An Alternative Synthesis of (\pm) -Dehydrogriseofulvin by Enzymic Phenolic Oxidation by Homogenised Potato Peelings

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WE have reported that head-to-tail coupling of 1,2,3,4tetrahydro-7-hydroxy-1-(4-hydroxyphenethyl)-6-methoxy-2-methylisoquinoline by enzymic phenolic oxidation gives the expected promelanthioidine. Similarly, N-methylcoclaurine undergoes enzymic phenolic oxidation with homogenised potato peelings-hydrogen peroxide.2 Since the formation of dehydrogriseofulvin (II), a precursor of griseofulvin, has been assumed to be by phenol oxidation of griseophenone A (I),3 many attempts to obtain (II) in vitro by phenol oxidation of (I) with potassium ferricyanide4 and horseradish-hydrogen peroxide⁵ have been carried out. Here, we report an alternative conversion of (I) into (II) with homogenised potato peelings-hydrogen peroxide.

A phosphate-buffered solution (pH 7·6—7·7) of griseophenone A (I), derived from natural griseofulvin, was mixed with homogenised potato peelings in the presence of hydrogen peroxide and ethanol and set aside for 2 days at 4-8°. A further and similar quantity of homogenised potato peelings was then added. The mixture was worked

up after 4 days and gave starting material (I) and (±)dehydrogriseofulvin (II), m.p. (benzene) 288—209° [lit.,7 m.p. $288-290^{\circ}$], $[\alpha]_D = 0^{\circ}$, (12%) yield) whose i.r. (in CHCl₃) and n.m.r. (in CDCl₃) spectra were superimposable on those of an authentic sample. The compound was optically inactive.

$$\underbrace{\begin{array}{c} OMe \\ OH \\ CI \end{array}}_{OH} \underbrace{\begin{array}{c} MeO \\ MeO \\ OH \\ \end{array}}_{MeO} \underbrace{\begin{array}{c} O\\ MeO \\ CI \\ \end{array}}_{(II)} \underbrace{\begin{array}{c} OMeO \\ MeO \\ CI \\ \end{array}}_{(III)}$$

We thank Dr. M. Murakami and Mr. R. Kawata, The Central Research Laboratory, Yamanouchi Pharmaceutical Co. Ltd., for a gift of natural griseofulvin.

(Received, November 25th, 1968; Com. 1603.)

¹ T. Kanetani, S. Takano, and T. Kobari, Tetrahedron Letters, 1968, 4565; J. Chem. Soc. (C), in the press.

² T. Kametani, H. Nemoto, and S. Takano, to be published.

³ D. H. R. Barton and T. Cohen, 'Festschrift A. Stoll', Birkhauser, Basle, 1957, p. 117.

A. C. Day, L. Nabney, and A. I. Scott, J. Chem. Soc., 1961, 4067.
A. Segal and E. H. Taylor, J. Pharm. Sci., 1968, 57, 874.
D. Tajb, C. H. Kuo, H. L. Slates, and N. L. Wendler, Tetrahedron, 1963, 19, 1.