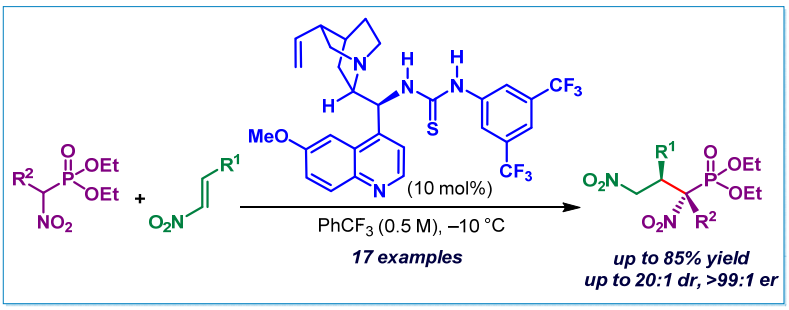
Synopsis

The thesis entitled "**Lewis Base and Hydrogen-Bonding Catalysis by Thioureas: from Chemoselective Alcohol Oxidation to Asymmetric Iodofunctionalizations of Alkenes and Dienes**" is divided into four chapters.

Chapter 1: *Catalytic Asymmetric Synthesis of α,β-Disubstituted α,γ-Diaminophosphonic Acid Precursors by Michael Addition of α-Substituted Nitrophosphonates to Nitroolefins*

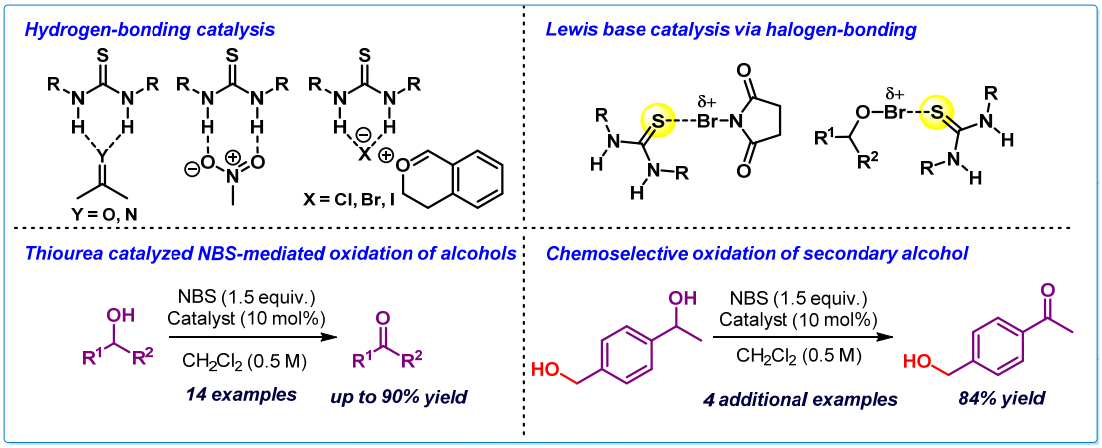
In this chapter, a highly diastereo- and enantioselective catalytic Michael addition of α-substituted nitrophosphonates to nitroolefins has been discussed. In the presence of 10 mol% of a quinine-derived bifunctional thiourea catalyst, a wide range of nitroolefins with diverse steric and electronic environment reacted smoothly to afford α,β-disubstituted α,γ-dinitrophosphonates in good yield with high dr and er. The products of this reaction, consisting of adjacent quaternary and tertiary stereocenters, represent immediate precursors of α,β-disubstituted α,γ-diaminophosphonic acids.



Reference: Tripathi, C. B.; Kayal, S.; Mukherjee, S. *Org. Lett.* **2012**, *14*, 3296-3299.

Chapter 2: *Lewis Base Catalysis by Thiourea: N-Bromosuccinimide-Mediated Oxidation of Alcohols*

This chapter deals with a novel mode of activation by thiourea derivatives. During the last decade, (thio)urea derivatives have emerged as one of the most popular class of small molecule organocatalysts. Initial reports have been confined to the direct activation of electrophilic substrates by means of double hydrogen bonding and a wide range of asymmetric transformations has been accomplished by chiral (thio)urea derivatives. More recently, anion-binding property of (thio)ureas has been exploited in asymmetric catalysis. However, in all these cases, substrate activation is based on the hydrogen bond donor ability of (thio)urea derivatives. Herein another activation mode by thiourea derivatives, namely Lewis base catalysis has been described. The proof of this concept is demonstrated for the *N*-bromosuccinimide (NBS)-mediated oxidation of alcohols. Mild reaction conditions developed here enabled selective oxidation of secondary alcohols in the presence of primary alcohols in high yields with outstanding chemoselectivity.

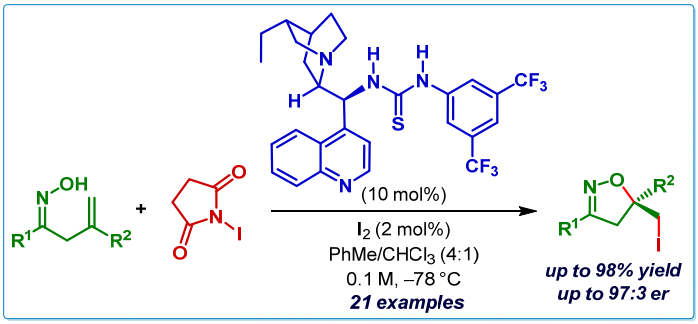


Reference: Tripathi, C. B.; Mukherjee, S. *J. Org. Chem.* **2012**, *77*, 1592-1598.

Chapter 3: *Catalytic Enantioselective Iodocyclization of β,γ-Unsaturated Oximes and Hydrazones*

In this chapter, the first catalytic enantioselective iodocyclizations of ketone derived nucleophiles, namely β,γ-unsaturated oximes and hydrazones, have been discussed.

In the presence of 10 mol% of a dihydrocinchonidine-derived bifunctional thiourea catalyst, a variety of β,γ-unsaturated ketoximes were cyclized using commercially available *N*-iodosuccinimide (NIS) to furnish Δ^2-isoxazolines containing a quaternary stereogenic center in high yield with excellent enantioselectivity. The synthetic utility of the products was demonstrated through a series of synthetic transformations in outstanding efficiency and with complete stereochemical fidelity. Due to the abundance of Δ^2-isoxazolines in biologically active compounds and as synthetically useful chiral building blocks, this protocol is expected to be highly useful across various disciplines.

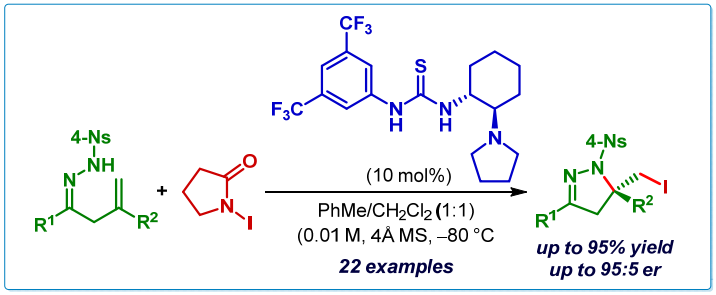


Reference: (1) Tripathi, C. B.; Mukherjee, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8450-8453.

(2) Tripathi, C. B.; Mukherjee, S. *Synlett* **2014**, *25*, 163-169. (*Synpact*)

After successfully demonstrating the catalytic enantioselective iodoetherification of β,γ-unsaturated oximes, a bifunctional thiourea-catalyzed asymmetric iodocyclization of another ketone derived nucleophile – hydrazones has been developed. Starting from β,γ-unsaturated 4-nitrobenzenesulfonyl (4-Ns) hydrazones as the substrate and *N*-iodopyrrolidinone as the electrophilic iodine source, several Δ^2-pyrazolines containing a

quaternary stereocenter were obtained in good yields with high enantioselectivities. This is the first example of the use of hydrazones as nucleophile in olefin halofunctionalization reaction. Given the diverse biological activities of pyrazoline derivatives, this method can be useful for generating such compounds in enantioenriched form.

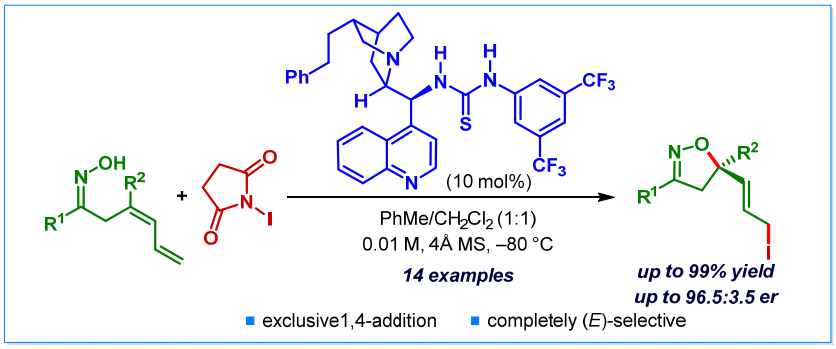


Reference: Tripathi, C. B.; Mukherjee, S. *Org. Lett.* **2014**, *16*, 3368-3371.

Chapter 4: *Catalytic Enantioselective 1,4-Iodofunctionalizations of Conjugated Dienes*

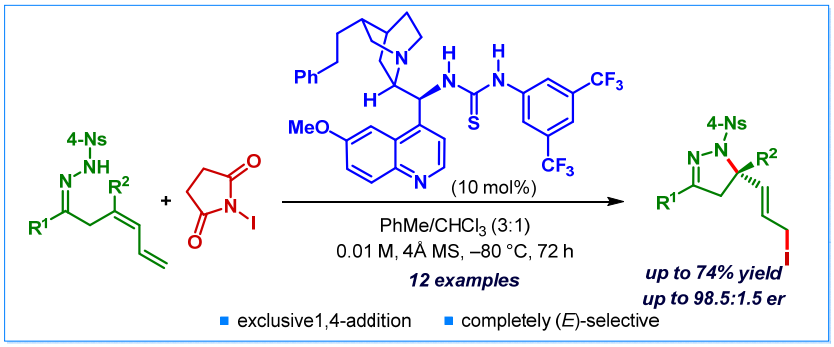
Catalytic enantioselective halofunctionalization reactions of unactivated olefins have received considerable attention only during the past few years, however despite tremendous progress in this area, the same transformation with conjugated π-systems remained far less developed. The reason behind this paucity possibly lies in the challenging regiochemical requirement (1,2- vs. 1,4-halofunctionalization). This chapter deals with the first catalytic enantioselective 1,4-iodofunctionalizations of conjugated dienes.

In the presence of 10 mol% of a cinchonidine-derived bifunctional tertiary amino-thiourea derivative, several β,γ,δ,ε-unsaturated oximes underwent cyclization, exclusively in 1,4-fashion, to furnish Δ^2-isoxazoline derivatives containing an allyl iodide unit at the quaternary stereogenic center generally in high yield with impeccable diastereoselectivity (with respect to the olefin geometry) and excellent enantioselectivity. The potential utility of the products was demonstrated through a series of synthetic transformations.



In addition, to the 1,4-iodoetherification, 1,4-iodoaminocyclization of related hydrazone derivatives has also been described. A bifunctional thiourea catalyst has been employed for accomplishing this transformation. Under the newly devised protocol, a wide range of β,γ,δ,ε-unsaturated (4-nitrobezenesulfonyl) hydrazones underwent 1,4-iodoaminocyclization to afford Δ^2-pyrazoline derivatives, containing a quaternary stereogenic center in high yield

with good to excellent enantioselectivity and impeccable diastereoselectivity. The utility of these Δ^2-pyrazoline derivatives were demonstrated through several transformations including the synthesis of an analog of a potent kinesin spindle protein (KSP) inhibitor.



Reference: Tripathi, C. B.; Mukherjee, S. *Org. Lett.* **2015**, *17,* 4424-4427.