The Structure of Albidin—an *X*-Ray Crystallographic Study

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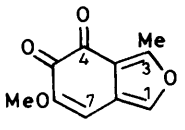
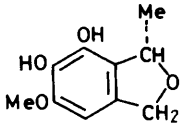
The fungistatic red pigment albidin, a secondary metabolic product of *Penicillium albidum*, is shown to be 6-methoxy-3-methylisobenzofuran-4,5-dione

A fungistatic optically inactive red pigment of composition $C_{10}H_8O_4$, containing one OMe and one CMe group, was isolated[1] from a *Penicillium* sp. considered at the time to fall within the *P. nigricans-janczewskii* series. Following the publication[2] of an authoritative treatise, the fungus was identified as *P. albidum* Sopp, and the pigment acquired the trivial name albidin,[3] a far from felicitous choice. The structure of this pigment has now been determined as 6-methoxy-3-methylisobenzofuran-4,5-dione (**1**).



(**1**)



(**2**)

Albidin formed a mono-dinitrophenylhydrazone. It gave a leucodiacetate of composition $C_{14}H_{14}O_6$ on reductive acetylation, and a quinoxaline derivative $C_{16}H_{12}N_2O_2$ with *o*-phenylene diamine. These reactions suggested that albidin contained an *o*-benzoquinone moiety (δ_C 174.4, 178.2) with the remaining two oxygen atoms present in ether linkages. The presence of OMe (δ_H 3.81; δ_C 56.1) and RRC=CRMe (δ_H 2.65; δ_C 14.3) substituents was confirmed by physical methods. In the ^1H n.m.r. spectrum both of the remaining H atoms were present as singlets at δ_H 6.49 and 7.33; the latter was severely deshielded for an olefinic hydrogen and was likely to be due to a proton present in an RRC=CH–O group. The composition of albidin required that a furan ring be fused to the quinone moiety and the absence of allylic coupling to the CMe group indicated the possibility of an isobenzofuran skeleton, a skeleton consistent with the formation of oxonium salts.[1]

The mass spectrum showed the sequential loss of $^{\cdot}CH_3$ and CO (twice), giving fragment ions at *m/z* 177, 164, 149, and 121, but provided no additional reliable evidence as to the position and relationship of the OMe and Me substituents. This information was therefore obtained by *X*-ray crystallography, and the structure is shown in the Figure which includes the atomic numbering scheme adopted for crystallographic purposes. Atomic co-ordinates are listed in the Table. Albidin is therefore 6-methoxy-3-methylisobenzofuran-4,5-dione (**1**), a type of quinone hitherto unavailable from natural sources or by synthesis. However, the analogous reduced structure (**2**) has been assigned[4] to curvulol, a metabolic product of the fungus *Curvularia siddiqui*.

Experimental

M.p.s were taken on a Kofler hot-stage apparatus and are corrected. I.r. spectra were determined on Nujol mulls and u.v. spectra were obtained in methanol. N.m.r. spectra were obtained at 360 MHz (^1H) or 90.55 MHz (^{13}C) in $CDCl_3$ with

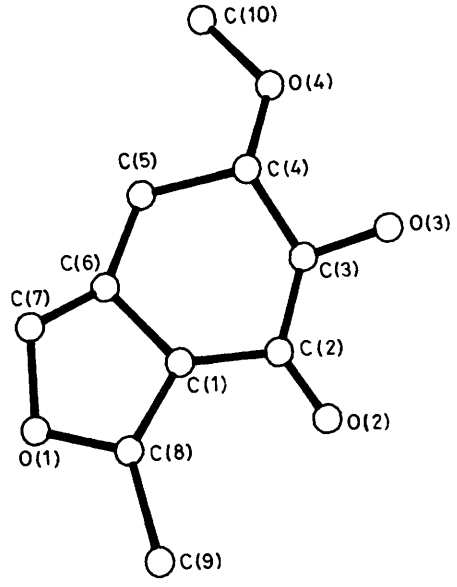


Figure. *X*-Ray molecular structure of albidin, showing the crystallographic numbering scheme

$SiMe_4$ as internal standard. CH_3/CH and CH_2/Cq ^{13}C subspectra were generated by spin-echo pulse sequences. In analytical t.l.c., Merck silica gel HF_{254} was used in chloroform–methanol (9:1) as developer.

Albidin (*6-Methoxy-3-methylisobenzofuran-4,5-dione*).—This compound was obtained as described previously,[1] R_F 0.63; $\nu_{max.}$ 3 110w, 3 076w, 1 692w, 1 661, 1 645, 1 615, 1 592, 1 551, 1 060, 910, 875, and 810 cm^{-1}; $\lambda_{max.}$ 240, 350, and 434 nm (log ε 4.02, 3.27, and 3.50 respectively); δ_H (all s) 2.65 (3 H, CMe), 3.81 (3 H, OMe), 6.49 (7-H), and 7.33 (1-H); δ_C 14.3 (CCH_3), 56.1 (OCH_3), 105.7 (CH), 116.4 (q), 119.6 (q), 138.3 (CH), 152.7 (q), 165.3 (q), 174.4 (CO), and 178.2 (CO); *m/z* 192 (M^+, 100%), 177 (5), 164 (22), 149 (63), 135 (35), 121 (65), 93 (20), 79 (33), and 65 (60).

The *2,4-dinitrophenylhydrazone* formed deep red needles, m.p. >350 °C (from ethanol) (Found: C, 51.4; H, 3.0; N, 14.5. $C_{16}H_{12}N_4O_7$ requires C, 51.6; H, 3.2; N, 15.0%).

The *quinoxaline*, prepared in acetic acid, crystallised from ethanol in citrine needles of a *solvate*, m.p. 65 °C (loss of solvent) and 145—150 °C (decomp.); R_F 0.72 (Found: C, 69.75; H, 5.2; N, 9.6%; M^+, 264. $C_{16}H_{12}O_2N_2 \cdot C_2H_6O$ requires C, 69.7; H, 5.8; N, 9.0%; M^+, 264); $\nu_{max.}$ 3 400br and 1 640 cm^{-1}; $\lambda_{max.}$ 262, 270, and 436 nm (log ε 4.55, 4.55, and 3.96).

The *leucodiacetate*, prepared in pyridine–acetic anhydride in the presence of zinc powder, was precipitated by the addition of water, and was obtained as an amorphous solid, R_F 0.72 (Found: C, 60.1; H, 5.0%; M^+, 278. $C_{14}H_{14}O_6$ requires C, 60.4; H, 5.1%; *M*, 278).

Table. Fractional atomic co-ordinates ($\times 10^3$) with estimated standard deviations in parentheses

	x	*y*	*z*
O(1)	397(6)	105(2)	552(5)
O(2)	876(6)	226(2)	286(5)
O(3)	822(5)	370(1)	357(4)
O(4)	450(5)	419(1)	508(4)
C(1)	571(5)	205(1)	450(4)
C(2)	728(7)	250(2)	363(6)
C(3)	672(9)	321(3)	383(6)
C(4)	515(9)	354(2)	508(7)
C(5)	312(11)	300(3)	545(8)
C(6)	340(8)	226(3)	528(6)
C(7)	285(7)	169(2)	610(6)
C(8)	589(10)	128(3)	470(8)
C(9)	788(10)	69(3)	434(8)
C(10)	228(9)	441(3)	569(7)

Crystal Data for Albidin.—$C_{10}H_8O_4$, M = 192.2, monoclinic, space group $P2_1/c$, a = 5.996(3), b = 18.926(13), c = 7.742(10) Å, β = 90.0(1)°, V = 878.5 Å^3, D_c = 1.45 g cm^{-3}. Monochromated Mo-K_α radiation, λ = 0.710 69 Å, μ = 1.1 cm^{-1}.

Crystallographic Analysis of Albidin.—The compound crystallised as very thin red needles. The best one that could be found was *ca.* 1.0 × 0.10 × 0.02 mm. No attempt was made to cut it since the crystals usually shattered easily. The diffraction data were extremely limited, but as no better crystal could be obtained they were used in the analysis. The crystal was mounted on an Enraf-Nonius CAD4 diffractometer and intensities for unique data with $2 < \theta < 25°$ were measured by an ω–2θ scan with a maximum scan time of 2 min. No correction was made for absorption. Out of 1 885 reflections measured, only 236 with $|F^2| > 3\sigma(F^2)$ were used in the refinement, where $\sigma(F^2) = [\sigma^2(I) + (0.04I)^2]^{\frac{1}{2}}/Lp$.

The structure was solved by direct methods using MULTAN.[5] Initially only an incorrectly positioned fragment of the structure could be located. This was finally developed into the correct solution by working in the reduced symmetry space group $P1$ and using successive Fourier syntheses to locate the symmetry-related molecules. The final structure was then refined by full-matrix least-squares in the correct space group using only isotropic temperature factors because of the lack of data. No attempt was made to include H atoms. Refinement converged at R = 0.153, R' = 0.161 with a weighting scheme of $w = 1/\sigma^2(F)$. A final difference map was everywhere < 0.5 e Å^{-3}. The negative temperature factor for C(1) and the fairly wide spread of calculated distances and angles are results of the paucicity of data, but we feel that the molecular structure is correctly defined. All calculations were done on a PDP11/34 computer using the Enraf-Nonius SPD-Plus program package.*

* Tables of intramolecular distances and bond angles, and isotropic temperature factors, are available as a Supplementary Publication [SUP No. 56520 (3 pp.)]. For details of the Supplementary Publications Scheme, see *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1. Structure factors are available from the editorial office on request.

Acknowledgements

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