Napyradiomycin Synthesis for Antibiotics and Antitumor Agents

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Drug development for antibiotics and colon cancer drugs: The napyradiomycins are a novel family of natural products isolated from terrestrial strains of Streptomyces bacteria. Many of these compounds demonstrated in vitro and in vivo antibacterial activity against gram-positive bacteria, including strains of methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecium (VREF), as well as antitumor potency against colon carcinoma cells. But their polycyclic frameworks and halogenation pattern are challenging to chemical synthesis. Very few synthetic routes with stereocontrol are reported. Although biosynthesis may provide good stereoselectivity, it is difficult to have modification for new compounds. Therefore, new synthetic solutions, particularly those with high enantioselective ones are needed.

Syntheses of napyradiomycin for use in antibiotics and antitumor drugs: This invention describes the first asymmetric syntheses of napyradiomycin members, with shorter routes, better stereocontrol and facile access to simplified and altered structures. It starts with a cheap and widely-available material and achieves the target compounds in several linear steps, featuring the asymmetric chlorination with high yield and enantiomeric excess. Key elements include a two-step synthesis of flaviovin, a highly asymmetric chlorination of an isolated alkene and a Johnson-Claisen rearrangement to forge a quaternary C next to a glucal-like O.

Applications: • Development of new antibiotic agents, especially those with activity against MRSA and VREF • Development of new antitumor agents • A new method of asymmetric olefin chlorination

Advantages: • Using an inexpensive and widely-available starting material • Fewer steps and higher stereoselectivity than reported routes • Facile access to simplified and altered structures compared to biosynthesis • Easy to prepare analogous routes based on the developed chemistry • Able to complete a nice collection of napyradiomycins which could be screened broadly in search of additional activity

Patent Status: Patent Pending

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