3-Cycloethylene Ketal of Cortisone B.M.D. (XVIII).—Ethylene glycol (40 cc.) was added to a solution of cortisone B.M.D. (XVII) (3.0 g.) in benzene (400 cc.) containing *p*-toluenesulfonic acid monohydrate (200 mg.) and heated under reflux with a water separator for 8 hours. Sodium bicarbonate solution (20 cc., 5%) and water (250 cc.) were added and the product isolated with benzene. Removal of the solvent and crystallization of the product from benzene–hexane afforded the 3-cycloethylene ketal of cortisone B.M.D. (XVIII) (1.75 g.), m.p. 188–192°, raised by several crystallizations from benzene–hexane to 200–202°, $[\alpha]_D$ −88°; XVIII exhibited no selective absorption in the ultraviolet.

Anal. Calcd. for $C_{25}H_{34}O_7$: C, 67.24; H, 7.67; O, 25.09. Found: C, 66.79; H, 7.73; O, 25.26.

Permonophthalic Acid Oxidation of the 3-Cycloethylene Ketal of Cortisone B.M.D. (XVIII).—Permonophthalic acid (3.8 g.) in ether (50 cc.) was added dropwise over 15 minutes to a solution of the cycloethylene ketal of cortisone B.M.D. (XVIII) (4.75 g.) in chloroform (50 cc.) at −10°. After keeping at 0° for 16 hours the solution was washed with cold 5% sodium bicarbonate solution until it was acid free and then with water to neutrality. Removal of the solvent after drying over sodium sulfate afforded a product which was adsorbed from benzene onto alumina (200 g.). Elution with benzene–ether (80:20, 1.5 l.) afforded the 3-cycloethylene ketal of cortisone B.M.D.-5α,6α-epoxide (XIXa) (2.55 g.), m.p. 293–297°. The analytical sample from ethyl acetate–hexane had m.p. >300°, $[\alpha]_D$ −90°.

Anal. Calcd. for $C_{25}H_{34}O_8$: C, 64.92; H, 7.41; O, 27.67. Found: C, 64.76; H, 7.63; O, 27.88.

Potassium Cyanide Cleavage of the 3-Cycloethylene Ketal of Cortisone B.M.D.-5α,6α-epoxide (XIXa).—Potassium cyanide (2.5 g.) was added to a solution of the epoxide XIXa (1.23 g.) in ethylene glycol (50 cc.) and heated under reflux for 45 minutes. Addition of water and isolation with ethyl acetate afforded a product which was adsorbed from benzene onto alumina (50 g.). Elution with benzene (750 cc.) afforded the Δ^5-6-cyano-3-cycloethylene ketal (XXa) (250 mg.), m.p. 262–264°, raised by several crystallizations from benzene–hexane to 267–269°, $[\alpha]_D$ −138°, λ_{max}^{EtOH} 224 mμ, ε 10,075.

Anal. Calcd. for $C_{26}H_{33}O_7N$: C, 66.22; H, 7.05; N, 2.97. Found: C, 66.59; H, 7.15; N, 3.34.

Further elution with benzene–ether (90:10, 750 cc.) afforded by the 6-cyano enol ether XXIa (420 mg.), m.p. 192–197°, raised by several crystallizations from benzene–hexane to 209–211°, $[\alpha]_D$ −139°, λ_{max}^{EtOH} 284–286 mμ, ε 18,200.

Anal. Calcd. for $C_{26}H_{33}O_7N$: C, 66.22; H, 7.05; N, 2.97. Found: C, 66.76; H, 7.02; N, 3.14.

Potassium Cyanide Cleavage of Cortisone Bis-ketal-5α,6α-epoxide (XIXb).—Potassium cyanide (4.0 g.) was added to a solution of cortisone bis-ketal-5α,6α-epoxide[63] (XIXb) (2.0 g.) in ethylene glycol (80 cc.) and heated under reflux for 1 hour. Addition of water to the cooled solution and extraction with ethyl acetate gave a product which was adsorbed from methylene dichloride–benzene (1:30, 500 cc.) onto alumina (80 g.). Elution with ether–acetone (90:10, 1 l.) afforded after one crystallization from acetone–hexane 6-cyano-Δ^5-pregnene-17α,21-diol-11-one-3,20-bis-cycloethylene ketal acetate (XXb) (440 mg.), m.p. 273–275°, raised by several crystallizations from acetone–hexane to 277–279°, $[\alpha]_D$ −56°; λ_{max}^{EtOH} 224 mμ, ε 11,000; λ_{max}^{KBr} 3450, 2200 and 1705 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{35}O_7N$: C, 65.94; H, 7.45; N, 2.96. Found: C, 65.64; H, 7.66; N, 3.07.

Further elution with ether–acetone (70:30, 800 cc.) afforded 6-cyano-3-(2′-hydroxyethyl)-$\Delta^{3,5}$-pregnadiene-17α,21-diol-11-one-20-cycloethylene ketal (XXIb) (370 mg.), m.p. 247–249°, raised by several crystallizations from ethyl acetate–hexane to 248–250°, $[\alpha]_D$ −59°; λ_{max}^{EtOH} 284–286 mμ, ε 17,800; λ_{max}^{KBr} 3450, 2200, 1690 and 1625 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{35}O_7N$: C, 65.94; H, 7.45; N, N, 2.96. Found: C, 65.64; H, 7.66; N, 3.06.

6α-Cyanocortisone (XXII).—Perchloric acid (3.7 cc., 35%) was added to a solution of 6-cyano-3-(2′-hydroxyethyl)-$\Delta^{3,5}$-pregnadiene-17α,21-diol-11,20-dione-20-cycloethylene ketal (XXIb) (220 mg.) in tetrahydrofuran (7.4 cc.). After 3 hours at room temperature water was added and the product extracted with ethyl acetate. The combined extracts were washed with sodium bicarbonate solution (5%), water and then dried over sodium sulfate. Removal of the solvent afforded 6α-cyanocortisone (XXII) as an amorphous solid, m.p. 152–162°, which resisted crystallization; $[\alpha]_D$ −22° (dioxane); λ_{max}^{EtOH} 220–222 and 286–288 mμ, ε 4,300 and 10,800, respectively; λ_{max}^{KBr} 3500, 2200, 1720(sh), 1700, 1670 and 1625 cm.$^{-1}$. The analysis for XXII was unsatisfactory.

Anal. Calcd. for $C_{22}H_{27}O_5N$: C, 68.55; H, 7.06; N, 3.63. Found: C, 67.56; H, 7.31; N, 2.95.

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

The Infrared Spectra of Steroid Lactones

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RECEIVED FEBRUARY 20, 1959

Characteristic features of the infrared spectra of twenty-six types of steroid lactones are summarized and discussed. For saturated γ- and δ-lactones it is observed that, in the absence of direct perturbing influences such as the inductive effects of vicinal substituents, the C=O stretching frequency in solution is negligibly influenced by the location of the lactone group with respect to the steroid ring system. The ranges previously assigned to the positions of the C=O stretching bands of saturated γ- and δ-lactone systems are confirmed, and other absorption specific to different types of steroid lactones is noted between 1450 and 1350 cm.$^{-1}$. The unsaturated lactone systems of $\Delta^{20(22)}$-cardenolides and $\Delta^{20,22}$-bufadienolides exhibit two bands in the C=O stretching region of the spectrum; the relative intensities of the two bands show large solvent effects, but they are not significantly influenced by the formal extension of the conjugated system into ring D.

Numerous publications during the past few years have served to focus attention on the prevalence of lactone groups in naturally occurring compounds; typical examples are the bitter principles, such as pictrotoxin and limonin, the santonins, nepetalactone, and gibberellic acid. Lactones are also encountered in steroids; unsaturated γ- and δ-lactone ring systems characterize the cardiac, squill and bufalin aglycones while various types of saturated steroid lactones have been obtained in the course of synthetic and degradative studies.

Infrared spectrometry has been used extensively to distinguish between γ- and δ-lactone ring systems in natural products; a range of 1780–1760 cm.$^{-1}$ is commonly reported for the C=O stretching frequency in saturated γ-lactones and 1750–1735 cm.$^{-1}$

(1) Published as Contribution No. 5303 from the Laboratories of the National Research Council of Canada, and No. XXXII in the series "Studies in Steroid Metabolism."

for saturated δ-lactones.[2] Nevertheless, the spectroscopic distinction between γ- and δ-lactones has not always been reliable. In columbin, a dilactone, Barton and Elad[3] observed carbonyl bands at 1750 and 1725 cm.$^{-1}$ in chloroform solution; they assigned the band at 1725 cm.$^{-1}$ unequivocally to a saturated δ-lactone group, but they could not differentiate spectroscopically between a γ- and δ-lactone ring for the second carbonyl band. Subsequent chemical investigations established it to be a β,γ-unsaturated-α-hydroxy-δ-lactone.

The positions of lactone carbonyl bands have been recorded along with other analytical data in several papers dealing with the structure of individual natural products, and some lactone carbonyl frequencies have been reported for steroids.[4-8] However, the characterizing features of such lactone spectra have not hitherto been considered collectively. The object of this paper is to amplify and coördinate such scattered observations on the infrared spectra of steroid lactones and, in particular, to draw attention to the anomalous absorption associated with the $\Delta^{20(22)}$-cardenolide and $\Delta^{20,22}$-bufadienolide structures. A subsequent paper[9] will report in greater detail certain features of lactone spectra that are exhibited to better advantage in simpler model compounds.

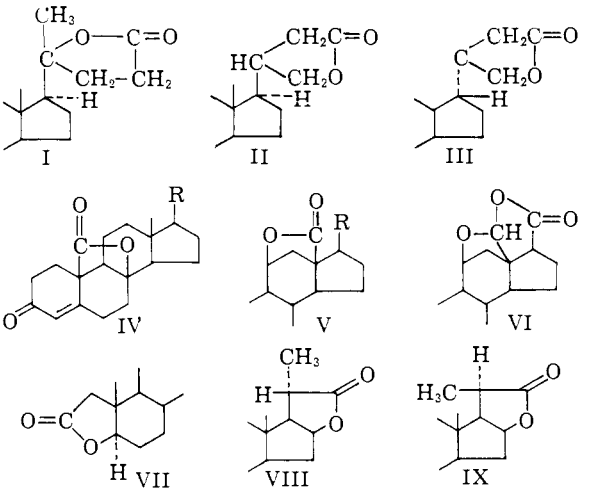
Experimental

The spectra measured in our laboratories were determined on Perkin–Elmer model 112 and model 21 spectrometers. Calcium fluoride prisms were used above 1300 cm.$^{-1}$ and sodium chloride prisms below. The estimated precision of the reported band positions is ±2 cm.$^{-1}$. The steroids were acceptable "analytical" samples and none exhibited any spectrographically recognizable impurity. The sources of the individual compounds are acknowledged in the footnote to Table I. The complete spectra, together with the spectra of related model compounds will be published separately.[10]

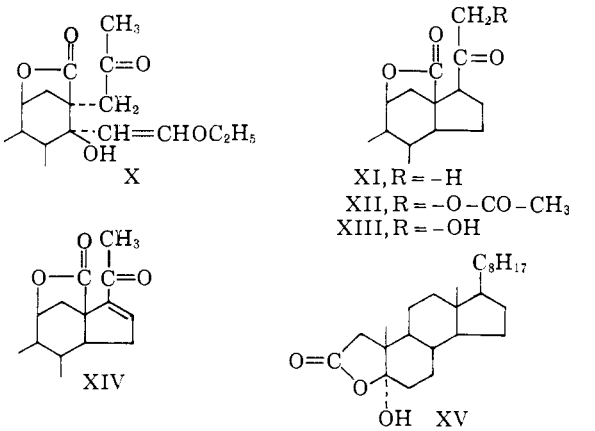
Results and Discussion

In Table I the characteristic group frequencies are listed for the individual steroid lactones. The complete data including values taken from other publications are summarized in Table II. Many of the compounds also contained other carbonyl groups but, in general, there was no difficulty in recognizing the lactone carbonyl absorption.

Saturated γ-Lactones.—Lactones of types I–IV have been examined in our laboratories and the infrared spectra of several additional types of γ-lactones have been reported in the literature, these include structures V[7,11] VI,[7,11] VII,[12] VIII[13] and IX.[13]



Structures I–VII exhibit sharp intense carbonyl bands between 1789 and 1777 cm.$^{-1}$ in carbon tetrachloride solution, and between 1782 and 1772 cm.$^{-1}$ in chloroform solution. This agrees with values commonly reported for monocyclic compounds. Neighboring carbonyl groups, such as those occurring in 11,17-diketones and 21-acetoxy-20-ketones, are known to induce characteristic displacements of C=O stretching frequencies, but no comparable effects are apparent in the oxygenated lactone structures X–XIV described by Wettstein and collaborators,[7] all of which show the lactone carbonyl band between 1779 and 1770 cm.$^{-1}$ in methylene chloride solution. For the lactol XV a C=O stretching band at 1764 cm.$^{-1}$ has been reported[14]; here the lowering might be attributed to the vicinal hydroxyl group but the extent of the displacement cannot be fully assessed since the solvent is not stated. The lactones of types VIII and IX, derived from steroidal sapogenins, are also reported to absorb at a significantly lower frequency (1773 cm.$^{-1}$ in carbon disulfide and 1764 cm.$^{-1}$ in methylene dichloride).[13]



In IV the carbonyl band of the Δ^4-3-ketone group occurs at 1686 cm.$^{-1}$ in carbon tetrachloride solu-

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(14) F. L. Weisenborn, D. C. Remy and T. L. Jacobs, *ibid.*, **76**, 552 (1954). The stereochemistry of XV at C(5) is not specifically defined but the hydroxyl group is presumably α.

TABLE I

CHARACTERISTIC ABSORPTION BANDS IN THE INFRARED SPECTRA OF STEROID LACTONES

Structure	Compound[a]	Source[b]	Solvent	Characteristic bands, cm.$^{-1}$: Carbonyl[c]	Other[d]
	A. Saturated γ-lactones				
I	3β-Acetoxy-20-hydroxy-Δ^5-cholenic acid lactone	1	CCl_4	1777, *1733*	1425,[e] 1392,[f] 1202[g,h]
	3β-Benzoxy-20-hydroxy-Δ^5-cholenic acid lactone	1	CCl_4	1778, *1718*	1424,[e] 1392,[f] 1202.[g,h]
	20-Hydroxy-3-keto-Δ^4-cholenic acid lactone	1	CCl_4	1778, *1679*	1424,[e] 1390,[f] 1200[g,h]
II	3β-Acetoxy-14-hydroxy-cardanolide (dihydroxy-digitoxigenin acetate)	2	CCl_4	1786, *1736*	1424,[e] 1176[g,h]
			$CHCl_3$	1775, *1727*	
III	3β-Acetoxy-14-hydroxy-17α-cardanolide (17-iso-dihydroxy-digitoxigenin acetate)	2	CCl_4	1789, *1736*	1422,[e] 1168[g,h]
			$CHCl_3$	1776, *1728*	..
IV	8-Hydroxy-3,20-diketo-Δ^4-pregnen-19-oic acid lactone	3	CCl_4	1781, *1710, 1686*	1163[g,h]
			$CHCl_3$	1772, *1705, 1677*	1165[g]
	8-Hydroxy-3,20-diketo-Δ^4-17α-pregnen-19-oic acid lactone	3	CCl_4	1782, *1709, 1686*	1170[g,h]
			$CHCl_3$	1772, *1704, 1675*	..
	8,21-Dihydroxy-3,20-diketo-Δ^4-pregnen-19-oic acid 8:19-lactone	3	$CHCl_3$	1775, *1716, 1680*	1170[g]
	8,21-Dihydroxy-3,20-diketo-Δ^4-17α-pregnen-19-oic acid 8:19-lactone	3	$CHCl_3$	1777, *1714, 1678*	1174[g]
	B. Saturated δ-lactones				
XVI	5-Hydroxy-3:5-*seco*-4-norcholestan-3-oic acid lactone	1	CS_2	1744	1420,[e] 1078,[g] 1050[g]
	5,17β-Dihydroxy-3:5-*seco*-4-norandrostan-3-oic acid 3:5-lactone	1	CCl_4	1747	1417,[e] 1078,[g] 1047[g]
	5,17β-Dihydroxy-3:5-*seco*-4-nor-17-methylandrostan-3-oic acid 3:5-lactone	1	CS_2	1742	[i] [i] [i]
	5,20-Dihydroxy-3:5-*seco*-4-norallopregnan-3-oic acid 3:5-lactone	1	CS_2	1745	[i] [i] [i]
XVII	3β,16-Dihydroxy-16:17-*seco*-Δ^5-androsten-17-oic acid 16:17-lactone	4	CCl_4	1740	1401,[j] 1155,[g,h] 1110,[g,h] 1045[g,h]
	3β-Acetoxy-16-hydroxy-16:17-*seco*-Δ^5-androsten-17-oic acid lactone	4	CCl_4	1739[k]	1401,[j] 1154,[g,h] 1108,[g,h] 1048[g,h]
XVIII	3-Acetoxy-13-hydroxy-13:17-*seco*-Δ$^{1,3,5(10)}$-estratrien-17-oic acid lactone (estrololactone acetate)[l]	5, 6	CS_2	*1767*, 1742	[i] [i]
	3α,13-Dihydroxy-13:17-*seco*-androstan-17-oic acid 13:17-lactone (andrololactone)	7	$CHCl_3$	1718	1118[g]
	3α-Acetoxy-13-hydroxy-13:17-*seco*-androstan-17-oic acid lactone (andrololactone acetate)	7	CCl_4	1737[k]	1422,[e] 1116[g,h]
	3β-Acetoxy-13-hydroxy-13:17-*seco*-androstan-17-oic acid lactone (isoandrololactone acetate)[l]	5, 8	CS_2	1742[k]	[i] [i]
	3α,13-Dihydroxy-13:17-*seco*-etiocholan-17-oic acid 13:17-lactone (3α-etiocholanololactone)	7	$CHCl_3$	1718	[i] 1114[g]
	3β-Acetoxy-13-hydroxy-13:17-*seco*-etiocholan-17-oic acid lactone (3β-etiocholanololactone acetate)[l]	8	CS_2	1742[k]	[i] [i]
XVIII	13-Hydroxy-3-keto-13:17-*seco*-Δ$^{1:4}$-androstadien-17-oic acid lactone	7	CCl_4	1743	[i] [i]
			$CHCl_3$	1722	[i] 1103[g]
	13-Hydroxy-3-keto-13:17-*seco*-Δ^4-androsten-17-oic acid lactone	9	CCl_4	1742	1420[e] [i]
			$CHCl_3$	1723	[i] 1102[g]
XIX	3β-17-Dihydroxy-16:17-*seco*-Δ^5-androsten-16-oic acid 16:17-lactone	4	CCl_4	1744	1418,[e] 1401,[j] 1180,[g,h] 1037[g,h]
	3β-Acetoxy-17-hydroxy-16:17-*seco*-Δ^5-androsten-16-oic acid lactone	4	CCl_4	1742[k]	1419,[e] 1400,[j] 1192,[g,h] 1042[g,h]
	C. Unsaturated γ-lactones				
XXVII	3β-14-Dihydroxy-Δ$^{20(22)}$-cardenolide (digitoxigenin)	2	$CHCl_3$	1787,[m] 1747[n]	1619[o]
XXVIII	3β-Acetoxy-14-hydroxy-Δ$^{20(22)}$-cardenolide (digitoxigenin acetate)	2	CS_2	1783,[m] 1756,[n] *1738*	
			$CHCl_3$	1784,[m] 1745,[n] *1730*	1620[o]
XXIX	3β,5,14-Trihydroxy-19-oxo-Δ$^{20(22)}$-cardenolide (strophanthidin)	2	$CHCl_3$	1790,[m] 1748,[n] 1718[p]	1624[o]
XXX	3β,16-Diacetoxy-Δ$^{14(15),20(22)}$-cardadienolide (14-anhydrogitoxigenin diacetate)	2	CS_2	1784,[m] 1758,[n] *1739*	
			$CHCl_3$	1787,[m] 1752,[n] *1730*	1628[o]
XXXI	3β,14-Dihydroxy-Δ$^{16(17),20(22)}$-cardadienolide (16-anhydrogitoxigenin)	2	$CHCl_3$	1790,[m] 1748[n]	1624[o]
XXXII	3β-Acetoxy-14-hydroxy-Δ$^{16(17),20(22)}$-cardadienolide (16-anhydrogitoxigenin acetate)	2	CS_2	1783,[m] 1755,[n] *1737*	
			$CHCl_3$	1788,[m] 1748,[n] *(1732)*	1622[o]
XXXIII	3β-Acetoxy-Δ$^{14(15),16(17),20(22)}$-cardatrienolide (14,16-dianhydrogitoxigenin acetate)	2	CS_2	1780,[m] 1750,[n] *1735*	
			$CHCl_3$	1786,[m] 1738[k,n]	1612,[o] 1568[o]
	D. Unsaturated δ-lactones				
XXXVII	3β,14-Dihydroxy-Δ^{20,22}-bufadienolide (bufalin)	2	$CHCl_3$	(1740), 1718	1636[o]
XXXVIII	3β,5,14-Trihydroxy-19-oxo-Δ^{20,22}-bufadienolide (hellebrigenin)	2	$CHCl_3$	(1740), 1718[p]	1638[o]
XXXIX	3β-Acetoxy-5,14-dihydroxy-19-oxo-Δ^{20,22}-bufadienolide (hellebrigenin acetate)	2	$CHCl_3$	1740,[k] 1718[p]	1636[o]
XL	3β,16-Diacetoxy-Δ$^{14(15),20,22}$-bufatrienolide (14-anhydrobufotalin diacetate)	2	CS_2	1751, 1736[p]	
			$CHCl_3$	(1748), 1729[p]	1638
XLI	3β-Acetoxy-Δ$^{14(15),16(17),20,22}$-bufatetraenolide (14,16 dianhydro-desacetyl-bufotalin acetate)	2	CS_2	1740[k]	
			$CHCl_3$	1723[k]	1632,[o] 1600[o]

[a] The nomenclature used here has been modified from that of our previous publications to conform more closely with the recommendations of the I.U.P.A.C. as reported in *Chemistry & Industry*, pp. SN1-SN11 (June 23rd, 1951). [b] (1) B. J. Brent, Organon, Inc., Orange, N. J.; (2) T. Reichstein, University of Basel, Basel, Switz.; (3) M. Ehrenstein, University of Pennsylvania Medical School, Philadelphia, Pa.; (4) G. Papineau-Couture and G. A. Grant, Ayerst, McKenna and Harri-

son Ltd., Montreal, Can.; (5) R. F. Jacobsen, Worcester Foundation for Experimental Biology, Worcester, Mass., (6) W. W. Westerfeld, Syracuse University, N. Y.; (7) compound synthesized at the Sloan–Kettering Institute, New York, N. Y.; (8) D. A. Prins, Cleveland Clinic, Cleveland, O.; (9) J. Fried, Squibb Laboratories, New Brunswick, N. J. [c] Bands not associated with the lactone carbonyl are italicized; inflections are given in parentheses. [d] See text. [e] Band assigned to $-CH_2-CO-O-$ group. [f] Band assigned to C(18) methyl group. [g] Band assigned to C–O stretching vibration of lactone group. [h] Measured in carbon disulfide solution. [i] Region not measured. [j] Band tentatively assigned to $CO-O-CH_2-$, group in a six-membered ring. [k] Overlapped by acetate absorption. [l] The carbonyl bands of these compounds were reported previously in ref. 4 where they were assigned erroneously to structure XVII; see also ref. 21. The C=O frequencies reported here are based on new and more precise measurements than those reported in ref. 4. [m] "Abnormal band." [n] "Normal" band. [o] C=C stretching band. [p] Overlapped by C(19) aldehyde absorption.

TABLE II

SUMMARY TABLE OF STEROID LACTONE BAND POSITIONS

	Structure	Solvent	C=O stretching band,[c] cm.$^{-1}$	Other bands, cm.$^{-1}$
	A. Saturated γ-lactones			
I	20-Hydroxy-cholanic acid lactone	CCl_4	1778–1777	1425–1424,[e] 1392–1390[f], 1202–1200[g,h]
II	Cardanolide	CCl_4	1786	1424,[e] 1176[g,h]
		$CHCl_3$	1775	
III	17-α-Cardanolide	CCl_4	1789	1422,[e] 1168[g,h]
		$CHCl_3$	1776	
IV	8-Hydroxy-19-oic acid lactone	CCl_4	1782–1781	1174–1165[h]
		$CHCl_3$	1777–1772	
V	11β-Hydroxy-18-oid acid lactone[a]	$CHCl_3$	1782	
		CH_2Cl_2	1779–1770	
VI	11β,18-Epoxy-18-hydroxy-20-oic acid lactone[a]	$CHCl_3$	1779	
VII	5-Hydroxy-2:5-*seco*-3,4-bisnor-2-oic acid lactone[b]	CCl_4	1785	
VIII	16β-Hydroxy-bisnorallocholanic acid lactone	CS_2	1773	1175,[g] 1017[g]
		CH_2Cl_2	1764	1184,[g] 1017[g]
IX	16β-Hydroxy-20-isobisnorallocholanic acid lactone	CS_2	1773	1184,[g] 1016[g]
		CH_2Cl_2	1764	1171,[g] 1016[g]
XV	5,5-Dihydroxy-2:5-*seco*-3,4-bisnor-2-oic acid lactone[b]	..	1764	
	B. Saturated δ-lactones			
XVI	5-Hydroxy-3:5-*seco*-4-nor-3-oic acid lactone	CS_2	1744–1742	1078,[g] 1050,[g]
		CCl_4	1747	1420–1417,[e] 1078,[g] 1047[g]
XVII	16-Hydroxy-16:17-*seco*-17-oic acid lactone	CCl_4	1740–1739	1401,[j] 1155–1154,[g,h] 1110–1108[g,h] 1048–1045[g,h]
XVIII	13ξ-Hydroxy-13:17-*seco*-17-oic acid lactone	CS_2	1742	1116[g]
		CCl_4	1743–1737	1422–1420[e]
		$CHCl_3$	1723–1718	1118–1102[g]
XIX	17-Hydroxy-16:17-*seco*-16-oic acid lactone	CCl_4	1744–1741	1419–1418,[e] 1401–1400,[j] 1192–1190[g,h] 1042–1037[g,h]
XX	5-Chloro-5-hydroxy-3:5-*seco*-4-nor-3-oic acid lactone[d]	..	1770	
	C. Saturated ε-lactones			
XXIV	13ξ-Hydroxy-12:13-*seco*-5α,22α-spirostan-12-oic acid lactone	CS_2	1727	
		$CHCl_3$	1705	
XXV	11-Keto-13ξ-hydroxy-13:17a-*seco*-D-homo-17a-oic acid lactone	$CHCl_3$	See text, p. 13	
	D. Unsaturated γ-lactones			
XXVII–XXIX	$\Delta^{20(22)}$-Cardenolide	CS_2	1783,[m] 1756[n]	
		$CHCl_3$	1790–1784,[m] 1748–1745[n]	1624–1619[o]
XXX	16β-Acetoxy-$\Delta^{14(15),20(22)}$-cardadienolide	CS_2	1784,[m] 1758[n]	
		$CHCl_3$	1787,[m] 1752[n]	1628[o]
XXXI–XXXII	$\Delta^{16(17),20(22)}$-Cardadienolide	CS_2	1783,[m] 1755[n]	
		$CHCl_3$	1790–1788,[m] 1748[n]	1624–1622[o]
XXXIII	$\Delta^{14(15),16(17),20(22)}$-Cardatrienolide	CS_2	1780,[m] 1750[n]	
		$CHCl_3$	1786,[m] 1738[k,n]	1612,[o] 1568[o]
XXXVI	5-Hydroxy-2:5-*seco*-3:4-bisnor-Δ^5-2-oic acid lactone	CCl_4	1806	1705[o]
XXXVII–XXXIX	$\Delta^{20,22}$-Bufadienolide	$CHCl_3$	(1740), 1718	1636[o]
XL	16β-Acetoxy-$\Delta^{14,15),20,22}$-bufatrienolide	CS_2	1751, 1736	
		$CHCl_3$	(1748), 1729[k]	1638[o]
XLI	$\Delta^{14(15),16(17),20,22}$-Bufatetraenolide	CS_2	1740[k]	
		$CHCl_3$	1723[k]	1632,[o] 1600[o]
XLII	5-Hydroxy-Δ^5-4-nor-3-oic acid lactone[b,d]	CCl_4	1757–1756	1667[i,o]

[a] See ref. 7, 11. [b] See ref. 14. [c] Points of inflection indicated by parentheses. [d] See ref. 28. [e,f,g,h,i,k,m,n,o] See footnote to Table I. [j] This value is reported for a series of compounds in ref. 31; 1682 cm.$^{-1}$ has been reported subsequently for one compound in ref. 12. [l] See ref. 12.

tion. This is higher than the normal position at 1681–1677 cm.$^{-1}$. In chloroform solution IV absorbs at 1680–1675 cm.$^{-1}$, while the normal range is 1668–1660 cm.$^{-1}$. The Δ^4 C=C stretching vibration is also displaced in these compounds from 1619–1613 to 1635 cm.$^{-1}$ ($CHCl_3$ soln.). It would appear therefore that the bridging of ring B by the lactone group increases the rigidity of the A/B ring system and so induces steric strains in the conjugated ketone structure. Dipole–dipole interactions between the two carbonyl groups could also raise the ketone and C=C stretching frequencies, but if this were so, the lactone carbonyl frequency would also be affected.

Saturated γ-lactones exhibit characteristic features in the region between 1500 and 1300 cm.$^{-1}$ associated primarily with deformation vibrations of C–H bonds. Representative examples are

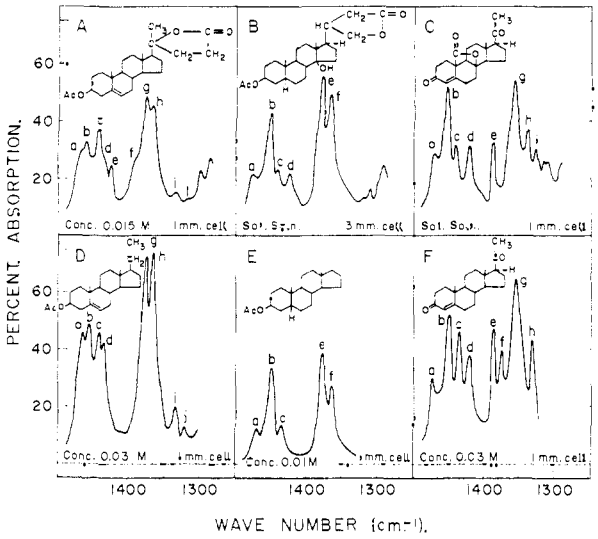


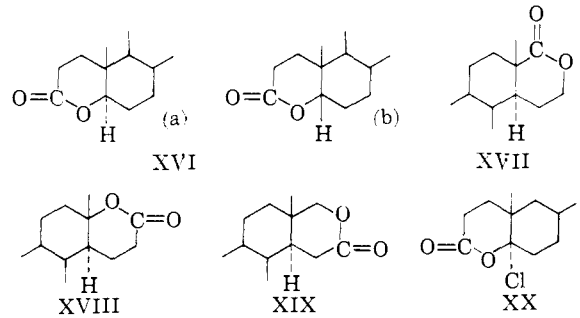
Fig. 1.—C–H deformation vibrations of saturated γ-lactones in CCl_4 solution: A, structure I, comparison with D demonstrates characteristic bands e and f. Band e is assigned to the α-methylene group of the lactone ring and band f to the C(18)-methyl group displaced to higher frequency in the lactone spectrum. B, structure II, comparison with E demonstrates characteristic band d assigned to the α-methylene group of the lactone ring. C, structure IV, comparison with F demonstrates no new absorption in the lactone spectrum, but band f, assigned to the C(19)-methyl group, is lost.

shown in Fig. 1, where the spectra of the lactones are compared with the spectra of closely related steroids lacking the lactone group. In the spectra of ketones and acyl esters containing a methylene group in the α-position to carbonyl, a small band is observed near 1420 cm.$^{-1}$. This has been shown by selective deuteration to involve the α-methylene hydrogen atoms and has been assigned to the scissoring vibration of the C–H bonds.[15,16] The lactones I–III, which likewise contain an α-methylene group, exhibit a small band near 1425 cm.$^{-1}$ (Fig. 1A, band e; Fig. 1B, band d); this band is lacking from the spectra of the comparison compounds in Figs. 1D and 1E and can be assigned to the α-methylene scissoring vibration.

In the spectrum shown in Fig. 1C, band d at 1420 cm.$^{-1}$ is associated with the scissoring vibration of the C(2) methylene and is not derived from the lactone group. A band of comparable intensity is present in the curve in Fig. 1F; similar bands have been noted in the spectra of other Δ^4-3-ketones and they disappear on substitution at C(2).[17] From Figs. 1C and 1F it is also seen that band f is not present in the spectrum of the lactone. This is undoubtedly the C(19) methyl symmetrical bending vibration; between 1400 and 1300 cm.$^{-1}$, the curve in Fig. 1C closely resembles the spectrum of 19-norprogesterone[18] which also lacks this band.

Lactones, like esters, exhibit strong absorption in the region 1200–1100 cm.$^{-1}$ probably associated with stretching vibrations of the C–O linkages. Lactones of structures II–IV exhibit such a band near 1170 cm.$^{-1}$ whereas for structure I the analogous band occurs at 1200 cm.$^{-1}$ (Table I).

Saturated δ-Lactones.—The saturated steroid δ-lactones we have examined are of types XVI–XIX. Three of these contain the lactone group in an enlarged ring D; these compounds, obtained initially by oxidation of 17-ketosteroids[19,20] and 17-α-hydroxy-20-ketosteroids,[21] have been a subject of study by several investigators[19–25] and the earlier literature has been summarized in the paper by Murray, Johnson, Pederson and Ott.[25]



XVI XVII

XVIII XIX XX

All four types of δ-lactones exhibit the typical C=O stretching band between 1747 and 1737 cm.$^{-1}$ in carbon disulfide and carbon tetrachloride solution. These observations are consistent with data in the literature for simpler monocyclic saturated δ-lactones and acyl ester carbonyl groups in strainless systems.[26] In his recent monograph,[2] Bellamy discusses the possibility that the δ-lactone carbonyl frequency may be enhanced where the lactone forms part of a strained polycyclic ring system. This may well be true, but the example cited by Bellamy unfortunately was based on a typographical error in one of our earlier publications[5] which was later corrected.[27] For the chlorolactone XX Turner[28] has reported the C=O band at 1770 cm.$^{-1}$ (solvent not stated).

The absorption of representative δ-lactones in the region 1500–1300 cm.$^{-1}$ is shown in Figs. 2 and 3. The structures shown in Figs. 2A, 3A and 3B exhibit the small band at 1422–1418 cm.$^{-1}$ assigned to the methylene group vicinal to the lactone carbonyl; these spectra should be compared with Figs. 2C, 3C and 3D and also with the lactone in Fig. 2B which have no α-methylene group.

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

(16) M. E. Isabelle and L. C. Leitch, *Can. J. Chem.*, **36**, 440 (1958).

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

(18) See Chart 417 of ref. 6.

(19) W. W. Westerfeld, *J. Biol. Chem.*, **143**, 177 (1942).

(20) R. P. Jacobsen, *ibid.*, **171**, 61 (1947).

(21) N. S. Leeds, D. K. Fukushima and T. F. Gallagher, THIS JOURNAL, **76**, 2265 (1954).

(22) C. v. Seemann and G. A. Grant, *ibid.*, **72**, 4073 (1950).

(23) J. Jacques, A. Horeau and R. Courrier, *Compt. rend.*, **229**, 321 (1949).

(24) N. L. Wendler, D. Taub and H. L. Slates, THIS JOURNAL, **77**, 3559 (1955).

(25) M. F. Murray, B. A. Johnson, R. L. Pederson and A. C. Ott, *ibid.*, **78**, 981 (1956).

(26) According to Gual, Dorfman and Rosenkrantz,[8] estrololactone, a steroid of structure XVIII, exhibits an anomalously low carbonyl frequency when measured in a potassium bromide disk. The acetate of this compound absorbs normally in solution (Table I) and the band displacement of the free alcohol in the solid state must result from intermolecular hydrogen bonding in the crystal lattice. This provides an excellent example of the hazards associated with structural assignments based on spectra measured in the solid phase.

(27) Page 22 of ref. 6.

(28) R. B. Turner, THIS JOURNAL **72**, 579 (1950)

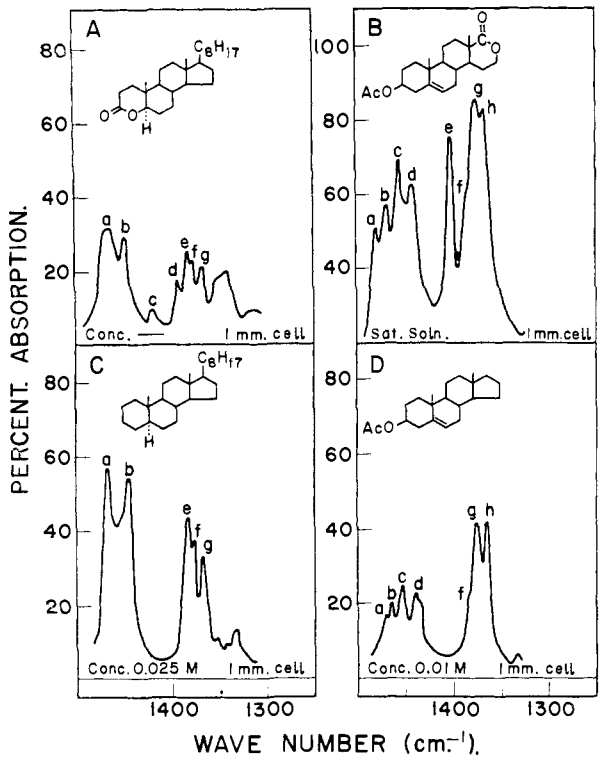


Fig. 2.—C–H deformation vibrations of saturated δ-lactones in CCl_4 solution: A, structure XVIa. comparison with C demonstrates characteristic bands c and d. Band c is assigned to the α-methylene group of the lactone ring and band d to the C(19)-methyl group displaced to higher frequency in the lactone spectrum. B, structure XVII, comparison with D demonstrates characteristic band e tentatively assigned to the –CO–O–CH_2–system in a six-membered ring.

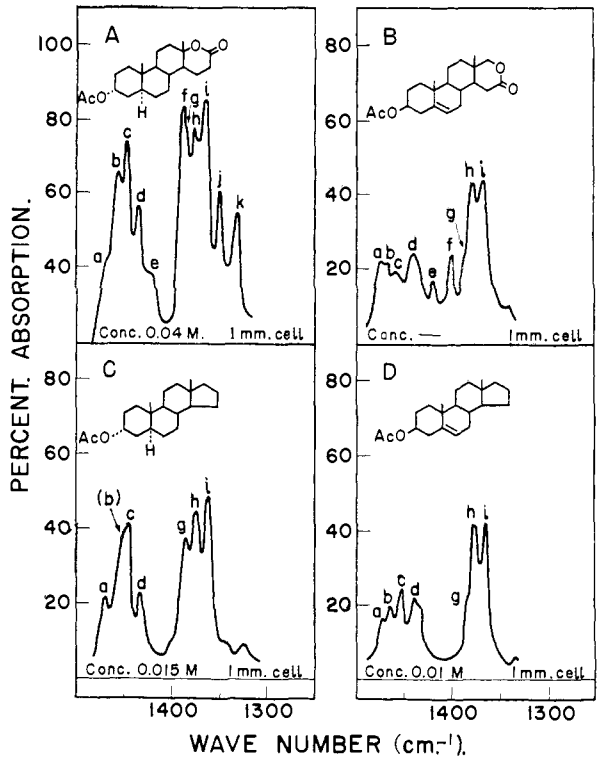
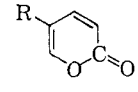


Fig. 3.—C–H deformation vibrations of saturated δ-lactones in CCl_4 solution: A, structure XVIII, comparison with C demonstrates characteristic bands e and f. Band e is assigned to the α-methylene group of the lactone ring and band f is unassigned. B, structure XIX, comparison with D demonstrates characteristic bands e and f. Band e is assigned to the α-methylene group of the lactone ring, and band f to the –CO–O–CH_2– system in a six-membered ring.

Compounds of structure XVII and XVIII show a prominent narrow band near 1400 cm.$^{-1}$ (Fig. 2B, band e; Fig. 3B, band f) which must also be associated with the lactone group. Comparison of the structures of the four types of δ-lactones suggests this band may require the presence of the group –$COOCH_2$– in a six-membered ring. A similar band is observed in XXI, but not in XXII or XXIII, and a strong band at 1402 cm.$^{-1}$ is reported in the spectrum of δ-valerolactone.[29] No analogous band is seen in open chain esters of the type R–CO–O–CH_2–R′, nor in II or III where the same grouping occurs in a five-membered ring, and the association of this band with the –$COOCH_2$– group is speculative.

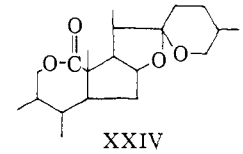
XXI



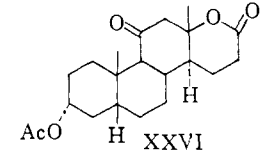
XXII, R = –H
XXIII, R = –CH_3

δ-Lactones show prominent bands in the lower frequency region between 1250 and 1000 cm.$^{-1}$ as noted in the right hand column of Table I. The position of these bands is variable in the different types of δ-lactones. Where other functional groups are also present in the molecule these bands are difficult to recognize, and their use for structural diagnosis is limited unless similar steroids lacking the lactone group are available for comparison.

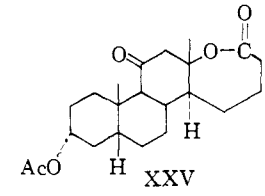
Saturated ε-Lactones.—Meager information is available concerning steroids possessing ε-lactone groups; compounds containing the structures XXIV[30] and XXV[24] have been described. The



XXIV



XXVI



XXV

lactone carbonyl group of XXIV is reported to absorb at 1727 cm.$^{-1}$ (CS_2) and 1705 cm.$^{-1}$ ($CHCl_3$), and these band positions are significantly lower than those reported for δ-lactones (*cf.* Table II).

(29) R. S. Rasmussen and R. R. Brattain, THIS JOURNAL, **71**, 1073 (1949).

(30) E. S. Rothman, M. E. Wall and C. R. Eddy, *ibid.*, **76**, 527 (1954).

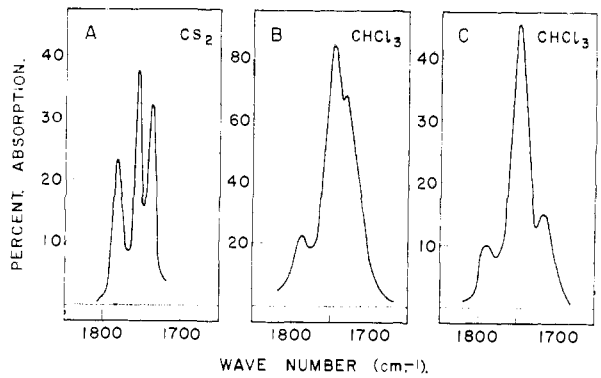
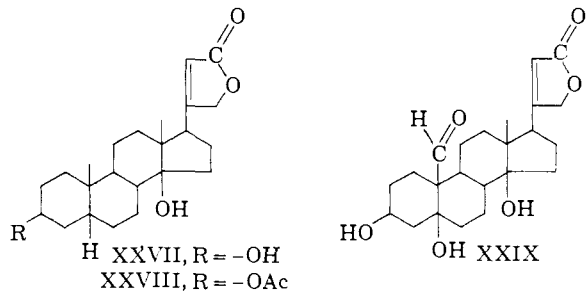
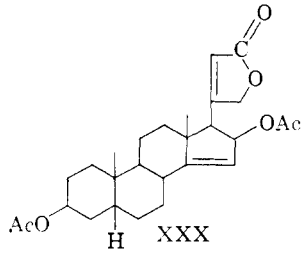
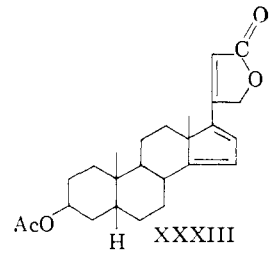


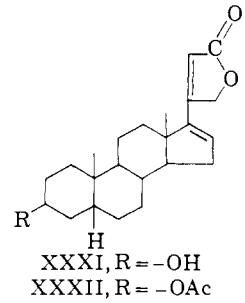
Fig. 4.—Infrared spectrum in C=O stretching region: A, digitoxigenin acetate (XXVIII) in CS_2 soln. (satd. soln., 1-mm. cell); B, digitoxigenin acetate (XXVIII) in $CHCl_3$ soln. (0.006 *M*, 1-mm. cell); C, strophanthidin (XXIX) in $CHCl_3$ soln. (satd. soln., 1-mm. cell).

For XXV bands are reported at 1724 and 1709 cm.$^{-1}$ in chloroform. The homolog with a δ-lactone structure (XXVI) absorbs at 1730 and 1706 cm.$^{-1}$ in the same solvent. In view of the several carbonyl functions present, the lactone frequency cannot be assigned with certainty, though it would appear that in this case the band









position is not significantly affected by the ring enlargement. However the relative intensities of the two carbonyl bands are not reported, and if the lower frequency band were significantly more intense in XXV than in XXVI the ε-lactone group might be contributing to the 1709 cm.$^{-1}$ band of XXV and the δ-lactone group to the 1730 cm.$^{-1}$ group of XXVI. This would be consistent with the observations on XXIV in indicating a fall in the carbonyl frequency with ring enlargement.

Unsaturated γ-Lactones.—The α,β-unsaturated γ-lactone group of the $\Delta^{20(22)}$-cardenolide side chain is unusual in exhibiting two prominent bands in the region commonly associated with the C=O stretching vibration. Observations on a series of model compounds containing this ring system[9] have established that the phenomenon is specific to the lactone ring and does not involve intra- or intermolecular association with hydroxyl or other functional groups on the steroid ring system. The relative intensities of the two peaks are little influenced by concentration, but they are sensitive to changes in solvent polarity and to temperature. The spectroscopic and structural significance of the two bands will be considered in connection with the model compounds in another publication[9] and here we shall deal only with the bands as observed in steroid spectra.

The spectrum of digitoxigenin acetate (XXVIII) in carbon disulfide solution exhibits three bands between 1800 and 1700 cm.$^{-1}$ (Fig. 4A). The band at lowest frequency (1738 cm.$^{-1}$) can be assigned to the C(3) acetate group and the doublet at 1783 and 1756 cm.$^{-1}$ to the lactone ring. The 1756 cm.$^{-1}$ band can be considered "normal" since conjugation would be expected to lower the C=O frequency by 20–30 cm.$^{-1}$ from the position at 1786 cm.$^{-1}$ in the dihydro compound II. The band at 1783 cm.$^{-1}$ is the "abnormal" one. In more polar solvents the intensity of this abnormal band diminishes greatly while that of the normal band increases, as is shown for the same compound in chloroform solution in Fig. 4B. While change of solvent polarity produces a large effect on the relative intensities of the two bands, the frequency shifts are small. The spectrum of strophanthidin (XXIX) in chloroform solution (Fig. 4C) illustrates the cardenolide lactone doublet uncomplicated by overlapping acetate absorption, as the C(19) aldehyde carbonyl absorption is well separated at its normal position[31] (1719 cm.$^{-1}$).

The spectra of several cardiac aglycone derivatives unsaturated in ring D also have been examined. The spectrum of 14-anhydrogitoxigenin diacetate (XXX) shows the α,β-unsaturated γ-lactone carbonyl doublet with the additional absorption of the superimposed acetate bands at their normal positions (Fig. 5). In 16-anhydrogitoxigenin acetate (XXXII) formal conjugation exists between the $\Delta^{20(22)}$-double bond of the cardenolide ring and the Δ^{16}-bond of ring D; nevertheless the C=O stretching absorption is closely similar to that of digitoxigenin acetate (Fig. 6). The same holds true for 14,16-dianhydrogitoxigenin acetate (XXXIII), the spectrum of which is shown in Fig. 7.

The insensitivity of the lactone carbonyl frequency to extended conjugation in ring D suggested initially that steric resistance might be preventing the lactone ring from taking up a configuration coplanar with ring D. Experiments with atom

(31) W. J. Nowaczynski, P. R. Steyermark, E. Koiw, J. Genest and R. N. Jones, *Can. J. Biochem. Physiol.*, **34**, 1023 (1956).

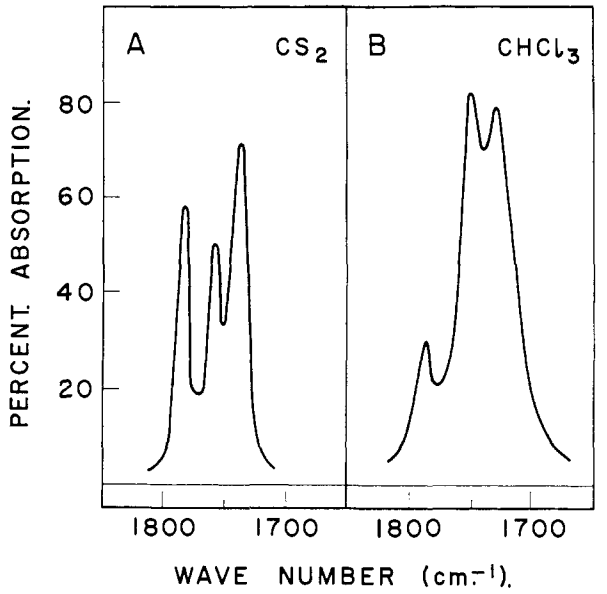


Fig. 5.—Infrared spectrum C=O stretching region: A, 14-anhydrogitoxigenin diacetate (XXX) in CS_2 soln. (satd. soln., 1-mm. cell); B, 14-anhydrogitoxigenin diacetate (XXX) in $CHCl_3$ soln. (0.005 *M*, 1-mm. cell).

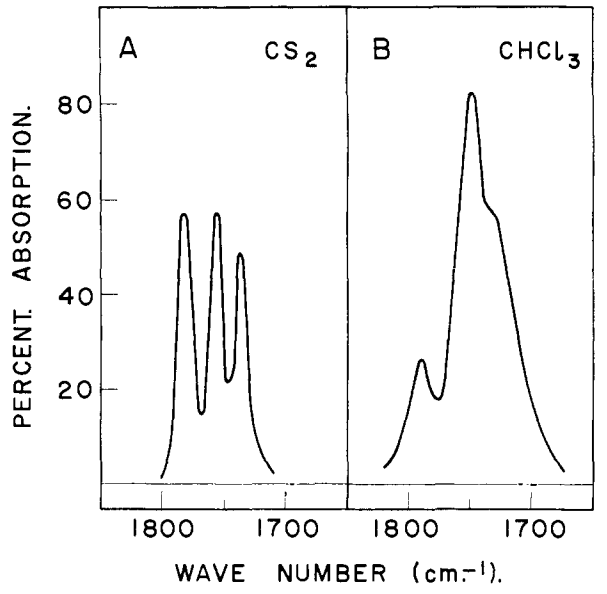
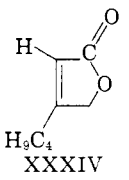
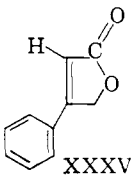


Fig. 6.—Infrared spectrum C=O stretching region: A, 16-anhydrogitoxigenin acetate (XXXII) in CS_2 soln. (satd. soln., 1-mm. cell); B, 16-anhydrogitoxigenin acetate (XXXII) in $CHCl_3$ soln. (0.005 *M*, 1-mm. cell).

models demonstrated, however, that, if present at all, such an effect must be small. Furthermore the lactone carbonyl frequencies of XXXIV and XXXV are also quite similar[9] and here there can be no question of a steric barrier to coplanarity. It



XXXIV



XXXV

was pointed out several years ago by Cromwell and collaborators[32] that the extension of conjugation from an α,β-unsaturated ketone to an $\alpha,\beta;\gamma,\delta$-di-unsaturated ketone induced only a small additional lowering of the carbonyl stretching frequency: extended conjugation influences the electronically excited states much more than the ground state of the molecule and consequently the ultraviolet spectrum is affected much more than the infrared spectrum.

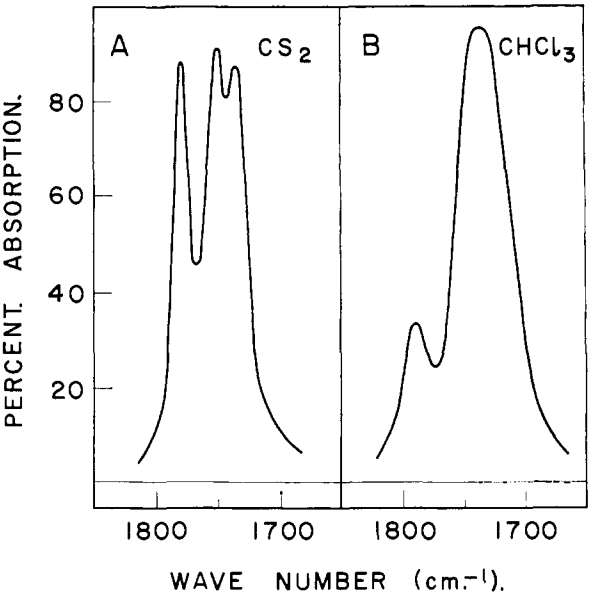
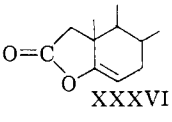


Fig. 7.—Infrared spectrum in C=O stretching region: A, 14,16-dianhydrogitoxigenin acetate (XXXIII) in CS_2 soln. (0.007 *M*, 1-mm. cell); B, 14,16-dianhydrogitoxigenin acetate (XXXIII) in $CHCl_3$ soln. (0.007 *M*, 1-mm. cell).

In chloroform solution the C=C stretching bands of these structures are also observed, and in all cases except XXXIII the $\Delta^{20(22)}$ C=C vibration is noted as a weak band between 1620 and 1630 $cm.^{-1}$ (Tables I and II). Compound XXXIII shows two very strong C=C stretching bands at 1612 and 1578 $cm.^{-1}$; these are probably vibrations of the ring D diene system, and the weaker cardenolide C=C band may be submerged beneath them.

Another type of unsaturated γ-lactone (XXXVI) has been observed by Jacobs and Takahashi[12]



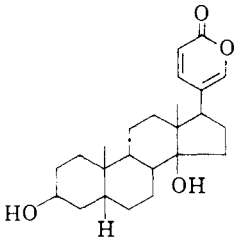
XXXVI

to give strong bands at 1806 and 1705 $cm.^{-1}$ in a carbon tetrachloride solution. These bands can be assigned respectively to the C=O and C=C stretching modes, and their high frequencies are consistent with similar vibrations of acyl enol esters.

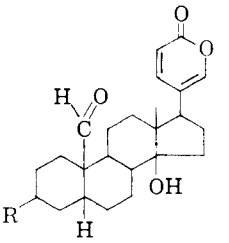
Unsaturated δ-Lactones.—The di-unsaturated δ-lactone system characteristic of the bufadienolide side chain exhibits a doublet carbonyl spectrum

(32) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank and D. J. Wallace, THIS JOURNAL, **71**, 3337 (1949).

similar to that of the $\Delta^{20(22)}$-cardenolides, but with both bands displaced to lower frequency, consistent with extended conjugation and the increase in the ring size. Because of the poor solubility of the steroid bufadienolides in carbon disulfide or carbon tetrachloride, the sensitivity of the relative band intensities to the solvent polarity is observed more effectively with model compounds, such as 5-methyl-α-pyrone[9] (XXIII), but the discussion here will be restricted to the steroid aglycone spectra.



XXXVII



XXXVIII, R = -OH
XXXIX, R = -OAc

The spectra of bufalin (XXXVII) and hellebrigenin (XXXVIII) in chloroform solution exhibit the low frequency band at 1718 cm.$^{-1}$ and the high frequency band as an inflection at 1740 cm.$^{-1}$ (Fig. 8). In the case of hellebrigenin the C(19) aldehyde also contributes to the absorption at 1718 cm.$^{-1}$.

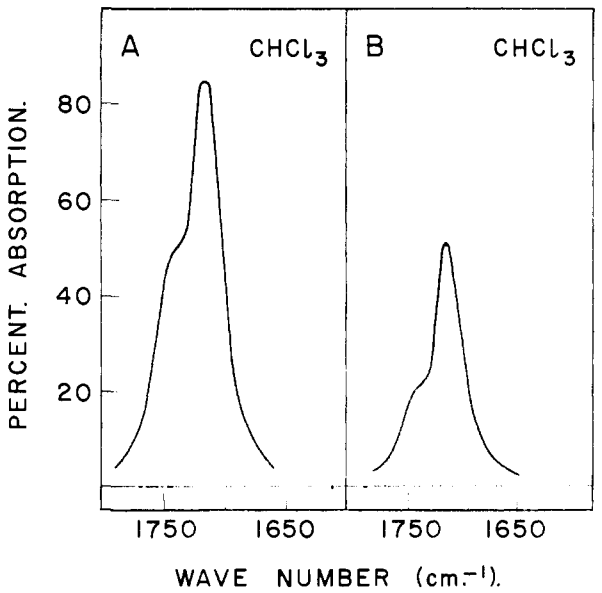
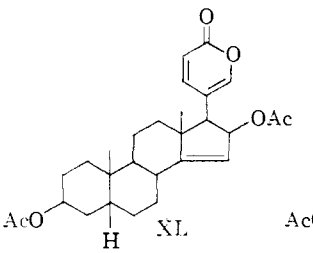


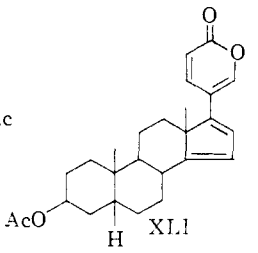
Fig. 8.—Infrared spectrum in C=O stretching region: A, bufalin (XXXVII) in $CHCl_3$ soln. (satd. soln., 1-mm. cell); B, hellebrigenin (XXXVIII) in $CHCl_3$ soln. (satd. soln., 1-mm. cell).

The spectrum of 14-anhydrobufatalin diacetate (XL) both in carbon disulfide and in chloroform is shown in Fig. 9. Here the intensification of the high frequency band in the less polar solvent is clearly demonstrated. In the C=C stretching region chloroform solutions of the bufadienolides all absorb weakly near 1636 cm.$^{-1}$.

Structure XLI exhibits a broad carbonyl band with maximum at 1723 cm.$^{-1}$ in chloroform solution. Although the lactone absorption cannot be



XL



XLI

separated from that of the C(3)-acetate group, it is evident that here, as with the γ-lactones, there can be little if any coupling between the unsaturated systems of the lactone ring and ring D in the electronic ground state.

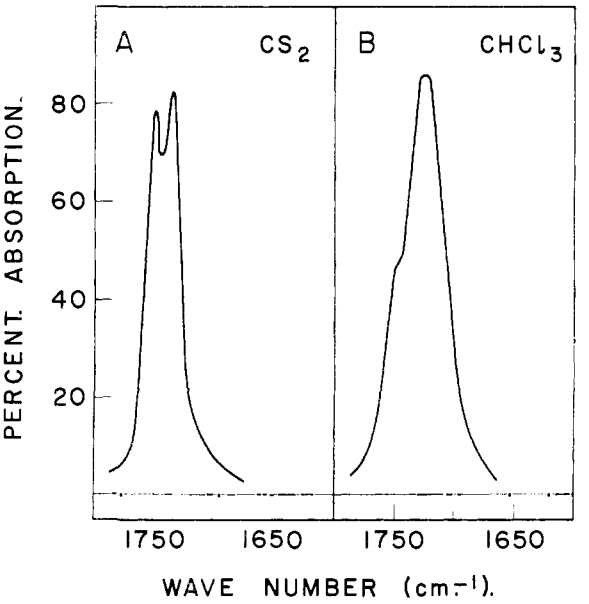
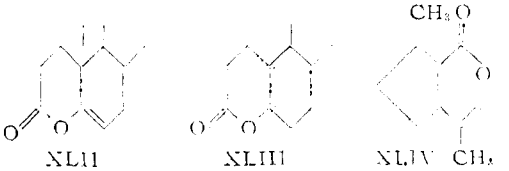


Fig. 9.—Infrared spectrum in C=O stretching region: A, 14-anhydrobufatalin diacetate (XL) in CS_2 soln. (satd. soln., 1-mm. cell); B, 14-anhydrobufatalin diacetate (XL) in $CHCl_3$ soln. (0.005 *M*, 1-mm. cell).

Unsaturated δ-lactones of the enol ester type (XLII) have been examined by Rosenkrantz and Gut[33] and by Jacobs and Takahashi.[12] As would be anticipated, the C=O frequency is raised (1757 cm.$^{-1}$ in CS_2 soln.) and the C=C frequency is also increased (Table II). The spectra of fully cyclic enol lactones of structures XXXVIII have not been studied in the steroid series, but for nepetalactone[34] (XLIV) C=O and C=C bands have been reported at 1764 and 1686 cm.$^{-1}$.



XLII XLIII XLIV

Summarizing Remarks.—The C=O stretching bands in the spectra of steroid lactones measured in solution can be used effectively for differentiating

(33) H. Rosenkrantz and M. Gut, *Helv. Chim. Acta*, **36**, 1000 (1953).

(34) J. Meinwald, THIS JOURNAL, **76**, 4571 (1954). The conditions under which the spectrum is determined are not specifically stated, but presumably a liquid film was employed.

between γ- and δ-lactone ring systems, but they are little influenced by the mode or position of attachment of the lactone group, and are not selective enough to distinguish among various types of lactones of the same ring size. No specific examples of the perturbation of these bands by other neighboring carbonyl groups have been encountered, though there is limited evidence to show that the lactone carbonyl frequency may be depressed by the hydroxyl group in the structure -CO-O-C(OH)- and elevated by the halogen in the structure -CO-O-C(Cl)-. In enol lactones of types XXXVI, XLII and XLIV the C=O frequency is raised. The C=O frequency range for enolic δ-lactones may overlap the range for γ-lactols of the type discussed above (*cf.* XV with XLII and XLIV) and caution must be used in evaluating the lactone ring size where the C=O frequency lies in the range between 1770 and 1755 cm.$^{-1}$. ε-Lactones may absorb at significantly lower frequencies than δ-lactones, but the available evidence is inconclusive.

The presence of two "carbonyl" bands associated with the $\Delta^{20(22)}$-cardenolide and $\Delta^{20,22}$-bufadienolide systems is unusual. The most plausible explanation is a Fermi type resonance between the true C=O stretching vibration and a second vibration, possibly an overtone of a low frequency fundamental. Such an hypothesis is difficult either to confirm or to refute; our investigations on simple butenolides and pyrones fully confirm the generality of the behavior but, as yet, have not provided a satisfactory explanation. Whatever the cause, this solvent effect offers a useful diagnostic method for the identification of such lactone ring systems in compounds of unknown structure. Where solubility conditions permit, this region of the spectrum should be routinely investigated in solvents of both low and high polarity.

The various types of saturated lactones show characteristic differences between 1500 and 1300 cm.$^{-1}$ though the α-methylene bands cannot be distinguished from similar bands of ketones and straight chain esters. The strong "C-O stretching bands" between 1250 and 1000 cm.$^{-1}$ are also sensitive to the type of lactone ring, but they are difficult to recognize where other functional groups are also present unless the curves for appropriate non-lactonic steroids are available for comparison purposes.

Acknowledgment.—The authors wish to thank the several investigators, listed individually in a footnote to Table I, who kindly made available many of the compounds. We are particularly grateful to Prof. T. Reichstein who provided the unique series of cardanolide and the bufanolide derivatives. We also wish to thank Dr. D. Fleischer of the Sloan-Kettering Institute and Dr. D. Taub of the Merck Laboratories for several valuable suggestions, and Mr. D. S. Keir, Mr. R. Lauzon and Mrs. M. A. Mackenzie for technical assistance with the measurement of the spectra.

This investigation was supported, in part, by a grant from the American Cancer Society and a research grant (CY3207) from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

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Glycol Fission in Rigid Systems. II. The Cholestane-3β,6,7-triols. Existence of a Cyclic Intermediate[1]

BY S. J. ANGYAL AND R. J. YOUNG

RECEIVED MARCH 6, 1959

The four diastereomeric cholestane-3β,6,7-triols have been synthesized and their configurations determined. Their rates of oxidation by lead tetraacetate, phenyl iodosoacetate and periodate have been measured; the 3β,6β,7α-isomer, which contains a diaxial glycol group, is not attacked by either reagent. The results support a mechanism for the glycol fission involving a cyclic intermediate (or transition state).

In the preceding paper[2] it has been shown that glycol fission is extremely slow when the projected valency angle (between the two C–OH bonds, viewed along the C–C axis) in a vicinal glycol is rigidly held at 120°. Subsequently it appeared desirable to investigate a case where the projected valency angle is rigidly held at 180°. Such an angle occurs, for example, between axial groups on vicinal carbon atoms in a cyclohexane ring; but to assure the rigidity of that angle the ring must be prevented from changing into other conformations. This can be achieved by *trans*-fusion to the ring of two other cyclohexane rings: ring B of cholestane is thus immobilized. A derivative of cholestane containing two axial hydroxyl groups at C6 and C7 was chosen for study and, to have a sound basis for comparison, its three diastereomers were also prepared and investigated. Cholesterol served as the starting material for their synthesis; hence the four glycols also had a 3β-hydroxyl group; its presence, however, has no effect on the glycol fission.

Wintersteiner and Moore[3] prepared the only previously known cholestane-3β,6,7-triol by hydroxylation of 3β-acetoxycholest-6-ene (III) with osmium tetroxide, but they did not assign a configuration to it. By nature of the reaction it must be a *cis*-glycol; and since hydroxylation of

(1) Abstracted from part of the Ph.D. Thesis of R. J. Young, Sydney, 1958.

(2) S. J. Angyal and R. J. Young, THIS JOURNAL, **81**, Oct. 20 (1959).

(3) O. Wintersteiner and M. Moore, *ibid.*, **72**, 1923 (1950).