Vývoj metod syntézy vedoucích k fumagillinu, jeho derivátů a příbuzných přírodních látek

Development of synthetic methods suitable for the synthesis of fumagillin, its derivatives and related natural products

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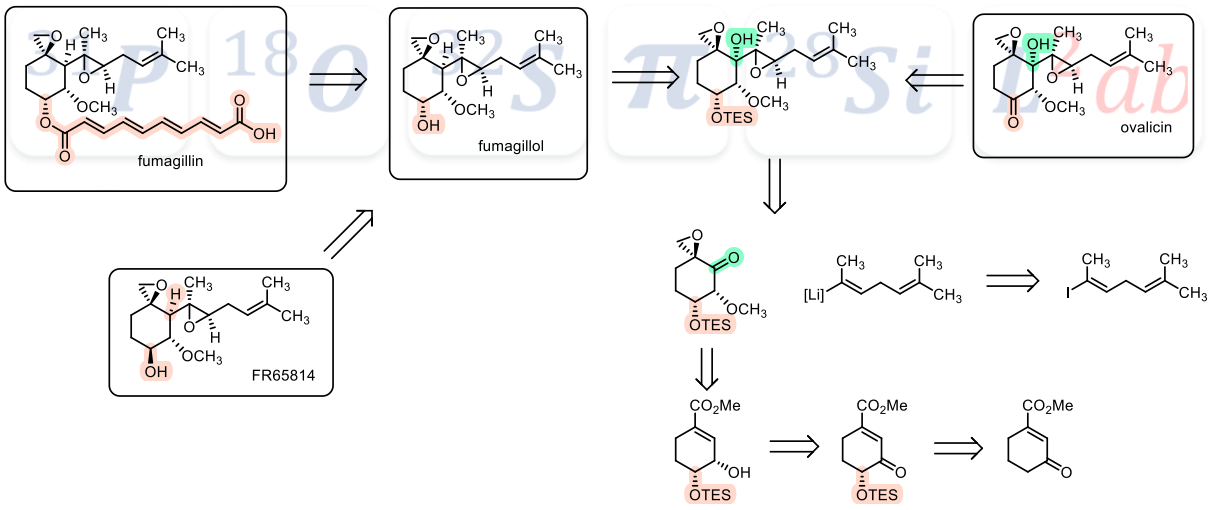
The synergistic effect of various drugs and/or natural products that is a very important topic of now a days pharmacology. In many cases, clinicians observe the synergy effects when a mixture of prescribed drugs with different mode of action and/or for various illnesses is used. Such observations are in most cases based on empirical bases and no relevant scientific follow-up is made to determine what happens in the human body. Since recently, however, several natural drugs with expected/observed biological activity e.g. against the bacteria or fungi were used in the presence of certified drugs with known mode of action and the effect was studied.[1]

In our group we are interested in such activity, and we are wishing to evaluate the influence of various polyketides to known polyaminoacid-based drugs (compounds are commercially available and mode of action is known). Before the study starts, however, we need to prepare several polyketide scaffolds with known or expected biological activity. One of the studied polyketide scaffold are compounds related to fumagillol structural motive.[2] Our retrosynthesis is depicted bellow.



The aim of the theses is:

1) To write a literature review about synergistic effects between polyketides and polyamines.
2) To explore the synthetic route to targeted compounds
3) To characterize all prepared compounds with help of available characterization techniques

Litterature

(1) Adams, J. M. E.; Moulding, P. B.; El-Halfawy, O. M. Polyamine-Mediated Sensitization of Klebsiella Pneumoniae to Macrolides through a Dual Mode of Action. *ACS Infect. Dis.* **2024**, *10* (6), 2183–2195. https://doi.org/10.1021/acsinfecdis.4c00157.
(2) Yamaguchi, J.; Hayashi, Y. Syntheses of Fumagillin and Ovalicin. *Chem. Eur. J.* **2010**, *16* (13), 3884–3901. https://doi.org/10.1002/chem.200902433.