The thesis entitled "Novel Strategies for Heterocyclic Constructions via 1,4-Dipolar Intermediates" embodies the results of extensive investigations carried out to gain some insight into the reactivity of 1,4-dipolar intermediates generated from nitrogen heterocycles (pyridine and its benzoanalogues) and dimethyl acetylenedicarboxylate (DMAD) with various dipolarophiles such as aldehydes, N-tosylimines and benzoquinones.

A general introduction and a brief survey of 1,4-dipolar cycloaddition reactions is presented in chapter 1. A definition of the present work is also incorporated in this chapter.

The second chapter describes the unusual reactivity of 1,4-dipolar intermediate generated from pyridine and DMAD with aromatic aldehydes, resulting in the facile synthesis of benzoyl fumarates via the elimination of pyridine. A typical example is given in scheme 1.

\[
\text{CHO} + \text{I} \xrightarrow{\text{Pyridine (20 mol%)}} \text{II} \xrightarrow{\text{Dry DME, -10 °C to RT, 3 h}} \text{III} \xrightarrow{\text{85%}} \text{IV}
\]

Scheme 1

A similar reaction of the 1,4-dipolar intermediate with N-tosylimines, provided a facile entry into highly substituted 1-azadienes, in good yields (Scheme 2).

\[
\text{NTs} + \text{I} \xrightarrow{\text{Pyridine (20 mol%)}} \text{II} \xrightarrow{\text{dry DME, -10 °C to RT, 3 h}} \text{III} \xrightarrow{\text{66%}} \text{IV}
\]

Scheme 2

The introduction of 1,2-dicarbonyl compounds such as N-substituted isatins as dipolarophiles in this reaction resulted in a novel three component condensation, yielding spiro pyrido[2,1-b][1,3]oxazino derivatives as mixture of diastereomers via 1,4-dipolar cycloaddition pathway (Scheme 3).
The third chapter describes the interception of 1,4-dipolar intermediate from isoquinoline and DMAD with N-tosylimines, resulting in the diastereoselective synthesis of 2H-pyrimido[2,1-a]isoquinoline derivatives in high yields, thus constituting a novel multicomponent reaction (Scheme 4).

A similar multicomponent reaction of isoquinoline, DMAD and aromatic aldehydes resulted an inseparable diastereomeric mixture of [1,3]oxazino[2,3-a]isoquinoline derivatives (Scheme 5).

The fourth chapter deals with the trapping of 1,4-dipolar intermediate from isoquinoline and DMAD by 1,2-benzoquinones affording novel spiro[1,3]oxazino[2,3-a]isoquinoline derivatives in high yields (Scheme 6).
A logical extension of this reaction to 1,4-benzoquinones as dipolarophiles also afforded the expected spiro[1,3]oxazino[2,3-a]isoquinoline derivatives (Scheme 7).

Scheme 6

Scheme 7

In conclusion, we have unraveled some novel and interesting reactivity of 1,4-dipoles derived from pyridine and its analogues towards dipolarophiles such as aldehydes and N-tosylimines. A general method for the synthesis of benzoyl fumarates under mild conditions was developed along with a novel synthesis of highly substituted 1-azadienes, which are important precursors of saturated amino acids. A diastereoselective synthesis of 2H-pyrimido[2,1-a]isoquinolines and [1,3]oxazino[2,3-a]isoquinolines was also developed; such compounds are known to possess therapeutically important biological activities. It is conceivable that the novel synthetic strategies described herein will be applicable to the synthesis of a variety of interesting heterocycles.
LIST OF PUBLICATIONS


6. Multicomponent Reaction *via* 1,4-Dipolar Cycloaddition: A Facile Route to Condensed Isoquinoline Heterocycles Nair, V.; Sreekanth, A. R. (to be communicated to *J. Org. Chem.*).

Posters Presented at Symposia