

Structural Revision and Synthesis of a Novel Fungal Diaryl Ether

By J. R. CANNON, T. M. CRESP, B. W. METCALF, M. V. SARGENT*

(Department of Organic Chemistry, University of Western Australia, Nedlands, Western Australia)

and J. A. ELIX

(Chemistry Department, School of General Studies, Australian National University, Canberra, Australia)

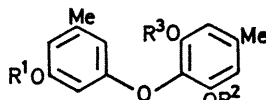
Summary The structure 2-hydroxy-6-methoxy-4-methylphenyl 3-hydroxy-5-methylphenyl ether (**1**) proposed for the fungal metabolite LL-V125 α has been revised to 2-hydroxy-4-methoxy-6-methylphenyl 3-hydroxy-5-methylphenyl ether (**2**); this has been confirmed by synthesis.

THE isolation of a diaryl ether, LL-V125 α , from a fungus of the order Sphaeropsidales has recently been reported.¹ The erroneous structural assignment (**1**) for this metabolite followed from an incorrect interpretation of the ¹H n.m.r. spectra of this compound and its derivatives. We now report an amended structure (**2**) for LL-V125 α , and a synthesis of this metabolite.

We have interpreted the data reported for this natural product in terms of structure (**2**), and hence structures (**3**), (**4**), and (**5**) follow for the di-*O*-methyl ether, the demethylation product, and the diacetate, respectively. Tri-*O*-methylalectol (**3**), a depsidone degradation product, had previously been synthesised by Asahina and Fuzikawa² in 0.2% yield by Ullmann condensation between mono-*O*-methylorcinol (**6**) and di-*O*-methyl-2-bromo-orcinol⁴ (**7**). Modification of this method gave (**3**), m.p. 94.5–96° (lit.,² 96°) (ca. 20%); mass spectrum, M^+ , m/e 288; τ (CDCl₃; all 60 MHz) 3.67 (m, 5H, ArH), 6.25 (s, 3H, OMe), 6.31 (s, 6H, OMe), and 7.77 and 7.87 (each s, 3H, Me). Demethylation of (**3**) gave alectol† (**4**); mass spectrum, M^+ , m/e 246; τ (CDCl₃) 3.18br (s, 2H, D₂O-exchangeable OH), 3.74 (m, 6H, 5 × ArH and 1 × D₂O-exchangeable OH), 7.82 and 8.02 (each s, 3H, Me). The physical properties of both (**3**) and (**4**) are similar to those reported for the di-*O*-methyl ether, and the demethylation product, respectively, of LL-V125 α .¹

Ullmann condensation between mono-*O*-benzylorcinol‡ (**8**) and (9)§ gave (**10**) (ca. 25%), which on hydrogenolysis afforded LL-V125 α (**2**) (98%), m.p. 121–122° (lit.,¹ 121.5–122.5°); mass spectrum, M^+ , m/e 260; τ (CDCl₃) 3.72 (m, 5H, ArH), 4.42 and 4.62 (each br s, 1H, OH), 6.23 (s, 3H, OMe), and 7.78 and 7.94 (each s, 3H, Me) virtually identical with that reported for natural LL-V125 α . The i.r. spectra of the natural and synthetic products, kindly determined by Dr. E. L. Patterson, were identical. The diacetate (**5**) of synthetic LL-V125 α had m.p. 72–73° (lit.,¹ 75–76°).

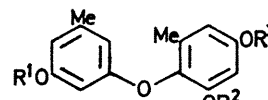
In contrast to these results, Ullmann condensation between (**6**) and di-*O*-methyl-4-bromo-orcinol¶ (**11**) gave (**12**), m.p. 141–142°; mass spectrum, M^+ , m/e 288; τ



(1) R¹ = R² = H; R³ = Me

(12) R¹ = R² = R³ = Me

(13) R¹ = R² = R³ = H



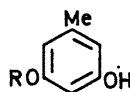
(2) R¹ = R² = H; R³ = Me

(3) R¹ = R² = R³ = Me

(4) R¹ = R² = R³ = H

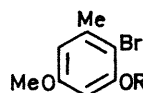
(5) R¹ = R² = Ac; R³ = Me

(10) R¹ = R² = CH₂Ph; R³ = Me



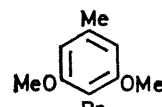
(6) R = Me

(8) R = CH₂Ph



(7) R = Me

(9) R = CH₂Ph



(11)

(CCl₄) 3.65 (s, 2H, ArH), 3.80 (m, 1H, ArH), 3.93 (m, 2H, ArH), 6.30 (s, 6H, OMe), 6.33 (s, 3H, OMe), and 7.70 and 7.78 (each s, 3H, Me). Demethylation of (**12**) gave (**13**), m.p. 148–150°; mass spectrum, M^+ , m/e 246; τ (CDCl₃) 3.69br (s, 5H, 2 × ArH and 3 × D₂O-exchangeable OH), 3.80 (m, 3H, ArH), and 7.87 and 7.97 (each s, 3H, CH₃).

The above evidence indicates that LL-V125 α has structure (**2**).

(Received, January 18th, 1971; Com. 080.)

† All new compounds gave satisfactory elemental analyses or high-resolution mass spectra.

‡ Obtained by partial hydrogenolysis of di-*O*-benzylorcinol.

§ Prepared by bromination of mono-*O*-methylorcinol followed by benzylation.

¶ Readily obtained by treatment of 4-lithio-di-*O*-methylorcinol with 1,2-dibromoethane.

¹ W. J. McGahren, W. W. Andres, and M. P. Kunstmann, *J. Org. Chem.*, 1970, **35**, 2433.

² Y. Asahina and F. Fuzikawa, *Ber.*, 1934, **67**, 163.

³ Prepared in 98% yield by monodemethylation of di-*O*-methylorcinol by the general method of G. I. Feutrill and R. N. Mirrington, *Tetrahedron Letters*, 1970, 1327.

⁴ See D. D. Ridley, E. Ritchie, and W. C. Taylor, *Austral. J. Chem.*, 1970, **23**, 147; we found the direct bromination of di-*O*-methylorcinol to be more convenient.