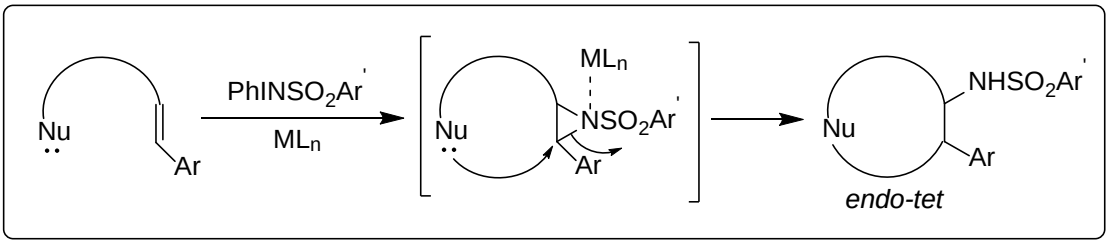
Catalytic Asymmetric Domino Aminolactonization and Aminoarylation Reactions for the Synthesis of γ-Lactones, δ-Lactones, Tetrahydroquinolines and Tetrahydrobenzazepines

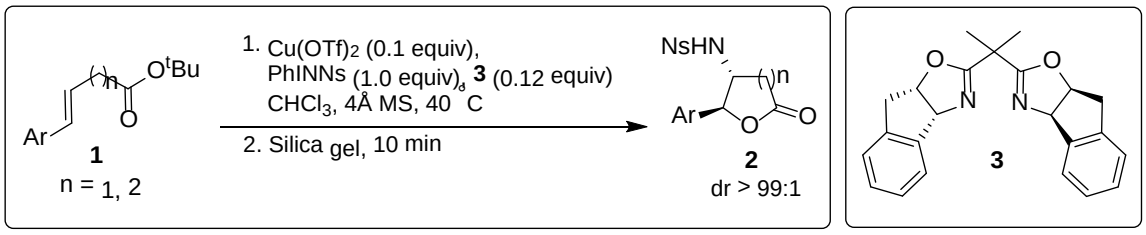
The concept of aminocyclization *i.e.* asymmetric aziridination and sequential intramolecular opening of the newly-born aziridine has been exploited throughout the thesis. Olefinic substrates with pendent nucleophiles were employed in such cyclizing transforms using proper reagents in ambient conditions that ended up in comprising stereodefined heterocycles (Scheme 1).



Scheme 1. The concept of aminocyclization

p-Nitrophenylsulphonyliminoiodinane (PhINNs) was accounted to deliver the nitrene to olefinic double bond and further one pot selective *endo-tet* cyclizations were deeply investigated and demonstrated in versatile methods. $Cu(OTf)_2$ as catalyst performed dual functions in these aziridination-cyclization transforms and that chelated with bisoxazoline ligand **3** offered a balanced combination towards regiospecific and stereoselective construction of bifunctionalised heterocycles.

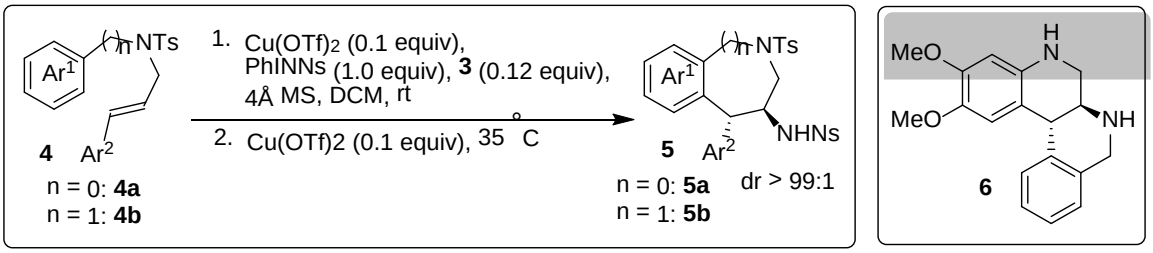
Internal carboxylate nucleophile initiated aziridine opening cyclizing concept was unfolded as aminolactonization reactions that procreate five-membered or six-membered stereodefined aminolactones **2** starting from *tert*-butyl homocinnamates **1**. The method was developed and cultivated with synthetically useful yields and enantioselectivities (up to 94% ee).



Scheme 2. Catalytic asymmetric aminolactonization

The strategy was illustrated even in synthesizing δ-aminolactones with all-carbon quarternary stereo-centres (up to 98% ee).

The idea of catalytic enantioselective nitrogen transfer to olefins followed by internal functionalization was further explored to the synthesis of annulated heterocyclic nucleus. Tethered π-excess arene neucleophile led aziridine opening Friedel-Crafts cyclizations, emerged as aminoarylation reactions, were designed in persuasion of pharmacologicaly important Dopamine D1 agonist architectures. One such method was evolved to afford *trans*-3-amino-4-aryltetrahydroquinolines **5a** (up to 97% ee) from *N*-tosyl-*N*-cinnamylanilines **4a**, aiming to synthesize *N*-bioisostere of dihydrexidine **6**. The present work reached to a matured stage toward its goal (Scheme 3).



Scheme 3. Catalytic asymmetric aminoarylation

In continuation, another conceptually similar annulation technique was adopted for the synthesis of *trans*-4-amino-5-aryltetrahydro-2-benzazipienes **5b** (up to 97% ee) from *N*-tosyl-*N*-cinnamylbenzylamines **4b** (Scheme 3).

Keywords: Asymmetric; Catalytic; Enantioselective; Aminolaconization; Aminoarylation; Aziridine; Aminoactone; Friedel-Crafts cyclization; $Cu(OTf)_2$; Bis-oxazoline; Dopamine D1 agonist; *N*-bioisostere; Dihydrexidine; *trans*-3-Amino-4-aryltetrahydroquinolines; *trans*-4-amino-5-aryltetrahydro-2-benzazipienes.