A Highly Selective, Organocatalytic Route to Chiral 1,2-Oxazines and Pyridazines and Their Application to Natural Product Synthesis

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Finding efficient ways of selectively preparing heterocyclic systems still provides a significant challenge in organic chemistry. Enantiopure 1,2-oxazines are potentially useful target heterocycles as they are not only present in biologically active natural products but can also be further derivatised into various useful groups by straightforward chemistry. A sequential, organocatalytic asymmetric one-pot reaction to access chiral 1,2-oxazines and 3,6-pyridazines from achiral aldehyde and ketone starting materials has been achieved, which proceeds in excellent enantioselectivity and moderate to good yields. Further efforts to evaluate the use of these methods and their application to natural product synthesis are currently being undertaken. A specific target is Lydiamycin A, an antibiotic with strong antituberculosis activity. A combination of its biological activity and our ability to generate the core piperazic acid with our recent chemistry has led us to focus the current work on its total synthesis, which will be discussed.