962. *Optical Rotatory Dispersion: Application of the Octant Rule to Some Structural and Stereochemical Problems.*[1]

By CARL DJERASSI and W. KLYNE.

The octant rule, regarding rotatory dispersion curves of saturated ketones, has been applied to a wide range of compounds in which the carbonyl group is in a six-membered ring, including decalones, sesquiterpenes, diterpenes, steroids, and triterpenes.

The problems considered are related to (*a*) relative configurations or structure, (*b*) absolute configurations, and (*c*) preferred conformations. These are fields in which rotatory dispersion often provides information which is not readily available by use of other physical methods.

The amplitude of a Cotton effect curve is recognized as a useful measure of the asymmetry of the surroundings of the carbonyl group.

THE octant rule, which provides a generalization about the rotatory dispersion curves of saturated ketones, has been stated in a previous paper,[2] and potential applications to decalones and steroids were indicated there. In the present paper we consider applications

of this rule to a variety of structural and stereochemical problems, chiefly in terpene and steroid chemistry, in relation to compounds where the keto-group is in a six-membered ring. For general reviews of recent work on optical rotatory dispersion see refs. 3—5.

The problems might be classified as relating to (i) relative configurations or structure, (ii) absolute configurations, and (iii) preferred conformations, although in many cases two or more aspects must be considered together. Here rotatory dispersion offers information that is often not available by use of other physical methods.

For our present purpose we consider the molecular amplitude as a roughly quantitative measure of the Cotton effect. The molecular amplitude, a, is defined as the difference between the molecular rotation at the extremum (peak or trough) of longer wavelength $[\phi]_1$ *minus* the molecular rotation at the extremum of shorter wavelength $[\phi]_2$, divided by 100 for convenience: $a = 10^{-2}([\phi]_1 - [\phi]_2)$. (In our previous proposals [6] we did not suggest division by 100.) Amplitude values are shown in parentheses thus, $(+52)$, (-21). The symbol ! is used to indicate curves where the extremum of shorter wavelength could not be measured; the amplitudes thus marked represent minimum values; the true amplitudes may be larger.

It is appreciated that the fully quantitative treatment using reduced rotational strengths (R_K) which is being developed by Dr. A. Moscowitz [7] may in some instances replace the use of amplitudes; nevertheless the amplitudes, which are simpler to obtain, can give much useful information.

Our results have been obtained with Rudolph spectropolarimeters; where necessary, results are distinguished by the authors' initials (C. D. = Djerassi; W. K. = Klyne). Some of them arose in connection with problems presented to us by colleagues; we are greatly indebted to the many colleagues concerned for the use of samples.

Most measurements refer to methanol solution; where other solvents were used these are indicated as follows: C, chloroform; D, dioxan; H, "iso-octane" or any other hydrocarbon solvent.

Enantiomers.—In order to facilitate comparisons between compounds, use will frequently be made of such expressions as " the dispersion curve of $(+)$-X was . . . "— when, in fact, the material X was the $(-)$-enantiomer and the signs of rotations have been changed accordingly. The letter E is used to indicate " enantiomer of."

Symbols on Octant Projections.—The following symbols are used when necessary to indicate the contributions of atoms:

X	X	atoms symmetrically disposed; contributions cancel out.
●		atom in back octant; positive contribution
○		atom in back octant; negative contribution.
▲		atom in front octant; positive contribution.
△		atom in front octant; negative contribution.
✳		atom in vertical xy plane (no contribution).

For projections of complex structures, where several rings are superimposed, it is convenient to show the cyclohexanone ring itself and those directly fused to it in full lines, whilst other rings are shown in broken lines. The horizontal and vertical lines which represent the projection of the symmetry planes are shown by dotted lines.

DECALONES, INCLUDING SESQUITERPENES AND DITERPENES.

trans-*Decalones.*—A wide range of decalones, both simple and complex, has now been studied. Data for many of the *trans*-decalones (for which there is in normal circumstances

[3] Djerassi, " Optical Rotatory Dispersion," McGraw Hill, New York, 1960.

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

[5] *Tetrahedron*, 1961, **13**, 1—240; conference at Rancho Santa Fe, California, January 1960.
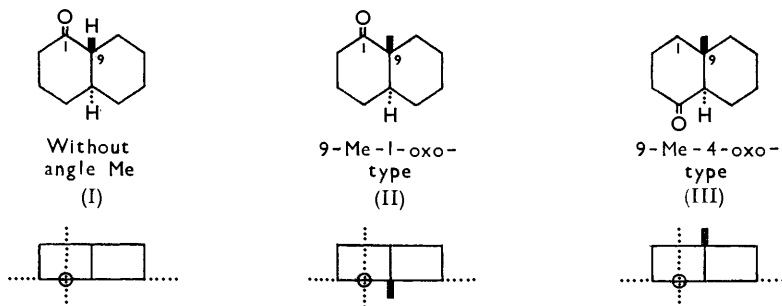
[6] Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55.

[7] Moscowitz and Snyder, Amer. Chem. Soc. Meeting, St. Louis, March 1961, Abs. Papers, p. 7R; cf. Moscowitz, *Tetrahedron*, 1961, **13**, 48; ref. 3, chap. 12.

TABLE 1.

Amplitudes of *trans*-1-decalones.

General types [decalin numbering but always starting with 1 next to the angular methyl group (9)].

Without angle Me (I)	9-Me-1-oxo-type (II)	9-Me-4-oxo-type (III)

Without angle methyl (I)			9-Methyl-1-oxo-type (II)			9-Methyl-4-oxo-type (III)		
Subst.	*a*	Note	Subst.	*a*	Note	Subst.	*a*	Note
None	−40 (E)	a	None	+27	c	None	−15 ! (E)	h
4β-OH	−16 !	b	2α-CH₂·OMe	+33	d	5,6-Lactone (IV)	−28	i
5α-OH	−63	c	4β-Me, 7-OH			6,7- ,, (V)	−25	j
			6-CHMe·CO₂H }	+17	e	5-Me, 5-CO₂H (EVI) }		
			2α-Me, 4β-OH }			1-Spiro-lactone }	−33 (E)	f
			5-Me, 5-CO₂H }	+52 (E)	f	5α-OH, 6-Prⁱ	−71	k
			3β-Pr, 8β-Me	−109	g	5β-Me, 3β-Prⁱ	−40 (E)	k
						5,6-CH₂⁻ (EVII)	−84 (E)	l
						1-R, 2α-Me, 5,5-Me₂	−52 (E)	m
						1-R, 2β-Me, 5,5-Me₂	−62 (E)	m

(a) Ref. 8. This value is estimated from observations on material of 70% optical purity. Configuration allotted by octant rule and by axial halogeno-ketone rule; cf. Prelog, unpublished observations. (b) Ref. 9; see text. (c) Ref. 10. (d) Ref. 11; see text. (e) Hydroxy-acid from ψ-santonin; see refs. 12, 13. The positive Cotton effect here is less than for the simple decalone, because of the negative contribution of the propionic acid side-chain (upper right octant). (f) Derivatives from marrubiin;[14] for comment on a derivative which gives an abnormal curve, see text. (g) *trans*-Tetrahydroeremophilone. The unstable isomer formerly referred to as *cis*.[10] A major anomaly, probably due to a "twist" conformation (Ref. 14a). (h) Estimated from data[15] for equilibrium mixture of *trans*- and *cis*-isomers. (i) From junenol.[16] (j) Norketone from telekin.[17] (k) From junenol.[18] (l) Nor-maalione;[19] see text. (m) 6-Oxolabdan-15-oic acids; from cativic acid or 6-oxocativic acid; R = [CH₂]₂·CHMe·CH₂·CO₂H.[20]
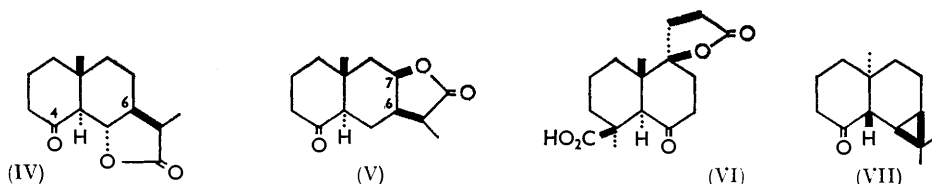
[8] Djerassi and Staunton, *J. Amer. Chem. Soc.*, 1961, **83**, 736.
[9] Baumann and Prelog, *Helv. Chim. Acta*, 1958, **41**, 2362, 2379; Feldman and Prelog, *ibid.*, p. 2396.
[10] Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.
[11] Djerassi, Halpern, Halpern, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 4001.
[12] Dauben, Hance, and Hayes, *J. Amer. Chem. Soc.*, 1955, **77**, 4609.
[13] Chopra, Cocker, Edward, McMurray, and Stuart, *J.*, 1956, 1828.
[14] Burn and Rigby, *J.*, 1957, 2964.
[14a] Djerassi and Klyne, *Proc. Nat. Acad. Sci. U.S.A.*, 1962. **48**, 1093.
[15] Djerassi and Marshall, *J. Amer. Chem. Soc.*, 1958, **80**, 3986.
[16] Shaligram, Rao, and Bhattacharyya, *Chem. and Ind.*, 1961, 671.
[17] Benešova, Herout, and Šorm, *Coll. Czech. Chem. Comm.*, 1961, **26**, 1350.
[18] Herout, Motl, and Šorm, *Coll. Czech. Chem. Comm.*, 1954, **19**, 990; 1957, **22**, 785; Bhattacharyya, Rao, and Shaligram, *Chem. and Ind.*, 1960, 469.
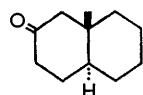[19] Büchi, von Wittenau, and White, *J. Amer. Chem. Soc.*, 1959, **81**, 1968; 1960, **82**, 2327.
[20] Halsall and Moyle, *J.*, 1960, 1324.

only one favoured double-chair conformation) are summarized in Tables 1 and 2. Comments on points of interest follow the Tables.
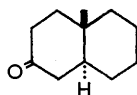
TABLE 2.

Amplitudes of *trans*-2-decalones.

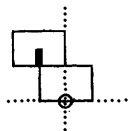No example without either angular methyl group is available.
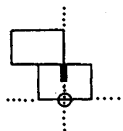


(VIII)

9 - Methyl - 2 - oxo - type

(IX)

9 - Methyl - 3 - oxo - type

9-Methyl-2-oxo-type (VIII)

9-Methyl-3-oxo-type (IX)

Subst.	a	Note	Subst.	a	Note
8-Me	+71!	a	None	+51 (E)	f
4-Me, 6-Pr^i	+11	b	5-Me	+32 (E)	g
5-Me, 3-CHMe·CO$_2$H	+40! to +69 } (E)	c	5,5-Me$_2$	+32	h
1β-Me, 5,6-lactone	+36 to +79! } (E)	d	4α-Me, 5,6-lactone (X)	+33	
			,, (11-epi)	+66 }	i
			,, (6-epi, 11-epi)	+57	
1β-R, 5,5-Me$_2$ (cf. XIII)	+100 to +130 }	e	4α-Me, 5,6-lactone, 7-OH	+30	j
			4α-Me, 6,7-lactone	+59	k
			4α-Me, 6-CHMe·CO$_2$H	+70	l
			1-R, 2α, 5,5-Me$_3$ (EXI)	+28 } (E)	m
			1-R, 2β, 5,5-Me$_3$	+61	

(a) Djerassi *et al.*[22a] (b) Tetrahydronootkatone, probable structure (Erdtman, *Acta Chem. Scand.*, in the press). (c) Four values, for two acids epimeric at C-11 and their methyl esters (W. K.); samples from Professor W. Cocker, Dublin;[21] cf. values for acid (+40!)[22] and for ester (+60!)[23] (C. D.). (d) Compounds from lumisantonin.[24] (e) Nor-diterpenes, see text, p. 4933; R is a large alkyl group. (f) In dioxan, a +44; note small solvent effect. (g) Ref. 15. (h) Ketone from widdrol; used for allotment of absolute configurations (Enzell, *Acta Chem. Scand*, 1961, **15** 1191; Norin and Enzell, *2nd Internat. Symp. Natural Products*, 1962, *Abstracts*, p. 53). (i) Tetrahydrosantonins; see text for effect of 4β(ax)-methyl group. (j) Tetrahydroartemisin.[25] (k) 3-Oxoalantolactone derivative from isotelekin.[26] (l) Ref. 27; configuration allotted from dispersion curves by Djerassi *et al.*[11] (m) From 6-oxocativic acid.[20]
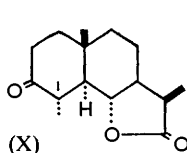
(X)
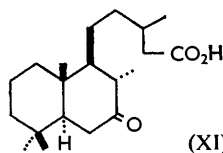
(XI)
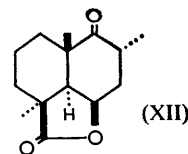
(XII)

(i) *Simple derivatives.* Recent microbiological work (Prelog and his colleagues[9]) has yielded a number of optically active decalones not carrying angle methyl groups. Absolute configurations were allotted by asymmetric synthesis; they may be confirmed by application of the octant rule to the dispersion curves.

Examples with substituents somewhat larger than methyl are provided by the 2-methoxymethyl derivatives [11] of 9-methyl-*trans*-1-decalone.

[21] Cocker, Hopkins, McMurray, and Nisbet, *J.*, 1961, 4721.
[22] Ukita and Nazakawa, *J. Amer. Chem. Soc.*, 1960, **82**, 2224.
[22a] Djerassi, Mitscher, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 947.
[23] Tsuda, Tanabe, Iwai, and Funakashi, *J. Amer. Chem. Soc.*, 1957, **79**, 5721.
[24] Barton and Gilham, *Proc. Chem. Soc.*, 1959, 391; *J.*, 1960, 4596.
[25] Sumi, *J. Amer. Chem. Soc.*, 1958, **80**, 4869.
[26] Benešova, Herout, and Klyne, *Coll. Czech. Chem. Comm.*, 1962, **27**, 498.
[27] Abe, Harukawa, Ishikawa, Miki, Sumi, and Toga, *J. Amer. Chem. Soc.*, 1956, **78**, 1416.

The simple methyldecalone (without a methoxymethyl substituent) shows a positive Cotton effect (+27). The related compound (with an equatorial 2-methoxymethyl substituent) has a similar Cotton effect (+33); the effect of the equatorial substituent is negligible.

The corresponding axial 2-methoxymethyl substituent has a negative Cotton effect (−36!), showing that the large axial substituent in the lower left octant has a large negative contribution (−70 or more). It is possible that repulsion between the axial 2- and 9-substituents distorts ring A to a partial boat or " twist " form.[14a, 28]

(ii) *Diterpene derivatives (α-decalones).* The keto-lactone (XII) from marrubiin[14] shows an anomalous amplitude (+84), presumably owing to conformational distortion. The value (−84) for nor-maalione[19] (VII) shows that distortion of the ring system by a cyclopropane ring at a distance from the carbonyl group does not seriously influence the Cotton effect, unlike the behaviour of an adjacent cyclopropane ring (unpublished work).

(iii) *Diterpene derivatives (β-decalones).* The *trans*-decalones of types (XIIIA and B), which provided the proof for the discovery of the " abnormal " 10α-configuration in several diterpenes, give a series of values for the 9-methyl-2-oxo-type with equatorial alkyl substituents of various kinds at the carbon atom adjacent to the carbonyl group.

(XIIIA) Normal

(XIIIB) = E(XIIIA) "Abnormal"
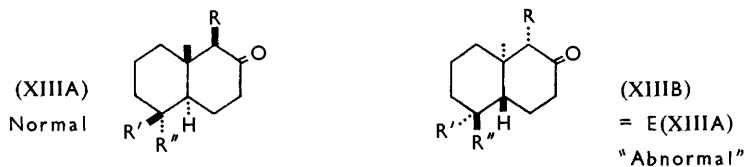
R′ = R″ = Me except where stated otherwise.

Compounds (XIII)

	a		a	Ref.
From labdanolic acid, R = CH$_2$·CH$_2$·CHMe·CO$_2$Me	−77 D	From eperuic acid, R = CH$_2$·CH$_2$·CHMe·CO$_2$Me	+97! D	29
From manõol, R = CH$_2$·CH$_2$·CO$_2$H	−123! D			29
From onocerin, R = CH$_2$ (OAc at C-3)	−130! D			29*
From agathic acid, R = CH$_2$·CH$_2$·CO$_2$·H, R′ = CO$_2$H, R″ = Mc	−131	From daniellic acid, R = CH$_2$·CH$_2$·CO$_2$H, R′ = CO$_2$H, R″ = Me	+131	30
		From andrographolide, R = CH$_2$·CO$_2$Me, R′ = CH$_2$OAc, R″ = Me (OAc at C-3)	+123	31
From neoabietic acid, R = CH$_2$·CH$_2$·CO$_2$H, R″ = CO$_2$H, R′ = Me	−119	From polyalthic acid, R = CH$_2$·CH$_2$·CO$_2$H, R″ = CO$_2$H, R′ = Me	+104†	32

* Value is for " half-molecule." † Sample slightly discoloured.

It is significant that the compounds represented by formula (XIII), *i.e.*, those in which the carbon atom (C-1) adjacent to carbonyl (C-2) carries a large equatorial alkyl substituent, show much larger amplitudes than the other sub-groups which have no such substituent. The comments of Djerassi *et al.*[33] on the effects of t-butyl α to carbonyl are relevant to this point.

cis-*Decalones.*—A *cis*-decalin derivative can exist in two possible two-chair conformations, unless its conformational freedom is restricted by ring fusion. In many cases it

[28] Johnson, Bauer, Margrave, Frisch, Dreger, and Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606.
[29] Djerassi and Marshall, *Tetrahedron*, 1957, **1**, 238.
[30] Haeuser, Lombard, Léderer, and Ourisson, *Tetrahedron*, 1961, **12**, 205.
[31] Cava and Weinstein, *Chem. and Ind.*, 1959, 851; Cava, Chan, Haynes, Johnson, and Weinstein, *Tetrahedron*, 1962, **18**, 397.
[32] Gopinath, Govindachari, Parthasarathy, and Viswanathan, *Helv. Chim. Acta*, 1961, **44**, 1040.
[33] Djerassi, Warawa, Berdahl, and Eisenbraun, *J. Amer. Chem. Soc.*, 1961, **83**, 3334.

may be predicted that Cotton effects of the two possible conformational isomers of the same *cis*-decalone will be of opposite sign (cf. ref. 2); the experimental determination of the rotatory dispersion curve of a *cis*-decalone thus often indicates the preferred conformation; this is not to say, of course, that all of the compound exists in the preferred conformation (cf. the discussion of bromodecalones in ref. 8).

In addition to the simple *cis*-decalones discussed elsewhere,[2] a number of natural products and their derivatives, which are the *cis*-analogues of the *trans*-compounds discussed in Tables 1 and 2, may now be considered. In several cases *cis*- and *trans*-compounds are treated together here; in some of these examples the allotment of configurations (as well as of conformations) has been made with the help of rotatory dispersion curves.

(i) *Tetrahydrocyperones.* The alkali-stable *cis*-tetrahydro-epi-α-cyperone [34] (XIV) was allotted by the original authors the configuration and conformation shown. The positive Cotton effect found experimentally (*a*, +29) supports this allotment.

The alternative conformation (XV) (with the other *configuration* at C-4) is improbable because it has an axial isopropyl group; its octant diagram indicates a weakly positive Cotton effect.

(XIV)   (XV)

(XVI)   (XVII)   (XVIII)

(XIXA)   (XIXB)
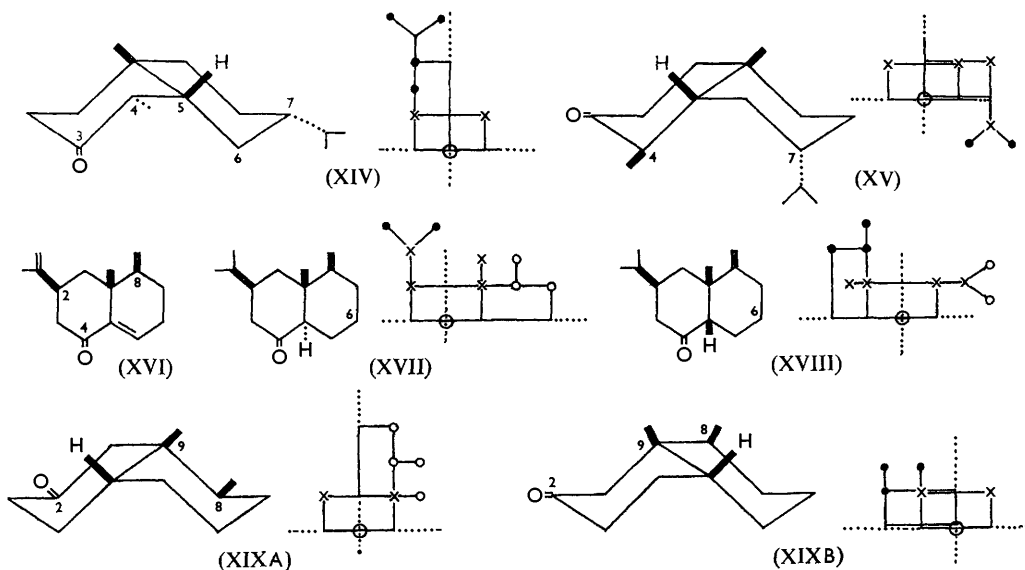
The *cis*-tetrahydrocyperone with the "natural" 7β-configuration of the isopropyl group [34] must have the steroid-like conformation (as XV, with equatorial 7β-isopropyl group). If the 4-methyl group is also β (equatorial), the octant diagram indicates a small negative Cotton effect (the methyl groups of the isopropyl cancel out). In fact, the Cotton effect is negative (−11 !) and resembles that of 5β-cholestan-3-one. If the 4-methyl group were α (axial), it would have a strong positive contribution and the Cotton effect would be positive. Thus the octant rule permits the allotment of configuration at C-4 and confirms the preferred conformations of both the *cis*-decalones.

(ii) *Eremophilone derivatives.* Eremophilone has long been of interest as one of the few sesquiterpenes which does not follow the biogenetic isoprene rule.[35] Work in one of our laboratories has established in all details the relative and absolute [36] stereochemistry

[34] Howe and McQuillin, *J.*, 1958, 1194.
[35] Ruzicka, *Experientia*, 1953, **9**, 357.
[36] Djerassi, Mauli, and Zalkow, *J. Amer. Chem. Soc.*, 1959, **81**, 2914, 3424; Zalkow, Markley, and Djerassi, *ibid.*, 1960, **82**, 6359.

of eremophilone (XVI) and its derivatives. The absolute configuration proves to be the opposite of that which was allotted previously [10] by comparison of dispersion curves of eremophilone itself and analogous steroid αβ-unsaturated ketones, a comparison which has proved to be unjustified because of conformational distortion in eremophilone. Here we shall consider only the saturated ketones.

The two tetrahydroeremophilones (XVII, XVIII) were allotted the configurations shown.[36] The stable *cis*-isomer (XVIII; called *trans* in ref. 10) has a small negative amplitude (−37) which agrees with the octant diagram. The unstable *trans*-isomer (XVII) is discussed elsewhere in connection with the " twist " conformation.[14a] Note that the atom C-6 (decalin numbering) is almost certainly in the near octant and therefore has a *negative* contribution; furthermore the negative contribution of the β-isopropyl group may be larger than that of a β-methyl or β-methylene group, depending on the preferred conformation about the bond joining CHMe₂ to C-2. The " non-steroid " conformation corresponding to (XVIII) need not be considered, since it would have all substituents axial.

The degradation product (XIX) of eremophilone provides a reference value [36] for the 9-methyl-*cis*-2-decalone type not hitherto available.

The conformation (XIXA) would be preferred on energetic grounds since the 8β-methyl is equatorial. Cotton effects predicted are strongly negative for (XIXA) and positive for (XIXB). The observed negative Cotton effect confirms that (XIXA) is preferred.

Santonin Derivatives.—Santonin [37] and its derivatives provide a rich field for stereochemical studies of many kinds. Here we shall consider only reduced compounds—the tetrahydrosantonins and corresponding hydroxy-acids. Configurations at C-11 in santonin derivatives are shown in accordance with the latest *X*-ray and chemical [38] evidence.

(XX)   (XXI)
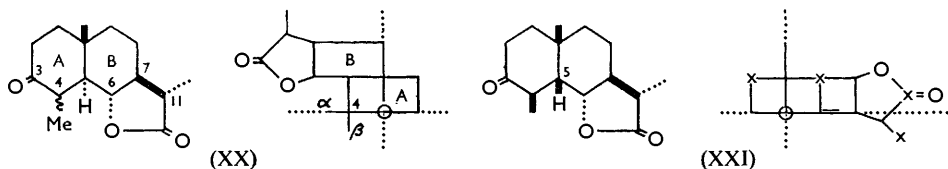
The three tetrahydrosantonins [10] (XX, 4-Me α or β; and XXI) of the "natural" 6β(H), 11β(H)-series and the corresponding 11-epi-santonins [Cocker; [39] 6β(H), 11α(H)] all have *trans*-fused lactone rings; in the case of the *cis*-decalones (XXI) this additional ring will hold the molecule in the " steroid-like " conformation shown. The results are collected in Table 3.

TABLE 3.

Tetrahydrosantonins and related compounds.

All are 3-oxo-compounds.

S = " Steroid-like " conformation.   NS = " Steroid-unlike " conformation.

	5α (A/B *trans*)		5β (A/B *cis*)		
	4α-Me (eq) *a*	4β-Me (ax) *a*	Config. of 4-Me	Conformn.	*a*
12→6-*Lactones*					
Ordinary series, 6β(H), 11β(H)	+33	+5	{ β { α	S S	−23 +20
11-Epi-series, 6β(H), 11α(H)	+66	+27	β	S	{ −15! { −18!
6-Epi, 11-epi-series, 6α(H), 11α(H) ...	+57	0	?α	?S or NS	+21
As above with additional 8α-OH					
6β(H), 11β(H)	+31	+3	β	S	−24

[37] For absolute stereochemistry, see Bruderer, Arigoni, and Jeger, *Helv. Chim. Acta*, 1956, **39**, 858 (chemical evidence); also ref. 10 (dispersion evidence).
[38] Asher and Sim, *Proc. Chem. Soc.*, 1962, 111; Nakazaki and Arakawa, *Proc. Chem. Soc.*, 1962, 151.
[39] Cocker, Dodds, and McMurray, *Tetrahedron*, 1958, **3**, 160.

The general pattern, which is in accordance with the octant diagrams, may be summarized as follows:

5α-Configuration, with 4α-(equatorial)methyl   +;

5α-   ,,   ,, 4β-(axial)   ,,   less +.

(Note the negative contribution of 4β-methyl, as expected.)

5β-Configuration, with 4β(equatorial)-methyl in
" steroid-like " conformation.   —

In the " ordinary " series, the fourth isomer [5β, with 4α(*ax*)-methyl] is available;[40] here the 4α-methyl group makes a positive contribution, as expected.

The only compound which appears to be doubtful, in either configuration or conformation, is the *cis*-decalone of the 6-epi, 11-epi-series.[40]

The compounds of the artemisin series[25] with an additional 8α-hydroxyl group follow the general santonin pattern.

Two keto-acids (XXIIA, B) prepared by Abe *et al.*[27] represent ring-opened versions of (XX) and (XXI), with the hydroxyl group removed (3-oxoeudesman-12-oic acids). Their dispersion curves, from which configurations were allotted by Djerassi *et al.*[11] show Cotton effects of the sign and magnitude expected.

The *cis*-8-oxo-acid (XXIII)[22] is one of the few ketones which give a very small Cotton effect (a, —6!). The compound presumably takes up the " steroid-like " conformation shown so as to keep the propionic acid side-chain equatorial. The octant projection
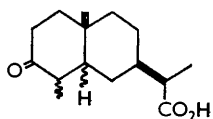
(XXIIA) 5α-H, 4α-Me: a, +70.
(XXIIB) 5β-H, 4β-Me: a, —47.

shows that mutual cancellation of substituent effects might well yield an almost " plain " curve; the alternative " steroid-unlike " conformation would give a strongly positive Cotton effect.

(XXIII)
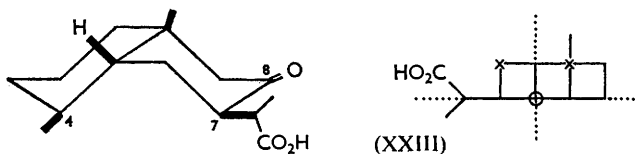
Tricyclic Ketones: Perhydrophenanthrenes and Related Compounds.

A considerable range of perhydrophenanthrene ketones and hexahydrobenzindanones has now been studied. These provide the next stage in complexity after the decalones. We shall restrict our attention here to compounds with a ketone group in a six-membered terminal ring.

Des-D-*Steroid Ketones.*—Three series are available, namely, 14-, 13-, and 12-ketones (steroid numbering).

(i) 14-*Ketones.* These perhydrophenanthrene ketones, obtained as degradation products[41] of cholesterol and as intermediates in a total synthesis of steroids[42] are of the general type (XXIV; R = H or Me).

[40] Cocker, Gobinsingh, McMurray, and Nisbet, *J.*, 1962, 1432.
[41] Billeter and Miescher, *Helv. Chim. Acta*, 1950, **33**, 388.
[42] Cornforth and Robinson, *J.*, 1949, 1855.

(XXIV)   (XXV)   OAc

In a previous discussion [43] we assumed on conformational grounds that the 13-methyl group (steroid numbering) is in the equatorial position. Consideration of the dispersion curves of a pair of compounds which differ only in the presence or absence of this methyl group supports this. The dispersion curves for compounds (XXIV; R = H and Me) are almost identical (*a*, −54, −60), showing that the methyl group adjacent to carbonyl must be equatorial since an axial (β-)methyl 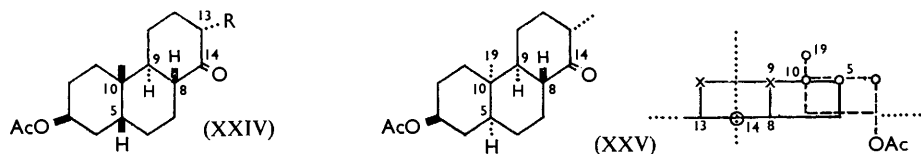group in this position would have a strong negative contribution (cf. some 13-ketones). These compounds are of the natural (*cis-anti-trans*) series. Since the surroundings of C-13 and C-14 are the same in all the other compounds to be discussed, there is good reason for assuming that the 13-methyl group is equatorial in all of them.

It is now possible to test by the octant rule the conclusions, reached in our previous paper [43] by analogy only, regarding the absolute configuration of the " unnatural " *cis-syn-trans*-ketones (Cornforth and Robinson's series A [42]). We previously allotted the configuration (XXV) to the A(+)-ketones. The octant diagram for this configuration shows that a negative Cotton effect would be expected, and this is found experimentally (*a*, −62, −54). The previous conclusions are thus supported.

For the natural series, inversion of configuration at C-5 makes little difference to the Cotton effect of a 14-ketone; the 5β-ketones (XXIV; R = H or Me) have *a*, −54, −60. The 5α-ketone (XXVI) has *a*, −54, −57 (duplicate determinations).

Introduction of a *gem*-dimethyl group at C-4 causes no change in amplitude. The 4,4-dimethyl analogue of compound (XXVI) without the 13-methyl group has *a* ∼ −58 (we are indebted to Dr. M. Marsh, Eli Lilly & Co., Indianapolis, for this result; the qualitative nature of the curve is mentioned by Turner and Shaw [44]). However, compound (XXVII) shows a greatly reduced amplitude (*a*, −13) because of the general flattening of the AB-ring system by the 5,6-double bond (cf. octant projection).

(XXVI)   OH   (XXVII)   OAc
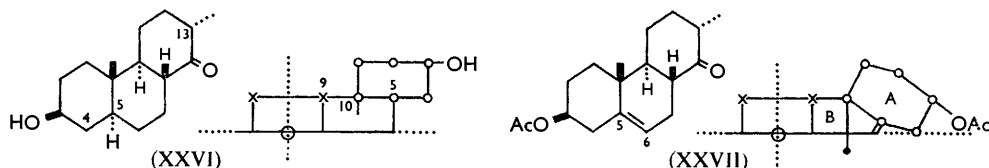
An analogue of compound (XXIV) with an axial 13-methyl group and a large equatorial 13α-substituent [CH(CO₂Me)·CH₂·CO₂Me; the remains of ring D and the cardenolide side-chain; Meyer [45]] shows, as expected from the octant projection, a greatly increased negative amplitude (*a*, −134).

(ii) *13-Ketones.* Two sets of compounds are available: (i) oxidation products of, and synthetic intermediates for, the phyllocladene group of diterpenes, and (ii) oxidation products of cassaic acid.

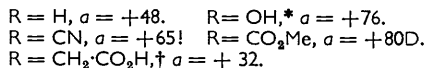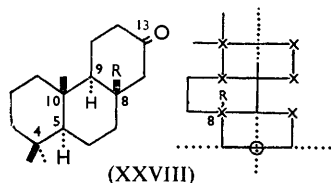Compounds (XXVIII) related to phyllocladene [46] show the effect of different substituents at C-8, *i.e.*, β to the carbonyl group.

[43] Djerassi and Klyne, *Chem. and Ind.*, 1956, 988.
[44] Turner and Shaw, *Tetrahedron Letters*, 1960, No. 18, 24.
[45] Meyer, unpublished work.
[46] Grant, *J.*, 1959, 860; Grant and Hodges, *Chem. and Ind.*, 1960, 1300; Hodges, *Tetrahedron*, 1961, 12, 215.

7 U

(XXVIII)

R = H, a = +48.   R= OH,* a = +76.
R = CN, a = +65!   R= CO_2Me, a = +80D.
R = $CH_2 \cdot CO_2H$,† a = + 32.

* Haeuser et al.[30] find (+46) for the compound with
4β-CO_2Me in place of Me.   † This compound was measured
as its enantiomer derived from steviol;[47] the 9-epimer has
a = +27.

A compound from cassaic acid (as XXVIII, R = H; with 4β-CO_2H, and with 14β-Me; ref. 48) is free from complications in the position β to carbonyl; the value for this is a, +61!.

(iii) *12-Ketones.* These have recently become available by degradation and reduction of podocarpic acid.[49]   Both B/C-*trans*- and B/C-*cis*-compounds are available (XXIX; XXX); their relative configurations were allotted with the help of the octant rule, as follows: *trans*-$8\beta,9\alpha$, a, +71; *cis*-$8\alpha,9\alpha$, a, —7.

(XXIX)   [Y = CO_2H]   (XXX)
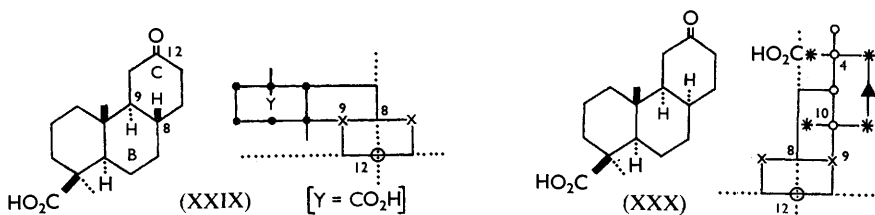
* Close to octant symmetry plane.

Des-A-steroids.—(i) *5-Ketones.* These compounds, studied extensively in Manchester and in Oxford,[50] are all steroids in which ring A has been opened (XXXIA,B) and then removed in whole or in part. They include compounds with the normal *trans*-B/C-ring fusion ($8\beta,9\alpha$) and the two different " abnormal " *cis*-B/C-fusions ($8\alpha,9\alpha$ and $8\beta,9\beta$). Within each configurational class there are two series, (XXXIA; with a single methyl group at C-10; presumed equatorial in each case) and (XXXIB; with methyl and carboxyethyl groups at C-10, in the same configuration as in the original steroid).
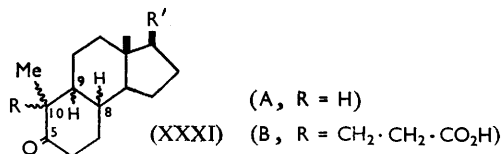
(XXXI)   (A, R = H)
(B, R = $CH_2 \cdot CH_2 \cdot CO_2H$)

Three types of ring fusion in the 10-methyl compounds are represented by the formulæ and projections (XXXII—XXXIV), and the signs predicted for the Cotton effects by the octant rule agree with those found experimentally:

		Cotton effect	
Ring fusion		Predicted	Found
XXXII; $8\beta,9\alpha$ (normal)		—	—76
XXXIII; $8\beta,9\beta$		+	+63!
XXXIV; $8\alpha,9\alpha$		Small +	+21

Compound (XXXIV) is the *des*-A-ketone from pyrocalciferol, provisionally allotted this formula by Jones *et al.*[50] A possible alternative considered by the Oxford workers would be the $8\beta,9\alpha$-isomer, with an unstable (10β-)methyl group. This should differ from

[47] Dolder, Lichti, Mosettig, and Quilt, *J. Amer. Chem. Soc.*, 1960, **82**, 246; Mosettig, Quilt, Beglinger, Waters, Vorbrueggen, and Djerassi, *ibid.*, 1961, **83**, 3163.
[48] Mathieson, unpublished work.
[49] Bible and Burtner, *J. Org. Chem.*, 1961, **26**, 1174.
[50] Jones, Meakins *et al.*, *J.*, 1959, 1159; 1960, 2627, 2785, 2792, 2800.

the 8β,9α-isomer (XXXII; with 10α-methyl) in amplitude by about +50; its *a* value should thus be about −25. The observed amplitude (+21) supports formula (XXXIV).

(XXXII)   (XXXIII)   (XXXIV)
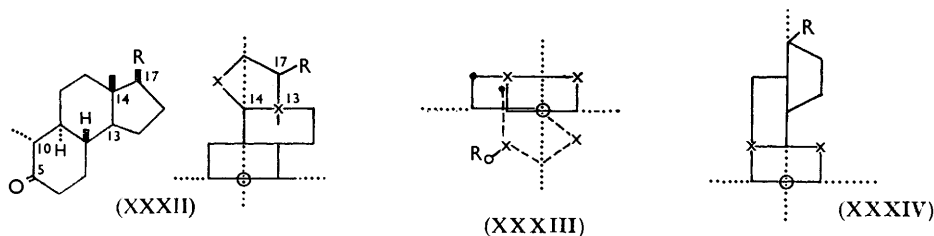
Further examples of the "normal" 8β,9α-type (XXXII) with different 17-side-chains are also available, namely: R = OH, *a* = −79; R = OAc, *a* = −39!; R = OBz, *a* = −48; R = C_8H_{17} (Inhoffen's ketone) *a* = −94.

The 10-carboxyethyl-10-methyl series (XXXIB) (the Windaus acids) differs from that discussed in the preceding two paragraphs by the presence of an axial 10-substituent (methyl or $CH_2 \cdot CH_2 \cdot CO_2H$). The differences in amplitude (Δ*a*) from series (XXXIA), which may be attributed to this axial substituent, are all of the expected sign. The magnitudes of the Δ*a* values could not, however, have been predicted from other available results because we do not know the preferred conformation of the flexible $CH_2 \cdot CH_2 \cdot CO_2H$ side-chain.

In the 8β,9α-series (normal), two isomers are available (XXXVA, 10α-Me; XXXVB, 10β-Me). The axial substituents would be expected to make a positive contribution (positive Δ*a* values). The observed Δ*a* values are:

XXXVB − XXXII (R = C_9H_{19}):   Δ*a* = −69 − (−76) = +7.

XXXVA − XXXII (R = C_8H_{17}):   Δ*a* = +15 − (−76) = +91.

For 8β,9α-compounds (XXXVI), the additional axial substituent should give a negative contribution, and this is found to be the case:

(XXXVI) − (XXXIII):   Δ*a* = +11 − (+63!) = −52!

(ii) *6-Ketones.* One simple ketone of this series has been measured, namely, Summers's acid (XXXVII; R = H),[51] which shows a negative Cotton effect (*a*, −23), as expected. A derived α-monobromo-ketone (R = Br) gave a very strong negative curve (*a*, −369); this fact was used to allot the position of the bromine substituent as 5α (a 7α-bromine

(XXXV)   (XXXVA)   (XXXVI)
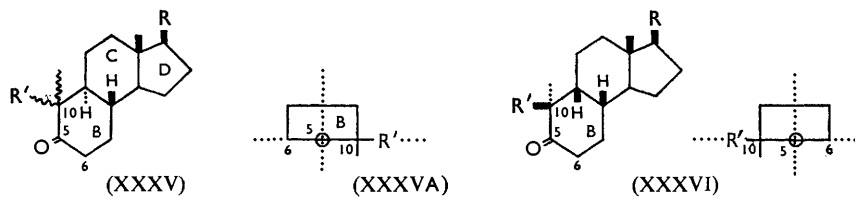
R' = $CH_2 \cdot CH_2 \cdot CO_2H$ in (XXXV) and (XXXVI).

Projections show ring B only.

	R'	10-Me	R	*a*
XXXVA	α	β	C_9H_{19}	+20
			C_8H_{17}	+15 (C. D.)
			C_8H_{17}	+18 (W. K.)
XXXVB	β	α	C_9H_{19}	−69
XXXVI	β	α	—	+11

[51] Summers, unpublished work.

substituent would have given a strong positive contribution; cf. the axial halogeno-ketone rule).[52]
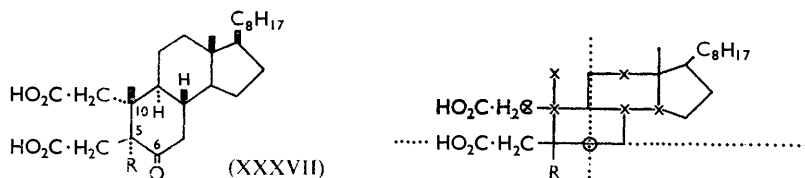
(XXXVII)

Diterpenes.—1-, 2-, and 3-Ketones of the diterpene series, which are now available in the manoyl oxide series,[46] have been measured.

The negative value (*a*, —34D) for the 1-ketone (XXXVIII) contrasts sharply with the positive value for the corresponding 9-methyl-*trans*-1-decalone, and must be due to

(XXXVIII)   (XXXIX)
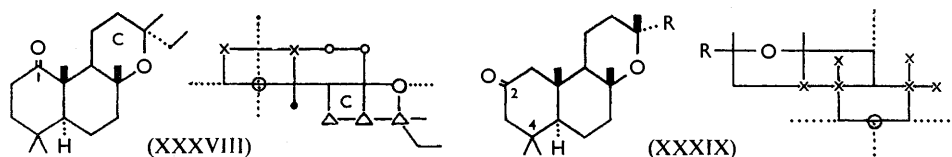
(XXXIX): R = Et, *a* = +85 (W. K.), +68! (G. O.*), +76 (C. D.); R = CH:CH₂, *a* = +66 (W. K.);
R = C:CH, *a* = +77 (W. K.).

* Professor G. Ourisson, Strasbourg.

" near-octant " effects from ring c.   The small positive value (+25!D) for the 3-ketone analogous to (XXXIX) agrees with those for the 8β-methyl-substituted triterpenoid 3-ketones (cf. refs. 11 and 53) and for the similarly substituted 3-ketones of the diptero-carpol series.[54]

Extended Decalones.—The preceding compounds include three types which represent extended *trans*-β-decalones, *viz.*, the 13- and 12-oxo-des-D-steroids (XXVIII and XXIX)

(XXVIII) *a* = +48   (XXIX) *a* = +71   (E XXXII) *a* = +79
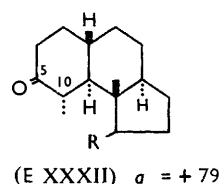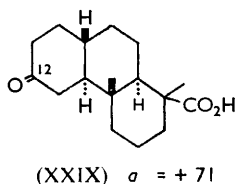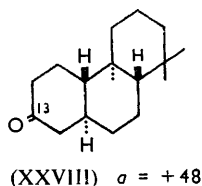
and the 5-oxo-des-A-steroids (XXXII), which may be rewritten as annexed to emphasize their relationships; (XXXII) is shown here as its enantiomer.   It is seen that the position and nature of the third ring make little difference to the amplitude, which is essentially determined by the stereochemistry of the decalone system.

STEROIDS.

A previous paper [2] dealt with the commoner types of steroid ketones; this section deals with some compounds with unusual configurations and unusual substituents.

3-Oxo-steroids.—(i) 5α,10α-*Type.*   3-Oxo-5α,10α-steroids, in which the B/C ring junction is normal (8β,9α) provide further examples of ketones which give dispersion curves without

[52] Djerassi and Klyne, *J. Amer. Chem. Soc.*, 1957, **79**, 1506; Djerassi, Osiecki, Riniker, and Riniker, *ibid.*, 1958, **80**, 1216.
[53] Djerassi, Osiecki, and Closson, *J. Amer. Chem. Soc.*, 1959, **81**, 4587.
[54] Hanna, Levisalles, and Ourisson, *Bull. Soc. chim. France*, 1960, 1936.

apparent Cotton effects; one such is 17α-ethyl-17β-hydroxy-19-nor-5α,10α-androstan-3-one (XL).[55] Here the large collection of atoms 11, 12, 13, 16, 17, and 18 (positive) counterbalances the two nearer atoms 6 and 7 (negative). The dispersion curve is apparently plain. A similar plain curve was given by the corresponding 17β-acetoxy-compound (without 17α-ethyl).[56]

(XL)
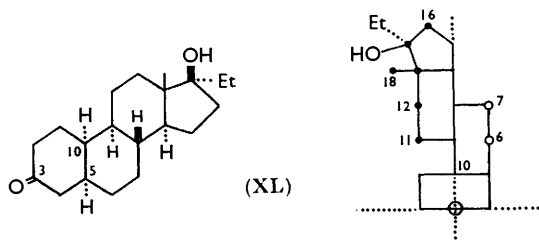
A set of three 3-oxo-19-nor-steroids recently prepared by Counsell[57] provides further useful values, as tabulated.

17β-Acetoxy-19-norandrostan-3-ones (amplitudes).

	19-Nor- series	" Ordinary " * series
5α,10β, " normal," *trans*	+64	+54
5β,10β, " normal," *cis*	−30	−25
5α,10α, " reversed," *cis* (XL)	0	—

* With angular 10-methyl group.

(ii) *Lumistanones.* These compounds, which are all 3-oxo-10α-steroids with different types of ring-fusion, have been studied extensively by E. R. H. Jones, Meakins, and their colleagues.[50] Lumistanone-A (5β,10α,9β,8β), a *trans-anti-cis*-compound (XLI), may be considered as an extended 9-methyl-*trans*-3-decalone of type enantiomeric with the ordinary steroids. The observed Cotton effect (−52) is in accord with this. Lumistanone-C, stated[50] to be a 5α,10α,9β,8β,14β-compound (XLII), is prepared by hydrogenation of the 8(14)-unsaturated derivative. As Jones *et al.*[50] have pointed out, " conformational analysis of structure (XLII) [compound (VIII) in their paper] shows the somewhat unexpected result that two all-chair forms are possible." In the first, the 3β-substituent is equatorial and the C/D ring fusion " unfavourable " (in Dreiding's sense),[58] while the 3β-substituent is axial and the ring-fusion " favourable " in the second. Chemical and infrared evidence[50] indicates adoption of the first form (XLII), and the positive Cotton effect (+22) supports this conclusion.

5α-Hexahydropyrocalciferone has a 5α,10α,9α,8β-structure (as XL; with 10-Me). This is a 10-methyl analogue of the 19-nor-5α,10α-compounds already discussed (XL) which show no Cotton effect. The small positive Cotton effect (+12) of this calciferone derivative is thus compatible with the configuration allotted on chemical grounds.

(iii) 9β-*Type.* In any 5α,10β,9β-steroid one of the two middle rings (B or C) must have a boat[59] or a modified boat (twist[28]) conformation. This makes application of the octant rule more difficult, at any rate to those compounds carrying the keto-group in ring B or C.

A 3-oxo-5α,9β-steroid[60] has a positive Cotton effect (+44); examination of models of possible twist conformations corresponding to the boat conformations previously

[55] Rapala and Farkas, *J. Org. Chem.*, 1958, **23**, 1404.
[56] Sawai, Tsurumi Research Laboratory of Chemistry, Yokohama, Japan, unpublished work.
[57] Counsell, *Tetrahedron*, 1961, **15**, 202.
[58] Dreiding, *Chem. and Ind.*, 1954, 992.
[59] See Table I in Djerassi, Frick, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1953, **75**, 349; Crawshaw, Henbest, Jones, and Wagland, *J.*, 1955, 3420.
[60] Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathaway, Oughton, and Thomas, *J.*, 1953, 2921.

discussed [59] shows that most of them would give positive Cotton effects; the dispersion curve, therefore, does not indicate the preferred conformation.

(XLI)   (XLII)   Ring C behind A
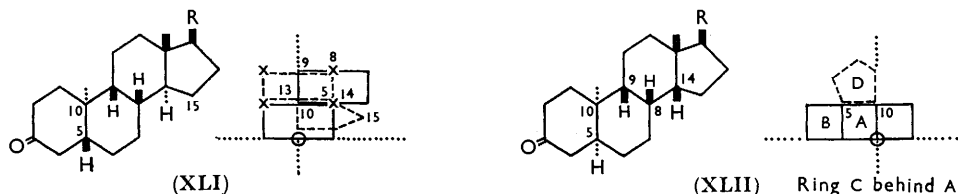
(iv) *3-Oxo-compounds with double bonds in a normal skeleton.* Some further curves are available confirming and extending earlier observations.[11] The (5α-)6-en-3-ones have been discussed (with Sondheimer, Summers *et al.*[61]). Amplitudes (*a*) are: unsubst. and 2α-Me, nearly plain; 2β-Me, −41; 2,2-Me$_2$, −54. The negative amplitude for the 2β-methyl compound must be due to an abnormal conformation of ring A.

The (5β-)6-en-3-one, provided by Dr. A. Nickon (Baltimore), has been measured in both our laboratories. The very large amplitude [*a*, −135 (W. K.); −118, −122 (C. D.)] must reflect an abnormal conformation.

For (5α-)7-en-3-ones, recent results confirm earlier ones,[11] and extend them to the 4-monomethyl substituted derivatives: [62] new values of the amplitude (*a*) are: unsubst. +56! (C. D.), +63 (W. K.); 4α(*eq*)-Me, +59; 4,4-Me$_2$, −26 (C. D.), −32 (W. K.).

The steroid 4,4-dimethyl-8(14)-en-3-one (*a*, −22) is a new type: the 8(14)-double bond does not make the curve for a 4,4-dimethyl-substituted compound positive, as the 8(9)-double bond does [11] [cf. the studies by Léderer's school [63] on darutigenol (XLIII); the enantiomeric 3-ketone (XLIV) has *a*, +42!].

(XLIII;   R = CH(OH)·CH$_2$·OH)   (as enantio-   (as des-A-
(XLIV;   R = Me   :O at posn. 3)   steroid)   triterpene)
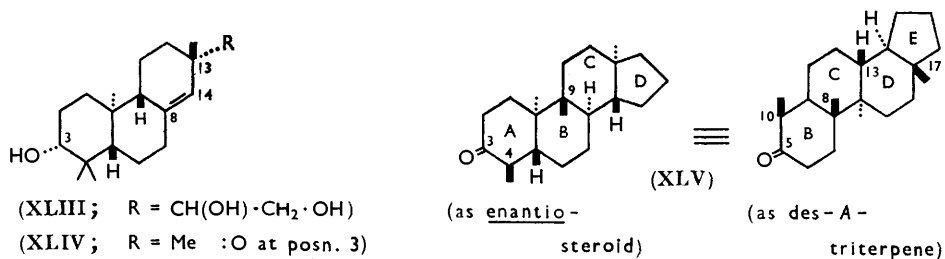
The 5-oxo-des-A-triterpenes recently prepared by E. R. H. Jones and his colleagues [62] are *enantio*-4α,9α-dimethyl-5α-3-oxo-steroids (XLV), *i.e.*, they are enantiomeric with 3-oxo-5α-steroids to which two methyl groups have been added (4α, known to make a negligible contribution on the Cotton effect, and 9α). The amplitudes found (−49, −50), when compared with that for a 4α-methyl-3-oxo-5α-steroid (as enantiomer *a* = −51), show that the effect of the 9α-methyl group is negligible.

(v) *3-Oxo-5β-steroids.* Few modified compounds of this type are available. The

(XLVI)   (XLVIA)
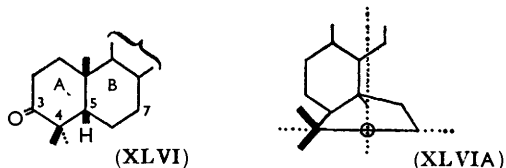
[61] Sondheimer, Klibansky, Haddad, Summers, and Klyne, *J.*, 1961, 767.
[62] Jones *et al.*, unpublished work.
[63] Pudles, Diara, and Léderer, *Bull. Soc. chim. France*, 1959, 693; Diara, Asselineau, and Léderer *ibid.*, 1960, 2170.

4,4-dimethyl derivative (XLVI) [64] shows an amplitude (−27) very similar to that for the unmethylated compound. This may imply that the *gem*-dimethyl group at position 4 "straddles" the carbonyl group, as in (XLVIA) in which ring A approximates to the 1,4-right-handed twist conformation; this would relieve non-bonded interaction between C-7 and the 4α-methyl group.

11-*Oxo-compounds.*—Two compounds with abnormal ring-fusions are available here. The 11-oxo-9β-steroid [60] must have at least one intermediate ring in a non-chair conformation. At least three twist conformations are possible,[14a] corresponding to the three boat conformations discussed previously.[60] These forms, namely B 6,9 " right-twist," C 8,12 " left-twist," and C 11,14 " right-twist," would all apparently give positive Cotton effects; it is thus impossible to choose the preferred conformation on the basis of the dispersion curve.
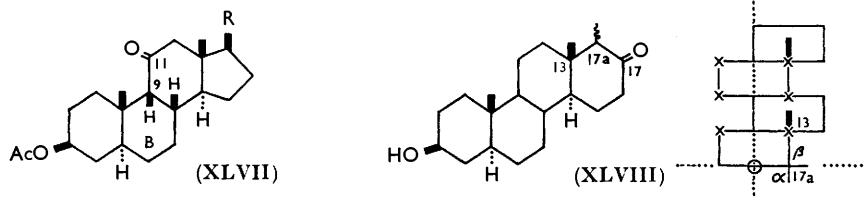
The 11-oxo-13α-steroid, 3β,17α-dihydroxy-5α,13α-androstan-11-one, prepared by Barton *et al.*,[65] gives a very strong negative Cotton effect (*a*, −187), which cannot be rationalized in terms of an all-chair conformation. It appears to be compatible with a twist conformation.[14a]

An 11-oxo-14β-steroid [65a] gives a less strong negative Cotton effect (−82); this may also be due to a similar abnormal conformation of ring C.

12-*Oxo-compounds.*—A 12-ketone of the dammarane type, 3α,20β-dihydroxy-8β,14α-dimethyl-18-nor-5α-pregnan-12-one,[66] (*a*, −37) may be compared with a normal 12-ketone (*a*, +10).

17-*Oxo-*D-*homo-compounds* (XLVIII).—17aα- and 17aβ-Methyl-substituted compounds [66a] have been used by Djerassi *et al.*[10] to illustrate the effects of axial and equatorial methyl substitution. The 17a,17a-dimethyl compound [67] has now been measured; unlike the 4,4-dimethyl-3-ketones, this does not give rise to an anomaly: addition of the (equatorial) 17aβ-methyl group to the 17aα-methylated compound has no significant effect. Amplitudes (*a*) for the D-homo-17-ketones (XLVIII) are: without 17a-Me −89!; 17aβ(*eq*)-Me −96; 17aα(*ax*)-Me, −21; 17a,17a-Me$_2$, −18.

17a-*Oxo-*D-*homo-compounds.*—17a-Ketones of the D-homoandrostane series (XLIX) were measured some years ago [10] and found to give curves with no apparent Cotton effect.
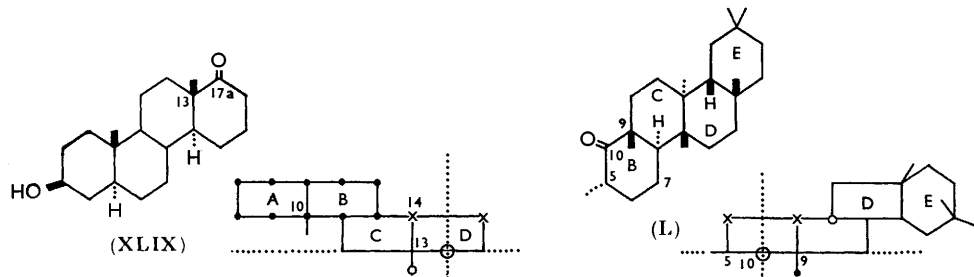
[64] Chaudhry, Halsall, and Jones, *J.*, 1961, 2725.
[65] Barton, Campos-Neves, and Scott, *J.*, 1957, 2698.
[65a] Djerassi, Halpern, Halpern, Schindler, and Tamm, *Helv. Chim. Acta*, 1958, **41**, 250.
[66] Fischer and Seiler, *Annalen*, 1959, **626**, 185.
[66a] Ramirez and Stafiej, *J. Amer. Chem. Soc.*, 1956, **78**, 644.
[67] Uskoković, Gut, Trachtenberg, Dorfman, and Klyne, *J. Amer. Chem. Soc.*, 1960, **82**, 4965.

This rather surprising finding was subsequently rationalized in terms of the octant rule.[2] It was pointed out that the apparent plain curve (a, ∼ 0) resulted from the balance of contributions by the angular 13-methyl group (negative) and by the many atoms in rings C, B, and A (positive). Measurements of other compounds of this series not carrying substituents in the neighbourhood of C-17a have confirmed this. Furthermore, a 17α-(*eq*)-methyl-17a-ketone [68] (related to the urane series [69]) also gave a plain curve as expected. However, the 17β-methyl-17a-ketone [68] gave a grossly abnormal curve, which is discussed elsewhere in terms of the " twist " conformation.[14a]

<div align="center">DES-A-TRITERPENE KETONES.</div>

Corey and Ursprung [70] described two des-A-triterpenes of the friedelane series with 10- and 7-keto-groups, respectively [ring systems as in (L)], which represent further D-homosteroid types.

The 10-ketone (a, −24!) [L; 5-methyl probably, but not certainly, equatorial (α)] is an extended 9-methyl-*trans*-1-decalone, in which the positive Cotton effect of the bicyclic system (+27) is more than balanced by a large number of weak negative contributions from eleven atoms in rings D and E. This is essentially the enantiomer of a 17α-methyl-17a-oxo-D-homosteroid (cf. XIX).

The 7-ketone is formed by catalytic hydrogenation of a 5-en-7-one; rear attack seems probable, and the 5-methyl is probably axial (β). This compound (a, +55) may also be considered to be an extended *trans*-1-decalone. The negative Cotton effect of the related 9-methyl-*trans*-4-decalone (−15!) must be counterbalanced by a positive contribution from the 5-methyl group (whatever its configuration), and by some weak positive contributions from rings D and E. There are, however, also some weak negative contributions from the near lower right-hand octant.

<div align="center">TRITERPENES.</div>

4,4-Dimethyl-3-oxo-compounds.—The anomalous effects of gem-dimethyl groups at position 4 in 3-oxo-steroids and triterpenes have been discussed at length elsewhere.[3,4,11,71] The most satisfactory explanation appears to be that of Lehn, Levisalles, Ourisson, and Witz,[71a] who represent the A-rings as distorted chairs.

Ring-E Ketones.—Experience has shown that the application of the octant rule is simpler for ketones carrying their carbonyl group in a terminal ring than for those with the carbonyl in an intermediate ring. Each type of ring-E ketone (see LI) may be considered as an extended *trans*- or *cis*-decalone (see Table).

30-Nortaraxastan-20-ones.—These two ketones (LIIA,B) have *trans*-D/E ring-fusion, and their configurations were allotted by Ames *et al.*[73] on the evidence of reaction mechanisms. They are of interest because the compound (LIIB) carrying an axial 19β-methyl group is unexpectedly the more stable. This fact has been rationalized [73] on the grounds that the equatorial 19α-methyl group in (LIIA) is subject to steric compression from the 12-methylene group. The dispersion curves are also anomalous.[11] From the diagrams, it would be expected that the 19β-compound would have the more negative Cotton effect owing to the negative contribution of this group in the lower left-hand octant, as against the negligible effect of an (equatorial) 19α-methyl group. In fact the 19β-methyl compound has a more positive Cotton effect (a, +30D) than the 19α-isomer (+10D).

[68] Fukushima, Dobriner, and Rosenfeld, *J. Org. Chem.*, 1961, **26**, 5025.
[69] Marker *et al.*, *J. Amer. Chem. Soc.*, 1938, **60**, 210, 1061, 1561, 2719; Klyne, *Nature*, 1950, **166**, 559; Klyne and Shoppee, *Chem. and Ind.*, 1952, 470.
[70] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041.
[71] Hanna, Sandris, and Ourisson, *Bull. Soc. chim. France*, 1959, 1454; Lehn, Levisalles, and Ourisson, *Tetrahedron Letters*, 1961, 682; Holker and Whalley, *Proc. Chem. Soc.*, 1961, 464; Allinger and Da Rooge, *Tetrahedron Letters*, 1961, 676.
[71a] Lehn, Levisalles, Ourisson, and Witz, *2nd Internat. Symp. Natural Products*, 1962, *Abstracts*, p. 72.

(LI)
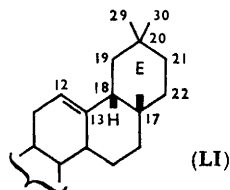
Triterpene E-ring ketones.

Bicyclic analogues are all *cis*-decalones in the " steroid-like " conformation.

Type (cf. LI) 18β-	Amplitude	Ref.	Bicyclic analogue	Cotton effect predicted
19-Oxo-	+110	53	3,3,9-Trimethyl-*cis*-4-decalone	+ +
20-Oxo- (29,30-di-nor)	−73D	11, 72	9-Methyl-*cis*-3-decalone	−
21-Oxo-	−127D	53	3,3,9-Trimethyl-*cis*-2-decalone	− −
22-Oxo-	−123D	53	3,3,9-Trimethyl-*cis*-1-decalone	− −

These compounds are extended 4,9-dimethyl-*trans*-3-decalones and may be compared with the 3-oxo-5α-santonanic acids (p. 4932). Now the 3-oxosantonanic acid carrying a 4α-methyl group has a, +70, and the isomer carrying an axial 4β-methyl group has an amplitude of about 50 units less (*ca.* +20). The amplitude of the 19β-methyl-20-ketone (LIIB) (a, +30D) corresponds well with the latter value; the equatorial isomer (LIIA) is thus presumably the anomalous one.

A, 19α−Me; B, 19β−Me

The projection shows the D and E rings as twist conformations.*
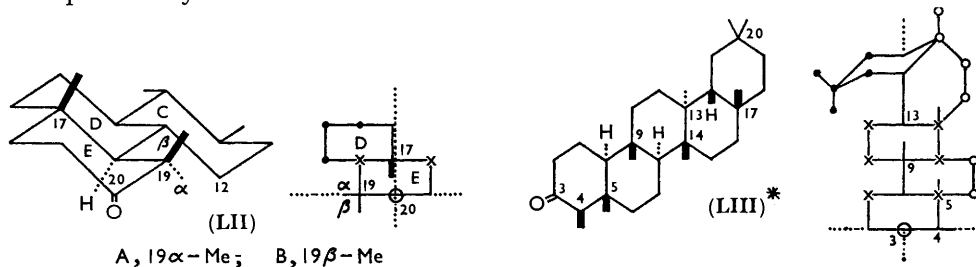
* Djerassi *et al.* [53] have pointed out that an all-chair conformation for the friedelane skeleton is virtually excluded because the 13α- and the 20α-methyl group would be very close together. Of the possible modified conformations of rings D and E, that with D-15, 18 left twist and E-17, 20 left twist seems favourable. The shapes of rings D and E will, of course, have little effect on the amplitude of a 3-ketone.

FRIEDELANE DERIVATIVES.

Friedelin (friedelan-3-one) (LIII) provides another example of the " weighting " of a decalone by remote groups (for stereochemistry, see Corey and Ursprung [70]). Friedelin may be considered as a 1,9-dimethyl-*trans*-2-decalone (cf. EVIII; a, −71 !) with five weak negative and five weak positive contributions from the more remote rings. A close analogy is available in the 17aβ-methyl-17-oxo-D-homosteroid (LII; a, −96D). In accordance with expectation, the Cotton effect [10] of friedelin is strongly negative (a, −110D)

EXPERIMENTAL

Rotatory dispersion curves were measured with Rudolf photoelectric spectropolarimeters: by C. Djerassi in the Department of Chemistry, Wayne State University, Detroit, Michigan, in the laboratories of Syntex S.A., Mexico City, and now in the Department of Chemistry, Stanford University, Stanford, California; and by W. Klyne at the Postgraduate Medical School, London, W.12., in the Organic Chemistry Department, Imperial College of Science

[72] Corey and Cantrell, *J. Amer. Chem. Soc.*, 1958, **80**, 499.
[73] Ames, Beaton, Bowers, Halsall, and Jones, *J.*, 1954, 1905.

Formula	Laboratory	Compound	Extrema [θ]	λ (mμ)	[θ]	λ (mμ)	Amplitude, a	Solvent	Refs.
		trans-1-Decalones							
I	D	trans-1-Decalone	+1530°	309	−2460°	267.5	+40	M	8
	D	,, , 4β-OH	−1080	305	+470l	280	−16l	M	9
	D	,, , 5α-OH	−2050	307	+4200	267.5	−63	M	9
II	D	trans-1-Decalone, 9β-Me	+1940	310	−720	270	+27	M	10
	D	,, , 2α-MeO·CH₂-9β-Me	+2100	315	−1200	270	+33	M	11
	D	,, , 2β-MeO·CH₂-9β-Me	−1840	320	+1750l	287.5	−36l	M	11
	D	4α,5α,11β(H)-8-Hydroxy-1-oxoeudesman-12-oic acid	+2120	307.5	+400	277.5	+17	D	10
III	D	trans-1-Decalone, 4β-OH-2α,5α,9β-Me₃-5β-CO₂H	−2620	310	+2590	272.5	−52	M	14
IV	D	trans-1-Decalone, 8β,9β-Me₂-3β-Pr^i (trans-tetrahydroeremophilone)	−4800	310	+6080	270	−109	M	10
V	D	trans-4-Decalone, 9β-Me	+555	305	−940l	265	+15l	M	15
VI	D	6α-Hydroxy-4-oxo-4-nor-5α,11β(H)-eudesman-12-oic acid lactone	−2100	313	+730	268	−28	M	16
	K	6α,8-Dihydroxy-4-oxo-7,8-lactone from telekin	+2610	323	+92	283	+25	M	17
	K	Spirolactone from marrubiin	+2370	302.5	−920	265	+33	M	14
VII	D	trans-4-Decalone, 5α-OH-9β-Me-6β-Pr^i	−2890	312.5	+4210	275	−71	M	18
	D	,, , 5β,9β-Me₂-3β-Pr^i	−2200	317.5	+2130	282.5	−40	M	18
	D	,, , 9β-Me-5α,6α-CMe₂	+3910	305	−4480	267.5	+84	M	19
	K	6-Oxo-8α(H)-labdan-15-oic acid	+2900	310	−3250	280	+61	M	20
	K	6-Oxo-8β(H)- ,, ,, ,,	+2110	320	−3110	270	+52	M	20
		trans-2-Decalones							
	D	trans-2-Decalone, 8,9β-Me₂	+3160°	307.5	−3970°l	270	+71l	M	22^a, 36
	K	,, , 4,9-Me₂-6-Pr^i (tetrahydronootkatone)	+1640	305	+490	280	+11	M	—
	K	8-Oxo-4α,5α,11β(H)-eudesman-12-oic acid	−2740	312.5	+3560	272.5	−64	M	22
	D	,, ,, ,,	−1180	317.5	+2780l	265	−40l	M	23
	K	,, ,, ,, Me ester	−3520	312.5	+3400	270	−69	M	22
	K	8-Oxo-4α,5α,11α(H)-eudesman-12-oic acid	−2880	310	+3110l	275	−60l	M	24
	K	,, ,, ,, Me ester	−2840	312.5	+3600	275	−64	M	22
	K	enantio-6β-Hydroxy-1β-methyl-2-oxo-4-nor-5α,7α-11β(H)-eudesman-12-oic acid lactone	−1930	312.5	+3480l	272.5	−55l	M	22
	K	enantio-6α-Hydroxy-7β(H)-isomer	−3720	310	+4160l	280	−79l	M	25
IX	K	trans-3-Decalone, 9β-Me	−2380	302.5	+1230	270	−36	M	25
	D	,, , 5,9β-Me₂	−2220	305	+2920	262.5	−51	M	—
	D	,, , 8,9β-Me₂	−1650	317.5	+1620	285	−33	D	14
	K	,, , 5,5,9-Me₃	+1890	307.5	−2360l	270	+43l	M	22^a
XI	K	7-Oxo-8β(H)-labdan-15-oic acid	+1630	312.5	−1570	275	+32	M	20
	K	7-Oxo-8α(H)	−1260	310	+1550	272.5	−28	M	20
		,, ,,	−2860	310	+3220	272.5	−61	M	20
		Labdan-8-ones and enantio-derivatives							
XIIIA	D	From labdanolic acid	−4440°	317.5	+3240°	277.5	−77	D	29
XIIIB	D	(enantio) From eperuic acid	+4890	317.5	−4780l	280	+97l	D	29
XIIIA	D	From manool	−6500	317.5	+5840	280	−123l	D	29
,,	D	From onocerin	−12,700	317.5	+13,160l	275	−130l*	D	29

* Value for " half-molecule."

Formula	Laboratory	Compound	[θ]	λ (mμ)	[θ]	λ (mμ)	Amplitude, a	Solvent	Refs.
					Extrema				
		Labdan-8-ones and enantio-derivatives							
XIIIB	D	(*enantio*) From andrographolide	+6530°	305	−5800°	267·5	+123	M	31
XIIIA	K	(*enantio*) From polyalthic acid	+4400	312·5	−6020	272·5	+104	M	32
	K	From neoabietic acid	−5230	312·5	+6660	270	−119	M	32
		cis-Decalones							
XIV	D	4β,5β,7β(H)-Eudesman-3-one (*cis*-tetrahydroepi-α-cyperone)	+1530°	305	−1400°	267·5	+29	M	34
	D	7α(H)-Isomer (*cis*-tetrahydro-α-cyperone)	−640	302·5	+440i	275	−11i	M	34
XVII	D	*cis*-Tetrahydroeremophilone	−890	312·5	+2760	272·5	−37	M	10
XIX	D	8β,9β-Dimethyl-*cis*-2-decalone (5β-H)	−320	315	+413i	307·5	−7i	M	36
		Tetrahydrosantonins							
		3-Oxoeudesman-12-oic acid 12 ⟶ 6-lactones:							
XX	D	4β,5α,11β(H)-6α-Hydroxy-	+1870°	307·5	−1400°	270	+33	M	10
XXI	D	4α,5α,11β(H)-	+1270	305	+725	277·5	+5	M	10
	D	4α,5β,11β(H)- ,,	−675	305	+1620i	257·5	−23i	M	10
	D	4β,5β,11β(H)- ,,	+350	305	−2100	275	−8i	M	10
	K	4α,5β,11α(H)- ,,	−125	310	+790i	275	+20	M	10
	D	,, ,,	−772	305	+790i	270	−15i	M	39
	K	4β,5α,11α(H)- ,,	+100	305	+1900i	265	−18i	M	39
	K	4α,5α,11α(H)- ,,	+43	305	−6550	262·5	+66	M	39
	K	4β,5α,11α(H)-6β-Hydroxy-	−1500	305	−4200	265	+27	M	39
	K	4α,5α,11α(H)- ,,	+790	307·5	−5080	263	+59	M	40
	K	4α,5α,11α(H)- ,,	Plain curve				0	M	40
	K	4β?,5β,11α(H)- ,,	+190	310	−1930	270	+21	M	40
		Tetrahydroartemisins							
		3-Oxoeudesman-12-oic acid 12 ⟶ 6-lactones:							
	D	4β,5α,11β(H)-6α,8α-Dihydroxy-	+1940°	310	−1120°	267·5	+31	M	25
	D	4α,5α,11β(H)- ,,	+900	312·5	+580	282·5	+3	M	25
	D	4α,5β,11β(H)- ,,	−450	305	+1970	275	−24	M	25
		Related keto-acids							
XXIIA	D	4β,5α(H)-3-Oxoeudesman-12-oic acid	+2720°	310	−4280°	267·5	+70	M	11, 27
XXIIB	D	4α,5β(H)- ,, ,,	−1060	305	+3600	265	−47	M	27
XXIII	D	4α,5β(H)-8-Oxoeudesman-12-oic acid	+565	320	+1160i	282·5	−6i	M	22
	K	4,5α,11(H)-8α-Hydroxy-3-oxoeudesman-12-oic acid 12 ⟶ 8-lactone (tetrahydro-3-oxoalantolactone)	−1590	307·5	−4300	265	+59	M	26
		Tricyclic ketones: Des-D-steroids							
XXIV	D	Des-D-5β-androstan-14-one, 3β-OAc	−2350°	312·5	+3080°	277·5	−54	D	41, 43
XXV	D	18-Nor- ,, ,, 3α-OAc	−1870	305	+4100	270	−60	M	42, 43
	D	Des-D-5α,10α-androstan-14-one, 3β-OAc	−1590	307·5	+4100	267·5	−62	M	41, 43
	D	18-Nor- ,, ,, 3β-OAc	−860	310	+4500	260	−54	M	42, 43
XXVI	K	Des-D-5α-androstan-14-one, 3β-OAc {	−2380	307·5	+3020	275	−54	M	41
			−2360	307·5	+3300	272·5	−57	M	41

Formula	Laboratory	Compound	Extrema [θ]	λ (mμ)	Extrema [θ]	λ (mμ)	Amplitude a	Solvent	Refs.
		Tricyclic ketones: Des-D-steroids							
XXVII	K	Des-D-androst-5-en-14-one, 3β-OAc	−1510	310	−218	280	−13	M	41
XXVIII:	K	Des-D-5β-androstan-14-one, 3β-OAc-13α-CH(CO₂Me)·CH₂·CO₂Me	−4750	310	+8700	270	−134	M	45
R = H	D	Des-D-18-nor-5α-androstan-13-one, 4,4-Me₂	+2130	307.5	−2660	267.5	+48	M	46
OH	D	" " " ,8β-OH	+3540	305	−4060	262.5	+76	M	46
CO₂Me	D	" " " ,8β-CO₂Me	+2840	317.5	−5130	277.5	+80	D	46
CN	K	" " " ,8β-CN	+2940	310	−3540!	265	+651	M	46
CH₂CO₂H	D	enantio-Des-D-18-nor-5α-androstan-13-one, 8β-CO₂Me-4α-Me-4β-CO₂Me	−2380	310	+870	272.5	−32	M	47
"	D	9β(H)-Isomer of above	+40	310	−2620!	275	+271!	M	47
"	K	Des-D-18-nor-5α-androstan-13-one, 4α,14β-Me₂-4β-CO₂H	+3120	305	−2940!	265	+611	M	48
XXIX	K	Des-D-18-nor-5α,8β-androstan-12-one, 4α-Me-4β-CO₂H	+3390	307.5	−3660	267.5	+71	M	49
XXX	K	8α(H)-Isomer of above	+130	315	+850	280	−7	M	49
		Des-A-steroids							
XXXII	K	Des-A-androstan-5-one, 17β-OH	−3120°	310	+4780°	265	−79	M	50
"	K	" " , 17β-OAc	−2640	302.5	+1300!	280	−39!	M	50
"	K	" " , 17β-OBz	−2060	305	+2760	282.5	−49	M	50
XXXII	D	8β,9α-Des-A-ergostan-5-one	−3770	305	+3840	270	−76	M	50
XXXIII	D	8β,9β- " "	+1100	305	−5220!	255	+631	M	50
XXXIV	D	8α,9α- " "	+1630	305	−480	275	+21	M	50
XXXIV	D	8β,9α-Des-A-cholestan-5-one (Inhoffen's ketone)	−2920	307.5	+6430	262.5	−94	M	50
XXXVB	D	5-Oxo-3,5-seco-4-nor-8β,9α,10α(Me)-ergostan-3-oic acid	−3520	315	+3350	270	−69	M	50
XXXVA	D	5-Oxo-3,5-seco-4-nor-8β,9α-ergostan-3-oic acid	+960	322.5	−1090	275	+20	M	50
XXXVA	D	5-Oxo-3,5-seco-4-nor-8β,9α-cholestan-3-oic acid	+1490	315	−330	275	+18	M	50
XLVI	D	5-Oxo-3,5-seco-4-nor-8β,9β,10α(Me)-ergostan-3-oic acid	+1660	320	+120	280	+15	M	50
XLVII	D	Me₂ 6-oxo-2,3-seco-5α-cholestane-2,3-dioate	+586	312.5	−502	285	+11	M	51
XLVII	K	5α-Bromo-deriv. of above	−1380	307.5	+860	270	−23	M	51
			−14,600	327.5	+22,300	280	−369	M	51
		Diterpenes							
XXXIX R = CH:CH₂	D	2-Oxomanoyl oxide	+3950°	310	−3650°	270	+76	M	46
"	K	" "	+3480	310	−3160	280	+66	M	46
			+3400	312.5	−3220	275	+66	M	46
XXXIX R = Et	K	Dihydro-2-oxomanoyl oxide	+3430	310	−5100	265	+85	M	46
XXXIX R = C:CH	K	2-Oxomanoyl oxide (with triple bond in side-chain)	+3630	310	−4060	270	+77	M	46
XLIV	D	enantio-Des-D-androst-8(14)-en-3-one, 4,4,13-Me₃ (ketone from darutigenol)	+1230	315	−3010!	260	+421	M	63
		Steroids							
XL	D	19-Nor-5α,10α-androstan-3-one, 17α-Et, 17β-OH	None	None			0	M	55
"	D	" " , 17α-Et, 17β-OAc	None	None			0	M	56
"	K	19-Nor-5α,10β-androstan-3-one, 17β-OAc	+2970°	310	−3420°	265	+64	M	57
"	K	19-Nor-5β,10β-androstan-3-one, 17β-OAc	−950	315	+2060	270	−30	M	57

Formula	Laboratory	Compound	Extrema [θ]	λ (mμ)	[θ]	λ (mμ)	Amplitude a	Solvent	Refs.
		Steroids							
XL	K	19-Nor-5α,10α-androstan-3-one, 17β-OAc	None		None		0	M	57
XLI	D	Lumistanone A	−2320	310	+2920	270	−52	M	50
XLII	D	„ C	+1200	307	−1000	270	+22	M	50
	D	5α-Hexahydropyrrocalciferone	+460	312.5	−720	275	+12	M	50
	D	5α,9β-Ergostan-3-one	+3000	307.5	−1320	275	+43	M	60
	K	5α-Cholest-6-en-3-one	−2040	307.5	−1650	300	−4	M	61
	K	2α-Methyl-5α-cholest-6-en-3-one	−1200	327.5	−890	320	−3	M	61
	K	2β-Methyl-5α-cholestan-6-en-3-one	−2900	312.5	+1160	275	−41	M	61
	K	2,2-Dimethyl-5α-cholest-6-en-3-one	−4430	312.5	+970	275	−54	M	61
	D	5β-Cholest-6-en-3-one	−6980	307.5	+4830	265	−118	M	—
	K	5α-Ergost-7-en-3-one	−6550	307.5	+6950	267.5	−135	M	11
	D	5α-Cholest-7-en-3-one	+2380	317.5	−3300!	275	+56!	D	11
	K	4,4-Dimethyl-5α-cholest-7-en-3-one	−2320	305	−3880	262.5	+63	M	—
	D	„ „	−1520	310	+860	277.5	−32	M	11
	K	4,4-Dimethyl-5α-cholest-8(14)-en-3-one	−1650	315	+1070	275	−26	M	62
			−2080	300	+530	280	−22	M	62
XLV	K	*enantio*-4α,9α-dimethyl-5α-androstan-3-one	−2940	302.5	+2120	267.5	−51	M	62
EXLV	K	4,9α-Dimethyl-5α-androstan-3-one	+1980	307.5	−3500	262.5	+55	M	62
	K	9α-Methyl-5α-androstan-3-one	+2100	310	−2940	270	+50	M	62
XLVI	K	4,4-Dimethyl-5β-cholestan-3-one	−1480	310	+1240	275	−27	M	63
XLVII	D	5α,9β-Ergostan-11-one, 3β-OAc	+4770	320	−4400	275	+92	D	60
	D	5α,13α-Androstan-11-one, 3β,17α-(OAc)$_2$	−9930	320	+8770	280	−187	M	65
	D	Me 11-oxo-5β,14β-etianate, 3α-(O·CO·CH_2·CH_2·CO_2Me)	−2260	322.5	−5960	285	−82	D	65a
	K	8β,14α-Dimethyl-18-nor-5α-pregnan-12-one, 3α,20β-(OH)$_2$	−875	307.5	+2800	267.5	−37	M	66
		D-Homosteroids							
		d-Homo-5α-androstanes:							
XLVIII	K	17-one, 3β-OH	−4760°	307.5	+4180°[1]	270	−89[1]	M	—
	D	17-one, 17aα-Me-3β-OH	−1500	320	+600	280	−21	D	10
	D	17-one, 17aβ-Me-3β-OH	−5470	315	+4170	275	−96	D	10
XLIX	K	17-one, 17a,17a-Me$_2$-3β-OAc	−1070	300	+760	275	−18	D	7,68
	K	17a-one, 17α-Me-3β-OAc	None		None		0	M	8,69
		Des-A-triterpenes							
L	D	Des-A-friedelan-10-one	−180°	320	+2240°[1]	280	−24[1]	D	70
	D	Des-A-friedelan-7-one	+2750	315	−2790	275	+55	D	70
		Triterpenes							
LI	D	Me 19-oxo-olean-12-en-28-oate, 3β-OAc	+7050°	317	−4100°	277	+110	M	53
„	D	29,30-Dinorurs-12-en-20-one, 3β-OBz	−1710	320	+5600	295	−73	D	11,72
„	D	Me machaerate (21-oxo-olean-12-en-28-oate, 3β-OH)	−5020	320	+7720	275	−127	D	53
	D	Olean-12-en-22-one, 3β,16β,28-(OAc)$_3$	−6200!	327.5	+6200!	280	−123!	D	53
LIIA	D	19β(H)-30-Nortaraxastan-20-one	+1570	310	+550	277.5	+10	D	11,73
LIIB	D	19α(H)- „	+1530	320	−1450	280	+30	D	11,73
LIII	D	Friedelan-3-one	−5620	315	+5020	275	−106	D	10,70

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Experimental details are as in ref. **3**, chap. **3** (solvent usually methanol or dioxan; tube 0·5 or 1 dm.; 18—25°; *c*, 0·1 mg./c.c. or less).

The data for extrema (peaks and troughs) and amplitudes of curves are collected in the Table. Results are quoted as molecular rotations; some have been presented previously as specific rotations. The data for the extremum of longer wavelength are cited first in all cases, whether this extremum is a peak or a trough. Dioxan is denoted D, methanol M.

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