765. *Studies in the Synthesis of Cortisone. Part XX.* The Infrared Absorption of α-Halogeno-oxo-steroids.*

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The infrared absorption between 4000 and 400 cm.$^{-1}$ of *cyclo*hexanones, oxo-steroids, oxo-steroidal sapogenins, α-halogeno-oxo-steroids, α-bromo-oxo-triterpenoids, and related substances has been examined and the effect of α-halogen substituents on the carbonyl frequency of oxo-steroids and -triterpenoids is discussed. Low-frequency skeletal and carbon–hydrogen deformation bands that appear to be characteristic of ketone and acetate groups have been identified and are distinguished from " halogen-sensitive " bands characteristic of the type of halogen substituent. An equatorial α-halogen substituent absorbs at a higher frequency than the corresponding axial one.

THE carbonyl-stretching region of the infrared absorption spectra of α-bromo-oxo-steroids has received considerably more attention than the low-frequency region in which halogen linkages absorb. Jones, Ramsay, Herling, and Dobriner [1] (see also Corey [2] and Corey and

* Part XIX, *J.*, 1957, 1175.

[1] Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828; see also Corey, *ibid.*, 1953, **75**, 4832, and Fieser and Huang, *ibid.*, p. 4837.

[2] Corey, *ibid.*, 1953, **75**, 2301, 3297; 1954, **76**, 175.

TABLE 1. *Carbonyl stretching frequencies* (CS_2 *solution*) *and steric configurations for halogeno-oxo-steroids and -oxo-triterpenoids.*

No.	Compound	Ref.	Frequency (cm.$^{-1}$) Acetate	Ketone	Δ on halogn.*	Conformn. of C–Hal linkages
1	Cholestan-2-one	*a*	—	1712	—	—
2	3α-Chlorocholestan-2-one	*a*	—	1714	2	a *
3	3α-Bromocholestan-2-one	*a*	—	1715	3	a
4	3α-Iodocholestan-2-one	*b*	—	1708	−4	a
5	Cholestan-3-one	*c*	—	1715	—	—
6	2α-Chlorocholestan-3-one	*d*	—	1735	20	e *
7	2β-Chlorocholestan-3-one	*a*	—	1724	9	a
8	2 : 2-Dichlorocholestan-3-one	*e*	—	1737	22	e : a
9	2α-Bromocholestan-3-one	*c*	—	1730	15	e
10	4α-Bromocholestan-3-one	*f*	—	1730	15	e
11	2 : 2-Dibromocholestan-3-one	*c*	—	1732	17	e : a
12	2α : 4α-Dibromocholestan-3-one	*c*	—	1754	39	e : e
13	2α-Chloro-2β-bromocholestan-3-one	*e*	—	1736	21	e : a
14	2α-Chloro-4α-bromocholestan-3-one	*e*	—	1756	41	e : e
15	2α-Iodocholestan-3-one	*c*	—	1723	8	e
16	2α-Iodo-4α-bromocholestan-3-one	*c*	—	1750	35	e : e
17	Cholest-1-en-3-one	*c*	—	1677	—	—
18	2α-Bromocholest-1-en-3-one	*g*	—	1694	17	e
19	4α-Bromocholest-1-en-3-one	*h*	—	1692	15	e
20	Cholest-4-en-3-one	*c*	—	1674	—	—
21	2α-Chlorocholest-4-en-3-one	*e*	—	1692	18	e
22	2α-Bromocholest-4-en-3-one	*i*	—	1690	16	e
23	6α-Bromocholest-4-en-3-one	*j*	—	1680	6	e
24	6β-Bromocholest-4-en-3-one	*j*	—	1678	4	a
25	Ergosta-3 : 11-dione	*h*	—	1708	—	—
26	2α-Bromoergosta-3 : 11-dione	*h*	—	1706 1728	20	e
27	2α : 4α-Dibromoergosta-3 : 11-dione	*h*	—	1706 1754	46	e : e
28	11β-Hydroxyergostan-3-one	*h*	—	1712	—	—
29	2α-Bromo-11β-hydroxyergostan-3-one	*h*	—	1730	18	e
30	4α-Bromo-11β-hydroxyergostan-3-one	*h*	—	1728	16	e
31	2α : 4α-Dibromo-11β-hydroxyergostan-3-one	*h*	—	1755	43	e : e
32	Ergost-9(11)-en-3-one	*h*	—	1712	—	—
33	2α : 4α-Dibromoergost-9(11)-en-3-one	*h*	—	1754	42	e : e
34	Lanostan-3-one	*l*	—	1704	—	—
35	2α-Bromolanostan-3-one	*l*	—	1726	22	e
36	2β-Bromolanostan-3-one	*l*	—	1732	28	e
37	2 : 2-Dibromolanostan-3-one	*l*	—	1716	12	e : a
38	Lanost-8(9)-en-3-one	*l*	—	1703	—	—
39	2α-Bromolanost-8(9)-en-3-one	*l*	—	1728	25	e
40	2β-Bromolanost-8(9)-en-3-one	*l*	—	1734	31	e
41	*allo*Betulone (IV)	*a*	—	1704	—	—
42	2α-Bromo*allo*betulone	*h*	—	1724	20	e
43	5α-Chlorocholestan-6-one	*m*	—	1718	4?	a
44	Coprostan-6-one	*m*	—	1705	—	—
45	3α-Chlorocoprostan-6-one	*n*	—	1705	0	e
46	3β-Chlorocoprostan-6-one	*n*	—	1708	3	a
47	7-Oxocholestan-3β-yl acetate	*o*	1737	1713	—	—
48	6α-Bromo-7-oxocholestan-3β-yl acetate	*o*	1735	1735	22	e
49	6β-Bromo-7-oxocholestan-3β-yl acetate	*o*	1735	1712	−1	a
50	11-Oxoergostan-3β-yl acetate	*p*	1735	1706	—	—
51	9α-Bromo-11-oxoergostan-3β-yl acetate	*q*	1730	1703	−3	a
52	12α-Bromo-11-oxoergostan-3β-yl acetate	*r*	1730	1705	−1	a
53	12α-Chloro-23*a*-bromo-11-oxotigogenin acetate	*s*	1734	1716	6?	a
54	12α : 23*a*-Dibromo-11-oxotigogenin acetate	*t*	1735	1710	0?	a
55	11-Oxotigogenin acetate	*t*	1730	1708	—	—
56	12β-Chloro-11-oxotigogenin acetate		1733	1733	25	e
57	23*a*-Bromohecogenin	*u*	—	1710	—	—
58	11α : 23*a*-Dibromohecogenin	*u*	—	1730	20	e
59	23*a*-Bromohecogenin acetate	*u*	1736	1712	—	—
60	11α : 23*a*-Dibromohecogenin acetate	*u*	1730	1730	18	e
61	23*b*-Bromohecogenin acetate	*v*	1734	1710	—	—
62	11α : 23*b*-Dibromohecogenin acetate	*w*	1732	1732	22	e

Burke [3]) have shown that if the bromine atom enters at an equatorial position on the *cyclo*hexanone ring in the chair configuration the carbonyl band is displaced by about 20 cm.$^{-1}$ to a higher frequency; bromination at an axial position causes little or no frequency displacement. A positive frequency displacement on bromination is accompanied by a 25% decrease in the integrated absorption intensity of the carbonyl band. Jones and his colleagues [1] attributed the increase in carbonyl frequency on α-bromination to the reduction in single-bond character of the carbonyl linkage by the adjacent, almost co-planar, C→Br dipole, a field effect that would be almost at a minimum for an axial bromine substituent. These observations form the basis of an important method for determining the conformations of bromine linkages in bromo-oxo-steroids.

We have examined, for carbon disulphide solutions over both the carbonyl and the low-frequency spectral regions, a wider range of chloro-, bromo-, and iodo-oxo-steroids than Jones and his colleagues examined and have extended the survey to α-chloro- and α-bromo-oxo-*iso*sapogenins and to α-bromo-oxo-triterpenoids. Our carbonyl-frequency values for α-bromo-oxo-steroids (see Table 1) are, when comparable with those reported by Jones and his colleagues,[1,4] about 1—3 cm.$^{-1}$ lower, but show that their carbonyl-frequency displacement hypothesis [1] holds for α-halogenated 2-, 3-, 6-, 7-, 11-, and 12-oxo-steroids. An equatorial chlorine substituent causes a slightly greater carbonyl-frequency displacement (18—25 cm.$^{-1}$) than an equatorial bromine substituent (15—22 cm.$^{-1}$), which in turn produces a larger displacement than an equatorial iodine substituent (about 8 cm.$^{-1}$); an axial chlorine substituent produces a smaller displacement (2—9 cm.$^{-1}$) than an equatorial one (18—25 cm.$^{-1}$), but a larger displacement than axial bromine (−3 to +3 cm.$^{-1}$) and axial iodine substituents (about −4 cm.$^{-1}$). These displacements are of the same order as those reported for α-halogeno*cyclo*hexanones.[2,3]

The infrared measurements on the epimeric 6-bromo-7-oxocholestan-3β-yl acetates are among the first to be reported on oxo-steroids brominated in ring B; the α- and β-configurations of their bromine atoms have been established chemically.[5] The carbonyl bands at 1712 and 1735 cm.$^{-1}$ in the spectrum of the 6β-bromo-7-ketone are assigned to the 7-ketone and the 3-acetate group, respectively. However, the integrated absorption intensity of the single carbonyl band at 1735 cm.$^{-1}$ in the spectrum of the 6α-bromo-7-ketone corresponds with that for one ketone and one acetate group and shows that the 7-ketone absorption band has been displaced by about 22 cm.$^{-1}$ and superimposed on that for the 3-acetate group. Thus an equatorial 6-bromine atom displaces by about 22 cm.$^{-1}$ the absorption frequency of the 7-ketone group; an axial 6-bromine atom has no effect.

Halogen atoms that are not adjacent to a ketone group have little or no effect on the carbonyl frequency. Thus equatorial and axial 6-bromine and equatorial and axial 3-chlorine atoms affect only slightly the carbonyl frequencies of cholest-4-en-3-one and coprostan-6-one, respectively. This effect is consistent with the electrostatic field theory of Jones *et al.*[1]

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* a = axial; e = equatorial; Δ = displacement.

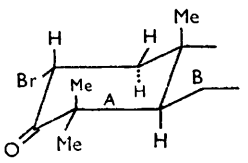
(*a*) Supplied by Professor D. H. R. Barton, F.R.S. (*b*) Bird and Cookson, unpublished work, (*c*) Ref. 28. (*d*) Beereboom, Djerassi, Ginsburg, and Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 3500. (*e*) Beereboom and Djerassi, *J. Org. Chem.*, 1954, **19**, 1196. (*f*) Ref. 11. (*g*) Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1947, **69**, 2404. (*h*) Prepared by Dr. A. G. Long. (*i*) Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003. (*j*) Bird, Cookson, and Dandegaonker, *J.*, 1956, 3675. (*l*) Ref. 6. (*m*) Supplied by Professor C. W. Shoppee, F.R.S. (*n*) Shoppee, Bridgwater, Jones, and Summers, *J.*, 1956, 2492. (*o*) Barr, Heilbron, Jones, and Spring, *J.*, 1938, 334. (*p*) Heusser, Eichenberger, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106. (*q*) Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477. (*r*) Henbest and Wrigley, *J.*, submitted for publication. (*s*) Schmidlin and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 1241. (*t*) Cornforth, Osbond, and Phillipps, *J.*, 1954, 907. (*u*) Elks, Phillipps, Walker, and Wyman, *J.*, 1956, 4330. (*v*) Mueller and Norton, *J. Amer. Chem. Soc.*, 1954, **76**, 749. (*w*) Ref. 19.

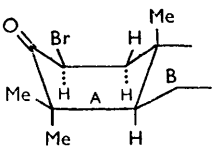
[3] Corey and Burke, *J. Amer. Chem. Soc.*, 1955, **77**, 5418.

[4] Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252.

[5] Fieser and Fieser, "Natural Products related to Phenanthrene," 3rd edn., Reinhold, New York, 1949, p. 270.

Barton, Lewis, and McGhie's observation [6] that ring A of 2α-bromo- and of 2β-bromolanostan-3-ones has a chair (I) and a boat conformation (II), respectively, is supported by our infrared measurements. The spectra of both epimeric lanostanones show positive carbonyl-frequency displacements of 22—25 and 28—31 cm.$^{-1}$, respectively, indicating that the carbon–bromine linkage in both compounds is equatorial; the displacements are slightly greater than those (15—22 cm.$^{-1}$) observed for α-bromo-oxo-steroids. The carbon–bromine linkages of both 2α-bromolanostan-3-one, in which ring A has a chair conformation, and 2β-bromolanostan-3-one, in which ring A has a boat conformation, are equatorial and would be expected to cause positive carbonyl-frequency displacements (see Jones [7]). If ring A of 2β-bromolanostan-3-one had a chair conformation, powerful 1 : 3-interactions

(I) 



(II)

would occur between the axial bromine atom and the axial 4- and 10-methyl groups; these interactions are avoided by a boat conformation. It is noteworthy that 2 : 2-dibromo- has a lower carbonyl frequency (1716 cm.$^{-1}$) than either 2α- (1726 cm.$^{-1}$) or 2β-bromolanostan-3-one (1732 cm.$^{-1}$).

The carbonyl frequency of cholestan-3-one (1715 cm.$^{-1}$) is decreased by the introduction of α-*gem*-dimethyl groups. Thus lanostan-3-one and 2 : 2 : 4 : 4-tetramethylcholestan-3-one absorb at 1704 and 1698 cm.$^{-1}$, respectively. A similar trend is seen in the carbonyl-frequency data for α-alkyl- and α-aryl-*cyclo*hexanones reported by Cherrier [8] and Conroy and Firestone [9] (see also Lukes, Poos, Beyler, Johns, and Sarett [10]). The frequency displacements induced by α-alkyl groups are much smaller than, in the opposite direction to, and apparently less consistent than, those produced by α-halogen atoms. Conroy and Firestone [9] attributed the decrease in carbonyl frequency occurring on alkylation at both α-carbon atoms in *cyclo*hexanone to the tendency of the two α-alkyl substituents to widen the carbonyl angle; this effect of disubstitution at both α-carbon atoms might explain the unexpectedly low carbonyl frequency of 2 : 2-dibromolanostan-3-one.

Low-frequency Spectra.—The carbonyl frequency method is not satisfactory for determining the conformations of halogen substituents in α-halogeno-oxo-steroids, such as bromo-21-acetoxy-17α-hydroxy*allo*pregnane-3 : 11 : 20-triones, which have several carbonyl groups; the carbonyl region of the spectra of such compounds is fairly complex and it is not always possible to distinguish small frequency displacements in them.[11] It therefore appeared reasonable to find out whether our observation,[12] that an equatorial carbon–halogen linkage in a simple halogeno-steroid absorbs at a higher frequency than the corresponding axial linkage, could be applied to halogeno-oxo-steroids. Such an extension might provide information to supplement that derived from a study of carbonyl-stretching frequencies. Dr. G. Eglinton (see Barton, Campos-Neves, and Cookson [13]) has suggested that some of the absorption bands previously [12] shown to be characteristic of equatorial and axial halogen substituents may correspond with polarised or coupled carbon–hydrogen deformation modes rather than with simple carbon–halogen stretching vibrations; these will therefore be referred to as " halogen-sensitive " bands. A change of this kind in the

[6] Barton, Lewis, and McGhie, *J.*, in the press.
[7] Jones, *J. Amer. Chem. Soc.*, 1953, **75**, 4839.
[8] Cherrier, *Compt. rend.*, 1947, **225**, 1063.
[9] Conroy and Firestone, *J. Amer. Chem. Soc.*, 1956, **78**, 2290.
[10] Lukes, Poos, Beyler, Johns, and Sarett, *ibid.*, 1953, **75**, 1707.
[11] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.
[12] Barton, Page, and Shoppee, *J.*, 1956, 331.
[13] Barton, Campos-Neves, and Cookson, *J.*, 1956, 3500.

assumed origin of the bands would not affect our empirical correlation of band frequency with halogen conformation.

The halogen-sensitive bands for halogeno-oxo-steroids occur in the low-frequency spectral region, in which the skeletal and carbon–hydrogen deformation bands associated with ketone and acetate groups would be expected to appear. However, since little is known about the behaviour of such bands, it was first necessary to examine the low-frequency spectra of simple unhalogenated *cyclo*hexanones and oxo-steroids.

TABLE 2. *Frequencies (cm.$^{-1}$) and apparent molecular extinction coefficients (in parentheses) for low-frequency absorption bands of* cyclo*hexanones and related substances* (CS_2 *solution*).

No.	Compound	Absorption bands
63	*cyclo*Hexane	522(4)
64	*cyclo*Hexanol	788(6), 652(4), 554(16), 475(7)
65	2-Methyl*cyclo*hexanol	772(4), 561(14), 517(10), 434
66	Methyl 2-methyl*cyclo*hexanyl ether	778(4), 554(7), 506(8)
67	*cyclo*Hexanone	748(20), 650(7), 489(24), 410
68	2-Methyl*cyclo*hexanone	721(11), 655(5), 513(7), 500(9), 425
69	3-Methyl*cyclo*hexanone	751(10), 639(4), 512(26), 489(12), 436(5)
70	2 : 2-Dimethyl*cyclo*hexanone	691(7), 651(5), 553(9), 512(14), 439(7)
71	2 : 6-Dimethyl*cyclo*hexanone	752(12), 586(5), 411
72	2 : 2 : 6-Trimethyl*cyclo*hexanone	735(9), 559(8), 549(8), 455(5), 416
73	2 : 2 : 6 : 6-Tetramethyl*cyclo*hexanone	758(5), 548(12), 453(6)

The prominent absorption bands appearing above 1350 cm.$^{-1}$ in the infrared spectra of steroids are mainly of simple contour and can be identified with vibrations of specific bonds or small atomic groups. At lower frequencies the spectra are more complex and are highly specific for individual compounds.[14] The bands below 700 cm.$^{-1}$ in the spectra of compounds containing carbon, hydrogen, and oxygen only are probably associated with skeletal and coupled deformation vibrations of carbon–hydrogen linkages. The frequency and intensity of the bands will be readily affected by small changes in the molecule and any structural assignments are, therefore, likely to be more specific, but of more limited application, than those made at higher frequencies. The bands are usually much weaker than the carbonyl and carbon–oxygen stretching bands found at higher frequencies.

The low-frequency (700—400 cm.$^{-1}$) spectra of *cyclo*hexanones and oxo-steroids have received scant attention. Thompson and Torkington [15] examined the low-frequency spectra of simple alkyl acetates and identified at 640 and 612 cm.$^{-1}$ absorption bands that they thought were associated in some way with the $CH_3{\cdot}CO$ or $CH_3{\cdot}CO{\cdot}O$ parts of the molecule. Recently, a series of absorption bands at about 600, 520, and 400 cm.$^{-1}$ in the spectra of simple non-branching aliphatic ketones have been assigned by Lecomte, Josien, and Lascombe [16] to individual deformation vibrations of the carbonyl group; the spectra of branched-chain ketones were more complex, and the bands could not be fully assigned.

*Low-frequency spectra of α-methyl*cyclo*hexanones and related substances.* Our values for the frequencies and apparent molecular extinction coefficients of the principal bands between 800 and 400 cm.$^{-1}$ in the spectra of α-methyl*cyclo*hexanones and related substances are summarized in Table 2. The apparent molecular extinction coefficient values (see p. 3857) provide information on the relative, but not the absolute, band intensity.

*cyclo*Hexane shows only one weak band at 522 cm.$^{-1}$; the introduction of a ketone or hydroxyl group leads to the appearance of three additional bands, the *cyclo*hexanone bands being stronger than the *cyclo*hexanol ones. The *cyclo*hexanone bands at 650, 489, and 410 cm.$^{-1}$ appear to correspond with those at 600, 520, and 400 cm.$^{-1}$ in the spectra of the unbranched long-chain aliphatic ketones examined by Lecomte and his colleagues,[16] and it is tempting to assume that the bands are associated with Lecomte's ν_5, ν_3, and ν_6 vibrations, respectively. However, since the ring is less planar, the skeletal vibration

[14] Jones, Nolin, and Roberts, *J. Amer. Chem. Soc.*, 1955, **77**, 6331.
[15] Thompson and Torkington, *J.*, 1945, 640.
[16] Lecomte, Josien, and Lascombe, *Bull. Soc. chim. France*, 1956, 163.

modes for *cyclo*hexanone are more complex than those for unbranched long-chain aliphatic ketones. Jones, Nolin, and Roberts[14] have indicated for *cyclo*hexanone eight sets of vibrations that could arise from coupling of the fundamental ketone in-plane skeletal

TABLE 3. *Frequencies (cm.$^{-1}$) and apparent molecular extinction coefficients (in parentheses) for low-frequency absorption bands of steroids and triterpenoids* (CS_2 *solution*).

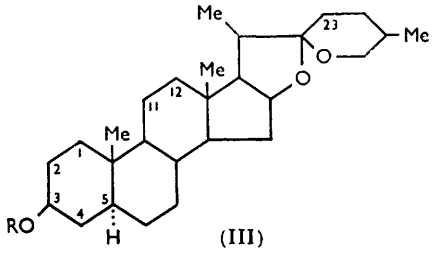
No.	Compound	Absorption bands
74	*allo*Pregnan-3β-ol	759(11), 713(10), 641(11), 606(13), 513(18), 477(21)
75	Cholestan-3β-ol	732(11), 634(7), 556(9), 531(8), 494(13)
76	Cholesterol	735(15), 625(8), 606(8), 592(14), 501(11)
77	Cholestan-3β-yl acetate	732(10), 663(12), 608(28), 540(12), 476(9), 446(9)
78	Cholesteryl acetate	734(12), 668(6), 620(14), 607(30)
79	Tigogenin acetate (III; R = Ac)	673(16), 663(18), 606(28), 575(12), 541(23), 533(17), 508(13), 477(12), 453(16)
50	11-Oxoergostan-3β-yl acetate	797(9), 662(10), 632(50), 606(32), 587(15), 557(9), 543(15), 503(11), 485(10), 447(10)
55	11-Oxotigogenin acetate	782(18), 663(20), 623(20), 606(33), 601(33), 542(31), 508(14), 474(11), 453(15)
80	Hecogenin acetate	794(12), 779(14), 757(8), 644(8), 605(32), 584(18), 566(12), 538(24), 519(9), 486(8)
5	Cholestan-3-one	760(10), 736(14), 682(7), 536(10), 508(10), 502(12), 449(5)
81	Cholest-5-en-3-one	795(33), 772(10), 735(11), 608(7), 584(21), 505(22)
82	Coprostan-3-one	767(14), 733(10), 680(9), 606(9), 529(30)
17	Cholest-1-en-3-one	778(114), 746(12), 554(7), 502(17), 448(20)
20	Cholest-4-en-3-one	778(26), 733(11), 683(33), 653(10), 567(11), 536(12), 512(23), 460(14)
83	Cholesta-1 : 4-dien-3-one	702(30), 686(29), 559(9), 521(17), 515(20), 483(22)
84	Cholesta-4 : 6-dien-3-one	775(17), 754(28), 736(8), 703(8), 665(19), 624(18), 548(11), 515(19), 482(8)
28	11β-Hydroxyergostan-3-one	798(9), 763(12), 743(13), 625(18), 587(8), 547(17), 523(16), 512(20), 464(18)
25	Ergosta-3 : 11-dione	763(8), 742(10), 633(43), 548(22), 501(21), 465(17)
34	Lanostan-3-one	731, 583, 494
38	Lanost-8(9)-en-3-one	732, 653, 578, 522, 494
41	*allo*Betulone (IV)	766(54), 578(28)

motions with stretching motions of the C_α–C_β linkages in different phase relationships. These vibrations, however, cannot be identified with normal vibration modes, since the latter may involve resultant motions not necessarily directed along the bond axes and not readily to be predicted for such asymmetric structures. It is therefore only possible at present to make empirical structural assignments.

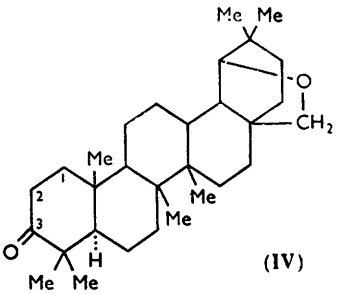
The spectra of the α-methyl*cyclo*hexanones are comparable with those of the branched-chain ketones examined by Lecomte *et al.*[16] The bands between 550 and 480 cm.$^{-1}$ in the spectra of α-methyl*cyclo*hexanones are weaker than those for *cyclo*hexanone, suggesting that the bands are associated with coupled α-methylene deformation vibrations of the ketone group; such bands would be expected to be weaker in the spectra of α-methyl ketones.

Low-frequency spectra of steroids. The low-frequency spectra of steroids, *iso*sapogenins, and triterpenoids [see Table 3 (bands with an apparent molecular extinction coefficient of less than 5 have been omitted from the Table)] are more complex and contain stronger bands than those of *cyclo*hexanones. However, the 550—500 cm.$^{-1}$ bands for cholestan-3β-ol are weaker than those for cholestan- and coprostan-3-one (cf. *cyclo*hexanol and *cyclo*hexanone). Cholestan-3-one has three bands of medium intensity in this region at 536, 508, and 502 cm.$^{-1}$, but coprostan-3-one shows a single strong band at about 529 cm.$^{-1}$. These bands probably have an origin similar to that of the corresponding bands in the spectrum of *cyclo*hexanone and represent coupled α-methylene deformation vibrations of the 3-ketone group; the frequency and intensity of the band or bands depend on the nature of the neighbouring substituents. If the 3-ketone group is conjugated with a double bond, as in cholest-1-en- and cholest-4-en-3-one, the band pattern changes and a medium intensity band appears at 460—448 cm.$^{-1}$. A 4-*gem*-dimethyl group, as in lanostan-3-one, displaces the stronger band to higher frequencies, namely, 583—578 cm.$^{-1}$.

It is further seen from Table 3 that 11-oxo- and 11β-hydroxy-steroids absorb relatively strongly at about 632—623 and 625 cm.$^{-1}$, respectively, and are distinguished from 3β-acetoxy-steroids, which have prominent bands at 608—605 cm.$^{-1}$. These empirical assignments are tentative, but they are supported by our measurements on halogeno-oxo-steroids; the bands are usually about 2—3 times as strong as the other bands in this spectral region and are readily identified. The 3β-acetate bands at 608—605 cm.$^{-1}$ are



(III)



(IV)

probably related to the alkyl acetate bands at about 640 and 612 cm.$^{-1}$, which were first reported by Thompson and Torkington.[15] The relatively strong bands in the 900—750 cm.$^{-1}$ region of the cholestenone spectra are associated with out-of-plane carbon–hydrogen bending vibrations of the conjugated ethylenic linkages: they have been discussed by Jones, Herling, and Katzenellenbogen.[17]

Steroidal sapogenins, such as tigogenin acetate (III; R = Ac) and hecogenin acetate, which [18] absorb so strongly between 1000 and 850 cm.$^{-1}$, show in the low-frequency region several weak bands, but no strong bands that can be assigned to the *iso*sapogenin side-chain. The triterpenoid, *allo*betulone (IV), however, has a strong band at 766 cm.$^{-1}$, which also appears in the spectra of other *allo*betulin derivatives and is probably associated with ring E of the *allo*betulin molecule.

Low-frequency spectra of α-halogeno-oxo-steroids and -oxo-triterpenoids. The low-frequency spectra of α-halogeno-oxo-steroids contain halogen-sensitive bands, which must be distinguished from the skeletal and carbon–hydrogen deformation bands associated with ketone and acetate groups. Since ethylenic double bonds absorb in the low-frequency region, we have excluded from this survey halogenated αβ-unsaturated oxo-steroids.

The skeletal and carbon–hydrogen deformation ketone bands for α-halogeno-oxo-steroids (see Table 4) appear at slightly higher frequencies than, but have similar apparent molecular extinction coefficients to, those for the corresponding unhalogenated oxo-steroids. The frequency and apparent molecular extinction coefficient of the bands depend on the nature and conformation of the halogen atom. The ketone bands for 2α-chloro- (595 cm.$^{-1}$), 2α-bromo- (564 cm.$^{-1}$), and 2α-iodo-cholestan-3-one (560—540 cm.$^{-1}$) appear in the expected order (see Figs. 1, 2, and 3); 2α-chlorocholestan-3-one (595 cm.$^{-1}$), which has an equatorial chlorine substituent, absorbs at a slightly higher frequency than the corresponding 2β-chloro-epimer (588 cm.$^{-1}$). The ketone band is either absent from, or has an apparent molecular extinction coefficient of less than 20 in, the spectra of 2-bromolanostan-3-ones and of 2α : 4α-dibromo-3-oxo-5α-steroids. This is in harmony with the suggestion that the bands are associated with carbon–hydrogen deformation vibrations of the methylene group adjacent to the ketone.

The carbon–hydrogen deformation band for the 11β-hydroxyl group of a halogeno-11β-hydroxy-3-oxo-5α-steroid appears in the same region (656—629 cm.$^{-1}$) as that for the corresponding unhalogenated steroid; the band for 4α-bromo-11β-hydroxyergostan-3-one splits into two relatively weak components absorbing at about 656 and 637 cm.$^{-1}$.

[17] Jones, Herling, and Katzenellenbogen, *J. Amer. Chem. Soc.*, 1955, **77**, 651.

[18] Wall, Eddy, McClennan, and Klumpp, *Analyt. Chem.*, 1952, **24**, 1337; Jones, Katzenellenbogen, and Dobriner, *J. Amer. Chem. Soc.*, 1953, **75**, 158.

The spectra of α-halogeno-3-oxo-5α-steroids show one strong halogen-sensitive band and one or two of medium intensity between 850 and 670 cm.$^{-1}$ that are readily distinguished from carbon–hydrogen deformation ketone bands, which appear at lower frequencies; all the bands are listed in Table 4. The relatively strong bands (apparent molecular extinction

TABLE 4. *Structural assignments and apparent molecular extinction coefficients (in parentheses) for low-frequency absorption bands (cm.$^{-1}$) in CS_2 solution spectra of mono-α-halogeno-oxo-steroids.*

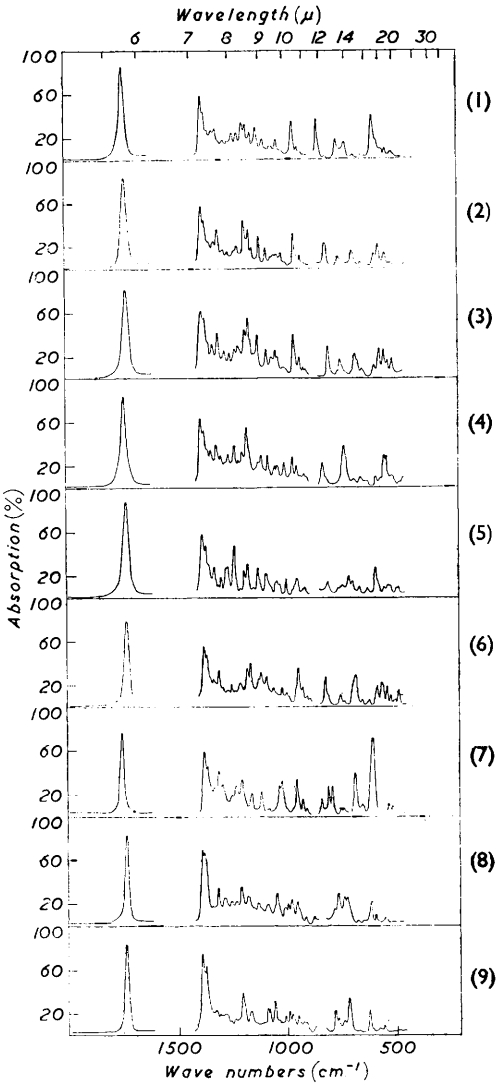
No.	Compound	Conformn. of C–Hal linkage	Halogen-sensitive	3-Ketone	6-Ketone	11-Ketone	3-Acetate
2	3α-Chlorocholestan-2-one	a	735(33), 702(28)	566(57), 470(25) †	—	—	—
3	3α-Bromocholestan-2-one	a	670(24)	531(55), 455(30) †	—	—	—
4	3α-Iodocholestan-2-one	a	645	534, 482 †	—	—	—
6	2α-Chlorocholestan-3-one	e	841(54), 752(23), 714(20)	595(58)	—	—	—
9	2α-Bromocholestan-3-one	e	814(44), 750(21), 698(27)	564(36)	—	—	—
29	2α-Bromo-11β-hydroxy-ergostan-3-one	e	816(46), 753(21), 703(32)	562(34), 534(30)	—	629(25) *	—
26	2α-Bromoergosta-3 : 11-dione	e	814(40), 754(13), 696(26)	561(56)	—	633(47)	—
15	2α-Iodocholestan-3-one	e	800(52), 744(31), 686(36)	560(48), 540(46)	—	—	—
7	2β-Chlorocholestan-3-one	a	708(24), 694	588(35), 486(10)	—	—	—
10	4α-Bromocholestan-3-one	e	727(50)	548(36), 539(36)	—	—	—
30	4α-Bromo-11β-hydroxy-ergostan-3-one	e	730(48), 703(18)	548	—	656, 637 *	—
23	6α-Bromocholest-4-en-3-one	e	788(41), 726(47), 685(50)	508(19)	—	—	—
24	6β-Bromocholest-4-en-3-one	a	700(53), 685(34), 649(23)	535(29)	—	—	—
43	5α-Chlorocholestan-6-one	a	756	—	N.I.	—	—
45	3α-Chlorocoprostan-6-one ‡	e	751(95)	—	625, 590, 555	—	—
46	3β-Chlorocoprostan-6-one ‡	a	711(50)	—	597	—	—
48	6α-Bromo-7-oxocholestan-3β-yl acetate	e	765, 735, 678	—	—	—	608
49	6β-Bromo-7-oxocholestan-3β-yl acetate	a	734, 686, 609	—	—	—	609
51	9α-Bromo-11-oxoergostan-3β-yl acetate	a	785(35), 744(55)	—	—	633(60)	605(29)
53	12α-Chloro-23*a*-bromo-11-oxotigogenin acetate	a	762	—	—	663, 643	606
52	12α-Bromo-11-oxoergostan-3β-yl acetate	a	717(51)	—	—	643(30)	608(34)
54	12α : 23*a*-Dibromo-11-oxotigogenin acetate	a	715	—	—	660, 640	606
56	12β-Chloro-11-oxotigogenin acetate	e	806	—	—	N.I.	N.I.

* 11β-Hydroxy. † 2-Ketone. ‡ 5β-Steroid. N.I., not examined in 700—400 cm.$^{-1}$ region.

coefficient, 54—40) at 841, 816—814, and 800 cm.$^{-1}$ in the spectra of 2α-chloro-, 2α-bromo-, and 2α-iodo-3-oxo-5α-steroids, respectively, follow the general order, chlorine, bromine, iodine (see Figs. 1, 2, and 3). The corresponding band for 4α-bromo- (730—727 cm.$^{-1}$) appears about 85 cm.$^{-1}$ lower than that for 2α-bromo-3-oxo-5α-steroids (see Fig. 4). The medium-intensity bands occurring between 755 and 685 cm.$^{-1}$ in the spectra of α-halogeno-3-oxo-steroids, although showing a small progressive frequency displacement with change in halogen substituent, probably represent coupled carbon–hydrogen deformation modes.

Axial halogen substituents in general absorb at a lower frequency, and frequently yield weaker absorption bands, than the corresponding equatorial substituents; this is consistent with our suggested basis for distinguishing between equatorial and axial

linkages.[12] The equatorial halogen substituents in 2α-chlorocholestan-3-one, 6α-bromo-7-oxocholestan-3β-yl acetate, and 3α-chlorocoprostan-6-one absorb at 841 (see Fig. 1), 678, and 751 cm.$^{-1}$, respectively, and the axial substituents of the corresponding halogen epimers at 708 (see Fig. 5), 609, and 711 cm.$^{-1}$, respectively. The axial halogen substituents in 3α-chloro-, 3α-bromo-, and 3α-iodo-cholestan-2-one absorb at 735, 670, and 645 cm.$^{-1}$, respectively, compared with 841, 814, and 800 cm.$^{-1}$, respectively, for the equatorial halogen substituents in 2α-chloro-, 2α-bromo-, and 2α-iodo-cholestan-3-one. The axial bromine substituents of 9α-bromo- and of 12α-bromo-11-oxoergostan-3β-yl acetate have



FIGS. 1—9.

Infrared spectra (2000—400 *cm.*$^{-1}$) *of* 2·0% (*w*/*v*) *solutions of*:

(1) 2α-*Chlorocholestan*-3-*one*.
(2) 2α-*Bromocholestan*-3-*one*.
(3) 2α-*Iodocholestan*-3-*one*.
(4) 4α-*Bromocholestan*-3-*one*.
(5) 2β-*Chlorocholestan*-3-*one*.
(6) 2 : 2-*Dibromocholestan*-3-*one*.
(7) 2α : 4α-*Dibromocholestan*-3-*one*.
(8) 2α-*Bromolanostan*-3-*one*.
(9) 2β-*Bromolanostan*-3-*one*
in CS_2.

unexpectedly high absorption frequencies, namely, 744 and 717 cm.$^{-1}$, respectively; the 12α-bromine value is supported by our measurements on 12-halogeno-11-oxotigogenins.

The low-frequency spectra of 23*a*-bromo*iso*sapogenins [12,19] have a strong bromine band at about 726 cm.$^{-1}$, but otherwise do not show bands characteristic of the 23*a*-bromo*iso*-sapogenin side-chain; the 726 cm.$^{-1}$ band has been excluded from Table 4. The other

[19] Dickson and Page, *J.*, 1955, 447.

low-frequency bands in the spectra of α-halogeno-oxo-steroidal sapogenins are as expected from a study of simpler steroids. We were unable with certainty to identify bands associated with 11α-bromine in the low-frequency spectra of 11α : 23*a*- and 11α : 23*b*-dibromohecogenins.

The low-frequency spectrum of a 2 : 2-dihalogeno- is more complex than that of a 2α : 4α-dihalogeno-3-oxo-5α-steroid (see Table 5 and Figs. 6 and 7); this is in harmony with Fox and Martin's observation [20] (see also Bergmann and Pinchas [21] and Page [22]) that repetition of an absorbing substituent on the same carbon atom causes splitting of the

TABLE 5. *Structural assignments and apparent molecular extinction coefficients (in parentheses) for low-frequency absorption bands (cm.$^{-1}$) in CS_2 solution spectra of di-α-halogeno-3-oxo-steroids.*

No.	Compound	Conformn. of C–Hal linkages	Halogen-sensitive	3-Ketone	11-Ketone
8	2 : 2-Dichlorocholestan-3-one	e : a	838, 722	N.I.	N.I.
11	2 : 2-Dibromocholestan-3-one	e : a	823(44), 685(52), 588(31), 566(34)?	546(29), 492(23)?	—
13	2α-Chloro-2β-bromocholestan-3-one	e : a	826(33), 758(45), 715(58), 697(37), 595(54)	569(31), 535(27)	—
12	2α : 4α-Dibromocholestan-3-one	e : e	686(63), 608(112)	546(12), 529(9)	—
31	2α : 4α-Dibromo-11β-hydroxy-ergostan-3-one	e : e	690(64), 608(118)	527(14), 515(12)	638(46) *
33	2α : 4α-Dibromoergost-9(11)-en-3-one	e : e	692(80), 606(101	549(14), 539(13)	—
27	2α : 4α-Dibromoergosta-3 : 11-dione	e : e	690(61), 608(81)	541(19), 508(20)	643(70)
14	2α-Chloro-4α-bromocholestan-3-one	e : e	706(54), 687(30), 635(27), 625(42), 608(55)	572(8), 549(9), 535(7)	—

* 11β-Hydroxy. N.I., not examined in 700—400 cm.$^{-1}$ region.

absorption band. The strongest bromine-sensitive bands for a 2 : 2-dibromo- and a 2α : 4α-dibromo-3-oxo-5α-steroid appear at about 823 and 685 and at 692—686 and 608—606 cm.$^{-1}$, respectively; the bands occurring between 600 and 560 cm.$^{-1}$ in the spectrum of the 2 : 2-dibromo-isomer may also be bromine-sensitive.

The low-frequency spectrum of a 2α : 4α-dibromo-3-oxo-5α-steroid is unexpectedly simple (see Fig. 7). The two bromine bands are surprisingly strong (apparent molecular extinction coefficients, 80—61 and 118—81, respectively) and have lower frequencies (692—686 and 608—606 cm.$^{-1}$, respectively) than those for other equatorial bromine substituents. The carbon–hydrogen deformation ketone bands usually appearing between 570 and 540 cm.$^{-1}$ and having an apparent molecular extinction coefficient of about 50 in the spectra of mono-α-bromo-3-oxo-5α-steroids are either absent or have an apparent molecular extinction coefficient of less than 20.

The strong bromine-sensitive bands at 762—760 cm.$^{-1}$ and at 716—715 cm.$^{-1}$ in the spectra of 2α-bromo- and 2β-bromo-lanostanones (see Table 6 and Figs. 8 and 9) provide additional evidence that the bromine substituents in both compounds are equatorial and confirm the view that ring A in these compounds has a chair (I) and a boat conformation (II), respectively (see Barton, Lewis, and McGhie [6]). 2α-Bromo*allo*betulone shows in addition to the bromine-sensitive band at 762 cm.$^{-1}$ an equally strong band at 766 cm.$^{-1}$, which appears to be characteristic of the *allo*betulin molecule (see above).

The effect of an adjacent ketone group on the absorption frequency and apparent molecular extinction coefficient of the halogen-sensitive vibration for 2- and 3-halogenocholestanes is shown in Table 7. The frequency values of α-halogenocholestanones are

[20] Fox and Martin, *Proc. Roy. Soc.*, 1938, *A*, **167**, 257.
[21] Bergmann and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 161.
[22] Page, *J.*, 1955, 2017.

taken from Table 4 of this paper, but those for halogenocholestanes are based on values reported previously.[12] An adjacent ketone group displaces the frequency of an equatorial

TABLE 6. *Structural assignments and apparent molecular extinction coefficients (in parentheses) for low-frequency absorption bands (cm.$^{-1}$) in CS_2 solution spectra of α-bromo-oxo-triterpenoids.*

No.	Compound	Conformn. of ring A	Conformn. of C–Br linkages	Bromine-sensitive	3-Ketone
35	2α-Bromolanostan-3-one	Chair	e	760(50,) 736(44), 724(40)	588(12), 549(10)
39	2α-Bromolanost-8(9)-en-3-one	,,	e	762(59), 734(54)	548(20)
42	2α-Bromo*allo*betulone	,,	e	762(56), 730(30)	584(19), 531(10)
36	2β-Bromolanostan-3-one	Boat	c	781(35), 768(22), 715(56)	553(14)
40	2β-Bromolanost-8(9)-en-3-one	,,	e	788(30), 755(23), 716(54)	558(20), 515(10)
37	2 : 2-Dibromolanostan-3-one	—	e : a	780(31), 723(33), 630(25), 588(48)	539(28)

chlorine or bromine substituent by about 85 cm.$^{-1}$ to higher frequencies; the frequency of an axial substituent suffers a smaller displacement (about 20 cm.$^{-1}$) in either a positive or a negative direction. The apparent molecular extinction coefficients of the bands for

TABLE 7. *Comparison of frequencies (cm.$^{-1}$) and apparent molecular extinction coefficients (in parentheses) of halogen-sensitive bands for simple halogenocholestanes and α-halogeno-cholestanones.*

Halogen	Conformn. of C–Hal linkage	Halogeno-cholestane	α-Halogeno-cholestanone	Frequency displacement
2α-Chloro	e	755(95)	841(54) *	+86
2β-Chloro	a	693(80)	708(24) *	+15
3α-Chloro	a	707(62)	735(33) †	+28
2α-Bromo	e	754—708(90—50)	816—814(46—40) *	+84
3α-Bromo	a	690(46)	670(24) †	−20

* 3-Ketone. † 2-Ketone.

both equatorial and axial halogen substituents are, however, reduced. Mizushima and his colleagues [23] (see also McBee and Christman [24]) have shown that in the more stable form of compounds, such as bromo- and chloro-acetyl chloride and chloroacetone, in which the halogen atom is *cis* with respect to the carbonyl oxygen, namely, equatorial, the carbon–halogen frequency rises.

EXPERIMENTAL

The *cyclo*hexanones, steroids, *iso*sapogenins, and triterpenoids were examined over the 4000—650 cm.$^{-1}$ spectral region as either 1·0% or 2·0% (w/v) carbon disulphide solutions in 0·8 mm. cells by means of a Perkin-Elmer Corporation, model 21, double-beam infrared spectrophotometer fitted with a sodium chloride prism (see Dickson, Page, and Rogers [25]) and over the 1000—400 cm.$^{-1}$ region as a 2·0% (w/v) carbon disulphide solution in a 2·0 mm. cell in the same spectrophotometer fitted with a potassium bromide prism (see Barton, Page, and Shoppee [12]). The spectral slit width was about 6 cm.$^{-1}$ at 1700 cm.$^{-1}$ (sodium chloride prism) and 3 cm.$^{-1}$ at 600 cm.$^{-1}$ (potassium bromide prism). The apparent molecular extinction coefficients were calculated from the relation, $\varepsilon = (1/cl) \log_{10} (T_0/T)$, where T_0 and T are, respectively, the % radiation transmitted by the solvent and by the solution at the frequency of the absorption band, c is the solute concentration in moles per l., and l is the cell thickness in cm. (cf. refs. 26).

[23] Nakagawa, Ichishima, Kuratani, Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1952, **20**, 1720; Mizushima, Shimanouchi, Miyazawa, Ichishima, Kuratani, Nakagawa, and Shido, *ibid.*, 1953, **21**, 815.

[24] McBee and Christman, *J. Amer. Chem. Soc.*, 1955, **77**, 755.

[25] Dickson, Page, and Rogers, *J.*, 1955, 443.

[26] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72; Jones, Ramsay, Keir, and Dobriner, *ibid.*, p. 80.

All the compounds, with the exception of those acknowledged below, were prepared in these laboratories; their physical properties have been described either by Attenburrow *et al.* (α-methyl*cyclo*hexanones) [27], by Shoppee and Shoppee (simple steroids and steroidal sapogenins),[28] or in the references listed in Table 1.

We thank Professor D. H. R. Barton, F.R.S. (Glasgow University) for specimens (1), (2), (3), (7), (34), (35), (36), (37), (38), (39), (40), (41), (47), (48), and (49), Dr. R. C. Cookson (Birkbeck College, London) for specimens (4), (15), (23), and (24), Dr. H. B. Henbest (King's College, London) for specimens (51) and (52), and Professor C. W. Shoppee, F.R.S. (Sydney University) for specimens (43), (44), (45), and (46).

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[27] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.
[28] Shoppee and Shoppee, " Chemistry of Carbon Compounds," ed. E. H. Rodd, Elsevier, Amsterdam, 1953, Vol. II B, pp. 765, 876, and 983.