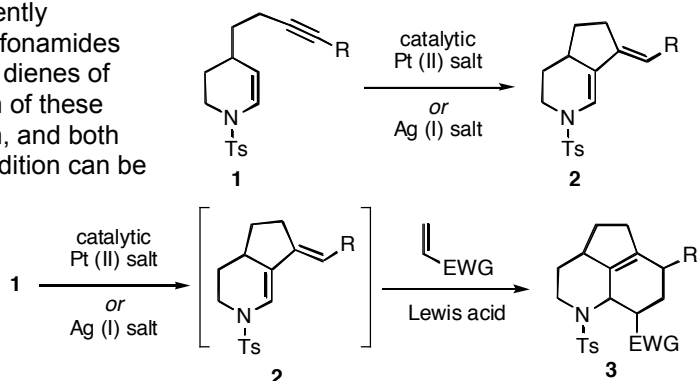


Metal Catalyzed Annulation-Gregory Dake
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My research group (Tyler Harrison, Monserrat Corbella-Pane, Jennifer Kozak, Krystle Guieb, and Jennifer Dodd) has been examining the ability of latent nucleophiles such as enesulfonamides (e.g. **1, 6** or **8**) and related compounds such as enamides (e.g. **10**) to react with alkynes activated by metal catalysis.

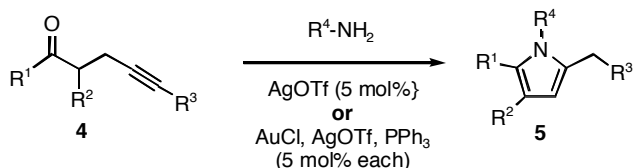
Either platinum (II) or silver (I) salts efficiently catalyze the cycloisomerization of enesulfonamides of general structure **1** to produce bicyclic dienes of type **2**. An important synthetic application of these dienes uses the Diels-Alder cycloaddition, and both the catalyzed cyclization and the cycloaddition can be carried on in one reaction flask. In one synthetic operation, tricycles such as **3** are prepared.



We discovered by chance that certain compounds formed pyrroles under these catalysis conditions.

These results led us to investigate

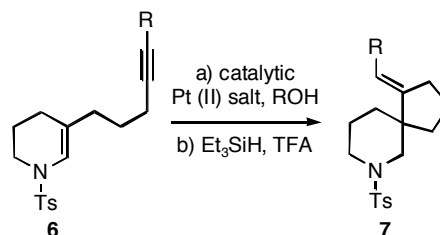
silver(I) and gold(I) catalyzed hydroaminations of imines formed "in situ" to alkynes forming pyrroles (**4** to **5**). This useful heterocyclization reaction could have interesting applications in synthesis



Our most recent work is the spirocyclization reactions of compounds of general

structure **6, 8** or **10** using platinum (II) catalysis. These reactions form quaternary carbon centers in an efficient manner.

Substituting the alkyne with an aryl group provides an alternative reaction path. In addition to the platinum-catalyzed spirocyclization reaction, the arene ring undergoes a "Friedel-Crafts" or "Pictet-Spengler" type addition to the (presumably formed) azacarbenium ion (**8** to **9**). This enables a reaction pathway in which multiple rings are formed from a simple precursor. Different modes of cyclization ("5-exo" vs. "6-endo") are also possible, and these can, in principle, be modified with adjustment of the reaction catalyst.



Reactions of bicyclic compounds to form tricyclic enamides also proceed efficiently (**10** to **11**). In accord with our expectation, high stereoselectivity is observed in these reactions. We have successfully applied this reaction methodology within a synthesis of the natural product *fawcettidine*. At this stage I am interested in further applications of this reaction methodology in the context of alkaloid total synthesis.

