Natural Product Synthesis Through (4+3) Cycloaddition: (+/-)-Frondosin B and (+/-)-Liphagal

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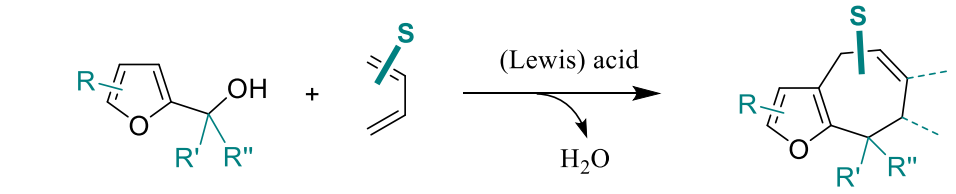
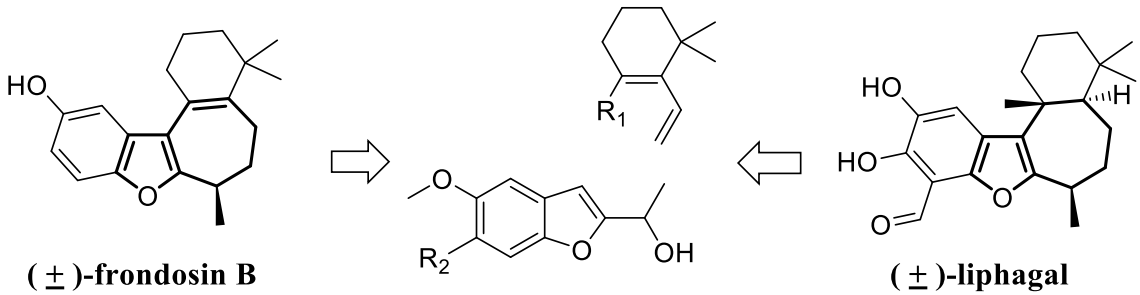
Previous work in our laboratory revealed a new type of (4+3) cycloaddition that proceeds via an oxyallyl-type cation producing hard to synthesize 7-membered rings. This synthetic method is very useful in the field of natural product (NP) synthesis since many of these NPs contain furan fused cycloheptenes or straightforward synthetic derivatives thereof. The scope of this conversion has already been demonstrated using simple furanol precursors and diene systems.[1]





(±)-frondosin B **(±)-liphagal**

R_1= Me, R_2= OMe (±)-liphagal
R_1= H, R_2= H (±)-frondosin B

A more recent study aimed at more elaborate polycycles containing cyclohepta[b]furan substructures in accordance to existing NPs. We envisaged a total synthesis for frondosin B and liphagal as obvious targets for our method, also the latter NP was identified as inhibitor for one isoform of the phosphatidylinositide 3-kinase (PI3K) enzyme and had already been the subject of research.[2] Herein, we present a full account of our investigations towards a new and short synthesis of (+/-)-5epi-liphagal and frondosin B.[3]

References

[1] Winne, J. M., Catak, S., Waroquier, M. and Van Speybroeck, V. (2011), Angew. Chem. Int. Ed., 50: 11990–11993.
[2] Day, J. J., McFadden, R. M., Virgil, S. C., Kolding, H., Alleva, J. L. and Stoltz, B. M. (2011), Angew. Chem. Int. Ed., 50: 6814–6818.
[3] Laplace, D.R., Verbraeken, B., Vanhecke, V.H., Winne, J.M. (2014), Chem. Eur. J, 20: 253-262.