TOTAL SYNTHESIS OF CALLYSPONGIOLIDE

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Callyspongiolide was isolated in 2014 from the marine sponge *Callyspongia* sp. The macrolide displays potent cytotoxicity against human lymphocytes and thus represents a potential lead compound for the development of new anticancer agents. A total synthesis of this molecule would not only provide more material for further clinical studies, but also an evaluation of the stereochemical assignment.[1]

Previous approaches towards callyspongiolide, comprising of late-stage trans-hydroelementation failed due to steric bias, as such a novel synthetic approach based on ring closing alkyne metathesis (RCAM) of a ynoate derivative was developed.[2] This strategy bore considerable risk as there are only few recorded examples of RCAM on simple ynoates.[3] Highlighting the performance of the latest generation of molybdenum-based catalysts, this total synthesis illustrates the first example of a RCAM on a highly complex ynoate. Another key-step of the devised synthesis was the subsequent Z-selective semi-reduction of the resulting ring-internal alkyne. An optimized nickelboride-catalyzed hydrogenation ensured the efficient reduction of the alkyne, tolerating alkene and vinyl iodide functionalities. Finally, via Sonogashira reaction the unique enyne side-chain was installed, concluding the efficient total synthesis of (+)-callospongiliolide in 20 steps and 4 % overall yield.