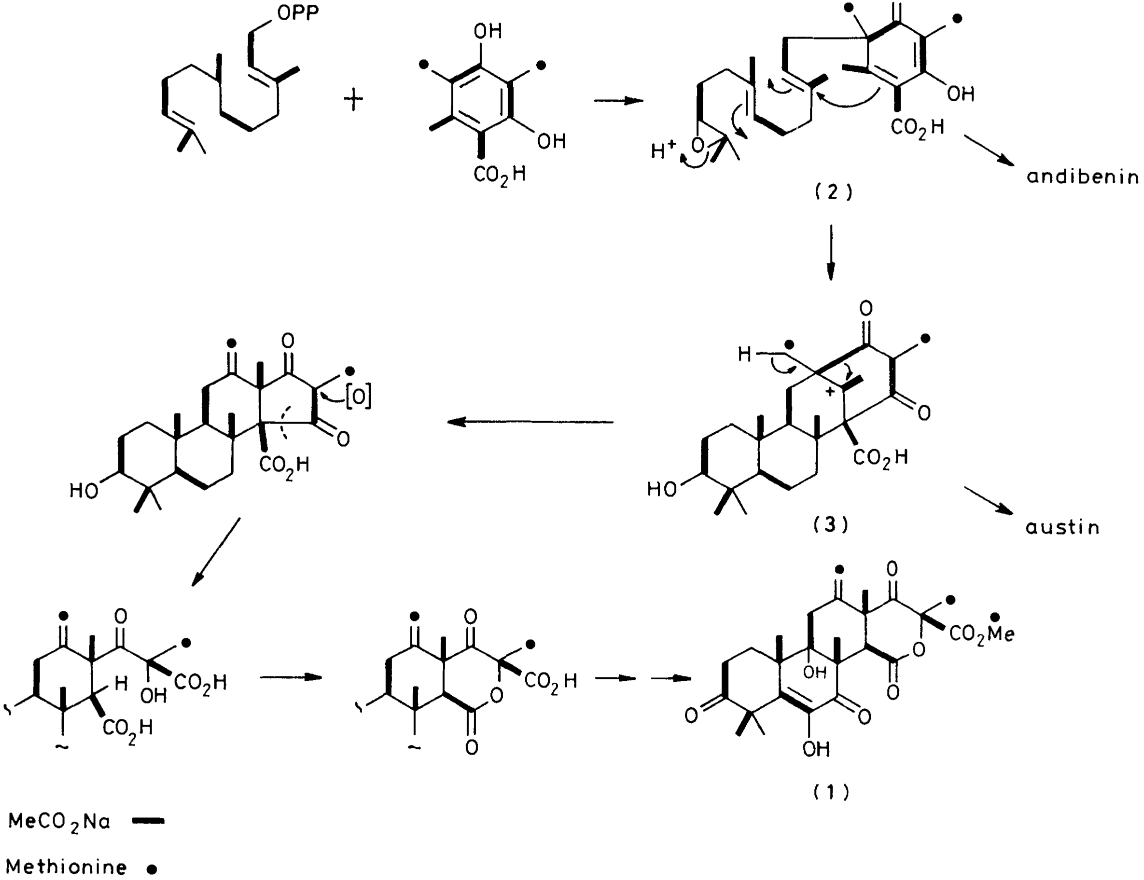
Biosynthesis of Terretonin, a Polyketide-terpenoid Metabolite of *Aspergillus terreus*

By C. RUPERT MCINTYRE and THOMAS J. SIMPSON*
(*Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh* EH9 3JJ, *Scotland*)

Summary Incorporations of [1,2-$^{13}C_2$]acetate and [*Me*-^{13}C]-methionine into the mycotoxin terretonin, a metabolite of *Aspergillus terreus*, indicate its formation by a mixed polyketide–terpenoid pathway.

ANDIBENIN[1] and anditomin,[2] metabolites of *Aspergillus variecolor*, and austin,[3] a metabolite of *Aspergillus ustus*, have been shown to be formed by a novel variation of the triprenyl–phenol biosynthetic pathway in which *C*-



SCHEME. Biosynthesis of terretonin in *Aspergillus terreus* alkylation of 3,5-dimethylorsellinate by farnesyl pyrophosphate gives the key intermediate (**2**) which is then subject to further elaboration to produce the above metabolites. We suggested[2] that the mycotoxin terretonin (**1**), a metabolite of *Aspergillus terreus* for which a triterpenoid origin has been proposed,[4] could also be a product of this pathway. We now report studies which support this proposal.

Incorporation of [*Me*-^{13}C]methionine and [1,2-$^{13}C_2$]acetate by cultures of *A. terreus* (NRRL 6273) resulted in terretonin being labelled as indicated in the Scheme.† This labelling pattern can be best accounted for by the pathway summarised in the Scheme in which cyclisation of (**2**) as in austin biosynthesis gives the intermediate (**3**), which by ring contraction, followed by retro-Claisen reaction, hydroxylation, and lactonisation as indicated to generate the ring D keto-lactone system, and oxidative modification of the bicyclofarnesyl moiety, gives terretonin. Further studies to establish the timing and mechanisms of these processes are in progress.

The support of the S.R.C. and microbiological assistance by Miss S. Christie are gratefully acknowledged.

(*Received*, 1*st July* 1981; *Com.* 772.)

---

† Details of ^{13}C n.m.r. assignments, enrichments, and ^{13}C–^{13}C couplings will be reported in full elsewhere.

[1] J. S. E. Holker and T. J. Simpson, *J. Chem. Soc., Chem. Commun.*, 1978, 626.
[2] T. J. Simpson, *Tetrahedron Lett.*, in the press.
[3] T. J. Simpson and D. J. Stenzel, *J. Chem. Soc., Chem. Commun.*, in the press.
[4] J. P. Springer, J. W. Dorner, R. J. Cole, and R. H. Cox, *J. Org. Chem.*, 1979, **44**, 4852.