Interaction between Non-adjacent Benzoate Groups: an Extension of the Dibenzoate Chirality Rule

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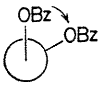
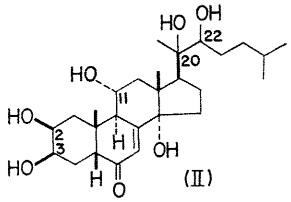
Summary Application of the dibenzoate chirality rule to ajugasterone C and metagenin indicates that the rule can be extended to determine the chiralities of non-adjacent hydroxy-groups.

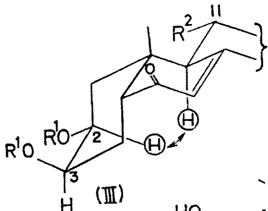
AN extension of the "benzoate sector rule"[1] has shown that in the dibenzoates or *p*-substituted dibenzoates of cyclic secondary α-glycols, interaction of the two aromatic chromophores results in splitting of the original Cotton effects associated with the isolated benzoate chromophore (c.d. Cotton effect at *ca.* 225 nm., Δε *ca.* 3·5, for unsubstituted benzoates) so that a very intense first Cotton effect is observed at 233 nm., Δε 10—15; in most cases, a second Cotton effect of opposite sign is observed at 219 nm. (Davydov splitting).[2] Moreover, the sign of the 233 nm. Cotton effect is coincident with the sense of screwness of the α-dibenzoates, *i.e.*, if they are twisted as in (I), which is defined as positive, then the Cotton effect sign is also positive, and *vice versa*. ("dibenzoate chirality rule").[2]



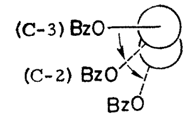
(I)



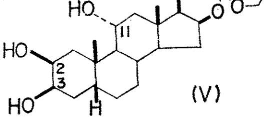
(II)



(III)



(IV)



(V)

The phytoecdysone ajugasterone C (II)[3] is a particularly interesting example of the dibenzoate chirality rule, as it indicates that the rule can be extended to determine the spatial dispositions, *i.e.*, configurations or conformations, of non-adjacent hydroxy-groups in polyhydroxy-compounds, as well as in cyclic 1,2-diols and 1,2,3-triols.[2]

Ajugasterone C 20,22-acetonide-2,3,11-tribenzoate, m.p. 93—94°, was prepared by benzoylation of the 20,22-monoacetonide, which in turn was prepared by selective removal of the 2,3-acetonide group from the 2,3; 20,22-diacetonide by treatment of the latter with 25% aqueous dioxan containing 1% HCl for 24 hr. at room temperature. In ajugasterone C acetonide tribenzoate (see partial structure III; R^1 = Bz, R^2 = OBz) the 3β- and 2β-benzoates constitute a left-handed screw, while the 2β- and 11α-benzoates also form a left-handed screw (IV). The 237 nm. Cotton effect is accordingly negative, and the Δε has the very large value of −30, which is in contrast to the Δε values of 10—15 for ordinary α-dibenzoates. It is clear from the Figure that the Cotton effects associated with the ring-B enone chromophore are too weak to interfere with the observation of the large Cotton effects at 237 and 221 nm. caused by the dipole–dipole interactions between the electric transition moments of the three benzoate groups.

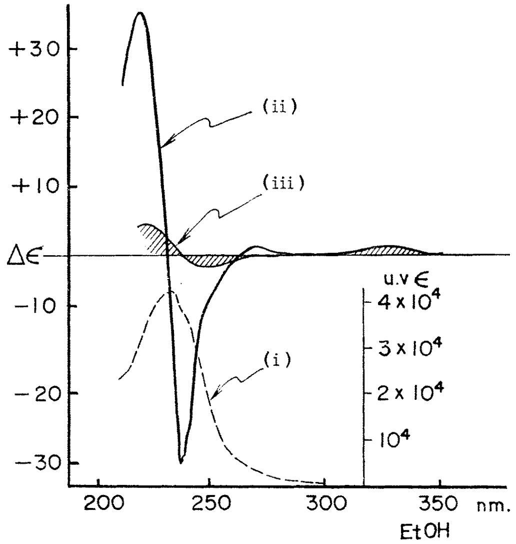


FIGURE. *C.d. and u.v. curves in ethanol. Ajugasterone C* 20,22-*acetonide* 2,3,11-*tribenzoate.*

(i) ------: *u.v.* λ_{max} 231 nm. (ε 40,300)
(ii) ——[a]: *c.d.* $\Delta\epsilon_{237}$ −30, $\Delta\epsilon_{221}$ +34
Ajugasterone C
(iii) —— (*shaded area*):
c.d. $\Delta\epsilon_{328}$ +1·5 ($n \rightarrow \pi^*$)
$\Delta\epsilon_{250}$ −3·0 ($\pi \rightarrow \pi^*$)

[a] The small positive c.d. Cotton effect at 272 nm. in curve (ii) is due to interactions between the 280 nm. transitions of the benzoate chromophores.[1b]

This superposition of two left-handed interactions thus corroborates the configurations deduced for C-2,-3,-11, and -5 (A/B *cis*) in ajugasterone C,[3] and also indicates that ring A adopts the chair conformation. The 2,3,11-tribenzoate of metagenin (V),[4] m.p. 278—279° (decomp.), in which the benzoates are again arranged as in (IV), also shows a strongly negative c.d. Cotton effect at 237 nm., Δε −24·4, and a positive Cotton effect at 220 nm., Δε +20 (in ethanol).

Another useful method for collectively establishing the C-2,-3, and -5 configurations and the ring-A conformation of ecdysones is measurement of the n.m.r. intramolecular nuclear Overhauser effect (NOE).[5] Irradiation of the 9α-H signal of the ecdysones having the familiar 2β,3β-dihydroxy-5β-7-en-6-one moiety causes a *ca.* 10% increase in the integrated intensity of the 2α-H signal,† *e.g.*, ponasteroside A,[6] ponasterone A [2,3-diacetate 20,22-acetonide (partial structure III; R^1 = Ac, R^2 = H; irr. 9H results in 10% NOE for 2α-H, but 0% NOE for 3α-H)], ecdysterone, *etc.*

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† Measured for a perdeuterioacetone solution.

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