

## Absolute Stereochemistry of the Sesquiterpenoid, Alliacolide

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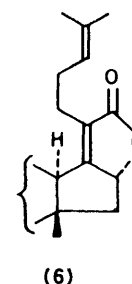
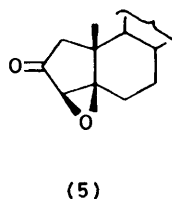
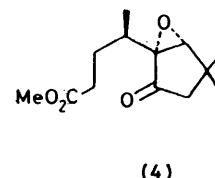
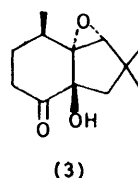
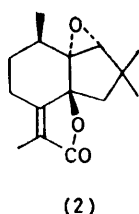
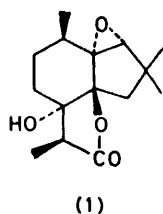
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The absolute stereochemistry of alliacolide (1) has been determined by a series of circular dichroism measurements.

ALLIACOLIDE (1) is a fungal sesquiterpenoid with a unique carbon skeleton and is one of a group of metabolites that have been isolated<sup>1</sup> from *Marasmius alliaceus*. Its structure and relative configuration were established by X-ray diffraction. In connection with biosynthetic studies of this unusual skeleton and the structure determination of the related metabolites,<sup>2,3</sup> we have determined the absolute configuration of alliacolide by degradation and circular dichroism (c.d.) measurements.

Dehydration of alliacolide with phosphoryl chloride in pyridine afforded the butenolide (2).<sup>1</sup> Cleavage of the butenolide with potassium permanganate and sodium periodate in aqueous *t*-butyl alcohol containing potassium carbonate afforded the  $\alpha$ -hydroxy- $\beta$ -epoxy-ketone

stereochemistry (3). Finally, the butenolide (2) had a positive Cotton effect ( $\Delta\epsilon +4.49$ ,  $\lambda$  260 nm), as does the lactone (6), derived from fusidic acid.<sup>5</sup> This model suggests that (2) also has a 'left-handed chirality'<sup>5</sup> and gives the absolute stereochemistry of the  $\alpha\beta$ -unsaturated lactone as shown in (2). Hence the overall absolute stereochemistry of alliacolide is (1) in agreement with that drawn in the original communication.



(3). The i.r. and <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra were consistent with this structure showing, in particular, the singlet ( $\delta$  3.24) associated with the epoxide C-H and the AB doublets [ $\delta$  1.20 and 1.76 ( $J$  14 Hz)] assigned to the isolated methylene on the five-membered ring. When the crude mixture from the potassium permanganate-sodium periodate reaction was further oxidized with methanolic periodic acid, the ketol was cleaved and the epoxy-cyclopentanone (4) was obtained. The <sup>1</sup>H n.m.r. spectrum of the product retained the 1 H singlet ( $\delta$  3.35) of the epoxide C-H and clearly revealed the AB doublets [ $\delta$  1.80 and 2.23 ( $J$  17.5 Hz)] now shifted downfield and associated with a rigid methylene-ketone.

The c.d. curve of the epoxy-ketone (4) had a positive Cotton effect ( $\Delta\epsilon + 2.29$ ,  $\lambda$  310 nm). This compares with a positive Cotton effect reported<sup>4</sup> for the  $\Delta$ -nor-steroid, 3 $\beta$ ,5 $\beta$ -epoxy-nor-5 $\beta$ -cholestan-2-one (5), and hence is in accord with the absolute stereochemistry shown in (4). Secondly the  $\alpha$ -hydroxy- $\beta$ -epoxy-ketone (3) had a positive Cotton effect ( $\Delta\epsilon +0.17$ ,  $\lambda$  328;  $+0.19$ , 318 nm) although the curve was anomalous in shape and position. Here the dominant effect is that of the epoxide group and of the five-membered ring in a positive octant suggesting that the ketone has the absolute

### EXPERIMENTAL

*Oxidation of Dehydroalliacolide* (2).—Sodium periodate (5.35 g) and potassium permanganate (98.8 mg) were dissolved in water (250 ml). Dehydroalliacolide (200 mg)<sup>1,3</sup> in *t*-butyl alcohol (20 ml) was added to a mixture of this solution (40 ml), *t*-butyl alcohol (30 ml), water (130 ml), and potassium carbonate (138 mg) during 1.5 h. The mixture was then stirred at room temperature for a further 2 h. Aqueous sodium hydrogensulphite was added, the solution was acidified, and then extracted with ethyl acetate. The solvent was dried and evaporated to afford a gum which was chromatographed on silica. Elution with chloroform-ethyl acetate-acetic acid (40 : 10 : 1) gave 3 $\alpha\beta$ -hydroxy-2,2,7-trimethyl-4-oxo-1 $\alpha$ ,7 $\alpha\alpha$ -epoxyindane (3) (50 mg) which crystallized from ether as needles, m.p. 111–114 °C,  $[\alpha]_D^{20} +12^\circ$  (*c* 0.2, CHCl<sub>3</sub>) (Found: C, 68.5; H, 8.5. C<sub>12</sub>H<sub>18</sub>O<sub>3</sub> requires C, 68.5; H, 8.6%);  $\nu_{\max}$  3 320 and 1 728 cm<sup>-1</sup>, <sup>1</sup>H n.m.r. ([<sup>2</sup>H]chloroform)  $\delta$  1.09 and 1.20 (3 H, s), 1.37 (3 H, d,  $J$  7 Hz), 1.20 and 1.76 (each 1 H, d,  $J$  14 Hz), 2.45 (1 H, s, OH), and 3.24 (1 H, s); <sup>13</sup>C n.m.r.  $\delta$  18.1(q), 24.3(q), 24.8(q), 29.1(t), 31.5(d), 35.3(t), 38.3(s), 43.2(t), 69.0(d), 72.2(s), 83.4(s), and 209.4(s).

*Preparation of the Keto-ester (4).*—Dehydroalliicolide (379 mg) in *t*-butyl alcohol (65 ml) was oxidized as above and then stirred overnight. After recovering in ethyl acetate, the crude product was treated with periodic acid (696 mg) in aqueous methanol (20 ml) overnight. The methanol was removed under reduced pressure, aqueous sodium chloride (20 ml) was added, and the product was recovered in ethyl acetate. The residue was chromatographed on silica in chloroform–ethyl acetate–acetic acid (40:10:1) to afford 2-(3-methoxycarbonyl-1-methylpropyl)-4,4-dimethyl-1-oxo-2,3-epoxycyclopentane (4) (234 mg) as an oil,  $[\alpha]_D^{25} +13.5^\circ$  (*c* 0.9, CHCl<sub>3</sub>) (Found: C, 64.95; H, 8.3. C<sub>13</sub>H<sub>20</sub>O<sub>4</sub> requires C, 65.0; H, 8.4%);  $\nu_{\max}$ , 1735 cm<sup>-1</sup>; <sup>1</sup>H n.m.r. (in [<sup>2</sup>H]chloroform)  $\delta$  0.99 (3 H, d, *J* 7 Hz), 1.03 (3 H, s), 1.20 (3 H, s), 1.60 (1 H, m), 1.80 (1 H, d, *J* 17.5 Hz), 1.90 (1 H, m), 2.0 (1 H, sextuplet, *J* 7 Hz), 2.23 (1 H, d, *J* 17.5 Hz), 2.35 (2 H, m), 3.35 (1 H, s), and 3.64 (3 H); <sup>13</sup>C n.m.r.  $\delta$  15.1(q), 23.7(q), 25.4(q), 27.7(t), 29.1(d), 31.9(t), 34.2(s), 47.1(t), 51.5(q), 67.3(s), 69.7(d), 173.5(s), and 209.7(s).

*Circular Dichroism Data.*—Compound (2) (dehydroalliicolide)  $\lambda$  285,  $\Delta\epsilon$  0; 260, +4.49; 250, 0; 232, -19.3; 214, 0; and 198 nm, +22.25. Compound (3)  $\lambda$  350,  $\Delta\epsilon$  0; 328, +0.17; 323, +0.16; 318, +0.19; 304, 0; 290, -0.12; 250 0; and 214 nm, -0.41. Compound (4)  $\lambda$  350  $\Delta\epsilon$  0; 310, +2.29; 250, 0; and 201 nm, -2.76.

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