The Absolute Configuration of the Orsellinate of Armillol; Application of the Coupled Oscillator Theory

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The absolute configuration of armillol as shown in (**6**) was determined by applying coupled oscillator theory to the strong negative circular dichroism (c.d.) couplet of (**7**), utilizing the published atom co-ordinates obtained from *X*-ray diffraction.

Various Basidiomycetes are known to produce sesquiterpenoid metabolites whose carbon skeleton may arise by cyclisation of farnesyl pyrophosphate *via* a humulene intermediate. Among these fungal metabolites with established structures are illudol (**1**),[1] illudin M (**2**) and S (**3**)[1a,2] isolated from *Clytocybe illudens,* fomannosin (**4**)[1b,3] from *Heterobasidion annosum* (Fr.) Bref. [syn. *Fomes annosus* (Fr.) Cooke], marasmic acid (**5**)[4] from *Marasmium conigenus,* and the orsellinate of armillol (**6**)[5] from *Armillaria mellea.*

The *X*-ray analyses of derivatives of (**1**) and (**5**) were used for the determination of their partial stereochemistries;[6] the absolute configuration of illudin S (**3**) was established by application of the dibenzoate chirality rule.[7] Two methods were used in the study of the absolute configuration of fomannosin (**4**); firstly, circular dichroism (c.d.) measurement on dihydrofomannosin[8] and secondly, the *X*-ray structure determination of the (−)-camphanate ester of the same compound.[9]

Proof for the structure and relative stereochemistry of the orsellinate of armillol (**6**) was provided by single crystal analysis of its oxidation product, the β-hydroxy-aldehyde (**7**).[5] We now report the determination of the absolute configuration of armillol by application of the coupled oscillator theory to the oxidation product (**7**).

The u.v. spectrum of the natural compound armillol orsellinate (**6**) shows a strong band at 263 nm (MeOH, ε 14 400)[5] which is due to the orsellinate chromophore. The corresponding aldehyde (**7**) has a u.v. band in the same range (262 nm) of even greater magnitude (ε 19 310) indicating the presence of a second stronger absorption in the same wavelength area, which must be the 'conjugation band' of the ene–aldehyde (calculated 246 nm without taking into account the strain introduced by the four-membered ring). The c.d. spectrum† of (**7**) shows in the same wavelength range a typical c.d. couplet (Δε −24.1 at 270 nm and +21.0 at 250 nm), which is highly indicative of a chiral coupling between the strong electric transition moment of the orsellinate chromophore within its 'conjugation band' and the similarly strong electric transition moment for the transition of the conjugated aldehyde. Harada and Nakanishi[10] have cited many examples of such typical 'exciton couplings,' and several successful applications to the determination of absolute configuration of (substituted) benzoates of hydroxylated conjugated enones.

In order to evaluate the absolute configuration from the (negative) sign of the c.d. couplet one has to find the relative positions in space of these two electric transition moment vectors. In the case of a conjugated enone this vector is directed approximately along the line connecting the oxygen with the C_β-atom, whereas for a *p*-hydroxybenzoic acid it is practically directed along the long axis of that moiety. The additional *o*-hydroxy group will introduce a small deviation from this direction; on the other hand this will in part be compensated by the influence of the methyl group in the second *ortho*-position. A few test calculations taking into account the principal geometry of the molecule as given by the *X*-ray diffraction data,[5] allowing also for small deviations from these aforementioned directions and positions, gave consistently a medium to strong positive c.d. couplet. The absolute configuration of the aldehyde (**7**) derived from the natural

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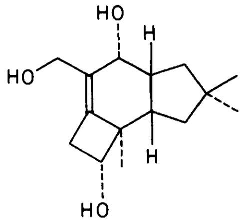
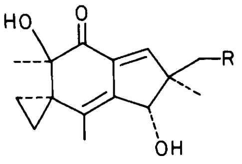
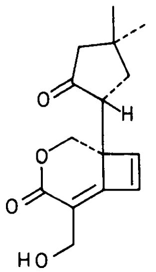
† C.d. measurements were performed in acetonitrile solution at a concentration of 0.46 mmol/l on an ISA-Jobin-Yvon Mark III dicrograph connected on-line to a PDP-8/e computer; curve smoothing was done by the Golay–Savitzky algorithm.



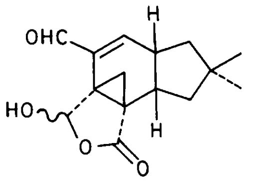
(1)



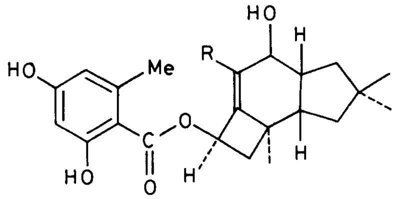
(2) R = H
(3) R = OH



(4)



(5)



(6) R = CH_2OH
(7) R = CHO

armillol orsellinate (**6**) must, therefore, be opposite to the configuration (deliberately chosen) described in Figure 1 of ref. 5 and determined by the published co-ordinates,[5] *i.e.* it is actually that depicted in (**7**). It follows thus from the c.d.-spectrum that armillol has the absolute configuration suggested on the basis of biogenetic reasoning. The other three Cotton effects around 384 nm ($\Delta\varepsilon$ +0.3), 336 (−0.8), and 300 (+2.0) cannot be used for an unambiguous determination of the absolute configuration of (**7**) because of lack of sufficiently reliable rules.

Received, 4th November 1983; Com. 1442

References

1 (a) T. C. McMorris, M. S. R. Nair, and M. Anchel, *J. Am. Chem. Soc.*, 1967, **89**, 4562; (b) M. F. Semmelhack, S. Tomoda, and K. M. Hurst, *ibid.*, 1980, **102**, 7567.

2 T. C. McMorris and M. Anchel, *J. Am. Chem. Soc.*, 1963, **85**, 831; 1965, **87**, 1594; K. Nakanishi, M. Ohachi, M. Tada, and Y. Yamada, *Tetrahedron*, 1965, **21**, 1231.

3 J. A. Kepler, M. E. Wall, J. E. Mason, C. Basset, A. T. McPhail, and G. A. Sim, *J. Am. Chem. Soc.*, 1967, **89**, 1260.

4 J. J. Dugan, P. de Mayo, M. Nisbet, J. R. Robinson, and M. Anchel, *J. Am. Chem. Soc.*, 1966, **88**, 2838.

5 D. M. X. Donnelly, S. Sanada, J. O'Reilly, J. Polonsky, T. Prangé, and C. Pascard, *J. Chem. Soc., Chem. Commun.*, 1982, 135.

6 P. D. Cradwick and G. A. Sim, *J. Chem. Soc., Chem. Commun.*, 1971, 431.

7 N. Harada and K. Nakanishi, *J. Chem. Soc., Chem. Commun.*, 1970, 310.

8 G. Snatzke, Festschrift Fonds der Chemischen Industrie, Frankfurt, 1975, p. 31.

9 D. E. Cane and R. B. Nachbar, *Tetrahedron Lett.*, 1977, 4277.

10 N. Harada and K. Nakanishi, 'Circular Dichroic Spectroscopy – Exciton Coupling in Organic Stereochemistry,' University Science Books, Mill Valley, 1983, ch. 7 in particular.