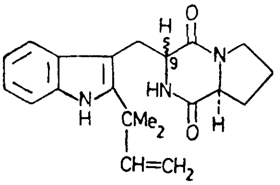
Synthesis of Deoxybrevianamide E

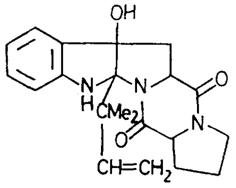
By Robert Ritchie and J. Edwin Saxton*
(*Department of Organic Chemistry, The University, Leeds* LS2 9JT)

Summary The proposed structure of deoxybrevianamide E has been confirmed by synthesis from 3-(3-dimethylaminomethylindol-2-yl)-3-methylbut-1-ene.

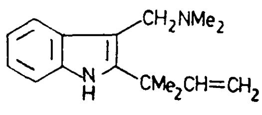
We report the synthesis of deoxybrevianamide E [L-prolyl-2-(1′,1′-dimethylallyl)-L-tryptophyldiketopiperazine] (**1a**), a metabolite of *Aspergillus ustus* (Bainier) Thom and Church,[1] and a degradation product of brevianamide E (**2**), a metabolite of *Penicillium brevicompactum*;[2] this provides final confirmation of structure (**1a**), which was based mainly on spectroscopic evidence and plausible biogenetic argument.



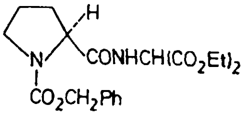
(**1a**); α-H at C(9)
(**1b**); β-H at C(9)



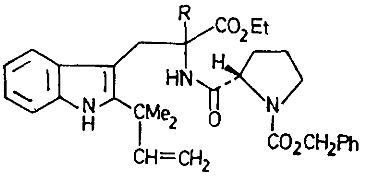
(**2**)



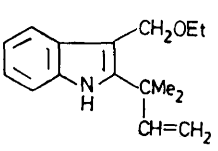
(**3**)



(**4**)



(**5**); R = CO$_2$Et
(**7**); R = H



(**6**)

3-(3-Dimethylaminomethylindol-2-yl)-3-methylbut-1-ene (**3**)[3] was converted into its methosulphate, which was condensed with the sodium salt of diethyl *N*-benzyloxycarbonyl-L-prolylaminomalonate [derived from (**4**), m.p. 74—75 °C] in ethanol to give the amido-diester (**5**) (42%), together with the ether (**6**) (10%). Partial hydrolysis of (**5**) (2N-NaOH–EtOH) followed by decarboxylation afforded the mono ester (**7**) (52%), which was treated with 2N-HBr–AcOH at room temperature to remove the benzyloxycarbonyl group. The free amino-ester was liberated and cyclised by refluxing in toluene with 4A molecular sieves. Chromatography of the product gave deoxybrevianamide E (**1a**) as a colourless glass (20%), $[\alpha]_D^{22}$ − 58° ($CHCl_3$), and its diastereoisomer, L-prolyl-2-(1′,1′-dimethylallyl)-D-tryptophyldiketopiperazine (**1b**), also a colourless glass (14%), $[\alpha]_D^{22}$ − 30° ($CHCl_3$).

The t.l.c. behaviour, the i.r., u.v., and n.m.r. spectra, and the optical rotation of (**1a**) were identical with those of authentic deoxybrevianamide E, $[\alpha]_D^{22}$ − 59 °C ($CHCl)_3$.

Attempted oxidation of deoxybrevianamide E by means of iodosobenzene diacetate in aqueous acetonitrile furnished an inseparable mixture of products (diastereoisomers?), whose complex n.m.r. spectrum contained all the absorptions appropriate to brevianamide E (**2**).†

We are indebted to Dr. P. S. Steyn for supplying a sample of deoxybrevianamide E, and for information concerning its aerial oxidation.

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† We have not examined this reaction further in view of Dr. Steyn's report that deoxybrevianamide E is slowly converted into brevianamide E by aerial oxidation. The synthesis of deoxybrevianamide E thus constitutes, in a formal sense, the synthesis also of brevianamide E.

[1] P. S. Steyn, *Tetrahedron Letters*, **1971**, 3331; *Tetrahedron*, **1973**, **29**, 107.
[2] A. J. Birch and J. J. Wright, *Tetrahedron*, **1970**, **26**, 2329.
[3] E. Houghton and J. E. Saxton, *J. Chem. Soc.* (*C*), **1969**, 595.