NOTE

DEGRADATION STUDIES OF NAPHTHOMYCIN*

MARIO BRUFANI** and LUCIANO CELLAI
Laboratorio di strutturistica chimica
"G. Giacomello" del C.N.R.
00016 Monterotondo Stazione, Italy

WALTER KELLER-SCHIERLEIN
Organisch-chemisches Laboratorium der
Eidg. Technischen Hochschule,
CH-8092 Zürich, Switzerland
(Received for publication October 2, 1978)

Naphthomycin is an antibacterial antibiotic originally isolated from cultures of Streptomyces cohnii, strain Tü-1055. On the basis of an extensive 1H-nmr study including paramagnetically induced chemical shifts Williams 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 to revise the structure of naphthomycin to II with the phenolic hydroxyl group in position 6 (numbering according to Prelog and Oppolzer).

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, C14H14O7. It shows properties very similar to those of a degradation product (IV) of rifamycin S: ir. (KBr) 1745, 1735, 1703 cm⁻¹; nmr (CDCl₃) 1.65 (s, 3H), 2.34 (s, 3H), 3.89 (s, 3H), 3.98 (s, 3H), 4.88 (s, OH), 8.04 (s, 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: C₁₅H₁₅O₃ (M⁺ 324); nmr (CDCl₃) 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; C₁₄H₁₅O₇; nmr (CDCl₃) 2.27 (s, 3H), 3.82 (s, 3H), 3.90 (s, 3H), 7.98 (s, 1H).

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

References
3) WILLIAMS, T. H.: Naphthomycin, a novel ansa

