

## Chiroptical Studies. Part 90.<sup>1</sup> The Circular Dichroism of Cyclopentanones and Related Compounds. A Proposed Octant-dissignate Effect of C-H Bonds

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An analysis of c.d. data ( $n \rightarrow \pi^*$ ) for chiral cyclopentanone rings suggests that the  $C_\alpha$ -H bonds make the dominant contributions, in the octant-dissignate ('anti-octant') sense. The *magnitude* of a  $C_\alpha$ -H contribution is considered to be given approximately by the empirical expression  $\delta\Delta\epsilon = 6.2 \sin^2\omega$ , where  $\omega$  is the torsion angle between the  $C_\alpha$ -H and C=O bonds. On this basis, *all* common  $\alpha$ -substituents probably contribute in the octant-dissignate sense to the c.d. of a ketone, most appearing to have an octant-consignate effect only because they replace a more dissignate  $\alpha$ -hydrogen atom. This new method for calculation of chiroptical effects has been applied to some compounds thought to contain twisted cyclohexanone rings, and to some monocyclic cyclopentanone derivatives.

THE success of the Octant Rule<sup>2</sup> in relating the o.r.d. and c.d. characteristics of chiral ketonic compounds to their stereochemistry has been of great value in assignments of structure or configuration; it has, however, diverted attention from an important feature of the underlying phenomenon of the dissymmetric perturbation of the carbonyl  $n \rightarrow \pi^*$  transition by molecular structure. The present paper is wholly concerned with the  $n \rightarrow \pi^*$  transition.

A footnote to the original statement of the Octant Rule<sup>2</sup> acknowledged that neglect of the contributions of hydrogen atoms was a practical convenience, but was not necessarily justified. The largest accumulation of chiroptical data refers to ketones of the extended decalone type,<sup>3</sup> with the cyclohexanone ring in its usual preferred chair conformation. Such compounds have *local*  $C_2$  symmetry in the cyclohexanone ring itself, but are chiral by virtue of additional rings or substituents at the ' $\alpha$ '- or ' $\beta$ '-carbon atoms. A conformationally rigid ' $\alpha$ '-axial bromocyclohexanone (Figure 1), for example, exhibits chiroptical behaviour which is commonly considered to manifest an octant-consignate<sup>4</sup> ('pro-octant') effect of the bromo-substituent.<sup>5</sup> In fact, assuming additivity of effects of substituents, we observe the *difference* (or the algebraic sum) of the

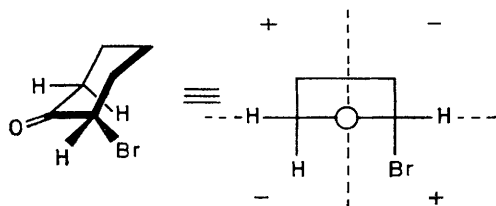


FIGURE 1 ' $\alpha$ '-Axial bromocyclohexanone, and rear-octant diagram

separate contributions of the ' $\alpha$ '-axial bromo-substituent and the ' $\alpha$ '-axial hydrogen atom. The symmetry characteristics of an undistorted cyclohexanone in the chair conformation preclude the use of such experimental data alone to separate the substituent and hydrogen atom contributions. Tables of data representing contributions of structural features to chiroptical

<sup>1</sup> Part 89, D. N. Kirk and W. Klyne, *J.C.S. Perkin I*, 1976, 762.

<sup>2</sup> W. Moffitt, R. B. Woodward, A. Moscovitz, W. Klyne, and C. Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

<sup>3</sup> D. N. Kirk and W. Klyne, *J.C.S. Perkin I*, 1974, 1076, and references therein.

properties of cyclohexanone analogues,<sup>3</sup> while being valuable for structural and stereochemical studies, contain insufficient information to permit the derivation of *absolute* values for the chiroptical effects of substituents; all reported data for such compounds are relative to hydrogen at the same location.

A different situation pertains for chiral cyclopentanone derivatives,<sup>1</sup> however, for the chiroptical properties are associated mainly with twisting of the cyclopentanone ring itself.<sup>6,7</sup> Substituent effects, though often not negligible, are usually relatively small.<sup>1</sup> The custom of representing cyclopentanone rings by diagrams (Figure 2)

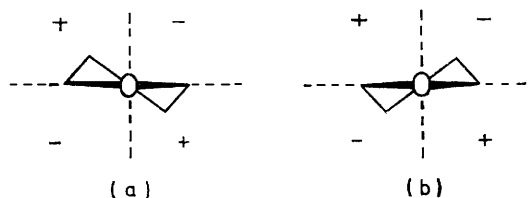


FIGURE 2 Conventional octant diagrams for chiral cyclopentanone rings: (a) c.d. positive; (b) c.d. negative

which show only the dissymmetrically arranged carbon atoms, and the fact that application of the Octant Rule to such diagrams has correctly predicted signs corresponding to those of the Cotton effects observed experimentally,<sup>6,7</sup> have unfortunately diverted attention from the possibility of major contributions coming from hydrogen atoms or C-H bonds.

After reconsideration of chiroptical data<sup>1</sup> for compounds containing a chiral cyclopentanone ring it is now suggested that the apparently consignate chiroptical behaviour of a cyclopentanone ring is really a manifestation of dominant *octant-dissignate*<sup>4</sup> ('anti-octant') behaviour of ' $\alpha$ '-quasi-axial C-H bonds (Figure 3), rather than of consignate behaviour of ring carbon atoms or C-C bonds. Moreover a quantitative though empirical analysis of the data which emerged from our recent study of hexahydroindanones<sup>1</sup> has afforded quite large estimated values of *octant-dissignate* contributions of ' $\alpha$ '-axial C-H bonds (p. 2174). If the magnitudes estimated for dissignate C-H effects have any validity,

<sup>4</sup> W. Klyne and D. N. Kirk, *Tetrahedron Letters*, 1973, 1483.

<sup>5</sup> C. Djerassi and W. Klyne, *J. Chem. Soc.*, 1963, 2390.

<sup>6</sup> W. Klyne, *Tetrahedron*, 1961, **13**, 29.

<sup>7</sup> W. Klyne, *Bull. Soc. chim. France*, 1960, 1396.

they imply that many if not all of the ' $\alpha$ '-axial substituents most commonly studied (*e.g.* Me, Cl, Br, and I) \* also exert dissignate rather than consignate effects; the effects of substituents give the appearance of being consignate only because they are normally being compared with even more dissignate contributions of the hydrogen atoms (or C-H bonds) which they replace. This conclusion regarding effects of individual bonds may be concealed in the results which have come from MO-based theoretical treatments of the chiroptical properties resulting from dissymmetric perturbation of the carbonyl chromophore,<sup>8</sup> but does not appear to have been stated explicitly even when attention has been focused on bonding patterns.<sup>11</sup>

Some recent theoretical studies, however, have produced findings similar to ours, although the authors have not laid any emphasis upon the dissignate C-H effects implied by their results. Emeis<sup>12</sup> used SCF wave functions to calculate the rotational strength of *trans*-hexahydroindan-2-one, and presented conclusions implying that the larger part of the  $n \rightarrow \pi^*$  Cotton

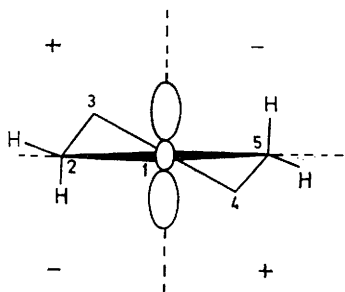


FIGURE 3 Octant diagram for a 'twisted' cyclopentanone ring, showing  $C_{\alpha}$ -H bonds

effect can be attributed to perturbation by the ' $\alpha$ '-quasiaxial hydrogen atoms of C-H bonds (octant-dissignate); a much smaller dissignate contribution (*ca.* 10% of the total) is due to the  $C_{\alpha}$ - $C_{\beta}$  bonds of the cyclopentanone ring. Bouman and Lightner,<sup>13</sup> using a CNDO method for the calculation of rotational strengths of a large number of chiral ketones (mainly of cyclohexanone or decalone type), also present data with the implication that the contributions associated with both  $C_{\alpha}$ -H and  $C_{\alpha}$ - $C_{\beta}$  bonds are generally dissignate. These theoretical treatments are strictly concerned with complete wave-functions, in contrast to the principle underlying our recent empirical analyses of c.d. data for extended decalone<sup>3</sup> and hexahydroindanone<sup>1</sup> derivatives. Our assumption that the contributions of suitably chosen structural features are characteristic

\* See footnote references to Table 2.

<sup>8</sup> J. C. Tai and N. L. Allinger, *J. Amer. Chem. Soc.*, 1966, **88**, 2179; O. E. Weigang and E. G. Höhn, *ibid.*, p. 3673; Y.-H. Pao and D. P. Santry, *ibid.*, p. 4157; T. D. Bouman and A. Moscovitz, *J. Chem. Phys.*, 1968, **48**, 3115; G. M. Robinson and O. E. Weigang, *J. Amer. Chem. Soc.*, 1969, **91**, 3709; J. M. Howell, *J. Chem. Phys.*, 1970, **53**, 4152; A. D. Buckingham and P. J. Stiles, *Accounts Chem. Res.*, 1974, **7**, 258; see also references 9 and 10.

<sup>9</sup> R. R. Gould and R. Hoffmann, *J. Amer. Chem. Soc.*, 1970, **92**, 1813.

and additive was generally found to lead to satisfactory results, and has been employed again in the present study.

*Empirical Considerations.*—Cyclopentanone ring conformations have been classified for convenience as either

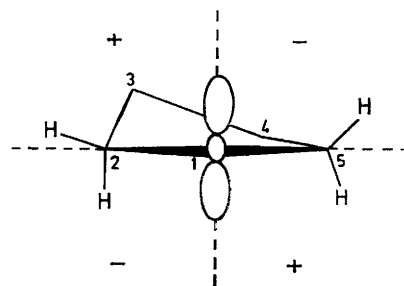


FIGURE 4 Octant diagram for a 'folded' cyclopentanone ring, showing  $C_{\alpha}$ -H bonds

'twisted' or 'folded'.<sup>1</sup> Twisted rings are those in which C-3 and C-4 lie on opposite sides of the 'horizontal' plane defined by the oxygen atom and C-1, C-2, and C-5 (Figure 3), and folded conformations are those in which C-3 and C-4 lie on the same side of the 'horizontal' plane (Figure 4). The boundary case is the 'envelope' conformation, with only one methylene carbon atom out-of-plane. To a first approximation, the c.d. of a chiral cyclopentanone ring is considered to be the sum of the contributions of its component 'halves,' which lie on either side of the vertical plane defined by the carbonyl  $\pi$ -orbital (Figures 3 and 4). We therefore regard a chiral cyclopentanone as being made up of two 'chiral units' of the type illustrated in Figure 5. A 'chiral unit' represents the superimposition of three chiral four-centre components (Figure 6), each of which

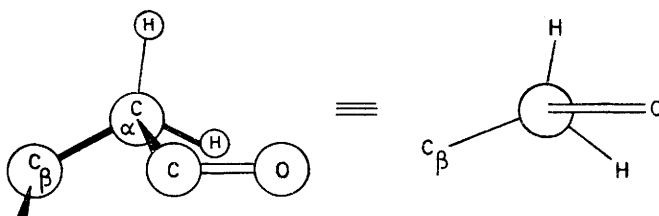


FIGURE 5 A chiral 'half' of a cyclopentanone ring: chiral unit comprising the carbonyl group,  $C_{\alpha}$ , and the atoms attached to  $C_{\alpha}$  (shown also in Newman projection)

comprises the  $O=C-C_{\alpha}$  system and one of the three other atoms or groups (R) attached to  $C_{\alpha}$ . The c.d. contribution associated with a chiral 'half' of the ring is then regarded as the sum of contributions, from the three

<sup>10</sup> J. A. Schellman, *J. Chem. Phys.*, 1966, **44**, 55; E. H. Höhn and O. E. Weigang, *ibid.*, 1968, **48**, 1127; G. Wagnière, *J. Amer. Chem. Soc.*, 1966, **88**, 3937.

<sup>11</sup> R. M. Lynden-Bell and V. R. Saunders, *J. Chem. Soc. (A)*, 1967, 2061; J. Hudec, *Chem. Comm.*, 1970, 829; M. T. Hughes and J. Hudec, *ibid.*, 1971, 805; G. P. Powell and J. Hudec, *ibid.*, p. 806.

<sup>12</sup> C. A. Emeis, Thesis, Leiden, 1968.

<sup>13</sup> T. D. Bouman and P. A. Lightner, *J. Amer. Chem. Soc.*, 1976, **98**, 3145. I thank Professor Bouman for a copy of this manuscript before publication.

chiral four-centre units (*cf.* Whiffen<sup>14</sup> and Brewster<sup>15</sup>). It seems reasonable to regard the contribution of a chiral four-centre unit as being given by some function of the torsion angle  $\omega$  between the  $C_\alpha$ -R bond and the C=O bond (Figure 6). The angle  $\omega$  may usually be crudely estimated from a Dreiding model, or in some cases may be evaluated more accurately from X-ray data.

From symmetry considerations, the c.d. contribution of a chiral four-centre component O=C- $C_\alpha$ -R (Figure 6) must be zero when  $\omega = 0$  or  $180^\circ$ , and should reach a maximum value for some intermediate value of  $\omega$ , probably near  $90^\circ$  when the  $C_\alpha$ -R bond is aligned with the  $p$  orbital at the carbonyl carbon atom. [Gould and Hoffmann<sup>9</sup> have calculated that the rotational strength of acetaldehyde would be at a maximum for the conformation where one of the methyl C-H bonds makes a torsional angle ( $\omega$ ) of  $90^\circ$  with the carbonyl bond axis.] The choice of a sine function for empirical investigation

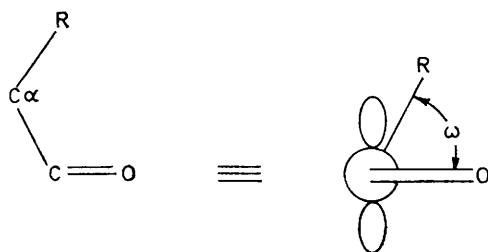


FIGURE 6 Chiral 'four-centre component' of a ketone, comprising the carbonyl group, one of the  $\alpha$ -carbon atoms, and an atom or group (R) attached to  $C_\alpha$  (shown also in Newman projection)

of the angular dependence of the c.d. therefore seemed reasonable, and the simple equation (i) was adopted,

$$\delta\Delta\epsilon = k \sin^2 \omega \quad (i)$$

where  $\delta\Delta\epsilon$  is the notional contribution of the bond  $C_\alpha$ -R to the total value of the Cotton effect,  $\Delta\epsilon$ ;  $\omega$  is the torsion angle defined above (Figure 6), and  $k$  is a proportionality constant, expected to take a characteristic value for each type of atom or group R bonded to  $C_\alpha$ . Coefficients  $k$  for particular atoms or groups are indicated by subscripts, *e.g.*  $k_H$  for a  $C_\alpha$ -H bond,  $k_O$  for the  $C_\alpha$ - $C_\beta$  bond of a cyclopentanone, *etc.*

Equation (i) is identical in form with the equation used previously<sup>1</sup> to relate methyl substituent effects to the torsion angle  $\omega$ . The only difference in the present analysis is that equation (i) is here used to express the *absolute* contribution  $\delta\Delta\epsilon$  of a bond or group, whereas the previous analysis was concerned with substituent effects relative to hydrogen.

The alternative equation (ii) was also tested briefly, but gave unsatisfactory results (see Appendix).

$$\delta\Delta\epsilon = k \sin \omega \quad (ii)$$

<sup>14</sup> D. H. Whiffen, *Chem. and Ind.*, 1956, 964.

<sup>15</sup> J. H. Brewster, *J. Amer. Chem. Soc.*, 1959, **81**, 5475, 5483, 5493; *Tetrahedron*, 1961, **13**, 106.

<sup>16</sup> C. Coulombeau and A. Rassat, *Bull. Soc. chim. France*, 1971, 516.

The following calculations are concerned with the combined effects of the three bonds originating from  $C_\alpha$  (Figure 5), each of which makes its own torsion angle with the carbonyl group. For convenience, the torsion angle  $\omega$  is given the value appropriate to the  $C_\alpha$ - $C_\beta$  bond of the cyclopentanone ring; the values of torsion angles for the two  $C_\alpha$ -H bonds are then taken to be  $(\omega + 120)^\circ$  and  $(\omega - 120)^\circ$ , respectively, with the assumption of perfect tetrahedral bond angles for simplicity.

Use of equation (i), a function of  $\sin^2 \omega$ , gives a positive-signed term which can afford only the *magnitude* of  $\delta\Delta\epsilon$ . Terms for the three individual bonds from  $C_\alpha$  in each chiral unit (Figure 5) were therefore given the signs expected from the Octant Rule, with the assumption, for convenience, that each of the three bonds lies in a rear octant. The question of whether the space around a carbonyl group should be divided into *quadrants*, reflecting the true symmetry of the chromophore, or *octants*, which imply a third boundary surface separating 'front' from 'rear' regions, has been the subject of much discussion.<sup>10</sup> Recent experimental results<sup>16-18</sup> give support to the octant treatment, although the precise shape of the 'third' surface is not agreed.<sup>13,16</sup> The present analysis employs the 'octant' pattern for the following reasons: (a) the use of an 'octant' framework for carbonyl compounds has become customary; (b) the generally 'octant-consignate' behaviour (relative to hydrogen) of alkyl, chloro, and bromo substituents ' $\alpha$ ' to carbonyl, whether in cyclopentanones ( $50^\circ < \omega < 90^\circ$ ) or in cyclohexanones ( $\omega$  *ca.*  $115^\circ$  for axial substituents) is consistent with the assumption that all three bonds radiating from  $C_\alpha$  are in rear octants, for otherwise a change of sign of substituent effects would be expected at some intermediate value of  $\omega$ ; (c) as a matter of terminology, taking account of the definitions proposed for the terms 'consignate' and 'dissignate';<sup>4</sup> the 'octant-dissignate' contributions described in this paper correspond to the older term 'anti-octant,' whereas a quadrant frame would require use of the confusing expressions 'quadrant-consignate' for the proposed effects of C-H bonds, and 'quadrant-dissignate' for the *differences* associated with  $\alpha$ -substitution.

A composite equation (iii) for the combined contributions of the component bonds of Figure 5 was constructed as the algebraic sum of expressions for its three components, each signed as indicated above. This

$$\delta\Delta\epsilon = k_O \sin^2 \omega + k_H [\sin^2 (\omega + 120^\circ) - \sin^2 (\omega - 120^\circ)] \quad (iii)$$

simplifies to equation (iv). For a complete cyclopentanone ring, two equations of type (iv), each written

$$\delta\Delta\epsilon = k_O \sin^2 \omega - \sqrt{3}(k_H \sin 2\omega)/2 \quad (iv)$$

with appropriate signs for its individual terms, were summed to give an expression for the total value of  $\Delta\epsilon$ .

<sup>17</sup> D. A. Lightner and D. E. Jackman, *J. Amer. Chem. Soc.*, 1974, **96**, 1938; D. A. Lightner and T. C. Chang, *ibid.*, p. 3015.

<sup>18</sup> D. N. Kirk, W. Klyne, and W. P. Mose, *Tetrahedron Letters*, 1972, 1315.



or  $k = 1.6$  to express the effects of unstrained methyl substituents at quaternary or tertiary carbon, respectively, relative to hydrogen at the same position. Strain effects will be discussed in a separate paper.<sup>19</sup>

150°. The model (Figure 7a) shows, however, that the 13 $\beta$ -methyl and 16 $\beta$ -hydrogen groups suffer mutual compression which should lead to a preference for a dissymmetric conformation. By flexing the model so

TABLE 3  
C.d. data for compounds thought to include cyclohexanone rings in the 'twist' conformation

|  | $\Delta\epsilon$ (obs.)                               | $\Delta\epsilon$ (calc.) <sup>a</sup>                 |              |  |
|--|---|---|--------------|--|
|  |   | 'All-chair'   | $C_2$ twist  | Others                                 |
| 17 $\beta$ -Methyl-17 $\alpha$ -oxo-D-homo-steroid (1) | +3.6 (C <sub>6</sub> H <sub>14</sub> )<br>+4.2 (MeOH) | +0.8 (C <sub>6</sub> H <sub>14</sub> )<br>+1.4 (MeOH) | +6.5         | +4.2 <sup>b</sup><br>+1.4 <sup>c</sup> |
| <i>trans</i> -Tetrahydroeremophilone (2)               | -2.7 <sup>d</sup>                                     | -2.35   | -5.9         | -3.7 <sup>c</sup>                      |
| 11-Oxo-13 $\alpha$ -steroid (3)                        | -4.6 <sup>d</sup>                                     | -1.05   | -6.7         |  |
| 1 $\beta$ -Methyl-3-oxo-5 $\alpha$ -steroid (4)        | +1.8 <sup>d</sup>                                     | +0.5  | Inaccessible | +1.3 <sup>c</sup>                      |

<sup>a</sup> No allowance was made for variations of solvent unless otherwise indicated. <sup>b</sup> For estimated 'minimum-strain' conformation—see text, p. 2176. <sup>c</sup> For 'envelope' conformation. <sup>d</sup> From  $\Delta\epsilon = a/40.28$  (S. F. Mason, *Quart. Rev.*, 1963, 17, 10).

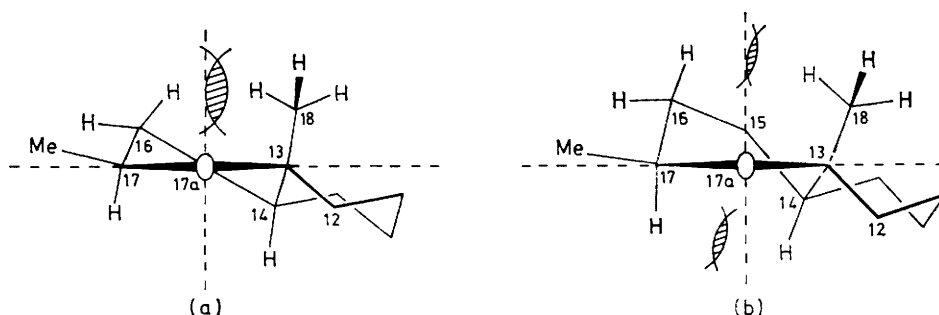


FIGURE 7 Octant projections of the 17 $\beta$ -methyl-D-homo-17 $\alpha$ -oxo-steroid (1): (a) with ring D in symmetrically-twisted ( $C_2$ ) conformation; (b) with ring D in asymmetrically-twisted 'minimum energy' conformation, to relieve 16 $\beta$ -H/18-H interaction

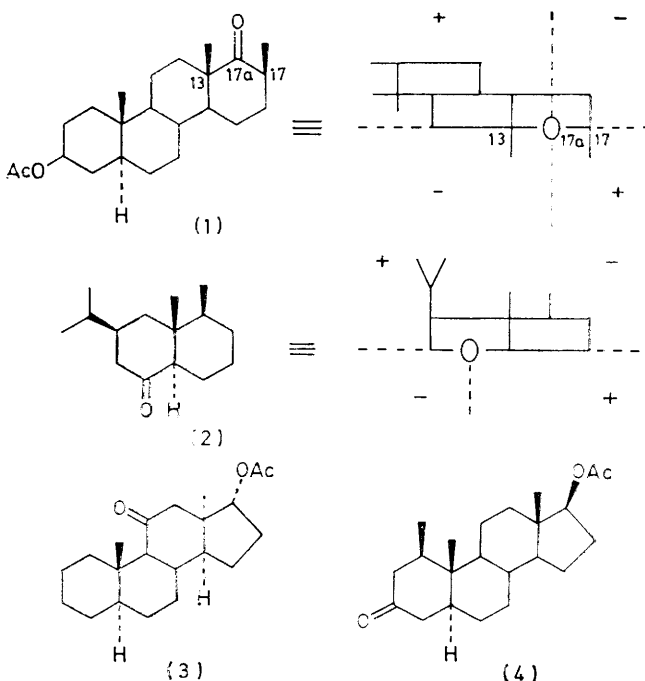
*Applications.*—(a) *Compounds thought to contain 'twisted' cyclohexanone rings.* Abnormal amplitudes (o.r.d.) found for some decalone derivatives led to the suggestion<sup>20</sup> that the cyclohexanone ring component had adopted the twist conformation in order to relieve gross steric compression which destabilises the chair form. The compounds in question were the 17 $\beta$ -methyl-D-homoandrostan-17 $\alpha$ -one (1), *trans*-tetrahydroeremophilone (2), an 11-oxo-13 $\alpha$ -steroid (3), and a 1 $\beta$ -methyl-3-oxo-5 $\alpha$ -steroid (4). By using data from our work on decalones<sup>3</sup> it is now possible to calculate the  $\Delta\epsilon$  values to be expected if these four ketones had all-chair conformations. Table 3 gives these calculated  $\Delta\epsilon$  values together with those derived from experimental data. *trans*-Tetrahydroeremophilone no longer appears as a gross anomaly, for the reasons given below. The other three compounds all exhibit  $\Delta\epsilon$  values considerably larger than those calculated on the 'all-chair' assumption, although signs are correct.

The procedure described above for calculating  $\Delta\epsilon$  for cyclopentanones can be extended to 'twist' forms of the cyclohexanone ring. There is little energy difference amongst various twist conformations of an unsubstituted cyclohexanone ring; the twist  $\rightarrow$  boat change requires only *ca.* 1 kcal mol<sup>-1</sup>.<sup>21</sup> The 17 $\beta$ -methyl-17 $\alpha$ -oxo-D-homo-steroid (1), if we assume a perfect twist form (local  $C_2$  symmetry) of ring D, has torsion angles  $\omega$  which were estimated from a Dreiding model to be *ca.*

<sup>19</sup> D. N. Kirk, in preparation.

<sup>20</sup> C. Djerassi and W. Klyne, *Proc. Nat. Acad. Sci., U.S.A.*, 1962, 48, 1093.

that the 14 $\alpha$ -H/17 $\alpha$ -H and 16 $\beta$ -H/18-H separations become equal (Figure 7b), torsion angles with respect to



C=O become *ca.* 130° for C-16 and 165° for C-14. Values of  $\Delta\epsilon$  calculated for both these conformations are given

<sup>21</sup> G. M. Kellie and F. G. Riddell, *Topics Stereochem.*, 1974, 8, 261.

in Table 3. Calculations are based on equation (iii), with  $k_H = -6.2$ ,  $k_C = -4.6$  at C-16 (for tertiary carbon), and  $k_C = -4.3$  at C-13 (for quaternary carbon). These coefficients  $k_C$  are the ones appropriate for  $C_\alpha$ -C bonds which are considered to be strain-free, since six-membered rings are involved. They are calculated from  $k_H = -6.2$  by allowing consignate (positive) methyl-substitution effects of  $+1.6$  and  $+1.9$  units, respectively,<sup>3</sup> for the  $C_\alpha$ -C bonds, here regarded as equivalent to  $C_\alpha$ -Me bonds.

The calculated value of  $\Delta\epsilon$  ( $+4.2$ ) for the dissymmetric 'minimum-energy' conformation (Figure 7b) is close to the experimental values ( $+3.6$  or  $+4.2$ ). The calculated value of  $\Delta\epsilon$  is very sensitive to the pair of torsion angles adopted: a further small variation to  $125^\circ$  and  $172.5^\circ$ , respectively, reduced the calculated value of  $\Delta\epsilon$  to  $+2.9$ , and distortion of ring D as far as the 'envelope' conformation gave  $\Delta\epsilon +1.4$ . These calculations suggest that the true torsion angles probably lie within the regions  $125$ – $130^\circ$  for C-16 and  $165$ – $172.5^\circ$  for C-14.

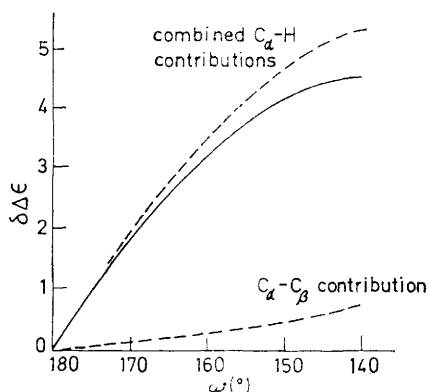


FIGURE 8 Graph of the equation  $\delta\Delta\epsilon = -5.4 \sin 2\omega - 1.9 \sin^2\omega$  (solid line) representing the contribution of one chiral 'half' of a cyclopentanone ring to the total value of  $\Delta\epsilon$  (broken lines indicate the separate contributions of the terms:  $-5.4 \sin 2\omega$  for combined effects of the two  $C_\alpha$ -H bonds;  $1.9 \sin^2\omega$  for effect of  $C_\alpha$ - $C_\beta$  bond, where  $\omega$  is the  $O=C-C_\alpha-C_\beta$  torsion angle)

Results of similar calculations for twisted conformations of compounds (2)–(4) are included in Table 3. They suggest that *trans*-tetrahydroremophilone (2), despite earlier impressions,<sup>20</sup> exists largely in the 'all-chair' conformation; the 'calculated' value of  $\Delta\epsilon$  now makes allowance for the  $8\beta$ -methyl group, which extends a primary zig-zag, and includes a weakly dissignate effect for the ' $\beta$ '-axial 2 $\beta$ -isopropyl group, considered here as being approximately equivalent in its c.d. effect to a methyl group in the same location. The 11-oxo-13 $\alpha$ -steroid (3) appears to be largely in a twist conformation, although the likely torsion angles cannot easily be estimated from models. The 1 $\beta$ -methyl-3-oxo-5 $\alpha$ -steroid (4) is unable to attain the *symmetrical* twist conformation, but probably exists largely in an *unsymmetrically* twisted form in which the sum of the

1 $\beta$ -Me/11-CH<sub>2</sub> and 1 $\beta$ -Me/10 $\beta$ -Me interactions is minimised.

(b) *Monocyclic cyclopentanone derivatives.* Insertion of the derived values of  $k_H$  and  $k_C$  into equation (iv) leads to two equations, (v) and (vi), for the contributions of 'halves' of a chiral cyclopentanone ring to the observed value of  $\Delta\epsilon$ . For positive values of the  $O=C-C_\alpha-C_\beta$  torsion angle  $\omega$  we have equation (v), and for negative

$$\delta\Delta\epsilon = -1.9 \sin^2 \omega - 5.4 \sin 2 \omega \quad (v)$$

values of  $\omega$ , equation (vi). In practice, it may often be

$$\delta\Delta\epsilon = +1.9 \sin^2 \omega - 5.4 \sin 2 \omega \quad (vi)$$

convenient to ignore the first term, which expresses the contribution of the  $C_\alpha$ - $C_\beta$  bond. Its omission affects the calculated value of  $\delta\Delta\epsilon$  negligibly for values of  $\omega$  between  $180$  and  $160^\circ$ , and only becomes significant (error  $\geq 0.5$  unit, or *ca.* 10% of total) for values of  $\omega \leq 150^\circ$ , not found except in highly skewed cyclopentanones. Figure 8 gives a graphical representation of equation (v) and its component terms.

The preferred conformation of an unsubstituted cyclopentanone ring is a twist form,<sup>22</sup> with  $C_2$  symmetry and torsional angles  $\omega$  probably close to  $165^\circ$ . The expected value of  $\Delta\epsilon$  for the enantiomeric twist forms is  $\pm 5.2$  units ( $2 \times 2.6$ ), with the sign following the sign of  $\omega$ , or the twist of the ring (Figure 2).

Cyclopentanone itself necessarily exists as an equimolar mixture of enantiomeric twist conformations, but a substituent would be expected to disturb the equilibrium by preferring to adopt the equatorial or quasi-equatorial conformation, so that one or other of the two twist conformations of the cyclopentanone ring will predominate. Simple calculations, on the assumption that the material is wholly distributed between the two extreme twist conformers, lead to the conclusions summarized in Table 4.

A 2-methyl substituent is considered to make its own contribution [equation (i)], as well as deciding the conformer populations. 3-Alkyl substituents are assumed to act only by stabilizing the conformations in which they are equatorial, since their contributions to the c.d. of 'twisted' cyclopentanones are negligible.<sup>1</sup> The conformer populations do not yet appear to have been determined experimentally for alkylcyclopentanones. The available c.d. data were therefore used to calculate a conformer ratio for each of the compounds in Table 4; the conformational free-energy differences  $\Delta G^\circ$  which would account for the calculated conformer ratios are also listed. The value of  $\Delta G^\circ$  ( $0.52 \pm 0.14$  kcal mol<sup>-1</sup>) estimated for 3-methylcyclopentanone agrees well with the value ( $0.54$  kcal mol<sup>-1</sup>) reported by Pitzer and Donath<sup>23</sup> for the hydrocarbon methylcyclopentane. The present calculated value for 2-methylcyclopentanone ( $\Delta G^\circ 0.09 \pm 0.13$  kcal mol<sup>-1</sup>) is smaller than that used by Ouannes and Jacques ( $0.25$

<sup>22</sup> C. Ouannes and J. Jacques, *Bull. Soc. chim. France*, 1965, 3601; N. L. Allinger, M. T. Tribble and M. A. Miller, *Tetrahedron*, 1972, 28, 1173.

<sup>23</sup> K. S. Pitzer and W. E. Donath, *J. Amer. Chem. Soc.*, 1959, 81, 3213.

kcal mol<sup>-1</sup>),<sup>24</sup> which would correspond to a 60 : 40 ratio of conformers, and by the present method of calculation gives  $\Delta\epsilon = -2.1$ . The discrepancy seems small in view of the approximations used in the derivation.

The estimates of conformational free energy differences ( $\Delta G^\circ$ ) in Table 4 imply rather low sensitivity to substitution type, with the maximum conformational preference in the case of a 3-t-butyl group, as expected. It is surprising that *cis*-4-isopropyl-2-methylcyclopentanone and *trans*-2,3-dimethylcyclopentanone gave such very low  $\Delta G^\circ$  values.

a cyclopentanone. In this case the composite equation simplifies to (iia). Equation (iia) cannot afford unique

$$\delta\Delta\epsilon = (k_O - k_H) \sin \omega \quad (\text{iia})$$

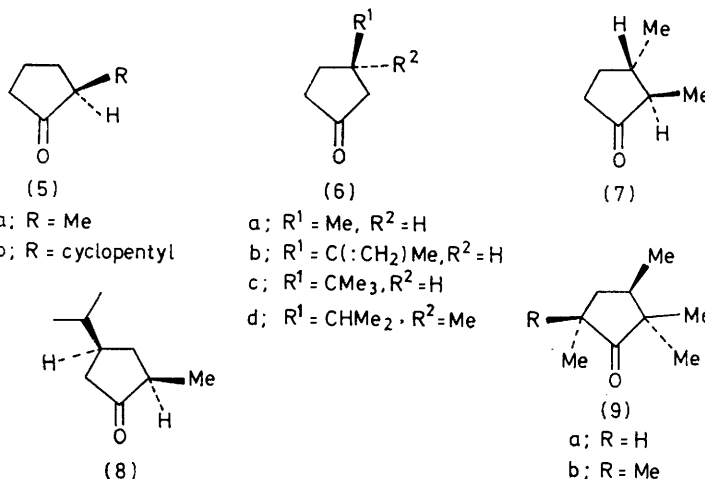
values of  $k_O$  and  $k_H$ , but can only give their difference. Insertion of  $\Delta\epsilon$  and  $\omega$  values for cyclopentanones (Table 1) gave four different numerical values of the difference  $k_O - k_H$  (5*t*2, +7.4; 5*c*2*eq*, +7.5; 5*t*3; +10.6; 5*c*3, +10.2; mean value +9). This result would imply that the effect of replacing an 'α'-axial hydrogen by a methyl group would be a consignate change of nearly

TABLE 4  
C.d. data and calculated conformer populations and  $\Delta G^\circ$  for alkylcyclopentanones

| Cyclopentanone derivative   | $\Delta\epsilon$ (obs.) * | $\Delta\epsilon$ (calc.)   |                      | % Quasi-equatorial conformer (calc.) † | $\Delta G^\circ$ /kcal mol <sup>-1</sup> for quasiequatorial conformer † |
|---|---------------------------|----------------------------|----------------------|--|--|
|   |                           | Quasi-equatorial conformer | Quasiaxial conformer |  |  |
| ( <i>R</i> )-2-Methyl (5a)  | -1.45 <sup>a</sup>        | -6.0                       | +3.7                 | 53 ± 5                                 | -0.07 ± 0.13   |
| ( <i>R</i> )-2-Cyclopentyl (5b)                                   | +0.8 <sup>b</sup>         | +6.0 ‡                     | -3.7 ‡               | 46 ± 6                                 | +0.09 ± 0.13   |
| ( <i>R</i> )-3-Methyl (6a)  | +2.1 <sup>b</sup>         | +5.2                       | -5.2                 | 70 ± 5                                 | -0.52 ± 0.14   |
| ( <i>R</i> )-3-Isopropenyl (6b)                                   | +2.3 <sup>b</sup>         | +5.2 ‡                     | -5.2 ‡               | 72 ± 5                                 | -0.57 ± 0.14   |
| ( <i>R</i> )-3- <i>t</i> -Butyl (6c)                              | +3.2 <sup>b</sup>         | +5.2 ‡                     | -5.2 ‡               | 81 ± 5                                 | -0.87 ± 0.19   |
| ( <i>R</i> )-3-Isopropyl-3-methyl (6d)                            | +2.4 <sup>b</sup>         | +5.2 ‡                     | -5.2 ‡               | 73 ± 5                                 | -0.60 ± 0.15   |
| (2 <i>R</i> ,3 <i>S</i> )- <i>trans</i> -2,3-Dimethyl (7)         | -1.7 <sup>b</sup>         | -6.0                       | +3.7                 | 57 ± 4                                 | -0.16 ± 0.10   |
| (2 <i>R</i> ,4 <i>S</i> )- <i>cis</i> -4-Isopropyl-2-methyl (8)   | -2.0 <sup>b</sup>         | -6.0 ‡                     | +3.7 ‡               | 60 ± 4                                 | -0.24 ± 0.10   |
| (3 <i>R</i> ,5 <i>R</i> )- <i>trans</i> -2,2,3,5-Tetramethyl (9a) | +0.5 <sup>c</sup>         | +2.9                       | -5.2                 | 70 ± 7                                 | -0.52 ± 0.18   |
| (3 <i>R</i> )-2,2,3,5,5-Pentamethyl (9b)                          | +1.2 <sup>c</sup>         | +3.6                       | -3.6                 | 67 ± 2                                 | -0.41 ± 0.07   |

<sup>a</sup> J. J. Partridge, N. K. Chadhar, and M. R. Uskokovic, *J. Amer. Chem. Soc.*, 1975, **97**, 532. <sup>b</sup> Ref. 24. <sup>c</sup> A. Collet, J. Jacques, B. Chion, and J. Lajzerowicz, *Tetrahedron*, 1975, **31**, 2243.

\* Italicised values from  $\Delta\epsilon = a/40.28$ . † The ranges of uncertainty are based upon the assumption that 'calculated' values of  $\Delta\epsilon$  are each ±0.5 units (*cf.* Table 1, and data in ref. 1). ‡ Calc. for the corresponding cyclopentanone with methyl substitution in place of other alkyl groups: alkyl substituents at C-3 or C-4 are assumed to have no direct effect on  $\Delta\epsilon$  (see text, p. 2176).



Alternative calculations of  $\Delta\epsilon$  for alkylcyclopentanones, in which the conformational free-energy data calculated by Ouannes and Jacques,<sup>24</sup> by an early version of the 'molecular mechanics' procedure, were combined with the use of equation (iv), gave no significant improvement in values of  $\Delta\epsilon$ .

*Appendix.—The unsuitability of equation (ii) ( $\delta\Delta\epsilon = k \sin \omega$ ). Equation (ii) was used to construct composite equations, similar to equation (iii), for the total contributions of C<sub>α</sub>-R bonds at each of the α-carbon atoms of*

**9** units in  $\Delta\epsilon$ , a far larger alkyl-substitution effect than any observed for the carbonyl  $n \rightarrow \pi^*$  transition. The maximum  $\delta\Delta\epsilon$  value for 'α'-axial methyl or methylene substitution is about 2 units.<sup>1,3</sup>

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<sup>24</sup> C. Ouannes and J. Jacques, *Bull. Soc. chim. France*, 1965, 3611.