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# Multi-gram scale synthesis of hunanamycin A, an antibiotic natural product from the marine source

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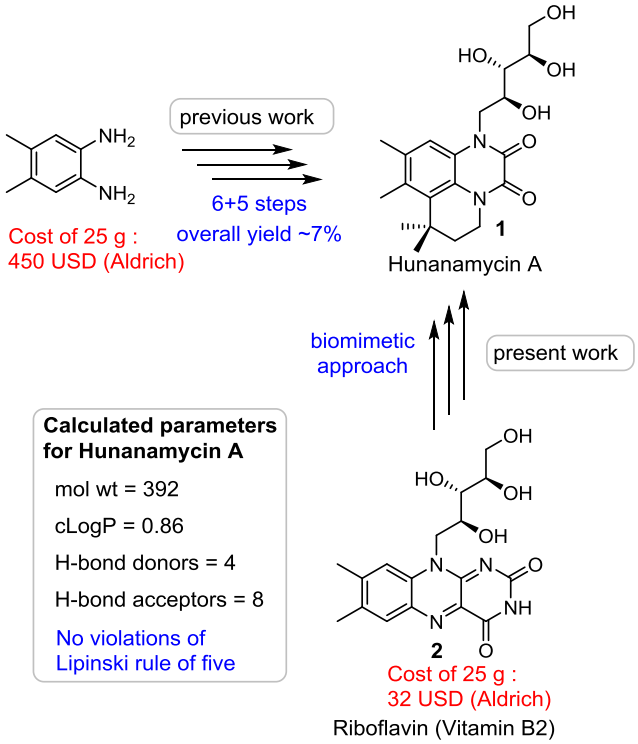
ABSTRACT

A simple, practical and biomimetic approach to access antibiotic natural product hunanamycin A starting from readily available inexpensive material Riboflavin is disclosed here. The present synthesis consists of three operationally simple, protecting group free steps and it is far superior when compared with previous route. Using this route one can make multi-gram quantities of the natural product which will help in further biological assays, in particular exploring the potential of treating food infections



Hunanamycin A (**1**), was isolated (0.8 mg) from a marine-derived *Bacillus hunanensis* by MacMillan et al.[1] It is the first natural product with a pyrido[1,2,3-*de*]quinoxaline-2,3-dione core related to a degradation product of riboflavin (vitamin-B2). Hunanamycin A was reported to have shown interesting antimicrobial activity against bacterial strains (*Salmonella enterica*) that lacked riboflavin transport mechanisms.[1] It was shown to have minimum inhibitory concentration (MIC) of 4.8 µg/mL against *Salmonella enterica*. It is estimated that Salmonella bacteria is one of the major cause for outbreaks associated hospitalizations.[2] According to very recent WHO report, the global burden of foodborne diseases shows that almost 420,000 people die every year by eating contaminated food.[3] The same also estimated that the African and South-East Asia Regions have the highest burden of foodborne diseases.[3] Hence there is a need for finding new drugs with novel mechanism. In addition to interesting antibacterial activity, hunanamycin A also complies all the rules of Lipinski, frequently practiced in medicinal chemistry suggesting that this is a promising lead for further studies. Interesting biological activity, drug-like properties and scarcity of the natural material prompted our group[4] and others[5] to initiate total synthesis programs. Recently, we have accomplished the first total synthesis of the hunanamycin A starting from 4,5-dimethylbenzene-1,2- diamine in ~7% overall yield (scheme 1).[4] Although we have synthesized the natural product for the first time, the route has some drawbacks such as poor yields, use of costly starting material and multiple steps. Our continued efforts to have an improved synthesis of hunanamycin A, resulted in multi-gram scale synthesis of **1** using operationally simple steps. Details are presented here.




**Scheme 1**. Synthetic approaches to hunanamycin A

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