NOTE

DEGRADATION STUDIES OF NAPHTHOMYCIN*

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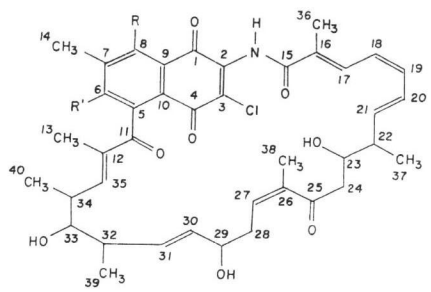
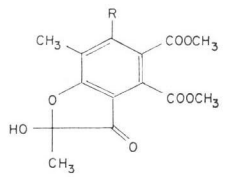
Naphthomycin is an antibacterial antibiotic originally isolated from cultures of *Streptomyces collinus*, strain Tü-105[2]. On the basis of an extensive ^{1}H-nmr study including paramagnetically induced chemical shifts WILLIAMS[3] proposed the structural formula **I** for this compound. However, the chemical shift of the phenolic proton (9.63 ppm) is not in agreement with an OH group in *peri*-position of a naphthoquinone system. This prompted RINEHART[4] to revise the structure of naphthomycin to **II** with the phenolic hydroxyl group in position 6 (numbering according to PRELOG and OPPOLZER[5]).

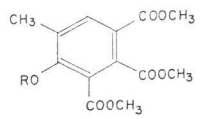
A chemical degradation of naphthomycin carried out in our laboratories strictly confirmed RINEHART's suggestion. Ozonization of the antibiotic in acetic acid at room temperature, oxidation of the ozonides with hydrogen peroxide in acetic acid and subsequent treatment of the mixture of products with diazomethane yielded, besides other products (chromatography on silica gel), a crystalline ester (**III**), m.p. 150~151°C, $C_{14}H_{14}O_7$***. It shows properties very similar to those of a degradation product (**IV**) of rifamycin S[6]: ir. (KBr) 1745, 1735, 1703 cm^{-1}; nmr ($CDCl_3$) 1.65 (s, 3H), 2.34 (s, 3H), 3.89 (s, 3H), 3.98 (s, 3H), 4.88 (s, OH), 8.04 (s,



I R = OH, R' = H
II R = H, R' = OH



III R = H
IV R = OCH_3



V R = CH_3CO
VI R = H

1H). Compound **III** was further degraded with sodium periodate (in water, 5 hours, 20°C). Methylation of the crude product with diazomethane gave the liquid ester **V**: $C_{15}H_{16}O_8$ (M^+ 324); nmr ($CDCl_3$) 2.31 (s, 3H), 2.36 (s, 3H), 3.88 (s, 3H), 3.92 (s, 6H), 7.92 (s, 1H). The O-acetyl group of **V** is derived from a part of the hemiketal ring of **III**. This same ester (**V**) was also obtained by acetylation of **VI**, another product isolated from the esterified ozonization mixture by chromatography: m.p. 102~105°C; $C_{13}H_{14}O_7$; nmr ($CDCl_3$) 2.27 (s, 3H), 3.82 (s, 3H), 3.90 (s, 6H), 7.98 (s, 1H).

The cyclic hemiketal structure of compound **III** definitely proves the 6-position of the phenolic hydroxyl group.

* Metabolites of microorganisms, 180th communication. For preceding communication see reference[1].

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*** Satisfactory analyses were obtained for all degradation products.

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