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MICROBIAL TRANSFORMATION OF 2′-PROPOXY ANALOGS OF (−)-AND (+)-DEHYDROGRISEOFULVIN AND(+)-2′-DEMETHOXYDEHYDROGRISEOFULVIN BY *STRFPTOMYCES CINEREOCROCATUS**

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In connection with the previous studies, the microbial treatment of 2′-propoxy analog of (−)-dehydrogriseofulvin (**1**) by *S. cinereocrocatus* under previously described conditions gave **4** as the reduction product and the recovered material, which were separated by silica gel column chromatography. On the other hand, the same microbial treatment of 2′-propoxy analog of (+)-dehydrogriseofulvin (**2**) was performed and its results were compared with those of the enantiomer (**1**). The results indicate that reactions of **1** proceed more rapidly that those of **2** by comparisons of the yields of the reduction product and the recovered material(s). Moreover, the comparisons of susceptibilities to microbial transformations between (−)- and (+)-dehydrogriseofulvin and their 2′-propoxy analogs indicate that the propoxy analogs are less transformed by *S. cinereocrocatus*. Furthermore, the relative ratios of these compounds clearly demonstrate that both substrates were transformed into the optically pure 2′-propoxy analog of (+)-griseofulvin in spite of a fact that recovered dehydrogriseofulvin analogs were a mixture of (+)- and (−)-enantiomers in the microbial treatment of 2′-propoxy analog (**2**) of (+)-dehydrogriseofulvin. Further, it is of importance to notice that in the microbial treatment by *S. cinereocrocatus* 2′-propoxy analog (**2**) of (+)-dehydrogriseofulvin was not transformed into the corresponding hydrogenated product (**5**). These results are summarized in Scheme 1.

In order to extensively elucidate the microbial transformation, (+)-2′-demethoxydehydrogriseofulvin (**3**) was synthesized as the substrate. The microbial treatment of (+)-2′-demethoxydehydrogriseofulvin (**3**) by *S. cinereocrocatus* for 12 hr under the same conditions described above afforded (+)-2′-demethoxygriseofulvin (**6**) (12%) and a mixture of (−)- and (+)-2′-demethoxy-2′,3′-dihydrodehydrogriseofulvin (**7** and **8**), whose relative ratio was calculated as 19 : 81 from the value of its circular dichroism. These results are summarized in Scheme 2. Furthermore, the formation of (+)-2′-demethoxy-2′,3′-dihydrodehydrogriseofulvin (**8**) suggests that the microorganism has the abilities of the isomerization of the substrate (**3**) into the enantiomer (**9**) and of the subsequent reduction of the latter.

Hence, we conclude that in the treatment with *S. cinereocrocatus*, the analogs of (−)- and (+)-dehydrogriseofulvin which have or have not substituents at 2′-position are

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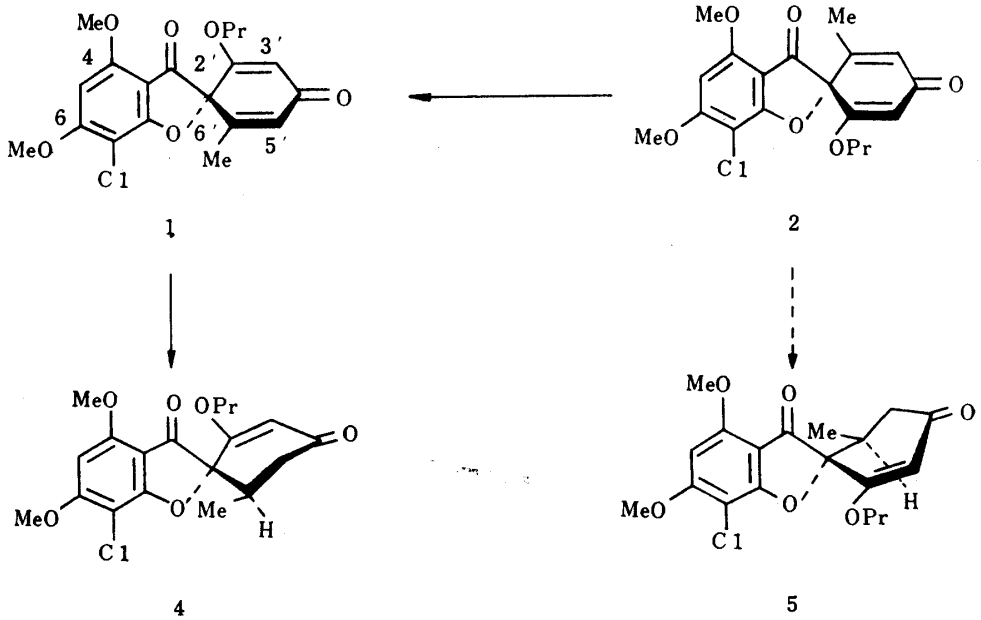
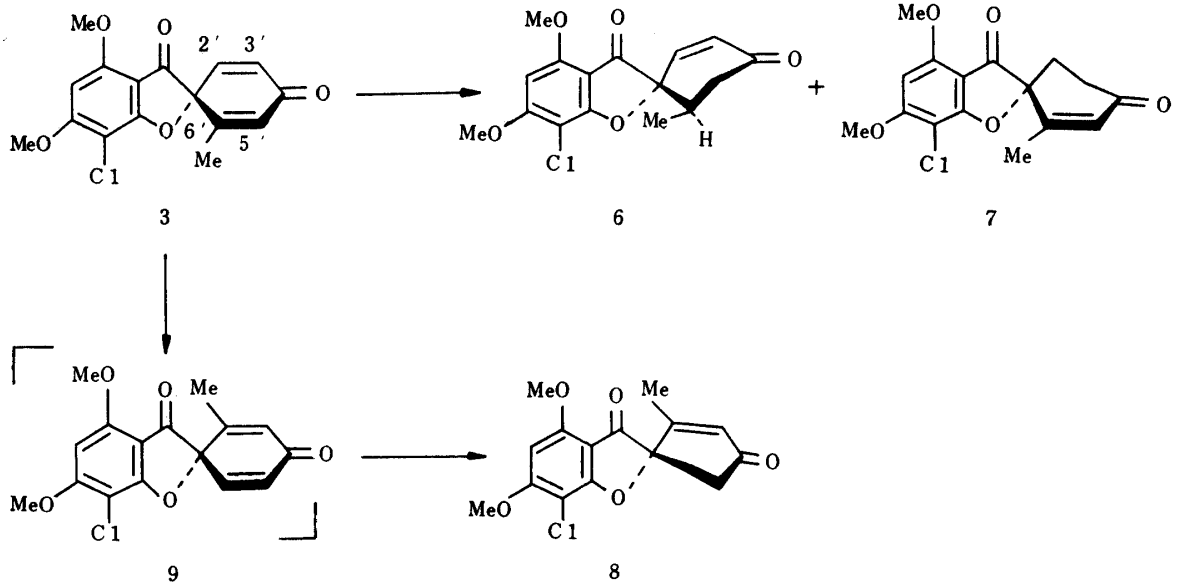


Scheme 1.



Scheme 2.

reduced directly or after isomerization into the corresponding enantiomers, yielding (+)- and/or (−)-dihydro compound(s) as the transformation products.