THERMAL REARRANGEMENT AND IN VITRO ACTIVITY OF TOROMYCIN AGAINST ANAEROBIC BACTERIA. SIGNIFICANCE OF REARRANGEMENT STUDIES ON THE NATURE OF CHRYSOMYCIN AND THE STRUCTURE OF GILVOCARCIN A.

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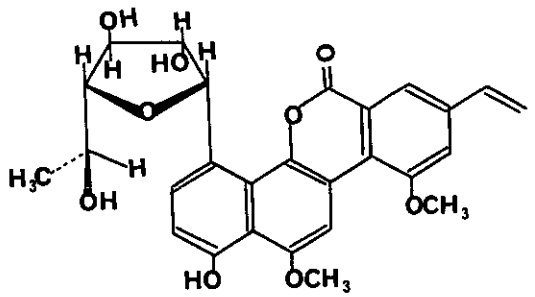
By means of chemical and spectroscopic methods we independently deduced the stereostructure of toromycin (AAC-324) implicit in 1 (Jain et al., Tetrahedron, 39, 599, 1983). This structure has been confirmed by single-crystal X-ray crystallography of gilvocarcin M (Hirayama et al., Bull. Chem. Soc. Japan, 54, 1338, 1981). In the course of these studies, it was observed that thermal treatment of toromycin yields two rearranged products, 2 and 3, wherein the former predominates. Similar results were obtained upon refluxing an aq. HOAc solution of dihydrotoromycin.



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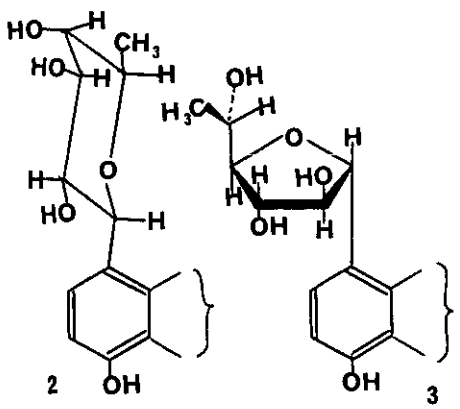

2 3

The rearranged structure 2 referred to as toromycin isomer A bears a striking resemblance to chrysomycin A (Weiss et al., J. Antibiotics, 35, 1194, 1982), the significance of which will be discussed in some detail. Interestingly, our studies of the rearrangement of toromycin under a variety of conditions provide a key to rationalization of previously unexplained spectroscopic and biological data relating to toromycin reaction products reported in the literature. This will be discussed with special reference to the structure and biology of gilvocarcin A.

Toromycin (AAC-324) displayed a remarkable spectrum of activity against several isolates of anaerobic bacteria and we compared its in vitro activity with that of clindamycin, chloramphenicol, rifamycin, and other antibiotics. Neither the facile rearrangement nor the anaerobic activity of the molecule reported herein has been described previously, despite several reports on toromycin from different laboratories.