..	..

TABLE I (*Continued*)

Compound[a]	Source[b]	Absorption bands (See Table II) A	B	C,C'	D	E	F	G	H	I	J	K	L	M	N	O	Other bands
III. Acetates																	
Cyclohexanol acetate	[d]	1467	..	1452	..	..	..	..	..	..	..	..	1379	..	1365	..	1434[g,u]
Androstanol-3α acetate	20[d]	1474	..	*1454*, 1448	..	..	..	..	..	1385	..	1376	1376	..	1362	..	1433[m,u]
Androstanol-3β acetate	20[d]	1474	..	1452	..	..	..	..	..	*1387*	..	1378	1378	..	1366	..	..
Androstanol-17β acetate	20[d]	1472, *1469*	..	1449	..	..	..	..	..	1388	..	*1380*	1372	..	1360	..	*1428*[u]
Androstanediol-3α,17β-diacetate	8	1475	..	1455	..	..	..	..	..	*1385*	..	1380	1373	..	1369	..	1438[u]
Pregnanetriol-3α,12α-20β monoacetate-12	8	1464	..	1451	..	..	..	..	..	1375	..	1375	1375	..	..	..	
Pregnanol-20α acetate	15	*1471, 1464*	..	1452, *1447*	..	..	..	..	..	*1378*	..	*1378*	1374	..	1370	..	..
Pregnanetriol-3α,12α,20β-diacetate-3,12	8	1468	..	1452	..	..	..	..	..	*1382*	..	1376	1376	..	1365	..	*1430*,[u] 1402
Pregnanetriol-3α,12α,20β-diacetate-3,20	8	1468	..	1450	..	..	..	..	..	1378	..	1378	1370	..	1365	..	*1440*[u]
Pregnanetriol-3α,12α,20β triacetate	8	*1468*	..	1450	..	..	..	..	..	*1382*	..	1376	1376	..	1365	..	*1434*[u]
Cholestanol-3β acetate*	7	..	1468	1452	..	..	..	..	..	1382	1382	1382	1382	1367	1367	..	..
Ergostanol-3β acetate	11[d]	..	1466	1453, 1448	..	..	..	..	..	*1386*	1378	1378	1378	1367	*1360*	..	*1428*[u]
Stigmastanol-3β acetate (*fucostanol acetate*)	11, 22	..	1467	1453, 1448	..	..	..	..	..	1386	1379	1379	1379	1368	*1362*	..	..
Δ^5-Androstenediol-3β,17β-acetate-17	18	1470	..	1455	..	1442	..	..	..	1388	..	1375	1375	..	1365	..	..
Δ^5-Cholestenol-3β acetate	7[d]	..	1468	*1455*	..	1441	..	..	..	1383	1375	1375	1375	1366	*1366*	..	1436,[u] 1357[v]
$\Delta^{5,8}$-Cholestadienol-3β acetate	2[d]	..	1470	1454	..	..	..	..	..	1379	1379	1379	1369	1369	1361	..	1447[m,c] 1428[m,c]
Zymosterol acetate	2	..	1468	1455, 1446	..	1435	..	..	..	1378	1378	1378	1373	..	1361	..	..
Δ^7-Ergostenol-3β acetate	2	..	1468	1450	..	1435[v]	..	..	..	1378	1378	1378	1378	1365	1365	..	..
$\Delta^{8,14}$-Ergostenol-3β acetate	11	..	1465	1452	..	1436	..	..	..	1380	1380	1380	1380	1368	1368	..	..
Δ^{14}-Ergostenol-3β acetate	2[d]	..	1466	1456, 1450	..	*Abs.*	..	..	..	*1386*	1378	1378	1378	1370	*1365*	..	..
Δ^{22}-5-Isoergostenol-3α acetate	2[d]	*1465*	..	1455, 1450	..	*Abs.*	..	..	..	*1384*	1379	1379	1379	1372	1363	..	..
Lumisterol$_2$ acetate*	11	..	..	1458	..	*1440*	..	..	..	1382		1374	1374	1374	1362	..	1418
α-Spinasterol acetate	2	1472	1462	1448	..	?	..	..	..	1384	1377	1377	1377	1366	1366	..	..
Fucosterol acetate	11	..	1468	*1458, 1446*	..	1442	..	..	..	*1381*	1375	1375	1375	1366	1366	..	..
IV. Other Esters																	
Δ^{11}-3α-Hydroxybisnorcholenic acid methyl ester	16	*e*	*e*	*1454*	1438	..	..	..	..	1375	?	1375	..	..	..	..	1460[g], 1394[v] *1365*[f]
Δ^{11}-3α-Hydroxynorcholenic acid methyl ester	16, 23	*e*	*e*	1455, 1450	1438	..	..	..	..	*1380*	?	1375	..	..	..	..	1460,[g] 1393[v] *1365*, 1355[f]
Δ^{11}-3α-Hydroxycholenic acid methyl ester	23	*e*	*e*	1455	1438	..	..	..	..	1375	?	1375	..	..	..	..	1460[g], 1393[v] 1365[f]
Δ^8-Cholestenol-3β formate	8	..	1468	1458	..	1442	..	..	..	1382	1382	1382	..	1368	..	..	..
Cholestanol-3β acetoacetate	1	..	1468	1450	..	..	..	..	..	1385	*1376*	*1376*	..	1365	..	..	1417[m,o]
Δ^5-Cholestenol-3β acetoacetate		..	1468	1448	..	1437	..	..	..	1382	1382	1382		1368	..	..	1412[m,o] 1359[g,h]

TABLE 1 (*Continued*)

Compound[a]	Source[b]	Absorption bands (See Table 11) A	B	C,C'	D	E	F	G	H	I	J	K	L	M	N	O	Other bands
β-Sitosterol acetoacetate	1	..	1467	1450	..	?	..	..	..	*1386*	1378	1378	..	1368	..	..	1415[m,g] 1360[g,h]
Δ[5,22]-Stigmastadienol-3β acetoacetate	1	..	1466	1450	..	*1345*	..	..	..	*1385*	1379	1379	..	1368	..	..	1415[m,g] 1360[g,h]
V. Monoketones and Hydroxyketones																	
8-Methyl-*trans*-hydrindanone-1	13	1468	..	1454	..	..	..	..	1406[i]	..	..	1372[i]	..	..	..	..	..
8-Methyl-*cis*-hydrindanone-1	13	1462	..	1446	..	..	..	..	1408[i]	..	..	1372[i]	..	..	..	..	..
9-Methyl-*cis*-decalone-1	13	1460	..	1450	..	..	1428[j]	..	..	1378[j]	..	..	..	..	..	..	..
Androstanone-3	20	1472	..	1452, 1448	..	..	..	*1425*, 1418	..	1386	..	1379	..	..	..	..	1364[v], 1353[v]
Androstanol-17β-one-3	20	1473	..	1454, 1449	..	..	..	*1426*, 1420	..	1382	..	1382	..	..	..	..	..
Etiocholanol-17β-one-3	5			1455, 1448	..	..	..	1422	..	1378	..	1378	..	..	..	..	1395[v]
Cholestanone-3	11	..	1469	1448	..	..	..	*1425*, 1419	..	1385	1377	1377	..	1368	..	..	1352[v]
2,2-Dibromocholestanone-3*	6	..	1470	1449	..	..	..	1426	..	1384	*1378*	*1378*	..	1368	..	..	
Coprostanone-3	7	..	1469	1456, 1447	..	..	..	1424	..	1384	1380	1380	..	1368	..	..	1355[m]
Cholestanone-4	17	..	1468	1455, 1446	..	..	1430	..	..	1384	1384	*1378*	..	1368	..	..	1487[v]
3-Bromocholestanone-6	10	..	1468	1446	..	..	1428	..	..	1388	1382	*1374*	..	1367	..	..	..
i-Cholestanone-6	10	..	1470	1464, *1454*	..	..	..	..	..	*1385*	1377	1377	..	1368	..	..	1433[m,k] 1412[m,k]
Pregnanone-7*	19	1464		1454	..	..	1437	..	..	1380	..	1380	..	..	..	..	1392[v]
Cholestanone-7	11	..	1469	1450	..	..	1433	..	..	1384	1384	1377	..	1368	..	..	1356[v]
Pregnanone-12*	19	1464	..	1452	..	..	1434	..	..	1379	..	1379	..	..	..	..	..
Androstanone-17	20	1470	..	1455, 1448	..	..	..	..	1410	*1380*	..	1374	..	..	..	..	*1365*[v]
Androstanol-3α-one-17	7	1470	..	1455, 1448	..	..	..	..	1409	1385	..	1372	..	..	..	..	1434[v]
Androstanol-3β-one-17	20	1470	..	1454	..	..	..	..	1409	*1385*	..	1375	..	..	..	..	*1445*
Etiocholanol-3α-one-17	7	1472	..	1454	..	..	..	..	1409	*1384*	..	1374	..	..	..	..	..
Etiocholanol-3β-one-17	5	1479	..	*1454*, 1450	..	..	..	..	1408	*1385*	..	1375	..	..	..	..	..
i-Androstanol-6-one-17	4	1474	..	1456	..	..	..	..	1408	1376	..	1376	..	..	..	..	1436[m,k] 1404[m,k]
Pregnanol-3α-one-20	7	1472	..	1452	..	..	..	..	..	1386	..	1378	..	..	..	1358	1420[w]
Δ[4]-Androstenone-3*	20	*1472*	..	1455	..	1440	..	1423	..	1380	..	1380	..	..	..	..	1355[m]
Δ[4]-Androstenol-17β-one-3* (*Testosterone*)	12, 20	1470	..	1454	..	1438	..	1422	..	1378	..	1378	..	..	..	..	1353[m]
Δ[4]-17-Methylandrostenol-17β-one-3*	20	1468	..	1452	..	1438	..	1422	..	1377	..	1377	..	..	..	..	1352[m]
Δ[4]-17-Vinylandrostenol-17β-one-3*	20	1472	..	1454	..	1438	..	1420	..	1380	..	1380	..	..	..	..	1356,[m] 1350[m]
Δ[4]-2-Bromocholestanone-3*	6	..	1468	1453	..	1440	..	*Abs.*	..	*1386*	1378	1378	..	1368	..	..	..
Δ[4,6]-Cholestadiene-one-3*	7	..	1470	1450	..	*Abs.*	..	1420	..	1382	1382	1382	..	1368	..	..	1354[s]
Δ[8,14]-Ergostenone-3	2	..	1464	1453	..	1437	..	*1424*, 1420	..	*1384*	1380	1380	..	1369	..	..	..
Δ[22]-Ergostenone-3	2	..	..	1460, 1450	..	*Abs.*	..	1422	..	1386	1374	1374	..	1374	..	..	..
Δ[7,22]-Ergostadiene-one-3	2	..	..	1460	..	1438	..	1425, 1420	..	*1380*	1374	1374	..	1374	..	..	1355
Δ[4,22]-Ergostadiene-one-3		1468	..	1456	..	?	..	1426, 1420	..	1383	1383	1372	..	1372	..	..	1358[v]

TABLE I (*Continued*)

Compound[a]	Source[b]	Absorption bands (See Table II) A	B	C,C′	D	E	F	G	H	I	J	K	L	M	N	O	Other bands
Δ^{2}-Androstenone-17*	15	1473	..	1457, 1449	..	*1438*	..	..	1408	1382	..	1376	..	..	..	..	..
Δ^{5}-Androstenol-3β-one-17	20	1472	..	1456	..	1438	..	..	1408	*1386*	..	1374	..	..	..	..	..
Δ^{5}-Pregnenol-3β-one-20	12	1475, 1464	..	1452	..	1437	..	..	..	1387	..	*1376*	..	..	..	1356	..
Δ^{5}-16,17-Methylenepregnenol-3β-one-20	5	1465	..	1455	..	1437	..	..	.	1378	..	1378	..	..	..	1366[f]	1392[f]
VI. Di- and Polyketones and Hydroxyketones																	
Androstanedione-3,17	7	1472	..	1454, 1448	..	..	..	*1425*, 1418	1409	1386	..	1376	..	..	..	..	1365[f]
Etiocholanedione-3,17	7	1470	..	1456	..	..	..	1422	1409	1380	..	1374	..	..	..	..	..
17-Methyl-D-homoandrostanetrione-3,11,17a (*"Uranetrione"*)	18	1470	..	1454	..	..	1430	1420	..	1388	..	1378	..	..	..	..	1362[m,f]
Allopregnanedione-3,20	15	1475	..	1450	..	..	..	1422	..	1387	..	1387	..	..	..	1357	..
Pregnanedione-3,20	7	1472	..	1451	..	..	..	1425	..	1386	..	1380	..	..	..	1358	1436[f]
Pregnanol-3α-dione-11,20*	19	*1475*	..	1454	..	..	1435	..	..	1390	..	1378	..	..	..	1358	..
Pregnanetrione-3,11,20	23	1475	..	1461, 1450	..	..	1433	*1420*	..	1390	..	1380	..	..	..	1358	..
Cholestanedione-3,7	2		1467	1455	..	..	1438	1422	..	1384	*1377*	*1377*	..	1367	..	..	..
Δ^{1}-Androstenedione-3,17*	6	1474	..	1452	..	*Abs.*	..	1415	1409	1378	..	1378	..	..	..	..	1398[m]
Δ^{4}-Androstenedione-3,17	20	1472	..	1454	..	1436	..	1422	1408	1376	..	1376	..	..	..	..	1355[m]
$\Delta^{1,4}$-Androstadienedione-3,17	6	1470	..	1456	..	1445	..	*Abs.*	1404	1374	..	1374	..	..	..	..	..
Δ^{4}-19-Norandrostenedione-3,17	5	1472	..	1454	..	1432	..	1422	1409	1375	..	*Abs.*	..	..	..	..	1358[m]
Δ^{4}-Pregnenedione-3,20 (*Progesterone*)	12	1475	..	1454	..	1438	..	1423	..	1387	..	1377	..	..	..	1359	..
Δ^{4}-19-Norpregnenedione-3,20	5	1475	..	1452	..	1432	..	1422	..	1387	..	*Abs.*	..	..	..	1357	..
VII. Ketoesters																	
Androstanol-3α-one-17 acetate	7	1473	..	1454	..	..	..	..	1409	1387	..	1375	1375	..	1365	..	1437[c,s]
2,2-Dibromoandrostanol-17β-one-3 acetate	6	1470	..	1449	.	..	..	1425	..	1392	..	1374	1374	..	1362	..	..
2-Iodo-4-bromoandrostanol-17β-one-3 acetate	7	1472	..	*1454*, 1449	..	..	..	*Abs.*	..	1392	..	1382	1374	..	1362	..	..
Allopregnanol-3β-one-20 acetate*	18	1474	..	1450	..	..	..	..	..	1385	..	1378	1378	..	*1365*	1358	..
Pregnanol-3β-one-20 acetate	15	1474	..	1450	.	..	..	..	..	1386	..	1377	1377	..	1365	1357	1437[m,s]
Pregnanediol-3α,17α-one-20-formate-3	8	1467	..	1452	.	..	..	..	..	1385	..	1372	..	..	..	1357	
Pregnanediol-3β,17α-one-20-acetate-3	8	1474	..	*1454*, 1450	.	..	..	..	..	*1385*	..	1378	1378	..	1365	1357	1437[m,s]
Allopregnanediol-3β,17α-one-20-acetate-3	5	1470	..	1450	..	..	..	..	..	*1386*	..	1378	1378	..	1365	1357	1437[m,f]
Pregnanediol-3β,21-one-20-acetate-21	19	*1470*	..	1452	..	..	..	..	..	1386	..	1372	1372	..	..	..	1442[s], 1412[s]
2,4-Dibromo-3-ketoetioallocholanic acid methyl ester	6	..	..	1452	1438	..	..	*Abs*	..	1384	..	1384	..	..	..	..	1358[m,f]
3α,9α-Epoxy-11-ketonorcholanic acid methyl ester	23	e	e	1458, 1450	1438	..	*1426*	..	..	1387	..	1376	..	..	..	..	1468[c], 1358[m,f]

TABLE 1 (*Continued*)

Compound[a]	Source[b]	Absorption bands (See Table II) A	B	C,C'	D	E	F	G	H	I	J	K	L	M	N	O	Other bands
3α,9α-Epoxy-11-ketocholanic acid methyl ester	23	e	e	1458, 1452	1438	..	*1426*	..	..	1387	..	1376	..	..	..	..	1468[e], 1358[v,f]
Δ⁵-Androstenol-3β-one-17 acetate	15	1468	..	1453	..	1439	..	..	1408	*1382*	..	1372	1372	..	1363	..	..
Δ⁵-Androstenol-3β-one-17 acetoacetate	1	1470	..	*1454*, 1450	..	1442	..	..	1410	1376	..	1376	..	..	..	..	1415[g], 1358[h]
Δ¹-3-Ketoetioallocholenic acid methyl ester	6	1472	..	1452	1438	..	..	1418	..	1384	..	1374	..	..	..	..	1358[f]
Δ¹,⁴-3-Ketoetioallocholadienic acid methyl ester	6	1472	..	1454	1440	1440	..	*Abs.*	..	1386	..	1372	..	..	..	..	1403, 1358[f]
Δ⁴-2-Bromo-3-ketoetioallocholenic acid methyl ester	6	*1468*	..	1455	1440	1440	..	*Abs.*	..	*1386*	..	1378	..	..	..	..	1358[f]
Δ⁵-Pregnenol-3β-one-20 acetate	20[d]	1472, 1469	..	1453	..	1441	..	..	..	1387	..	1376	1376	..	1366	1359	1436[u]
Δ⁴-Pregnenol-21-dione-3,20 acetate (*Desoxycorticosterone acetate*)	20	*1473*	..	1452	..	1437	..	1422	..	1388	..	1374	1374	..	..	*Abs.*	1415[v]
Δ⁴-2-Carbomethoxycholestenone-3	10	..	1468	1450	1438	1438	..	*Abs.*	..	*1382*	1378	1378	..	1365	..	..	*1356*[f]
Δ⁴-4-carbomethoxycholestenone-3	10	..	1468	1452	1435	1435	..	1421	..	1384	1377	1377	..	1365	..	..	1358[f]
Δ⁵-27-Norcholestenol-3β-one-25 acetate	12	..	1468	1456	..	1441	..	..	..	*1382*	1375	1375	1375	..	1365	..	1412[p], 1356[q]
VIII. Steroids Containing Aromatic Rings																	
Estradiol diacetate	7	1475	..	1455, 1450	..	1435	..	..	..	..	..	1385	1370	..	..	..	1495[r]
Estrone methyl ether	13	1465	..	1458	..	1438	..	..	1408	..	..	1375	..	..	..	..	1502[r]
Estrone acetate	12[d]	1475, 1468	..	1456	..	1437	..	..	1408	..	..	*1376*	..	..	1368[t]	..	1495[r], 1422
13-Isoestrone methyl ether (*Lumiestrone methyl ether*)	13	..	..	1453	..	1437	..	..	1411	..	..	1376	..	..	..	..	1503[r], 1467 *1428*, 1353
Δ⁵,⁷,⁹-Estratrienol-17β	15	1474	..	1452	..	1438	..	..	..	..	..	1376	..	..	..	..	1485[r], 1462, 1417, 1398, 1350
Δ⁵,⁷,⁹-Estratrienol-17β acetate	15[d]	1474	..	1450	..	1437	..	..	..	..	..	1387	1372	..	1360[t]	..	1485,[t] 1461 1417, 1353
dl-Equilenin methyl ether*	13	1465	..	1458	..	1438	..	..	1410	..	..	1376	..	..	..	..	1488,[t] 1352
Cholestanol-4β-benzoate	2	..	1469	1453, 1448	..	..	..	..	..	1386	1386	*1376*	..	1368	..	..	..
Fucosterol benzoate	11, 22	..	1470	1454	..	*1440*	..	..	..	1382	1382	1376	..	1364	..	..	..
Estrone benzoate	9	1472	..	1454	..	1437	..	..	1410	..	..	1374	..	..	..	..	1495[r], 1422
Equilin benzoate	9	1472	..	1454	..	1430	..	..	1410	..	..	1374	..	..	..	..	1495[r]
Equilenin benzoate	9	..	..	1458, 1453	..	1438	..	..	1410	..	..	1374	..	..	..	..	1480[r]
Δ⁵-Cholestanol-3β benzoylacetate	1	..	1469	1455	..	*1440*	..	..	..	1380	1380	1380	..	1368	..	..	1498[r], 1416[s]
Fucosterol 3,5-dinitrobenzoate	11	..	1468	1460	..	1440	..	..	..	1382	1382	1372	..	*1360*	..	..	1348[s]

[a] Compounds are arranged in order of increasing skeletal chain length, with unsaturated compounds listed apart from saturated compounds. The configuration of the 17-hydroxyl group is designated β when it is the same as in testosterone. Figures in parentheses indicate points of inflection. *Abs.* in a column of band positions indicates that the absence of the band is of specific structural significance. An asterisk following the name of the compound indicates the measurements were made with a sodium chloride prism. [b] (1) A. R. Bader, Pittsburgh Plate Glass Co., Milwaukee, Wis.; (2) D. H. R. Barton, Imperial College, London, England; (3) H. M. Crooks, Parke, Davis and Co., Detroit, Mich.; (4) E. Dingemanse, University of Amsterdam, Holland, and N. Fuson, Fisk University, Nashville, Tenn.; (5) C. Djerassi and G. Rosenkranz, Syntex S. A. Mexico City, Mexico; (6) C. Djerassi and C. R. Scholz, Ciba Pharmaceutical Products, Inc., Summit, N. J.; (7) K. Dobriner, Sloan-Kettering Institute, New York, N. Y.; (8) T. F. Gallagher, Sloan-Kettering Institute, New York, N. Y.; (9) G. A. Grant, Ayerst, McKenna and Harrison Ltd., Montreal, P. Q.; (10) R. D. H. Heard, McGill University, Montreal, P. Q.; (11)

Sir I. M. Heilbron, Imperial College, London, England; (12) E. B. Hershberg, The Schering Corp., Bloomfield, N. J.; (13) W. S. Johnson, University of Wisconsin, Madison, Wis.; (14) E. R. H. Jones, University of Manchester, Manchester, England; (15) O. Kamm, Parke, Davis and Co., Detroit, Mich.; (16) E. C. Kendall, The Mayo Clinic, Rochester, Minn.; (17) W. Klyne, Postgraduate Med. School, London, England; (18) R. E. Marker, Pennsylvania State College, State College, Penna.; (19) T. Reichstein, University, Basel, Switzerland; (20) C. R. Scholz, Ciba Pharmaceutical Products Inc., Summit, N. J.; (21) M. L. Tainter, Sterling-Winthrop Research Inst., Rensselaer, N. Y.; (22) D. Thorn, Mt. Allison University, Sackville, N. B.; (23) R. Turner, Harvard University, Cambridge, Mass. [c] $\Delta^{6,8}$-Diene system. [d] Compound acetylated in our own laboratory by Dr. B. Nolin. [e] The 1460–1470 cm.$^{-1}$ region in the spectra of carbomethoxy esters is being further investigated. [f] A band at 1355–1360 cm.$^{-1}$ is frequently observed in the spectra of carbomethoxy esters and may be associated with the ester methyl group. [g] Acetoacetate methylene group absorption. [h] Acetoacetate acetoxy methyl group absorption. [i] These methylhydrindanone stereoisomers may be regarded as models for the C and D steroid ring system and the bands at 1406 cm.$^{-1}$ and 1375 cm.$^{-1}$ are assigned on this basis. [j] Model for the A and B ring system (see *i*). [k] These bands at 1436–1433 and 1412–1404 cm.$^{-1}$ may be characteristic of *i*-steroids. [l] The displacement of band H to higher frequency by 10 cm.$^{-1}$ may be caused by the 16,17-methylene group. [m] Medium strength band. [n] May be attributed to the 17a-methyl group. [o] Attributed to C_{21}-methylene group. [p] Attributed to C_{24}-methylene group. [q] Attributed to C_{25}-methyl group. [r] Aromatic ring absorption. [s] Strong band. [t] Phenolic acetate methyl group. [u] Probably associated with the acetate group. [v] Weak band.

phatic hydrocarbons it has been shown[7] that the principal absorption bands between 1350 and 1500 cm.$^{-1}$ are associated with vibrations of methyl and methylene groups.

This region has tended to be overlooked in the investigation of steroid solution spectra since it is opaque in carbon disulfide solution and in Nujol suspensions. It may be investigated conveniently in carbon tetrachloride solution at path lengths up to 3 mm. and many steroids show good solubility in this solvent.

The present paper is concerned with the identification of bands characteristic of specific methyl and methylene groups from the comparative study of the spectra of a large number of steroids of established structure. In the following paper[8] evidence is presented in support of these assignments based on a study of the spectra of steroids in which selected CH_2 and CH_3 groups have been replaced by CD_2 and CD_3 groups.

Experimental

The spectra were measured on a Perkin–Elmer Model 12c single beam spectrometer equipped with a calcium fluoride prism. Some earlier measurements made with a sodium chloride prism are also included and are indicated by an asterisk in Table I. The spectra were plotted as percentage absorption against wave number, corrections for water vapor absorption being obtained from a solvent control spectrum determined immediately before or after the experimental run, using the same absorption cell. A rapid stream of dry nitrogen was passed through the spectrometer during the measurement to reduce water vapor absorption.

All compounds were dissolved in carbon tetrachloride, usually at a concentration of about 0.035 molar, in a cell of 1 mm. thickness. A few substances of limited solubility were examined in a 3 mm. cell. The sources of the compounds are indicated in Table I.

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

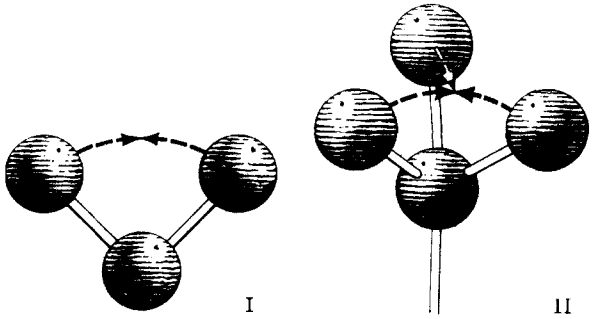
(8) R. N. Jones, A. R. H. Cole and B. Nolin, THIS JOURNAL, **74**, 5662 (1952).

Results

The positions of all absorption maxima between 1350 and 1500 cm.$^{-1}$ in the spectra of some 150 steroids and related compounds included in this survey are given in Table I. The majority of the bands, which are identified by the letters A–O in Tables I and II, are assigned to vibrations of specific methyl and methylene groups in accordance with the structural correlations summarized in Table II. These correlations are discussed in detail below and also in the following paper.[8] In some instances one absorption band has been assigned to two or more vibrations where there is reason to believe that two or more overlapping bands are actually present. Some unassigned bands of medium or weak intensity were also observed, and these are listed in the right hand column of Table I.

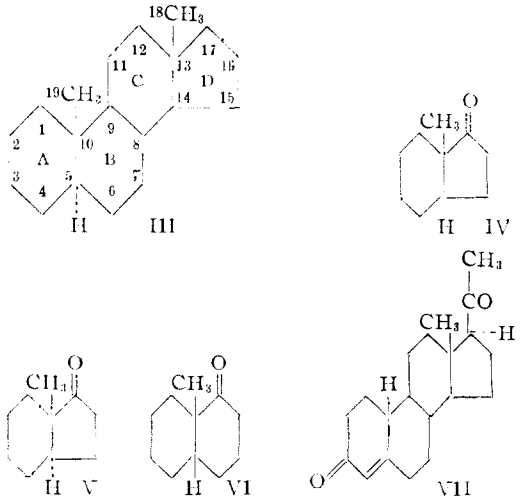
Discussion

The bending vibration of the C–H bonds (I) is one of the characteristic modes of vibration of the methylene group. It occurs near 1450 cm.$^{-1}$ and is illustrated in the spectrum of cyclohexane in Fig. 1A. The symmetrical "breathing" vibration of the C–H bonds of the methyl group (II) gives rise to a band near 1375 cm.$^{-1}$ and is seen in the spectrum of methylcyclohexane in Fig. 1B.



I II

Angular Methyl Group Vibrations. Bands I and K.—The spectrum of the simple steroid hydrocarbon androstane (III) is shown in Fig. 1C. The bands at 1384 and 1378 cm.$^{-1}$ can be assigned to vibrations of the angular methyl groups, and similar bands are observed in the spectra of all steroids containing two angular methyl groups.



H III H IV

H V H VI VII

TABLE II

SUMMARY OF CHARACTERISTIC GROUP VIBRATION FREQUENCIES BETWEEN 1502 AND 1350 CM.$^{-1}$ IN STEROID SPECTRA

Band	Frequency,[a] cm.$^{-1}$	Intensity[b]	Structure assignment
..	.. (1502 – 1480)	s	Aromatic A or B ring. Not shown by benzoate esters of non-aromatic steroids
A	1470 (1475 – 1464)	m	Attributed tentatively to "unperturbed" methylene groups in C_{19} and C_{21} steroids
B	1468 (1470 – 1462)	s	Unperturbed side chain methylene groups in C_{27}, C_{28} and C_{29} steroids. Distinguished from A by intensity which is equal to or greater than that of the C,C′ bands
C,C′	1453, 1448 (1464 – 1446)	s	One or more strong bands in all steroid spectra. Assigned to unperturbed methylene groups of the ring system. The contour of this complex band group varies considerably; several overlapping bands are involved, possibly including weak methyl group vibrations
D	1438 (1440 – 1435)	m–s	Carbomethoxy ester. Does not require an unsubstituted α-methylene group
..	.. (1440 – 1430)	w–m	Band in many, but not all acetates
E	1438 (1445 – 1432)	w–m	Unsubstituted methylene group adjacent to a double bond or to an aromatic ring. Very weak in Δ^7-steroids and not observed in Δ^{14}-steroids
F	1434 (1438 – 1426)	w–m	Ketosteroids with a free α-methylene group next to a carbonyl group at C_4, C_6, C_7, C_{11} and C_{12}
G	1422 (1426 – 1415)	m	3-Ketosteroid with free α-methylene group at C_2 or C_4
..	.. (1415 – 1412)	w	21-Acetoxy-20-ketone; probably C_{21} methylene group absorption
H	1408 (1411 – 1404)	m	17-Ketosteroid with free α-methylene group at C_{16}
I	1385 (1392 – 1374)	m	Angular methyl group (C_{19} ?)
J	1380 (1386 – 1374)	m	Side chain methyl groups at C_{21} and C_{28}
K	1377 (1383 – 1372)	m	Angular methyl group (C_{18} ?). Bands I, J, and K overlap and are rarely resolved when all three types of methyl group are present. The exact positions and intensities probably depend on structural and stereochemical factors which remain to be elucidated
L	1375 (1382 – 1369)	s	Acetate methyl group; given by phenolic as well as 3-, 12-, 17- and 20-acyl acetates
M	1368 (1374 – 1360)	m	In C_{27}, C_{28} and C_{29} steroids; attributed to terminal gem dimethyl group of side chain. Tends to occur above 1368 cm.$^{-1}$ in ergostane and stigmastane derivatives and below 1368 cm.$^{-1}$ in cholestane derivatives
N	1365 (1370 – 1360)	s	Acetate methyl group in 3- and 17-steroid acetates
O	1357 (1359 – 1356)	s	C_{21} methyl vibration of 20-keto-21-methyl group
..	.. (1365 – 1356)	m	Band in many carbomethoxy esters; possibly methyl group vibration

[a] The figure in the left column is the band position as determined from compounds in which there is no appreciable overlap with neighboring absorption bands. The figures in parentheses indicate the extreme range of absorption attributed to the group vibration in Table I, and includes cases where the band may be reduced to an inflection by overlap. [b] The rough indication of the intensity ranges of these bands is based on comparison with the C,C′ band group. Bands which, in the majority of compounds are of equal or greater intensity than the C,C′ bands are classed as s (strong); m (medium) bands are at least half this intensity on a %-absorption scale, and the remainder are classed as w (weak).

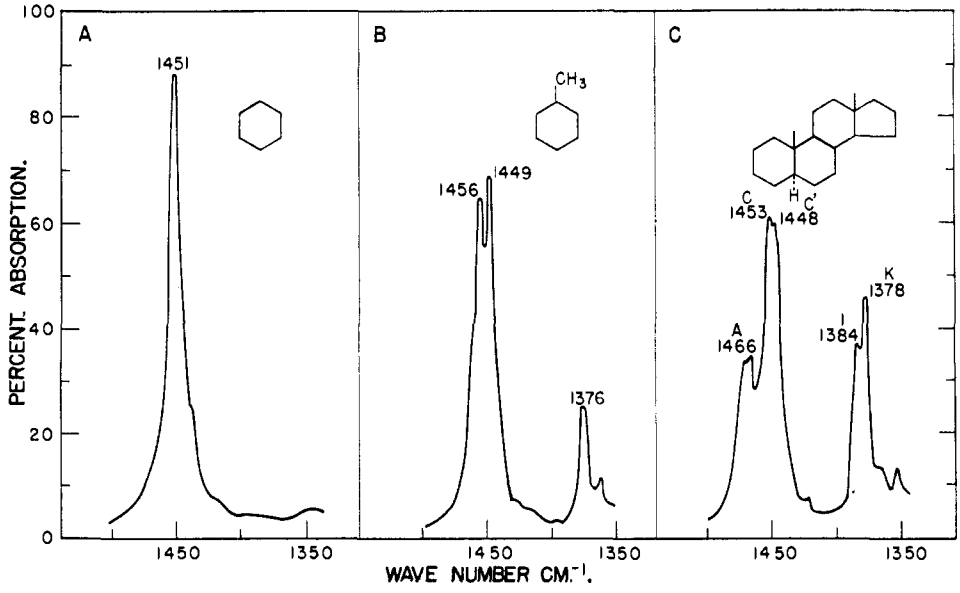


Fig. 1.—Infrared spectra in methyl–methylene bending region: A, cyclohexane; B, methylcyclohexane; C, androstane.

In Table I, 13 compounds are included which lack the angular methyl group at the A/B ring junction.[9] In the spectra of these compounds only one band is observed in this region, and it may be inferred that each of the two bands in the spectra of the C_{19}-steroids is to be attributed to a vibration of an individual methyl group. In ten of the 19-norsteroids the methyl band occurs between 1375 and 1378 cm.$^{-1}$, which would suggest that it is band K which is associated with the C_{18} angular methyl group at the C/D ring junction, and band I, at a somewhat higher frequency, with the C_{19}-methyl group. In this connection it may also be significant that in the *cis* and *trans* isomers of 8-methylhydrindanone-1 (IV, V) the angular methyl group absorbs at a lower frequency (1372 cm.$^{-1}$) than in *cis*-9-methyldecalone-1 (VI) (1378 cm.$^{-1}$).

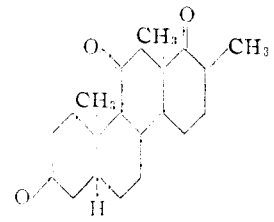
In the present state of our knowledge, too much emphasis cannot be placed on the exact positions of these methyl bands, since in three of the 19-norsteroids (Δ^4-19-norpregnenedione-3,20 (VII), estradiol diacetate, $\Delta^{5,7,9}$-estratrienol-17β acetate) the C_{18} angular methyl vibration appears to be located near 1387 cm.$^{-1}$, and it seems probable that the exact positions and relative intensities of these angular methyl vibrations are subject to the influence of neighboring groups or stereochemical factors.

In pregnane and allopregnane derivatives in which there is a $-CH_2-CH_3$ or a $-CH(OH)-CH_3$ side chain, only one band is usually resolved in this region. It is probable that the C_{21}-methyl group is also contributing to the absorption, and the superimposed bands of the three methyl groups overlap too closely to be separated.

Cyclic Methylene Group Vibrations, Bands A,C,C′.—All steroid spectra possess a group of strong absorption bands near 1450 cm.$^{-1}$, and by analogy with the spectrum of cyclohexane this absorption may be attributed to the C–H bending vibrations of the methylene groups in the steroid ring system. In many instances (*e.g.*, androstane, Fig. 1C), this absorption may be resolved into two peaks (C,C′) near 1448 and 1453 cm.$^{-1}$ and in addition there is usually weaker absorption near 1470 cm.$^{-1}$ (band A).

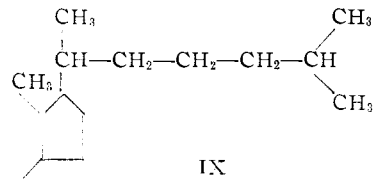
A number of reasons may be advanced in explanation of the complex character of this absorption. Chains or rings of methylene groups may be expected to produce multiple bands due to in-phase and out-of-phase couplings between the vibrations of neighboring groups. Small differences might also be expected between the bending frequencies of methylene groups in different molecular environments.[10] Thirdly, there is also an unsymmetrical C–H bending vibration of the *methyl* group observed near 1460 cm.$^{-1}$ in the spectra of many simple hydrocarbons, esters and ketones, and this also may be contributing to the absorption in this region.

Although the evidence at present available does not allow the nature of this group vibration to be defined precisely, it will suffice for present purposes to assign it to predominant vibrations of "unperturbed" methylene groups in the ring system and to differentiate it from absorption below 1440 cm.$^{-1}$ in steroids containing carbonyl groups or double bonds, and from *strong* absorption above 1462 cm.$^{-1}$ in steroids containing aliphatic side chains.

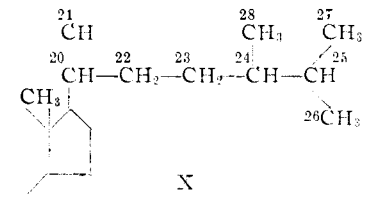


VIII

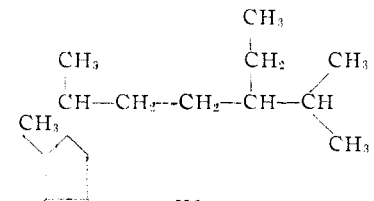
Methyl and Methylene Absorptions of Steroid Side Chains, Bands B, J, M.—The aliphatic side chains of cholestane (IX), ergostane (X) and sitostane (XI) derivatives give rise to additional methyl and methylene bands (Figs. 2A, 2B). In the methyl bending region a band occurs at 1368 cm.$^{-1}$ (band M) and there is also additional absorption superimposed on the angular methyl bands near 1380 cm.$^{-1}$ (band J). It is probable that the band at 1368 cm.$^{-1}$ is associated with the terminal



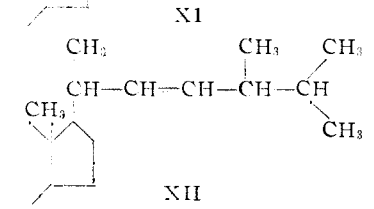
IX



X



XI



XII

(9) Estranol-17β; 19-norandrostanedione-3,17; Δ^4-19-norpregnene dione-3,20; estradiol diacetate; estrone methyl ether; estrone acetate; 13-isoestrone methyl ether; $\Delta^{5,7,9}$-estratrienol-17β; $\Delta^{5,7,9}$-estratrienol-17β acetate; *dl*-equilenin methyl ether; estrone benzoate, equilin benzoate; equilenin benzoate.

(10) The possibility has been considered that the weak absorption near 1470 cm.$^{-1}$ (band A) arises from bending vibrations of the methylene groups in the five-membered ring. This is discounted by the observation that a similar weak band occurs in the spectrum of 17a-methyl-D-homoandrostanetrione-3,11,17 (VIII), where ring D is six-membered. This compound "uranetriane" was prepared by Marker, Kamm, Oakwood, Wittle and Lawson (THIS JOURNAL, **60**, 1061 (1938)) and assigned the structure 9-isopregnanetrione-3,11,20. The 17-methyl-D-homoandrostanetrione structure is based on more recent work of Klyne (*Nature*, **166**, 559 (1950)). The spectrum of "uranetrione" does not show the strong absorption at 1357 cm.$^{-1}$ (band O) associated with the 20-keto-21-methyl side chain, and this supports Klyne's formulation for the uranes.

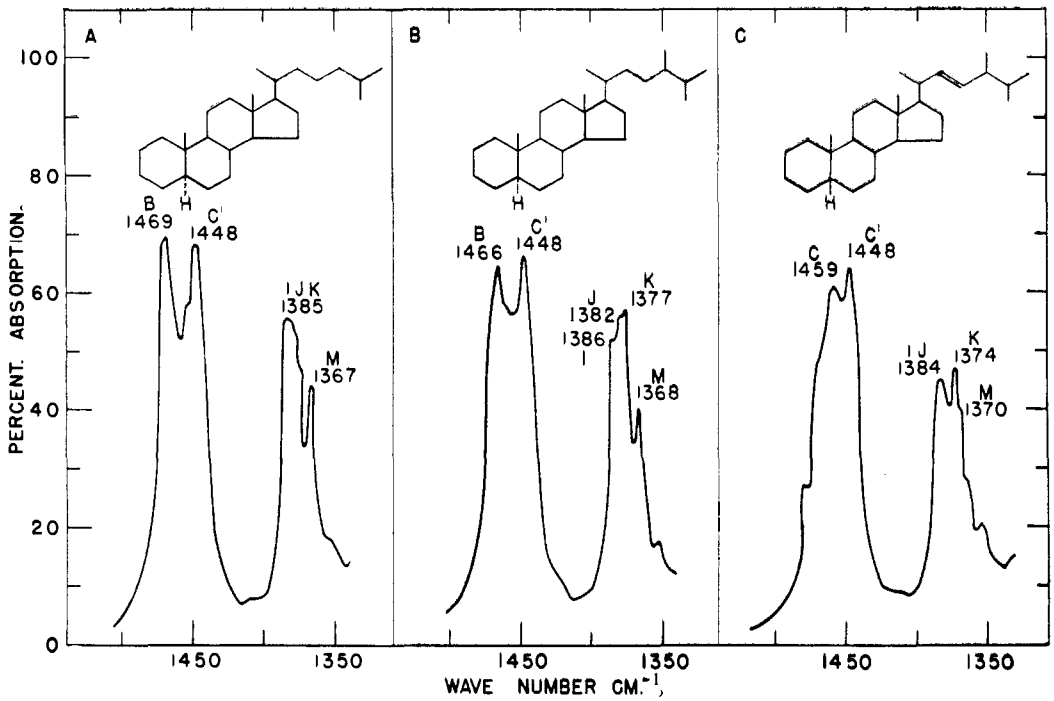


Fig. 2.—Infrared spectra illustrating bands B, J and M associated with side chain group: A, cholestane; B, ergostane; C, Δ^{22}-ergostene.

gem-dimethyl group and the additional absorption at 1380 cm.$^{-1}$ with the methyl groups at C_{21} and C_{28}, but this remains to be confirmed.

The linear methylene groups in steroid side chains give rise to a prominent maximum at 1466–1469 cm.$^{-1}$ (band B) (Figs. 2A, 2B) on the high frequency side of the bands assigned to the cyclic methylene groups (1448–1456 cm.$^{-1}$). This linear methylene band is more intense in cholestane derivatives (Fig. 2A) which possess three linear methylene groups than in ergostane derivatives (Fig. 2B) where only two occur. In Δ^{22}-ergostene compounds (XII), where there are no methylene groups in the side chain, this band is absent (Fig. 2C).

Effects of Introducing Carbonyl Groups. Ring Ketosteroids, Bands F, G, and H.—In steroids containing the group $-CH_2-CO-$ additional absorption bands occur between 1400 and 1440 cm.$^{-1}$. In the spectrum of androstanone-3, shown in Fig. 3A a band is observed at 1418 cm.$^{-1}$ in addition to the methyl and methylene absorption bands possessed by androstane (*cf.* Fig. 1C). A band near 1418 cm.$^{-1}$ is observed in many other 3-ketones (Table I) (band G) and appears whenever there is

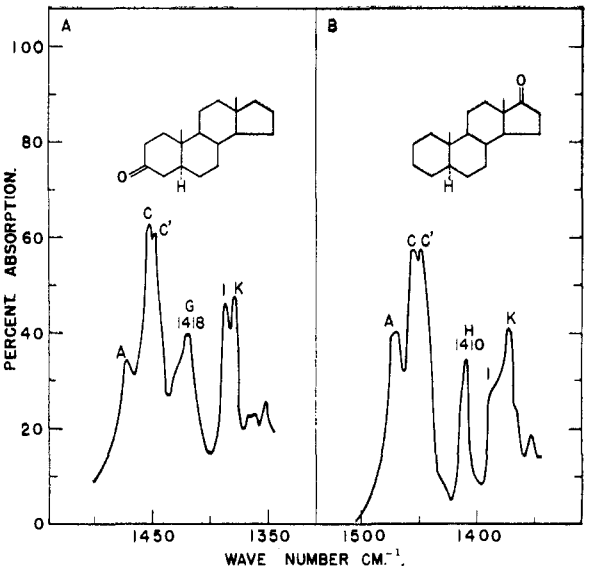
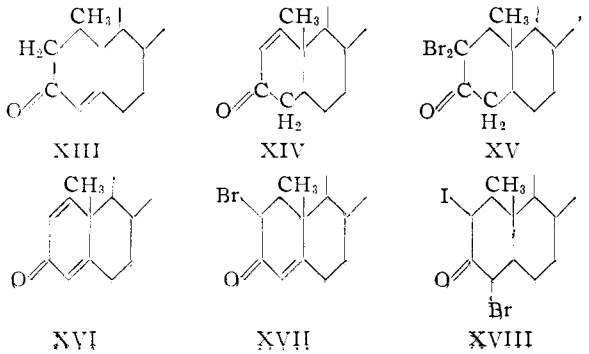


Fig. 3.—Infrared spectra illustrating effect of carbonyl groups on methylene and methyl absorption (bands G and H): A, androstanone-3; B, androstanone-17.



at least one unsubstituted methylene group at either C_2 *or* C_4. Thus it occurs in the spectra of Δ^4-3-ketones (XIII), Δ^1-3-ketones (XIV) and 2,2-dibromo-3-ketones (XV), but is absent from the spectra of $\Delta^{1,4}$-diene-3-ketones (XVI), Δ^4-2-bromo-3-ketones (XVII) and 2-iodo-4-bromo-3-ketones (XVIII). It is suggested that this band arises from the bending vibration of a methylene group at C_2 and C_4 lowered from the normal position (1450 cm.$^{-1}$) by a perturbing effect of the adjacent carbonyl group, and additional evidence in support of this interpretation is provided by the studies on deuterated compounds discussed in the following paper.[8]

In many 3-ketosteroids in which the methylene groups both at C_2 and C_4 are unsubstituted, this band exhibits an inflection on the high frequency side near 1425 cm.$^{-1}$, which may indicate a small difference in the vibration frequencies of the methylene groups at C_2 and C_4.

In steroids containing carbonyl groups at positions 4, 6, 7, 11 or 12 a similar band occurs near 1434 cm.$^{-1}$ (band F) (Fig. 7B) and in 17-ketosteroids there is a characteristic band at 1408–1410 cm.$^{-1}$ (band H) (Fig. 3B). These bands are also attributed to vibrations of the methylene groups adjacent to the respective carbonyls.

The 20-Ketone Side Chain, Band O.—Steroids containing the 20-keto-21-methyl side chain (XIX) have no α-methylene group and there are no absorption bands between 1400 and 1435 cm.$^{-1}$ associated with this group. There is however a strong band at 1356 cm.$^{-1}$ (Fig. 4A) which may be assigned to the bending vibration of the C_{21}-methyl perturbed by the C_{20} carbonyl (band O).

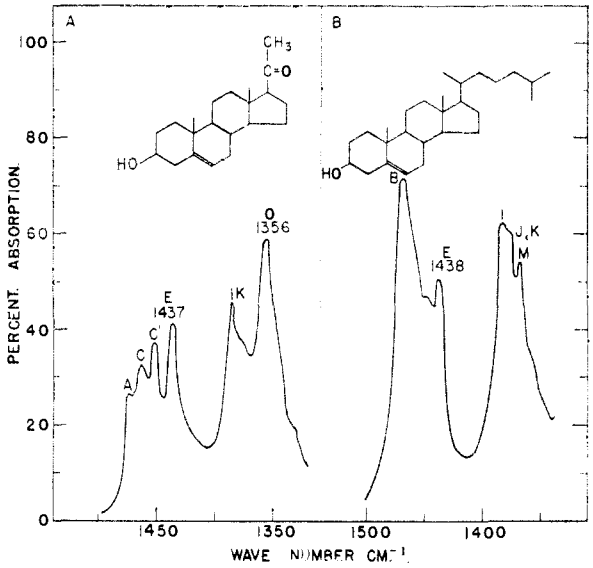
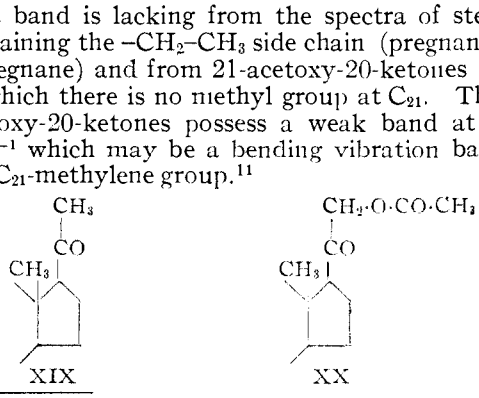


Fig. 4.—Infrared spectra illustrating effects of unsaturation (band E) and of the 20-ketone group (band O): A, Δ^5-pregnenol-3β-one-20; B, Δ^5-cholestenol-3β.

This band is lacking from the spectra of steroids containing the $-CH_2-CH_3$ side chain (pregnane, allopregnane) and from 21-acetoxy-20-ketones (XX) in which there is no methyl group at C_{21}. The 21-acetoxy-20-ketones possess a weak band at 1414 cm.$^{-1}$ which may be a bending vibration band of the C_{21}-methylene group.[11]

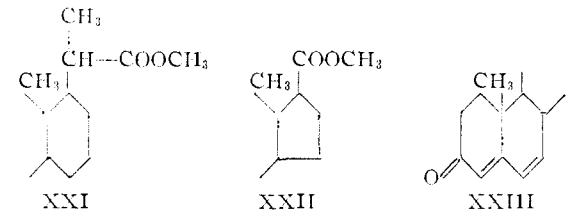


(11) The 1356 cm.$^{-1}$ band should be lacking also from the spectra of 21-hydroxy-20-ketones, which might show a methylene band between 1400 and 1435 cm.$^{-1}$. The low solubility of 21-hydroxy-20-ketosteroids in carbon tetrachloride has precluded their examination. The region 1350–1410 cm.$^{-1}$ is accessible to study in chloroform solution at 1 mm. path length, but whether or not the polarity of this solvent will affect the characteristic band positions awaits future investigation.

Steroid Alcohols and Ethers.—In the spectra of *hydroxy-steroids* no bands are observed in these regions which can be related either directly to the hydroxyl group or to its influences on neighboring methyl or methylene groups; the same holds true also for the ether groups of methoxy steroids and steroid 3,9-epoxides.

Steroid Esters.—In steroid *acyl acetates*, strong bands occur in the methyl region. 3-Acetates and 17-acetates possess two well resolved bands at 1375 and 1365 cm.$^{-1}$ (bands L and N) (Figs. 5B, 5C). Two similar bands occur also in the spectrum of cyclohexanol acetate (Fig. 5A). In 20-acetates only one acetate methyl band is resolved. The presence of two methyl absorption in the 3- and 17-acetate spectra may be dependent on stereochemical factors, and it recalls the splitting of the C–O stretching band (near 1240 cm.$^{-1}$) which is very pronounced in the spectra of certain types of 3-acetoxy steroids.[12] A weak band near 1437 cm.$^{-1}$ is also noted in the spectra of some acetates (including cyclohexanol acetate) but it is absent from others. In *phenolic steroid acetates* (*e.g.* estrone acetate)[13] there is a single acetate methyl band at 1372–1374 cm.$^{-1}$. *Acyl formates* and *acyl benzoates* show no characteristic absorption between 1350 and 1500 cm.$^{-1}$; *acyl 3,5-dinitrobenzoates* possess a very strong band at 1344 cm.$^{-1}$; *acyl acetoacetate* esters and *acyl benzoylacetate* esters absorb strongly at 1412–1417 cm.$^{-1}$.

In steroid *carbomethoxy esters*, there is a moderately intense band at 1438–1440 cm.$^{-1}$ (band D). The obvious assignment of this to the perturbing influence of the carbomethoxy group on an adjacent methylene group must be discounted, since the band occurs in methyl esters of bisnorcholanic acid (XXI) and etiocholanic acid (XXII) where there is no α-methylene group present. Most carbomethoxy esters also absorb at 1356–1360 cm.$^{-1}$ and some show a weak band near 1420 cm.$^{-1}$. Similar bands are observed also in the spectra of methyl esters of fatty acids and are at present the subject of more detailed investigation.



Unsaturated Steroids.—In many unsaturated steroids an absorption band occurs near 1438 cm.$^{-1}$ (band E). A band at the same position is seen also in the spectrum of cyclohexene and seems to require the presence of a methylene group in a six-membered ring adjacent to an unsaturated linkage. The band is strong in Δ^5-steroids (Figs. 4A, 4B) and in Δ^2, $\Delta^{8,9}$ and $\Delta^{8,14}$-steroids, but it is very weak in Δ^7-steroids. It is not observed in

(12) R. N. Jones, P. Humphries, F. Herling and K. Dobriner, THIS JOURNAL, **73**, 3215 (1951).

(13) Steroids containing aromatic A or B rings possess strong absorption bands between 1475 and 1500 cm.$^{-1}$; these are probably due to vibrations of the benzene ring and do not involve methyl or methylene groups.

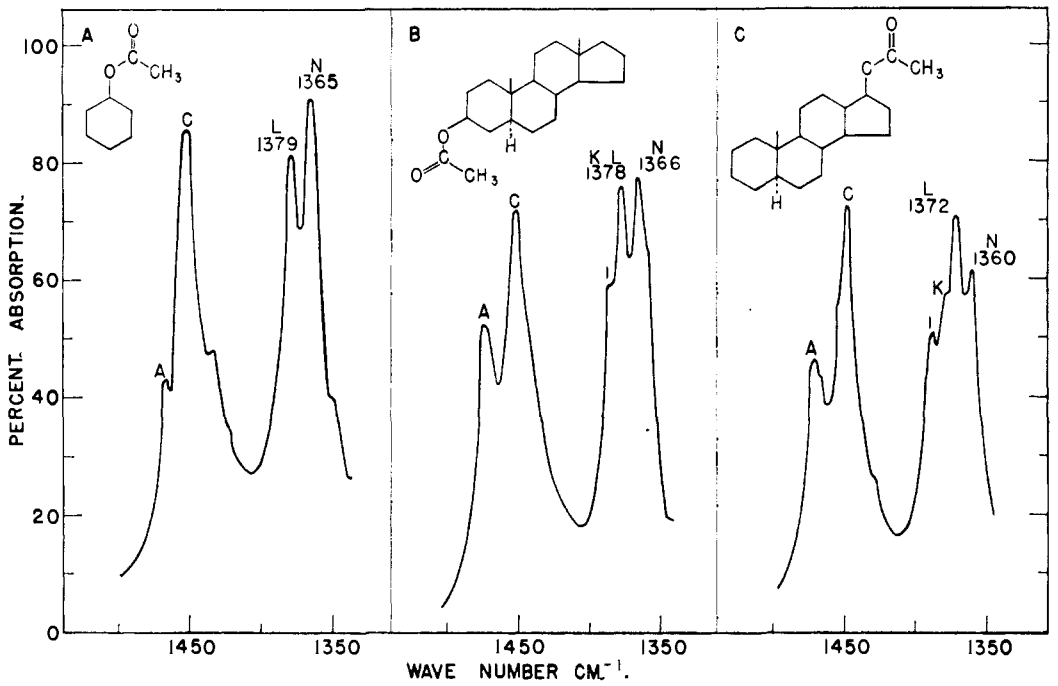


Fig. 5.—Infrared spectra illustrating absorption characteristic of the acetate group (bands L and N): A, cyclohexanol acetate; B, androstanol-3β acetate; C, androstanol-17β acetate.

Δ^{14}-ergostenol where the only methylene group adjacent to the double bond is in the 5-membered ring, nor does it occur in Δ^{22}-ergostene derivatives (XII) where there are no α-methylene groups.

The same band is observed also in $\alpha\beta$-unsaturated ketones, provided the necessary conditions are met. Thus it occurs in Δ^4-3-ketones (XIII) and $\Delta^{1,4}$-diene-3-ketones (XVI) which have a free methylene group at C_6 but not in Δ^1-3-ketones (XIV) nor in $\Delta^{4,6}$-diene-3-ketones (XXIII). A band at 1435–1440 cm.$^{-1}$ is observed also in the spectra of steroid estrogens and other steroids in which rings A or B are aromatic, and in $\Delta^{4,6}$- and $\Delta^{5,7}$-dienes.[14]

It seems plausible to attribute these bands to the bending vibration of the α-methylene group, perturbed by the adjacent unsaturated linkage, but this interpretation has not yet been checked by observations on suitable deuterated compounds.

Applications to Determinations of Structure.—The value of this region of the spectrum in the elucidation of molecular structure is potentially considerable, and it is enhanced by the fact that the specific methyl and methylene band positions are retained when two or more functional groups are present. Thus in androstanedione-3,17 bands occur both at 1408 and 1420 cm.$^{-1}$ characterizing the methylene groups at C_{16} and at C_2 and C_4, respectively.

An excellent illustration of the independence of these vibrations is provided by the spectrum of Δ^4-19-norpregnenedione-3,20 (VII) shown in Fig. 6. The six bands which occur between 1350 and 1500 cm.$^{-1}$ are cross referenced by the letters A, C, E, G, K, O to the characteristic band positions listed in Table II. Bands A and C can be assigned to the six unperturbed cyclic methylenes at C_1, C_7, C_{11}, C_{12}, C_{14} and C_{15}; band E to the methylene at C_6 adjacent to the Δ^4-double bond; band G to the C_2 methylene adjacent to the C_3-carbonyl; band K to the angular methyl group at C_{13} and band O to the C_{21}-methyl group next to the C_{20}-carbonyl. From the C=O and C=C stretching regions shown also in Fig. 6 the 20-ketone group, the Δ^4-3-ketone group and the Δ^4-double bond are characterized by the position of bands α, β and γ. Thus an analysis of these two regions of the spectrum provided a fairly complete interpretation of the whole structure of this steroid.

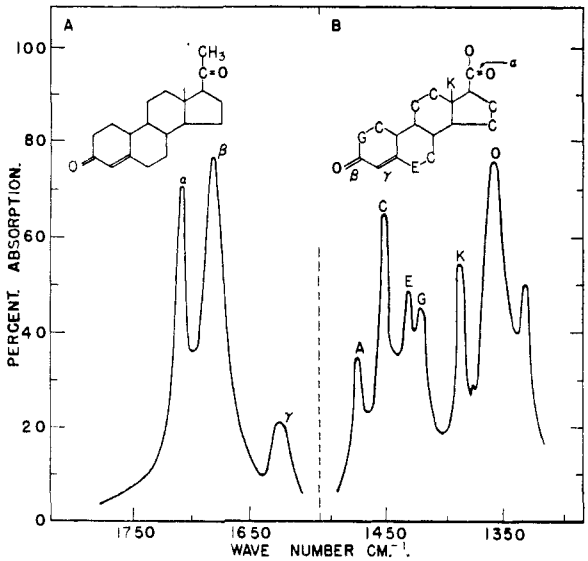


Fig. 6.—Infrared spectrum of Δ^4-19-norpregnenedione-3,20: A, C=O and C=C stretching regions; B, methylmethylene bending region; letters on structural formula relate to band assignments (see text).

(14) $\Delta^{4,6}$-Dienes also possess a band at 1428 cm.$^{-1}$. The interpretation of the methylene region in the spectra of conjugated dienes is still unclear and merits further investigation.

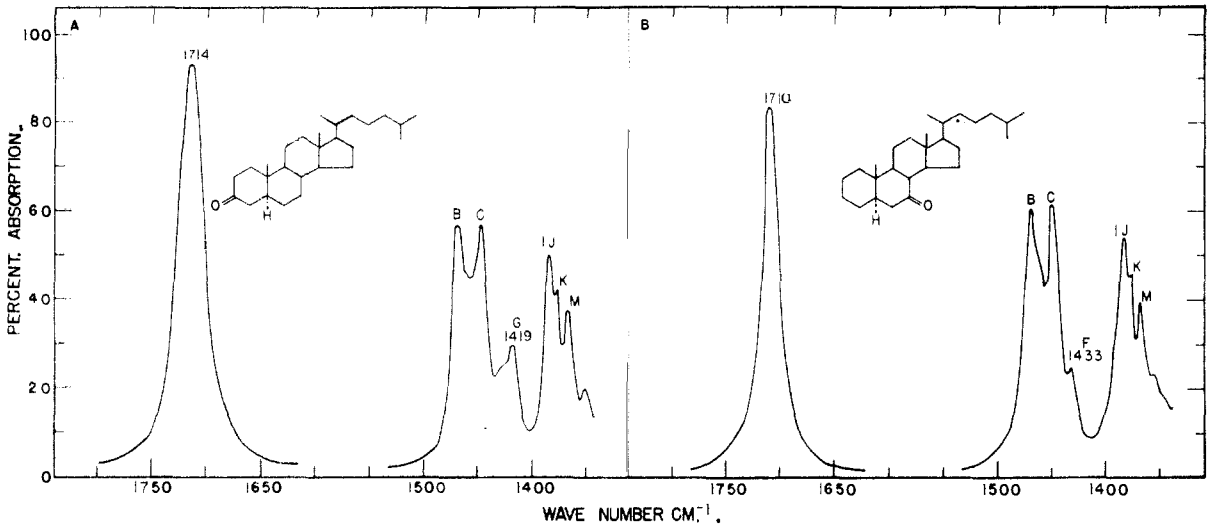
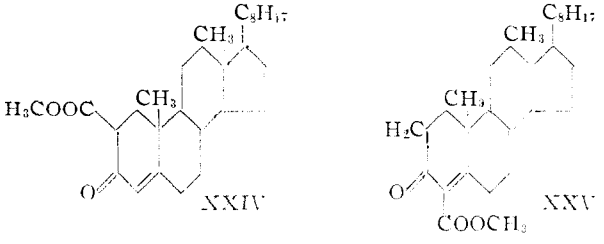


Fig. 7.—Infrared spectra of cholestanone-3 and cholestanone-7 illustrating the use of bands F and G to differentiate between the carbonyl positions.

Absorption in the methyl–methylene region has also proved useful in determining the location of carbonyl groups in steroids. From observation of the position of C=O stretching bands it is not possible to distinguish unequivocally among steroids containing non-conjugated carbonyl groups at C_3, C_4, C_6, C_7, C_{11}, C_{12} or C_{20}, since these groups give C=O stretching bands in overlapping ranges between 1706 and 1719 cm.$^{-1}$ in carbon disulfide or carbon tetrachloride solution.[3,5] However, the methylene groups α- to the 3-ketone absorb at 1419 cm.$^{-1}$ and can be easily distinguished from the corresponding band at 1434 cm.$^{-1}$ in 4, 7, 11 or 12-ketones; an example illustrating this is shown in Fig. 7. In 20-ketones in which there is a methyl group at C_{21} there is the characteristic methyl absorption at 1356 cm.$^{-1}$.

The necessity of a free α-methylene group for absorption between 1400 and 1435 cm.$^{-1}$ may also be useful in distinguishing among substituted ketosteroids. The spectra of Δ^4-2-carbomethoxycholestenone-3 (XXIV) and Δ^4-4-carbomethoxycholestenone-3 (XXV) are shown in Fig. 8. In XXV which contains a free methylene at C_2 the expected band



at 1421 cm.$^{-1}$ is observed, while in XXIV where the carbomethoxy group is introduced at C_2 this band is missing.

Finally, it may also be pointed out that this region of the spectrum can be particularly valuable for distinguishing among steroid homologs containing the same functional groups. In Fig. 9 are shown the spectra of Δ^{22}-5-isoergostenol-3α (XXVI) and Δ^{22}-5-isostigmastenol-3α (XXVII), two ster-

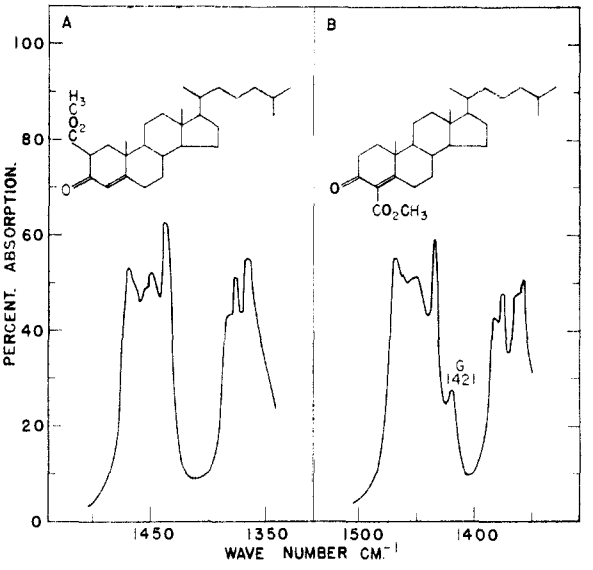
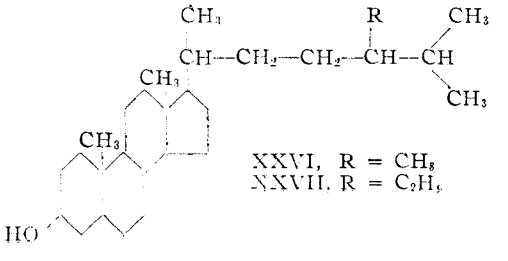


Fig. 8.—Infrared spectra illustrating use of band G to differentiate between 2-substituted and 4-substituted Δ^4-3-ketones.

oids which differ only in the presence of a methyl or an ethyl group at C_{24}. In the regions accessible to study in carbon disulfide solution these curves are almost identical, and might reasonably be mistaken for the spectra of the same compound. In the methyl bending region the spectra of XXVI and XXVII differ quite significantly, XXVI possessing two resolved maxima and two inflections while XXVII possesses three resolved peaks.



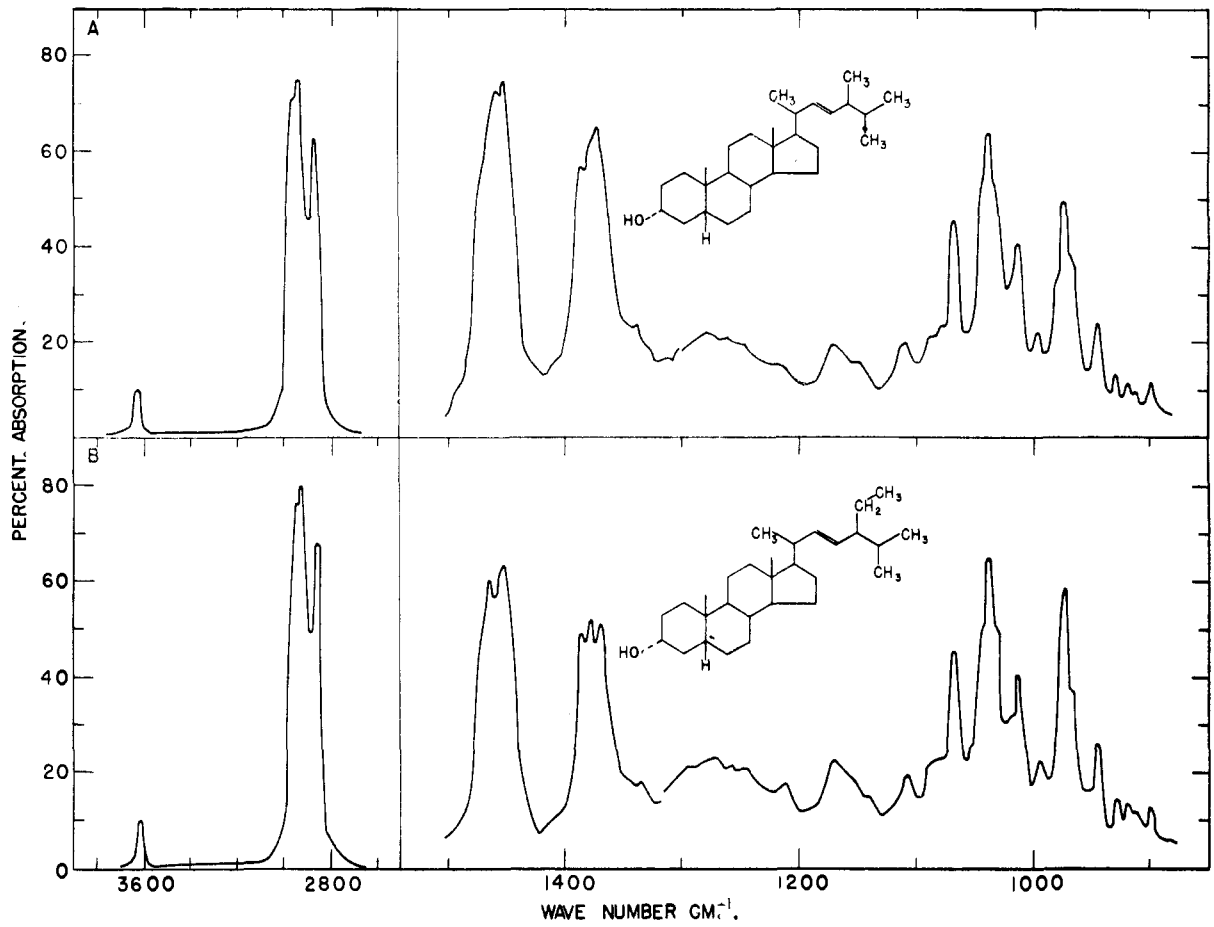


Fig. 9.—Infrared absorption spectra illustrating use of methyl–methylene region to differentiate between steroid homologs: A, Δ^{22}-5-isoergostenol-3α; B, Δ^{22}-5-isostigmastenol-3α.

Discussion of the more general aspects of this investigation will be deferred for consideration in the following paper.

Acknowledgments.—During the course of these investigations the authors have enjoyed the opportunity of frequent discussion with the late Dr. Konrad Dobriner of the Sloan–Kettering Institute, New York, and his interest in the work is gratefully acknowledged. We wish to thank the several investigators, listed individually in a footnote to Table I, who made available many of the compounds to us and Dr. B. Nolin who provided the spectra of a number of the steroid acetates and monoketones. Thanks are also due to Miss L. Groth, Mr. D. S. Keir, Mr. R. Lauzon and Mrs. M. MacKenzie for technical assistance in the determination of the spectra.

OTTAWA, CANADA