Rationalisation of 'Dissignate' and 'Front Octant' Effects of Chiral Ketones by a Quadrant Rule

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Summary Theoretical study of a number of 2-alkanones reveals that both the normal and the abnormal (front octant and dissignate effect of substituents in rear octants) chiroptical behaviour of substituents in certain relative orientations with respect to the carbonyl group can be rationalised by a quadrant rule supplemented by a definition of the through-bond path that connects the substituent and the chromophore; the new rules are rationalised in terms of the change in the mixing of the x and y components of the total n MO orbital induced by the substituent.

THE shape[1-3] or even the necessity[4] for the third nodal surface of the C=O group that bisects the π^* orbital (generating a quadrant rule) has been a matter of discussion for some time. The planar surface of the original Octant Rule[1] was made convex in order to account for the dissignate behaviour of β-axial Me groups.[2] It was recently changed into a concave one in order to account for observed front octant behaviour; 'holes' were inserted into back octants in order to account for the β-axial Me groups.[3]

We have shown in one of the accompanying communications that the optical activity of ketones can be estimated by the twist ($\Delta\theta$) of the delocalised oxygen n and π^* orbitals[5] (due to mixing of oxygen $2p_x$, $2p_y$ and π, π^* orbitals). We have applied the relationships in this accompanying article to the above question of the third nodal surface, using Me-substituted model 2-alkanones, in appropriate conformations.[6] Our results are presented in Figures 1 [idealised cyclohexanone geometry Figure 1(b)] and 2 (idealised bicyclo[2.2.2]octanone geometry).

The inspection of the data ($\Delta\theta$) confirms both sets of calculations;[2,3] Me groups in direct coupling paths are all consignate and $\Delta\theta$ decreases as the number of intervening C–C bonds increases. Me groups in noncoupling paths are either dissignate or very weakly consignate. These calculations confirm beautifully the recently derived conclusions for alkyl substituents based on the analysis of the c.d. spectra of decalones and steroidal ketones[7] [Figure 1 (b)].

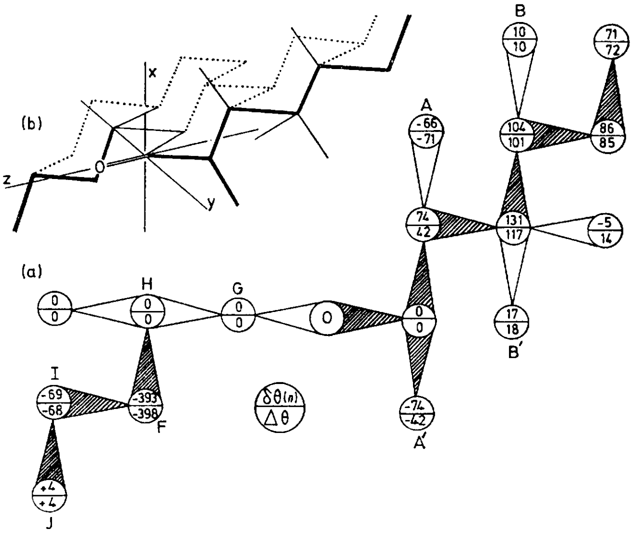


FIGURE 1. (a) $\Delta\theta$ and $\delta\theta(n)$ values for 2-alkanones which serve as models for decalinoidal and steroidal ketones generalised in (b): darkened (or thick) bonds represent coupling paths; light (or thin) bonds represent non-coupling paths.

The analysis of the calculations allows us to construct a general MO diagram for the delocalised n_0 orbital (Figure 3). Its inspection reveals that when certain pairwise H atoms (which have identical mixing interaction with the x and y components of the n MO) are substituted by a methyl group, the mixing is affected identically irrespective of their position in space. Thus the pairs of Me groups, A, A′ and C, C′, decrease the mixing; A′ and C′ will be consignate but A and C will be dissignate. Me groups B, B′, and D (D′ in the *yz* plane) hardly affect the mixing and thus would be expected to show only a very small contribution to $\Delta\epsilon$.

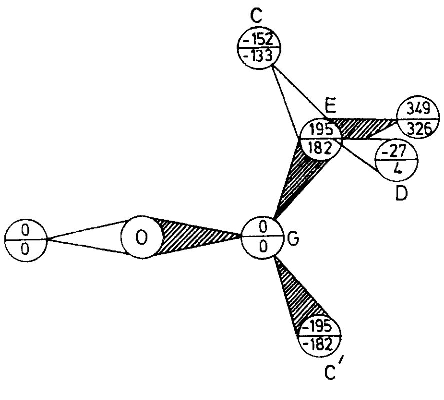


Figure 2. $\Delta\theta$ and $\delta\theta(n)$ values for bicyclo[2.2.2]octanone model.

The consignate (front octant) contribution of methyl group F is expected to be in contrast to methyl group E (mirror image) because the nodal properties of the C atom H to which it is attached have changed relative to C atom G (Figure 3). However, C atoms I and J are in a coupling path and thus will be expected to decrease the overall consignate effect. We can predict with confidence that compounds such as (**1**) will be dissignate (Octant Rule) in contrast to compounds of type (**1**) without ring X[8] which are weakly consignate.

These results force us to conclude that the chiroptical properties of substituted ketones cannot be satisfactorily rationalised either by Quadrant or Octant Rules alone. However, the use of a Quadrant Rule supplemented by a rule for recognition of coupling and non-coupling paths between the carbonyl group and the substituent does account for all known anomalies. Further generalisation for substituents other than methyl groups also requires the knowledge of the effect of the substituent on the mixing;[5] the retention of the Octant Rule[1] would require a plethora of variously shaped third surfaces not only for each substituent but also for each different orientation of that substituent about the various C–C bonds as well as the C–X bond if X has a lone pair (N, O, or S).

Rules for a recognition of coupling paths: (1) Replace C=O group in a substituted ketone with a CH_2.

(2) Replace C–X bond by C–H_x (if H_x will not be expected to couple (n.m.r. long range *J*[9]) with either H in CH_2, the path will be non-coupling. If it will couple, mark the H atom involved).

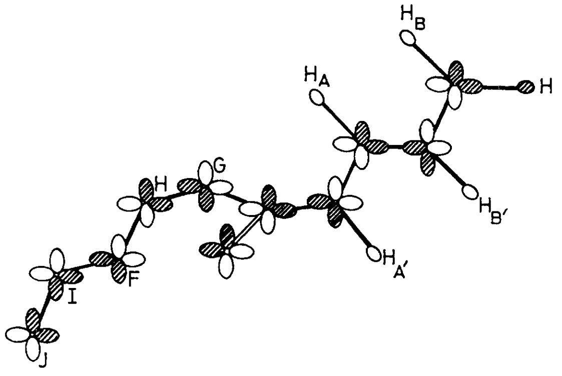
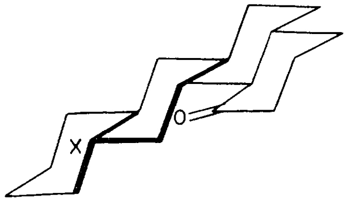


Figure 3. Generalised representation of the delocalised oxygen *n* MO.

(3) Replace the lone pair on X with X–H_y (if H_y couples with the marked H of CH_2 group, coupling path obtains, otherwise non-coupling).

(4) If more than one path is available, the one with the least number of intervening C–C bonds will dominate the twists.

Rule 3 is unimportant for symmetrical substituents such as halogens, Me, freely rotating NR_2, SR, OR, S^-, O^-, *etc.* but crucially important for bridged N, O, and S compounds.



(1)

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