Andilesin, a C_{25} Polyisoprenoid from *Aspergillus* sp. *X*-Ray Crystallographic and Spectroscopic Determination of the Structure

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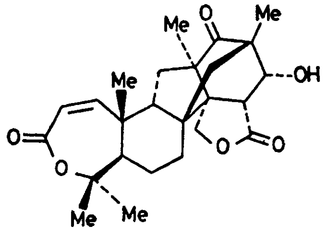
Summary The structure of a previously reported C_{25} polyisoprenoid, 'dihydroandibenin,' a metabolite of *Aspergillus* species, has been elucidated by *X*-ray and c.d. analysis.

Extraction of the mother liquors from a static culture of a pure strain of the fungus, *Aspergillus variecolor*, yielded three C_{25} polyisoprenoids (possibly sesterterpenes) named andibenin, dihydroandibenin, and deoxyandibenin;[1] subsequently, a fourth member of this series has been isolated. Dihydro- and deoxy-andibenin were named as derivatives of andibenin simply on the basis of the relationship of their molecular formulae, spectroscopic (^{1}H n.m.r., i.r., u.v.) similarity to andibenin, and a common fungal origin. The structure of andibenin was determined by *X*-ray and c.d. analysis.[1] The ^{1}H n.m.r. spectra of dihydroandibenin ($C_{25}H_{32}O_6$, mass spectrometry), deoxyandibenin ($C_{25}H_{30}O_5$), and the new compound just reported ('deoxydihydroandibenin,' $C_{25}H_{32}O_5$) showed sufficient differences from andibenin to suggest a skeletal difference between them and andibenin. We report here the structure of 'dihydroandibenin' which, because of skeletal differences from andibenin, is re-named andilesin.



(I)

Andilesin, $C_{25}H_{32}O_6$, m.p. 310 °C (decomp.) (from Pr^{i}OH) showed $[\alpha]_D^{27}$ $-9{\cdot}5°$ and u.v. 'end absorption' only; ν_{max} 3620, 1775, 1710, 1680, and 1595 cm^{-1}; δ 5·9 and 5·72 (C*H*=C*H*–C=O, *J* 12 Hz), 4·23 and 4·08 (–CH_2–O–, *J* 10 Hz), 4·05 and 2·91 (C*H*OH–C*H*–C=O, *J* 8 Hz), 1·78 (s, OH, exchanges with D_2O), 1·00—2·10 (m, 10H), and 1·44, 1·35, 1·30, 1·14, and 1·12 (each s, CMe).

An *X*-ray study of andilesin indicated structure (**1**). Andilesin crystals were orthorhombic with $a = 7{\cdot}557(3)$, $b = 28{\cdot}023$ (7), $c = 12{\cdot}674$ (4) Å, space group $P2_12_12_1$, and included propan-2-ol of crystallization, $Z = 4$ ($C_{25}H_{32}O_6.C_3H_8O$). Intensity measurements were made with Mo-K_α radiation ($\lambda = 0{\cdot}71069$ Å; graphite monochromator) on a Hilger–Watt four-circle diffractometer to θ 22·5°. A total of 1212 unique reflections with a net count of 3σ were found and deemed observed. The structure (**1**) was solved after much difficulty using a recent version of MULTAN.[2] Refinement proceeded by Fourier and least-squares methods which immediately revealed the region in which the solvent molecule was located but this was ill defined and is probably disordered. Refinement of the major terpene molecule proceeded smoothly and appeared to be unambiguously determined to the extent that, after anisotropic convergence, a difference map revealed the majority of the hydrogen atoms and these were subsequently included in the computations at fixed positions. Oxygen atoms were identified by their temperature factors and by the heights of the corresponding Fourier peaks. Final stages of refinement were with the terpene atoms in one least-squares block and the solvent atoms (treated isotropically) in a second block. Currently, the maximum shift per standard deviation is 0·26 with the average being much less than 0·1 (*R* is 8·8%).†

The absolute stereochemistry shown (**1**) was obtained from the c.d. curve. The only long-wavelength u.v. absorption expected for structure (**1**) would lie near 290 nm for the $n \rightarrow \pi^*$ transition of the carbonyl group in the saturated six-membered ring. Other absorption maxima due to this carbonyl and those in the γ- and ϵ-lactone would be expected at a much shorter wavelength.[3] The c.d. curve was negative at 296 nm (ΔE $-1{\cdot}76$). Consideration of the octant rule[4] and a Dreiding molecular model of structure (**1**) showed that almost all the structure must lie in the negative quadrants behind the carbonyl group, in keeping with the observed negative c.d. curve.

The unexpectedly much smaller difference between the chemical shifts of the hydrogens on the double-bond of the ϵ-lactone in andilesin (δ 5·9 and 5·72) compared with that for the hydrogens on the corresponding double-bond in the δ-lactone of andibenin (δ 6·74 and 6·06) may be accounted for by reduced π-bonding in andilesin. Thus, the torsional angle between the carbonyl group and the double-bond in

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

andilesin is 16° rather than 0° and the bond angles about the unsaturated carbon atoms differ by between 1 and 12° from those required for sp^2-hybridization.

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[2] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368; I. P. Declercq, G. Germain, and M. M. Woolfson, *Acta Cryst.*, 1975, **A31**, 367.

[3] See for example, A. I. Scott, 'Interpretation of the UV Spectra of Natural Products', Pergamon, Oxford, 1964, pp. 79–83.

[4] See for example, P. Crabbé, 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry', Holden-Day, San Francisco, 1965, pp. 72–158.