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CIRCULAR DICHROISM - LIX [1]

ON THE APPARENT FAILURE OF THE OCTANT RULE IN THE TWISTANE - SERIES

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CHIROPTICAL Methods have been used to determine the absolute configuration of twistane by two groups of workers.[2,3,4] Adachi et al.,[2] by application of the octant rule [5] to the positive Cotton effect of the intermediate ketone (-)-I, predicted its absolute configuration to be enantiomeric with that shown below. They came to a similar conclusion in the case of the (+)-2-twistanone (II) (positive CD), chemically correlated with (-)-I, by using the rule of Djerassi and Klyne. [6] Tichý and Sicher [3] applied this same rule to (+)-4-twistanone (III), also exhibiting a positive Cotton effect, and were led to the same conclusion about the absolute configuration of twistane.

On the other hand, CD-measurements of derivatives of cis-4,5-twistanediol [4] (dibenzoate, [7] $(DPM)_3Eu$ complex, [8] thiocarbonyl derivative [9]) and application of the appropriate rules lead to the opposite absolute configuration of twistane, in accordance with chemical correlations. [4]

We would like to show here that the ketone rules for prediction of the CD are also in agreement with the revised absolute configuration, [4] if applied correctly.

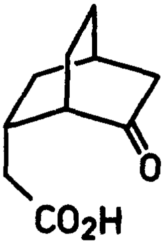
(-)-I: First we assume D_{3d}-symmetry for the bicyclo[2.2.2]octane skeleton; from the octant type projection [5] one can see that the carbonyl group is incorporated into two chiral second spheres [10] enantiomeric with each other, so that their contributions to the CD compensate each other. The CH_2CO_2H -

grouping lies formally in a "negative octant", [5] but it is positioned similarly to a ß-axial substituent of a cyclohexanone in a chair conformation. It has been shown [11,12,13] that in such an arrangement the sign of the contribution to the Cotton effect is usually opposite to that predicted from the original octant rule, [5] so that for the enantiomer drawn below a positive CD is indeed expected, and not a negative one as assumed by Adachi et al. [2] If on the other hand the skeleton is twisted so that only D_3-symmetry applies, then the magnitudes of the chiralities (chirality can be measured quantitatively *e.g.* by an appropriate chirality function, *cf.* Ruch and Schönhofer [14]) of the two chiral second spheres are not the same, which leads only to partial compensation of the respective contributions to the CD. However, such small distortions will be approximately equally possible in both senses, so the overall contribution of the two second spheres to the Cotton effect will again be zero or at least very small. Thus the CD in this case also will be determined by the third-sphere-contributions of the side chain, which follow, however, an "anti-octant-rule", as mentioned above.

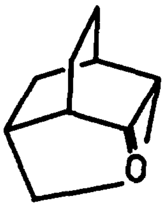
(+)-II: The carbonyl group of 2-twistanone is incorporated into three different six-membered rings, each of them forming a chiral second sphere. In their discussion, however, Adachi et al. [2] considered only the middle ring, hatched in the drawing below, where the C=O lies in the "point" of the twist. [6] For *(+)-II* this ring adopts M-helicity, for which a negative contribution to the CD is predicted. [6] However, the chirality of both other ("outer") rings is such that according to the same rule a positive Cotton effect is predicted for them. Experience shows that with two chiral second spheres of opposite sense of chirality the smaller ring determines the sign of the Cotton effect (*e.g.* camphor, certain kaurane derivatives, etc.). Without making detailed calculations there is no *a priori* reason why the middle ring of *II* should be given priority over the other two in determining the sign of the Cotton effect, and obviously the combined positive contributions coming from the two "outer" rings override the negative contribution of the middle ring.

(+)-III: The carbonyl group of 4-twistanone is also part of two different chiral second spheres of the same ring size (cyclohexanones). The one

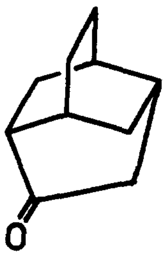
hatched in the drawing below gives rise to a negative CD, as in case of (+)-II, the other to a positive one. According to the octant rule the rest of the molecule will also give a weak positive contribution to the Cotton effect. One might have been inclined to ascribe a greater contribution to that chiral second sphere with C_2-symmetry (the hatched ring) than to the other ring on the basis of experience with cyclohexanones or cyclopentanones containing only a single second chiral sphere, but the example of (+)-III clearly shows that no such preference can be assigned in a case of two chiral spheres of same ring size.



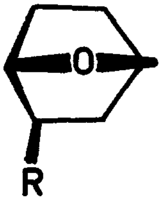
(-)-I

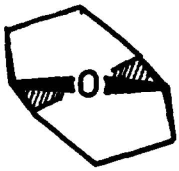


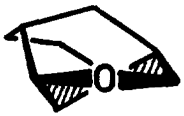
(+)-II



(+)-III







Thus also in the case of the twistanones a systematic application of the division of chiral molecules into different spheres [10] helps to avoid incorrect assignments caused by arbitrary disregard of essential parts of the molecules in question.

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