Rhodium-Mediated Substrate- and Catalyst-Controlled Synthesis of 1,2-, 1,3-, and 1,4-Diamines

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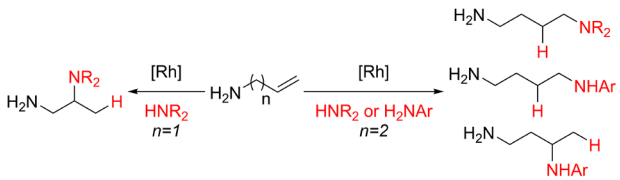
The catalytic addition of an amine across an unsaturated C–C bond has been one of the most intractable challenges in organometallic chemistry for decades. However, hydroamination is complicated by high activation energies and negative entropic values. To promote this otherwise demanding transformation, we have shown that remote Lewis-basic directing groups can be used to bind the metal center and increase the reactivity of an otherwise electronically unactivated olefin. In addition, this group often enforces a high degree of regioselectivity as it proceeds through a favored metallacycle intermediate.

While employing secondary amine nucleophiles, N-allyl imines and amines undergo Rh-catalyzed hydroamination to form 1,2-diamines. In contrast, with secondary amine nucleophiles, homoallyl amines form 1,4-diamines. These reactions are tolerant of a variety of secondary amines and functional groups, and show a high degree of diastereoselectivity. Finally, when primary arylamines are employed as nucleophiles with homoallylic amines, the 1,3- or 1,4-diamine product (of Markovnikov or anti-Markovnikov hydroamination respectively) can be preferentially formed.



Complexity-to-Diversity: Sinomenine

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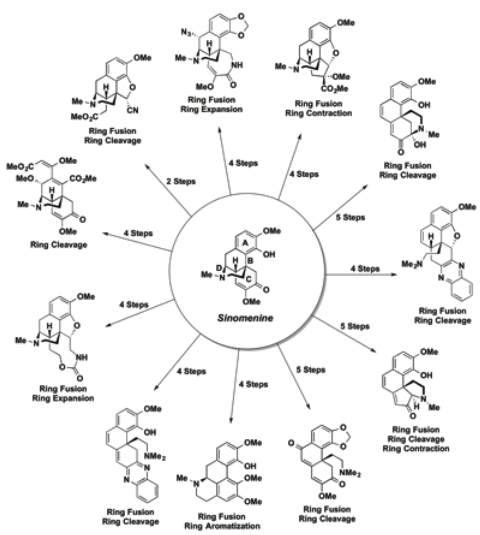
The Complexity-to-Diversity (CtD) project developed in the Hergenrother laboratory allows for the distortion of rings in complex, readily available natural products. The alkaloid sinomenine, isolated from the Chinese and Japanese plant *Sinomenium acutum*, has been subjected to the CtD strategy.[1] To date, 15 scaffolds (12 novel) have been generated in five steps or less by combining various ring distortion reactions (Figure 1). The sinomenine library consists of 56 total compounds and is expected to increase in size as more derivatives and scaffolds are generated. Future work will include assessing the library for biological activity in various mammalian cell lines.



Ref. [1] *Acta Med. Okamaya*. **1976**, 30, 1-20.
Figure 1 (Right). Selection of sinomenine CtD library.