

MICROBIAL CONVERSION
OF ANTIBIOTICS. IIDEACYLATION OF MARIDOMYCIN
BY ACTINOMYCETES

Sir:

A previous paper¹⁾ in this series has described that maridomycin III (MDM III) and 9-propionylmaridomycin III (PMDM III), macrolide antibiotics, are hydrolyzed to 4''-depropionylmaridomycin III (MDM III-M) and 4''-depropionyl-9-propionylmaridomycin III (PMDM III-M), respectively, by *Bacillus megaterium* 91277. Leucomycin^{2,3)} and SF-837⁴⁾ have also been reported to be hydrolyzed by fungi. But the deacylation of macrolide antibiotics by actinomycetes is not known.

This paper deals with the deacylation of MDM III, PMDM III and PMDM III-M by *Streptomyces pristinaespiralis* IFO 13074 and *Streptomyces olivaceus* 219.

Actinomycetes were grown in a medium (pH 7.2) containing 2% dextrin, 0.5% peptone, 0.5% yeast extract, 0.5% beef extract and 0.5% CaCO₃ in deionized water at 28°C for 72 hours on a rotary shaker.

MDM III (2.9 g) was added to culture broth of *S. pristinaespiralis* IFO 13074 (5.8 liters), and the culture broth was incubated at 28°C for 72 hours with shaking. Thin-layer chromatogram of the culture broth indicated that MDM III added was almost completely converted to MDM III-M. After the incubation, the culture broth was adjusted to pH 8.5 and extracted with ethyl acetate. The extract was washed with water and extracted with 0.05M citrate buffer (pH 3.0). The buffer layer was reextracted with ethyl acetate at pH 8.5. The extract was washed with water and concentrated *in vacuo*. The concentrate was chromatographed on a silica gel column using a solvent system consisting of benzene-acetone (2:1, v/v), and the eluate containing MDM III-M was concentrated *in vacuo* to give MDM III-M (1,374 mg) as a white powder.

PMDM III (3 g) was added to culture broth of *S. pristinaespiralis* IFO 13074 (6 liters), and the culture broth was incubated at 28°C for 72 hours with shaking. PMDM III added was almost completely converted to MDM III-M, in contrast to the deacylation by *B. megate-*

rium 91277 which converted PMDM III to PMDM III-M.¹⁾ The purification of MDM III-M formed in the culture broth was carried out similarly to that described above to give MDM III-M (889 mg) as a white powder.

PMDM III-M (1.8 g) was incubated with culture broth of *S. pristinaespiralis* IFO 13074 (3.6 liters) at 28°C for 72 hours. PMDM III-M added was almost completely converted to MDM III-M during the incubation. The purification was carried out to give MDM III-M (469 mg) as a white powder.

MDM III (1.9 g) was added to culture broth of *S. olivaceus* 219 (3.8 liters), and the culture broth was incubated at 28°C for 72 hours with shaking. Thin-layer chromatogram of the culture broth indicated that MDM III added was almost completely converted to MDM III-M during the incubation. The purification was carried out to give MDM III-M (600 mg) as a white powder.

PMDM III (1.3 g) was incubated with culture broth of *S. olivaceus* 219 (2.6 liters) at 28°C for 72 hours. PMDM III added was almost completely converted to PMDM III-M, but not to MDM III-M even if further incubation was continued. The purification was carried out to give PMDM III-M (334 mg) as a white powder.

Although PMDM III-M was completely converted to MDM III-M by *S. pristinaespiralis* IFO 13074, it was not converted at all by *S. olivaceus* 219.

IR, NMR and mass spectra and thin-layer chromatographic patterns of the deacylation products thus obtained were identical with those of authentic samples prepared as described previously.⁵⁾

The deacylation of MDM III, PMDM III and PMDM III-M by these actinomycetes are summarized in Fig. 1.

Of 219 strains of actinomycetes tested, 19 strains were found to hydrolyze MDM III and PMDM III with the high conversion rates. Among these actinomycetes, 12 strains hydrolyzed PMDM III to MDM III-M similarly to *S. pristinaespiralis* IFO 13074, and 7 strains hydrolyzed PMDM III to PMDM III-M but not to MDM III-M similarly to *S. olivaceus* 219. Thus, it seems that there are two types of actinomycetes which hydrolyze PMDM III. One hydrolyzes PMDM III at C₄' and

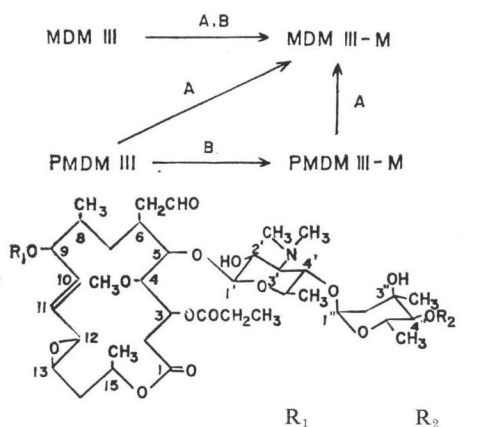
C₆, and the other only at C₄'.

On the other hand, it was found that several strains gave other conversion products which were detected by TLC. These results will be presented elsewhere in the near future.

Fig. 1. Deacylation of MDM III, PMDM III and PMDM III-M by actinomycetes.

A: Deacylation by *S. pristinaespiralis* IFO 13074

B: Deacylation by *S. olivaceus* 219



	R ₁	R ₂
Maridomycin III (MDM III)	H	COCH ₂ CH ₃
4''-Depropionylmaridomycin III (MDM III-M)	H	H
9-Propionylmaridomycin III (PMDM III)	COCH ₂ CH ₃	COCH ₂ CH ₃
4''-Depropionyl-9-propionylmaridomycin III (PMDM III-M)	COCH ₂ CH ₃	H

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