The thesis entitled "**Electrophile Intiated Reactivity of Functional Alkynes Involving Azide as Amine Surrogate for Medicinally Important Scaffolds**" is divided into four chapters.

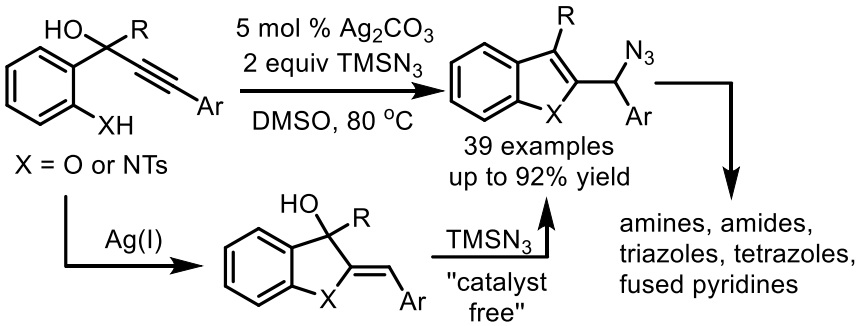
Chapter 1: An Overview on Azide as Nitrogen Surrogate

The development of versatile methodologies to employ azides as aminating agents for the formation of nitrogen-containing compounds has attracted significant attention in synthetic chemistry. This review examines recent developments in the tandem reaction of azides with alkynes and alkynols. The formation of diverse nitrogen containing compounds is classified in this review according to the types of reactions. Nitrogen-containing compounds, such as nitriles, azoles,amides, isoquinolines, quinolines, pyridines, pyrroles etc., are important scaffolds found in numerous natural products, biologically and pharmaceutically active compounds as well as functional materials. These compounds have been extensively studied for their biological and therapeutic activities. In addition, intramolecular processes in this area could be powerful strategies for the synthesis of important heterocyclic compounds. With continuous research in the tandem reaction of azides with alkynes and alkynols, novel reactions and new approaches can be anticipated to appear in the future and be applied extensively in practical synthesis.

Chapter 2A: Synthesis of Benzofuranyl and Indolyl Methyl Azides by Tandem Silver-Catalysed Cyclization and Azidation

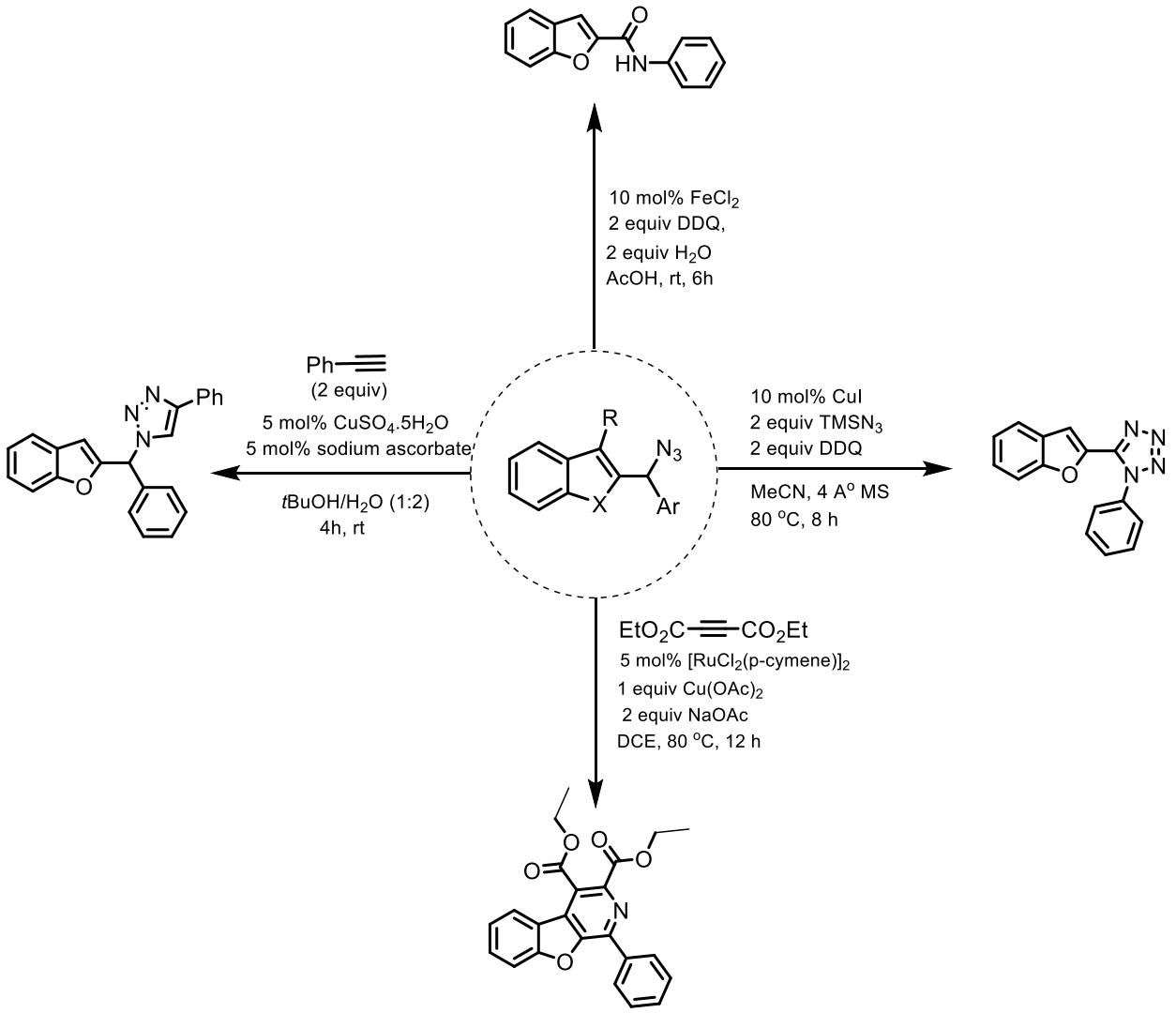
Ag(I)-catalyzed synthesis of 2-azidomethyl benzofurans/indoles from linear and readily available hydroxyl /amino-phenyl propargyl alcohols is described*via* a highly regioselectiveC-O and C-N bond formations. Control experiments reveal that the reaction involves the sequential Ag(I)-catalyzed*5-exo-dig*

Scheme 1:



cyclization and a catalyst free γ-allylic azidation. The synthetic utility of this method has been demonstrated by using azidomethyl unit of the above synthesized heterocycles as base for variety of other functionalizations, like triazole-, tetrazole-, amide-, amine-, pyrido-derivatives.

Scheme 2: Synthetic application



Conclusion:

In summary, an efficient synthetic route to 2-azidomethyl benzoheteroles based on tandem Ag(I)-catalyzed intramolecular cyclization and aromatization driven γ-azidation from readily available linear propargyl alcohols is reported. While it did not require exclusion of air or moisture, the reaction was applicable over a wide range of substrates. The synthetic utility of the reaction was demonstrated by the conversion of azido methyl unit to various other useful functionalities *via* reduction, oxidation and cyclization reactions.

Chapter 2B: In vitro Antitubercular Activity of a Series of Benzofuran And Indole Derivatives

Phosphorylation and dephosphorylation are the key mechanisms for mycobacterial physiology and play critical roles in mycobacterial survival and in its pathogenesis. Mycobacteria evade host immune mechanism by inhibiting phagosome – lysosome fusion in which mycobacterial protein tyrosine phosphatase A (TP) plays an indispensable role. Tyrosine kinase (TK) activated by autophosphorylation; phosphorylates TP, which subsequently leads to increase in its phosphatase activity. The activated TP after getting phosphorylated is secreted in phagosome of macrophage. In present study we have shown that the phosphorylation at two sites of TP; Y128 and Y129 are critical for TK mediated phosphatase activity. The disruption of this interaction between TK and TP inhibits activation of later which further leads to the decrease in intracellular survival of mycobacteria. Further, the proof of concept has been established using Benzyl benzofurans and Benzofuranamides which inhibit the growth and intracellular survival of mycobacteria, associate with the functional sites of TP and contend with the TK.

Table 1. Screening series of compounds against PtpA

Sl. no.	**Compound**	**%Inhibition at 25 µM**	**MIC** (µM)	**CC_{50}**
1	S015-2211	64	50	≤100
2	S015-2212	96	> 50	>100
3	S015-2213	76	> 50	>100
4	S015-2214	74	> 50	>100
5	S015-2215	68	> 50	≤100
6	S015-2216	1	> 50	>100
7	S015-2217	65	50	≤100
8	S015-2218	63	> 50	≤100
9	S015-2219	47	> 50	>100
10	S015-2220	58	> 50	>100
11	S015-2221	51	50	≤100
12	**S015-2222**	**71**	**50**	**>100**
13	S015-2223	6	50	≤100
14	**S015-2224**	**100**	**50**	**>100**
15	S015-2225	50	50	≤100

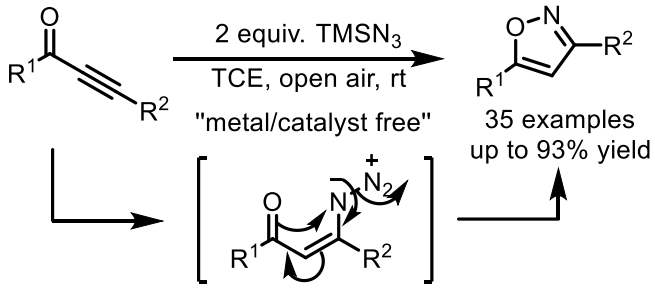
16	S015-2226	46	> 50	>100
17	S015-2227	22	> 50	>100
18	S015-2228	74	> 50	>100
19	S015-2229	62	> 50	>100
20	S015-2230	57	> 50	≤100
21	S015-2231	88	> 50	>100
22	S015-2232	44	> 50	>100

In conclusion these compounds were evaluated for their roles in intracellular survival of Mtb infected macrophage cell line. Both these inhibitors disrupt the TK-TP interaction *in vitro,* and S015-2224 proved to reduce the Mtb survival up to 50 percent at 3.12μM to 25μM concentration.

Chapter 3: **A Direct Access to Isoxazoles from Ynones using Trimethylsilyl Azide as Amino Surrogate under Metal/Catalyst free Conditions**

In this chapter, A general method for isoxazoles from readily available ynones using trimethylsilyl azide as amino surrogate, likely *via* an unprecedented hydroazidation of alkyne and denitrogenative cyclization, is demonstrated. The method neither required any catalyst nor demanded the unusual conditions to afford the products with outstanding functional group compatibility. we herein presented a direct access to isoxazoles from ynones using $TMSN_3$ as amino surrogate. This new method is step economical and it does not require (1) assistance of any metal/catalyst, (2) harsh reaction conditions, and (3) exclusion of air or moisture.

Scheme 3: Synthesis of isoxazoles



Conclusion:

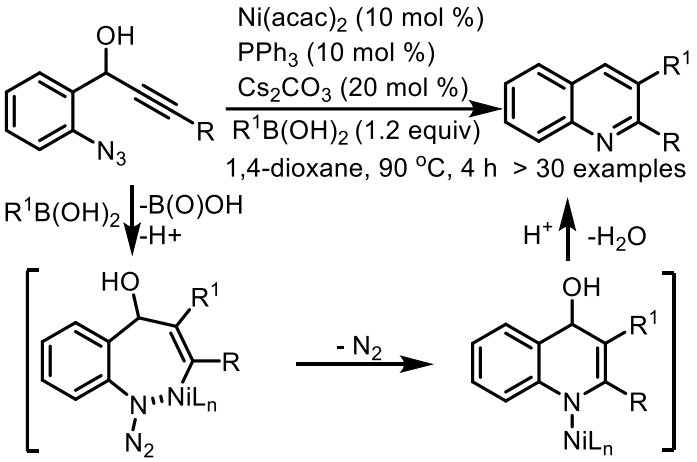
In this chapter we have illustrated a highly general and straightforward method for the synthesis of isoxazoles from readily available ynones using $TMSN_3$ as amino surrogate. The reaction likely proceeds *via* tandem azidation and denitrogenative cyclization (providing a new set of disconnections), offering a single pot C-N and O-N bond formation. Further, a high reaction scope with respect to both terminals of

ynone together with excellent product yields makes it a practical approach for the highly privileged scaffold.

Chapter 4: **A Nickel-Catalyzed *anti*-Carbometallative Cyclization of Alkyne-Azides With Organoboronic Acids: Synthesis of 2,3-Diarylquinolines**

An *anti*-carbonickelative cyclization *via* reversible alkenylnickel *E/Z* isomerization of 2-azido phenyl propargyl alcohols with aryl boronic acids is achieved using $Ni(acac)_2$ as the catalyst to access 2,3-diaryl quinolines. It represents a rare example of trapping the vinyl metal intermediate with a nitrogen center, a non-carbon center electrophile.

Scheme 4: Synthesis of 2,3-Diarylquinolines



Conclusion:

azidophenyl propargyl alcohols could be cyclized to 2,3-diaryl quinolines *via* arylation with aryl boronic acids under Ni(II)- catalysis. Selective carbonickelation, *E/Z* isomerization of the nickel intermediate and capture of the C-M centre by an internal azide as a rare non-carbon electrophile were highlights of the redox-free catalytic process. A thorough verification of substrate scope with respect to both boronic acids and the alkyne-azides was done to prove the practicality of the method.