

ABSOLUTE CONFIGURATION OF CARYOPTIN AND 3-EPICARYOPTIN —
AN EXCEPTION IN THE EXCITON CHIRALITY METHOD

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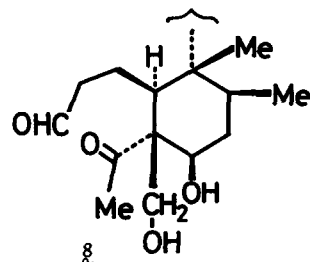
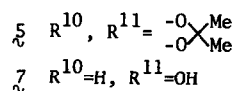
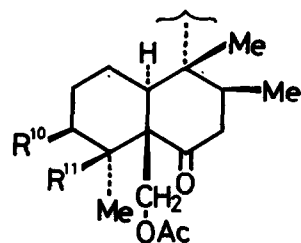
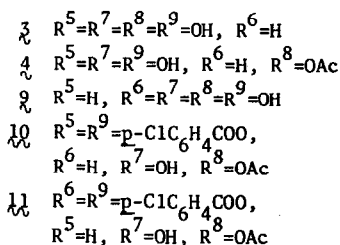
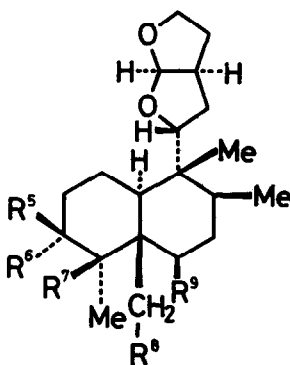
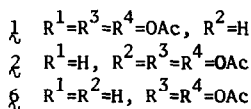
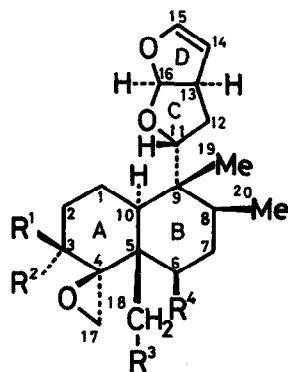
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The stereochemistry and structure of caryoptin (1)¹ and 3-epicaryoptin (2)², isolated from Caryopteris divaricata Maxim.³ and Clerodendron calamitosum L., respectively, were reported in the previous papers. And also, it has been shown that these diterpenes having the common clerodane skeleton have a bitter taste and the insect antifeeding activity⁴. We wish to report now the confirmation of the absolute configuration of 1 and 2 , and the noteworthy experimental results about the CD spectroscopy for these dibenzoate derivatives.

When the enol double bond and the epoxide ring remained unchanged as it is, 1 and 2 could not be derived to the stable carbonyl compounds. Therefore, the compounds for spectrometric determination were given from their dihydrotetraol derivatives as the following way. Catalytic reduction of 1 with Pd-C (EtOAc, 25°) followed by reduction with LiAlH₄ (dioxane, 20°, 12hr) gave dihydrocaryoptintetraol (3), m.p. 216-217°; C₂₀H₃₄O₆; [α]_D -22° (c 1.00, CHCl₃); δ(CDCl₃) 1.40(3H, s). Acetylation of 3 with acetic anhydride (1.2 equiv.) in pyridine (15°, 24hr) yielded dihydrocaryoptintetraol-18-acetate (4) in 54%, m.p. 180-181°; C₂₂H₃₆O₇; δ(CDCl₃) 2.05(3H, s) 5.18 and 4.88(ABq, J 12.5Hz). Treatment of 4 with 2,2-dimethoxypropane and p-TsOH in acetone (20°, 15min.) followed by oxidation with CrO₃-pyridine complex (CH₂Cl₂, 18°, 32hr) gave a 3,4-acetonide-6-keto-18-acetate derivative (5), ν_{max}(CCl₄) 1718, 1743 cm⁻¹; CD(EtOH) [θ]₃₀₁ +10.21 x10³; ORD(EtOH) [φ]₃₁₉^P +6.170x10³, [φ]₂₇₉^T -7.160x10³.

In order to confirm the absolute configuration of 1 by comparing with clerodin (6)⁵ of the known absolute configuration^{*}, 6 was derived in a similar manner via the hydrogenation, acetylation and oxidation reactions to deacetyltetrahydroclerodin-6-keto-18-acetate (7), ν_{max}(CCl₄) 3500, 1750, 1700 cm⁻¹; CD(EtOH) [θ]₃₀₉ +10.49x10³, [θ]_{301.5} +11.57x10³; ORD(EtOH) [φ]₃₂₇^P +7.725 x10³, [φ]₃₂₀^P +6.730x10³, [φ]₂₈₄^T -6.660x10³. Both ORD and CD curves of 5 and 7 showed the



positive Cotton effects which were expected from the ketone octant rule. In these derivatives, the C-18 primary carbinol group exerts the positive effect and the methyl group at C-4 may also contribute to the positive sign, since it situates in the positive quadrant of the front octants. Therefore, the absolute configuration of caryoptin is shown as λ and same as that of clerodin (δ) except the C-3 position.

The epimeric relationship at the C-3 acetoxy groups of λ and ζ was evidenced by the formation of the same keto-aldehyde derivative (δ), $[\alpha]_D +18^\circ$ (c 0.99, $CHCl_3$), which was derived from both ξ and 3-epidihydrocaryoptintetraol (θ) by the consumption of one equivalent of $NaIO_4$ for 2.5hr and 12hr, respectively, in $MeOH-H_2O$.

Harada and Nakanishi⁶ reported the CD spectra of para-substituted dibenzoates of 5 α -chole-
 stane-3 β ,6 β -diol as a convenient method for determining of the absolute configuration of the
 1,4-glycol system. When this exciton chirality method⁷ is applied to λ and ζ , it can be
 expected that the relationship of the absolute configuration between λ and ζ become more
 apparent. Treatment of λ with p-chlorobenzoyl chloride in pyridine followed by purification on
 PLC gave dihydrocaryoptintetraol-3,6-di-p-chlorobenzoate-18-acetate ($\lambda\theta$). The C-3 epimer ($\mu\theta$)
 of $\lambda\theta$ was derived from 3-epicaryoptin (ζ) in a similar manner as above. By inspection of the
 projection formula, the positive split Cotton effects must be given for the benzoylated 1,4-

glycol system of $\lambda\lambda$ on the basis of the exciton chirality method, while the negative effects should be predictable for that of the epimer ($\lambda\lambda$). However, the CD spectrum of both derivatives showed the reverse Cotton effects separated by a Davydov splitting that we had expected (Fig. 1). These facts are entirely in conflict with the conclusion which has been drawn from the Cotton effect on the carbonyl compounds.

If the exciton chirality method is invariant in principle to the any 1,4-glycol systems, the conflict may occur with that the chirality showing primarily the normal direction varies with the intramolecular interaction for the benzoyl group. The Y-axis (long axis)⁸ of the 3-benzoyl group of $\lambda\lambda$ is parallel to that of the 3-C—O bond, that is the axial direction at the normal state. When hydrogen-bonding is formed between the carbonyl group of the axial 3-benzoyl group and the equatorial 4-hydroxyl group, the Y-axis becomes to intersect the axis of the 3-C—O

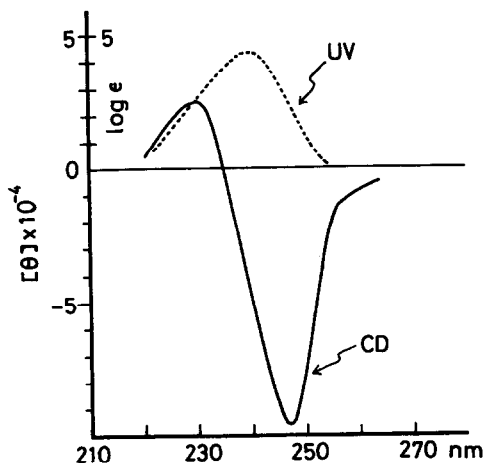


Fig. 1a CD and UV curves of $\lambda\lambda$
 CD* ; $[\theta]_{247.5} -9.49 \times 10^4$, $[\theta]_{230} +2.47 \times 10^4$
 UV** ; $\lambda_{max} 240$ nm (log ϵ 4.32)

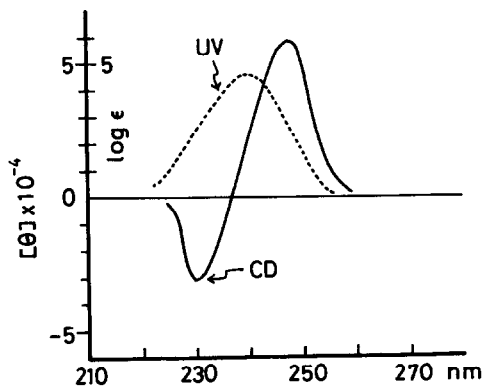


Fig. 1b CD and UV curves of $\lambda\lambda$
 CD* ; $[\theta]_{247.5} +5.87 \times 10^4$, $[\theta]_{230} -3.03 \times 10^4$
 UV** ; $\lambda_{max} 240$ nm (log ϵ 4.57)

* EtOH-dioxane(4:1), ** EtOH

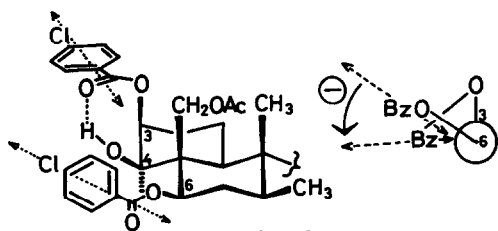


Fig. 2a

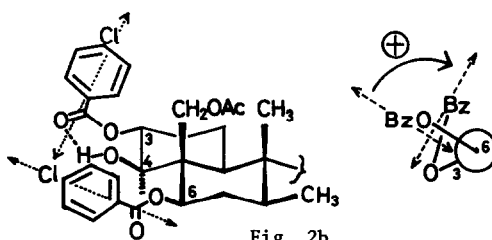


Fig. 2b

bond, in other words, to incline to the equatorial direction (Fig. 2a). In addition, it is necessary to take into account the deviation of the electric dipole transition moment of the benzoyl group from the Y-axis to the oxygen atom of the carbonyl group with angle of ca. $7^{\circ 8}$. It is understandable on the basis of these relationship for the reverse split Cotton effects by the dipole-dipole interaction between the electric transition moments of intramolecular charge-transfer band of two benzoate chromophors. And, if the carbonyl group of the equatorial 3-benzoyl group and the equatorial 4-hydroxyl group of 11 form the hydrogen-bonding, the reason of its reverse split Cotton effects can be best explained in a similar manner as 10 (Fig. 2b).

However, these reverse split Cotton effects may be explained by other reasons. Further details of these facts will be reported together with results on the model compounds.

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References and Footnote

1. S. Hosozawa, N. Kato, and K. Munakata, Phytochemistry, 12, 1833 (1973).
2. S. Hosozawa, N. Kato, and K. Munakata, ibid., 13, 308 (1974).
3. (a) Four new diterpenes, dihydrocaryoptin¹, caryoptin hemiacetal¹, caryoptinol^{3b}, and dihydrocaryoptinol^{3b}, and three known diterpenes¹, clerodin, dihydroclerodin-I, and clerodin hemiacetal, were also isolated from this plant.
(b) S. Hosozawa, N. Kato, and K. Munakata, Phytochemistry, 13, 1019 (1974).
4. S. Hosozawa, N. Kato, and K. Munakata, Agr. Biol. Chem., 38, 823 (1974): ibid., 38, 1047 (1974).
5. Clerodin had been isolated from Clerodendron infortunatum, see D.H.R. Barton, N.T. Cheung, A.D. Cross, L.M. Jackman, and M. Martin-Smith, J. Chem. Soc., 1961, 5061: I.C. Paul, G.A. Sim, T.A. Hamor, and J. Monteath Robertson, J. Chem. Soc., 1962, 4133.
6. N. Harada, S. Suzuki, H. Uda, and K. Nakanishi, J. Am. Chem. Soc., 93, 5577 (1971).
7. N. Harada and K. Nakanishi, Accounts Chem. Res., 5, 257 (1972).
8. J. Tanaka, Bull. Chem. Soc. Japan, 36, 833 (1963).
9. JASCO Model J-40 Instrument.
- *) Barton et al. reported that the Cotton effect of the ketone toluene-p-sulphonate which was obtained by the oxidation of deacetyldihydroclerodin-I monotonuene-p-sulphonate was enantiomeric to that of 6-keto-trans A/B steroid⁵. This result was confirmed in the X-ray analysis of clerodin bromolactone by J.M. Robertson et al⁵.