SYMMETRY-INSPIRED APPROACH TO MASSADINE

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The pyrrole-imidazole family of alkaloids is a diverse class of over 200 marine natural products with a wide spectrum of biological activities.[1] These structurally complex alkaloids are forged by desymmetrization of a single biogenic precursor, oroidin, which undergoes various cyclization, dimerization and tetramerization processes. Massadine, a hexacyclic member of the [3+2] dimeric subgroup of pyrrole-imidazole alkaloids, represents an upper echelon of complexity in the alkaloid family and displays potent antifungal and calcium signaling-disturbing activity.[2,3]

Thus, practical methods that allow rapid access to massadine and its analogs are required. Inspired by the efficacious desymmetrization in the biogenesis of massadine, we developed a novel, symmetry-breaking tandem aldolization/[3+2] cycloaddition, which leverages an alternative symmetry element hidden in intermediates *en route* to the natural product.

The shortest synthesis of the carbocyclic core of massadine, *i.e.* ring D, reported to date will be disclosed. Further elaboration to the A,D,C ring system will be discussed.

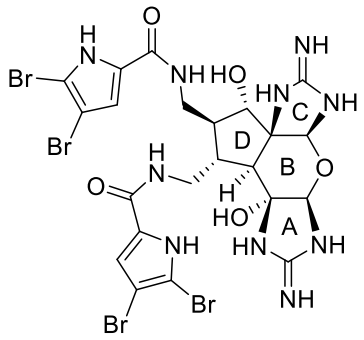

Figure 1. **Massadine.**

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