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CIRCULAR DICHROISM—LXIII[1]

THIRD-SPHERE CONTRIBUTION TO THE R-BAND COTTON EFFECT OF LACTONES

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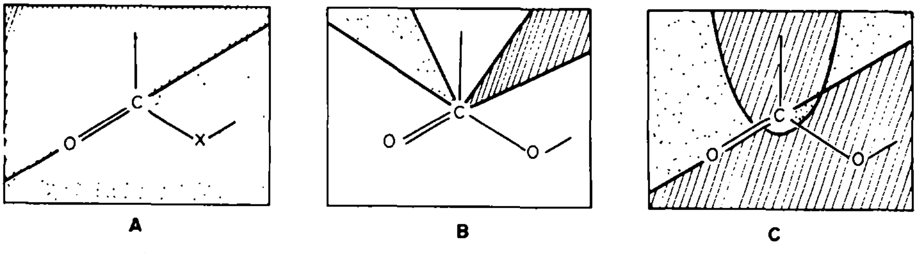
Summary—The Cotton effect within the n→π* band of the lactone chromophore of the halo lactones **3a–c**, prepared from (1S)-2-bromo adamantanedione-4.8 (**1**) is positive and can be used to determine unequivocally the sign of third-sphere contributions of the appropriate sector rule. An "axial" halogen (Cl, Br, I) substituent in a β-position to the keto group of these halogeno oxa-homoadamantanediones gives an antioctant contribution to the Cotton effect of the carbonyl chromophore as observed earlier for the corresponding halogeno-adamantanones.

Zusammenfassung—Der Cotton-Effekt im Bereich der n→π*-Absorptionsbande der Halolactone **3a–c**, die ausgehend von (1S)-2-Bromadamantandion-4.8 (**1**) dargestellt wurden, ist positiv. Die gemessenen Daten gestatten die eindeutige Bestimmung der Vorzeichen des Beitrags von Substituenten in der dritten Sphäre für die Lacton-Sektor-Regel. "Axiale" Halogensubstituenten in β-Position zur Ketogruppe zeigen—wie schon bei den entsprechenden Halogeno-adamantanonen gefunden—auch bei Oxa-homoadamantanonen Antioktantenverhalten für den Cotton-Effekt des Carbonylchromophors.

The sign of the R-band Cotton effect of lactones is in general determined by the torsion angle around the C_α–C(=O) — bond[2-4] within the ring, i.e. (according to our definition[5]) by the chirality of the second sphere. For third sphere contributions different rules have been proposed on theoretical[6,7] or on semiempirical[8] basis. Schellman and Oriel[6] treat the C(=O)–NH–chromophore (n→π*-band) as a weakly perturbed carbonyl chromophore with quasi-C_{2v} symmetry and derive a quadrant rule identical with that proposed by them for ketones. In their paper they mention that similar n→π*-transitions can be treated analogously (*cf* also[9]). The corresponding rule is shown in Fig 1A.

Klyne *et al*[7] regard the two canonical structures O=C—OR and O$^{(-)}$—C=O$^{(+)}$R of the carboxylic group as equivalent and, applying the octant rule[10] to both of them, deduce the sector rule depicted in Fig. 1B. Cooper[11] proposed to turn around these sectors by about 20° in the direction of the double bond in order to take care of the unequal contributions of double bond character of the two structures in question.

Snatzke *et al*[8] made allowance for a stronger perturbation of the "carbonyl" chromophore by the additional "ether"-oxygen by adding (Fig 1C) the nodal surface of the π_3*-orbital to the quadrants proposed by Schellman and Oriel.[6] In effect these



A B C

Fig 1. Sector rules for third sphere contributions to the lactone n→π* band CD. Signs refer to upper sectors; the plane of the paper is also a nodal plane.

▨ : positive contributions
▒ : negative contributions
□ : no contributions or negligible ones

A: Schellman's rule for lactams (X = NH),[6] analogously applied to lactones (X = O).
B: Sector rule proposed by Klyne *et al.*[7]
C: Lactone sector rule according to Snatzke *et al.*[8] (old version).

two rules show only a small difference: our rule gives two additional narrow sectors on that side of the n→π*-nodal plane, which is opposite to the "ether"-oxygen. Second sphere contributions were believed at the time of the proposal of this rule to be negligible, as for γ- and δ-lactones all ring atoms are situated in nodal surfaces, and according to the one-electron-theory the positive chiral residual field of nuclei, not completely screened by their electrons, determines the CD (*cf* the successful treatment of the carbonyl chromophore by Moscowitz[13]). As later on has been shown by Höhn and Weigang,[14] the octant rule for ketones can, however, also be obtained by application of the polarizability theory; here the position (and direction) of bonds have to be taken into account and not just the position of nuclei. As the bonds in the ring of a γ- or δ-lactone are not coplanar, it follows that indeed ring chirality, i.e. second-sphere contributions, should be regarded as important and determine the Cotton-effect.[2-4]

Hitherto there does not exist a single good model for testing the various rules for third-sphere contributions to the CD of carboxylic derivatives as lactone rings in general are not planar, and in the case of esters,[15] which lack second sphere contributions, the preferred conformation of the COOR-group is not known unequivocally. In the following we describe the preparation and chiroptical properties of three lactones in the adamantane series, which are ideal models for this purpose.

Fragmentation of the bromo-adamantanedione **1** with different bases yielded the bicyclic unsaturated keto-acid **2** in analogy with experiments described in literature.[16,17] Reaction with halogens in chloroform gave in excellent yield the corresponding halolactones **3a–c**. The structure of these compounds follows from reaction mechanism[18] and NMR-data. The CD-spectra within the keto n→π*-band support the stereochemistry assumed.[19]

In the lactones described here, the COO-grouping is incorporated into two chiral second spheres, which are exactly enantiomeric to each other. This is true for both, a coplanar lactone grouping as well as for a non-planar one, as in the latter case the two possible conformers should have the same energy and therefore be present in equal amounts; it is highly improbable that the antiperiplanar halogen-substituent could influence this equilibrium. According to the presence of two second spheres which are enantiomeric to each other (permanently or in time average) second sphere contributions cancel each other and the only one left, a third-sphere contribution to the CD, results from the halogen substituent.

The keto carbonyl group cannot appreciably influence the CD of the lactones as it is situated in a nodal plane. As seen from Fig 2 the CD for the compounds **3a–c** in the lactone R-absorption band is positive (the positive CD of the iodo lactone **3c** is obviously overcompensated by a stronger negative CD of the iodo chromophore and appears therefore as a negative minimum rather than as a positive maximum; *cf* the spectra of the corresponding "axial" iodo adamantanone[19] shown in Fig 2).

Fig 3 shows two different projections of the halo lactones **3** from which it is deduced that the sign

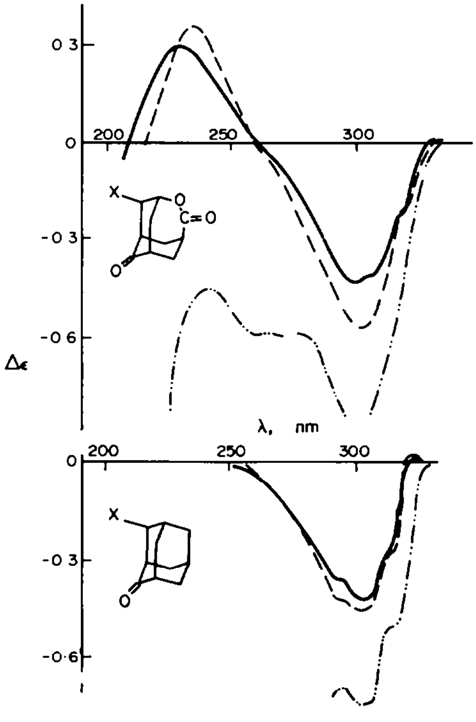
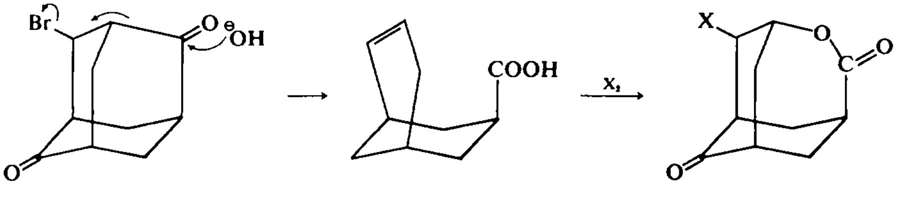


Fig 2. CD-spectra of halo-lactones **3a–c** (top) and "axial" β-halo-adamantanones (bottom).[19]

———— : X = Cl

---------- : X = Br

-··-··- : X = I



Reaction scheme

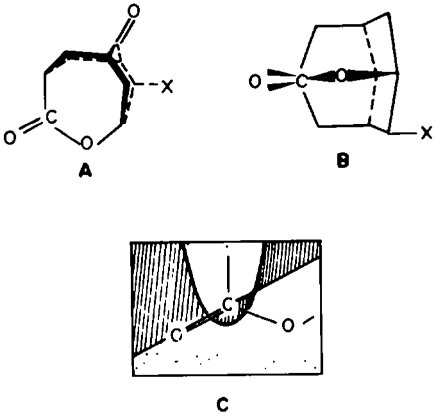


Fig 3. Revised sector rule for third-sphere contributions to the lactone $n \rightarrow \pi^*$ band CD.
A: Projection of 3 onto the plane of the lactone grouping
B: Projection of 3 along the bisectrix of the lactone grouping
C: Revised sector rule; Signs refer to upper sectors, the plane of the paper is also a nodal plane. Indication of signs as in Fig 1.

pattern of our lactone rule[8] has to be as is depicted in the same figure, and not as originally tentatively proposed[8] (*cf* Fig 1C). The rule suggested by Klyne and coll.[7] predicts a negative sign for the lactone CD in disagreement with our results; Schellman's rule for lactams[6,9] if applied analogously to lactones shows now identical sign pattern in corresponding sectors as this modified rule, proposed here. We believe that these three halo lactones are the first examples which can be used in order to determine the sign of the third-sphere contributions in the lactone series without any doubt.

Fig 2 shows also the Cotton effect of the keto chromophore of compounds **3a–c**. It is identical in magnitude as well as in sign with that of the corresponding "axial" halo adamantanones[18] proving thus again that the "anti-octant" behaviour of such axial groups in β-position to the keto chromophore in a cyclohexanone is not due to some special effects in the intact adamantane skeleton.

EXPERIMENTAL

For general procedures and recording of spectra *cf*[19], IR-spectra were measured in $CHCl_3$, NMR-spectra in $CDCl_3$, $\delta_{TMS} = 0$.

(1S)-2-*Bromoadamantanedione*-4.8 (**1**) was prepared from (+)-(1S)-2-Carboxyadamantanedione-4.8 as described in Ref. 20.

(1R)-7-*Carboxybicyclo* [3.3.1] *non*-2-*en*-9-*one* (**2**). 500 mg **1** were dissolved in 4 ml ethanol and after addition of 4 ml 10% aqueous NaOH kept at 100° for 7 h. Alcohol was removed *in vacuo* and the aqueous phase after acidification with 5 N HCl and saturation with NaCl was extracted with ether-CH_2Cl_2, yielding 340–360 mg acid **2**. An analytical sample was crystallized from acetone-petrol ether: mp 168°. (Found: C, 66·61; H, 6·71; $C_{10}H_{12}O_3$ requires: C, 66·65; H, 6·76%). IR: 3015, 2925, 2860 (CH); 1732, 1700 (CO). NMR: 11·9 (1H); 5·68 ($W_{1/2} = 8Hz$) (2H); 3·0–2·5 (7H); 2·4–2·0 (2H). UV: $\lambda_{max} = 292$ nm, $\epsilon = 24$, (methanol, c = 3·1 g/l). CD: 320 (0), 296 (+1·4), 245 (0) (Ethanol, c = 2·08 g/l). MS: M^+ = 180,07 (62%), *m/e* = 79 (100%).

1R,9R - 9 - *Chloro* - 2 - *oxa* - *homoadamantanedione* - 3·7 (**3a**). 150 mg **2** were dissolved in 2 ml of dry $CHCl_3$, the solution was saturated with Cl_2 at 0° and kept at room temperature for 3 h. After dilution with 50 ml $CHCl_3$ excess chlorine was reduced with $Na_2S_2O_3$, the organic phase was washed with $NaHCO_3$ and saturated brine. Evaporation of solvent yielded 160 mg crystalline material which was recrystallized from acetone-petrol ether: mp 189/236°. (Found: C, 56·02; H, 5·14; Cl 16·45; $C_{10}H_{11}Cl$ requires: C, 55·95; H, 5·16; Cl, 16·51%). IR: 3015, 2935, 2860, (CH); 1737 (CO). NMR: 4,7 ($W_{1/2} = 12Hz$) (2H); 3·35–2·60 (5H); 2·60–2·15 (6H). UV: $\lambda_{max} = 295$, $\epsilon = 24$; $\lambda_{max} = 230$, $\epsilon = 80$ (c = 0·8 g/l). CD: 330 (0), 317 (−0·75), 305 (−1·38), 298 (−1·45), 260 (0), 230 (+0·96), 210 (0). MS: M^+ = 214 (100%), *m/e* = 179 (12%).

Bromolactone **3b**. 149 mg of acid **2** were dissolved in 3 ml of dry chloroform, a diluted solution of Br_2 in CCl_4 was added dropwise until a light shade of yellow remained for 15 min. Decoloration of the solution at the beginning of the reaction took place very rapidly. Work up as described before yielded 196 mg pure compound, which after recrystallisation from acetone—benzene (1 : 10) gave thick needles, mp. 219·5° (Found: C, 46·32; H, 4·25; Br, 30·61; $C_{10}H_{11}BrO_3$ requires: C, 46·35; H, 4·29; Br 30·84%). IR: 3010, 2940, 2920, 2865 (CH); 1735 (CO). NMR: 4·70 (2H); 3·35–2·55 (5H); 2·55–1·15 (6H). UV: $\lambda_{max} = 296$, $\epsilon = 25$; $\lambda_{max} = 220$, $\epsilon = 280$ (c = 0·67 g/l). CD: 330 (0), 320 (−0·69), 302 (−1·83), 260 (0), 234 (+1·16). MS: M^+ = 260 (35%), *m/e* = 179 (100%).

Iodolactone **3c**. 150 mg of acid **2** were dissolved in 2 ml 10% aqueous $KHCO_3$ and treated with 10% excess $KI.I_2$. After 4 h standing at room temperature the reaction mixture was worked up as described for compound **3a**. The crude product (300 mg) was recrystallized from acetone–benzene to yield 228 mg of iodolactone, mp 189°. IR: 3010, 2940, 2920, 2855 (CH), 1730 (CO). NMR: 4·85 (1H); 4·80 (1H); 3·40–2·90 (3H); 2·90–2·60 (2H); 2·60–1·90 (6H). UV: $\lambda_{max} = 263$, $\epsilon = 565$; $\lambda_{max} = 220$ nm, $\epsilon = 1050$. CD: 330 (0), 299 (−0·87), 275 (−0·57), 260 (−0·59), 240 (−0·42), negative at shorter wavelengths. MS: M^+ = 509·9 (2·4%), *m/e* = 179 (100%).

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