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THE ABSOLUTE CONFIGURATION OF THE STERPURENE SESQUITERPENES

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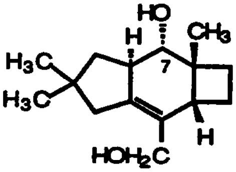
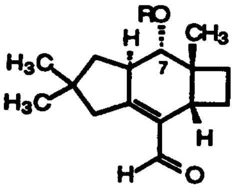
Summary: The absolute configuration of the sterpurene sesquiterpenes isolated from *Stereum purpureum* has been determined both by the use of the exciton chirality method on (2), a derivative of 7,12-dihydroxysterpurene (1) and from the ^{19}F NMR spectra of the Mosher's esters (3) and (4).

The sterpurenes comprise a recently discovered group of sesquiterpene fungal metabolites with a novel tricyclic skeleton, exemplified by 7,12-dihydroxysterpurene (1). All the sterpurene metabolites have been isolated from *Stereum purpureum*, the fungus responsible for the silver-leaf disease in fruit trees.[1] Biosynthetic experiments have established the isoprenoid nature of these compounds[2] and shown that the enzymic cyclisation of farnesyl pyrophosphate proceeds with carbon-carbon bond cleavage.[3] We report here the absolute stereochemistry of the sterpurene metabolites.

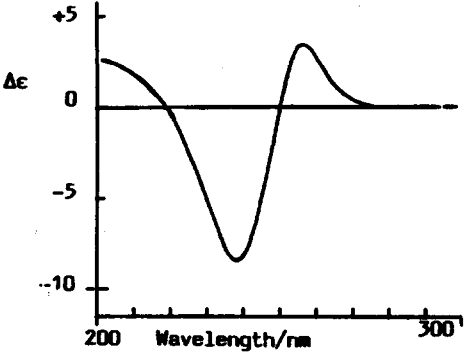
The major metabolite we isolate from surface cultures of *Stereum purpureum* grown on a malt extract broth is the diol 7,12-dihydroxysterpurene (1).[3] In order to determine the absolute configuration by the exciton chirality method a molecule must have two chromophores exhibiting strong $\pi \rightarrow \pi^*$ absorptions in a defined chiral orientation with respect to each other.[4] Suitable chromophores are present in the derivative (2). This was formed from (1) by oxidation of the allylic alcohol to the aldehyde using activated manganese dioxide in dichloromethane (λ_{max} 255 nm, aldehydic hydrogen at 9.8 p.p.m.), followed by esterification of the secondary alcohol with *p*-bromobenzoyl chloride in the presence of DMAP and triethylamine in dichloromethane. The *p*-bromobenzoate (2) (λ_{max} 244 nm, C<u>H</u>OR at 4.8 p.p.m.) was rigorously purified by chromatography.[5]



(1)



(2) $R = BrC_6H_4CO_2$-



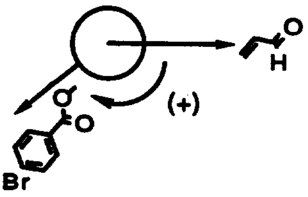
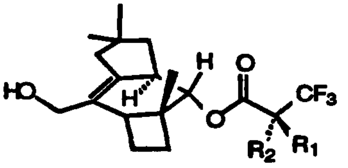


Fig.1. C.D. spectrum of (2)

The C.D. spectrum of (2) (Figure 1) was recorded in acetonitrile on a JASCO J40CS spectropolarimeter. The positive Cotton effect at 256 nm ($\Delta\varepsilon_{256}$ = +3.4, $\Delta\varepsilon_{238}$ = -8.4) caused by the interaction of the two chromophores (the enone and the p-bromobenzoyl groups) indicates a positive chirality of the two chromophores, consistent with the S configuration at C-7.

A parallel determination of the absolute configuration was performed using the ^{19}F NMR method pioneered by Mosher.[6] 7,12-Dihydroxysterpurene (1) was diesterified with Mosher's acid, (R)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid, using DCC as a coupling agent in the presence of DMAP in dichloromethane. The allylic ester was then selectively hydrolysed using potassium carbonate in 80% methanol-water to give the secondary ester (3).[7] In this way, starting with the R and then the S acid, the pair of complementary diastereomeric esters (3) and (4) were prepared.

The ^{19}F NMR spectrum of an unequal mixture of (3) and (4) in deuteriocyclohexane showed the signals for the CF_3 groups in the two compounds to be resolved by 0.04 p.p.m.. In deuteriobenzene the separation is increased to 0.1 p.p.m.. This separation is typical of values for this kind of determination.[9] In both spectra the signal for the ester derived from the R-acid comes at higher field. The model proposed by Mosher puts the secondary hydrogen on C-7, the carbonyl group , and the CF_3 group in the same plane and then considers how this alignment may be perturbed by steric interactions between the phenyl group and substituents on the alcohol.[8] In this case the phenyl group is predicted to have the greater interaction with the bulkier tertiary centre causing the CF_3 group to be twisted more out of the plane of the carbonyl group for (3) than (4). This moves the CF_3 group away from the deshielding region of the carbonyl group, i.e. to higher field. The predicted absolute configuration corresponds to that found using the chiral exciton coupling method. It is of interest to note that the sterpurenes have the same absolute stereochemistry as the illudins, marasmic acid and fomannosin which are antipodal to hirsutic acid.[10]



(3) R_1 = Ph, R_2 = OCH_3
(4) R_1 = OCH_3, R_2 = Ph

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7. (3) ^{19}F NMR δ(235 MHz, C_6D_6) 91.87; δ(C_6D_{12}) 92.75 p.p.m.. (4) ^{19}F NMR δ(235 MHz, C_6D_6) 91.97; δ(C_6D_{12}) 92.79 p.p.m. (both relative to 2,2,2-trifluoroethanol as internal standard at δ 86.12).
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