MICROBIAL CONVERSION OF
 ϵ -PYRROMYCINONE TO 1-HYDROXY-
 11-DEOXYCARMINOMYCIN II

Sir:

During our biosynthetic studies on anthracycline antibiotics, we isolated a blocked mutant of *Actinomadura roseoviolacea* MuW1 which converted ϵ -rhodomycinone to carminomycins¹⁾. The strain MuW1 was derived by NTG treatment of *A. roseoviolacea*, a carminomycin producer. It was selected as an antibiotic blocked mutant which could not produce the chromophore, and its ability to convert ϵ -rhodomycinone to carminomycins was assessed in preliminary shake flask trials. We wish to report herein the conversion of ϵ -pyrromycinone to a novel anthracycline glycoside by MuW1.

For the microbial conversion of ϵ -pyrromycinone, a medium of the following composition was used; 2.5% glucose, 1.5% soy bean meal, 0.2%

Fig. 1. The structure of 1-hydroxy-11-deoxycarminomycin II.

yeast extract and 0.4% CaCO_3 . One ml of seed culture was added to 100 ml of medium contained in a 500-ml Erlenmeyer flask. After 24-

Fig. 2. ^1H NMR spectrum of 1-hydroxy-11-deoxycarminomycin II (400 MHz in CDCl_3).

hour cultivation at 37°C on a rotary shaker, 1 ml of a dimethyl sulfoxide solution of ϵ -pyrromycinone (3 mg/ml) was added to the flask and the cultivation was continued for a further 48 hours.

After centrifuging the culture broth (10 liters), the mycelial cake was extracted with acetone. The acetone extract was concentrated to a small volume *in vacuo* and was then extracted with CHCl_3 - MeOH (9:1). The solvent fraction was evaporated to dryness *in vacuo* and the residue was subjected to silica gel column chromatography. The column was washed with CHCl_3 and a new anthracycline glycoside (MG1) was then eluted with CHCl_3 - MeOH (10:1). Further purification was achieved by HW-40 column chromatography with MeOH - AcOH (100:0.1) to give a pure sample of MG1 (3 mg).

Physico-chemical properties of MG1 are as follows: $\text{C}_{33}\text{H}_{41}\text{NO}_{13}$, FD-MS m/z 682 ($\text{M} + \text{Na}$)⁺, mp 210~212°C, $[\alpha]_{\text{D}}^{25}$ 20° (c 0.05, CHCl_3), UV λ_{max} (in MeOH) nm ($\text{E}_{1\%}^{1\text{cm}}$) 235 (687), 259 (375), 294 (155) and 492 (215). The ^1H NMR spectrum (Fig. 2) of MG1 was superimposable on that of carminomycin II²⁾ except for aromatic protons. Thus the ^1H NMR spectrum of carminomycin II showed the signals assignable to ϵ -rhodomycinone at δ 7.16 (d, $J=8.0$ Hz, H-3), 7.61 (dd, $J=8.0$, 8.0 Hz, H-2) and 7.68 (d, $J=8.0$ Hz, H-1), whereas that of MG1 showed resonances due to ϵ -pyrromycinone at δ 7.30 (s, 2H, H-2, H-3) and 7.65 (s, H-11). These results show that MG1 is 1-hydroxy-11-deoxycarminomycin II (Fig. 1). It is interesting to note that similar kind of transformation of anthracyclinone, *i.e.* conversion of ϵ -pyrromycinone and ϵ -isorhodomycinone to 1-hydroxy-13-dihydrodaunomycin and *N*-formyl-1-hydroxy-13-dihydrodaunomycin was reported to be catalyzed by a blocked mutant of *Streptomyces*

coeruleorubidus ME130-A4³⁾.

The cytotoxic activity (IC_{50}) of 1-hydroxy-11-deoxycarminomycin II on P388 leukemia cells *in vitro* was 4 ng/ml and that of carminomycin II was 1 ng/ml. Further studies on the anti-tumor activity of this compound are now in progress.

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