The Absolute Stereochemistry of Isoamijiol, a Dolastane Diterpene, as determined by the C.D. Allylic Benzoate Method

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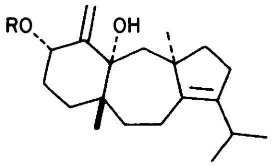
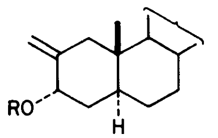
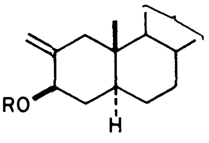
The absolute stereochemistry of isoamijiol, a dolastane diterpene isolated from the brown seaweed *Dictyota linearis,* has been found to be as shown in (**1**) by the c.d. allylic benzoate method.



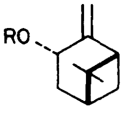
(**1**) R = H
(**2**) R = COC_6H_4-*p*-Br



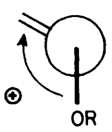
(**3**)



(**4**)



(**5**)



(**6**)

For (**3**) - (**6**): R = COC_6H_4-*p*-Br

The c.d. allylic benzoate method, a recently developed chiroptical tool[1,2] for determining the absolute configuration of allylic alcohols on the basis of the chiral exciton coupling mechanism, has been applied extensively to various natural and synthetic chiral organic compounds including both cyclic[3] and acyclic[4] systems. Recently one of us reported the structure of isoamijiol (**1**),[5] a dolastane[6] diterpene isolated from the brown seaweed *Dictyota linearis*. However, the absolute configuration of (**1**) and related compounds remained unknown. We report a chiroptical determination of the absolute stereochemistry of (**1**) by application of the c.d. allylic benzoate method.

There are some empirical rules, *e.g.*, Mills' rule[7] and Brewster's benzoate rule,[8] for the determination of the absolute configuration of allylic alcohols. However, these rules cannot be applied to allylic alcohols with an exocyclic double bond, because the former applies to allylic alcohols with an endocyclic double bond, and there are some exceptions to the latter.[9] On the other hand, consideration of the exciton theory suggests that the c.d. allylic benzoate method would cover such cases.

In order to verify this, two steroidal model compounds, 2-methylene-5α-cholestan-3α-yl and -3β-yl *p*-bromobenzoates, (**3**) and (**4**),[10] were prepared. From the half-width value, $w_{1/2}$, of the C-3 proton peak in the ^1H n.m.r. spectra, it was confirmed that the A-ring of both compounds (**3**) and (**4**) adopts a chair conformation: (**3**), δ 5.57, $w_{\frac{1}{2}}$ 5.6 Hz; (**4**), δ 5.44, $w_{1/2}$ 16.5 Hz. The c.d. spectrum of (**3**) exhibits a positive Cotton effect, λ_{ext} 243.4 nm, $\Delta\varepsilon$ +5.0 in ethanol, in line with a clockwise relationship between the 2-methylene and 3α-*p*-

bromobenzoate groups. On the other hand, compound (**4**) shows no clear c.d. extremum in the region of the *p*-bromobenzoate $\pi \rightarrow \pi^*$ transition, because the 3β-*p*-bromobenzoate and 2-methylene groups lie in the same plane, therefore providing no exciton chirality. Additional support was given by the c.d. data of the *p*-bromobenzoate (**5**) of (1*R*,3*S*,5*R*)-*trans*-pinocarveol: λ_{ext} 245.0 nm, $\Delta\varepsilon$ +5.7; ^{1}H n.m.r., δ 5.78 (d, *J* 8 Hz). It is thus apparent that the c.d. allylic benzoate method is applicable to allylic alcohols with an exocyclic double bond.

The *p*-bromobenzoate (**2**) of isoamijiol was prepared in the usual way: *p*-bromobenzoyl chloride in pyridine, at room temperature, overnight. The conformation of the six-membered ring was determined to be the chair form, by the ^{1}H n.m.r. data, δ 5.72, $w_{1/2}$ 4.0 Hz.† The u.v. spectrum of (**2**) shows a *p*-bromobenzoate $\pi \rightarrow \pi^*$ transition at 243.7 nm (ε 21 300), in which region the c.d. spectrum shows a positive Cotton effect, λ_{ext} 244.5 nm, $\Delta\varepsilon$ +7.9 in ethanol, indicating a clockwise relationship between the exocyclic double bond and *p*-bromobenzoate chromophores as shown in (**6**). The absolute stereochemistry of isoamijiol was thus found to be as shown in (**1**).

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† In the case of (**2**), the conformational analysis is not necessarily required, because the exciton chirality between the *p*-bromobenzoate and double bond chromophores is always positive, regardless of the conformational change of the methylene–cyclohexane ring.