1328. *Optical Rotatory Dispersion. Part XXIV.*[1] *Lactones*

By J. P. Jennings, W. Klyne, and Patricia M. Scopes

The optical rotatory dispersion curves have been measured for an extensive series of lactones, most of which give Cotton effects with a first extremum at about 225 mμ. A lactone sector rule is described which enables the rotatory dispersion of many lactones to be predicted from considerations of the asymmetric surroundings of the chromophore. The sector rule affords a satisfactory explanation of the empirical data for the great majority of the compounds studied.

Until recently, the measurement of optical rotatory dispersion (o.r.d.) curves has been restricted in general to that region of the spectrum above 260 mμ. Within this region, the $n \longrightarrow \pi^*$ transition of the carbonyl group gives rise to a weak absorption band at 290 mμ, and the Cotton effects associated with this band have been correlated with the

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[1] A preliminary account of this work has already appeared, J. P. Jennings, W. Klyne, and P. M. Scopes, *Proc. Chem. Soc.*, 1964, 412; Part XXIII, W. Klyne, R. J. Swan, B. W. Bycroft, D. Schumann, and H. Schmid, *Helv. Chim. Acta*, 1965, **48**, 443.

stereochemical environment of the carbonyl group in many types of compound.[2] The empirical correlations have been placed on a theoretical basis in the octant rule,[3] which permits the prediction of the rotatory dispersion behaviour of a saturated ketone from considerations of the geometry of the asymmetric surroundings of the chromophore. Compounds containing the carboxyl group show only plain curves above 270 mμ, but these have led to some useful correlations; particularly in extensive studies by Djerassi, Sjöberg, and their colleagues.[4] These authors in addition to studying the plain curves of carboxylic acids in the longer-wavelength region, have made important studies of acid derivatives containing chromophores which give Cotton effects in the previously accessible region above 270 mμ.[5]

The development of an automatic recording spectropolarimeter,[6] capable of measuring optical rotation to about 210 mμ has enabled us to examine compounds containing the carboxyl chromophore in the region of their weak absorption band at 215 mμ,[7] and it has been shown that these compounds have Cotton effects with a first extremum at about 225 mμ comparable with those of ketones at 300 mμ. Cotton effects have been observed for the carboxyl and related groups in acids,[8] and esters,[9] lactones [1,10] and amides (including peptides),[11] but no theoretical interpretation of the results, comparable to the octant rule for ketones, has been formulated.

Of these carboxyl compounds, lactones are the most useful group with which to investigate the relationship between the rotatory dispersion of a compound and the asymmetric environment of its chromophore. The carboxyl group, when converted into a lactone, is held in a more or less fixed conformation in a ring, instead of rotating freely (as in most carboxylic acids); furthermore, a wide range of compounds of known stereochemistry is readily available. Our present work has been carried out entirely with bicyclic and polycyclic compounds, in which the structure is even more rigid than in monocyclic compounds. In this we have followed the pattern used so succesfully by Djerassi in the study of ketones.[12] His early studies were done on steroids and bicyclic compounds of known conformation; the empirical rules and semi-theoretical treatment [3] developed from this work were then applied to monocyclic ketones, and subsequently, to a limited extent, to open-chain ketones. We hope to follow a similar course in this work on the carboxyl group, leading from bicyclic to monocyclic lactones and then to open carboxylic acids, esters, and their derivatives.

The lactones treated here may be considered as heterocyclic analogues of decalones (I, II) hexahydroindanones (III, IV) and bicyclo[3,3,0]octanones (V, VI), (cf. treatment of decalones [13]); each series exists in *cis*- and *trans*-forms,* and with the hetero-atoms in position 1 or 2 relative to the ring-junctions, thus giving twelve main stereochemical types. In this Paper we present an o.r.d. survey convering nine of these twelve types, represented

* The *cis*- and *trans*-forms of each of the types (I)—(VI) are indicated by (I*c*) and (I*t*), etc.

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[2] C. Djerassi and W. Klyne, *J.*, 1962, 4929; 1963, 2390.

[3] W. Moffitt, A. Moscowitz, R. B. Woodward, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

[4] B. Sjöberg, *Arkiv Kemi*, 1960, **15**, 481.

[5] For summaries, see C. Djerassi, *Proc. Chem. Soc.*, 1964, 314, and P. Crabbé, " Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," ch. 11, Holden-Day, San Francisco, 1965.

[6] E. J. Gilham and R. J. King, *J. Sci. Instr.*, 1961, **38**, 21; J. P. Jennings, *Biochem. J.*, 1963, **86**, 16P.

[7] S. F. Mason, *Quart. Rev.*, 1961, **15**, 287.

[8] J. P. Dirkx and F. L. Sixma, *Rec. Trav. chim.*, 1964, **83**, 522; W. Gaffield, *Chem. and Ind.*, 1964, 1460; J. P. Jennings, W. Klyne, and P. M. Scopes, *J.*, 1965, 294; A. Fredga, J. P. Jennings, W. Klyne, P. M. Scopes, B. Sjöberg, and S. Sjöberg, *J.*, 1965, 3928; A. Kjaer, W. Klyne, P. M. Scopes, and D. R. Sparrow, *Acta Chem. Scand.*, 1964, **18**, 2412.

[9] J. P. Jennings and W. Klyne, unpublished work.

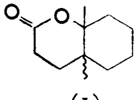
[10] T. Okuda, S. Marigaya, and A. Kiyomoto, *Chem. Pharm. Bull. Japan*, 1964, **12**, 504.

[11] R. Schwyzer, P. M. Scopes, and W. Klyne, unpublished observations.

[12] C. Djerassi, " Optical Rotatory Dispersion," McGraw-Hill, New York, 1960.

[13] W. Klyne, *Experientia*, 1964, **20**, 349.

by over seventy compounds.* With few exceptions, all the compounds considered have terminal lactone rings.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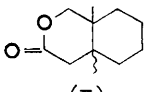
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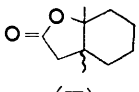
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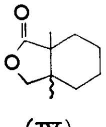
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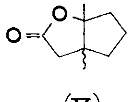
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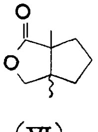
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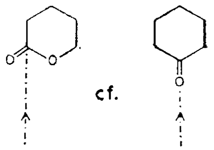
In order to facilitate comparisons between compounds of different types, use is made of the convention whereby some compounds are considered as their enantiomers. The expression " the enantiomer of X gave a positive curve. . ." indicates that the measured compound X was in fact the optical isomer with a negative curve, and that the signs have been changed accordingly. The prefix or suffix E indicates " enantiomer of " in the Tables and formulæ. As a convention the hetero-ring is drawn to the left of the formula with the upper angular substitutent β.

It is not possible at present to measure the full amplitude of the Cotton effect, and the data given are for the molecular rotations [ϕ] at the first extremum (peak or trough) at about 227 mμ. For compounds in which o.r.d. curves reached 220 mμ or below without attaining an extremum, the molecular rotation at 225 mμ is taken as an arbitrary value for reference and for application of the sector rule. The molecular rotation at this extremum, divided by 100, may be treated very approximately as a " half-amplitude," by analogy with the amplitude (peak *minus* trough) used in the discussion of ketonic Cotton effects.[3, 13, 15]

The data are interpreted here in terms of a lactone sector rule in which the molecule is viewed in the plane of the lactone group along the bisectrix of the O–C–O angle, *i.e.*, the line of the carboxyl group and its attached carbon atom (VII). (The lactone group may be considered to be roughly planar according to *X*-ray studies by Mathieson.[16]) The space around the lactone group may be divided into sectors by means of planes meeting at the carboxyl carbon, and from the available data it can be shown empirically that the signs used in the ketone octant rule,[3] must be *reversed* for lactone sectors. Thus atoms lying in the back upper right and lower left sectors make *positive* contributions to the



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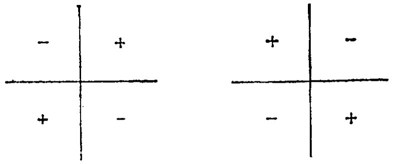

Lactone sectors Ketone octants

(VIII)

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* Another part of our work has been concerned with the study of the extended Hudson lactone rule [14] (jointly with Professor W. Cocker and colleagues in Dublin). The variable success of this rule in several fields of terpene chemistry over the last few years has made a re-examination of its limits very desirable; it seemed appropriate to do this with the newer technique of o.r.d. instead of monochromatic rotations, as in previous work.

[14] W. Klyne, *Chem. and Ind.*, 1954, 1198.

[15] W. Klyne, *Adv. Org. Chem.*, 1960, **1**, 239.

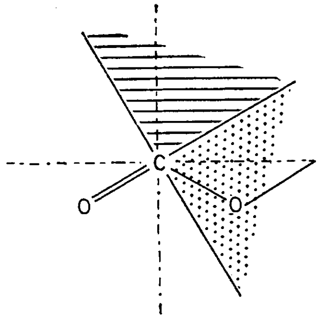
[16] A. McL. Mathieson, *Tetrahedron Letters*, 1963, 81, and references therein.

lactone Cotton effect, while atoms in the back upper left and lower right sectors make *negative* contributions (VIII).

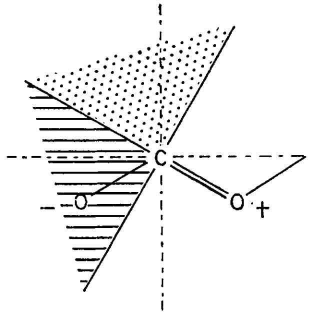
The following semi-quantitative treatment has been suggested to us by Dr. A. Moscowitz of the University of Minnesota, to whom we are greatly indebted for his interest and help. Both carbon–oxygen bonds are regarded as having some double-bond character; as no data seem to be available regarding the proportion of the two canonical forms in the resonance hybrid, we assume as a *very crude* approximation that the two –C–O– bonds are equivalent, and that the plane bisecting the carboxyl angle $(\mathrm{O}\overset{\mathrm{C}}{\diagup\diagdown}\mathrm{O})$ is a symmetry plane. Further refinements of the theoretical calculations will probably show that the nodal surfaces are non-planar, and that the vertical plane, does not in fact bisect the carboxyl angle; however, as a first approximation this treatment enables us to explain satisfactorily the signs of the contributions made by atoms and groups in these various sectors (cf. treatment of nitro-steroids by Snatzke [17]).

It is important to emphasise that our work so far has been concerned entirely with the contributions of alkyl groups and cycloalkane rings. Further studies will be necessary on the effect of halogen atoms, hydroxyl, and acetoxyl groups.*

Each carbon–oxygen bond of the lactone group is considered in turn as a double bond, and the signs of the contributions made by the atoms in different octants are allocated according to the ketone octant rule [3] (IXa and IXb). If these diagrams are superimposed the signs of the contributions in some sectors cancel in varying degrees (sectors A, C, D, F) while in other sectors the contributions reinforce one another giving, on balance, a *positive* contribution in the back upper right sector (E), and a *negative* contribution in the back upper left sector (B), in accordance with empirical observation (Xa). It must be emphasised that in view of the uncertainties regarding the orbital treatment of the lactone group (see above), the boundaries of the sectors are provisional. Furthermore, even without this proviso, atoms near a sector boundary, *e.g.*, in sector F, near the E/F boundary, will have a small but significant contribution (cf. Xb).



(IXa)



(IXb)

It is necessary to consider two views of each molecule in order to predict the sign of its Cotton effect from the lactone sector rule. These are (*a*) the view along the bisectrix of the O–C–O angle (the usual octant projection; XI, XIIIa, etc.) and (*b*) the view of the molecule from above, projected on to the plane of the lactone ring (the new sector projection; XIb, XIIIb, etc.). The signs given are those of the *back upper sectors, i.e.*,

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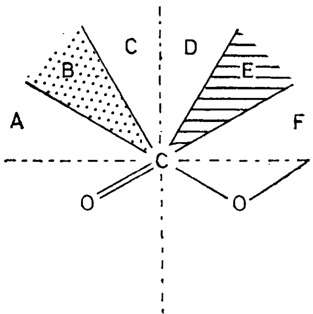
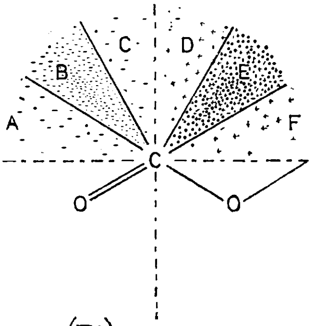
* Recently work has appeared by Okuda *et al.*[10] on the o.r.d. curves of some carbohydrate lactones. These authors have so far interpreted their results in terms of an octant rule (as for ketones) considering chiefly the effect of a hydroxyl group α to the lactone carbonyl.

[17] G. Snatzke, *J.*, 1965, 5002.



(Xa)



(Xb)

TABLE 1

O.r.d. curves of lactones: summary of Cotton effects at approx. 225 mμ

The prefix E indicates that the result is presented here for the enantiomer of the compound named and measured.

General type	Class of compound	Formula	Sign of lactone Cotton effect	
			Predicted from sector rule	Found
(I*t*)	1-*Oxa*-trans-*decalin*-2-*ones*			
	3-Oxo-4-oxa-5α-steroids	(XI)	+	+
	E 17-Oxo-17a-oxa-D-homo-steroids	(XII)	+	+
	E 5-Oxo-10-oxa-des-A-steroids	(XIII)	+	+
	12β-Hydroxysteroid-22-oic acid lactone	(XIV)	+	+
	E 7-Oxo-6-oxa-5α-steroids	(XV)	?	+
(I*c*)	1-*Oxa*-cis-*decalin*-2-*ones*			
	5-Oxo-10-oxa-des-A-9β-steroids	(XVI)	+	+
	E 3-Oxo-4-oxa-5β-steroids	(XVII)	+	+
	7-Oxo-6-oxa-5β-steroids	(XVIII)	?	+
(II*t*)	2-*Oxa*-trans-*decalin*-3-*ones*			
	3-Oxo-2-oxa-5α-steroids	(XIX)	—	—
	E 16-Oxo-17-oxa-D-homo-steroids	(XX)	—	—
(III*t*)	1-*Oxa*-trans-*hexahydroindan*-2-*ones*			
	6α-Hydroxy-5α-eudesman-13-oic acid lactone	(XXI)	+	+
	6α-Hydroxy-5β-eudesman-13-oic acid lactone	(XXII)	+	+
	E 8α-Hydroxy-5α-eudesman-13-oic acid lactone	(XXIII)	+	+
	E 6α-Hydroxy-2,3-seco-steroid-3-oic acid lactone	(XXIV)	+	+
	E 16-Oxo-17-oxa-steroids	(XXV)	+	+
	8α-Hydroxyiresan-11-oic acid lactone	(XXVI)	+	+
(III*c*)	1-*Oxa*-cis-*hexahydroindan*-2-*ones*			
	E 6β-Hydroxy-5α-eudesman-13-oic acid lactone	(XXVII)	+	+
	E 6β-Hydroxy-5β-eudesman-13-oic acid lactone	(XXVIII)	+ ? [a]	— [a]
	E Lactone from communic acid	(XXIX)	+	+
	E 8β-Hydroxyiresan-11-oic acid lactone	(XXX)	+	+
	8β-Hydroxy-5α-eudesman-13-oic acid lactone	(XXXI)	+	+
	6β-Hydroxy-2,3-seco-steroid-3-oic acid lactone	(XXXII)	+	+
(IV*t*)	2-*Oxa*-trans-*hexahydroindan*-1-*ones*			
	11-Hydroxyiresan-8aα-oic acid lactone	(XXXIII)	—	—
(IV*c*)	2-*Oxa*-cis-*hexahydroindan*-1-*ones*			
	E 11-Hydroxyiresan-8aβ-oic acid lactone	(XXXIV)	—	—
(V*c*)	2-*Oxa*-cis-*bicyclo*[3,3,0]*octan*-3-*ones*			
	E 16β-Hydroxysteroid-22-oic acid lactones	(XXXV)	+	+
	16α-Hydroxy-17-iso-steroid-22-oic acid lactone	(XXVI)	+	+
	17β-Hydroxysteroid-16β-ylacetic acid lactone	(XXXVII)	+	+
(VI*c*)	3-*Oxa*-cis-*bicyclo*[3,3,0]*octan*-2-*ones*			
	E 20β-Hydroxysteroid-16β-carboxylic acid lactone	(XXXVIII)	—	—
	20-Hydroxy-17-iso-steroid-16α-carboxylic acid lactone	(XXXIX)	—	—

[a] This anomaly may probably be ascribed to uncertainty about the conformation.

those above the plane of the lactone group. Since the lactone group lies in a true symmetry plane, the signs of the back lower sectors are necessarily opposite to those of the upper sectors. The signs of rotation contributions in the front sectors will presumably be opposite to those of back sectors but compounds with atoms in near sectors are not considered in the present survey. Along any radial line passing though the carboxyl carbon, the *quantitative* effect of a given substituent will decrease with increasing distance from the carboxyl group. However, the laws governing the magnitude of this effect are quite unknown.

For compounds in which the lactone ring is a terminal six-membered ring (not made rigid by additional constraints) this lactone ring could possibly take up a half-chair, half-boat, or intermediate conformation. Following the suggestions of Mathieson[16] we have based our drawings on the half-boat conformations in these cases—although the shape of the molecule with reference to the lactone chromophore is not very greatly altered when the half-chair form is used.

In this Paper the lactone sector rule is used to interpret the observed rotatory dispersion curves of an extensive range of simple but fairly rigid lactones of bicyclic and polycyclic types; the results are summarised in Table 1. It is hoped to extend the treatment to further lactones and to other related carboxyl types.

TABLE 2

O.r.d. of oxadecalones

The prefix E indicates that the result is presented here for the enantiomer of the compound named and measured.

No.	Compound	General formula	$10^{-2}[\varphi]$	λ (mμ)	Donor and reference
	1-*Oxa*-trans-*decalin*-2-*ones*				
1	17β-Hydroxy-17α-methyl-4-oxa-5α-œstran-3-one	(XI; R^1 = H)	+13 pk	227	D 2/1
2	4-Oxa-5α-cholestan-3-one	(XI; R^1 = Me)	+82 pk	227	A 2/2
3	17β-Hydroxy-4-oxa-5α-androstan-3-one	(XI; R^1 = Me)	+63 pk	226	A 2/2
4	17β-Hydroxy-17α-methyl-4-oxa-5α-androstan-3-one	(XI; R^1 = Me)	+47 pk	227	D 2/1
5	E 3β-Hydroxy-17a-oxa-D-homo-5α-androstan-17-one	(XII)	+35 *	225	B 2/3
6	E 3α-Hydroxy-17a-oxa-D-homo-5α-androstan-17-one	(XII)	+29 *	225	B 2/3
7	E 3α-Hydroxy-17a-oxa-D-homo-5β-androstan-17-one	(XII)	+30 *	225	B 2/3
8	E 3β-Acetoxy-17a-oxa-D-homo-5α-androstan-17-one	(XII)	+40 *	225	B 2/3
9	E 3β,16β-Diacetoxy-17a-oxa-D-homo-5α-androstan-17-one	(XII)	+60 *	225	P 2/4
10	E 10-Oxa-des-A-androstan-5,17-dione	(XIII)	+53 infl	227	T 2/5
11	3α-Acetoxy-12β-hydroxy-23,24-dinor-5β-cholane-22-carboxylic acid lactone	(XIV)	+26 *	225	F 2/6
12	3α,12β-Dihydroxy-23,24-dinor-5β-cholane-22-carboxylic acid 22 → 12β-lactone	(XIV)	+38 *	225	F 2/6
13	3β-Acetoxy-12β-hydroxy-20-iso-23,24-dinor-5β-cholane-22-carboxylic acid lactone	(XIV)	+52 *	225	F 2/6
14	E 6-Oxa-5α-cholestan-7-one	(XV)	+28!	233	A 2/7
	1-*Oxa*-cis-*decalin*-2-*ones*				
15	10-Oxa-des-A-9β-androstan-5,17-dione	(XVI)	+19 pk	224	T 2/5
16	E 4-Oxa-5β-cholestan-3-one	(XVII)	+14 pk	225	A 2/2
17	E 17β-Hydroxy-4-oxa-5β-androstan-3-one	(XVII)	+14 pk	230	A 2/2
18	E 17β-Hydroxy-17α-methyl-4-oxa-5β-androstan-3-one	(XVII)	+32 pk	225	D 2/1
19	6-Oxa-5β-cholestan-7-one	(XVIII)	+41 pk	233	A 2/7
20	17β-Hydroxy-6-oxa-5β-androstan-7-one	(XVIII)	+31 pk	233	A 2/7
	2-*Oxa*-trans-*decalin*-3-*ones*				
21	17β-Hydroxy-2-oxa-5α-androstan-3-one	(XIX)	−20 tr	219	C 2/8
22	17β-Hydroxy-17α-methyl-2-oxa-5α-androstan-3-one	(XIX)	−22!	227	C 2/8
23	E 4,4-Dimethyl-17-oxa-D-homo-5α-androstan-3,16-dione	(XX)	+6 tr	225	G 2/9

Solvent, methanol; pk = peak; infl = inflection; tr = trough; ! = lowest wavelength measured; * = value at 225 mμ, extremum not reached.

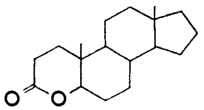
2/1, S. Szpilfogel, unpublished work. 2/2, N. W. Atwater and J. W. Ralls, *J. Amer. Chem. Soc.*, 1960, **82**, 2011. 2/3, N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1954, **76**, 2265. 2/4, S. Rakhit and M. Gut, *J. Org. Chem.*, 1964, **29**, 229. 2/5, C. Sih, *J. Amer. Chem. Soc.*, 1963, **85**, 2135. 2/6, T. R. Reichstein and M. Sorkin, *Helv. Chim. Acta*, 1944, **27**, 1631. 2/7, N. W. Atwater, *J. Amer. Chem. Soc.*, 1961, **83**, 3071. 2/8, R. Pappo and C. J. Jung, *Tetrahedron Letters*, 1962, 365. 2/9, J. S. E. Holker, unpublished work.

Note added in proof.—Since this Paper was submitted for publication, an important short Note has appeared by Dr. H. Wolf of Braunschweig (*Tetrahedron Letters*, 1965, 1075) on o.r.d. and circular dichromism curves of a series of lactones and lactams. Results for the compounds which have been run in both laboratories are generally in agreement—except for the compound (XII) (this Paper), for which further consideration is necessary.

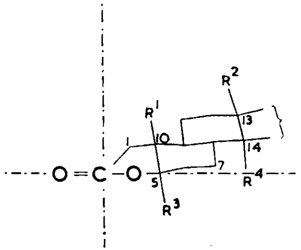
OXADECALONES

1-*Oxa*-trans-*decalin*-2-*ones*. For compounds of the general type (I*t*) the lactone sector rule predicts a positive Cotton effect at 227 mμ. This is in agreement with the empirical data for the compounds collected in Table 2.

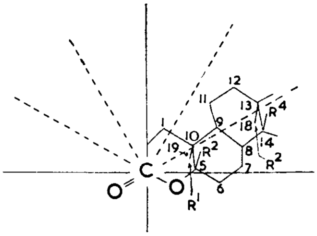
The simplest compound in this series is the steroid ring-A lactone derived from œstrane, 4-oxa-5α-œstran-3-one (with 17α-Me, 17β-OH) (general formula XI; $R^1 = R^3 = R^4 = H$, $R^2 = Me$), which has a positive Cotton effect, [ϕ] +1280 at the peak. This value may be compared with those for other 3-oxo-4-oxa-5α-steroids (XI; $R^3 = R^4 = H$, $R^1 = R^2 = Me$) having a methyl group at C-10 (androstane and cholestane series). As would be predicted, since the additional methyl group falls near to a positive sector, these compounds have an enhanced positive Cotton effect.*



(XI)

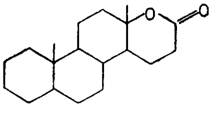


(XIa)



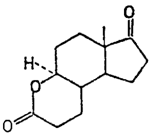
(XIb)

The 17-oxo-17a-oxa-D-homo-steroids (XII) may also be considered in this group. The actual compounds have negative o.r.d. curves (see Experimental section; Table 5) and therefore the *enantiomers* (which would be of the general type I*t*), would have positive curves (see Table 2). The octant and sector projections of these enantiomers are of the same type as those for the 3-oxo-4-oxa-5α-steroids (XIa and XIb; $R^1 = R^2 = H$, $R^3 = R^4 = Me$) and the positive curves are of comparable magnitude. These compounds show that, as with ketones, minor changes in substituents or stereochemistry at points remote from the chromophore have little effect on the o.r.d. curves.

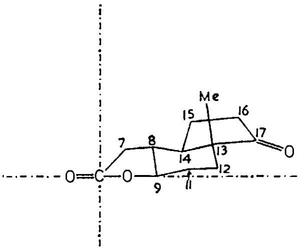


(XII)

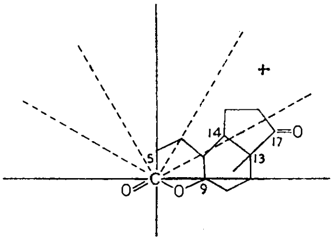
10-Oxa-des-A-androstane-5,17-dione (XIII) contains two optically active chromophoric groups (lactone and 17-ketone) and the corresponding Cotton effects can be observed in its rotatory dispersion curve. The actual compound (XIII) has a positive ketonic



(XIII)



(E XIII a)



(E XIII b)

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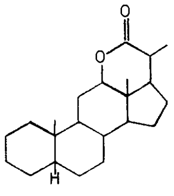
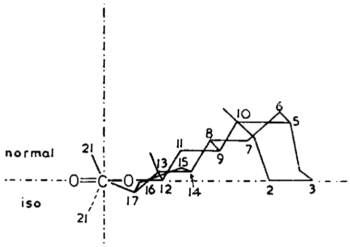
* The two projections for each type of compound (XIa and XIb, etc.) were drawn from Dreiding models.

Cotton effect for the 17-ketone, and a negative curve with an inflection at [ϕ] −5250 (227 mμ) in the region of the carboxyl absorption. The enantiomer of this compound (which is of the general group I*t*) would therefore have a positive o.r.d. curve at low wavelength with an inflection, corresponding to the carboxyl absorption, of [ϕ] +5250 (227 mμ). This is in accordance with the prediction of the sector rule [see (E XIIIa and E XIIIb)].

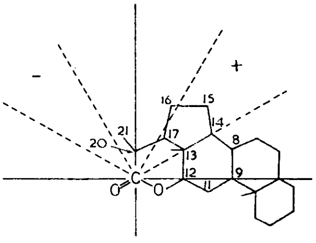
The steroid 22 $\longrightarrow$ 12β-lactones (XIV) may also be considered here; they differ from those compounds previously mentioned in carrying an additional bridge between C-4 and C-5 (decalin numbering); this bridge is in fact provided by C-15 and C-16 of the steroid D-ring. Of the three compounds examined, two 20-n-compounds, which differ only very slightly at a position remote from the lactone ring, have nearly identical curves, and the third, with the 20-iso * stereochemistry has a much larger Cotton effect (+5150 at 225 mμ as compared with +2580). This finding is in agreement with the sector rule which predicts an enchanced positive rotation for the compound with the 20-iso-arrangement, since the methyl group (C-21) then falls near to the lower positive sector close to the carboxyl group, whereas with the 20-normal stereochemistry, C-21 lies near to the upper negative sector [see (XIVa) and (XIVb)].



(XIV)

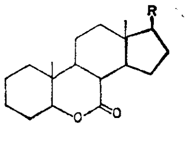


(XIVa)

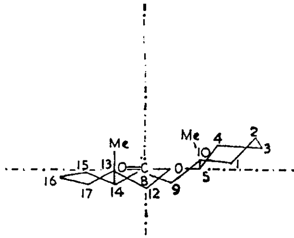


(XIV b)

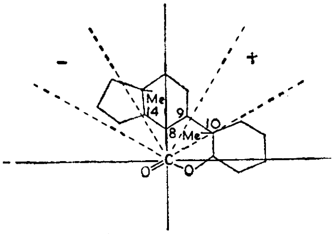
7-Oxo-6-oxa-5α-steroids (XV) also belong to this group, when considered as their enantiomers. The one example so far studied gives a medium positive Cotton effect. Compounds of the type (XV) have their lactone group in the *middle* ring of the polycyclic array; this complicates the treatment because significant atoms lie on both sides of the lactone group, and we report the data here for reference without attempting to interpret the sign of the curve.



(XV)



(E XVa)



(E XVb)

1-*Oxa*-cis-*decalin*-2-*ones*. The sector rule predicts positive Cotton effects for compounds of this general type (I*c*).

The simplest compound in the group, 10-oxa-des-A-9β-androstane-5,17-dione (XVI), contains two chromophores; a positive Cotton effect for the lactone is superimposed on a negative background, with a molecular rotation [ϕ] +1880 at the peak.

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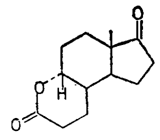
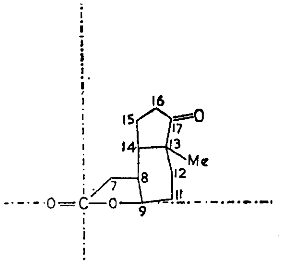
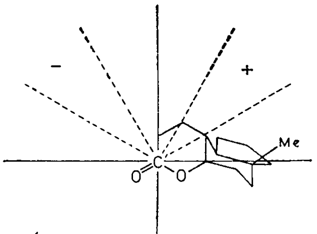
* The C-20-normal configuration is that with $20\alpha_F$H; the C-20-iso-configuration has $20\beta_F$H, as defined in I.U.P.A.C. *Information Bulletin*, No. 11, October 1960, p. 54.



(XVI)

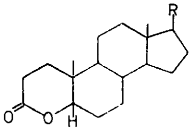


(XVIa)

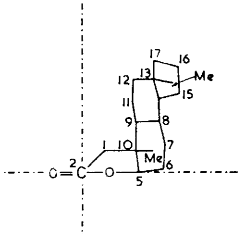


(XVIb)

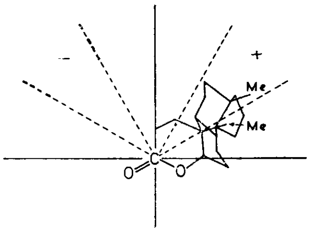
The most important members of this group are the 3-oxo-4-oxa-5β-steroids (XVII), considered here as their enantiomers. All the enantiomers have positive Cotton effects in accordance with the sector rule prediction but the molecular rotations at the peak are considerably smaller than for the 5α-analogues [+1250, +1400, and +3240 for enantio-



(XVII)

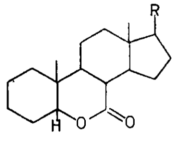


(E XVIIa)

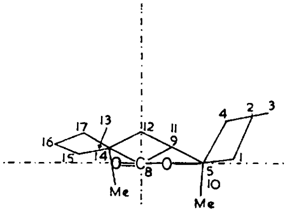


(E XVIIb)

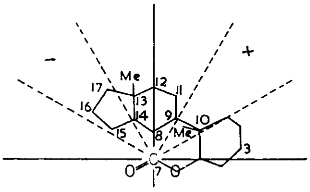
5β-compounds as compared with +5500, +6250, and +4670 for the similar 5α-structures (XI)]. A comparison of the projections (XIa) and (E XVIIa), show that for the 5α-compounds (XIa) the atoms of the C and D rings are separated from the chromophore by a large horizontal distance, whereas for the 5β-compounds (E XVIIa), the C and D rings are at a similar vertical distance from the chromophore. The observed difference in magnitude of the Cotton effects for these two types suggests that the effect of a remote substituent decreases more rapidly in a vertical direction than in the horizontal.



(XVIII)



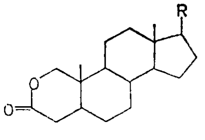
(XVIIIa)



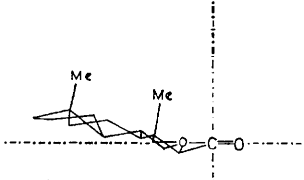
(XVIIIb)

7-Oxo-6-oxa-5β-steroids (XVIII) also fall in this group. Here the sector projections are complicated by the fact that the lactone group is in a middle ring; positive Cotton effects are observed.

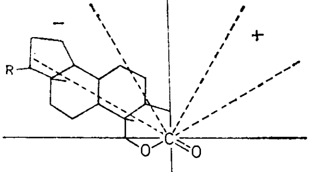
2-*Oxa*-trans-*decalin*-3-*ones*. The sector rule predicts a negative Cotton effect for the



(XIX)

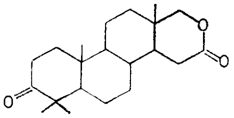


(XIXa)

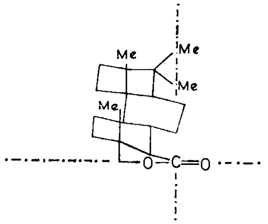


(XIXb)

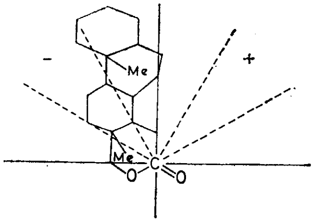
general type (II*t*) (Table 2), and this prediction is confirmed for the few examples available. The 3-oxo-2-oxa-5α-steroids (XIX) have troughs, $[\phi]$ −1960 and −2160, respectively. The enantiomer of 4,4-dimethyl-17-oxa-D-homo-5α-androstane-5,16-dione (E XX), also has a negative lactone Cotton effect superimposed on a strong positive background; first extremum $[\phi]$ +630 (trough).



(XX)



(E XX a)

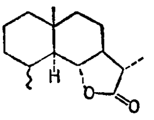


(E XX b)

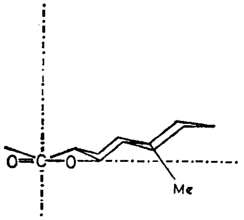
Oxahexahydroindanones

1-*Oxa*-trans-*hexahydroindan*-2-*ones*. Lactones based on the hexahydroindane skeleton have a five-membered lactone ring fused to a six-membered carbocyclic ring. This skeleton is very common particularly among sesquiterpene and steroid derivatives (see Table 3).

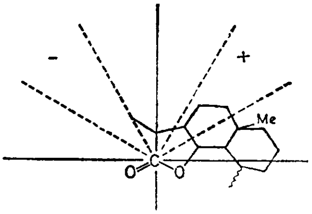
According to the sector rule, the 1-oxa-*trans*-hexahydroindan-2-ones (III*t*) should have positive Cotton effects at about 225 mμ, and this is found to be the case. One common structure of this general type is represented by the eudesmane 13 → 6-lactones with (5α,6β-H) stereochemistry (XXI); these have positive Cotton effects with $[\phi]$ about +2500 at the first extremum. The corresponding compounds with 5β-H at the ring junction (XXII) have considerably smaller values, +840, +920, and −80, respectively, at the peak. [The distinction between (XXII) and (XXI) is, for our present purposes, only a secondary stereochemical one; C-5 is at the junction of the third with the second ring, *not* between the second and the lactone ring, which is the main stereochemical feature considered here.]



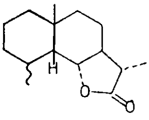
(XXI)



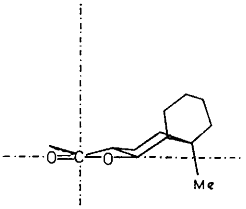
(XXI a)



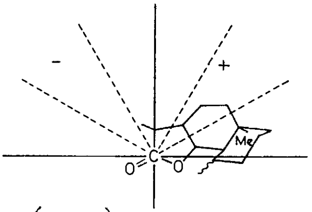
(XXI b)



(XXII)



(XXII a)



(XXII b)

Eudesman 13 → 8-lactones (with 5α,8β-H) (XXIII) (as their enantiomers) are closely similar to the corresponding 13 → 6-compounds; the Cotton effects are also positive and similar in magnitude to those for type (XXI).

TABLE 3

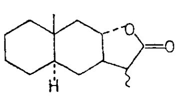
O.r.d. of hexahydro-oxaindanones

The prefix E indicates that the result is presented here for the enantiomer of the compound named and measured.

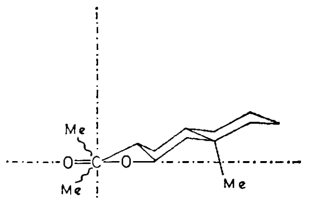
No.	Compound	General formula	$10^{-2}[\phi]$	λ (mμ)	Donor and reference
	1-*Oxa*-trans-*hexahydroindan*-2-*ones*				
24	4,5α(H),6,11β(H)-Eudesman-6,13-olide	(XXI)	+35 pk	230	M 3/1
25	4,5α(H),6,11β(H)-Eudesm-2-en-6,13-olide	(XXI)	+25!	260	M 3/1
26	3α-Acetoxy-4,5α(H),6,11β(H)-eudesman-6,13-olide	(XXI)	+23 pk	231	M 3/1
27	5α(H),4,6,11β(H)-Eudesman-6,13-olide	(XXI)	+23 pk	230	M 3/1
28	3α-Acetoxy-5α(H),4,6,11β(H)-eudesman-6,13-olide	(XXI)	+18!	236	M 3/1
29	3β-Acetoxy-5α(H),4,6,11β(H)-eudesman-6,13-olide	(XXI)	+28 pk	234	M 3/1
30	3α-Chloro-5α(H),4,6,11β(H)-eudesman-6,13-olide	(XXI)	+12 pk	233	M 3/1
31	3β-Acetoxy-4α(H),5,6,11β(H)-eudesman-6,13-olide	(XXII)	+53 pk	227	M 3/1
32	4,5,6,11β(H)-Eudesman-6,13-olide	(XXII)	− 1 pk	238	M 3/1
33	3α-Hydroxy-4,5,6,11β(H)-eudesman-6,13-olide	(XXII)	+ 9 pk	239	M 3/1
34	3β-Hydroxy-4,5,6,11β(H)-eudesman-6,13-olide	(XXII)	+ 8 pk	233	M 3/1
35	3β-Acetoxy-4,5,6,11β(H)-eudesman-6,13-olide	(XXII)	+52 pk	230	M 3/1
36 E	4,5,8,11β(H)-Eudesman-8,13-olide	(XXIII)	+28 pk	233	M 3/2
37 E	1ξ-Acetoxy-4,5,11α(H),8β(H)-eudesman-8,13-olide	(XXIII)	+25 inf	225	M 3/3
38 E	6α-Hydroxy-2,3-seco-5α-cholestane-2,3-dicarboxylic acid 3 → 6α-lactone methyl ester	(XXIV)	+34 pk	227	N 3/4
39 E	6α-Hydroxy-2,3-seco-5α-cholestane-2,3-dicarboyxlic acid 3 → 6α-lactone	(XXIV)	+33 pk	226	N 3/4
40 E	17-Oxa-5α-androstane-3,16-dione	(XXV)	+57 pk	227	P 2/4
41 E	17-Oxa-5α-androstane-3,16-dione 3-ethylene ketal	(XXV)	+45 pk	227	P 2/4
42 E	3β-Acetoxy-17-oxa-5α-androstan-16-one	(XXV)	+53 pk	227	P 2/4
43	8α-Hydroxyiresane-11-carboxylic acid lactone	(XXVI)	+51 pk	228	O 3/5
	1-*Oxa*-cis-*hexahydroindan*-2-*ones*				
44 E	4,5,6,11α(H)-Eudesm-2-ene-6,13-olide	(XXVII)	+ 3!	244	M 3/6
45 E	3α-Hydroxy-4,5,6,11α(H)-eudesman-6,13,olide	(XXVII)	+25 pk	232	M 3/6
46 E	3β-Hydroxy-5,6,11α(H),4β(H)-eudesman-6,13-olide	(XXVII)	+14 pk	233	M
47 E	3β-Acetoxy-5,6,11α(H),4β(H)-eudesman-6,13-olide	(XXVII)	+29 pk	230	M
48	(+)-α-Desmotroposantonin	(XXVII)	+62 pk	242	M 3/7
49	(+)-β-Desmotroposantonin	(XXVII)	+28 pk	240	M 3/7
50 E	3α-Hydroxy-4,6,11α(H),5β(H)-eudesman-6,13-olide	(XXVIII)	−18 tr	218	M 3/6
51 E	Methyl ester of C_{15} lactone from communic acid (8β → 12-lactone, steroid numbering)	(XXIX)	+ 4 pk	236	Q 3/8
52 E	8β-Hydroxy-(8α-methyl)-iresane-11-carboxylic acid lactone	(XXX)	+15 *	225	O 3/5
53	Tetrahydroivalin [2α-hydroxy-4,5,8α(H),11ξ(H)-eudesman-8,13-olide]	(XXXI)	+ 3 pk	235	R 3/9
54	Epitetrahydroivalin [2α-hydroxy-4,5,8α(H),11ξ(H)-eudesman-8,13-olide]	(XXXI)	+10 pk	232	R 3/9
55	6β-Hydroxy-2,3-seco-5α-cholestane-2,3-dicarboxylic acid 3 → 6β-lactone methyl ester	(XXXII)	+49 infl	227	N 3/4
	2-*Oxa*-trans-*hexahydroindan*-1-*ones*				
56	Isodihydroconfertifolin [11-hydroxyiresane-8aα-carboxylic acid lactone]	(XXXIII)	−47 tr	227	S 3/10
	2-*Oxa*-cis-*hexahydroindan*-1-*ones*				
57 E	Dihydroconfertifolin [11-hydroxyiresane-8aβ-carboxylic acid lactone]	(XXXIV)	−20 tr	230	S 3/10

Solvent, methanol; pk = peak; infl = inflection; tr = trough; ! = lowest wavelength measured; * = value at 225 mμ, extremum not reached.

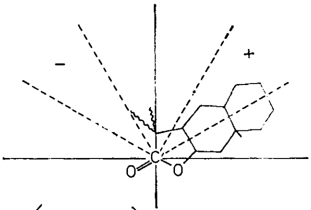
3/1, W. Cocker and T. B. H. McMurry, *J.*, 1956, 4549. 3/2, W. Cocker, L. O. Hopkins, T. B. H. McMurry, and M. A. Nisbit, *J.*, 1961, 4721. 3/3, N. M. Chopra, W. Cocker, J. T. Edward, T. B. H. McMurry, and E. R. Stuart, *J.*, 1956, 1828. 3/4, C. W. Shoppee, G. H. R. Summers, *J.*, 1952, 3374. 3/5, M. Hinder and M. Stoll, *Helv. Chim. Acta*, 1953, **36**, 1995. 3/6, W. Cocker, M. Gobinsingh, T. B. H. McMurry, and M. A. Nisbit, *J.*, 1962, 1432. 3/7, N. M. Chopra, W. Cocker, and J. T. Edward, *Chem. and Ind.*, 1955, 41. 3/8, V. P. Arya, M. Erdtman, and T. Kubota, *Tetrahedron*, 1961, **16**, 255. 3/9, W. Herz and G. Högenauer, *J. Org. Chem.*, 1962, **27**, 905. 3/10, H. H. Appel, J. D. Connolly, K. H. Overton, and R. P. M. Bond, *J.*, 1960, 4685.



(XXIII)



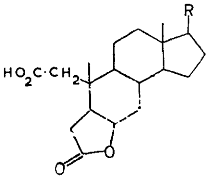
(E XXIII a)



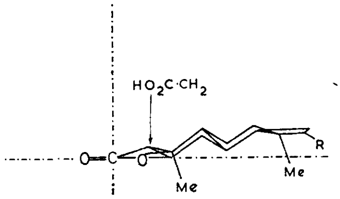
(E XXIII b)

Two types of steroid lactone belong to the general class (III*t*), 2,3-seco-steroid $6\alpha \longrightarrow 3$-lactones (XXIV) * and 16-oxo-17-oxa-steroids (XXV), both as enantiomers. In accordance with predictions, positive curves are observed for both types.

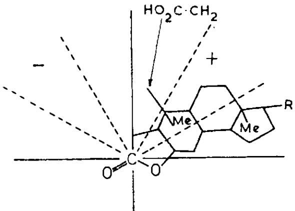
A lactone (XXVI) derived from bicyclohomofarnesol fits the general pattern of the group and is also included here.



(XXIV)

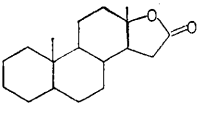


(E XXIV a)

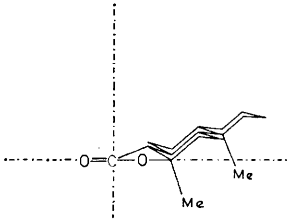


(E XXIV b)

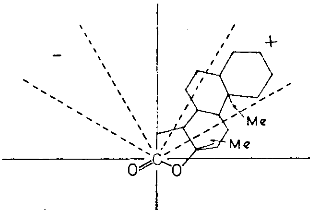
These results illustrate the effect of additional rings remote from the chromophore, on the magnitude of the Cotton effect (cf. general treatment of *trans*-decalones [13]). Compounds of the general types (XXI), (E XXIII), (E XXIV), (E XXV), and (XXVI) all have a common arrangement of rings A and B, with either one or two other remote rings from the possibilities shown in the Figure, which is a generalised sector projection for this class. [In the Figure, the letters A—D simply indicate the order in which the rings are joined together, A (the lactone ring) to B, B to C, and C to D. This designation applies only to the Figure and to the following paragraph, and has no reference to the convention



(XXV)

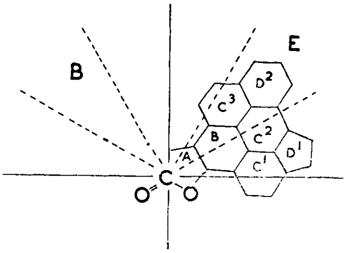


(E XXV a)



(E XXV b)

General formula	Rings	[ϕ] 10^{-2} at peak
(XXI)	A, B, C^1	+28
(E XXIII)	A, B, C^2	+25
(XXVI)	A, B, C^3	+50
(E XXIV)	A, B, C^2, D^1	+33
(E XXV)	A, B, C^3, D^2	+55
Contribution of the fourth ring		
(E XXV)—(XXVI)		+5
(E XXIV—(E XXIII)		+8



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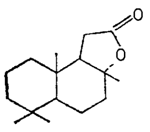
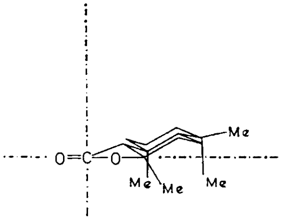
* It may be noted that the 2,3-seco-compounds of type (XXIV) carry an ester group, CH$_2$·CO$_2$Me, in addition to the lactone. However, evidence from other series indicates that a group of this kind (an acetic ester side-chain) has only a slight Cotton effect.

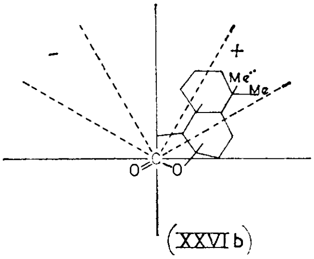
generally used elsewhere for any particular group of natural products]. The eudesmane 13 ⟶ 6-lactones (XXI) comprise the rings A, B, and C^1 ($[\phi]$, +2000 to +2800 at the peak) and the enantiomers (E XXIII) of the 13 ⟶ 8-lactones, with rings A, B, and C^2 have similar peak values. By contrast, the lactone (XXVI) derived from bicyclohomofarnesol with rings A, B, and C^3, has a significantly higher peak $[\phi]$, +5100. This is in accordance with the prediction of the sector rule, since C^3 falls within the sector (E) of high positive contribution (XXVIb) but C^2 is only partially within this sector, and C^1 is completely outside it.



(XXVI)



(XXVIa)

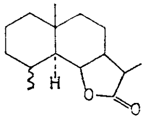


(XXVIb)

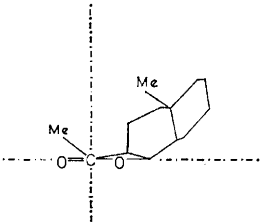
A similar situation arises with the tetracyclic compounds. Lactones of type (E XXV) (rings A, B, C^3, and D^2) in which C^3 and D^2 fall within the strongly positive sector, have much higher peaks ($[\phi]$, *ca.* +5000) than type (E XXIV) (rings A, B, C^2, and D^1) (peaks *ca.* +3000), in which rings C^2 and D^1 fall largely outside the positive sector.

A comparison of the peak values for compounds of types (XXV) and (XXVI) and of types (XXIV) and (XXIII) shows that the additional fourth ring (D), makes only a comparatively small contribution (less than 1000°) to the total rotation. This is in keeping with the distance of the fourth ring from the chromophore.

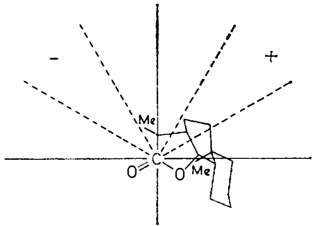
*1-Oxa-*cis*-hexahydroindan-2-ones.* The sector rule again predicts positive Cotton effects for type (III*c*) and the compounds examined give results in accordance with this prediction (see Table 3).



(XXVII)

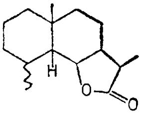


(E XXVIIa)

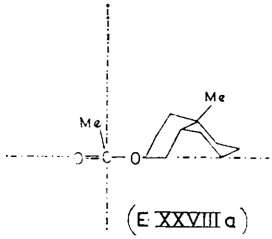


(E XXVIIb)

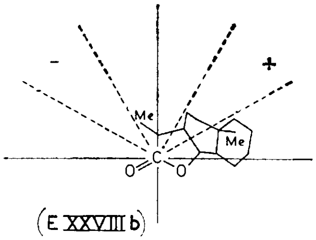
The enantiomers of eudesmane 13 ⟶ 6-lactones (with 5α,6α-H) (XXVII) give positive Cotton effects with values of about +2000 at the peak. The desmotroposantonins are derived from the eudesmane skeleton in which ring A is aromatic. They may be compared with type (XXVII) and also have positive Cotton effects. The only 13 ⟶ 6-lactone with 5β-H (*i.e.*, with a *cis*-decalin skeleton) (XXVIII) which has been examined gave a negative



(XXVIII)

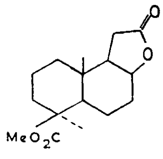


(E XXVIIIa)

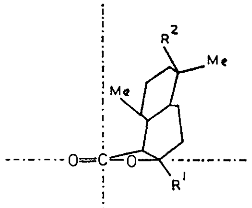


(E XXVIIIb)

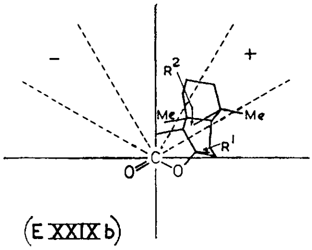
Cotton effect (trough [ϕ], −1840). If the *cis*-decalin system takes up the two-chair conformation shown in (E XXVIIIa), a positive Cotton effect would be expected. (The alternative two-chair conformation, although possible for such a compound, is highly unlikely because of non-bonded interactions.) The anomalous o.r.d. result presumably indicates a distorted decalin conformation, although we cannot say of what type this is. Other sesquiterpene lactones derived from communic acid (XXIX) and from ivalin (XXXI) have small positive Cotton effects.



(XXIX)

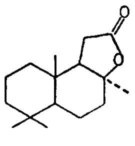


(E XXIXa)



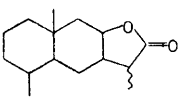
(E XXIXb)

2,3-Seco-steroids with 3 ⟶ 6β-lactone rings (XXXII) and the enantiomer of the isolactone from bicyclohomofarnesine (XXX) also belong to this class and give positive Cotton effects (larger than those of the eudesmane derivatives.)

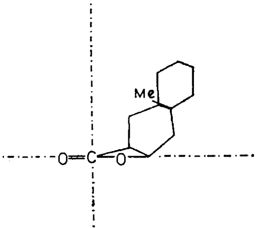


(XXX)

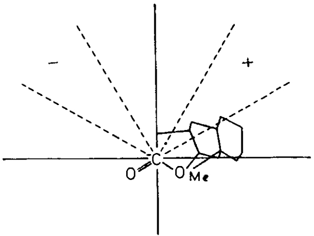
2-*Oxa*-trans- *and* -cis-*hexahydroindan*-1-*ones*. Compounds of types (IV*t*) and (IV*c*) in which the carbonyl group of the lactone is adjacent to the ring junction are comparatively rare (see Table 3), and only one example of each stereochemical type has been examined. Isodihydroconfertifolin (XXXIII) (*trans*) and the enantiomer (E XXXIV) of dihydroconfertifolin (*cis*) both give negative Cotton effects in accordance with prediction.



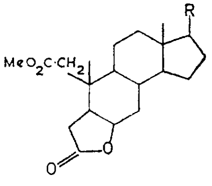
(XXXI)



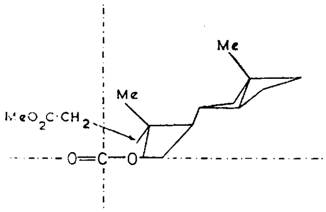
(XXXIa)



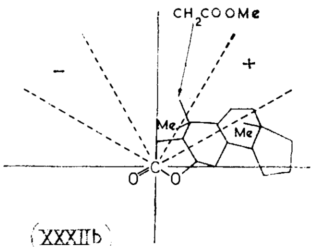
(XXXIb)



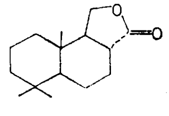
(XXXII)



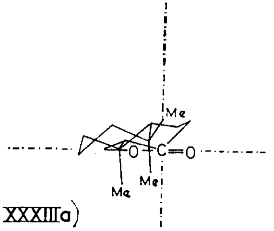
(XXXIIa)



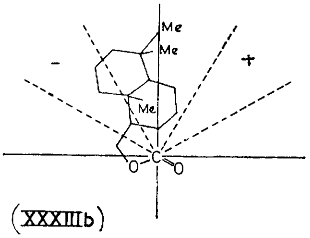
(XXXIIb)



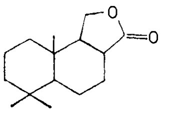
(XXXIII)



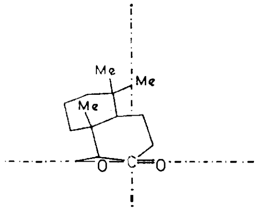
(XXXIIIa)



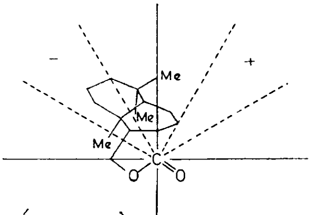
(XXXIIIb)



(XXXIV)



(E XXXIVa)



(E XXXIVb)

OXABICYCLO[3,3,0]OCTANONES

2-Oxa-cis-*bicyclo*[3,3,0]*octan*-3-*ones*. Lactones derived from the bicyclo[3,3,0]octane skeleton have a five-membered lactone ring fused to a five-membered carbocyclic ring. This system is stable when the two rings are *cis*-fused.

For lactones of the general type (V*c*), the sector rule predicts positive Cotton effects and this prediction is borne out by the three groups of compounds available (see Table 4)

TABLE 4

O.r.d. of oxabicyclo[3,3,0]octanones

The prefix E indicates that the result is presented here for the enantiomer of the compound named and measured.

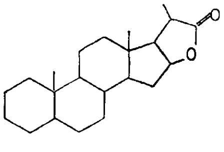
No.	Compound	General formula	$10^{-2}[\phi]$	λ (mμ)	Donor and reference
	2-Oxa-cis-*bicyclo*[3,3,0]*octan*-3-*ones*				
58	E 16β-Hydroxy-23,24-dinor-5α-cholane-22-carboxylic acid lactone	(XXXV)	+42 pk	227	4/1
59	E 3β-Acetoxy-16β-hydroxy-23,24-dinor-5α-cholane-22-carboxylic acid lactone	(XXXV)	+33 *	225	K 4/2
60	E 3β-Acetoxy-16β-hydroxy-23,24-dinor-20-iso-5α-cholane-22-carboxylic acid lactone	(XXXV)	+40 pk	227	K 4/2
61	E 2α,3β,15β,16β-Tetrahydroxy-23,24-dinor-5α-cholane-22-carboxylic acid 22 ⟶ 16β-lactone	(XXXV)	+34 *	225	H 4/3
62	3β-Acetoxy-16α-hydroxy-23,24-dinor-5α,17α-cholane-22-carboxylic acid lactone	(XXXVI)	+27 pk	227	K 4/2
63	3β,17β-Dihydroxyandrost-5-en-16β-ylacetic acid lactone	(XXXVII)	+11 pk	226	E 4/4
64	3β,17β-Dihydroxy-5α-androstan-16β-ylacetic acid lactone	(XXXVII)	+22 pk	230	E 4/4
	3-Oxa-cis-*bicyclo*[3,3,0]*octan*-2-*ones*				
65	E 3β-Acetoxy-20β-hydroxypregn-5-ene-16β-carboxylic acid lactone	(XXXVIII)	−9 tr	231	L 4/5
66	E 3β,20β-Dihydroxypregn-5-ene-16β-carboxylic acid 16β ⟶ 20β-lactone	(XXXVIII)	−15 tr	231	L 4/5
67	E 3β-Acetoxy-20β-hydroxy-5α-pregnane-16β-carboxylic acid lactone	(XXXVIII)	−34 tr	230	L 4/5
68	E 3β,20β-Dihydroxy-5α-pregnane-16β-carboxylic acid 16β ⟶ 20β-lactone	(XXXVIII)	−34 tr	230	L 4/5
69	3β-Acetoxy-20-hydroxy-17α-pregn-5-ene-16α-carboxylic acid lactone	(XXXIX)	−98 *	225	L 4/5
70	3β-Acetoxy-20-hydroxy-5α,17α-pregnane-16α-carboxylic acid lactone	(XXXIX)	−29 infl	228	L 4/5

Solvent, methanol; pk = peak; infl = inflection; tr = trough; ! = lowest wavelength measured; * = value at 225 mμ, extremum not reached.

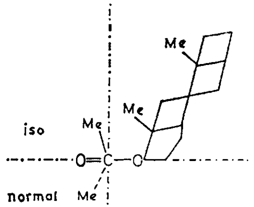
4/1, J. C. Danilewicz and W. Klyne, *J.*, 1965, 1306. 4/2, Y. Mazur, N. Danieli, and F. Sondheimer, *J. Amer. Chem. Soc.*, 1960, **82**, 5889. 4/3, D. L. Klass, M. Fieser, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1955, **77**, 3829. 4/4, P. Kurath and W. Cole, *J. Org. Chem.*, 1961, **26**, 1939. 4/5, P. Crabbé, L. M. Guerrero, J. Romo, and F. Sanchez-Viesca, *Tetrahedron*, 1963, **19**, 25.

dinorcholane 22 ⟶ 16β-lactones (XXXV) (as the enantiomers), 17-isodinorcholane, 22 ⟶ 16α-lactones (XXXVI), and androstan-16β-ylacetic acid lactones (XXXVII).

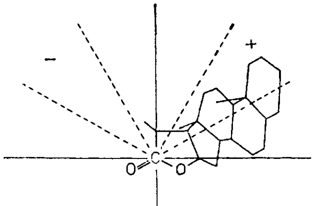
3-Oxa-cis-*bicyclo*[3,3,0]*octan*-2-*ones*. Two groups of compounds have been examined of the general type (VI*c*), 20β-hydroxypregnane-16β-carboxylic acid 16 ⟶ 20-lactones (XXXVIII) (as the enantiomers), and 20-hydroxy-17α-pregnane-16α-carboxylic acid 16 ⟶ 20-lactones (XXXIX). Both have negative Cotton effects in accordance with the predictions of the sector rule.



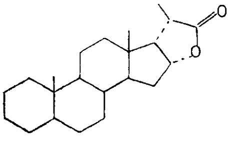
(XXXV)



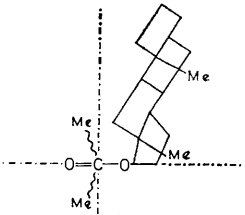
(E XXXVa)



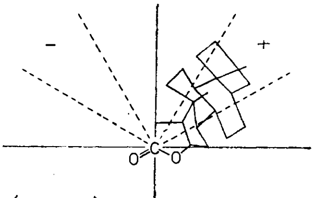
(EXXXVb)



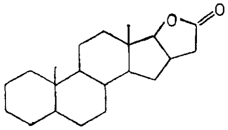
(XXXVI)



(XXXVIa)



(XXXVIb)



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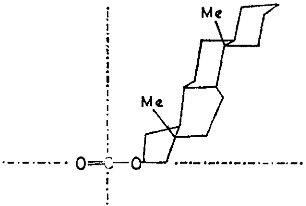

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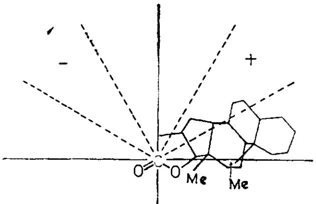

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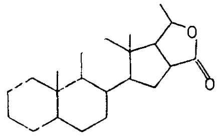

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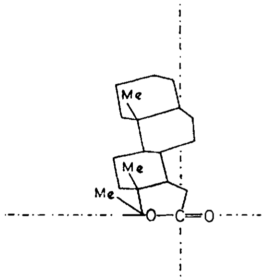
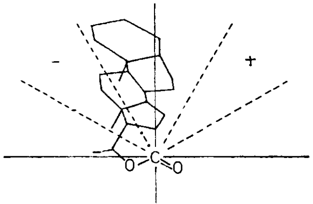
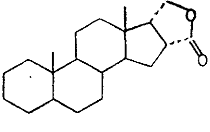


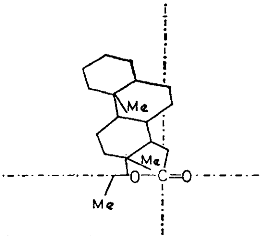
(E XXXVIII a)



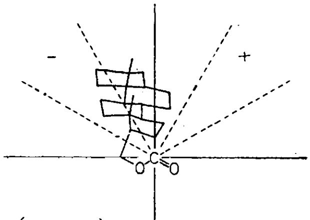
(E XXXVIII b)



(XXXIX)



(XXXIXa)



(XXXIXb)

Conclusion

The data in this Paper provide at least an extensive series of facts with the help of which useful empirical correlations of stereochemistry can be made. This is quite independent of any theoretical or semi-theoretical treatment of the problem; it may be compared with the extensive work done by Djerassi and his colleagues on ketones during the period 1954—1958, before the octant rule [3] was developed.

The problems which face us in seeking a theoretical treatment of the lactone and carboxyl groups are clearly much more complex than those for the simple ketonic carbonyl group. The positions and shapes of the nodal planes which define the sectors are as yet unknown. In these circumstances, the collection of data on rotatory dispersion curves (and, subsequently, circular dichroism curves) of lactones and carboxylic acids may help to serve as a probe for exploring the orbital character of the carboxyl and related groups. We hope that fundamental studies from a theoretical viewpoint, and studies by other physical techniques, will in due course enable us to be more precise. However, the sector rule suggested for the treatment of lactones appears to offer a preliminary working hypothesis.

In subsequent Papers, we hope to deal with other types of lactones, and then to go on to apply our knowledge of the rotatory dispersion behaviour of the $O{-}\dot{C}{=}O$ group thus gained, to the study of compounds where this group is not rigidly fixed, *i.e.*, in carboxylic acids themselves, in esters, amides, peptides, etc. Empirical work on these groups is proceeding at the present time.[9, 11, 18]

EXPERIMENTAL

Optical rotatory dispersion curves were measured on the Bellingham and Stanley/Bendix Ericsson autmatic recording spectropolarimeter " Polarmatic 62," modified as described in *J.*, 1965, 294. Solvent, methanol; l = 0·1 dm.; *t* = 20—25°; *c* = 1 mg./ml. or less.

TABLE 5

Experimental data

No.	General formula	[ϕ] at 400 mμ	[ϕ] at 300 mμ	[ϕ] at first extremum		[ϕ] at lowest wavelength		Donor and reference
	1-*Oxa*-trans-*decalin*-2-*ones*							
1	(XI)	+135	+285	+1280 pk	227	+1255!	220	D 2/1
2	(XI)	+900	+2090	+8150 pk	227	+4800!	208	A 2/2
3	(XI)	+565	+1380	+6250 pk	226	+3520!	211	A 2/2
4	(XI)	+205	+490	+4670 pk	227	+4200!	220	D 2/1
5	(XII)	−220	−555	−3460 *	225	−4670!	216	B 2/3
6	(XII)	−230	−400	−2880 *	225	−4760!	211	B 2/3
7	(XII)	−250	−415	−3010 *	225	−4150!	216	B 2/3
8	(XII)	−250	−605	−4010 *	225	−5150!	217	B 2/3
9	(XII)	−385	−870	−6000 *	225	−8700!	214	P 2/4
10	(XIII)	+540	†	−5250 infl	227	−6350!	212	T 2/5
11	(XIV)	+525	+975	+2580 *	225	+6800!	208	F 2/6
12	(XIV)	+520	+955	+3760 *	225	+6900!	213	F 2/6
13	(XIV)	+705	+1380	+5150 *	225	+9940!	206	F 2/6
14	(XV)	+310	−630	—		−2840!	233	A 2/7
	1-*Oxa*-cis-*decalin*-2-*ones*							
15	(XVI)	+765	‡	+1880 pk	224	−755!	210	T 2/5
16	(XVII)	+200	+335	−1400 tr	225	−800!	212	A 2/2
17	(XVII)	−110	−325	−1400 tr	230	−885!	218	A 2/2
18	(XVII)	−70	−260	−3240 tr	225	−2530!	213	D 2/1
19	(XVIII)	−100	−100	+4050 pk	233	−9800!	211	A 2/7
20	(XVIII)	−115	−275	+3120 pk	233	−8650!	214	A 2/7
	2-*Oxa*-trans-*decalin*-3-*ones*							
21	(XIX)	−30	−90	−1960 tr	219	−1910!	208	C 2/8
22	(XIX)	−150	−380	—		−2160!	227	C 2/8
23	(XX)	−440	−480	−630 pk	225	−1270!	217	G 2/9

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[18] Work on cyclic peptides with V. Prelog, cf. H. Gerlach, J. A. Owtschinnikow, and V. Prelog, *Helv. Chim. Acta*, 1964, **47**, 2294; and on alanyl peptides with G. W. Kenner, unpublished work.

TABLE 5 (*Continued*)

No.	General formula	[ϕ] at 400 mμ	[ϕ] at 300 mμ	[ϕ] at first extremum		[ϕ] at lowest wavelength		Donor and reference
	1-*Oxa*-trans-*hexahydroindan*-2-*ones*							
24	(XXI)	+300	+700	+3450 pk	230	+1950!	216	M 3/1
25	(XXI)	+325	+1300	—		+2510!	260	M 3/1
26	(XXI)	+145	+330	+2340 pk	231	−1390!	212	M 3/1
27	(XXI)	+145	+395	+2250 pk	230	+625!	215	M 3/1
28	(XXI)	−190	−200	—		+1760!	236	M 3/1
29	(XXI)	+395	+800	+2760 pk	234	+1920!	218	M 3/1
30	(XXI)	−115	−160	+1180 pk	233	−2460!	206	M 3/1
31	(XXII)	+585	+1380	+5300 pk	227	+3850!	213	M 3/1
32	(XXII)	−100	−210	−80 pk	238	−195!	206	M 3/1
33	(XXII)	+240	+495	+920 pk	239	+520!	222	M 3/1
34	(XXII)	+130	+230	+835 pk	233	+295!	222	M 3/1
35	(XXII)	+550	+1260	+5200 pk	230	+3940!	218	M 3/1
36	(XXIII)	−60	−220	−2820 tr	233	+1550!	208	M 3/2
37	(XXIII)	−520	−1045	−2450 infl	225	−10,400!	204	M 3/3
38	(XXIV)	−140	−405	−3360 tr	227	−670!	207	N 3/4
39	(XXIV)	−190	−465	−3280 tr	226	−1070!	208	N 3/4
40	(XXV)	+80	§	−5700 tr	227	−5480!	218	P 2/4
41	(XXV)	−410	−960	−4450 tr	227	−3700!	217	P 2/4
42	(XXV)	−445	−1050	−5290 tr	227	−4650!	216	P 2/4
43	(XXVI)	+30	+900	+5100 pk	228	+3800!	213	O 3/5
	1-*Oxa*-cis-*hexahydroindan*-2-*ones*							
44	(XXVII)	−190	−540	—		−300!	244	M 3/6
45	(XXVII)	−485	−960	−2450 tr	232	−2340!	214	M 3/6
46	(XXVII)	−310	−675	−1440 tr	233	−895!	208	M
47	(XXVII)	−360	−825	−2880 tr	230	−1130!	213	M
48	(XXVII)	+380	+430	+6220 pk	242	+3500!	233	M 3/7
49	(XXVII)	+520	¶	+2800 pk	240	+360!	229	M 3/7
50	(XXVIII)	+160	+320	+1840 pk	218	0!	209	M 3/6
51	(XXIX)	−10	−160	−350 tr	236	−140!	221	Q 3/8
52	(XXX)	−225	−450	−1540 *	225	−4970!	205	O 3/5
53	(XXXI)	+60	+60	+290 pk	235	−508!	219	R 3/9
54	(XXXI)	+240	+420	+1035 pk	232	+447!	217	R 3/9
55	(XXXII)	+670	+1610	+4860 infl	227	+6170!	205	N 3/4
	2-*Oxa*-trans-*hexahydroindan*-1-*ones*							
56	(XXXIII)	−110	−175	−4680 tr	227	+9450!	205	S 3/10
	2-*Oxa*-cis-*hexahydroindan*-1-*ones*							
57	(XXXIV)	−20	−65	+2000 pk	230	−4580!	212	S 3/10
	2-*Oxa*-cis-*bicyclo*[3,3,0]*octan*-3-*ones*							
58	(XXXV)	−490	−1265	−4200 tr	227	−3940!	220	4/1
59	(XXXV)	−515	−940	−3300 *	225	−5010!	205	K 4/2
60	(XXXV)	−300	−500	−4000 tr	227	0!	213	K 4/2
61	(XXXV)	−460	−1155	−3360 *	225	−3660!	213	H 4/3
62	(XXXVI)	+225	+510	+2660 pk	227	+2100!	219	K 4/2
63	(XXXVII)	−150	−230	+1050 pk	226	+750!	217	E 4/4
64	(XXXVII)	+185	+410	+2200 pk	230	−1260!	208	E 4/4
	3-*Oxa*-cis-*bicyclo*[3,3,0]*octan*-2-*ones*							
65	(XXXVIII)	−280	−585	+915 pk	231	−1180!	219	L 4/5
66	(XXXVIII)	−170	−420	+1450 pk	231	−570!	218	L 4/5
67	(XXXVIII)	+155	+340	+3360 pk	230	−220!	213	L 4/5
68	(XXXVIII)	+220	+390	+3380 pk	230	+220!	214	L 4/5
69	(XXXIX)	−1190	−2590	−9800 *	225	−10,650!	216	L 4/5
70	(XXXIX)	−320	−905	−2915 infl	228	−3700!	210	L 4/5

The E convention for representing enantiomers is not used. Solvent, methanol; pk = peak; infl = inflection; tr = trough; ! = lowest wavelength measured; * = value at 225 mμ, extremum not reached.

† Ketonic Cotton effect [ϕ] + 4920 pk (308 mμ), −5860 tr (271 mμ). ‡ Ketonic Cotton effect [ϕ] +4960 pk (312 mμ), −3500 tr (274 mμ). § Ketonic Cotton effect [ϕ] + 1350 pk (308 mμ), −4050 infl (259 mμ). ¶ Aromatic Cotton effect [ϕ] + 80 tr (296 mμ), +1750 infl (274 mμ).

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