Development of a Practical Manufacturing Route to a Pyrrolobenzodiazepine-Based (PBD) Linker-Drug

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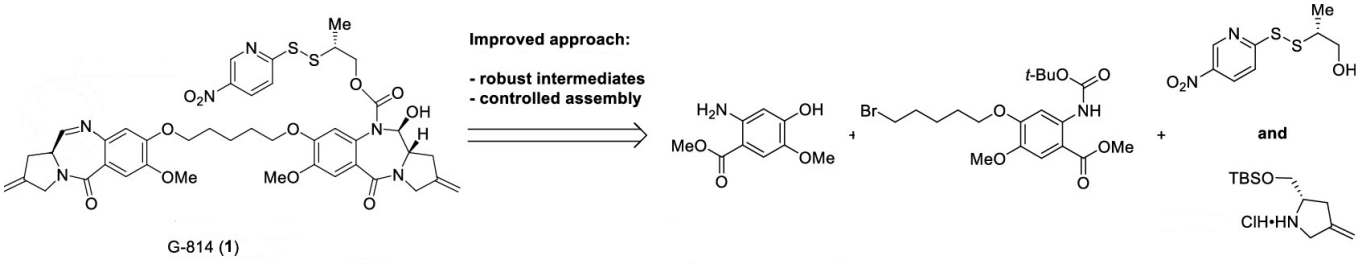
The synthetic strategy for the linker-toxin **1** was reconfigured in order to devise an efficient and unified supply chain for both compounds.[1] It involved establishing a novel chemical route to crystalline, monomeric building blocks that could be combined in a unique way for the molecular target.



This streamlined approach avoided challenging desymmetrization efforts en route to the target molecule as well as a drastically reduced need for multiple chromatographic purifications throughout the synthesis. The shared-building-block concept with other PBD Linker drugs enabled access to advanced intermediates from which the optimized endgame was implemented, ultimately resulting in a robust synthetic process.

[1] S.G. Koenig, R. Angelaud, C.M. Crittenden, K. Kurita, D.J. Russell, J-F. Marcoux, T. Matt, F. Gosselin, *Org. Process Res. Dev.*, **2022**, *26*, 2155−2175.