affording 6 mg. (3%), micro m.p. 86–88° (softening from 85°). A mixture with the sample prepared from bicyclohexyl-4,4′-dione gave no m.p. depression. No crystalline product could be isolated when the Oppenauer oxidation (aluminum *t*-butoxide, cyclohexanone, toluene, 0.5 hour at reflux) was used with III.

2-Methyl-4-(*trans*-4′-hydroxycyclohexyl)-cyclohexanone (XIV).—In a three-necked flask, fitted with a stirrer and under a nitrogen atomosphere, sodium methoxide was prepared from 435 mg. of sodium in 30 ml. of anhydrous methanol. To this was added the oily hydroxymethylene compound V prepared from 1.22 g. of the hydroxyketone VII, in 50 ml. of benzene. The homogeneous solution was refluxed 15 minutes, then 25 ml. of methyl iodide was added and refluxing continued. Additional methyl iodide was added after 12 and 22 hours and refluxing was continued for a total of 34 hours. The reaction mixture tested neutral to moist litmus. Isolation of the neutral fraction gave 1.329 g. of neutral oil. The alkaline washes gave 118 mg. (8%) of alkali-soluble oil. The neutral fraction was refluxed for two hours with a mixture of 100 ml. of methanol, 25 ml. of water and 20 ml. of concentrated hydrochloric acid. In this way 1.01 g. of neutral product was obtained and 126 mg. of alkali-soluble oil (corresponding to 9% O-methylation). The neutral product was dissolved in 50 ml. of ethyl acetate, adsorbed on 70 g. of alumina and eluted with 50-cc. portions of ethyl acetate. Fractions 4–11 (1006 mg.) were combined and recrystallized from ethyl acetate–cyclohexane giving 526 mg. (40%) of crystalline methyl derivative, m.p. 62–68°. Further recrystallizations from cyclohexane or ethyl acetate–cyclohexane gave thin plates melting at 72–76°, evidently a mixture of the two possible C-2 diastereoisomers of XIV.

Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.2; H, 10.54. Found: C, 74.4; H, 10.58.

Conversion of 2-Methylcyclohexanone to 10-Methyl-Δ^{1-9}-octalone-2 (XIII).—A solution of 10 g. (89 mmoles) of 2-methylcyclohexanone in 67 ml. of pyridine in a three-necked flask fitted with a stirrer and under nitrogen was treated with an ether solution of 180 ml. of 0.5 *N* triphenylmethylsodium solution (90 mmoles). Most of the ether was removed under reduced pressure with stirring, maintaining the nitrogen atmosphere, and a solution of the methiodide (prepared from 12.8 g. of 1-diethylamino-3-butanone) in 50 ml. of pyridine was added during 13 minutes, keeping the mixture at approximately 25°. Stirring was continued at room temperature for 2 hours, then a mixture of 22 g. of potassium hydroxide, 25 ml. of water and 225 ml. of methanol was added. After one hour stirring, the mixture was decanted into 800 ml. of saturated sodium chloride solution, concentrated hydrochloric acid was added and the mixture was extracted with ether. The extracts were dried over anhydrous sodium sulfate and evaporated to an oil. Addition of cold alcohol, trituration and filtration yielded 19.2 g. of triphenylmethane. The filtrate was concentrated to an oil and distilled giving 1.02 g. (10%) of recovered 2-methylcyclohexanone, b.p. 60–64° at 20 mm. Further distillation gave 10-methyl-Δ^{1-9}-octalone-2 in two fractions: 2.62 g. (18%), b.p. 82–88° at 0.2 mm. and 1.13 g. (8%) boiling slightly higher. The purity of each fraction was determined by conversion to the semicarbazone. The first fraction gave 2.38 g., m.p. 201–203.5°, and additional 0.64 g., m.p. 200–202°, for a total of 86%. The second fraction yielded 0.98 g. (64%), m.p. 201–203.5° (du Feu, McQuillin and Robinson reported m.p. 203.5–204°).[15]

Crude 10-Methyl-6-(*trans*-4′-hydroxycyclohexyl)-Δ^{1-9}-octalone-2 ((XV).—A solution of 905 mg. of 2-methyl-4-(*trans*-hydroxycyclohexyl)-cyclohexanone (XIV) (m.p. 65–70°) in 7 ml. of dry pyridine was treated with 18 ml. of 0.5 *N* triphenylmethylsodium solution in ether as described above for 2-methylcyclohexanone, the solvent removed and the enolate treated slowly with the methiodide from 740 mg. of 1-diethylamino-3-butanone in 11 ml. of pyridine. After three hours at room temperature and the further cyclization treatment with potassium hydroxide as above, the product was isolated as before. The neutral portion was adsorbed on 70 g. of alumina from benzene, the triphenylmethane being eluted by the same solvent. Fractions 9–28 (eluted with 50-cc. portions of ether–benzene 1:1, ether and ethyl acetate) were combined, and again adsorbed from ether onto 25 g. of alumina. Fractions 11–22 (eluted with ethyl acetate) were adsorbed from ether onto 30 g. of alumina and eluted with 25-cc. portions of ether, ether–ethyl acetate 2:1 to 1:2. Fractions 22–32, which had $\lambda_{\max}^{\mathrm{EtOH}}$ 238 mμ were combined to give 155 mg. of impure yellow oil, which from the ultraviolet absorption ($\lambda_{\max}$ 238 mμ, ϵ 6800) appeared to contain approximately 40% of the octalone derivative XV. This material was used for physiological testing.

MADISON 6, WISCONSIN

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

The Infrared Spectra of Ketosteroids Below 1350 Cm.$^{-1}$

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In the infrared spectra of ketosteroids several bands can be distinguished between 1350 and 650 cm.$^{-1}$, the position of which serves to characterize the location of the ketone group and its relationship to neighboring centers of unsaturation. Many of these bands also can be recognized in the spectra of diketones, keto-esters and keto-alcohols unless submerged beneath more intense absorption associated with the other functional substituents. Some of these characteristic frequencies may be perturbed by substitution in ring C.

Ketosteroids are most effectively characterized by the intense infrared absorption band between 1800 and 1650 cm.$^{-1}$ associated with the C=O stretching vibration, and the influence of the molecular structure on the position and intensity of this band has been a subject of detailed study.[3-5] Ketosteroids also absorb characteristically between 1475 and 1350 cm.$^{-1}$ due to bands associated with methyl and methylene groups vicinal to the carbonyl group.[6] The spectra of ketosteroids between 1350 and 650 cm.$^{-1}$ have not hitherto been surveyed for group vibrations specific to the ketone group, although it has been recognized that these compounds do possess prominent bands in this region of the spectrum.[7] Such a survey now has been carried out and several new bands have been identified.

Experimental Methods and Results

The spectra were determined on Perkin-Elmer model 12 and model 21 spectrometers. Many of the data are based

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Table I

Characteristic Group Frequencies in the Infrared Spectra of Ketosteroids Below 1350 Cm.$^{-1}$

(Carbon disulfide solution)

3-Ketones of normal series

Band Category[a]	A (II)	B (II)	C (III)	D (III)	E (I)	F (I)	G (II)	H (II)	I (II)	J (II)	K (II)	L (II)
Etiocholan-3-one (Fig. 1)	1353	1337	1319	1295	1264	1250	1221	1171	1146	1102	825	765
Coprostan-3-one	1354	1336	1320	1295	1266	1248	1220	1170	1150	1100	826	767
Etiocholane-3,17-dione	1354	1336	1318	1290	1265	1247[b]	1223	1170[b]	1147	1096[b]	827[b]	764
Pregnane-3,20-dione (Fig. 13)	[i]	1335	1318	1292[b]	1266	1248	1218[b]	1173[b]	1149	1102	824	766
Etiocholan-17β-ol-3-one	1353	1335	1317	1288	1264	1250	1222	1167	1148	1103	828	767
Etiocholan-17β-ol-3-one acetate	[c]	1335	1317	1288	[c]	[c]	1219	1171	1148	1104	829	766
Pregnan-21-ol-3,20-dione acetate	[c]	1336	1317	1292	1267	1248	[c]	1172	1150	1103	828	767

3-Ketones of allo series

Band Category	A (III)	B (1)	C (I)	D (I)	E (II)	F (II)	G (II)	H (II)	I (II)	J (II)
Androstan-3-one (Fig. 2)	1312	1272	1252	1228	1176	1151	1126	1116[e]	808	753
Allopregnan-3-one	1310	1271	1250	1226	1173	1153	1125	1116	812	760
Cholestan-3-one	1309	1272	1248	1228	1175	1154	1126	1116	805	757
Androstane-3,17-dione	1312	1272	1248	1228	1170[b]	1150	1128	1117[b]	804	760
Allopregnane-3,20-dione	1310	1272	1250	1229[b]	[f]	1158[b]	1126	1122	812	760
Androstan-17β-ol-3-one	1311	1272	1250	1228	1168	1154	1127	1121	812	760

Δ^{1}-3-Ketones of allo series

Band Category	A (II)	B (II)	C (III)	D (II)	E (III)	F (III)	G (II)	H (III)	I (II)	J (I)	K (III)
Δ^{1}-Cholesten-3-one	1270	1258	1223	1162	1107	949	935	918	816	779	744
Δ^{1}-Androstene-3,17-dione	1268	1258[b]	1224	1163[b]	1109[b]	951	934	916	816	778	746
Δ^{1}-Androsten-17β-ol-3-one (Fig. 3)	1270	1258	1223	1160	1109	951	934	918	816	777	745
Δ^{1}-Androsten-17β-ol-3-one hexahydrobenzoate	1272	1257	1222	[c]	1109	952	935	918	817	778	746
Δ^{1}-3-Keto-etioallocholenic acid methyl ester	1270	1256	1220	1166	1107	952	936	920	816	778	744
Δ^{1}-Allopregnene-21-ol-3,20-dione acetate	1269	1256	[c]	1160	1110	950	936	920	820	778	745

Δ^{4}-3-Ketones

Band Category	A (II)	B (I)	C (I)	D (I)	E (III)	F (III)	G (III)	H (III)	I (II)	J (II)	K (I)	L (II)	M (II)
Δ^{4}-Androsten-3-one (Fig. 4)	1332	1270	1230	1188	1124	1111	1024	1016	957	942	863	777	681
Δ^{4}-Cholesten-3-one	1330	1270	1230	1187	1126	1112	1029	1016	958	950	862	772	674
Δ^{4}-Androstene-3,17-dione (Fig. 12)	1328	1268	1226	1190	1123[b]	1109[b]	1030	1017	958	950	863	777	678
Δ^{4}-Pregnene-3,20-dione	1329	1269	1231[b]	1188[b]	1124[b]	1112	1028	1017		951[g]	865	777	683
$\Delta^{4,12}$-Pregnadiene-3,20-dione	1328	1271	1231	1192	1124	1109	1024	1017	[f]	948	864	777	[d]
Δ^{4}-Androsten-17β-ol-3-one	1330	1270	1233	1190	1130	1112	[h]	[h]	957	940	867	777	681
Δ^{1}-Androsten-17β-ol-3-one acetate	1330	1270	[c]	1190	1129	1112	[c]	[c]	958	942	867	776	683
Δ^{4}-Androsten-17α-ol-3-one acetate	1329	1268	[c]	1194	1128[e]	1117	[c]	[c]	957	942	864	775	684
Δ^{4}-Androsten-17β-ol-3-one benzoate	1330	[c]	1232	1188	1129[e]	[c]	[c]	[c]	956	940	863	774	682
17α-Vinyl-Δ^{4}-androsten-17-ol-3-one	1328	1271	1233	1187	1125	1110	[h]	[h]	957	945	862	774[g]	676

$\Delta^{1,4}$-Diene-3-ketones

Band Category	A (II)	B (II)	C (III)	D (III)	E (III)	F (II)	G (I)	H (II)	I (II)	J (II)	K (II)
$\Delta^{1,4}$-Cholestadien-3-one (Fig. 5)	1290	1242	1148	1102	956	927	887	816	805	701	685
$\Delta^{1,4}$-Androstadiene-3,17-dione (Fig. 14)	1291[b]	1243[b]	1149	1102[b]	952	931	887	814	806	701	683
$\Delta^{1,4}$-Androstadien-17β-ol-3-one (Fig. 15)	1290	1241	1147	1104	955	932	888	815	806	702	685
$\Delta^{1,4}$-Androstadien-17β-ol-3-one hexahydrobenzoate (Fig. 16)	1289	1245	1145[e]	1103	956	932	887	816	807	702	685
3-Keto-$\Delta^{1,4}$-etiocholadienic acid methyl ester (Fig. 17)	1290	1243	[c]	1102	955	931	887	816	807	702	687

$\Delta^{4,6}$-Diene-3-ketones

Band Category	A (III)	B (II)	C (I)	D (I)	E (II)	F (III)	G (III)	H (III)	I (III)	J (II)	K (II)	L (III)	M (I)	N (III)	O (II)	P (II)
$\Delta^{4,6}$-Cholestadien-3-one (Fig. 6)	1351	1324	1267	1222	1198	1180	1110	1084	990	967	945	924	874	827	772	752
$\Delta^{4,6}$-Androstadiene-3,17-dione	1353	1326	1268	1228	1199	1176	1110[b]	1088	988	967[b]	948	926	875	833[b]	779	752
$\Delta^{4,6}$-Pregnadiene-3,20-dione		1326	1246	1222[b]	1196[b]	1181	1112	1086[b]	990	965	947[b]	924	875	829	771	752

TABLE I (*Continued*)

3β-Acetoxy-Δ^{5}-7-ketones

Band Category	A (II)	B (II)	C (II)	D (II)	E (III)	F (II)	G (III)	H (II)	I (I)	J (I)	K (I)	L (I)	M (II)	N (III)	O (II)	P (II)	Q (III)	R (II)
Δ^{5}-Cholesten-3β-ol-7-one acetate (Fig. 7)	1318	1294	1236^{j}	1184	1130	1037^{j}	1018^{e}	988	956	938	919	905	867	854^{e}	825	813	716	700
3β-Acetoxy-7-keto-Δ^{5}-bis-norcholenic acid methyl ester	1318	1294	1238^{j}	1189	1132	1035^{j}	1018	988	955	935	919	903	866	851	824	812	716	699
Δ^{5}-Androsten-3β-ol-7,17-dione acetate	1318	1294	1236^{j}	1184	1136	1036^{j}	1019	987	958	939	921	905	869	843	818	813	716	698

17-Ketones of normal series

Band Category	A (II)	B (II)	C (III)	D (II)	E (II)	F (I)	G (I)	H (III)	I (II)	J (II)	K (II)
Etiocholan-17-one (Fig. 8)	1254	1243	1203	1167	1094	1050	1005	967	826	818	704
Etiocholane-3,17-dione	1257	1247^{b}	1205	1170^{b}	1096^{b}	1049	1016	966	827^{b}	818	707
Etiocholan-3α-ol-17-one	1255	1245	1208	1168	1088	1051	1007	967	829	822	708
Etiocholan-3α-ol-17-one acetate	^{c}	^{c}	^{c}	1170	1093	1051	1007	968	830	823	708
Etiocholan-3β-ol-17-one	1255	1243	1205	1170	1097	1050	1006	968	825	820^{e}	708
Etiocholan-3β-ol-17-one acetate	^{c}	^{c}	^{c}	1171	1101	1051	1008		829	820	708

17-Ketones of allo series

Band Category	a (III)	b (III)	c (III)	d (II)	e (II)	f (II)	g (II)	h (I)	i (I)	j (III)	k (II)	l (II)	m (II)
Androstan-17-one (Fig. 9)	1288	1256	1245	1202	1162	1121	1102	1057	1011	962	828	818	709
Δ^{2}-Androsten-17-one	1287	1256	1245	1200	1163	1125	1102^{e}	1053	1010	963	828	822	712
Androstan-3,17-dione	1288	1255^{e}	^{k}	1202	1170^{b}	1117^{b}	1102	1055	1009	965	830	821	712
Δ^{1}-Androstene-3,17-dione	1288	1258^{b}	1244^{e}	1208	1163^{b}	1130	1109^{b}	1047	1009	962	830	824	710
Androstan-3α-ol-17-one	1288	1255	1240^{g}	1204	1167	1123	1106	1058	1012	965	829	822	
Androstan-3α-ol-17-one acetate	1290^{e}	^{c}	^{c}	1205	1167	1121	1104	1058	^{c}	964	829	822	
Androstan-3β-ol-17-one	1292	1257	1249	1203	1170	1128	1100	1056	1009	963	831	822	710
Androstan-3β-ol-17-one acetate	1292	^{c}	^{c}	1206	^{f}	1123	1102	1058	1011	^{f}	831	822	710

The following 17-ketones containing a Δ^{4}- or Δ^{5}-bond have a pattern of absorption which conforms in general with the 17-ketosteroids of the allo series

Δ^{4}-Androstene-3,17-dione (Fig. 12)	1286	1254	1245	1202^{e}	^{f}	1123^{b}	1109^{b}	1053	1009	965	831	822	712
$\Delta^{1,4}$-Androstadiene-3,17-dione (Fig. 14)	1291^{b}	1257	1243^{b}	1199	1162	1118	1102^{b}	1056	1007	963	830	821	712
$\Delta^{4,6}$-Androstadiene-3,17-dione	1291	^{k}	1247	1210	^{f}	1127	1110^{b}	1050	1015	967^{b}	833^{b}	822	712
Δ^{5}-Androsten-3β-ol-17-one	1288	1257	1246	^{f}	1172	^{f}	1112	1053	1008	964	831	822	715
Δ^{5}-Androsten-3β-ol-17-one acetate	1288^{g}	^{c}	^{e}	^{f}	1165	1123	1110	1056	1006	962	829	820	712

20-Ketones of normal series

Band Category	a (II)	b (I)	c (I)	d (II)	e (I)	f (I)	g (III)	h (III)	i (III)	j (III)
Pregnan-3α-ol-20-one (Fig. 10)	1289	1234	1219	1192	1173	1155	1127	1086	972	942
Pregnan-3α-ol-20-one acetate	1289	^{c}	1217^{e}	1195	1176	1154	1128	1088	972^{e}	946
Pregnan-3β-ol-20-one acetate	1289	^{c}	^{e}	1193	1176	1155^{e}	1127^{e}	1084	972	946^{e}
Pregnane-3,20-dione (Fig. 13)	1292^{b}	1236	1218^{b}	1191	1173^{b}	1155	1124	1082	972	943

The following 20-ketones containing a Δ^{4}- or Δ^{5}-bond have a pattern of absorption which conforms in general with the 20-ketones of the normal series

Δ^{4}-Pregnene-3,20-dione	1291	1231^{b}	1210	1188^{b}	1163	1149	1124^{b}	1077	978^{e}	940^{e}
$\Delta^{4,6}$-Pregnadiene-3,20-dione	1290	1234^{e}	1222^{b}	1196^{b}	1167	1149	^{f}	1086^{b}	^{f}	947^{b}
Δ^{5}-Pregnen-3β-ol-20-one acetate	1289	^{c}	^{c}	1191	1168	1152	1127^{e}	1080	978	940

20-Ketones of allo series

Band Category	A (II)	B (I)	C (I)	D (III)	E (II)	F (I)	G (II)	H (II)	I (III)
Allopregnan-20-one	1290	1231	1208	1198	1177	1155	1071	954	920
Δ^{2}-Allopregnen-20-one	1291	1231	1213	1198^{e}	1180^{e}	1156	1072	960^{g}	920
Allopregnane-3,20-dione	1290	1229^{b}	1210	1198	1184	1158^{b}	1070	964	920
Allopregnan-3β-ol-20-one (Fig. 11)	1289	1232	1211	1198	1181	1154	1075	951	914
Allopregnan-3β-ol-20-one acetate	1290	^{c}	^{c}	1201	1178	1152	1073	953	915
$\Delta^{9(11)}$-Allopregnen-3β-ol-20-one acetate	1292	^{e}	^{e}	1202	1180	1155	1075^{e}	958^{g}	920

[a] For definitions of categories see text. [b] A band at this position is associated with both the carbonyl groups. [c] This region is obscured by strong ester absorption. [d] This region of the spectrum was not measured. [e] Inflection only. [f] Band not observed. [g] Broad band. [h] Region obscured by strong hydroxyl absorption. [i] Region obscured by absorption of C_{21}-methyl group. [j] 3-Acetate band. [k] Obscured by strong 3-ketone absorption.

TABLE II

SUMMARY OF KETOSTEROID GROUP FREQUENCIES

(Carbon disulfide solution)

Band	Frequency range, cm.$^{-1}$	Category^a
3-Ketones of normal series		
A	1354–1353	II
B	1337-1335	II
C	1320–1317	III
D	1295–1288	III
E	1267–1264	I
F	1250–1247	I
G	1223–1219	II
H	1173–1167	II
I	1150–1146	II
J	1104–1100	II
K	829–824	II
L	767–764	II
3-Ketones of allo series		
A	1312–1309	III
B	1272–1271	I
C	1252–1248	I
D	1228–1226	I
E	1176–1168	II
F	1154–1150	II
G	1127–1125	II
H	1122–1116	II
I	812–804	II
J	760–753	II
Δ^1-3-Ketones of allo series		
A	1272–1268	II
B	1258–1256	II
C	1224–1220	III
D	1166–1160	II
E	1110–1107	III
F	952–949	III
G	936–934	II
H	920–916	III
I	820–816	II
J	779–777	I
K	746–744	III
Δ^4-3-Ketones		
A	1332–1328	II
B	1271–1268	I
C	1233–1226	I
D	1194–1187	I
E	1130–1124	III
F	1117–1109	III
G	1030–1024	III
H	1017–1016	III
I	958–956	II
J	950–940	II
K	867–862	I
L	777–772	II
M	684–674	II
$\Delta^{4,6}$-Diene-3-ketones		
A	1353–1351	III
B	1326–1324	II
C	1268–1264	I
D	1228–1222	I
E	1199–1198	II
F	1181–1176	III
G	1112–1110	III
H	1088–1084	III
I	990–988	III
J	967–965	II
K	948–945	II
L	926–924	III
M	875–874	I
N	829–827	III
O	779–771	II
P	752	II
$\Delta^{1,4}$-Diene-3-ketones		
A	1290–1289	II
B	1245–1241	II
C	1149–1147	III
D	1104–1102	III
E	956–952	III
F	932–927	II
G	888–887	I
H	816–814	II
I	807–805	II
J	702–701	II
K	687–683	II
3β-Acetoxy-Δ^5-7-ketones		
A	1318	II
B	1294	II
C	1238–1236	II
D	1189–1184	II
E	1136–1130	III
F	1037–1035	II
G	1019–1018	III
H	988–987	II
I	958–955	I
J	939–935	I
K	921–919	I
L	905–903	I
M	869–866	II
N	851–843	III
O	825–818	II
P	813–812	II
Q	716	III
R	700–698	II
17-Ketones of normal series		
A	1257–1254	II
B	1245–1243	II
C	1208–1203	III
D	1171–1167	II
E	1101–1088	II
F	1051–1049	I
G	1016–1005	I
H	968–966	III
I	830–825	II
J	823–818	II
K	708–704	II
17-Ketones of allo series		
a	1292–1287	III
b	1257–1255	III
c	1249–1245	III
d	1208–1200	II
e	1170–1162	II
f	1130–1117	II
g	1106–1100	II
h	1058–1047	I
i	1012–1009	I
j	965–962	III
k	831–828	II
l	824–818	II
m	712–709	II
20-Ketones of normal series		
a	1289	II
b	1236–1234	I
c	1219	I
d	1195–1191	II
e	1176–1173	I
f	1155–1154	I
g	1128–1124	III
h	1088–1082	III
i	972	III
j	946–942	III
20-Ketones of allo series		
A	1292–1289	II
B	1232–1231	I
C	1213–1208	I
D	1202–1198	III
E	1184–1177	II
F	1156–1152	I
G	1075–1070	II
H	964–951	II
I	920–914	III

[a] See footnote to Table I.

on curves which have been published in atlas form[4] and details of the experimental techniques are given in the introductory section of that publication. Minor calibration corrections have been applied to a few of the curves discussed here; this has had the effect of lowering the frequencies by 2–4 cm.$^{-1}$ in the region between 1350 and 1200 cm.$^{-1}$ below those reported in the atlas.

The positions of the bands characterizing the ketone groups are listed for the individual compounds in Table I, and summarized in Table II. One representative example of each type of monoketosteroid spectrum is shown in Figs. 1–11; the specificity of the groups in diketones are illustrated in Figs. 12–14, while the persistence of a typical carbonyl absorption pattern in the presence of various other functional groups is demonstrated by Figs. 5 and 14–17 for the $\Delta^{1,4}$-diene-3-one system.

Discussion

The discussion here will be restricted to a consideration of the practical potentialities of these bands for characterizing saturated and conjugated ketone groups in steroids. The modes of molecular vibration with which these bands are associated are not known at present, although it is our intention to discuss this problem in a later paper.

Monoketones.—In the spectra of monoketones which contain no other functional groups all the bands listed in Table II are clearly recognizable. In Figs. 1–11 these bands are identified alphabetically, but it must be emphasized that the letters are introduced solely to provide easy cross-reference with the tables, and it is not implied that bands carrying the same identification letters in Figs. 1–11 are related.

Separate series of characteristic bands are reported for ketones of the normal and allo series; the differences are usually small, and consist for the most part of slight shifts in the ranges of bands which are probably of similar origin. Although not very striking in individual spectra, if these stereochemical distinctions are disregarded, the ranges which must be assigned to the characteristic groups are widened appreciably.

As would be anticipated, these stereochemical differences are most apparent in the 3-ketones. The normal 3-ketones usually can be recognized by weak bands at 829–824 and 767–764 cm.$^{-1}$ (bands K and L of Fig. 1) and the allo 3-ketones by bands at 812-804 and 760-753 cm.$^{-1}$ (bands I and J of Fig. 2). There also are differences between 1150

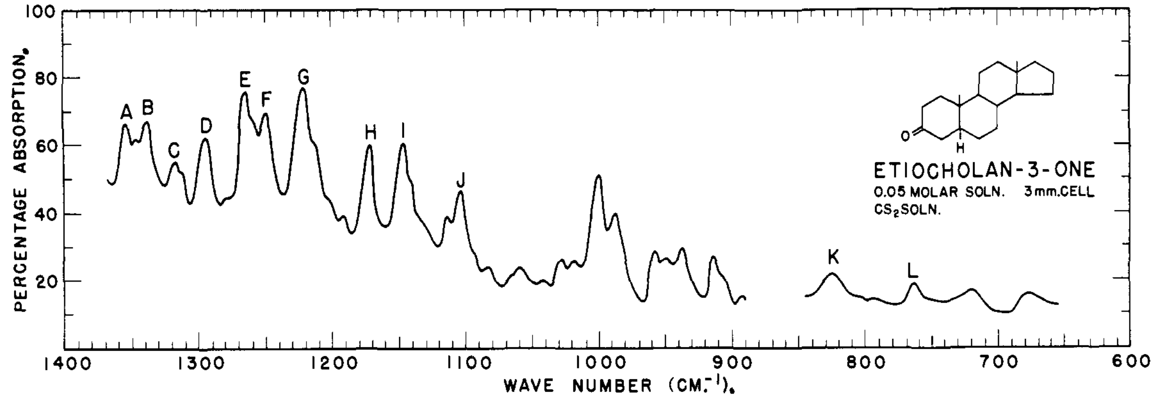


Fig. 1.—3-Keto-normal-steroid. The main characteristic bands lie between 1350 and 1100 cm.$^{-1}$ (A–J). Bands K and L may serve to differentiate from 3-keto allosteroids.

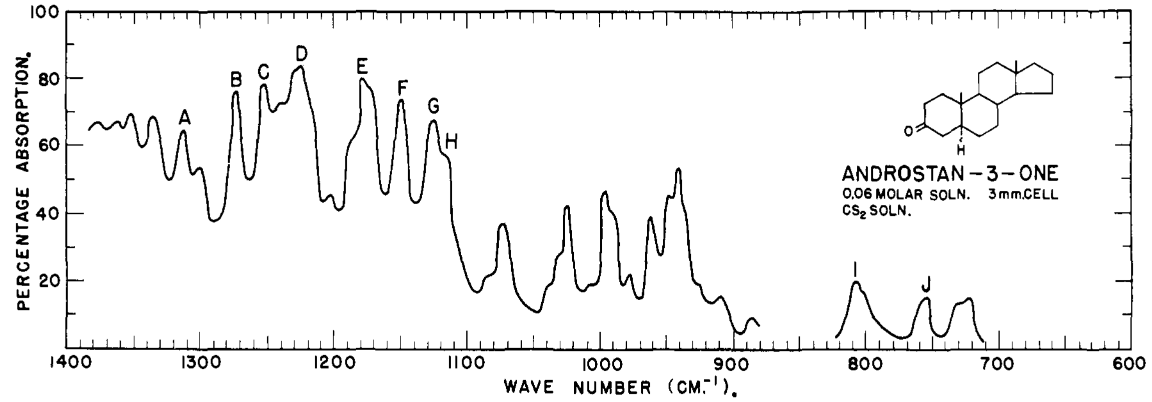


Fig. 2.—3-Keto-allo-steroid. The main characteristic bands lie between 1320 and 1100 cm.$^{-1}$ (A–H). Bands I and J may serve to differentiate from 3-keto normal-steroids (see above).

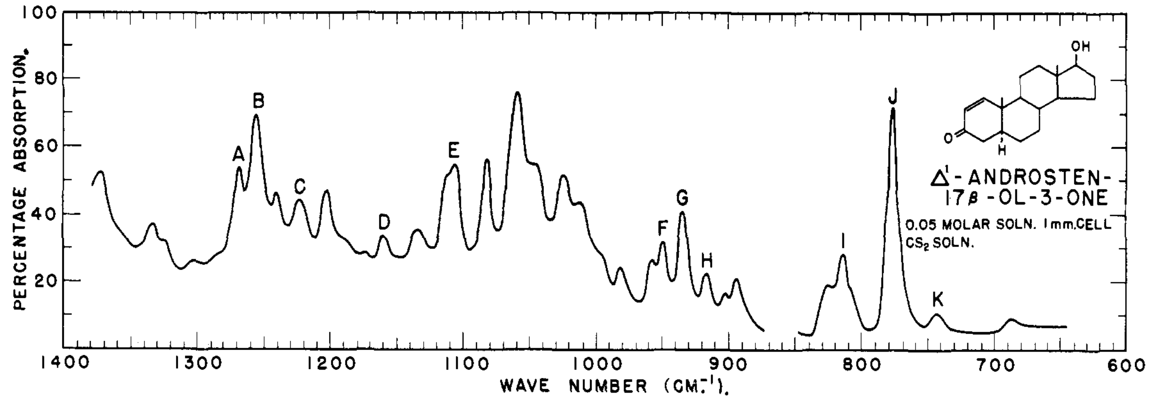


Fig. 3.—Δ^1-3-Keto-allo-steroid; primarily characterized by band J.

and 1080 cm.$^{-1}$, but the stronger bands between 1280 and 1150 cm.$^{-1}$ are more alike in the two stereochemical series. The differences above 1280 cm.$^{-1}$ are not so great as the tables might suggest since many 3-allo ketones possess bands in this region which have not been classified since they do not so readily fall into recognizable frequency ranges.

The 17-ketones of both the normal and allo series exhibit a similar pair of major bands near 1050 and 1010 cm.$^{-1}$ (bands F, G and h, i in Figs. 8 and 9). These are highly characteristic of the 17-ketone group and can be identified even in the presence of strong overlapping absorption in the spectra of hydroxy and acetoxy derivatives. The two stereochemical series differ mainly between 1150 and 1080 cm.$^{-1}$, but the differences do not involve any very prominent bands which would serve effectively to differentiate between the two stereochemical series in individual compounds.

The 20-ketones lack characteristic bands below 900 cm.$^{-1}$, probably because of the absence of α-methylene groups with which these low frequency bands in non-conjugated steroids may be associated. The differences between the 20-ketones of the normal and allo series consist mainly of small displacements in the frequency ranges of similar

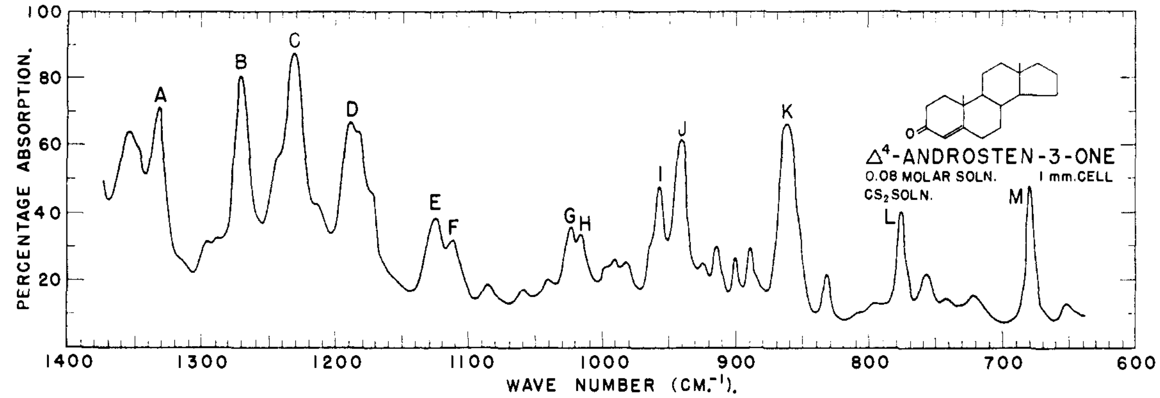


Fig. 4.—Δ^4-3-Ketosteroid; primarily characterized by band K supplemented by bands B, C and D. Anomalous behavior may be shown by 19-nor-Δ^4-3-ketosteroids (see text).

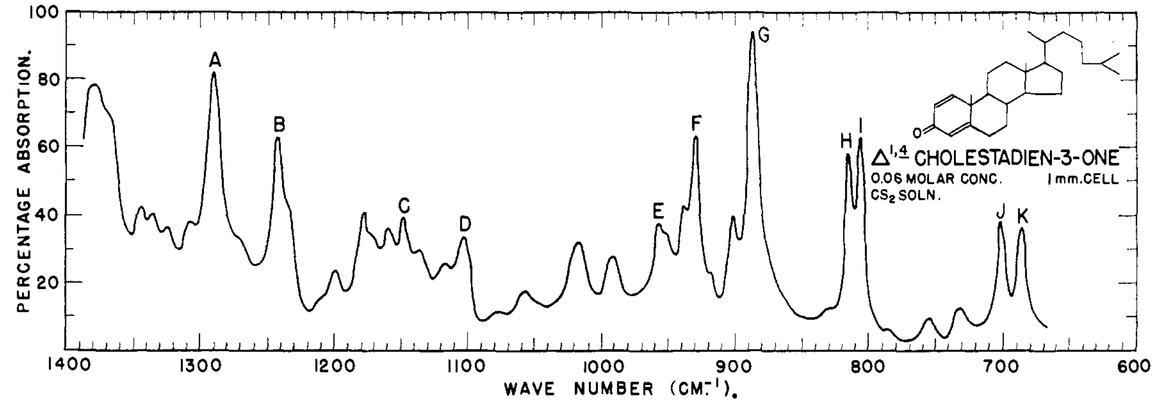


Fig. 5.—$\Delta^{1,4}$-Diene-3-ketosteroid; primarily characterized by band G supplemented by bands A and B and the doublet structures H, I and J, K (*cf.* Figs. 14–17).

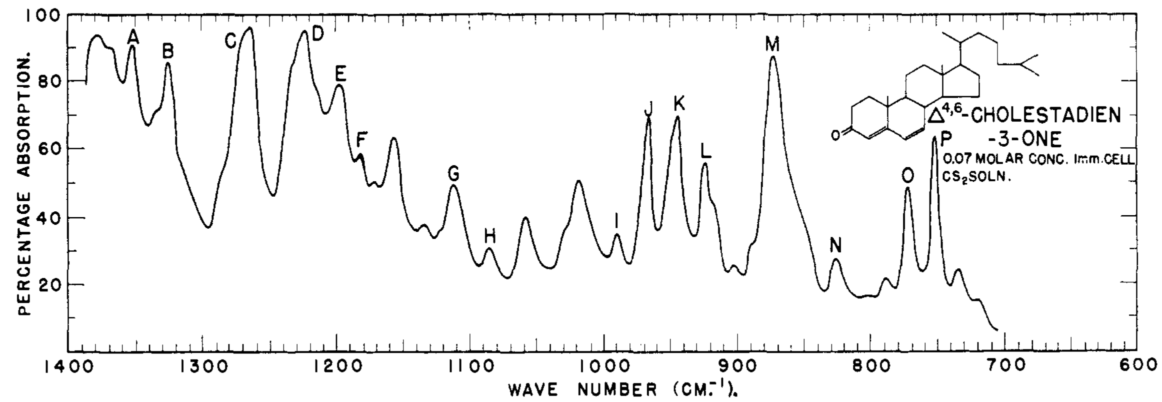


Fig. 6.—$\Delta^{4,6}$-Diene-3-ketosteroid; primarily characterized by band M supplemented by bands C and D and the doublet structures J,K and O,P.

bands (*cf.* bands a/A, b/B, c/C, d/D and e/E in Figs. 10 and 11).

Conjugated Ketones.—The conjugated ketones are best identified by the strong, well separated bands which they exhibit below 900 cm.$^{-1}$; some of these are no doubt associated with out-of-plane bending vibrations of the C–H bonds on the ethylenic linkages. This type of spectrum is particularly well illustrated in the $\Delta^{1,4}$-diene-3-one curves shown in Figs. 5 and 14–17. In addition to the very prominent band at 888–887 cm.$^{-1}$ this system is also characterized by the sharp bands at 932–927, 816–814, 807–805, 702–701 and 687–683 cm.$^{-1}$ (bands F–K of Figs. 5, 14–17). None of these bands are disturbed appreciably by the presence of other functional groups.

Diketones.—In the diketones included in Table I the two carbonyl groups are located in rings A, B, D or in the side chain and are well spaced from one another. Under these conditions most of the bands characteristic of each carbonyl group can be distinguished, although it is sometimes necessary to assign the same peak to both functional groups. Such cases are identified in Table I by a superscript

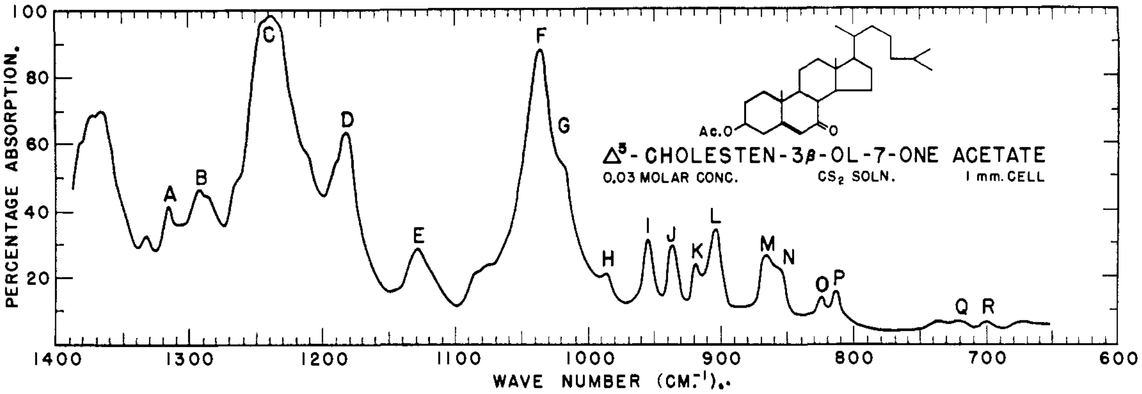


Fig. 7.—3β-Acetoxy-Δ^5-7-ketosteroid; the ketonic structure is primarily characterized by the quadruplet group of bands I, J, K and L. The strong bands C and F are associated with the acetate.

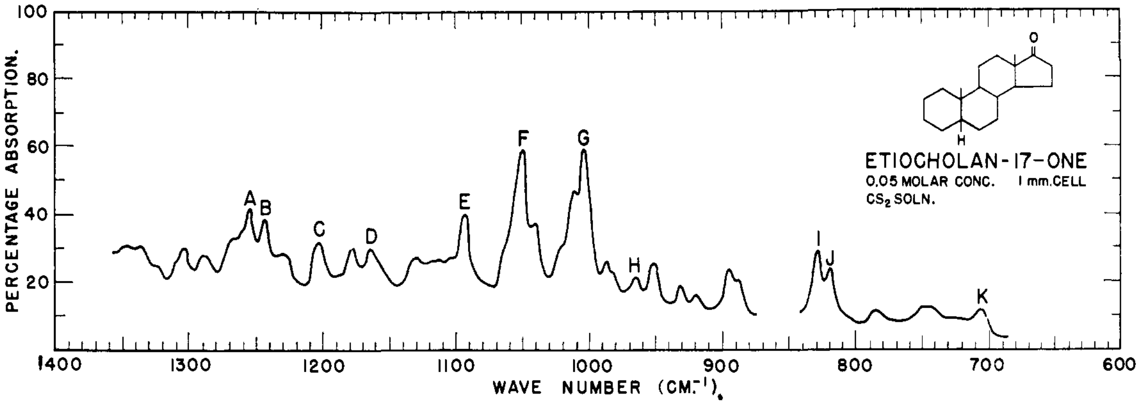


Fig. 8.—17-Keto-normal-steroid; primarily characterized by bands F and G.

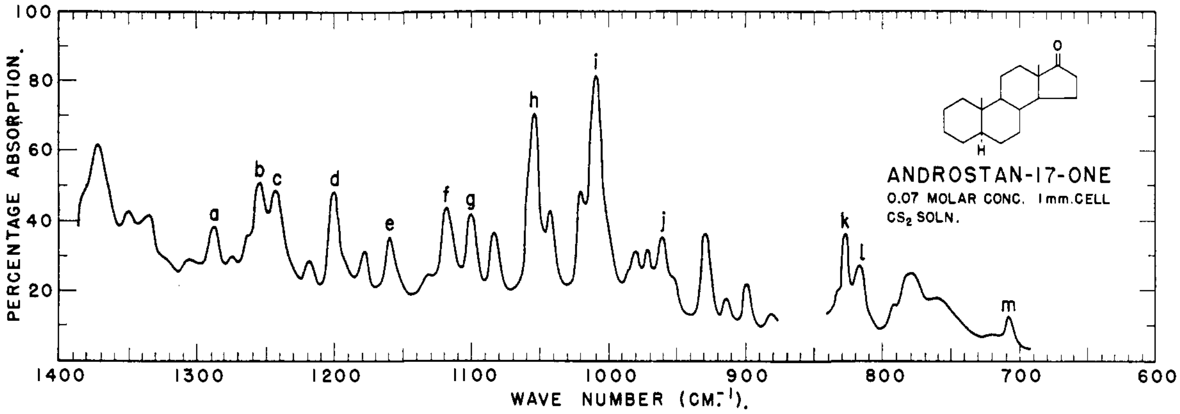


Fig. 9.—17-Keto-allo-steroid; primarily characterized by bands h and i.

b. In many instances it is possible that two superimposed bands are present, but this is difficult to establish. It cannot be inferred from the band intensity, since it is not unusual for bands in this region of the spectrum to be intensified in poly-substituted steroids even when such superposition effects can be discounted. The persistence of these carbonyl bands in diketone spectra is illustrated in Figs. 12–14 for Δ^4-androstene-3,17-dione, pregnane-3,20-dione and $\Delta^{1,4}$-androstadiene-3,17-dione; the bands assigned to each carbonyl group are indicated and may be identified by cross-reference with the monoketone spectra in Figs. 1, 4, 5, 9 and 10.

The introduction of substituents into ring C produces rather more significant changes, particularly for the 11-ketone group. Reserve must be exercised in applying these correlations where 11-ketosteroids are involved and it is our intention to deal with this problem separately in another paper.

Keto-alcohols and Keto-esters.—In keto-alcohols and keto-esters the ketone bands are usually distinguishable unless submerged under more intense absorption associated with the ester or alcohol groups. This is particularly liable to occur between 1280 and 1200 cm.$^{-1}$ in the spectra of keto-acetates, where the very intense ester C–O absorp-

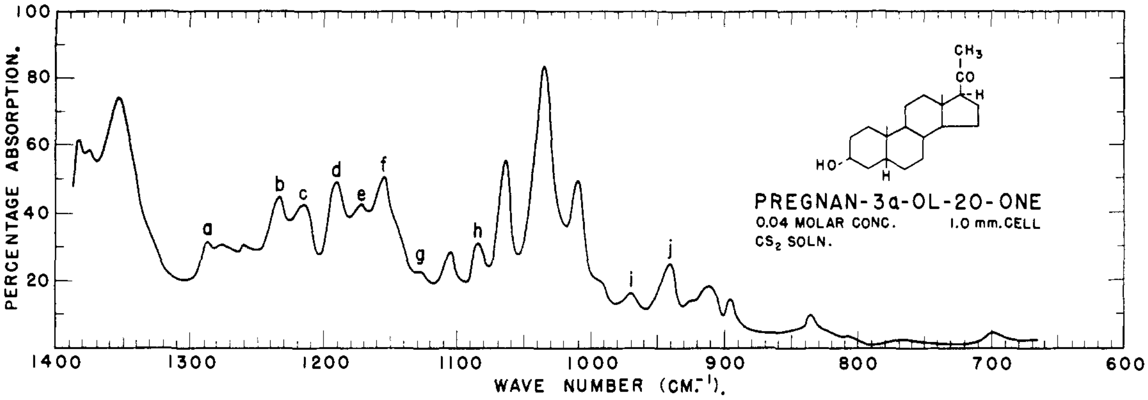


Fig. 10.—20-Keto-normal-steroid; primarily characterized by the group of bands b–f. Note the absence of significant structure below 900 cm.$^{-1}$.

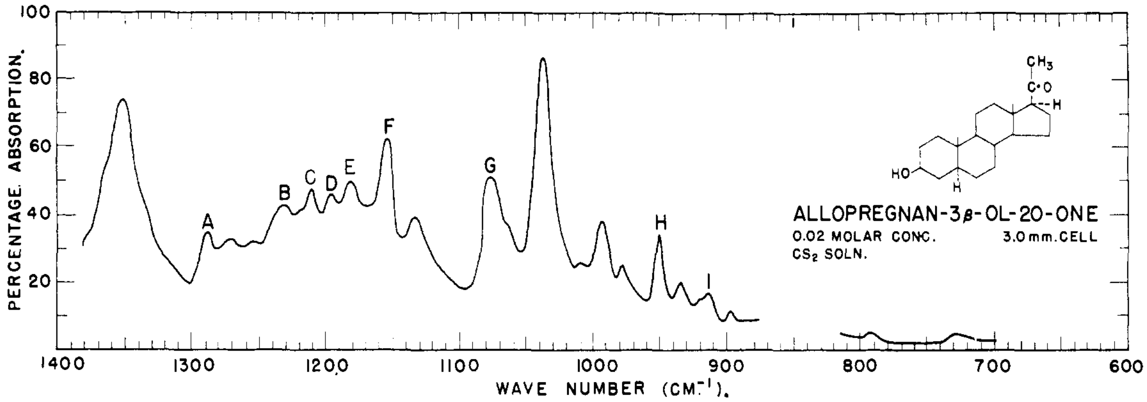


Fig. 11.—20-Keto-allo-steroid; primarily characterized by the group of bands B–F. Note the absence of significant structure below 900 cm.$^{-1}$.

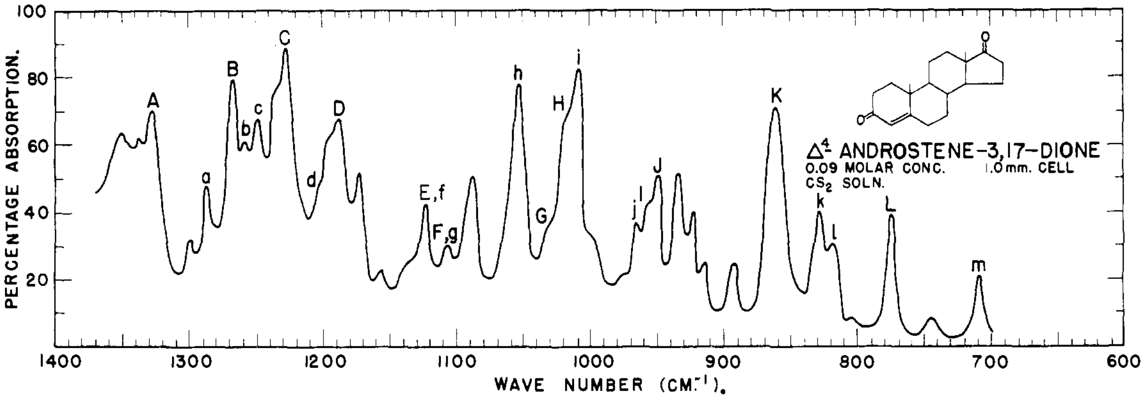


Fig. 12.—Δ^4-3,17-Diketosteroid; bands attributed to the characteristic absorptions associated with the Δ^4-3-ketone and 17-ketone groups are indicated (*cf.* Figs. 4 and 9).

tion obliterates the weaker ketone bands. The ketone groups in keto-alcohols and keto-esters are best identified from the bands in the lower frequency ranges.

In Table I, data are included for the 3β-acetoxy-Δ^5-7-ketone system; this has been treated as a single structural unit since Δ^5-7-ketones not acetylated at C_3 were unavailable. In view of the proximity of the groups it was not considered advisable to attempt to assign absorption separately to the ester and ketone groups.

Applications to Structure Identification.—The primary spectrographic characterization of carbonyl groups in steroids should be based on the position of the C=O stretching bands, but the additional characteristic absorption described here can be very helpful for confirmation purposes and in some cases may serve to distinguish systems which give C=O stretching bands at closely similar positions. This is true particularly of the various types of conjugated 3-ketones. The Δ^1-3-keto-allo-steroids and Δ^4-3-keto-steroids which both have

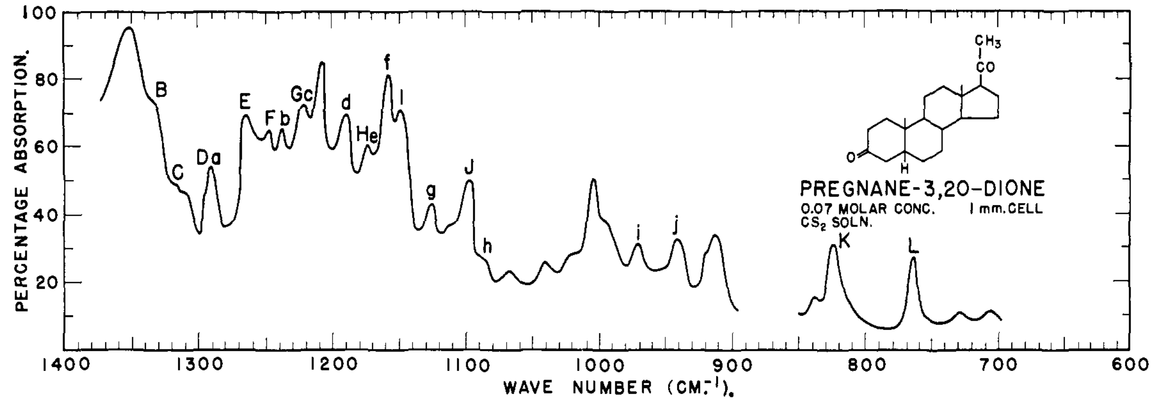


Fig. 13.—3,20-Diketo-normal-steroid; bands attributed to the characteristic absorption associated with the 3-normal ketone and 20-ketone groups are indicated (*cf.* Figs. 1 and 10).

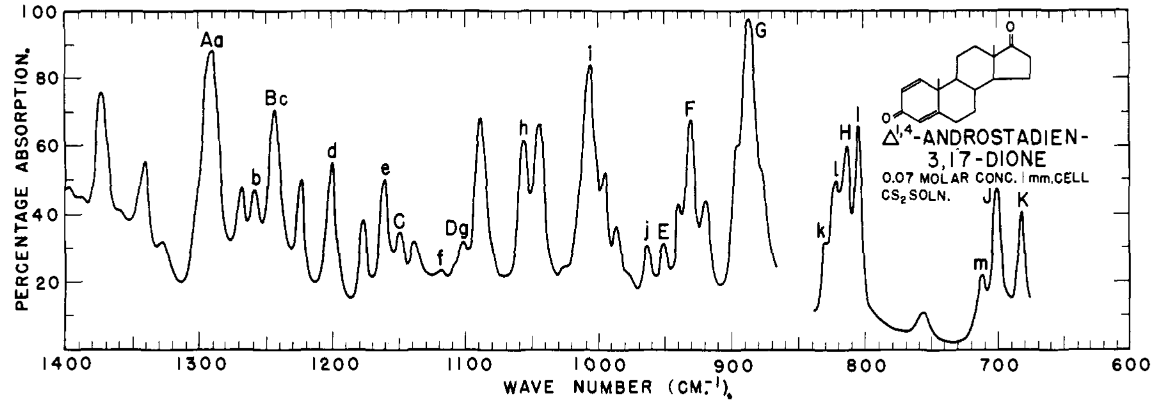


Fig. 14.—$\Delta^{1,4}$-Diene-3,17-diketosteroid; bands attributed to the characteristic absorption associated with the $\Delta^{1,4}$-diene-3-ketone and 17-ketone groups are indicated (*cf.* Figs. 5 and 9). Note particularly the characteristic pattern of low frequency absorption associated with bands G–K of the diene-one group.

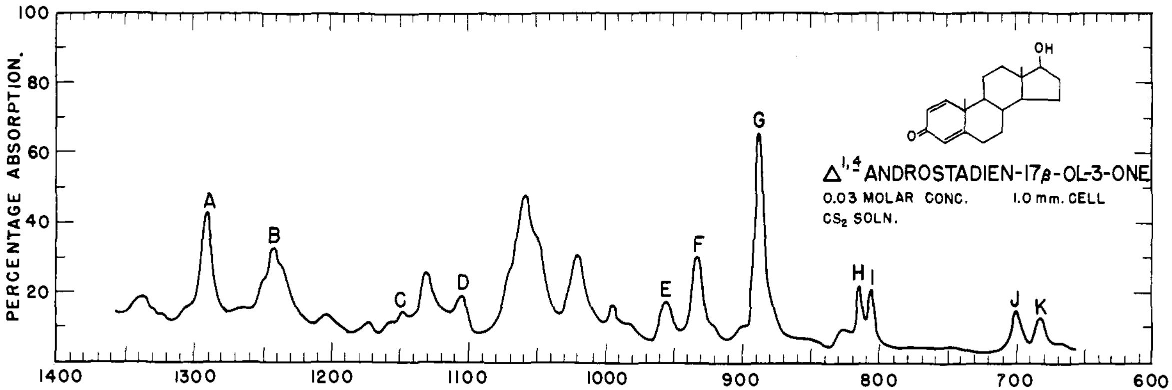


Fig. 15.—$\Delta^{1,4}$-Diene-17β-ol-3-one hydroxyketosteroid illustrating persistence of the characteristic diene-one absorption in the presence of the 17-hydroxyl group (*cf.* Fig. 5).

C=O stretching bands between 1684 and 1677 cm.$^{-1}$ in CS_2 or CCl_4 solution can be readily distinguished by the strong bands at 779-777 and 867-862 cm.$^{-1}$, respectively, while $\Delta^{1,4}$-diene-3-keto-steroids and $\Delta^{4,6}$-diene-3-keto-steroids which both absorb between 1671 and 1666 cm.$^{-1}$ are distinguished by bands at 888-887 and 875-874 cm.$^{-1}$, respectively.

In using these bands to identify the ketone type, attention should be paid to the over-all pattern of absorption, since accidental resonances may occasionally cause displacement of one or more of the individual bands. In the course of a survey of the "finger-print" region of steroids of all types it has become apparent that the region between 1150 and 1050 cm.$^{-1}$ is the most sensitive to individual variations from compound to compound and particular caution must be exercised in identifying characteristic group frequencies in this region.

The characteristic ketone bands discussed in this

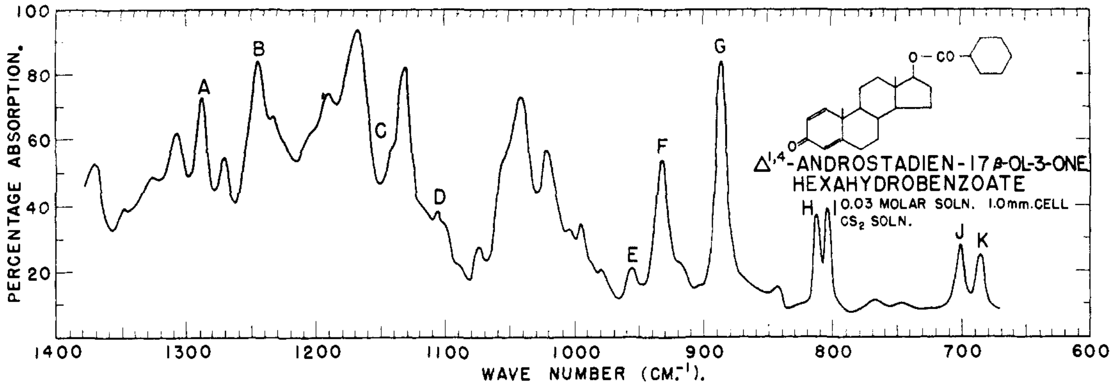


Fig. 16.—$\Delta^{1,4}$-Diene-17β-ol-3-one hexahydrobenzoate ester illustrating persistence of the diene-one absorption in the presence of the 17-ester group (*cf.* Fig. 5).

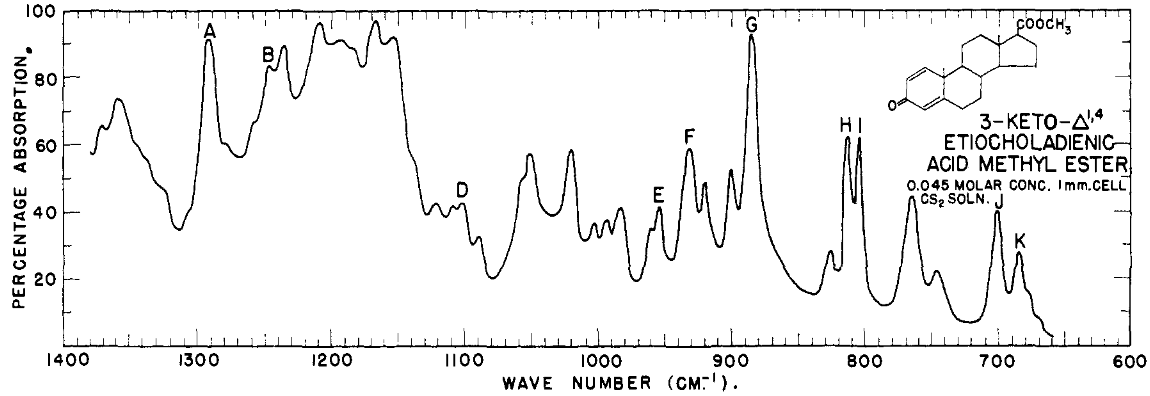
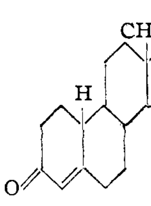


Fig. 17.—17-Carbomethoxy-$\Delta^{1,4}$-diene-3-one illustrating persistence of the diene-one absorption in the presence of the 17 carbomethoxy group (*cf.* Fig. 5).

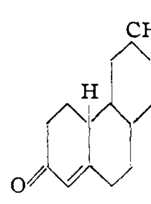
paper are classified into three categories (I, II and III) in their order of diminishing usefulness for identification purposes. Such a classification is of necessity based on rather intangible factors. In using these bands, attention should first be directed to recognition of category I bands, after which most of the category II bands will usually be found prominent enough to provide confirmatory evidence. The bands of category III are weaker; they show up in the simpler ketosteroids, but are liable to be lost by overlap or displacement in the more highly substituted compounds. They are included here since they may prove of interest when the nature of the vibrations responsible for these bands is better understood.

In preparing Tables I and II some additional bands also were surveyed, but were rejected for their failure to appear in one or two compounds or for other reasons. The tables therefore do not pretend to present a complete picture of the absorption pattern associated with the various types of ketone groups and additional bands may be added, or others withdrawn as more information becomes available.

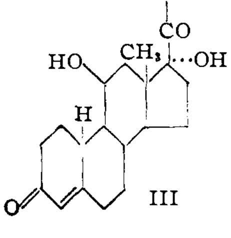
Effects of Conformational Isomerism.—The differences between the spectra of 3-ketones of the normal and allo series suggests that these bands may be helpful in the recognition of other forms of stereoisomerism such as conformational isomerism or boat-chair inversions in ring A. Although no well-authenticated examples of such effects have yet been established a curious anomaly has been noted in the spectra of 19-nor-Δ^4-3-keto-steroids. Of three such compounds which have been examined, two (I and II) exhibit a pattern of absorption very different from that of the Δ^4-3-ketones containing the C_{19} angular methyl group; only the minor A, and F bands of the Δ^4-3-ketone spectrum are identifiable. The spectra of I and II resemble each other, however, in absorbing at 1255, 1205, 965, 875, 853 and 760 cm.$^{-1}$; the 875 cm.$^{-1}$ band standing out prominently. The third 19-norsteroid (III) shows none of this absorption, but pos-



I



II



III

sesses the A, B, C, E, F, G, K, L and M bands of the ordinary Δ^4-3-ketone spectrum. Such differences might be understandable if III has the same A-ring conformation as the ordinary Δ^4-3-ketones while that of I and II is different. The spectra of all three compounds have been compared as Nujol mulls and of I and II also in carbon disulfide solution.

Acknowledgments.—We wish to express our gratitude to the many chemists who have provided the compounds on which these investigations are based; acknowledgments to the individual donors of most of the steroids discussed here have been made in our earlier publications. To these we wish to add our thanks to Dr. C. Djerassi of Wayne University for the three 19-norsteroids. The technical assistance of Miss B. Boland, Miss R. Connolly, Mr. R. Cohen and Mrs. M. MacKenzie is also gratefully acknowledged.

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The Reaction of Lead Tetraacetate with Progesterone and Testosterone

BY ROBERT L. CLARKE, KONRAD DOBRINER,[1] ARAM MOORADIAN AND CATHERINE M. MARTINI

RECEIVED APRIL 30, 1954

From the reaction of two or three moles of lead tetraacetate with one of progesterone were isolated 2α-hydroxyprogesterone acetate, 2α,21-dihydroxyprogesterone diacetate, and 1,4-pregnadien-21-ol-3,20-dione acetate. From the reaction of lead tetraacetate with testosterone acetate were isolated 2α-hydroxytestosterone diacetate, 2β-hydroxytestosterone diacetate and 1,4-androstadien-17β-ol-3-one acetate. Some reactions of these compounds are described. The rearrangement of 6-bromotestosterone acetate to 2-hydroxytestosterone diacetate was observed with isolation of the 2β-epimer rather than the previously reported 2α-epimer.

Several studies have been made of the mole for mole reaction of lead tetraacetate (LTA) with progesterone.[2–4] The products isolated were 2α-hydroxyprogesterone acetate, 2α,21-dihydroxyprogesterone diacetate, desoxycorticosterone acetate and an unidentified monohydroxyprogesterone.[2c]

Reichstein and Montigel[3] treated 1 mole of allopregnan-3-ol-20-one acetate with 1.8 moles of LTA to produce 53% acetoxylation at C-21 and 2% diacetoxylation at C-17, 21. 5-Pregnen-3-ol-20-one acetate with 3.2 moles of LTA gave a 19% yield of a 21-acetoxylated product. Mancera[5] acetoxylated 5-pregnen-3-ol-20-one benzoate at C-21 in 39% yield (1 mole LTA, if 100% pure), whereas Giral,[6] using this benzoate and more than a fourfold excess of LTA, obtained a 22% yield of an unknown[5] monoacetoxylated product, the only compound isolated. Thus, there are few cases of polyacetoxylation on record, even with excess LTA.

In this Laboratory the reaction of one mole of progesterone with two moles of LTA produced a complex mixture containing at least ten components as evidenced by infrared spectra. Diacetoxylated progesterones appear to constitute a rather large portion of the reaction products, but extensive work with solvents on the original oily product gave only a 2.5% yield of pure 2α,21-dihydroxyprogesterone diacetate. Chromatography on silica gel, which was only moderately effective, gave a mixture of diacetoxylated progesterones, a center cut of which (15% yield) showed an infrared spectrum very similar to that of the pure 2,21-diacetoxy compound; the purification of this mixture was so difficult that it was abandoned. 2α-Hydroxyprogesterone acetate[2c,4] (8%) and a new compound (I), $C_{23}H_{30}O_4$ (8%), were separated chromatographically and isolated in a pure state. I apparently results from the introduction of one acetoxy group and one double bond into the progesterone molecule.

Hydrogenation of I yielded allopregnan-21-ol-3,20-dione acetate,[7] pregnan-21-ol-3,20-dione acetate[8] and a trace of allopregnan-21-ol-20-one acetate[9] which were identical with the products obtained by the hydrogenation of desoxycorticosterone acetate under the same conditions. Thus the position of the acetoxyl group was fixed at C-21.

The hydrogenation experiment indicates that both unsaturated linkages in the molecule are conjugated with a carbonyl group, but the position and height of the ultraviolet absorption maximum rules out positions 6 or 16 for the second bond. Its location at position 1 is in accord with the data, a 1,4-dien-3-one showing the same absorption pattern as a 4-ene-3-one.[10] This was confirmed by a dienone–phenol rearrangement[11] of I to form a

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[1] Deceased.

[2] (a) G. Ehrhart, H. Ruschig and W. Aumüller, *Angew. Chem.*, **52**, 363 (1939); (b) British Patent 502,474; (c) *Chem. Ber.*, **72**, 2035 (1939).

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