

Optical Rotatory Dispersion and Circular Dichroism. Part LXXXII.¹ An Empirical Analysis of the Circular Dichroism of Decalones and their Analogues

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An empirical analysis of c.d. data ($n \rightarrow \pi^*$; ca. 290 nm) for a wide variety of ketones of the 'extended decalone' class has led to sets of numerical contributions for ring systems (Figure 8; Tables 9 and 14) and alkyl substituents (Table 3). These contributions can be summed to give $\Delta\epsilon$ values corresponding very closely to those observed (usually within ± 0.2 units, although a few exceptions are noted and discussed). This is the first such analysis to embrace, within a single scheme, compounds of both the *trans*- and *cis*-decalone types, as well as their polycyclic analogues. The treatment covers data obtained for solutions in four types of solvent: hexane, dioxan, acetonitrile, and methanol (or ethanol).

Further analysis of c.d. data for extended decalones indicates that certain coplanar zig-zag arrangements of C-C bonds (termed 'primary zig-zags': Figure 3) are probably responsible in many cases for a major part of the observed c.d., although other significant contributions may come from alkyl substituents in the vicinity of the carbonyl group. Atoms or bonds which form part of the alicyclic framework but do not lie on or adjacent to a primary zig-zag generally make little or no contribution to the value of $\Delta\epsilon$; structural features lying very close to the carbonyl group and in a 'front' octant are the main exceptions. Methyl substituents at the β -axial positions fall into the two distinct classes, having consignate or dissignate c.d. effects, respectively, according to the number of bonds comprising the primary zig-zag which passes through the particular β -carbon atom.

The scope and significance of these conclusions are discussed, and attention is drawn to some apparent correlations between c.d. and ¹³C n.m.r. data.

THIS is the first of a series of papers in which we shall present the results of a wide-ranging reassessment of the relationships between the structures and the chiroptical properties of ketones.

A review of the subject, in which we have surveyed some significant recent developments, has been presented elsewhere.² The present paper deals with decalones and their extended polycyclic analogues and is restricted to c.d. at the $n \rightarrow \pi^*$ (ca. 290 nm) transition of the carbonyl group,³ which has been the subject of many earlier papers⁴⁻⁷ from these and other laboratories. The short wavelength ($n \rightarrow \sigma^*$) transition,⁸ and the chiroptical properties of other classes of ketones, will be the subjects of later papers.

All early work³⁻⁶ was carried out on o.r.d. Some of the results were not of high accuracy, although a surprisingly large proportion have been essentially confirmed by comparison with recent more accurate c.d. data, using the theoretical relationship:⁹ $\Delta\epsilon = a/40.28$. The main conclusions are summarised in the familiar 'Octant Rule'⁴ which allowed the effects of α -axial substituents,† especially in rigid cyclohexanones, to be rationalised in simple geometrical terms. The fact that the commoner halogens (Cl, Br, and I) gave 'octant' contributions of

† Expressions of the type ' α -axial,' ' α -equatorial,' ' β -axial,' ' γ -equatorial,' etc. refer to the location and conformation of a substituent in relation to the carbonyl group in a cyclohexanone or decalone derivative (cf. Figure 4). When α - and β - follow locants (e.g. 3 β -, 6 α -, 17 β -) they refer to configurations, following the usual conventions of steroid nomenclature.

¹ Part LXXXI, F. Fernandez, D. N. Kirk, and M. Scopes, *J.C.S. Perkin I*, 1974, 18.

² W. Klyne and D. N. Kirk, in 'Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism,' ed. F. Ciardelli and P. Salvadori, Heyden and Son, London, 1973, pp. 89-107.

³ (a) P. Crabbé, 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' Holden-Day, San Francisco, 1965; (b) P. Crabbé, 'Applications de la Dispersion Rotatoire Optique et du Dichroïsme Circulaire Optique en Chimie Organique,' Gauthier-Villars, Paris, 1968; (c) L. Velluz, M. Legrand, and M. Grosjean, 'Optical Circular Dichroism,' Verlag Chemie, Academic Press, New York, 1965.

the same sign as alkyl groups lulled most workers in the field into easy acceptance of the simple geometrical picture, in which the Octant Rule was applied merely by considering the disposition of perturbing atoms in a dissymmetric pattern around the chromophore. Little thought was given to the possible significance of bonding patterns. The 'anomalous' behaviour of fluorine,¹⁰ which (in an α -axial position) gave effects of opposite sign to those of the other halogens, was ascribed to its lower polarisability. α -Hydroxy- and acetoxy-groups,¹¹ and also some nitrogen substituents,¹² have more recently been shown to give 'anti-octant' effects in certain situations.

The 'normal' behaviour of alkyl and cycloalkyl substituents appeared to be so regular that attempts were made, with moderate success, to allot amplitude contributions to groups of various kinds, on the assumption that these contributions were additive. Such analyses have been limited, however, to groups of closely related compounds, e.g. the *trans*-decalones^{5c} and some of their alkylated^{5a,13} and tricyclic analogues.⁶ No success has

⁴ W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

⁵ C. Djerassi and W. Klyne, *J. Chem. Soc.*, (a) 1962, 4929; (b) 1963, 2390; (c) W. Klyne, *Experientia*, 1964, **20**, 349.

⁶ D. N. Kirk, W. Klyne, and S. R. Wallis, *J. Chem. Soc. (C)*, 1970, 350.

⁷ C. Coulombeau and A. Rassat, *Bull. Soc. chim. France*, 1971, 516.

⁸ (a) D. N. Kirk, W. Klyne, W. P. Mose, and E. Otto, *J.C.S. Chem. Comm.*, 1972, 35; (b) D. N. Kirk, W. Klyne, and W. P. Mose, *Tetrahedron Letters*, 1972, 1315; (c) D. N. Kirk and W. Klyne, in preparation.

⁹ S. F. Mason, *Quart. Rev.*, 1963, **17**, 20.

¹⁰ C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 1216; J. Levisalles, and M. Rudler-Chauvin, *Bull. Soc. chim. France*, 1970, 664.

¹¹ J. R. Bull and P. R. Enslin, *Tetrahedron*, 1970, **26**, 1525; L. Bartlett, D. N. Kirk, W. Klyne, S. R. Wallis, H. Erdtman, and S. Thorén, *J. Chem. Soc. (C)*, 1970, 2678.

¹² J. Hudec, *Chem. Comm.*, 1970, 829.

¹³ (a) C. Djerassi, E. Lund, and A. A. Akhrem, *J. Amer. Chem. Soc.*, 1962, **84**, 1249; (b) C. Beard, C. Djerassi, J. Sicher, F. Šipoš, and M. Tichý, *Tetrahedron*, 1963, **19**, 919.

been reported to date in attempts to integrate data for *cis*-decalones and other classes of ketone into one empirical scheme.

The various recent attempts at theoretical treatments of chiroptical properties of ketones are summarised in Table I; no single treatment was applied to an extensive range of experimental data. It seems probable that each of the various features considered by theoreticians will find some place in a final complete mathematical description of chiroptical phenomena; however, the differences of approach, and the present inadequacy of theoretical treatments to predict $\Delta\epsilon$ values for any but the simplest compounds, suggest that there is still a great need for the empirical analysis of experimental data to guide the theoreticians, even if only by determining which structural features are of most importance in real compounds, as distinct from simplified models.

Recent Advances.—Challenges to the simple geometrical picture of perturbation of saturated ketones by 'atoms-in-space', as presented in the original Octant Rule,⁴

by Hudec,^{12,18} which has established a long-range effect of hetero-substituents upon the $n \rightarrow \pi^*$ Cotton effect of ketones. The magnitude and sign of the Cotton effect are dependent upon conformational features, apparently being pronounced only when there exists a suitable 'planar zig-zag' of bonds connecting the oxo-group and the hetero-atom (Figure 1; X = halogen, NR₂, OR, SR, etc.). The critical zig-zag of bonds is most readily illustrated for ketones of the extended decalone class. As defined by Hudec,¹⁸ the zig-zag (Figure 1; heavy lines) comprises one lobe of the *p*-orbital at the carbonyl carbon atom, the carbonyl-C_α bond, the C_α-C_β bond, the β-equatorial bond of the cyclohexanone ring, and any further C-C bonds which are alternately parallel to the C_α-C_β and the β-equatorial bonds. In ketones of other classes, any connecting zig-zag of C-C bonds having essentially the same orientation in space with respect to the carbonyl group is expected to lead to similar very pronounced effects of remote polar substituents. In such a situation, illustrated by Hudec for zig-zags of

TABLE I
Summary of recent attempts at theoretical treatment of c.d. of ketones ($n \rightarrow \pi^*$)

			Ref.
1966	J. A. Schellman and G. Wagnière	Octant vs. quadrant rules	a
1966	Y.-H. Pao and D. P. Santry	SCFMO; action through bonds; nodal surfaces.	b
1966	J. C. Tai and N. L. Allinger	One-electron; Hückel	c
1966—1968	E. G. Höhn and O. E. Weigang	Electron correlation: one electron and coupled oscillator.	d
1967	R. M. Lynden-Bell and V. R. Saunders	SCFMO: action through σ -bonds; extended Hückel.	e
1970	R. R. Gould and R. Hoffman	Extended Hückel.	f
1970	J. Hudec	Action through σ -bonds.	g

* Refs. 30a, c. ^b *J. Amer. Chem. Soc.*, 1966, **88**, 4157. ^c *J. Amer. Chem. Soc.*, 1966, **88**, 2179. ^d *J. Amer. Chem. Soc.*, 1966, **88**, 3673; also ref. 30b. ^e Ref. 20. ^f *J. Amer. Chem. Soc.*, 1970, **92**, 1813; see also Correction, *ibid.*, p. 7239. ^g Refs. 12 and 18.

have come from two important sets of recent observations, with c.d. measurements now superseding o.r.d. for most purposes.

One development is the recognition of the so-called 'anti-octant' effects in situations which cannot be simply interpreted on the original basis of relative polarisabilities of substituents. Most notable is the demonstration of 'anti-octant' behaviour of β-axial methyl groups in certain compounds (adamantanones;¹⁴ *cis*-2-decalones¹⁵). Although it has long been realised that polar β-axial substituents (halogens, CN, OH, etc.^{5b,16}) could introduce apparent anomalies, such behaviour of alkyl groups calls for a revision of the simple octant concept. 6α-Methyl groups in 3-oxo-5α-steroids similarly show apparent 'anti-octant' behaviour, which recently led Coulombeau and Rassat⁷ to propose a sharp curvature of the octant boundary surface bisecting the C=O bond, with the convex face of the surface towards the oxygen atom, so as to place the 6α-methyl group in a front octant. A similar suggestion has been made in relation to cyclopropyl ketones.¹⁷

The other and more important pointer to the limited scope of the early Octant Rule comes from recent work

¹⁴ G. Snatzke, B. Ehrig, and H. Klein, *Tetrahedron*, 1969, **25**, 5601.

¹⁵ H. J. C. Jacobs and E. Havinga, *Tetrahedron*, 1972, **28**, 135.

¹⁶ J.-C. Jacquesy and J. Levisalles, *Bull. Soc. chim. France*, 1962, **1866**; C. S. Barnes and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1962; also ref. 3a, pp. 103—104, and ref. 5a.

varying lengths by examples including π-camphor derivatives and 3-substituted 7-oxo-5α-steroids (1), the group X is considered to contribute two opposing

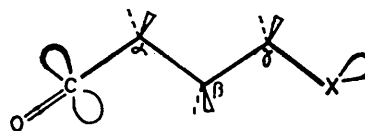


FIGURE 1 Planar zig-zag of bonds and orbital lobes

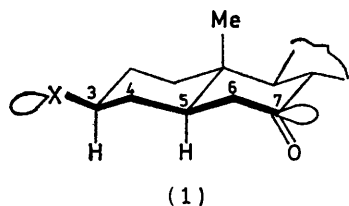
effects as follows. (a) The ($-I$) inductive (or inductomeric) effect of the atom or group X will tend to withdraw electrons from the carbonyl group. (b) The ($+E$) electromeric effect of a lone-pair at X may allow electron donation to the carbonyl group when required, provided that the axis of the lone-pair orbital extends the 'planar zig-zag'.

The observed signs and values of $\delta\Delta\epsilon_X$ (the change in $\Delta\epsilon$ due to the presence of the atom X), imply that a dominant electromeric ('back-donation') effect enhances 'octant' behaviour (e.g. when X = I, Br, or S⁻), whereas a dominant electron-withdrawing inductive effect causes 'anti-octant' behaviour (e.g. when X = F or OAc). These observations correlate in a qualitative sense with the Hammett σ and particularly the Taft σ^*

¹⁷ J. F. Tocanne, *Tetrahedron*, 1972, **28**, 389.

¹⁸ (a) M. T. Hughes and J. Hudec, *Chem. Comm.*, 1971, 805; (b) G. P. Powell and J. Hudec, *ibid.*, p. 806.

values for the substituents.¹⁹ In the 7-oxo-5 α -steroids (1),^{18b} the effect is revealed by pronounced 'octant' behaviour of those 3 β -substituents which can exhibit powerful electron donation, or, in sharp contrast, weak



'anti-octant' behaviour of strongly electronegative substituents (e.g. 3 β -F). All 3 α -heteroatom substituents, however, exhibit weak 'anti-octant' behaviour in these 7-oxo-5 α -steroids, corresponding to electron-withdrawal by the positive pole of the C(3)^{δ+}-X^{δ-} dipole, without the possibility of back-donation from the heteroatom lone pair, which no longer lies on the planar zig-zag path. This recognition, by Hudec, of the significance of conformational patterns of bonds and lone pairs, provided a powerful stimulus to the development of our own related treatment, as detailed later.

The concept of perturbation of carbonyl groups by substituent effects transmitted through σ -bonds has received recent support from a theoretical (SCFMO) treatment involving calculations of rotational strengths for simple models of α -substituted ketones.²⁰ The rotational strength of the ketone due to a substituent was shown to be related to the electronegativity of the substituent atom.

The primary objectives of our present work were: (a) to test anew the hypothesis^{5c} that the contributions ($\delta\Delta\epsilon$) of suitably chosen structural features should be additive (compare Zürcher's conspicuously successful and valuable analysis of substituent effects on the chemical shifts of the protons of angular methyl groups, in the n.m.r. spectra of steroids);²¹ and (b) assuming additivity to be established, to derive a reliable set of structural group increments, which would be useful both to organic chemists concerned with structural problems, and also to theoreticians studying chiroptical phenomena at the electronic level.

In both of these objectives we now report a considerable measure of success. The principle of additivity appears to apply to a wide variety of compounds, although a few instances are noted in later sections of this paper where the simultaneous presence of two separate structural features introduces a net c.d. contribution which, although essentially constant and characteristic, differs significantly from the sum of contributions of the two individual substituents.

During early attempts to evaluate the contributions of structural features (comprising only C,H systems), the signs and amplitudes (a) of o.r.d. Cotton effects of many polycyclic arrays of six-membered rings were

* Acetonitrile is a valuable solvent in being transparent to 185 nm, allowing study of the $n \rightarrow \sigma^*$ as well as the $n \rightarrow \pi^*$ transition, for compounds insufficiently soluble in hexane.

shown to be mainly dependent upon the bicyclic environment of the oxo-function.^{4,5} Most subsequent treatments have similarly discussed polycyclic compounds as extended decalones. Methyl groups in the α -axial position of a cyclohexanone^{4,13b} were found to make amplitude contributions (δa) of reasonably constant magnitude (about 65 to 70 units in the 'octant' sense). β -Equatorial methyl groups were also found to behave in predictable fashion, their contributions in 3-methylcyclohexanone,^{13b} 3 eq -methyladamantanone,¹⁴ and 3,9-dimethyl-*trans*-1-decalone^{13a} indicating a contribution (δa) of about 25 units.

Our investigation of solvent effects⁶ led to an analysis of some steroidal structures, yielding δa values for tricyclic fragments of the *trans*,*anti*,*trans*-perhydrophenanthrene type, and for methyl substituents at various positions on the cyclohexanone ring. Another recent study⁷ has provided a further set of structural contributions, and includes the suggestion that the 'third' boundary surface of the Octant Rule is sharply curved (p. 1077).

A major weakness of previous numerical analyses has been the failure to incorporate, within a single scheme, the available data for *cis*-decalones and 'middle-ring' ketones (e.g. 6-oxo- and 7-oxo-steroids); success has been limited largely to *trans*-decalone analogues. One of us (D. N. K.) tried unsuccessfully in 1964 to unify the limited o.r.d. data then available, with the assumption of characteristic and additive group increments.

Features evident from this early analysis included: (i) an apparently wide variation in the contributions of β -axial methyl groups in different situations; (ii) the apparent 'anti-octant' behaviour of a 6 α -methyl substituent in a 3-oxo-5 α -steroid; (iii) the total inadequacy of data for assessing either the sign or magnitude of 'front octant' contributions; and (iv) the unexpected behaviour of certain *cis*-decalones, some of which were then considered, from o.r.d. data, to exist in conformations which could not be explained adequately in energetic terms (p. 1094).

Present Work.—With improved instruments now available, and using c.d. measurements, it has been possible to carry out a thorough re-evaluation of chiroptical data for the $n \rightarrow \pi^*$ band of ketones, and also to explore the next transition of higher energy (ca. 190 nm; probably $n \rightarrow \sigma^*$).⁸ When materials were still available from earlier studies, their c.d. curves were determined for solutions in hexane, unless solubilities were too low. Our recent survey⁶ of changes in magnitude of Cotton effects with solvent, augmented by a further systematic survey (p. 1097) of key structural types in hexane, dioxan, acetonitrile,* and methanol (or ethanol),

¹⁹ H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191; R. W. Taft and I. C. Lewis, *J. Amer. Chem. Soc.*, 1958, **80**, 2436; R. W. Taft, in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956; L. P. Hammett, 'Physical Organic Chemistry,' 2nd edn., McGraw-Hill, New York, 1970.

²⁰ R. M. Lynden-Bell and V. R. Saunders, *J. Chem. Soc. (A)*, 1967, 2061.

²¹ R. F. Zürcher, *Helv. Chim. Acta*, 1961, **44**, 1300; 1963, **46**, 2054.

has afforded useful guidance for conversion of data from one solvent to another, so that published a or $\Delta\epsilon$ values for compounds no longer available could be 'corrected' for solvent variations.

More important in the present analysis has been the synthesis of certain new compounds (this page) required to resolve uncertainties of the type listed in points (i)—(iii) above. A stepwise numerical analysis of the data so obtained has now afforded a series of group increments ($\delta\Delta\epsilon$) which can be summed for any of a wide variety of 'extended decalones', to obtain estimates of $\Delta\epsilon$ values which agree closely (generally within ± 0.2) with experimental results in most cases. This new analysis combines, for the first time, data for *trans*- and *cis*-decalones, including 'middle-ring' ketones belonging to both classes.

Among the compounds examined during this work, almost none exhibited the complication of bisignate curves (c.d. curves with two 'humps' of opposite signs).² C.d. curves ($n \rightarrow \pi^*$) were in general almost perfectly symmetrical, of Gaussian shape,²² with width at half-height always close to 35 nm (usually ± 3 nm). Some curves, particularly those for solutions in hexane, showed partial resolution into vibronic bands:²³ in such cases the $\Delta\epsilon$ value used in the analysis was that of the strongest component band, which could be either the second or the third from the long-wavelength extreme of the c.d. band (some of the weaker vibronic bands were seen only as shoulders).

It would be desirable, on theoretical grounds, to use the rotational strength, R_K (obtained from the integrated area under the curve),²² rather than the molar coefficient of dichroic absorption, $\Delta\epsilon$; we have, however, based the present analysis on $\Delta\epsilon$ values for reasons of simplicity. Integration of band areas for twelve c.d. curves, selected at random from those used in the present work, showed that the band areas are closely proportional to the maximum values of $\Delta\epsilon$, even when the c.d. curve exhibits moderate or strong vibronic fine structure. Deviations did not exceed 10%, the more usual deviation being only 3–5%, which is hardly greater than the probable experimental error in measurement of $\Delta\epsilon$.

Wavelengths of c.d. maxima, including the wavelengths of maxima of individual vibronic bands, show little if any variations which could be related to structural type, indicating that alterations in the hydrocarbon framework, if they affect energy levels at all, influence the ground and excited states equally. Wavelengths of c.d. bands do, however, vary with solvent (p. 1097).

Terminology.—The colloquial expressions, 'octant' and 'anti-octant' have been used above and in all previous work on ketones. For reasons stated elsewhere,²⁴ we have adopted the terms 'consignate' and 'dissignate' for the designation of signs of group-

contributions to chiral properties. The chromophore is placed in a right-handed Cartesian co-ordinate frame. A structural feature at a point P is said to have a 'consignate' effect if the sign of its o.r.d. or c.d. contribution is the same as the sign of the product of the Cartesian co-ordinates of P; conversely the effect is 'dissignate' (pronounced 'dis-signate') if the two signs are opposite. For the carbonyl $n \rightarrow \pi^*$ transition, 'consignate' is synonymous with 'octant' behaviour (Figure 2a) and 'dissignate' with 'anti-octant' behaviour (Figure 2b) in terms of the original Rule.⁴

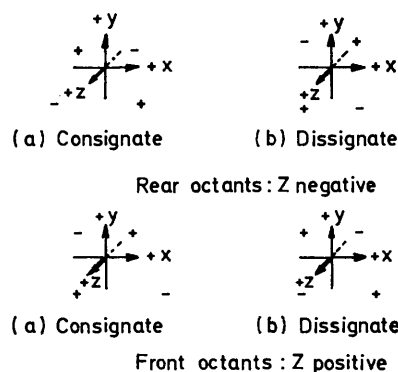


FIGURE 2 Designation of chiral properties

TABLE 2

New polycyclic ketones prepared for c.d. study

Formula no.	Compound	$\Delta\epsilon$ (hexane) *
Tricyclic		
(2)	(-)- <i>trans, syn, trans</i> -Perhydroanthracen-2-one	-1.40
(3)	Des-D-5 α ,13 β (H)-androstan-2-one	+1.50
(4)	Des-D-5 α ,13 β (H)-androstan-6-one	-0.70
(5)	Des-D-5 α ,13 β (H)-androstan-7-one	-0.35
Tetracyclic		
(6)	D-Homo-5 α -androstan-2-one	+1.75
(7)	5 α -Estran-4-one	-1.30
(8)	D-Homo-5 α -androstan-6-one	-0.50
(9)	5 α -Estran-6-one	-0.95
(10)	6 α -Methyl-5 β -cholestan-3-one	0.0
Pentacyclic		
(11)	2 α ,3 β -(4-Oxotetramethylene)-5 α -cholestane	-0.75

* $\Delta\epsilon$ values to nearest 0.05 unit. For details of $\Delta\epsilon$ values in various solvents, see Table 10.

EXTENDED ('ALL-*trans*') DECALONE SYSTEMS

Table 2 lists the new ketones (2)—(11) which have been synthesised²⁵ to provide answers to specific questions concerning the contributions of key structural features to chiroptical properties.

In addition to the compounds in the Table, samples of optically pure (+)-(9*S*,10*R*)-*trans*-1-decalone (12) and (-)-(9*R*,10*R*)-*trans*-2-decalone (13) have been prepared (by Dr. F. Fernandez²⁶): these ketones provided essential c.d. data for the parent bicyclic systems (previous papers quote only o.r.d. data), allowing estimation of contributions of extra rings and methyl substituents

²² C. Djerassi, 'Optical Rotatory Dispersion: Applications to Organic Chemistry,' McGraw-Hill, New York, 1960, ch. 12.

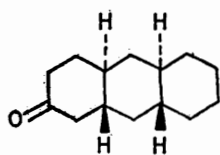
²³ O. Weigang, jun., *J. Chem. Phys.*, 1965, **43**, 3609.

²⁴ W. Klyne and D. N. Kirk, *Tetrahedron Letters*, 1973, 1483.

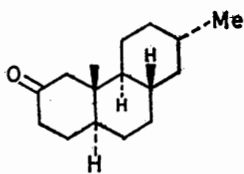
²⁵ D. N. Kirk, in preparation.

²⁶ F. Fernandez, D. N. Kirk, and P. M. Scopes, *J.C.S. Perkin I*, 1974, 18.

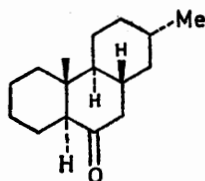
by pairwise comparisons with related but more complex molecules.



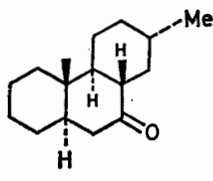
(2)



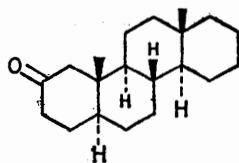
(3)



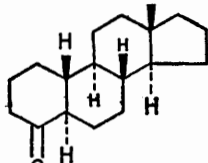
(4)



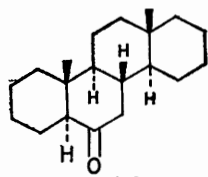
(5)



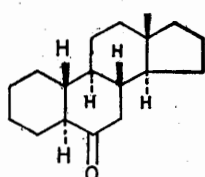
(6)



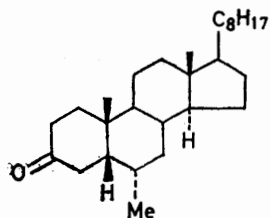
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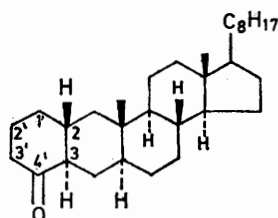
(8)



(9)



(10)



(11)

Some of the main conclusions from the study of c.d. data (Table 2; see also Table 10) for these new compounds are summarised here: their fuller implications will become apparent later.

(-)-trans,syn,trans-Perhydroanthracen-2-one (2)²⁶ (cf. Bloch's 3'-oxo 'pentacyclic' steroid analogue²⁷).

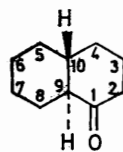
²⁷ J.-C. Bloch and G. Ourisson, *Bull. Soc. chim. France*, 1964, 3018.

²⁶ G. Shtatzke and F. Werner-Zamojska, *Tetrahedron Letters*, 1972, 4275.

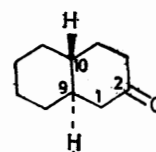
Comparison with *trans*-2-decalone shows that the 'third' ring makes a considerable contribution to $\Delta\epsilon$ (consignate; 0.3–0.5 units, depending upon solvent).

Des-D-5 α ,13 β (H)-androstan-2-one (3) and D-homo-5 α -androstan-2-one (6). The fourth ring in (6), though remote from the oxo-group, makes a consignate contribution which is by no means negligible (0.2–0.4 units). Ring D in an ordinary 2-oxo-5 α -steroid has a similar effect (p. 1085).

2 α ,3 β -(4-Oxotetramethylene)-5 α -cholestane (11). The $\Delta\epsilon$ values are not significantly different from those of



(12)



(13)

trans-1-decalone, showing that the third and further rings are without effect in this case.

5 α -Estran-4-one (7). Comparison of this 19-nor-compound ($\Delta\epsilon$ -1.3) with a typical 4-oxo-5 α -steroid containing the 10-methyl group ($\Delta\epsilon$ -1.6) shows that the β -axial methyl group here makes a consignate contribution, similar to the effect of a β -axial methyl group in a variety of steroids of the *trans*-2-decalone type (e.g. 2-oxo-5 α - and 5-methyl-3-oxo-5 α -steroids,^{5c} and some 3-oxo-compounds of 'unnatural' configuration¹⁵).

5 α -Estran-6-one (9). In sharp contrast to the 4-oxo-compounds, the 6-oxo-19-nor- and ordinary 6-oxo-steroids reveal a negligible or very weakly dissignate effect of the 10-methyl group. (This apparent anomaly had been a cause for concern earlier—see p. 1096.) Although dissignate behaviour of certain β -axial methyl or methylene substituents is now well recognised,^{14,15,28} the structural features which decide whether a β -axial C-C bond has a consignate or a dissignate effect have not hitherto been defined (but see p. 1081).

Des-D-5 α ,13 β (H)-androstan-7-one (5): front octant effects. Synthesis of the *des*-D-7-oxo-(tricyclic) compound (5)^{2b} and of D-homo-5 α -androstan-7-one²⁹ made it possible to determine directly for the first time the 'front octant' contributions of both the five-membered ring D in 5 α -androstan-7-one and the six-membered ring D in the D-homo analogue;^{2b} the results establish beyond doubt³⁰ that an octant rule rather than a quadrant rule applies to these compounds. The D-homo-ring makes a significant contribution, of the expected 'front octant' sign, whereas the five-membered D-ring in the normal androstane derivative makes a much smaller contribution, though of the same sign. These experimental results provide the first reliable values for the contributions of 'front octant' rings (for further discussion, see p. 1096).

The increments due to ring D in the 7-oxo-D-homo-²⁹ D. N. Kirk and M. A. Wilson, *J. Chem. Soc. (C)*, 1971, 414. ³⁰ (a) J. A. Schellman, *J. Chem. Phys.*, 1966, 44, 55; (b) E. G. Höhn and O. E. Weigang, *ibid.*, 1968, 48, 1127; (c) G. Wagnière, *J. Amer. Chem. Soc.*, 1966, 88, 3937.

steroid system are used later (p. 1084) in the evaluation of effects of further substituents in related structures.

6 α -Methyl-5 β -cholestan-3-one (10): '6 α -methyl group' effects. The dissignate behaviour of a 6 α -methyl group in a 3-oxo-5 α -steroid⁷ has now also been found in the 3-oxo-5 β -analogue. Molecular models show that the spatial relationships and bonding patterns between the carbonyl and the 6 α -methyl group in the 5 α - and 5 β -compounds are of enantiomeric type but otherwise identical. The 6 α -bond, which we label in the general case as γ' -equatorial (Figure 4), has analogies in structures of the 2-oxo-5 α - and 6-oxo-steroid type (the 9,11- and 14,15-bonds, respectively: see following paragraph).

Des-D-5 α ,13 β (H)-androstan-6-one (4) and D-homo-5 α -androstan-6-one (8). The des-D-ketone (4) shows a significantly more negative $\Delta\epsilon$ value (-0.7) than the D-homo-compound (8) ($\Delta\epsilon -0.5$). The latter ketone possesses the γ' -equatorial C(14)-C(15) bond, which is here exhibiting typical dissignate behaviour by making a contribution of positive sign (*cf.* preceding paragraph). Moreover, a comparison of $\Delta\epsilon$ for D-homo-5 α -androstan-6-one (8) with that for 5 α -androstan-6-one ($\Delta\epsilon -0.96$) reveals a significantly enhanced negative (consignate) contribution from the five-membered D-ring in the latter compound (*cf.* p. 1099). The D-ring is known to be a region of considerable strain, which resides largely in and around the C(13)-C(14) bond common to rings C and D;³¹ the observed enhanced c.d. effect is consistent with the hypothesis, proposed and developed below, concerning the special role of certain coplanar zig-zags of bonds. Recognition of the possibly enhanced effect of a highly strained bond calls for caution in the use of numerical data derived from compounds including such bonds. The phenomenon probably has analogies in the enhanced C-C hyperconjugation^{32a} and accelerated solvolytic rates^{32b} observed for compounds containing strained bonds; all these effects can be seen as consequences of enhanced polarisability of strained C-C bonds.

New Hypotheses.—Consideration of c.d. data for the new compounds mentioned above, and also of the wide range of reliable data now available for previously known ketones, permits the following generalisations.

(i) Those ketones of the extended 'all-*trans*'-decalone class which exhibit markedly enhanced Cotton effects, when compared with their parent bicyclic ketones, are those in which the additional rings (in rear octants) include bonds which add to the length of a planar zig-zag of bonds of the type defined on p. 1077 (Figure 1). Such compounds include (2), (3), (6), and (7) (*cf.* Table 2), as well as other steroidal ketones considered later. It seems to be immaterial whether the planar zig-zag is extended by rings added in the manner of a perhydroanthracene [*e.g.* (2)], or in that of a perhydrophenanthrene [*e.g.* (3), (6), and (7)]. Where the third and subsequent rings do not extend the critical zig-zag of

bonds [*e.g.* compound (11) and most *cis*-decalones; see p. 1095] there is no enhancement of the Cotton effect, which remains essentially that of the parent decalone.

We therefore offer the hypothesis that the length of the zig-zag of bonds defined above (which we shall term a 'primary zig-zag'; *cf.* Figure 3) is a major factor in determining the magnitude of the perturbation of the carbonyl chromophore, and in the observed dichroism of extended decalones. This hypothesis is examined in more detail later (pp. 1086 and 1100).

(ii) The special significance of primary zig-zags, proposed in hypothesis (i), also provides for a distinction between those structures in which a β -axial methyl substituent shows consignate or dissignate behaviour, respectively. Our second hypothesis is in two parts: (a) that the effect of a β -axial methyl group is *consignate* (*ca.* 0.5 unit) if that group is a substituent on a primary

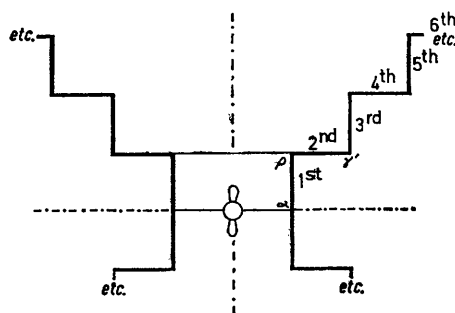


FIGURE 3 Primary zig-zags of bonds (heavy lines): octant projection

zig-zag which extends beyond the first two C-C bonds (*i.e.* the C α -C β bond and the β -equatorial bond of a cyclohexanone); (b) that the effect of a β -axial methyl group is weakly *dissignate* (*ca.* 0.1 unit), if the primary zig-zag carrying it comprises only one or two bonds. We cannot at present comment on the reasons underlying this distinction, but it has provided an empirical rationalisation of all the known β -axial methyl (or methylene) contributions of either type. Most significantly, it has permitted an interpretation of data for *cis*-decalones for the first time within the same scheme as *trans*-decalones (p. 1095).

The suggestion that chiroptical effects in ketones can be related to the lengths of primary zig-zags is, at present, entirely empirical. It is not meant to imply any particular mechanism of perturbation of the chromophore by the bonds of the zig-zag, although a mechanism may emerge from future theoretical considerations (see p. 1100). We note, however, the close parallel between our first hypothesis and that of Hudc¹⁸ concerning effects of hetero-atoms (p. 1077), and we draw attention to other phenomena which are thought to depend upon the special inductive, polarisability, or related properties of extended hydrocarbon chains. These include the ionisation potentials of hydrocarbons³³ and their functional derivatives,³⁴ the acidities of homologous fatty

³¹ C. Altona, H. J. Geise, and C. Romers, *Tetrahedron*, 1968, **24**, 13.

³² F. R. Jensen and B. E. Smart, *J. Amer. Chem. Soc.*, 1969, **91**, (a) 5686; (b) 5688.

³³ G. G. Hall, *Trans. Faraday Soc.*, 1953, **49**, 113; 1954, **50**, 319.

³⁴ L. S. Levitt and B. W. Levitt, *Tetrahedron*, 1973, **29**, 941; L. S. Levitt, B. W. Levitt, and C. Parkanyi, *ibid.*, 1972, **28**, 3369; B. W. Levitt and L. S. Levitt, *Chem. and Ind.*, 1972, 724, and references therein.

α -Equatorial methyl groups have been assigned contributions of 0.2 units in the three less polar solvents, or 0.15 units in methanol or ethanol, as the values giving the best overall fit with experimental data. In an early paper^{13b} concerned with the o.r.d. of monocyclic ketones, an amplitude a of 9 units was considered to be a maximum for the α -equatorial methyl group: larger values observed for $2eq$ -methylcyclohexanones were attributed to contributions from higher-energy conformers, including twisted rings. Although the α -equatorial methyl group is close to a nodal plane of the chromophore, the correct sign of its chiroptical contribution is best obtained by visualising the methyl group as projecting slightly 'above' this nodal plane (Figure 4; octant diagram), in contrast to the α -axial methyl group which clearly projects 'below' the plane.

β -Axial methyl contributions are divided into the two classes discussed above (p. 1081).

γ' -Axial and γ' -equatorial methyl contributions are taken from our own data for 6β - and 6α -methyl-3-oxo-steroids.

β' -Methyl substituents are found in very few of the present compounds (e.g. 10β -Me in 11-oxo-steroids, 14α -Me in certain 7-oxo-steroids). The two β' -C-C bonds make almost equal angles above and below the 'horizontal' nodal plane of the carbonyl group (Figure 4), so that the axial/equatorial distinction may be unimportant. β' -Substituents probably project into the front octant regions, the contributions of β' -methyl groups then appearing to be weakly octant-consignate, that is, their signs are the reverse of those for substituents in the corresponding rear octants. With so few examples available for study, a value of 0.2 for $\delta\Delta\epsilon$ (consignate) is provisionally adopted, irrespective of solvent.

Alkyl substituents other than methyl are not generally covered by the present work. It seems reasonable to use published increments where necessary for α -axial or equatorial isopropyl^{43a} or t -butyl groups,^{43b} with conversion of o.r.d. measurements (δa) into their c.d. equivalents ($\delta\Delta\epsilon$) by use of the formula:⁹ $\Delta\epsilon = a/40.28$. Table 3 includes suggested values of $\delta\Delta\epsilon$ for β -equatorial ethyl, isopropyl, and t -butyl groups, although little use is made of these in the present work.

Classification System for Polycyclic Extended Decalones.

—The following scheme was devised to simplify classification of polycyclic systems, and the recognition of structural and stereochemical features of molecules containing them.

The carbonyl group is used as the origin, and each ring is then related in turn to the cyclohexanone ring (assuming an undistorted 'diamond network' structure, comprising fused six-membered rings, each in the chair conformation).

Each ring is located unambiguously as follows:

- (1) The cyclohexanone ring is numbered as in Figure 5.
- (2) Configurations at ring junctions are defined by the abbreviations c for *cis* and t for *trans*.
- (3) The location of the second ring is given by the number of the carbon atom (2 or 3) which is its *nearest* point of attachment relative to the carbonyl group of the

cyclohexanone. Use of primed or unprimed locants allows a distinction between enantiomers: *unprimed* locants are used in the *clockwise* progression round the cyclohexanone ring, *primed* for *anticlockwise*. With the ring in the orientation illustrated, unprimed locants imply that the second ring is in a 'positive' octant, and primed locants that it is in a 'negative' octant.

(4) The *conformation* of the particular bond in the second ring located according to rule (3) is designated as *ax* (axial) or *eq* (equatorial) with reference to the first ring. This is necessary for *cis* junctions, but not for *trans* junctions, where it is always *eq*.

The second ring is uniquely defined by these rules, which provide convenient symbols (Figure 5) for the six decalone types (the enantiomers have primed digits in each case).

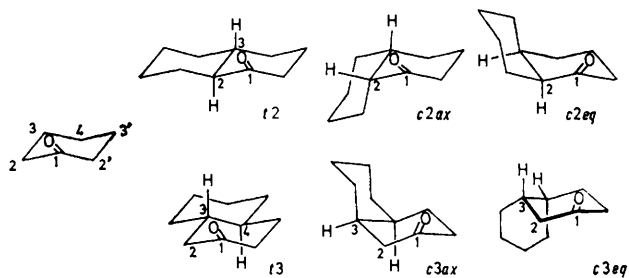


FIGURE 5 Classification system for decalones

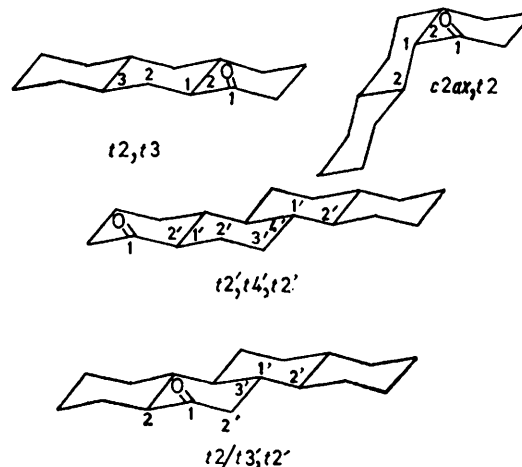


FIGURE 6 Examples of the classification of 'extended' decalones'

An extension of the rules allows us to define third and subsequent rings with equal ease. The n th ring is numbered from the carbon atom defining its coded point of fusion to the $(n - 1)$ th ring. This carbon atom is number 1 for the n th ring, which is then numbered sequentially *in the same sense* as the first ring, with locants primed or unprimed. The location (in this case 2, 3, or 4), and type (*ax* or *eq*) of the $(n + 1)$ th ring is then indicated according to rules (2)—(4).

This system provides compact descriptions of all the isomeric perhydrophenanthrenes and perhydroanthracenes, as well as tetracyclic and larger systems. 'Middle

⁴³ (a) C. Djerassi, P. A. Hart, and C. Beard, *J. Amer. Chem. Soc.*, 1964, **86**, 85; (b) C. Djerassi, P. A. Hart, and E. J. Warawa, *ibid.*, p. 78.

ring' ketones, that is those with 'second' rings to both left and right of the carbonyl group, like 6-oxo-steroids, are indicated by a combination of terms with primed and unprimed digits, separated by a solidus (/) to avoid confusion (for illustrations, see Figure 6).

TABLE 5
Contributions of bicyclic structures to c.d.
(actual values for *trans*-decalones)

Ketone	Ring symbol	$\Delta\epsilon$ ($n \rightarrow \pi^*$)			
		Hexane	Dioxan	MeCN	MeOH
(9 <i>S</i> ,10 <i>R</i>)- <i>trans</i> -1-Decalone (12)	<i>t2</i>	+0.81	+0.86	+0.85	+0.95 ^a
(9 <i>S</i> ,10 <i>S</i>)- <i>trans</i> -2-Decalone ^b [enantiomer of (13)]	<i>t3</i> ^b	+1.12	+1.28	+1.36	+1.37

^a Compare *a* + 40, ref. 3*a*. ^b Measurements were made on the enantiomer, (13) itself (9*R*,10*R*; *t3'*), which gave the corresponding $\Delta\epsilon$ values of negative sign.

These representations allow easy recognition of structural relationships. The system is of particular value in discussing *cis*-decalones, by providing a clear distinction

as a unit of structure. The next step was the derivation of contributions from 'third' rings of perhydrophenanthrene and perhydroanthracene analogues of the *trans*-decalones. Only one of the six parent tricyclic ketones (2) is so far available,²⁵ but estimates of the $\Delta\epsilon$ values for the others were made by inspection of data for accessible derivatives (including some new ketones listed in Table 2) and calculation of reference values as follows.

Each of the six tricyclic structures (Table 6) is represented by one or more steroid-like compounds of suitable structure. Estimates of $\Delta\epsilon$ values for the parent tricyclic systems were obtained by assuming additivity of structural contributions, and allowing appropriate increments ($\delta\Delta\epsilon$) for methyl substituents (Table 3), also for any extra rings (*e.g.* in *D*-homo-5 α -androstan-6-one, where ring A is regarded as contributing an increment corresponding to its character as a 'second' ring: Table 5); a few of the $\Delta\epsilon$ values used in Table 6 had to be estimated from published o.r.d. amplitudes (*a*) ($\Delta\epsilon = a/40.28$),⁹ when materials were no longer available for c.d. measurements. Comparisons of observed and

TABLE 6
Contributions of third rings to $\Delta\epsilon$
[(+) sign indicates consignate behaviour; (-) indicates dissignate behaviour]
Estimated $\Delta\epsilon$ ^b for parent tricyclic ketone (with no additional substituents)

Structure class	Compounds used in analysis ^a	Estimated $\Delta\epsilon$ ^b for parent tricyclic ketone (with no additional substituents)				Contribution ($\delta\Delta\epsilon$) of third ring ^a			
		Hexane	Dioxan	MeCN	MeOH or EtOH	Hexane	Dioxan	MeCN	MeOH or EtOH
<i>t2,t2</i>	Des-D-7-oxo-5 α -steroid (5) and D-homo-7-oxo-5 α -steroid (direct comparison)	(+) 1.45			(+) 1.95	(+) 0.65 ^d			(+) 1.0 ^d
<i>t2,t3</i>	2 α ,3 β -(4-Oxotetramethylene)-5 α -cholestane (11)	(+) 0.75			(+) 1.0	(-) 0.05			<i>ca.</i> 0
<i>t2,t4</i>	4-Oxo-5 α -steroid, 19-nor-4-oxo-5 α -steroid, des-D-14-oxo-5 α -steroid, and D-homo-17 α -oxo-5 α -steroid	(+) 1.2	(+) 1.35	(+) 1.4	(+) 1.6	(+) 0.4	(+) 0.5	(+) 0.55	(+) 0.65
<i>t3,t2</i>	Des-D-2-oxo-5 α -steroid (3) and D-homo-6-oxo-5 α -steroid (8)	(+) 1.05	(+) 1.15	(+) 1.2	(+) 1.35	(-) 0.05	(-) 0.15	(-) 0.15	<i>ca.</i> 0
<i>t3,t3</i>	2 α ,3 β -(3-Oxotetramethylene)-5 α -cholestane and analogous tricyclic ketone (2)	(+) 1.5	(+) 1.7	(+) 1.8	(+) 1.9	(+) 0.4	(+) 0.4	(+) 0.45	(+) 0.5
<i>t3,t4</i>	3-Oxo- (and 19-nor-) 5 α steroids, D-homo-17-oxo-5 α -steroids, and des-A-5-oxo-steroids	(+) 1.1	(+) 1.25	(+) 1.35	(+) 1.4	0	≥ 0.05	≥ 0.05	0

^a The enantiomeric form of the compound, with sign of $\Delta\epsilon$ reversed, was used for comparison where necessary. ^b For previous estimates, see ref. 6. ^c Values obtained by subtracting $\Delta\epsilon$ for the corresponding decalone from $\Delta\epsilon$ for the tricyclic ketone. ^d Ref. 8*b*.

between conformers hitherto often classed as either 'steroid-like' or 'non-steroid',⁴⁴ by comparison with the 5 β -steroid framework.

Analysis of C.d. Data for Extended trans-Decalones, in Terms of Ring Contributions.—Bicyclic ketones. Optical resolution of *trans*-1- and 2-decalols as their 3 β -acetoxy-eti-5-enates²⁶ allowed us to obtain c.d. data for the corresponding *trans*-decalones in a range of solvents (Table 5). Values of $\Delta\epsilon$ agree well with estimates based upon earlier o.r.d. data, supporting the reliability of the theoretical relationship:⁹ $a = 40.28\Delta\epsilon$.

Tricyclic ketones. The measured $\Delta\epsilon$ values for the bicyclic ketones (Table 5) were treated as representing the contributions ($\delta\Delta\epsilon$) of the 'second' ring, regarded

'calculated' $\Delta\epsilon$ values, whenever feasible, have generally given good agreement, with a maximum error of about ± 0.2 units. The present best estimates of $\Delta\epsilon$ values for the parent tricyclic ketones involved, in some cases, an element of judgement as to the reliability of each of several derived values, although in no cases did these values cover a very wide range. The best values are considered to be those which require fewest allowances for extra substituents, and which are based upon recent c.d. measurements.

An interesting and significant feature emerges from comparison of the 'third ring' contributions in the 4-oxo-5 α - and 2-oxo-5 α -steroid types (*t2,t4'* and *t3,t2*, respectively). 'Ring c' is in the same spatial relationship to the cyclohexanone ring (A) in each case, but the structures differ in the location of the second ring. Both

⁴⁴ See, for example, D. C. Hamsher, A. R. Pinder, and S. R. Wallis, *J. Chem. Soc. (C)*, 1968, 2941.

formulae (the 4-oxo-structure in its *enanti*-form) may be superimposed to give a single diagram (Figure 7).

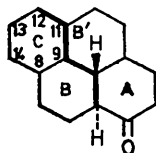


FIGURE 7 Comparison of 'third-ring' contributions in *t2,t4* and *t3,t2* structures (see Table 7)

TABLE 7

Comparison of 'third ring' contributions ($\delta\Delta\epsilon$) for ketones of the 4-oxo-5 α - and 2-oxo-5 α -steroid types (Figure 7)

	Solvent	Hexane	Dioxan	MeCN	MeOH
$\delta\Delta\epsilon$ Values (con-signate) for ring c in AB + c (<i>ent</i> -'4-oxo'-type: <i>t2',t4'</i>)	$\delta\Delta\epsilon$:	+0.4	+0.5	+0.55	+0.65
$\delta\Delta\epsilon$ Values (dissig-nate) for ring c in AB' + c ('2-oxo'-type: <i>t3,t2</i>)	$\delta\Delta\epsilon$:	-0.05	-0.15	-0.15	0.0
Differences		0.45	0.65	0.7	0.65

Table 7 compares the 'third ring' contributions, which differ considerably, for each of the two tricyclic structures. The reason for the estimated differences

γ' -equatorial type (*cf.* p. 1081) and therefore makes a small dissignate contribution, by analogy with a methyl substituent in the same location.

Fourth rings. Only a few of the numerous possible tetracyclic 'extended all-*trans* decalones' are represented by available compounds with a fourth cyclohexane ring. Some additional examples are provided by steroids where the fourth ring is five-membered, but these must be viewed with caution, since the effects of ring size and strain on c.d. may be appreciable (p. 1099). Table 8 contains data for those known tetracyclic ketones (*e.g.* perhydrocyclopentaphenanthrene and perhydrochrysene ketones) which appear to be useful models, and compares the $\Delta\epsilon$ values with those 'calculated' for their tricyclic analogues (from Table 6). Allowance is made in the 'tricyclic' columns of Table 8 for the contributions of any methyl groups present.

The fourth ring seems generally to make only a small contribution (<0.2), within the limits of experimental error. The only very significant exceptions, where the 'fourth-ring' contribution is too large to be ignored, are the 2-oxo-5 α -, 2-oxo-D-homo-5 α - and 16-oxo-D-homo-5 α -steroids, where the fourth ring in each case adds a bond or bonds to the primary zig-zag. The five-membered ring D in the normal 2-oxo-5 α -steroid contributes almost the same increment as the D-homo-ring: ring strain may possibly compensate for the marked divergence of the

TABLE 8
Contributions from fourth rings

Compound	Code *	$\Delta\epsilon$ (Typical value observed for tetracyclic compounds)		$\Delta\epsilon$ (Estimated for tricyclic analogue)†		$\delta\Delta\epsilon$ (Fourth ring) ‡	
		Hexane	MeOH	Hexane	MeOH	Hexane	MeOH
		1-Oxo-5 α -steroid	<i>t2',t2',t4'</i> *	-0.1	-0.4	+0.15	-0.25
2-Oxo-5 α -steroid	<i>t3,t2,t4</i> *	+1.7	+2.45	+1.5	+1.95	+0.2	+0.5
2-Oxo-D-homo-5 α -steroid	<i>t3,t2,t4</i>	+1.7	+2.3	+1.5	+1.95	+0.2	+0.35
3-Oxo-19-nor-5 α -steroid	<i>t3,t4,t2</i> *	+1.1	+1.4	+1.1	+1.4	0.0	0.0
3-Oxo-5 α -steroid	<i>t3,t4,t2</i> *	+0.8	+1.2	+0.85	+1.2	-0.05	0.0
4-Oxo-19-nor-5 α -steroid	<i>t2',t4',t2'</i> *	-1.2	-1.5	-1.2	-1.6	0.0	+0.1
4-Oxo-5 α -steroid	<i>t2',t4',t2'</i> *	-1.6	-2.0	-1.65	-2.2	+0.05	+0.2
4'-Oxo-'pentacyclic' steroid (11)	<i>t2',t3',t4'</i>	-0.75	-1.0	-0.75	-1.0	0.0	0.0
16-Oxo-D-homo-5 α -steroid	<i>t3',t2',t4'</i>	-1.1	-1.8	-0.8	-1.15	-0.3	-0.65
17-Oxo-D-homo-5 α -steroid	<i>t3',t4',t2'</i>	-1.5	-2.0	-1.55	-2.0	+0.05	0.0
17a-Oxo-D-homo-5 α -steroid	<i>t2,t4,t2</i>	-0.25	+0.05	-0.4	-0.1	+0.15	+0.15

* The fourth ring is coded here as if it were a cyclohexane, although in the cases marked by an asterisk it is a five-membered ring. † $\Delta\epsilon$ (estimated for tricyclic analogue) is the value 'calculated' for the corresponding tricyclic structure plus any methyl groups present. ‡ $\delta\Delta\epsilon$ (Fourth ring) = $\Delta\epsilon$ (observed for tetracyclic compound) - $\Delta\epsilon$ (estimated for tricyclic analogue).

between the two sets of contributions due to ring c is that in converting each bicyclic structure [either (A + B) or (A + B')] into the tricyclic structure, a different set of bonds (or atoms) is added. With 'ring c' numbered as in Figure 7, bonds 11,12, 12,13, 13,14, and 8,14 are added in each case, but the addition of ring c to AB also adds the 9,11-bond (or C-11), whereas the addition of ring c to AB' adds the 8,9-bond (or C-8).

The 'differences' in Table 7 therefore represent the differences between the individual contributions of these two C-C bonds (with their associated C-H bonds), assuming additivity of bond contributions. The 9,11-bond makes the larger (consignate) contribution, consistent with its location on the primary zig-zag (thickened bonds in Figure 7). The 8,9-bond, in contrast, is of the

C(15)-C(16) bond from coplanarity with the zig-zag extending from C(2) to C(15) (p. 1099). There is a possibility that the fourth-ring contribution in a 1-oxo-5 α -steroid also has some significance (p. 1096).

Although fourth-ring contributions have been evaluated here only for the solvents hexane and methanol, it seems reasonable to interpolate values for the two solvents of intermediate character, dioxan and acetonitrile (p. 1097).

With $\Delta\epsilon$ values generally becoming vanishingly small at the fourth ring, it seems reasonable to ignore the effects of any fifth and subsequent rings, with the possible exception of cases where a primary zig-zag is further extended, although even here any contributions of further rings would be very small.

Conclusions regarding contributions of rings to the total observed $\Delta\epsilon$ value for each of the four solvents are summarised in Figure 8.

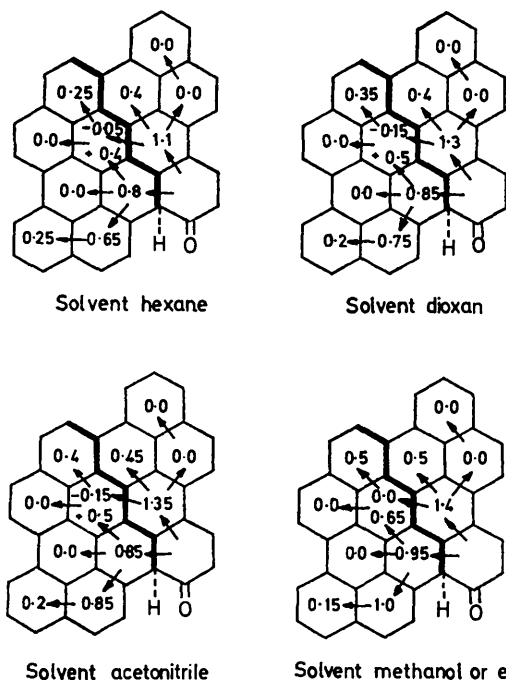


FIGURE 8 Contributions ($\delta\Delta\epsilon$) of individual rings (all-*trans*; arrows indicate connectivity of polycyclic systems)

By summing appropriate combinations of the values so far estimated for rings, we have 'calculated' values of $\Delta\epsilon$ for most of the unsubstituted 'all-*trans*' structures now available, or likely to become available in the near future. Table 9 lists calculated $\Delta\epsilon$ values for the known

TABLE 9
Contributions of arrays of *trans*-fused cyclohexane rings to the c.d. of cyclohexanones
($\Delta\epsilon$ values derived from data in Tables 5, 6, and 8)

		$\Delta\epsilon(n \rightarrow \pi^*)$			
		Hexane	Dioxan	MeCN	MeOH or EtOH
Bicyclic	Code †				
	<i>t2</i>	+0.8	+0.85	+0.85	+0.95
Tricyclic	<i>t3</i>	+1.1	+1.3	+1.35	+1.4
	<i>t2, t2</i>	+1.45	+1.6	+1.7	+1.95
	<i>t2, t3</i>	+0.75	+0.85	+0.95	+1.0
	<i>t2, t4</i>	+1.2	+1.35	+1.4	+1.6
	<i>t3, t2</i>	+1.05	+1.15	+1.2	+1.35
	<i>t3, t3</i>	+1.5	+1.7	+1.8	+1.9
	<i>t3, t4</i>	+1.1	+1.25	+1.35	+1.4
Tetracyclic	<i>t2, t2, t4</i>	+1.7	+1.8	+1.9	+2.1
	<i>t2, t3, t4</i>	+0.75	+0.85	+0.95	+1.0
	<i>t2, t4, t2</i>	+1.2	+1.4	+1.5	+1.6
	<i>t3, t2, t4</i>	+1.25	+1.4	+1.6	+1.8
	<i>t3, t3, t4</i>	+1.5	+1.7	+1.8	+1.9
	<i>t3, t4, t2</i>	+1.1	+1.25	+1.35	+1.4

† The ring systems coded here with unprimed digits (see p. 1083) all give $\Delta\epsilon$ values with a positive sign, as indicated; the enantiomeric ring systems, coded with primed digits, give the same $\Delta\epsilon$ values but with a negative sign.

fundamental (unsubstituted) skeletons based upon the *trans*-decalones, with up to four rings. These values may be used, along with increments for any methyl

substituents (Table 3), to 'predict' total $\Delta\epsilon$ values for a wide variety of polycyclic ketones based upon *trans*-decalones.

Table 10 compares the 'calculated' with the experimental values of $\Delta\epsilon$ for 68 compounds, which cover all the common 5 α -steroidal ketones, except the 6-, 11-, and 12-oxo-steroids with a normal five-membered ring D: these exceptional compounds are discussed later (p. 1097 and Table 16). A variety of other steroidal and *trans*-decalone derivatives are also included. Agreement in $\Delta\epsilon$ values is usually within ± 0.2 units, except for compounds which are known to be distorted from ideal geometry (see p. 1099).

Significantly large deviations of 'calculated' from observed values of $\Delta\epsilon$ in Table 10 are also found in the 7-oxo- and 12-oxo-D-homo-compounds (entries 42, 43, and 47). The 'calculated' values of $\Delta\epsilon$ deviate in the positive sense for the 7-oxo-compounds (by 0.3–0.4 units in hexane or 0.6 units in methanol), and in the negative sense for the 12-oxo-compounds (by –0.34 units in hexane or –0.45 units in methanol). The reasons for these deviations cannot be deduced from the available data, but we note that the departure from precise additivity is in each case of a sign such that either too large a contribution is being attributed to the *trans*-1-decalone (*t2*) fragment of each molecule, or too small a contribution is being attributed to the *trans*-2-decalone (*t3*) component. The 6-oxo-D-homo-compound (Table 10; entry 39) shows similar though smaller deviations which support this tentative generalisation.

It seems to follow that a 'middle-ring' ketone of the 'all-*trans*' perhydrophenanthrene class does not perfectly follow the principle of additivity of effects of individual rings. There is clearly a need for the synthesis of the parent tricyclic compound, *trans,anti,trans*-perhydrophenanthren-9-one, free from methyl substituents, so that its c.d. behaviour can be studied directly. Present data suggest a $\Delta\epsilon$ value for this compound of 0.6–0.7 unit, with the sign corresponding to that of the *t3* fragment. Algebraic addition of oppositely signed contributions from *t2* and *t3'* or *t2'* and *t3* rings gives $\Delta\epsilon$ values of only ± 0.3 –0.45 units, depending on the solvent (Table 9); these values are too small to reproduce accurately the observed $\Delta\epsilon$ values for 'middle-ring' ketones in Table 10 (see Discussion section, p. 1102).

The only other significant 'mistfit' of 'calculated' $\Delta\epsilon$ values is for friedelan-3-one (entry 64). This compound has a special structural feature shared by some *cis*-decalone analogues, and is discussed on p. 1094.

'PRIMARY ZIG-ZAGS' OF BONDS

The first stages of this analysis indicated that 'primary zig-zags' either are themselves, or play an important part in defining, the structural features largely responsible for the observed c.d. of many extended decalones. We next tried to evaluate the separate contributions of successive C–C bonds of the primary zig-zag towards the total value of $\Delta\epsilon$.

The carbonyl-C $_{\alpha}$ bond of a cyclohexanone ring lies in

TABLE 10

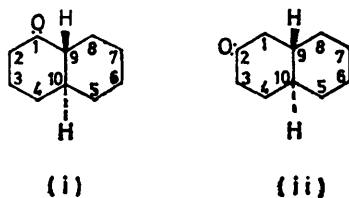
Comparison of 'calculated' ϵ and observed $\Delta\epsilon$ values for extended *trans*-decalones; $n \rightarrow \pi^*$ transition at *ca.* 290 nm ($\Delta\epsilon$ values in italics are derived from o.r.d. data by using the formula $\Delta\epsilon = a/40.28$; ref. 9)

Entry no.	Compound	Ring code	$\Delta\epsilon$ Values								Ref. ^b
			Hexane		Dioxan		Acetonitrile		MeOH or EtOH		
			Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	
5 α ,14 α -Steroids and simpler analogues											
1	1-Oxo	<i>t2',t2',t4'</i>	-0.1	-0.11	-0.15		-0.25	-0.25	-0.4	-0.39	
2	1-Oxo-3 β -Me	<i>t2',t2',t4'</i>	+0.4		+0.4	+0.59 ^c	+0.35		+0.2		aa
3	1-Oxo-19-nor ^d	<i>t2',t2',t4'</i>	-1.7		-1.8		-1.9		-2.1		
4	2-Oxo	<i>t3,t2,t4</i>	+1.7	+1.6	+1.9	+1.78	+2.15	+1.93	+2.4	+2.22 (+2.45)	aa
5	2-Oxo-3 β -Me	<i>t3,t2,t4</i>	+1.55		+1.8	+1.58 ^c	+1.95		+2.35		aa
6	2-Oxo-4,4-Me ₂	<i>t3,t2,t4</i>	+1.3	+1.44	+1.45		+1.7		+1.9		
7	2-Oxo-D-homo (6)	<i>t3,t2,t4</i>	+1.7	+1.73	+1.9		+2.15		+2.4	+2.28	
8	2-Oxo-des-D (3)	<i>t3,t2</i>	+1.5	+1.5	+1.65		+1.75		+1.95	+1.94 +1.99	
9	2-Oxo-19-nor	<i>t3,t2,t4</i>	+1.25		+1.4	+1.49	+1.6		+1.8		bb
10	3-Oxo-D-homo	<i>t3,t4,t2</i>	+0.85	+0.72	+1.0		+1.15	+1.0	+1.2		
11	3-Oxo	<i>t3,t4,t2</i>	+0.85	+0.79	+1.0	+1.03	+1.15	+1.18	+1.2	+1.18 +1.26	
12	3-Oxo-2 α -Me	<i>t3,t4,t2</i>	+0.65	+0.69 +0.68	+0.8	+0.84	+0.95	+0.99	+1.05	+1.07	
13	3-Oxo-2 β -Me ^e	<i>t3,t4,t2</i>	+2.05		+2.3		+2.55		+2.7	+1.8	cc
14	3-Oxo-4 α -Me	<i>t3,t4,t2</i>	+1.05	+0.9	+1.2		+1.35		+1.4	+1.2 +1.3	dd
15	3-Oxo-4 β -Me ^e	<i>t3,t4,t2</i>	-0.45	0.0	-0.3		-0.25	+0.21	-0.3		
16	3-Oxo-4,4-Me ₂ ^e	<i>t3,t4,t2</i>	-0.55	-0.32	-0.45		-0.3	-0.35	-0.35	-0.3	
17	3-Oxo-5 α -Me	<i>t3,t4,t2</i>	+1.3	+1.5	+1.5	+1.3	+1.7		+1.8	+1.8	ce
18	3-Oxo-6 α -Me	<i>t3,t4,t2</i>	+0.6	+0.51	+0.75		+0.85	+0.83	+0.9	+1.04	
19	3-Oxo-6 β -Me	<i>t3,t4,t2</i>	+0.75	+0.68	+0.85		+1.0	+1.09 +0.9	+1.0	+1.0	
20	3-Oxo-9 α -Me	<i>t3,t4,t2</i>	+0.85		+1.0		+1.15		+1.2	+1.25	ff
21	(-)- <i>trans, syn, trans</i> -Perhydroanthracen-2-one (2)	<i>t3',t3'</i>	-1.5	-1.37	-1.7	-1.64	-1.8	-1.76	-1.9	-1.86	
22	3'-Oxo-' pentacyclic ' f	<i>t3,t3,t4,t2</i>	+1.5	+1.62	+1.7	+1.73	+1.8	+1.82	+1.9	+1.98	
23	3-Oxo-19-nor	<i>t3,t4,t2</i>	+1.1	+1.02	+1.25	+1.27	+1.35	+1.3	+1.4 +1.45	+1.43 +1.37	
24	3-Oxo-2 α -Me-19-nor	<i>t3,t4,t2</i>	+0.9		+1.05	+1.2	+1.15		+1.25		gg
25	3-Oxo-2 β -Me-19-nor	<i>t3,t4,t2</i>	+2.3		+2.55	+2.9	+2.75		+2.9		gg
26	3-Oxo-4 α -Me-19-nor	<i>t3,t4,t2</i>	+1.3		+1.45		+1.55		+1.55	+1.35	hh
27	3-Oxo-19-nor-4,4-Me ₂	<i>t3,t4,t2</i>	-0.3	-0.5	-0.2	-0.5	-0.1		-0.15	-0.5	cc, ii
28	3-Oxo-19-nor-5 α -Me	<i>t3,t4,t2</i>	+1.55	+1.45	+1.75		+1.9	+1.68	+2.0		
29	4-Oxo	<i>t2',t4',t2'</i>	-1.65	-1.66 -1.64	-1.9	-1.69	-2.05	-1.80	-2.2	-1.92	
30	4-Oxo-3 β -Me	<i>t2',t4',t2'</i>	-1.45		-1.7	-2.0 -1.48	-1.85		-2.05		aa, jj
31	4-Oxo-3 α -Me	<i>t2',t4',t2'</i>	-2.85		-3.2		-3.45		-3.75		jj
32	4-Oxo-5 α -Me	<i>t2',t4',t2'</i>	-0.05	+0.3	-0.25		-0.4		-0.5	-0.3	
33	4-Oxo-6 β -Me	<i>t2',t4',t2'</i>	-1.45	-1.32	-1.7		-1.85		-2.0		kk
34	4-Oxo-19-nor (7)	<i>t2',t4',t2'</i>	-1.2	-1.14 -1.28	-1.4	-1.37 -1.50	-1.5	-1.36 -1.50	-1.6	-1.38 -1.46	
35	4'-Oxo-' pentacyclic ' f (11)	<i>t2',t3',t4',t2'</i>	-0.75	-0.76	-0.85		-0.95		-1.0	-1.0	
36	5-Oxo-des-A-19-nor	<i>t3',t4'</i>	-1.1		-1.25		-1.35	-1.29	-1.4	-1.9	
37	6-Oxo-des-A-19-nor ^d	<i>t3',t2'</i>	-1.05		-1.15		-1.2		-1.35		
38	6-Oxo-13 β (H)-des-D (4)	<i>t2/t3'</i>	-0.65	-0.71	-0.8		-0.8		-0.75		
39	6-Oxo-D-homo (8)	<i>t2/t3',t2'</i>	-0.35	-0.52	-0.4	-0.53	-0.45	-0.60	-0.5	-0.56	
40	6-Oxo-5 α -Me-D-homo ^d	<i>t2/t3',t2'</i>	-1.95		-2.05		-2.1		-2.2		
41	6-Oxo-19-nor-D-homo ^d	<i>t2/t3',t2'</i>	-0.25		-0.3		-0.35		-0.4		
42	7-Oxo-des-D (5)	<i>t2/t3'</i>	-0.05	-0.35	-0.2		-0.3	-0.84	-0.25	-0.85	
43	7-Oxo-D-homo	<i>t2,t2/t3'</i>	+0.6	+0.17	+0.55		+0.55		+0.75	+0.13	
44	11-Oxo-D-homo	<i>t3/t2',t2'</i>	+0.3	+0.29	+0.4		+0.4	+0.39	+0.35	+0.2	ll
45	11-Oxo-18-nor-D-homo ^d	<i>t3/t2',t2'</i>	-0.15		-0.1		-0.15		-0.25		
46	11-Oxo-19-nor-D-homo ^d	<i>t3/t2',t2'</i>	+0.1		+0.2		+0.2		+0.15		
47	12-Oxo-D-homo	<i>t3,t2/t2'</i>	+1.75	+2.09	+1.8		+1.85		+1.9	+2.35	
48	13-Oxo-des-D-18-nor	<i>t3,t4</i>	+1.1		+1.3		+1.35		+1.4	+1.2	ff
49	14-Oxo-des-D-18-nor	<i>t2',t4'</i>	-1.1	-1.35	-1.2		-1.25		-1.4	-1.65	dd
50	14-Oxo-des-D-13 α -Me	<i>t2',t4'</i>	-0.9	-0.94	-1.0	-1.06	-1.05	-1.09	-1.25	-1.18 -1.24	
51	16-Oxo-D-homo	<i>t3',t2',t4'</i>	-1.0	-1.1	-1.15		-1.4		-1.6	-1.8	dd
52	17-Oxo-D-homo	<i>t3',t4',t2'</i>	-1.55	-1.53	-1.75		-1.9	-1.83	-2.0	-2.0	
53	17-Oxo-D-homo-17 α -Me	<i>t3',t4',t2'</i>	-0.35		-0.45	-0.5	-0.5		-0.5		ff
54	17-Oxo-D-homo-17 β -Me	<i>t3',t4',t2'</i>	-1.75		-1.95	-2.4	-2.1		-2.15		ff
55	17-Oxo-D-homo, 17 α ,17 α -Me ₂	<i>t3,t4,t2</i>	-0.15		-0.3		-0.45		-0.45	-0.45	ff
56	17 α -Oxo-D-homo	<i>t2,t4,t2</i>	-0.4	-0.25	-0.25	-0.18	-0.15	-0.07	-0.1	+0.06	
57	17 α -Oxo-D-homo-17 α -Me	<i>t2,t4,t2</i>	-0.6	-0.71	-0.45		-0.35		-0.25	-0.4 -0.2	
58	17 α -Oxo-D-homo-17 β -Me ^e	<i>t2,t4,t2</i>	+0.8	+3.56	+1.05		+1.25		+1.4	+4.19	
59	17 α -Oxo-D-homo-17,17-Me ₂ ^e	<i>t2,t4,t2</i>	+1.0		+1.2		+1.3		+1.45	-1.15	mm

TABLE 10 (Continued)

Entry no.	Compound	Ring code	$\Delta\epsilon$ Values								Ref. ^b
			Hexane		Dioxan		Acetonitrile		MeOH or EtOH		
			Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	
Other types of steroids and triterpenes											
60	3-Oxo-5 β ,9 β ,10 α	<i>t</i> 3', <i>c</i> 4' <i>ax</i> , <i>t</i> 2'	-0.85	-0.70	-1.0		-1.15	-1.17	-1.2	-1.13	
										-1.31	<i>nn</i>
61	3-Oxo-19-nor-5 β ,9 β ,10 α	<i>t</i> 3', <i>c</i> 4' <i>ax</i> , <i>t</i> 2'	-1.1		-1.25		-1.35		-1.4	-1.32	<i>nn</i>
62	3-Oxo-5 β ,8 α ,10 α	<i>t</i> 3', <i>c</i> 4' <i>eq</i> , <i>t</i> 2'	-0.85		-1.0		-1.15		-1.2	-1.26	<i>nn</i>
63	3-Oxo-19-nor-5 β ,8 α ,10 α	<i>t</i> 3', <i>c</i> 4' <i>eq</i> , <i>t</i> 2'	-1.1	-1.3	-1.25		-1.35		-1.4	-1.36	<i>nn</i>
64	Friedelan-3-one ^c	<i>t</i> 3', <i>t</i> 4', <i>t</i> 2', <i>c</i> 4' <i>ax</i>	-1.75	-2.16	-1.95	-2.85	-2.1	-2.32	-2.15	-2.56	
65	Friedelan-7-one	<i>t</i> 3/ <i>t</i> 2', <i>t</i> 2', <i>c</i> 4' <i>ax</i>	-0.1	-0.22	+0.05		0.0		-0.1		
<i>trans</i> -Decalones ^d (simple bicyclic examples)											
66	9 β -Me-1-decalone	<i>t</i> 2'	+0.8		+0.8		+0.8		+0.75	+0.7	<i>ff</i>
67	3 β ,9 β -Me ₂ -1-decalone ^e	<i>t</i> 2'	+1.3		+1.35		+1.35		+1.35	+1.2	<i>oo</i>
68	10 α -Me-1-decalone	<i>t</i> 2'	-0.7		-0.75		-0.75		-0.85	-0.41	<i>ff</i>
69	9 β -Me-2-decalone	<i>t</i> 3	+1.55		+1.8		+1.9		+2.0		
70	10 α -Me-2-decalone	<i>t</i> 3	+0.85	+0.64	+1.05		+1.15		+1.2	+1.2	<i>ff</i>
71	8 β ,9 β -Me ₂ -2-decalone	<i>t</i> 3	+1.3		+1.55		+1.6		+1.7	+1.81	<i>ff</i>
72	8 β ,10 α -Me ₂ -2-decalone	<i>t</i> 3	+0.6		+0.8		+0.85	+0.8	+0.9		<i>ff</i>
73	8,8,10 α -Me ₃ -2-decalone	<i>t</i> 3	+0.5		+0.65		+0.7		+0.7	+0.8	<i>ff</i>
74	4 α ,9 β -Me ₂ -6 β -isopropyl-2-decalone	<i>t</i> 3	+1.15		+1.35		+1.35		+1.4	+1.15	<i>pp</i>

^c 'Calculated' values are based upon $\delta\Delta\epsilon$ values in Tables 3 and 9. ^b See footnote references. Where no reference is given, c.d. data were obtained during the present work; italicised $\Delta\epsilon$ values are derived from o.r.d. data in ref. 6. ^e Solvent not stated. ^o No experimental data available; the $\Delta\epsilon$ values indicated here are predictions. ^f Compound expected to be distorted by non-bonded interactions—see p. 1099. ^g Pentacyclic compound derived from 2 α ,3 β -tetramethylene-5 α -cholestane [cf. formula (11) and ref. 26]. ^h See p. 1095. ^d These compounds are named and numbered as derivatives of the 1- and 2-decalone enantiomers (i) and (ii), i.e.



in the forms corresponding in orientation to rings A and B of steroids. Configurations of substituents are indicated as α or β , following the usual steroid convention. ¹ Data were recorded for the enantiomer; sign of $\Delta\epsilon$ reversed. ² B. Cocton and A. Crastes De Paulet, *Bull. Soc. chim. France*, 1966, 2947. ³ M. Fetizon and J.-C. Gramain, *Bull. Soc. chim. France*, 1968, 3301. ⁴ (i) C. Djerassi, O. Halpern, V. Halpern, and B. Riniker, *J. Amer. Chem. Soc.*, 1958, 80, 4001; (ii) P. Witz, H. Herrmann, J.-M. Lehn, and G. Ourisson, *Bull. Soc. chim. France*, 1963, 1101. ⁵ Ref. 6. ⁶ J.-C. Jacquesy and J. Levisalles, *Bull. Soc. chim. France*, 1962, 1866; also ref. 5b. ⁷ Ref. 5a. ⁸ Y. Yamato and H. Kaneko, *Tetrahedron*, 1965, 21, 2501. ⁹ B. Berkoz, E. P. Chavez, and C. Djerassi, *J. Chem. Soc.*, 1962, 1323. ¹⁰ J. M. Midgley, W. B. Whalley, G. F. Katekar, and B. A. Lodge, *Chem. Comm.*, 1965, 169. ¹¹ F. Kohen and R. Stevenson, *J. Org. Chem.*, 1965, 30, 2268. ¹² Sample kindly supplied by Dr. J. R. Bull, Pretoria. ¹³ N. M. Jones, D. N. Kirk, and W. Klyne, in preparation. ¹⁴ M. Uskoković, M. Gut, E. N. Trachtenberg, W. Klyne, and R. I. Dorfman, *J. Amer. Chem. Soc.*, 1960, 82, 4965. ¹⁵ Ref. 15. ¹⁶ Ref. 13a. ¹⁷ D. L. Robinson and D. W. Theobald, *Tetrahedron*, 1968, 24, 5227.

a symmetry plane of the carbonyl group, and cannot itself contribute to the dichroism. The C $_{\alpha}$ -C $_{\beta}$ bond of the cyclohexanone ring is therefore treated as being the first significant bond of the zig-zag. Because of the symmetry of the ring, the contribution of a C $_{\alpha}$ -C $_{\beta}$ bond cannot be evaluated directly, but its spatial relationship to the carbonyl group is essentially similar to that of an α -axial C-C bond (cf. Figure 4). The contribution of an α -axial methyl group (Table 3) is therefore regarded as the best available value for a 'one-bond zig-zag'.

Bonds to hydrogen atoms are not specifically included here, but the $\delta\Delta\epsilon$ values assigned to a particular C-C bond must include the effects of any associated C-H bonds. On the evidence provided by *cis*-decalones (p. 1095), methyl and methylene groups are nearly but not quite equivalent in their effects.

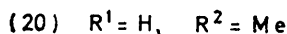
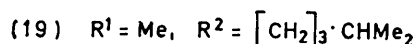
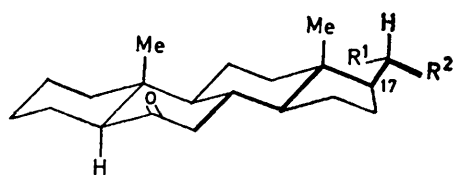
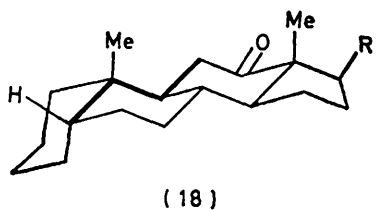
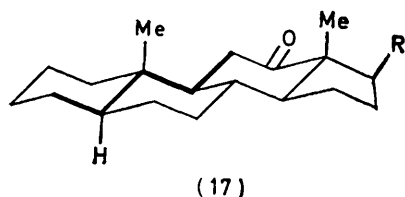
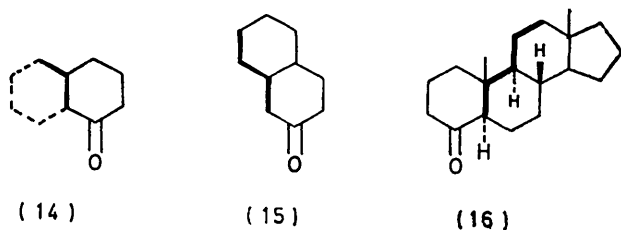
'Two-bond zig-zags' are represented by cyclohexanones with a β -equatorial C-C bond, which may be to a β -equatorial methyl group, or may be part of a second ring (14). The available compounds in this class (mainly *cis*-decalones) are listed in Table 11, with the numerical values (always consignate) of $\Delta\epsilon$. Estimated

contributions of any other C-C bonds, from the values for similarly situated C-Me bonds, are allowed for in arriving at the values ($\delta\Delta\epsilon$) in the final column of Table 11, which gives that part of the total $\Delta\epsilon$ value ascribed to the second bond of the 'primary zig-zag'. Values of $\delta\Delta\epsilon$ for the 'second' bond fall in the range 0.35–0.7 units, most being near the mean value of ca. 0.5 (for hexane as solvent).

'Three-bond zig-zags' are found mainly, but not exclusively, in *trans*-2-decalones (15): Table 11 lists the known examples. With the exception of the last compound listed in this group, which is the only one having a methyl group terminating the zig-zag, all $\delta\Delta\epsilon$ values lie between 0.95 and 1.15, with a mean of ca. 1.0–1.05. By comparison with the effect of the second bond alone (0.5), the third bond is seen to contribute a further 0.5 unit on average.

'Four-bond zig-zags' are limited at present to 'all-*trans*'-perhydrophenanthrene systems like rings A, B, and C (16) of a 5 α -4-oxo-steroid, and a single *trans,cis*-fused perhydroanthracene analogue (Table 11). With the exception of the last entry in this class, which is

based upon a published o.r.d. amplitude (a),²⁶ the values cluster around a mean of 1.25 units, indicating that the 'fourth' bond contributes *ca.* 0.25 units.



12-Oxo-steroids belong to a similar group, but include an uncertain contribution from the five-membered ring D (see p. 1099). However, 5 α -pregnan-12-one (17) ($\Delta\epsilon$ 1.35), and 5 β -cholan-12-one (18) ($\Delta\epsilon$ 1.0) have zig-zags differing by the additional presence of the 'fourth' bond C(5)-C(4) in the 5 α -isomer; the difference ($\delta\Delta\epsilon$ 0.35) is of the expected order of magnitude for the fourth bond [the difference in the side-chain at C-17 is ignored here, but may have some significance (p. 1099)].

'Five-bond zig-zags' are uncommon (Table 11); the perhydroanthracene derivative (2) provides one example. A 2-oxo-5 α -steroid may perhaps fall into this class, for the C(15)-C(16) bond is twisted out of the plane of the zig-zag extending from C(2) to C(15): strain

in ring D is likely, however, to complicate this system (p. 1085). 'Six-bond zig-zags' are found at present only in the 2-oxo-D-homo-5 α - (6) and 16-oxo-D-homo-5 α -steroids (Table 11). Direct comparison of the des-D- and D-homo-2-oxo-steroids indicates that ring D contributes a $\Delta\epsilon$ value of 0.25, which should be a measure of the combined contribution of the 5th and 6th bonds of the zig-zag. Mean $\Delta\epsilon$ values for the five- and six-bond zig-zags (excluding the first bond) are estimated as *ca.* 1.5 and 1.6 units, respectively, suggesting a limiting total contribution not much greater than 1.6 units for those bonds of a very long planar zig-zag which extend beyond the β -carbon atom of a cyclohexanone.

A further indication of increased contributions of zig-zags with length comes from a comparison of 5 α -cholestan-6-one (19) ($\Delta\epsilon$ -1.8), 5 α -pregnan-6-one (20) ($\Delta\epsilon$ -1.4), and 5 α -androstan-6-one (21) ($\Delta\epsilon$ -1.1) (all in dioxan, the latter two $\Delta\epsilon$ values being derived from o.r.d. data⁴⁵). Here any strain effect due to ring D is essentially constant, and the *differences* in $\Delta\epsilon$ values are probably related to the varying zig-zag lengths represented by the bonds from C-6 to C-17, extended by the pregnane or cholestane side-chains. The 5 β -isomers show a similar trend.⁴⁵

Our analysis of data for *cis*-decalones (p. 1095) shows that cyclohexanone analogues lacking any β -equatorial (primary) zig-zag exhibit very small $\Delta\epsilon$ values (generally ± 0.1).

The conclusions reached from data in Table 11 may be summarised to yield the estimated contributions of zig-zags, and of the separate bonds comprising them (Table 12). Values for methanol as solvent have been estimated from experimental data in the same manner as described above for hexane; values for dioxan and acetonitrile may reasonably be estimated by interpolation (p. 1097). It is apparent that the contributions of successive bonds do not fall off in a uniform manner. The possible significance of these values is discussed later (p. 1101).

This demonstration that $\Delta\epsilon$ values can be related to the lengths of primary zig-zags of C-C bonds may be of some significance in further consideration of the mode of interaction of structural features with the chromophore. As an empirical method for 'predicting' total values it is limited in its scope, but it proved to be a very useful concept in the next stage of our analysis, relating to extended *cis*-decalones.

cis-DECALONES

There are four classes of *cis*-decalone to be considered when conformational differences are taken into account (p. 1083). Table 13 lists the available data for *cis*-decalones and their extended analogues, grouped according to the *cis*-decalone class. O.r.d. amplitudes (a) have been converted into $\Delta\epsilon$ values (italicised) where necessary; these values are regarded as having a wider margin of uncertainty than $\Delta\epsilon$ values determined directly.

Table 13 includes a column for 'allowances' to be

⁴⁵ D. N. Jones and R. Grayshan, *J. Chem. Soc. (C)*, 1970, 2421.

TABLE 11
Estimated contributions ($\delta\Delta\epsilon$) of component C-C bonds of a primary zig-zag
($\Delta\epsilon$ values adjusted to hexane as solvent where necessary: see p. 1097)

Compound or class	$ \Delta\epsilon ^a$ (hexane)	Allowances for contributions of other bonds to $\Delta\epsilon^b$	Bond increment $\delta\Delta\epsilon$ (for 2nd bond only)
Compounds with a two-bond zig-zag			
3-Methylcyclohexanone	0.5	None	0.5
3 eq -Methyladamantanone	0.5	None	0.5
3-Oxo-5 β -steroids	0.3	10 β -Me -0.1	0.5
3-Oxo-19-nor-5 β -steroids	0.45	6,7-Bond (γ' - ax) -0.1	0.55
3-Oxo-5 α ,9 β ,10 α -steroid	0.3	6,7-Bond (γ' - ax) -0.1 10 α -Me -0.1	0.5
3'-Oxo-2 β ,3 β ,5 α ' pentacyclic ' steroid c	0.25	6,7-Bond (γ' - ax) -0.1	0.35
3'-Oxo-2 α ,3 α ,5 β ' pentacyclic ' steroid c	0.6	4,5-Bond (γ' - ax) -0.1	0.7
<i>trans</i> -1-Decalone	0.8	4,5-Bond (γ' - ax) -0.1 α - eq -CH ₂ <i>ca.</i> 0.2	0.6
Compounds with a three-bond zig-zag			
<i>trans</i> -2-Decalone	1.1	None	1.1
3-Oxo-5 α -steroids	<i>ca.</i> 0.8	10 β -Me -0.25	1.05
3-Oxo-19-nor-5 α -steroids	1.0-1.1	None	1.0-1.1
3-Oxo-5 β ,8 α ,10 β -steroid	0.7	10 α -Me -0.25	0.95
3-Oxo-5 β ,9 β ,10 α -steroid	0.7	10 α -Me -0.25	0.95
17-Oxo-D-homo-steroid	1.5	13 β -Me (β - ax) 0.45	1.05
5-Oxo-des-A-19-nor-steroid	1.05	None	1.05
6 β -Me-3-oxo-5 β -steroid	0.5	10 β -Me -0.1 6,7-Bond (γ' - ax) -0.1	0.7
Compounds with a four-bond zig-zag			
2-Oxo-des-D-5 α -steroid	1.5	10 β -Me 0.45	1.3
4-Oxo-5 α -steroids	1.6	9,11-Bond (γ' - eq), -0.25 10 α -Me 0.45	1.2
4-Oxo-19-nor-5 α -steroid	1.2	5,6-Bond (α - eq) 0.2 9,8-Bond (γ' - eq) 0.25 5,6-Bond (α - eq) 0.2	1.25
D-Homo-5 α -androstan-6-one	0.5	9,8-Bond (γ' - eq) -0.25 Ring A and 10 β -Me -0.7	1.45
D-Homo-17 α -oxo-steroid	0.25	14,15-Bond (γ' - eq) -0.25 13 β -Me -1.6	1.4
3'-Oxo-2 α ,3 β ,5 β ' pentacyclic ' steroid c	1.7	13,12-Bond (α - eq) 0.2 8,9-Bond (γ' - eq) -0.25 None	1.7
Compounds with a five-bond zig-zag			
3'-Oxo-2 β ,3 α ,5 α ' pentacyclic ' steroid c	1.6	None	1.6
(-)- <i>trans</i> , <i>syn</i> , <i>trans</i> -perhydroanthracen-2-one	1.4	None	1.4
2-Oxo-5 α -steroid (see text, p. 1085)	1.7	10 β -Me 0.45 9,11-Bond (γ' - eq) -0.25	1.5
Compounds with a six-bond zig-zag			
2-Oxo-D-homo-5 α -steroid	1.75	10 β -Me 0.45 9,11-Bond -0.25	1.55
16-Oxo-D-homo-5 α -steroid	1.1	13 β -Me -0.25 7,8-Bond (γ' - eq) -0.25	1.6

* Since the purpose is to compare numerical values, without regard to sign, data in this column are presented without signs.
^b Values taken from Tables 3 and 9; a negative sign in this column indicates that the substituent tends to reduce the numerical magnitude of $\Delta\epsilon$, in comparison with a compound lacking the substituent. c Compound of the 2,3-tetramethylenecholestone class: configurations at C-2, C-3, and C-5 refer to hydrogen atoms in each case (ref. 26).

TABLE 12

C.d. contributions ($\delta\Delta\epsilon$) estimated for primary zig-zags (taken from data in Table 11)

(a) Position of C-C bond in zig-zag:	1st	2nd	3rd	4th	5th	6th
Estimated contributions ($\delta\Delta\epsilon$) made by individual bonds:						
Solvent: Hexane	1.6	0.5	0.5	0.25	0.25	0.1
Methanol or ethanol	1.7	0.7	0.7	0.25	0.3	0.15
(b) Total length of zig-zag (no. of bonds)	1	2	3	4	5	6
Estimated total contribution of zig-zag to $\Delta\epsilon$ (± 0.2 units):						
Solvent: Hexane	1.6	2.1	2.6	2.85	3.1	3.2
Methanol or ethanol	1.7	2.4	3.1	3.35	3.6	3.8

TABLE 13
C.d. data for *cis*-decalones and their extended analogues

Compound (absolute configurations as in diagrams)	Ring code	$\Delta\epsilon$ (Italicised values calc. from $a = 40\Delta\epsilon$) (Solvent in parentheses ^a)	Allowances ($\delta\Delta\epsilon$) ^b for substituents	$\delta\Delta\epsilon$ for parent <i>cis</i> -decalone	$\Delta\epsilon$ ('calc.') ^c	Ref. ^d
Class <i>c2eq</i>						
7 β -Isopropyl-10 β -methyl- <i>cis</i> -1-decalone (22)	<i>c2'eq</i>	-0.36 (H) -0.20 (M)	β - <i>eq</i> -Me -0.5 (H) -0.6 (M)	+0.14 (H) +0.4 (M)	-0.35 (H) -0.2 (M)	<i>aa</i>
<i>cis</i> -Tetrahydroeremophilone (23)	<i>c2eq</i>	-0.9 (M)	β - <i>eq</i> -Me +0.6 (M) β - <i>eq</i> -Pr ¹ -1.1 (M)	-0.4 (M)	-0.4 (H) -0.9 (M)	<i>bb</i>
Des-D-9 β -7-ketone (abietic acid series) (24)	<i>c2eq/t3'</i>	-1.0 (M)	Ring A and 10 β -Me -1.2 (M) 4 α -CO ₂ Me, unknown 4 β -Me (γ' - <i>ax</i>) +0.2	ca. 0? (M)	-0.9 (H) -1.4 (M) (ignoring 4 α -CO ₂ Me)	<i>cc</i>
Nor-ketone derived from cistodiol (<i>cis</i> -clerodane series) (25)	<i>c2eq</i>	-1.6 (M)	α - <i>ax</i> -Me -1.7 (M)	+0.1 (M)	-1.45 (H) -1.3 (M)	<i>dd</i>
17 β -OH-17 α -Me-5 β -estrane-4-one (26)	<i>c2eq,t4,t2</i>	-0.11 (H) -0.22 (M)	None	-0.11 (H) -0.22 (M)	-0.15 (H) -0.4 (M)	
5 β -Androstan-4-one (27)	<i>c2eq,t4,t2</i>	+0.36 (H) +0.2, +0.1 (M)	β - <i>eq</i> -Me +0.5 (H) +0.6 (M)	-0.14 (H) -0.45 (M)	+0.35 (H) +0.2 (M)	
5-Methyl-5 β -cholestan-4-one (28)	<i>c2eq,t4,t2</i>	-1.9 (M)	β - <i>eq</i> -Me +0.6 (M) α - <i>ax</i> -Me -1.7 (M)	-0.8 (M)	-1.25 (H) -1.5 (M)	
Class <i>c2ax</i>						
7 α -Isopropyl-10 β -methyl- <i>cis</i> -1-decalone (29)	<i>c2'ax</i>	+2.7 (H) +2.75 (M)	β - <i>ax</i> -Me +0.1 (dis) isopropyl (3rd and 4th bonds of zig-zag) +0.75 (H) +0.9 (M)	+1.85 (H) +1.75 (M)	+2.65 (H) +3.0 (M)	<i>ee</i>
(-)-Valeranone [enantiomer of (30)]	<i>c2ax</i>	-2.75 (H) -3.04 (M)	As above, signs reversed, plus: α - <i>eq</i> -Me -0.2 (H) -0.15 (M)	-1.7 (H) -1.9 (M)	-2.85 (H) -3.15 (M)	
6 β ,7 β -Isopropylidene-10 β -methyl- <i>cis</i> -1-decalone (31)	<i>c2ax</i>	-2.7 (H) -2.9 (M)	β - <i>ax</i> -Me -0.1 (dis) cyclopropyl ring, unknown (-)	-2.6 (H) ^e -2.8 (M) ^e	-1.9 (H) ^e -2.1 (M) ^e	<i>aa</i>
17 β -CO ₂ Me-5 β -androstan-1-one (32)	<i>c2ax,t2,t4</i>	-3.1 (H) -3.95 (M)	β - <i>ax</i> -CH ₂ (C-11) -1.0 (H) -1.25 (M) -0.5 (H) (con) -0.6 (M)	-1.8 (H) -2.25 (M)	-3.1 (H) -3.7 (M)	<i>ff</i>
5 β -Cholestan-6-one (33)	<i>c2ax/t3',t2'</i>	-3.4 (H) -4.0 (M)	α - <i>eq</i> -Me +0.2 (H) +0.15 (M) 10 β -Me + rings c + d and side-chain ^f -1.8 (H) -2.0 (M)	-2.25 (M) -1.6 (H) -2.0 (M)	-3.7 (M) -3.6 (H) -4.0 (M)	<i>ff</i>
5-Methyl-19-nor-6-oxo-5 β -steroid (34)	<i>c2ax/t3',t2'</i>	-3.5 (H) -4.4 (M)	Rings c + d and side chain ^f -1.7 (H) -1.9 (M) α - <i>eq</i> -Me +0.2 (H) +0.15 (M)	-2.0 (H) -2.65 (M)	-3.3 (H) -3.75 (M)	<i>gg</i>
Class <i>c3eq</i>						
7 β -Isopropyl-10 β -methyl- <i>cis</i> -2-decalone (35)	<i>c3eq</i>	+0.36 (H) +0.55 (M)	γ - <i>eq</i> -Me -0.1	+0.46 (H) +0.65 (M)	+0.4 (H) +0.5 (M)	<i>aa</i>
Hexahydroisochamaecynone (36)	<i>c3'eq</i>	-1.0 (M)	γ - <i>eq</i> -Me +0.1	-1.1 (M)	-0.4 (H) -0.5 (M)	<i>hh</i>
<i>cis</i> -Tetrahydrocyperone (37)	<i>c3'eq</i>	-0.31 (M)	α - <i>eq</i> -Me -0.15 (M) γ - <i>eq</i> -Me +0.1 (M)	\geq -0.25 (M)	-0.6 (H) -0.65 (M)	<i>bb</i>
2-Oxo-5 α ,10 α -steroid (38)	<i>c3'eq,t2',t4'</i>	-0.5 (H), -0.28 (H) -0.85 (M)	β - <i>ax</i> -Me +0.1 (dis) γ' - <i>eq</i> -CH ₂ +0.25 (H); +0.3 (M)	-0.85 (H), -0.63 (H) -1.25 (M)	-0.15 (H) -0.2 (M)	
2-Oxo-19-nor-5 α ,10 α -steroid (38a)	<i>c3'eq,t2',t4'</i>	0.0 (M)	γ' - <i>eq</i> -CH ₂ +0.3 (M)	-0.3 (M)	-0.25 (H) -0.3 (M)	
3-Oxo-5 β -steroids (39)	<i>c3'eq,t4',t2'</i>	-0.37 (H) -0.4 (M)	γ - <i>eq</i> -Me +0.1	-0.47 (H) -0.5 (M)	-0.4 (H) -0.5 (M)	
2 β -Methyl-5 β -cholestan-3-one (40)	<i>c3'eq,t4',t2'</i>	-0.2 (D)	α - <i>eq</i> -Me +0.2 (D) γ - <i>eq</i> -Me +0.1 (D)	-0.5 (D)	-0.2 (D)	<i>ii</i>
3-Oxo-19-nor-5 β -steroids (41)	<i>c3'eq,t4',t2'</i>	-0.45 (H) -0.6 (M)	None	-0.45 (H) -0.6 (M)	-0.5 (H) -0.6 (M)	
5-Methyl-3-oxo-5 β -steroid (41a)	<i>c3'eq,t4',t2'</i>	-0.2 (H) -0.35 (M)	β - <i>ax</i> -Me +0.1 (dis) γ - <i>eq</i> -Me +0.1	-0.4 (H) -0.55 (M)	-0.3 (H) -0.4 (M)	
5-Methyl-19-nor-3-oxo-5 β -steroid (41b)	<i>c3'eq,t4',t2'</i>	-0.4 (H), -0.29 (H) -0.45 (M)	β - <i>ax</i> -Me +0.1 (dis)	-0.4 (H), -0.5 (H) -0.55 (M)	-0.4 (H) -0.5 (M)	<i>jj</i>

TABLE 13 (Continued)

Compound (absolute configurations as in diagrams)	Ring code	$\Delta\epsilon$ (Italicised values calc. from $a = 40\Delta\epsilon$) (Solvent in parentheses ^a)	Allowances ($\delta\Delta\epsilon$) ^b for substituents	$\delta\Delta\epsilon$ for parent <i>cis</i> -decalone	$\Delta\delta$ ('calc.')	Ref. ^d
5 α ,8 α ,10 α -Ergost-22-en-3-one (42)	<i>c3eq,c4eq,t2</i>	+0.46 (H)	γ - <i>eq</i> -Me -0.1	+0.56 (H)	+0.4 (H) +0.5 (M)	<i>jj</i>
17 β -Hydroxy-5 α ,8 α ,10 α -estrane-3-one (43)	<i>c3eq,c4eq,t2</i>	+1.53	None	+1.53	+0.6 (M)	<i>kk</i>
3-Oxo-5 α ,9 β ,10 α -steroid (44)	<i>c3eq,c4ax,t2</i>	+0.45 (M)	γ - <i>eq</i> -Me -0.1	+0.55 (M)	+0.4 (H) +0.5 (M)	
3-Oxo-19-nor-5 α ,9 β ,10 α -steroid (45)	<i>c3eq,c4ax,t2</i>	+0.53	None	+0.53	+0.5 (H) +0.6 (M)	<i>ll</i>
5 α -Methyl-3-oxo-19-nor-5 α ,9 β ,10 α -steroid (46)	<i>c3eq,c4ax,t2</i>	+0.06 (H) +0.53 (M)	β - <i>ax</i> -Me -0.1 (dis)	+0.16 (H) +0.63 (M)	+0.4 (H) +0.5 (M)	<i>jj</i>
2 β ,3 β -(3-Oxotetramethylene)-5 β -steroid (47)	<i>c3eq,c3ax,t4,t2</i>	+0.8 (H) +1.0 (D)	None	+0.8 (H) +1.0 (D)	+0.5 (H) +0.5 (D)	<i>mm</i>
2 α ,3 α -(3-Oxotetramethylene)-5 α -steroid [as (41)]	<i>c3'eq,t3',t4',t2'</i>	-0.24 (D)	None	-0.24 (D)	-0.5 (D)	<i>mm</i>
Class <i>c3ax</i>						
7,7,10-Trimethyl- <i>cis</i> -2-decalone (48)	<i>c3'ax</i>	+0.2 (M)	None	+0.2 (M)	+0.1 (M)	<i>nn</i>
7 α -Isopropyl-10 β -methyl- <i>cis</i> -2-decalone (49)	<i>c3ax</i>	-0.025 (M)	None	-0.025 (M)	-0.1 (M)	<i>nn</i>
Hexahydrochamaecynone (50)	<i>c3ax</i>	+0.7 (M)	α - <i>eq</i> -Me +0.15 (M)	+0.55 (M)	+0.05 (M) (or +0.6 ^e)	<i>hh</i>
<i>cis</i> -Tetrahydro- <i>epi</i> - α -cyperone (51)	<i>c3ax</i>	+0.7 (M)	α - <i>eq</i> -Me +0.15 (M)	+0.55 (M)	+0.05 (M) (or +0.6 ^e)	<i>bb</i>
8 β -9 β -Dimethyl- <i>cis</i> -2-decalone (52)	<i>c3'ax</i>	-0.21 (M)	β - <i>eq</i> -Me -0.6 (M)	< +0.4 (M)	-0.5 (M)	<i>bb</i>
6 β -7 β -Isopropylidene-10 β -methyl- <i>cis</i> -2-decalone (53)	<i>c3'ax</i>	-0.06 (H) -0.02 (M)	None	-0.06 (H) -0.02 (M)	+0.1	<i>aa</i>
6 β -7 β -Isopropylidene-1 α ,10 β -dimethyl- <i>cis</i> -2-decalone (54)	<i>c3'ax</i>	-0.84 (H) -0.92 (M)	α - <i>eq</i> -Me -0.2 (H); -0.15 (M)	-0.64 (H) -0.77 (M)	-0.1 (H) -0.05 (M) (or -0.6 ^e)	<i>aa</i>
8 α ,12-Ketone (des-D) (55)	<i>c3'ax,t2'</i>	-0.25 (H) -0.2 (M)	None	-0.25 (H) -0.2 (M)	+0.1	<i>bb</i>
2-Oxo-5 β -steroid (56)	<i>c3'ax,t2',t4'</i>	-0.77 (H) -0.78 (M)	β - <i>eq</i> -Me -0.5 (H); -0.6 (M)	-0.27 (H) -0.18 (M)	-0.5 (M)	
5 β -9 β -Ergost-22-en-3-one (57)	<i>c3ax,c4ax,t2</i>	+0.06	None	+0.06	-0.1	<i>jj</i>
3-Oxo-5 α ,10 α -steroid (58)	<i>c3'ax,t4',t2'</i>	+0.2 (M)	None	+0.2 (M)	+0.1 (M)	<i>bb</i>
3-Oxo-19-nor-5 α ,10 α -steroid (59)	<i>c3'ax,t4',t2'</i>	0.0	None	0.0	+0.1 (M)	<i>bb</i>
17 β -Hydroxy-5 β ,8 α ,10 β -estrane-3-one (60)	<i>c3ax,c4eq,t2</i>	+0.11	None	+0.11	-0.1	<i>kk</i>
7-Oxo-5 β -steroid (61)	<i>c3'ax,t2,t2</i>	+0.7 (M) +0.53 (D)	Rings c + D' +0.5 (M)	+0.2 (M)	+0.6 (M)	
2 β ,3 β -(3-Oxotetramethylene)-5 α -steroid (62)	<i>c3'ax,t3',t4',t2'</i>	<0.1	None	<0.1	+0.1	<i>mm</i>
2 α ,3 α -(3-Oxotetramethylene)-5 β -steroid (63)	<i>c3ax,c3eq,t4,t2</i>	+0.9 (H) +1.25 (M)	Very strained cage-like structure: effect unknown	+0.9 (H)? +1.25 (M)?	-0.1	<i>mm</i>

^a H = hexane; D = dioxan; M = methanol. ^b Values taken from Tables 3 and 12 except where otherwise indicated; con = consignate, dis = dissignate. ^c 'Calculated' values are obtained by summing the 'best value' (Table 14) of $\delta\Delta\epsilon$ for this *cis*-decalone and the contributions of any significant alkyl groups, as indicated in the column for 'allowances.' ^d Where no reference is indicated, data are our own. ^e The contribution of the cyclopropyl ring is unknown: its presence may enhance the negative contribution of the second ring through increased strain—see text, p. 1099. ^f The total contribution of rings c and D and the cholestane side chain was estimated from $\Delta\epsilon$ for the corresponding ketone of the 5 α -cholestane series, by subtracting the contribution due to ring A. ^g Alternative 'calculated' values, in parentheses, are based upon an enhanced consignate effect ($\delta\Delta\epsilon$ 0.7) when an α -*eq*-methyl and β -*ax*-substituent are both present—see text, p. 1095. ^h F. Fringuelli, A. Taticchi, F. Fernandez, D. N. Kirk, and P. M. Scopes, following paper. ⁱ Ref. 5a. ^j W. Herz and J. J. Schmid, *J. Org. Chem.*, 1969, **34**, 3473. ^k G. Berti, O. Livi, and D. Segnini, *Tetrahedron Letters*, 1970, 1401. ^l D. W. Theobald, *Tetrahedron*, 1966, **22**, 2869. ^m Ref. 6. ⁿ G. Snatzke and H. W. Fehlhaber, *Tetrahedron*, 1964, **20**, 1243. ^o T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, 1966, 3663. ^p P. Morand, J. M. Lyall, and H. Stollar, *J. Chem. Soc. (C)*, 1970, 2117. ^q Ref. 15. ^r R. Bucourt, D. Hainaut, J.-C. Gasc, and G. Nominé, *Tetrahedron Letters*, 1968, 5093. ^s J.-P. Berthelot and J. Levisalles, *Bull. Soc. chim. France*, 1971, 1888. ^t Ref. 26. ^u Ref. 46.

made for additional structural features. Values of $\delta\Delta\epsilon$ for methyl substituents are taken from Table 3, and those for additional rings or alkyl groups other than methyl are based upon the contributions of any component bonds forming part of a primary zig-zag (Table 12). The residual value, after deduction of these 'allowances' from the observed $\Delta\epsilon$ value, gives an estimate of the contribution of the bicyclic (*cis*-decalone) fragment.

For each class of *cis*-decalones the values of $\delta\Delta\epsilon$ thus

obtained generally fall within a fairly narrow range. The relatively few large deviations from the mode values of $\delta\Delta\epsilon$ are either attributable to special structural features such as excessive strain (p. 1099), or occur in $\Delta\epsilon$ values estimated from amplitudes a , some of which come from earlier published data of uncertain reliability.

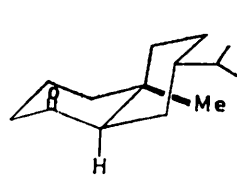
Conclusions for each class are as follows.

Class c2eq. Values of $\delta\Delta\epsilon$ cluster around 0.15 (hexane) or 0.4 (methanol) and are apparently dissignate (see p.

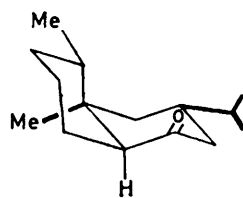
1095). The only significant deviations from these mode values are in compound (25), which may not have a rigid conformation, and in the 5β -methyl-4-ketone (28), an old result of uncertain reliability. We therefore

ably. Unfortunately, most of the available data are derived from a values, so there is some uncertainty as to the best $\Delta\epsilon$ values to adopt for this group.

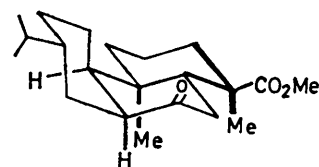
Class c3eq. The values of $\delta\Delta\epsilon$ considered most reliable



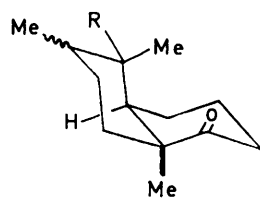
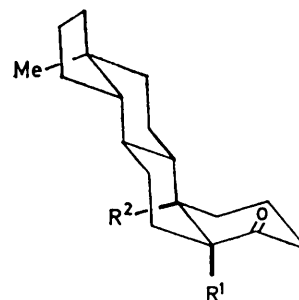
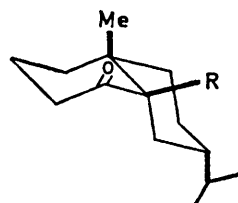
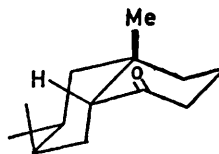
(22)



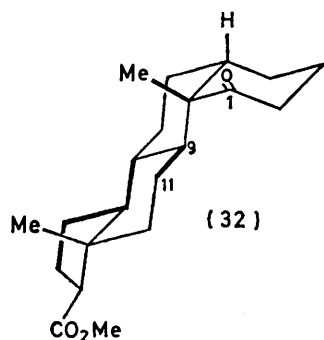
(23)



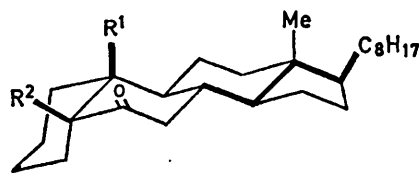
(24)

(25) $R = [CH_2]_2 \cdot CHMe \cdot CH_2 \cdot CH_2 \cdot OH$ (26) $R^1 = R^2 = H$ (27) $R^1 = H, R^2 = Me$ (28) $R^1 = R^2 = Me$ (29) $R = H$ (30) $R = Me$ 

(31)



(32)

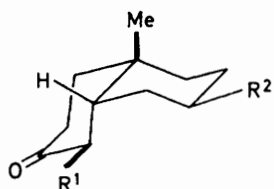
(33) $R^1 = Me, R^2 = H$ (34) $R^1 = H, R^2 = Me$

adopt the above $\Delta\epsilon$ values for the parent decalone system in this class.

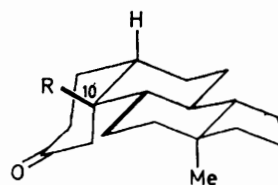
Class c2ax. Large values of $\delta\Delta\epsilon$ are found, ranging around 1.8 in hexane, or 2.0 in methanol (consignate). The major deviation occurs in compound (31), where the cyclopropyl ring must strain the 'second' ring consider-

and typical are grouped around 0.5 in hexane or 0.6 in methanol (consignate). Apart from $\Delta\epsilon$ values derived from o.r.d. data, a major deviation occurs only in one compound (43), which appears from a model to be highly strained. The structurally similar compound (42), however, is normal as to c.d. behaviour.

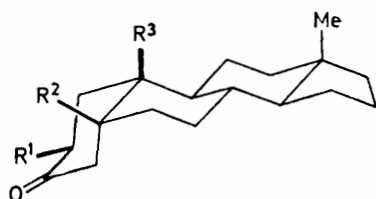
Class c3ax. Early work by Djerassi⁴⁶ with the two compounds (48) and (49), which had been expected to have the *c3ax* conformation, revealed apparently anomalous chiroptical behaviour, which led to the suggestion that these compounds might exist in conformations other than those predicted from consideration of molecular models. We now see that the experimental c.d. data agree well with expectation according to



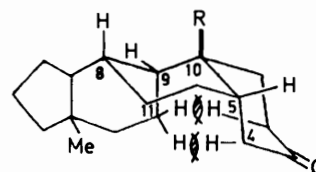
- (35) (enantiomer) $R^1 = H, R^2 = Pr^i$
 (36) $R^1 = H, R^2 = Et$
 (37) $R^1 = Me, R^2 = Pr^i$



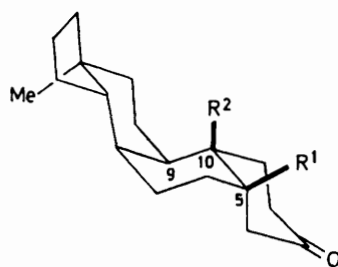
- (38) $R = Me$
 (38a) $R = H$



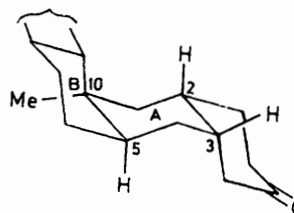
- (39) $R^1 = R^2 = H, R^3 = Me$
 (40) $R^1 = R^3 = Me, R^2 = H$
 (41) $R^1 = R^2 = R^3 = H$
 (41a) $R^1 = H, R^2 = R^3 = Me$
 (41b) $R^1 = R^3 = H, R^2 = Me$



- (42) $R = Me$
 (43) $R = H$



- (44) $R^1 = H, R^2 = Me$
 (45) $R^1 = R^2 = H$
 (46) $R^1 = Me, R^2 = H$



(47)

our new treatment, for the behaviour of these ketones is consistent with the general weakly dissignate behaviour of a β -axial bond (p. 1081), the only bond of the 'second' ring likely to make any significant contribution.

Values of $\delta\Delta\epsilon$ for the unsubstituted *cis*-decalone lie mostly between +0.2 and -0.2 (*i.e.* weakly consignate or weakly dissignate), irrespective of solvent. A large deviation (consignate) occurs for one compound (63), which appears from a model to have a congested, almost cage-like, structure, and must be highly strained.

The only other significant deviations are seen for three compounds with an α -equatorial methyl substituent, *viz.* (54) where the α -equatorial methyl group appears to contribute about -0.8 unit (consignate), in comparison with compound (53), and also compounds (50) and (51), which in comparison with (49) also reveal unusually large consignate effects (0.7) apparently associated with the α -equatorial methyl substituent. The usual value

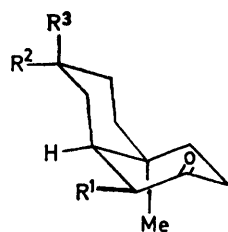
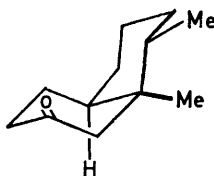
is *ca.* 0.2 (Table 3), implying an enhancement of the usual consignate effect by *ca.* 0.5 unit. We must, therefore, allow the possibility of an exceptionally large consignate contribution when an α -equatorial methyl group is adjacent to the β -axial bond of a *c3ax cis*-2-decalone.

Few other compounds having both α -equatorial and β -axial C-C bonds were available for careful scrutiny, but one such compound, friedelan-3-one, has already

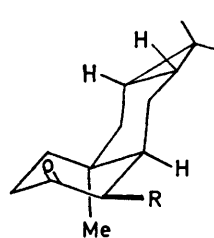
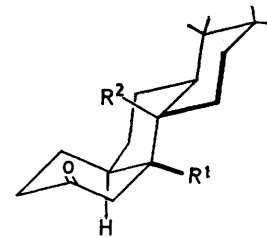
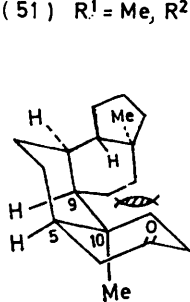
⁴⁶ C. Djerassi, J. Burakevich, J. W. Chamberlin, D. Elad, T. Toda, and G. Stork, *J. Amer. Chem. Soc.*, 1964, **86**, 465.

been noted (p. 1086) as one of the few extended *trans*-decalones which do not give $\Delta\epsilon$ values within about ± 0.2 units of the 'calculated' value. The average discrepancy is again about 0.4–0.5 unit, suggesting that the simultaneous presence of the 4 β - (α -equatorial) and 5 β - (β -axial) methyl groups is responsible. The 17 $\alpha\beta$ -methyl-D-homo-17-ketone (Table 10; entry 54) is

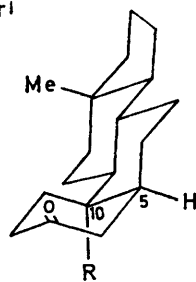
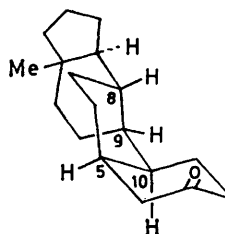
A further impression gained from scrutiny of data in the *c3ax* group is that, excepting the special relatively large consignate effects noted above, significant consignate effects of the second ring are limited to compounds (55) and (56), which are the only ones in the group having the *c3'ax,t2'* tricyclic structure. Here the β -axial carbon atom has an unusual pattern of substitution

(48) (enantiomer) $R^1 = H, R^2 = R^3 = Me$ (49) $R^1 = R^2 = H, R^3 = Pri$ (50) $R^1 = Me, R^2 = Et, R^3 = H$ (51) $R^1 = Me, R^2 = H, R^3 = Pri$ 

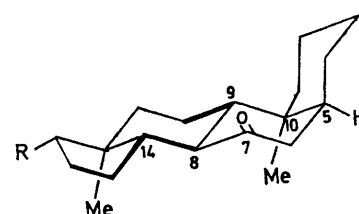
(52)

(53) $R = H$ (54) $R = Me$ (55) $R^1 = H, R^2 = Me$ (56) $R^1 = Me, R^2 = H$ 

(57)

(58) $R = Me$ (59) $R = H$ 

(60)



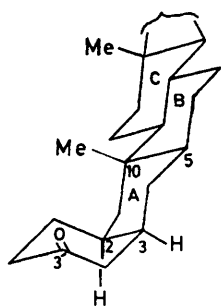
(61)

another compound of similar structure in the vicinity of the carbonyl group. Unfortunately we have only a $\Delta\epsilon$ value (-2.4) derived from a published o.r.d. amplitude, but this $\Delta\epsilon$ value is again enhanced by the expected

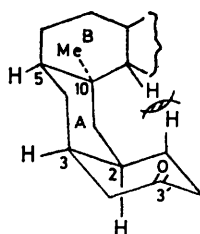
(heavy bonds in drawing), with one of the attached C–C bonds equatorial to the second ring, and extended by a further C–C bond parallel to the β -axial bond. Further examples are needed to test the possibility that these bonds of the third ring may constitute a 'secondary zig-zag', and contribute weakly in the consignate sense which just outweighs the normal dissignate effect of a β -axial methyl group.

All other *c3ax* compounds give zero or weakly dissignate $\Delta\epsilon$ values, which we regard as characteristic for the bicyclic system ($\delta\Delta\epsilon$ ca. 0.1; dissignate).

Empirical Calculations of C.d. Contributions of the cis-Decalones.—Our impression that the chiroptical properties of cyclohexanones stem largely from extended primary zig-zags, together with any alkyl substituents affecting the primary zig-zags, is further supported by a comparison of the foregoing $\Delta\epsilon$ values for *cis*-decalones with 'calculated' values. Calculations were based upon the contributions of only those bonds of the second ring which represent α - or β -substituents on the cyclohexanone ring, or form part of a primary zig-zag. Required bond increments are taken entirely from data obtained during our analysis of extended *trans*-decalones (Tables 3 and 12). The comparisons are presented in Table 14. The contribution ($\delta\Delta\epsilon$) of a C–CH₂ bond is assumed to



(62)



(63)

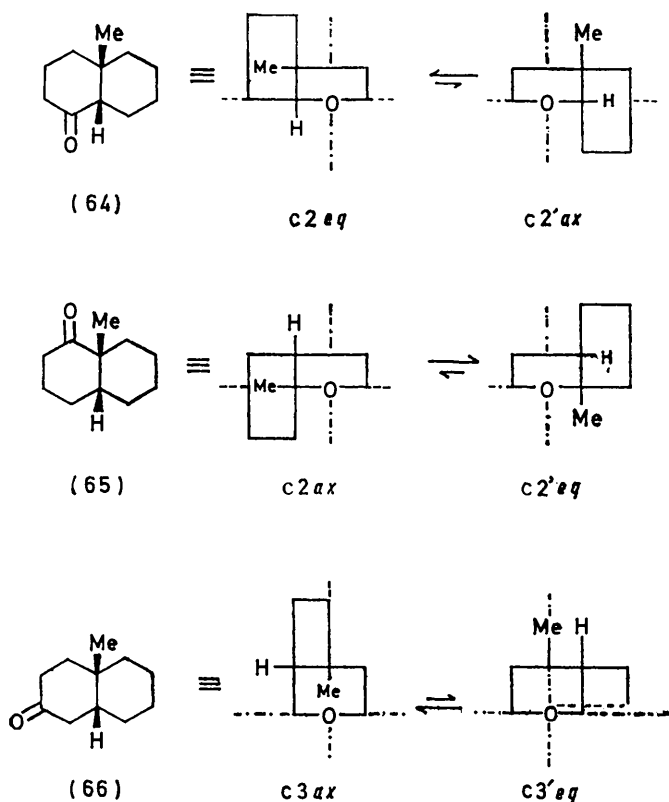
amount compared with the calculated value (-1.95). The apparent synergic effect therefore seems to be a genuine one. It may result from a subtle distortion by, or mutual interaction of, the adjacent α -equatorial and β -axial C–C bonds, which form a 'skew-butane' system (p. 1102). Such an effect would not be unreasonable, in view of the demonstrated sensitivity of β -axial group effects to other structural features.

be equivalent to that of a C-CH₃ bond (Table 3) in the same position.

Clearly, the agreement between 'calculated' $\Delta\epsilon$ values and those derived from experimental data is as good as could be expected in view of the assumptions made. The relatively small deviations which do occur may indicate that the effect of a C-CH₂ system is not exactly equivalent to that of C-methyl substitution.

The apparent weakly dissignate behaviour of the second ring, taken as a whole, in class *c2eq*, is explained by the dominant front-octant and dissignate contributions, respectively, of the 8,7- and 10,5-bonds.

cis-Decalones with Mobile Conformations.—Authors of previous papers^{4,47,48} have commented upon the c.d. behaviour of some *cis*-decalones (bicyclic) which have nothing in their structure to rigidify a particular conformation. Our estimates of c.d. contributions of the unsubstituted *cis*-decalones lead to the following conclusions, when suitable allowances are made for methyl substituents (*cf.* Table 3).



10-Methyl-cis-1-decalone (64). 'Calculated' $\Delta\epsilon$ values (in methanol) for the (*c2eq*) 'steroid-like' and alternative (*c2'ax*) forms are:

$$c2eq: \Delta\epsilon = +0.2; c2'ax: \Delta\epsilon = +2.1$$

The observed value of *a* (+11) ($\Delta\epsilon$ *ca.* +0.3) agrees well with the *c2eq* form, contrary to earlier conclusions.^{4,47}

⁴⁷ F. Sondheimer and D. Rosenthal, *J. Amer. Chem. Soc.*, 1958, **80**, 3995.

⁴⁸ N. L. Allinger and J. H. Siefert, *J. Amer. Chem. Soc.*, 1972, **94**, 8082.

9-Methyl-cis-1-decalone (65). 'Calculated' $\Delta\epsilon$ values are:

$$c2'eq: \Delta\epsilon = +2.1; c2ax: \Delta\epsilon = -1.85$$

The experimental value (*a* = +51; $\Delta\epsilon$ *ca.* +1.3) suggests that the *c2'eq* form is strongly favoured, consistent with the conclusions drawn from molecular models, and agreeing with the view of Moffitt *et al.*⁴

10-Methyl-cis-2-decalone (66). 'Calculated' $\Delta\epsilon$ values are:

$$c3'eq: \Delta\epsilon = -0.5; c3ax: \Delta\epsilon = -0.1$$

The experimental value (*a* = -11; $\Delta\epsilon$ *ca.* -0.27) agrees acceptably with the ratio of 70% *c3ax*: 30% *c3'eq* estimated by n.m.r.,⁴⁹ and agrees also with the views of Allinger,⁴⁸ but is contrary to those of Moffitt *et al.*⁴

FURTHER SPECIAL TOPICS

'Front Octant' Effects.—The 'front-octant' consignate behaviour of the third ring in compounds of the

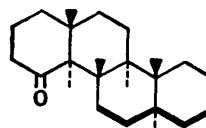


FIGURE 9 'Front octant' effects (see text)

trans,anti,trans-perhydrophenanthren-1-one (Figure 9) type (*cf.* Table 6) is imitated, though relatively weakly, when the 'third' ring is of cyclopentane type. Our published data^{8b} for 7-oxo-steroids (*cf.* p. 1080) have been augmented by recent data⁵⁰ for 5 α ,14 β -cholestan-7-one, where ring D makes a small negative contribution, contrasting in sign with its small positive contribution in the 14 α -isomer. We have suggested^{8b} that the interaction of a front octant ring with the carbonyl group operates through space, and falls off very rapidly with distance: angle deformation in an ordinary steroid certainly increases the distance of C-15 from the carbonyl group, compared with the un-deformed D-homo-compound.

The present work suggests, however, that a further effect cannot be ignored. The C-C bond of the third ring in a perhydrophenanthren-1-one (Figure 9) which lies closest to the carbonyl group is of the β' -type (Figure 4); we have assigned a $\delta\Delta\epsilon$ value of only 0.2 unit (Table 3) when the β' -substituent is methyl, so other C-C bonds of the third ring must augment this contribution when the ring is six-membered. Moreover the fourth ring of a 1-oxo-steroid (Table 8) probably makes a small additional contribution, despite its relatively great distance from the carbonyl group. On this limited evidence, we suggest the possibility that the zig-zag of bonds indicated by heavy lines (Figure 9) comprises another 'secondary zig-zag' (*cf.* p. 1095), and makes a significant contribution of front-octant sign. Like the other zig-zags which have been discussed, the general direction of this front-octant zig-zag is aligned so as to pass very

⁴⁹ K. L. Williamson and J. A. Spencer, *Tetrahedron Letters*, 1965, 3267.

⁵⁰ I. Midgley and C. Djerassi, *J.C.S. Perkin I*, 1973, 155.

close to the carbonyl group, a feature which seems likely to be important in considering the perturbation of the $n \rightarrow \pi^*$ transition by substituents.

Solvent Effects.—We have already reported and discussed the variations in o.r.d. data, according to solvent, for a wide variety of ketones.⁶ C.d. study of a more limited but similar range of ketones in hexane, dioxan, acetonitrile, and methanol (or ethanol) confirms that the

of the c.d. band, near 297 nm, although in a very few cases the second peak, near 306 nm, is of equal or stronger intensity. (b) The wavelength of $\Delta\epsilon(\text{max.})$ tends to shift progressively towards the blue as solvent polarity increases. The reasons for this effect, in terms of different solvation requirements of the ground and excited states, are well understood.^{3c} (c) The magnitude of $\Delta\epsilon$, like that of the o.r.d. amplitude a ,⁶ generally

TABLE 14

Empirical calculations of c.d. contributions ($\delta\Delta\epsilon$) of the four *cis*-decalone types: comparison with values estimated from experimental data

Decalone class ^a	Bond	Nearest equivalent substituent in a <i>trans</i> -decalone analogue ^b	$\delta\Delta\epsilon$ (bond and ring contributions taken from standard values for <i>trans</i> -series)	
			Hexane	MeOH or EtOH
<i>c2'eq</i>	9,8	α - <i>eq</i> -Me	-0.2	-0.15
	8,7	β' - <i>ax</i> -Me (front octant consignate)	+0.2	+0.2
	10,5	β - <i>ax</i> -Me (Class 2, dissignate)	+0.1	+0.1
		Calc. total for second ring	+0.1	+0.15
		Estimated from c.d. data for <i>cis</i> -decalone derivatives:	+0.15	+0.4
<i>c2ax</i>	9,8	First and second bonds of a primary zig-zag β - <i>eq</i> -Me	-2.1	-2.4
	8,7		+0.5	+0.6
	10,5			
		Calc. total for second ring	-1.6	-1.8
		Estimated from c.d. data for <i>cis</i> -decalone derivatives: <i>ca.</i>	-1.8	-2.0
<i>c3'eq</i>	9,8	β - <i>eq</i> -Me	-0.5	-0.6
	8,7	γ' - <i>ax</i> -Me	+0.1	+0.2
		Calc. total for second ring	-0.4	-0.4
		Estimated from c.d. data for <i>cis</i> -decalone derivatives:	-0.5	-0.6
<i>c3ax</i>	9,8	β - <i>ax</i> -Me (Class 2, dissignate)	-0.1	-0.1
		Calc. total for second ring	-0.1	-0.1
		Estimated from c.d. data for <i>cis</i> -decalone derivatives:	-0.1 ± 0.2	-0.1 ± 0.2

^a The *c2'eq* and *c2ax* forms illustrated are the alternative chair-chair conformations of (9*R*,10*R*)-*cis*-1-decalone; the *c3'eq* and *c3ax* forms are similarly alternative conformations of (9*R*,10*S*)-*cis*-2-decalone. ^b See Figure 4, and Tables 3 and 12.

variations in c.d. characteristics closely follow those found in o.r.d. Table 15 records data measured for portions of the same sample of ketone, and with experimental conditions virtually identical apart from the solvent. Methanol and ethanol seem to be interchangeable, within the limits of experimental error.

The main features of the data are: (a) maximum vibronic fine structure in hexane,²² and a trend to smoothing out of the curves with increasing solvent polarity; the maximum value of $\Delta\epsilon$ in hexane is generally reached at the *third* peak from the long-wavelength end

increases with solvent polarity, although the factors expressing this increase (Table 15) show quite wide variations according to structural type. In one case, that of the D-homo-17a-ketone, the magnitude of $\Delta\epsilon$ decreases with increasing solvent polarity, and even reverses sign in methanol. We have already commented on the reason for this abnormal trend, which is observed also in o.r.d.⁶ It stems from the differing sensitivities of the contributions of various structural features to changes in solvent. When all the contributing parts of a complex molecule lie in one octant, or in like-signed

TABLE 15.

C.d. data for various key types of ketone in different solvents.

Maximum values of $\Delta\epsilon$ in italics; values in square brackets are $\Delta\epsilon(\text{solvent})/\Delta\epsilon(\text{hexane})$ for $\Delta\epsilon_{\text{max}}$.

	Hexane		Dioxan		MeCN		MeOH (M) or EtOH (E)	
	$\Delta\epsilon$	λ/nm	$\Delta\epsilon$	λ/nm	$\Delta\epsilon$	λ/nm	$\Delta\epsilon$	λ/nm
(+)-3-Methylcyclohexanone	+0.23	317	+0.24	314				
	+0.42	307	+0.46	303	+0.48sh	300		
	+0.45	298	+0.49	295 [1.09]	+0.50	294 [1.11]	(M) +0.56	289 [1.24]
(+)-trans-1-Decalone (12)	+0.38	289	+0.41	286	+0.42sh	284		
	+0.44	315	+0.47sh	311	+0.46sh	310	+0.71sh	302
	+0.78	305	+0.82	301	+0.83	289		
	+0.81	296	+0.86	293 [1.06]	+0.85	292 [1.05]	(M) +0.95	295 [1.17]
	+0.66sh	289	+0.67sh	284				
(-)-trans-2-Decalone (13)	-0.55	317	-0.64sh	314	-1.30sh	300		
	-1.04	307	-1.21sh	303				
	-1.12	297	-1.28	295 [1.14]	-1.36	293 [1.21]	(M) -1.37	290 [1.22]
	-0.94sh	289	-1.10sh	288				
5 α -Cholestan-2-one	+0.83	318	+0.93sh	315	+1.06sh	311		
	+1.52	307	+1.66	303	+1.84sh	301		
	+1.61	298	+1.78	296 [1.10]	+1.93	294 [1.20]	(M) +2.22	290 [1.38]
	+1.35sh	291	+1.54sh	288				
5 α -Cholestan-3-one	+0.43sh	316						
	+0.74sh	304						
	+0.79	297	+1.03	295 [1.30]	+1.18	294 [1.49]	(M) +1.23	290 [1.56]
	+0.68	288					(E) +1.26	290
(-)-trans, syn, trans-Perhydroanthracen-2-one (2)	-0.67sh	317	-0.81sh	313				
	-1.25	306	-1.52sh	302	-1.62sh	301		
	-1.37	297	-1.64	295 [1.20]	-1.76	293 [1.28]	(M) -1.86	290 [1.36]
	-1.18sh	290						
2 α ,3 β -(3-Oxotetramethylene)-5 α -cholestane	+1.62	296	+1.73	294 [1.07]	+1.82	291 [1.12]	(M) +1.98	289 [1.22]
17 β -Acetoxy-5 α -androstan-3-one	+0.75	297	+1.04	294 [1.39]	+1.16	293 [1.55]	(E) +1.18	291 [1.57]
17 β -Acetoxy-2 α -methyl-5 α -androstan-3-one	+0.58	302	+0.84	297 [1.45]	+0.99	294 [1.71]	(E) +1.07	293 [1.84]
17 β -Acetoxy-5 α -estran-3-one	+0.51	316	+0.73	310	+1.25	299		
	+0.93	305	+1.18	300				
	+1.02	296	+1.27	295 [1.24]	+1.30	291 [1.27]	(E) +1.43	291 [1.40]
5 β -Cholestan-3-one	-0.19	317						
	-0.34	306						
	-0.37	297	-0.41	294 [1.11]	-0.39	294 [1.05]	(M) -0.40	290 [1.08]
	-0.32	287						
5 α -Estran-4-one	-0.64	315	-1.43	301	-1.45	300		
	-1.23	305						
	-1.28	295	-1.50	293 [1.17]	-1.50	291 [1.17]	(E) -1.46	294 [1.14]
5 α -Estran-6-one	-0.52	315	-0.70	311				
	-0.89	306						
	-0.89	297	-1.08	302 [1.21]	-1.24	292-294 [1.39]	(M) -1.39	292 [1.56]
	-0.72sh	189	-1.06	294				
D-Homo-5 α -androstan-6-one	-0.35	316	-0.36	312	-0.42	308	(E) -0.52sh	302
	-0.52	305	-0.53	303 [1.02]	-0.60	299 [1.15]	-0.56	295 [1.08]
	-0.45	297	-0.44	294	-0.49	293		
	-0.18	280						
5 α -Cholestan-6-one	-0.85	315	-0.92	311	-1.08	309		
	-1.36	306	-1.40	303 [1.03]	-1.59	300 [1.17]	(M) -1.71	293 [1.25]
	-1.29	296	-1.34	295	-1.52sh	293	(E) -1.72	295
	-1.01sh	289						
5 α -Cholestan-7-one	-0.41	297	-0.58	296 [1.41]	-0.65	294 [1.58]	(M) -0.71	292 [1.73]
D-Homo-5 α -androstan-17a-one	-0.14	318	-0.11	314	-0.05	314		
	-0.24	305	-0.15	303	-0.05	301		
	-0.25	293	-0.18	293 [0.72]	-0.07	292 [0.28]	(M) +0.06	297
	-0.22sh	286	-0.16	283				
Valeranone [enantiomer of (30)]	-1.55	319	-3.08	306	-2.81	304		
	-2.70	308	-3.08	297 [1.12]	-2.81	296 [1.02]	(M) -3.04	297 [1.11]
	-2.75	299						
	-2.26	291						

octants, the effect of summing their contributions reflects the general increase in group contributions with solvent polarity. However, a ketone perturbed by structural components in two octants of opposite signs gives a total $\Delta\epsilon$ value which is the algebraic sum of increments usually of opposite sign: the effect can be a small increase, or a small decrease, or even no net change in $\Delta\epsilon$ with solvent, depending upon the relative sensitivities of the effects of the component parts of

the molecule. The D-homo-17a-ketone, in particular, exhibits a $\Delta\epsilon$ value composed of a solvent-sensitive positive contribution due to the ring system (12,14,12), and a negative contribution, almost insensitive to solvent, from the 13-methyl group. Most 'middle ring' ketones likewise show very little variation of $\Delta\epsilon$ with solvent character.

It is now clear that the solvent variations in $\Delta\epsilon$ reflect those of $\delta\Delta\epsilon$ for the various ring systems (Table 9) and

with data for the androstane analogue. Deviations in $\Delta\epsilon$ values for the 12-oxo-spirostans are small, the observed values being comparable with those for 5 α -androstan-12-one; the 'side chain' (ring E and F) must be so placed as to exert no net effect on the carbonyl group. The conformationally mobile pregnane, cholane, and cholestane side chains, in contrast, cause larger deviations, which increase with increasing chain length, and significantly have the negative sign associated with 'front octant' behaviour; this is expected from the approximate equivalence of these alkyl chains to a β' -alkyl substituent (Figure 4). The reported o.r.d. data for β -nor-5 α - (68) and β -nor-5 β -cholestan-3-ones (69) imply that the strained 5,6-bond makes more than

DISCUSSION

All the main contributions to the c.d. of the classes of ketones under discussion, with the exception of front octant effects, seem to come from the atoms or bonds lying on primary zig-zags, or from substituents directly linked to the carbon atoms of primary zig-zags. If polarisability is the property with which we are concerned, it seems entirely reasonable that the polarisability of a hydrocarbon chain, like the ease of ionisation,³³ should increase with chain length, as implied by the c.d. data (Table 12). A simple qualitative orbital argument, of the type so elegantly expounded by Hoffmann,⁴¹ helps to make this clear. In the simplest pictorial representation for a four-carbon antiperiplanar

TABLE 16
C.d. data for steroidal ketones in which bonds of a five-membered ring lie on a primary zig-zag

Compound	Ring code ^a	$\Delta\epsilon$ Values				Deviation, $\delta\Delta\epsilon(\Delta\epsilon_{\text{obs.}} - \Delta\epsilon_{\text{calc.}})$	
		Hexane		Methanol or Ethanol		Hexane	MeOH or EtOH
		Calc. ^e	Obs.	Calc. ^e	Obs.		
β -Nor-5 α -cholestan-3-one ^b	<i>t3,t4,t2</i>	+0.85		+1.2	+2.5		+1.3
β -Nor-5 β -cholestan-3-one ^b	<i>c3'eq,t4',t2'</i>	-0.45		-0.65	-1.3		-0.65
5 α -Estran-6-one (9)	<i>t2/t3',t2'</i>	-0.25	-0.95	-0.4	-1.39	-0.7	-0.99
5 α -Androstan-6-one	<i>t2/t3',t2'</i>	-0.35	-0.96	-0.5	-1.26	-0.61	-0.76
5 β -Androstan-6-one	<i>c3ax/t3',t2'</i>	-3.15 ^e	-3.85 ^{e,d}	-3.65		-0.7 ^e	
5 α -Androstan-11-one	<i>t3/t2',t2'</i>	+0.3	+0.14	+0.35	+0.10	-0.16	-0.25
5 α -Androstan-12-one ^e	<i>t3,t2/t2'</i>	+1.75	+1.63	+1.9	+1.46	-0.12 ^f	-0.44 ^f
5 α -Pregnan-12-one	<i>t3,t2/t2'</i>	+1.55 ^g	+1.37	+1.7 ^g	+1.82	-0.18	+0.12
3 α -Hydroxy-12-oxo-5 β -cholanic acid, Me ester	<i>t3,c2eq/t2'</i>	+1.35 ^{e,g}	+0.94 ^{e,h}	+1.45 ^g		-0.41	-
5 β -Cholan-12-one	<i>t3,c2eq/t2'</i>	+1.35 ^g	+0.99	+1.45 ^g		-0.36	
3 α -Acetoxy-5 β -cholestan-12-one	<i>t3,c2eq/t2'</i>	+1.35 ^g	+0.70	+1.45 ^g	+0.52	-0.65	-0.93
(25 <i>R</i>)-3 β -Acetoxy-5 α ,20 β (<i>H</i>)-spirostan-12-one	<i>t3,t2/t2'</i>	+1.55 ^g	+1.61	+1.7 ^g	+1.90	+0.06	+0.2
(25 <i>R</i>)-3 β -Acetoxy-5 α ,20 α (<i>H</i>)-spirostan-12-one	<i>t3,t2/t2'</i>	+1.55 ^g	+1.63	+1.7 ^g	+1.90	+0.08	+0.2

^a Ring code and 'calculated' $\Delta\epsilon$ values are for the equivalent structure with all rings six-membered. ^b J. Joska, J. Fajkoš, and F. Šorm, *Coll. Czech. Chem. Comm.*, 1966, **31**, 2745; o.r.d. data converted into $\Delta\epsilon$ values. ^c In dioxan. ^d D. N. Jones and R. Grayshan, *J. Chem. Soc. (C)*, 1970, 2421; o.r.d. data converted into $\Delta\epsilon$ values. ^e Kindly provided by Dr. G. D. Meakins, Oxford. ^f The deviations for 5 α -androstan-12-one are distinctly greater (-0.34 in hexane; -0.89 in EtOH) if comparison is made with measured $\Delta\epsilon$ values for the D-homo-analogue (Table 10, entry 47). ^g 'Calculated' $\Delta\epsilon$ values based upon the arbitrary assumption that the 17 β -alkyl substituent has an effect equivalent to a 17 β -methyl group (β' -axial). ^h Ref. 3c.

the usual consignate contribution, found in the respective steroids with a normal ring B.

It is not possible at present to predict the magnitudes of enhancements in $\Delta\epsilon$ due to strain; the effect will certainly vary according to the amount and type of strain involved. There may even be compensating effects which tend to obscure the strain contribution; we suggested (p. 1089) for example, that a 2-oxo-5 α -steroid and its D-homo-analogue exhibit similar values of $\Delta\epsilon$ because the enhanced effect of the strained 14,15-bond in the ordinary steroid is balanced by a reduced effect of the 15,16-bond, which is twisted away from coplanarity with the zig-zag extending from C-2 to C-15. 11-Oxosteroids are similarly almost unaffected by the size of ring D.

Nonetheless, it seems reasonable to expect, empirically, that a strained bond in a primary zig-zag will generally give an enhanced consignate contribution; enhancements of up to one unit are common if the strained bond is not far removed from the carbonyl group, and is fully coplanar with the primary zig-zag.

zig-zag (Figure 10), the localised σ -bonding orbitals forming the C(1)-C(2) and C(3)-C(4) bonds, respectively, may combine in either a 'more-bonding' or a 'less-bonding' way to form two four-atom delocalised orbitals, both fully occupied in the ground state. As a result of splitting of energy levels, the 'less-bonding' combination is of higher energy than either of the localised σ -bonding orbitals from which it is considered to be formed; electrons occupying the 'less-bonding' combination orbital are therefore less firmly bound by the nuclei, so that the chain is more readily polarised. More elaborate treatments using methylene (CH_2) group orbitals⁵⁵ produce the same conclusion, and extensions of the concept of delocalised molecular orbitals lead to the expectation of progressively higher energy and polarisability of electrons in the highest occupied molecular orbital as the zig-zag is lengthened, although successive increments will tend to decrease in magnitude. Extended Hückel

⁵⁵ W. L. Jorgensen and L. Salem, 'The Organic Chemist's Book of Orbitals,' Academic Press, New York and London, 1973 p. 5.

calculations by Hoffmann⁵⁶ have shown that the energy of the highest occupied molecular orbital in n-alkanes follows just this pattern.

Alternate bonds of a planar zig-zag each belong to one of two parallel sets (parallel respectively to the $C_\alpha-C_\beta$ or the β -equatorial bonds). It seems reasonable that there should be a smooth fall-off in bond increments [$\delta\Delta\epsilon$; Table 12(a)] within the series formed by the 1st, 3rd, 5th... bonds, which are all parallel; the first ($C_\alpha-C_\beta$) bond is so aligned that some overlap with the carbonyl π -orbitals is possible (Figure 3).

The contributions of the 2nd, 4th, 6th... bonds, which lie roughly parallel with the carbonyl- C_α inter-nuclear axis, and cannot overlap with the π -orbital, form a separate decreasing series of lesser magnitude.

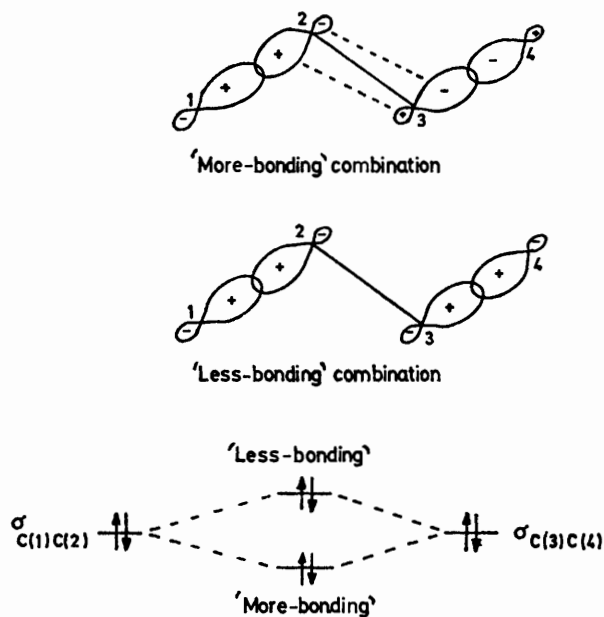


FIGURE 10 Simplified representation of the interaction of localised C-C bonding orbitals in a planar zig-zag to form delocalised orbitals

The values of $\delta\Delta\epsilon$ indicated in Table 12(a) suggest that the individual effects of odd-numbered bonds fall in roughly geometrical progression by a factor of about 1/2.5, the even-numbered bond contributions forming a similar series with corresponding terms proportionately smaller. It may be significant that increments in molar refractivities with increasing chain length show similar alternation for various groups of compounds.⁵⁷

Hudec's conclusions^{12,18} (p. 1079) concerning the effects of heteroatom substituents can also be integrated with

⁵⁶ R. Hoffmann, *J. Chem. Phys.*, 1963, **39**, 1397.

⁵⁷ R. J. W. LeFevre, *Adv. Phys. Org. Chem.*, 1965, **3**, 1.

⁵⁸ M. J. S. Dewar, 'Hyperconjugation,' Ronald Press, New York, 1962; R. Hoffmann, *Pure Appl. Chem.*, 1970, **24**, 585; R. Hoffmann, L. Radom, J. A. Pople, P. von R. Schleyer, W. J. Hehre, and L. Salem, *J. Amer. Chem. Soc.*, 1972, **94**, 6221; W. J. Hehre and L. Salem, *J.C.S. Chem. Comm.*, 1973, 754, and references therein.

⁵⁹ 'An Epistologue on Carbon Bonds,' ed. M. J. S. Dewar, *Tetrahedron*, 1962, **17**, 123; G. R. Underwood and J.-A. M. Iorio, *J. Org. Chem.*, 1971, **36**, 3987; J. P. Lowe, *J. Amer. Chem. Soc.*, 1972, **94**, 3718.

our findings. Remote substituents having high polarisability and electron-donor capability were found to act in the consignate sense if the heteroatom and one of its lone pairs lie on a primary zig-zag [e.g. as in Figure 1, and formula (1)]. We find that a CH_3 or CH_2R group in a similar location, extending a primary zig-zag, makes a smaller c.d. contribution though still in the consignate sense. The 'pseudo-atom' MO treatment of methyl and methylene groups^{55,58} which has been successful in explaining their interaction with adjacent orbitals of p -type symmetry, may be invoked here, along with the much-discussed and now widely accepted concept of a 'pseudo- π ' conjugative contribution to the bonding of saturated hydrocarbon chains.^{55,59} The methyl (or methylene) group extending a zig-zag evidently functions as if it were a weak electron donor (relative to hydrogen) in the carbonyl $n \rightarrow \pi^*$ transition, consistent with its known ability to stabilise carbonium ions and related species like benzenonium ions, probably through the 'hyperconjugation' mechanism. We envisage that the electron-donor properties of the methyl or methylene group come into play through the 'pseudo- π ' component of bonding, but only in response to an electron demand associated with carbonyl excitation (electromeric effect):⁶⁰ the detailed mechanism must remain a subject for future theoretical studies.

The c.d. effect of a methyl or methylene substituent present as a branch on a primary zig-zag may be of a different character. In the absence of the favourable 'hyperconjugation' path provided by extension of a coplanar zig-zag, the effect of the alkyl group seems likely to be mainly inductive.⁶⁰ The results of recent calculations (CNDO/2)⁶¹ of electron-density distribution in saturated hydrocarbons indicate that methyl substitution at a saturated carbon atom reduces the electron density on carbon in comparison with that found in the corresponding C-H compound. The reality of this effect is supported by ^{13}C n.m.r. data,^{62,63} which show that a methyl group in saturated hydrocarbons is generally electron-withdrawing in comparison with a hydrogen atom, so that methyl substitution in n-alkanes has a deshielding effect on the carbon atom concerned.

This view of an alkyl group as inductively accepting electronic charge places it in the same category as other electronegative substituents, when present as a branch anywhere on a primary zig-zag. The c.d. effect of the alkyl substituent should therefore be dissignate, although weakly so by comparison with strongly electronegative halogen or oxygen groups in the same location. This is found to be the case. The weakly dissignate effect of a γ' -axial or equatorial alkyl substituent (Table

⁶⁰ W. M. Schubert, R. B. Murphy, and J. Robins, *Tetrahedron*, 1962, **17**, 199.

⁶¹ J. A. Pople and M. S. Gordon, *J. Amer. Chem. Soc.*, 1967, **89**, 4253; W. J. Hehre and J. A. Pople, *ibid.*, 1970, **92**, 2191; see also ref. 56.

⁶² G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley-Interscience, New York, 1972, p. 38.

⁶³ B. V. Cheney and D. M. Grant, *J. Amer. Chem. Soc.*, 1967, **89**, 5319; J. Mason, *J. Chem. Soc. (A)*, 1971, 1038.

3) (e.g. 6 α - or 6 β -methyl in a 3-oxo-5 α -steroid) follows the stronger dissignate effects found for 6 α -F or Cl, and for 6 β -Cl, Br, or I.⁶⁴ We have also observed dissignate effects for 6 α - and 6 β -OH, OAc, and O-CO-CF₃ substituents.⁶⁵ We therefore visualise all dissignate effects of electronegative γ' -substituents, including those of methyl groups, as being due to inductive withdrawal of electrons from the primary zig-zag, just as was observed by Hudec for electronegative substituents at the more remote 3 α -position in a 7-oxo-5 α -steroid (p. 1077). It is now evident that the dissignate behaviour of a 6 α -methyl group in a 3-oxo-steroid (p. 1081), or of similarly-located alkyl groups in other systems, does not necessarily imply a 'front-octant' location (p. 1077) in relation to a curved nodal surface.

The dissignate behaviour of some β -axial methyl or methylene groups (Table 3, Class 2), as well as of β -axial heteroatom substituents in general,^{5b,16} may result at least in part from a similar inductive withdrawal of electrons from the primary zig-zag; some direct interaction with the carbonyl group through space cannot, however, be ruled out, in view of the proximity of the β -axial position to carbonyl.

Those β -axial methyl groups (Table 3, Class 1) attached to a longer primary zig-zag, and which appear to make a consignate contribution, must be viewed with caution. What we observe is the total effect of the simultaneous presence of a β -axial methyl group *and* the third (and any subsequent) bond of the primary zig-zag. To attribute the consignate enhancement to the β -axial substituent alone is logically unsound, for it may equally be argued from the data that the β -axial group is exerting its normal dissignate effect, but that in some way it enhances the consignate contribution of the third bond of the primary zig-zag. There seems to be no direct experimental way of separating the effects of the two structural components, since one can only observe their sum, which differs from the sum of the individual effects of the bonds. The same dilemma complicates study of the other two instances of non-additivity which we have uncovered [α -*eq* + β -*ax* (p. 1086) and 'middle-ring' ketones (p. 1086)].

¹³C N.m.r. spectroscopy and calculations of charge density distribution in hydrocarbons again provide the basis for a possible rationalisation of these examples of non-additivity. All three structural combinations where additivity breaks down contain a four-carbon (or three-bond) fragment of 'skew-butane' type. Moreover, one or more of the three C-C bonds in each case is part of a primary zig-zag (Figure 11). The mutual compression of hydrogen atoms on the terminal carbon atoms of a skew-butane system is known to result in a significant transfer of electronic charge from hydrogen to carbon,^{56,66} the increase in positive charges on the hydrogen atoms

being 'roughly proportional to their discomfort'.⁵⁶ ¹³C N.m.r. spectra of suitable hydrocarbons display the effect of 'steric perturbation', with consequent increased electronic charge around carbon nuclei, as an upfield shift of the signals due to carbon atoms of a skew-butane fragment. Axial methyl groups in cyclohexane [Figure 12(a)], for example, show an upfield ¹³C shift (ca. 6 p.p.m.) due to compression with axial hydrogen atoms at C-3 and C-5, the ¹³C signals for which are themselves also shifted upfield to a similar extent.^{67,68} Signals due to vicinal *cis*- (Figure 12b) or *trans*-diequatorial methyl substituents (Figure 12c) in cyclohexane,⁶⁷ or *cis*-1- and 2-methyl substituents in cyclopentane⁶⁹ show the same effect;

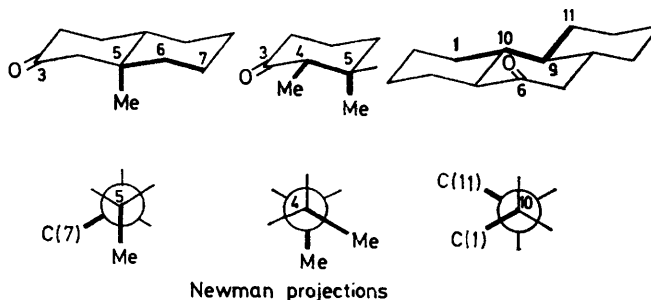


FIGURE 11 Structures exhibiting non-additivity of bond contributions: diagrams emphasising 'skew-butane' components

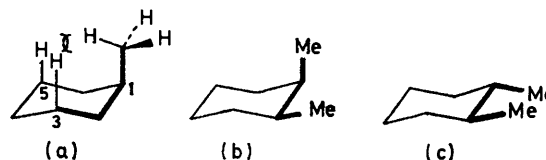


FIGURE 12 Systems with a 'skew-butane' component showing shielding (¹³C n.m.r.) due to steric perturbation of charge distribution

even in flexible open-chain hydrocarbons, where the 'skew-butane' conformation may be only one of several contributing forms, substitution of methyl for hydrogen at a carbon atom (C _{α}) results in a small upfield shift (ca. 2 p.p.m.) at C _{β} .^{62,63} The inner pair of carbon atoms of a skew-butane also shows the effect of strain in a slight upfield shift.^{62,67} We therefore suggest that the observed departures from additivity of c.d. contributions in some compounds containing a skew-butane fragment may be another manifestation of the phenomenon of steric perturbation of charge distribution, particularly when some of the atoms or bonds concerned lie on a primary zig-zag. Further investigations of charge distribution, and of correlations between c.d. and ¹³C n.m.r. data, seem likely to make a useful contribution to the understanding of chiroptical phenomena.

⁶⁴ C. S. Barnes and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1962; J.-C. Jacquesy and J. Levisalles, *Bull. Soc. chim. France*, 1962, 1866.

⁶⁵ D. N. Kirk, unpublished results.

⁶⁶ D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.*, 1967, **89**, 5315.

⁶⁷ D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, 1967, **89**, 6612; N. K. Wilson and J. B. Stothers, *Topics Stereochem.*, 1974, **8**, 1.

⁶⁸ F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, 1971, **93**, 258.

⁶⁹ M. Christi, H. J. Reich, and J. D. Roberts, *J. Amer. Chem. Soc.*, 1971, **93**, 3463.

EXPERIMENTAL

C.d. curves were measured for *ca.* 0.04% solutions in spectroscopic grade n-hexane, dioxan, acetonitrile, methanol, or ethanol, in a 1 cm cell, with a Roussel-Jouan Dichrograph 185 or Cary 61 instrument. Values of $\Delta\epsilon$ and λ_{max} determined on both instruments for each of a selection of ketones were virtually identical.

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