The thesis entitled **"Allenyl sulfones, sulfonamides and gold catalysts: A recipe for the rapid assembly of various nitrogen heterocycles"** is divided into four chapters.

CHAPTER- I: An introduction to homogeneous gold catalysis of organic reactions

Homogeneous gold catalysis has provided remarkable contributions to organic transformations in past few years. Gold(I)complexes are effective catalysts for the electrophilic homogeneous activation of alkynes and for construction of carbon-carbon and carbon-heteroatom bond formation. Gold(I) complexes selectively activate π-bonds of alkynes in complex molecules. Gold-alkyne complexes readily undergo nucleophilic addition to form *trans*-alkene intermediate, which upon de-auration with proton or electrophile results *trans*-addition product (Figure 1).

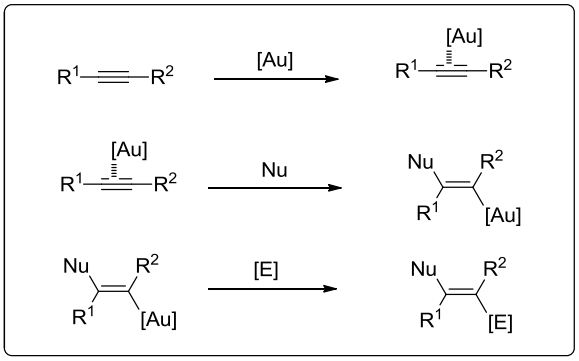


Figure 1: Gold catalyzed activation of alkynes and Markovnikov nucleophilic attack

Gold complexes activates alkynes towards nucleophilic attack, inter- or intra-molecularly, due to relativistic effect, gold complexes possess high carbophilicity as compared to oxyphilicity. This ability of C-C multiple bond activation of gold allows for development of efficient catalytic methods for the formation of C-C, C-N, C-O and C-S bonds and often cyclization reactions.

Transition metal catalyzed cycloisomerization of aza-enyne is a powerful method for construction of functionalized heterocycles. The significance of this process lies in the rapid increase of molecular complexity starting with relatively simple starting materials. Enyne cyclization pathways are highly influenced by substituents, the presence of electron-donating groups on alkyne favours *6-endo-dig* cyclization pathway and electron-withdrawing group on alkyne favours *5-exo-dig* cyclization. Enynes with terminal alkynes favours *5-exo-dig* cyclization, internal alkynes favours *6-endo-dig* cyclization (Figure 2).

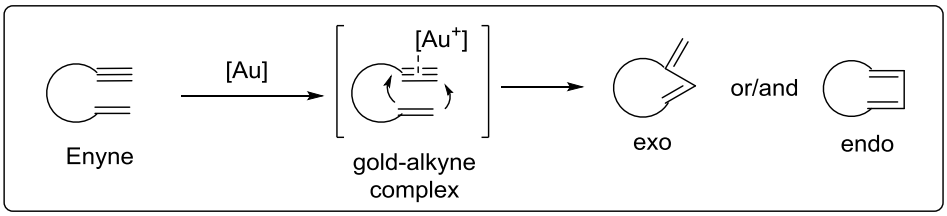
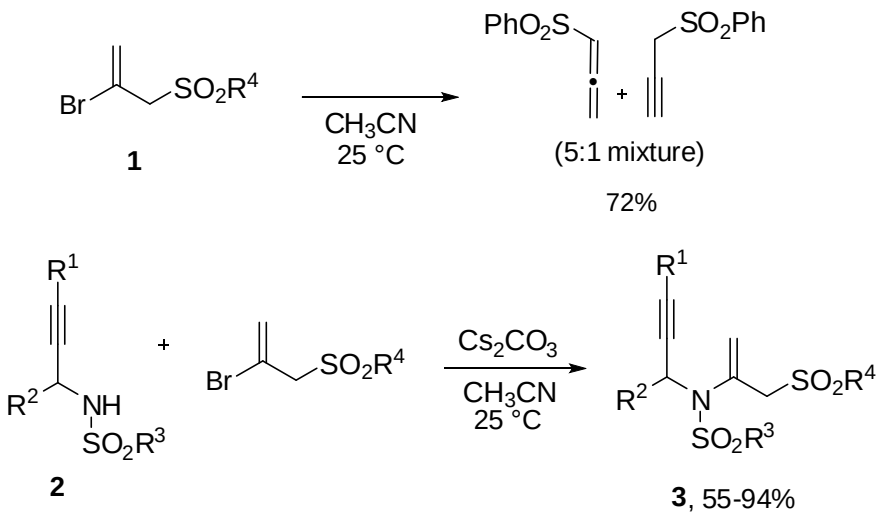


Figure 2: Gold catalyzed enyne cycloisomerization

<u>CHAPTER-II</u>: Base-mediated assembly of aza-enynes from allylbromo sulfones and their divergent gold-catalyzed cycloisomerization to pyrroles and dihydropyridines

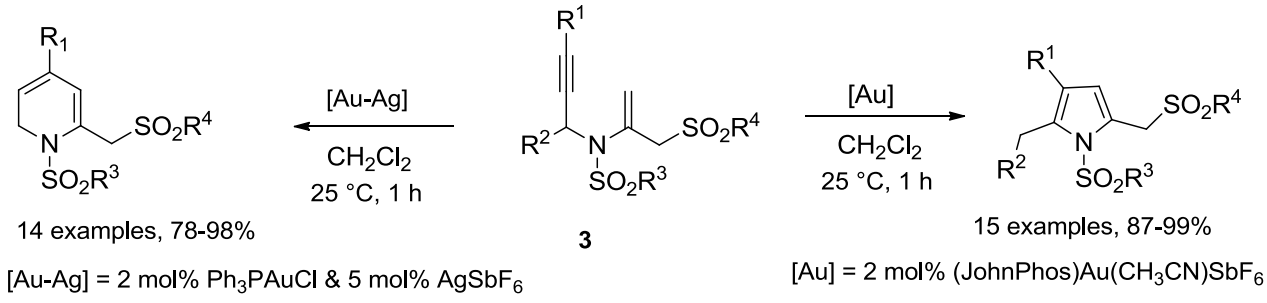
This chapter describes the base-mediated assembly of aza-enynes from bromoallyl sulfones and their divergent gold-catalyzed cycloisomerization to pyrroles and dihydropyridines. Divergent synthesis is strategy to synthesize a library of new chemical compounds from same building blocks with different reaction conditions. The work described in the chapter involves the divergent synthesis of pyrroles and dihydropyridines from the same set of reactants. A brief discussion on various divergent synthetic methods for heterocyclic construction, with an emphasis on aza-heterocycles, is presented in the beginning. The chemistry of allenyl sulfones remains less-explored due to the labile nature of this synthon and its anomalous behavior under various reaction conditions. A brief description of the chemistry of electrophilic allenes is presented in the introduction to put the results into perspective.

The work described in this chapter involves various layers of new reaction discoveries. First a stable, synthetic surrogate for the labile allenyl sulfone was developed. The studies showed that the previously known allyl bromosulfone **1** can function as an equivalent of allenyl sulfone under basic conditions. They react with sulfonamides **2** under basic conditions to provide enamine-like products **3** that hold potential for further synthetic manipulations. Remarkably the reaction constitutes a formal, vinylic displacement of a bromide without using any transition metals (Scheme 1).



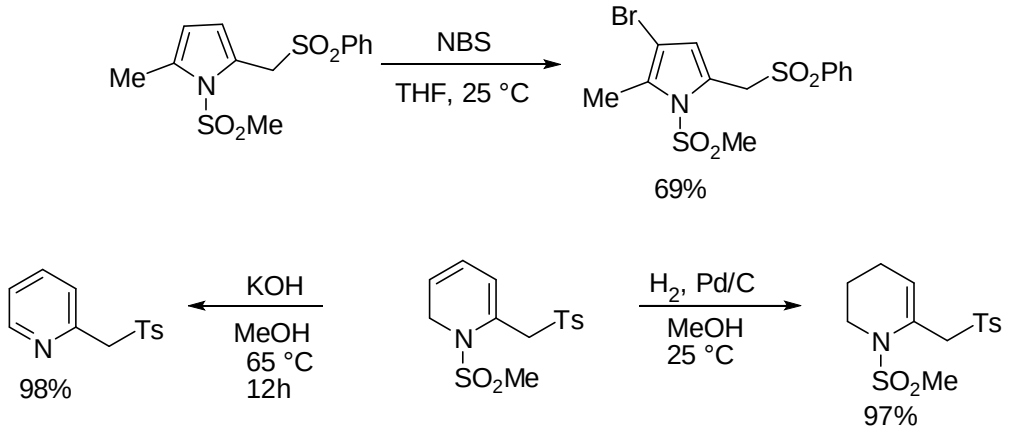
Scheme 1: Base-mediated formal vinylic displacement reaction of **1**

The products **3** thus obtained were examined for their utility as building blocks for nitrogen heterocycles under gold catalysis. Details of the optimization study are presented in the Results and Discussion section. It was revealed that divergent cycloisomerisation pathways for formation of pyrroles or dihydropyridines can be mediated by different Au-Ag catalyst combinations (Scheme 2).



Scheme 2: Au-Ag catalyzed divergent cycloisomerisation of aza-enynes **3**.

Details of the scope, generality and further synthetic operations possible on the products are described in detail in this chapter (Scheme 3).

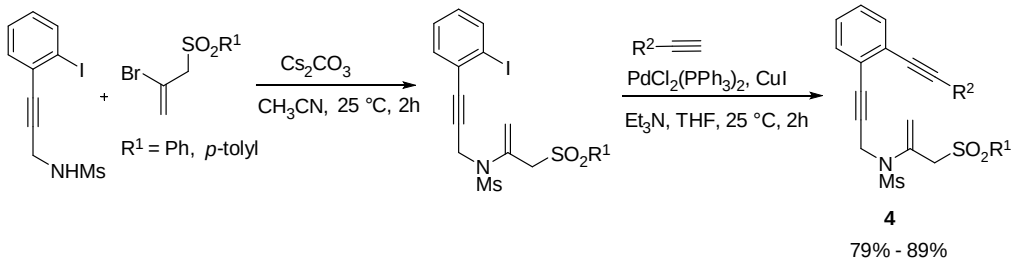


Scheme 3: Synthetic modifications of pyrrole and dihydropyridine products

A mechanistic postulate is also advanced wherein a propargyl-Claisen rearrangement is involved.

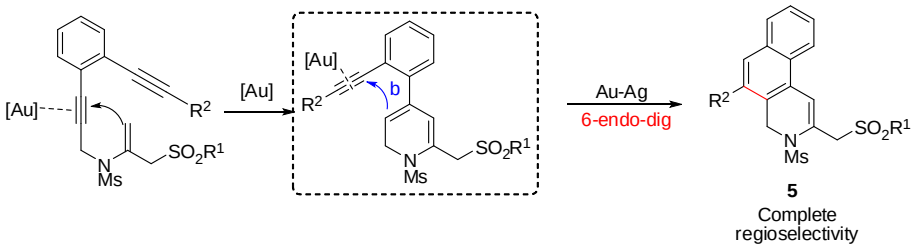
<u>CHAPTER-III</u>: **Cascade synthesis of substituted benzoisoquinoline derivatives via gold-catalyzed cascade cycloisomerization of enediynes**

This chapter describes the gold-catalyzed cascade cycloisomerization of ene-diynes synthesized using our formal vinylic displacement method. Cascade reactions, also known as a tandem or domino reactions, allows to carry out more than one transformation in an one-pot process without isolating any intermediate. The work described in this chapter involves the development of a god-catalyzed, cascade cycloisomerisation reaction of ene-diynes **4**. The latter compounds are synthesized in two steps as described in Scheme 4.



Scheme 4: Synthesis of ene-diynes **4** *via* formal vinylic displacement

Explorations on the development of cascade cycloisomerisation reaction of these ene-diynes are described in detail in this chapter. A facile reaction catalyzed by Au-Ag catalyst combination, that afforded 3,4-dihydrobenzo[*f*]isoquinolines **5** exclusively was discovered during these investigations (Scheme 5).



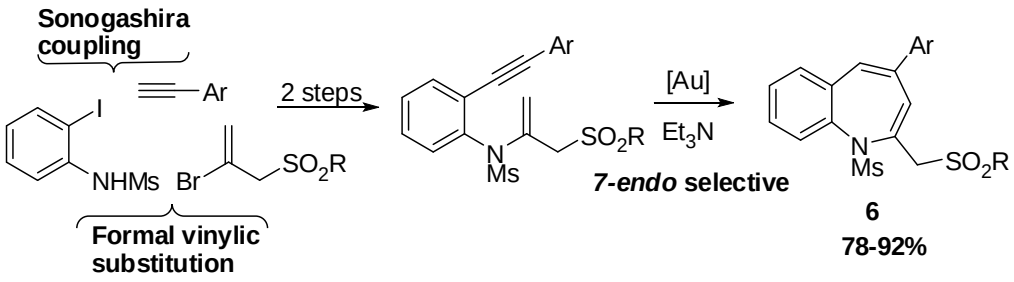
Scheme 5: Gold catalyzed cascade cycloisomerization of aza-ene-diyne.

Substrates with heteroaromatic and aliphatic substituents on the alkyne end (R^2) also produced good results, but in case of 2-ethynyl pyridine poor yield was observed. A mechanistic proposal and examples of further transformations of the product are also described in this chapter.

<u>CHAPTER-IV</u>: Regioselective synthesis of 1-benzoazepine derivatives via gold-catalyzed cycloisomerization of *N*-(*o*-alkynylaryl)-*N*-vinyl sulfonamides

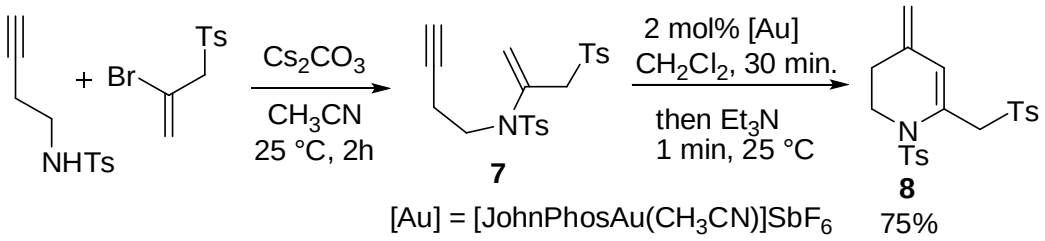
Benzo-fused, seven membered nitrogen heterocycles, commonly known as benzoazepines, are found in a variety of biologically active synthetic compounds. Benzoazepines are further classified based on the extent of unsaturation as well as the position of the nitrogen atom. Among them, the 1-benzoazepine moiety forms the core units of antagonists of *N*-methyl-D-aspartate (NMDA), vasopressin V_2 receptor, CC chemokine receptor-5 as well as anti-parasitic agents potentially useful for the treatment of leishmaniasis.

The combination of vinylic displacement-gold-catalyzed cycloisomerisation was applied successfully for the synthesis of 1-benzoazepine derivatives too. The results are described in detail in this chapter. The precursors for cycloisomerisation were assembled using the formal vinylic displacement route. Subsequent gold-catalyzed cycloisomerisation proceeded with exclusive 7-*endo* regioselectivity to afford excellent yields of benzoazepine products **6** (Scheme 6).



Scheme 6: Synthesis of *N*-(*o*-alkynylaryl)-*N*-vinyl sulfonamides and their gold catalyzed cycloisomerization.

Analogous reactions on an aliphatic derivative **7** proceeded with a different regioselectivity to afford tetrahydropyrdine derivative **8** as the exclusive product (Scheme 7).



Scheme 7: Gold-catalyzed cycloisomerization of aliphatic 3-aza-1,6-enyne **7** to afford a 4-methylene tetrahydropyrdine derivative **8**.

Summary: A brief description of the newly discovered methodologies, importance of the products and potential future applications are described in this section.