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

Sir:
During our biosynthetic studies on anthra-
cycline antibiotics, we isolated a blocked mutant of
Actinomadura roseoviolacea MuW1 which
converted ß-rhodomycinone to carminomycins\(^1\).
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 ß-rhodomycinone to car-
minomycins was assessed in preliminary shake
flask trials. We wish to report herein the con-
version of ß-pyrromycinone to a novel anthra-
cycline glycoside by MuW1.

For the microbial conversion of ß-pyrromycin-
one, a medium of the following composition was
used; 2.5% glucose, 1.5% soy bean meal, 0.2% 
yeast extract and 0.4% CaCO\(_3\). One ml of seed
culture was added to 100 ml of medium con-
tained in a 500-ml Erlenmeyer flask. After 24-

Fig. 1. The structure of 1-hydroxy-11-deoxy-
carminomycin II.

Fig. 2. \(\text{\textsuperscript{1}H}\) 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 CHCl₃ - 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 CHCl₃ and a new anthracycline glycoside (MG1) was then eluted with CHCl₃ - 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: C₃₃H₄₁NO₁₄, FD-MS m/z 682 (M⁺Na)⁺, mp 210-212°C, [α]D° 20° (c 0.05, CHCl₃), UV λmax (in MeOH) nm (E1%1cm) 235 (687), 259 (375), 294 (155) and 492 (215). The 1H NMR spectrum (Fig. 2) of MG1 was superimposable on that of carminomycin II 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-13-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 coerulescens ME130-A4³.

The cytotoxic activity (IC₅₀) of 1-hydroxy-13-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 antitumor activity of this compound are now in progress.

Masaya Nakagawa
Yoichi Hayakawa
Kanji Imamura
Haruo Seto
Noboru Ōtake

Institute of Applied Microbiology, University of Tokyo
Bunkyo-ku, Tokyo 113, Japan
'Applied Bioscience Laboratory, Kirin Brewery Co. Ltd.,
3 Miyahara, Takasaki-shi Gunma, Japan

(Received March 5, 1985)

References