

Isolation of C₂₅ Polyisoprenoids from *Aspergillus* sp: Crystal Structure of Andibenin

By ANDREW W. DUNN, ROBERT A. W. JOHNSTONE,* and BENJAMIN SKLARZ

(The Robert Robinson Laboratories, The University, Liverpool L69 3BX)

and TREVOR J. KING

(Department of Chemistry, The University, Nottingham NG7 2RD)

Summary Three C₂₅ polyisoprenoids, andibenin, dihydroandibenin, and deoxyandibenin have been isolated as fungal metabolites of *Aspergillus* sp; the structure of andibenin was elucidated by X-ray and c.d. spectroscopy.

THE fungus, Phomas NRRL 3188, has been reported to yield epoxydon (sphaeropsidin).¹ We were unable to confirm this report,² but we now find that the fungus we have worked with is in fact a pure strain of *Aspergillus varicolor* from which we now report the isolation of three, possibly related, possible sesterterpenes, andibenin, dihydroandibenin, and deoxyandibenin.

Extraction of the mother liquors from static cultures of the fungus afforded a brown semi-solid oil from which terrein was isolated by crystallization from acetone. The filtrate from the crystallization was chromatographed preparatively by t.l.c. on silica gel to give several fractions after elution with MeOH-CHCl₃ (2:98). Three of these fractions gave andibenin, m.p. 218–220 °C (from MeOH), dihydroandibenin, decomp. >300 °C (MeOH), and deoxyandibenin, decomp. >300 °C (MeOH). The structures of the latter two compounds are still under investigation.

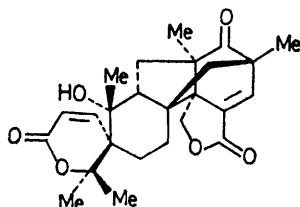
Andibenin, C₂₅H₃₀O₆ (mass spectrometry) showed $[\alpha]_D^{25}$ –277° and u.v. maxima at 249s (log ϵ 3.59) and 312 (2.91) nm; δ 7.04 (–CH=C–), 6.06 and 6.74 (CH=CH–C=O, J 10 Hz), 4.84 and 4.24 (–CH₂–O–, J 12 Hz), 2.55 (t showing

1.05 (each CMe); there was no extended proton coupling in the system.

The X-ray study of andibenin indicated structure (I). Andibenin crystals were tetragonal with $a = 8.388(2)$, $c = 60.53(1)$ Å, space group $P4_12_12$ or $P4_32_12$; determination of the chirality of the molecule showed that it was in fact the latter. Intensity measurements were made with Mo- K_α radiation ($\lambda = 0.71069$ Å, graphite monochromator) on a Hilger-Watt four-circle diffractometer out to θ 25°. 1422 Unique reflections with a net count of 3σ were found and deemed observed. The structure (I) was derived, with some difficulty, using MULTAN. Refinement was by full-matrix least-squares with carbon and oxygen treated anisotropically and with isotropic hydrogen atoms (found from a difference map) included in the calculation but not refined. The assignment of the hydroxy-group was made from a consideration of the temperature factors in the early stages of refinement (all atoms input as carbon) and confirmed later by the relevant bond length. At convergence the maximum positional shift was 0.05 σ and R was 0.057. Bond lengths and angles show no significant anomalies and the calculated estimated standard deviations for these quantities for (parameters not involving hydrogen) were 0.008–0.011 Å and ca. 0.6°.

The absolute stereochemistry shown in (I) was obtained from the c.d. curve. A six-membered ring $\beta\gamma$ -unsaturated ketone is known to give long wavelength $n \rightarrow \pi^*$ u.v. absorption near 300 nm.³ The skewed relative positions of the carbonyl group and the double bond give rise to helicity in the absorption, the right- or left-handedness being associated with positive and negative c.d. respectively.³ The c.d. curve was intensely negative, $\Delta\epsilon$ at 312 nm being –25.8, and the system must be left-handed; the large negative Cotton curve associated with this c.d. effect explains the large negative optical rotation observed at the sodium D-line.

The authors thank Professor W. Klyne and Dr. P. M. Scopes, Westfield College for measurement of the c.d. curve and the S.R.C. for a grant (A.W.D.).

(Received, 23rd January, 1976; Com. 067.)

(I)

further small coupling, J 14 and 3 Hz), 2.01–1.7 (m), and 1.64 (br s equivalent to 8H), and 1.47, 1.41, 1.38, 1.20, and

¹ J. H. Coats, M. E. Herr, and R. R. Herr, U.S.P., 3,585,11.

² A. W. Dunn, I. D. Entwistle, and R. A. W. Johnstone, *Phytochemistry*, 1975, 14, 2081.

³ For a discussion and several leading references, see P. Crabbé, 'Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' Holden-Day, San Francisco, 1965, pp. 232–237.