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Elucidate the biosynthesis of nucleoside moiety in albomycin

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A lbomycins are broad-spectrum antibiotics isolated from soil-dwelling *Actinomycetes*. The albomycins have a minimum inhibitory concentration (MIC) as low as 10 ng/mL against *Streptococcus pneumonia*. Studies revealed that albomycins are Trojan horse antibiotics that consist of a siderphore component that is indiscriminately taken up by bacteria as an iron source. Once inside the cell, the albomycins are hydrolyzed to release a nucleoside compound SB-217452, which works as an enzyme inhibitor of bacterial seryl-tRNA synthetase. Structurally different from other nucleoside antibiotics such as A-90289, caprazamycin, and muraymycin, the nucleoside moiety of albomycin has two features: 1) the stereo configuration of 5'-C-glycyluridine (GlyU) in albomycin is (5'R, 6'S), which is different from (5'S, 6'S) in the other nucleoside antibiotics and 2) A sulfur atom replaced the oxygen atom on the pentose ring in albomycin. Gene cluster analyzing indicated that AbmH, a homologue of LipK, is responsible for the incorporation of glycine moiety to the uridine aldehyde. LipK was functionally characterized as a L-threonine: uridine-5'-aldehyde transaldolase, which catalyzes the C-C bond-forming during the biosynthesis of the GlyU in A-90289. Further characterization of AbmH *in vitro* found that it covalent bonded a pyridoxal-5'-phosphate as cofactor. AbmH catalyzed an aldo-type reaction to incorporate the glycine moiety on L-threonine to uridine aldehyde to form the GlyU. The product GlyU was confirmed to have (5'R, 6'S) stereo configuration, same as the structure in albomycin. Different substrates test showed that L-*allo*-threonine could also be used as a substrate in reaction.

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New synthetic route for preparation of Cis (-) nucleosides

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Cis-nucleoside derivatives lamivudine (3TC) and emtricitabine (FTC) are useful in the treatment of retroviral infections caused by human immune deficiency virus (HIV), Hepatitis B virus (HBV) and Human T-Lymotropoic virus (HTLV). Lamivudine and emtricitabine are potent nucleoside analogue reverse transcriptase inhibitors (nRTI). These two drugs are synthesized by a four-stage process from the starting materials: Menthyl glyoxylate hydrate and 1,4-dithane-2,5-diol. All reagents and intermediates have been tested satisfactorily. Pharmaceutical development has been adequately described and also it has been shown as the most thermodynamically stable form. Although there are several different methods reported for the synthesis of lamivudine and emtricitabine as a single enantiomer, we required an efficient route, which was suitable for largescale synthesis to support the development of these compounds. In this process, we successfully prepared the intermediates of lamivudine and emtricitabine without using any solvents and catalyst, thus promoting the green synthesis.

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