How Much Difference Makes a Methyl in Total Syntheses of Bridged Pyrazinoquinazolinone Alkaloids

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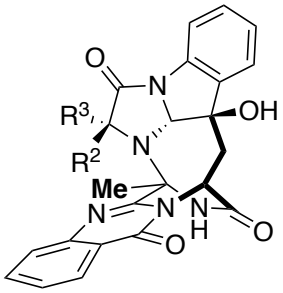
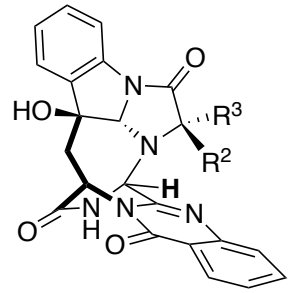
Pyrazinoquinazoline alkaloids, such as the fumiquinazolines and spiroquinazolinones or the pseudoenantiomeric cottoquinazolines or lapatins, are a diverse family of fungal metabolites that essentially differ in the amino acid precursors alanine for the former versus glycine for the latter.[1] They are produced in Nature by oxidative processes. However, their stereochemical features remain a matter of debate because of isolated amounts. Nonetheless, they display interesting bioactivities.

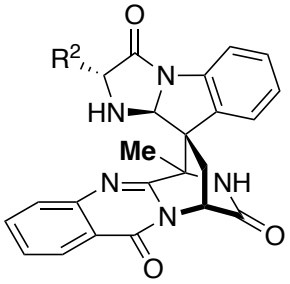


Fumiquinazoline K

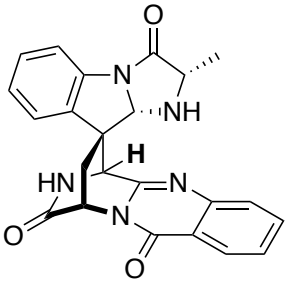
- Bioinspired approach
- Unified radical based
- Unambiguous elucidation of stereochemistry



Cottoquinazolines A-E



Spiroquinazolines



Lapatin A

Therefore, a short bioinspired unified approach to the fumiquinazolines and cottoquinazolines as well as to the spiroquinazolines is aimed for. Here we present results toward the total synthesis these natural products and demonstrate that the seemingly simple replacement of the proton for the methyl group may have significant consequences.

[1] D. Resende, P. Boonpothong, E. Sousa, A. Kijjoa, M. M. M. Pinto, *Nat. Prod. Rep.* **2019**, *36*, 7-34.