Allysilane-imine cyclizations
by Jun Li

A thesis submitted in partial fulfillment of the requirement for the degree of Master of Science in Chemistry
Montana State University

Abstract:
Allylsilane chemistry has been widely used in organic synthesis. The intramolecular nucleophilic addition of allylsilane to imine allows the construction of many ring systems in a convenient pathway. After the preparation of appropriate allylsilane-imine substrates, various conditions were applied to furnish the formation of pyrrolidine derivatives. It was found triftuoroacetyl triflate could effect such cyclization to form N-trifluoroacetyl-pyrrolidine with reasonable diastereoselectivity. F-19 NMR was applied to determine the ratio of two possible diastereomers conveniently. The structures were determined with H-1 NMR NOE measurements and confirmed by X-ray crystallography.

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APPROVAL

Of a thesis submitted by

Jun Li

This thesis has been read by each member of the thesis committee and had been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

Thomas Livinghouse — (Signature) — 7/18/01 (Date)

Approved for the Department of Chemistry and Biochemistry

Paul Grieco — (Signature) — 7-18-01 (Date)

Approved for the College of Graduate Studies

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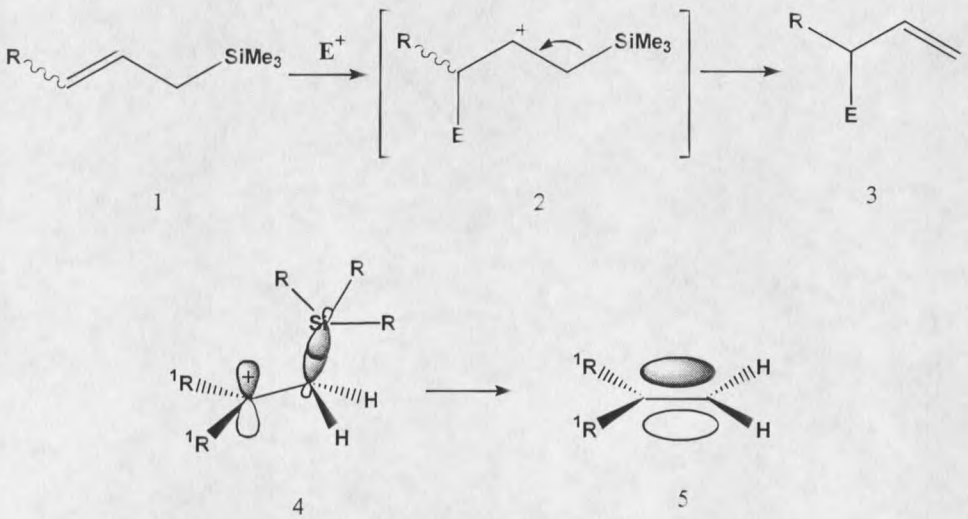
ABSTRACT

Allylsilane chemistry has been widely used in organic synthesis. The intramolecular nucleophilic addition of allylsilane to imine allows the construction of many ring systems in a convenient pathway. After the preparation of appropriate allylsilane-imine substrates, various conditions were applied to furnish the formation of pyrrolidine derivatives. It was found trifluoroacetyl triflate could effect such cyclization to form N-trifluoroacetyl-pyrrolidine with reasonable diastereoselectivity. F-19 NMR was applied to determine the ratio of two possible diastereomers conveniently. The structures were determined with H-1 NMR NOE measurements and confirmed by X-ray crystallography.

CHAPTER 1

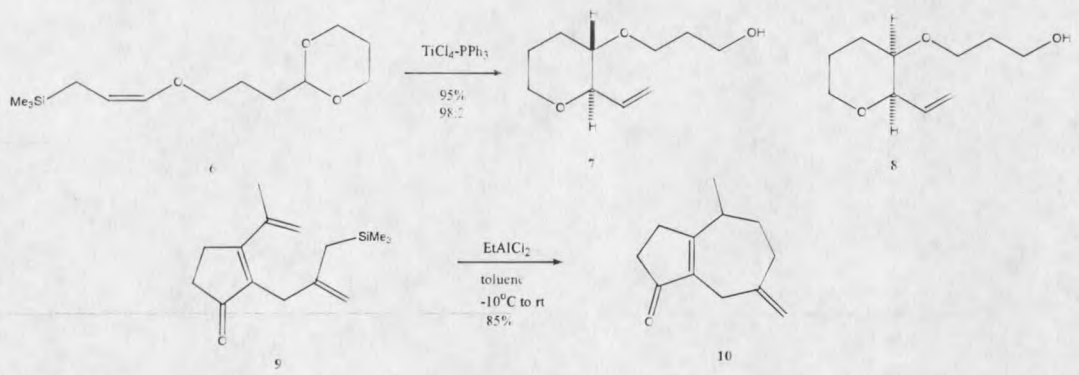
INTRODUCTION

Allylsilanes have proven to be among the most versatile of the silicon-containing carbon nucleophiles. The inter- or intramolecular addition of an allylsilane to carbon electrophiles has been widely used in organic synthesis, often with high level of stereocontrol.[1] A large majority of allylsilane chemistry is based on β-effect, the ability of silicon atom to stabilize the carbocation next to a C-Si bond. These systems tend to lose silyl group and form a double bond, thus give much higher regioselectivity than losing a proton in the analog without silyl group. (Scheme 1)



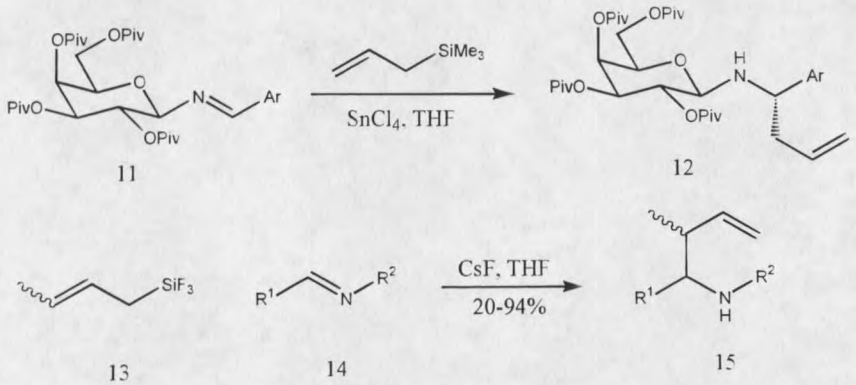
Scheme 1

The most commonly used substrates of allylsilane addition include aldehydes and ketones, acetals, α, β-unsaturated ketones. The intramolecular addition reactions have been widely used in construction of various ring systems. [2] (Scheme 2)



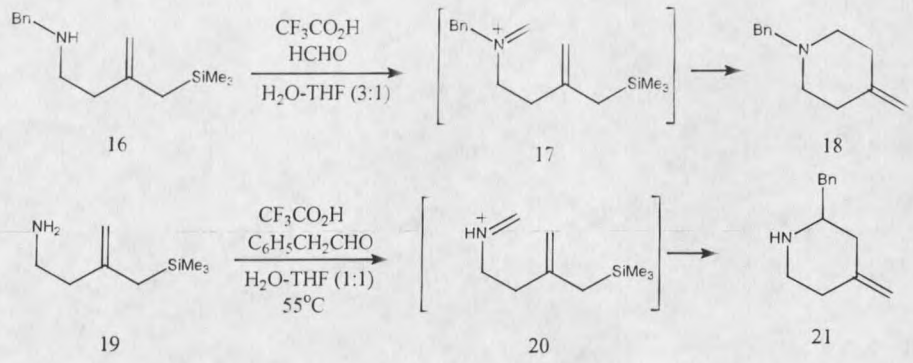
Scheme 2

Imines are also seen as substrates of allylsilane addition although not as widely used as the others. Compared to that of aldehydes, the reaction of imines with allylsilanes is sluggish even in the presence of Lewis acids. However, some examples have been reported.[3] (Scheme 3)



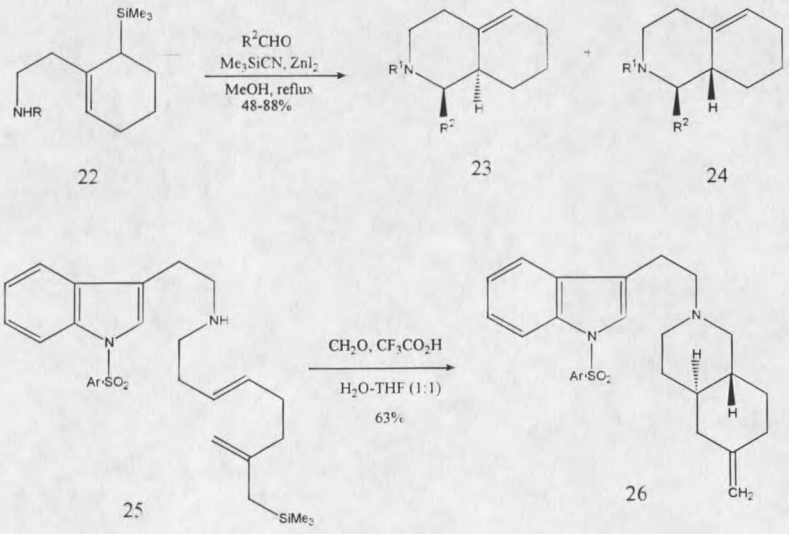
Scheme 3

It was reported that iminium salts, generated either from primary or secondary amine, are more reactive to the addition of allylsilane.[4] An intramolecular version gave rise to the adduct from simple phenylacetaldehyde. (Scheme 4)



Scheme 4

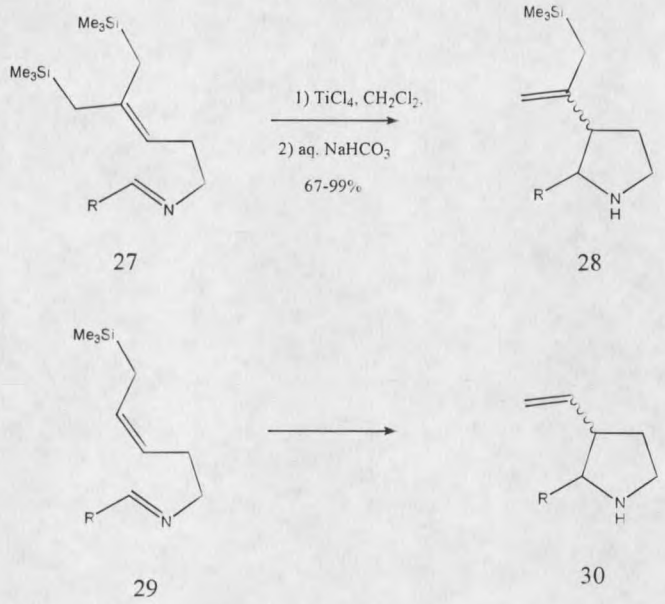
It was also reported that these reactions could be used in the construction of more complex ring system such as isoquinoline derivatives.[5] (Scheme 5)



Scheme 5

This project is directly related to what was done earlier in these laboratories. An intramolecular addition of allylbis(silane) was developed earlier, showing that the pyrrolidine ring can be constructed stereoselectively.[6] (Scheme 6) In most cases, these cyclizations showed interesting stereochemistry, with aromatic imines favoring *cis*-

pyrrolidines and aliphatic imines favoring *trans*- pyrrolidines. The goal of this project was to explore the appropriate conditions for similar cyclizations of the analogous allylsilane-imines and their stereochemistry.

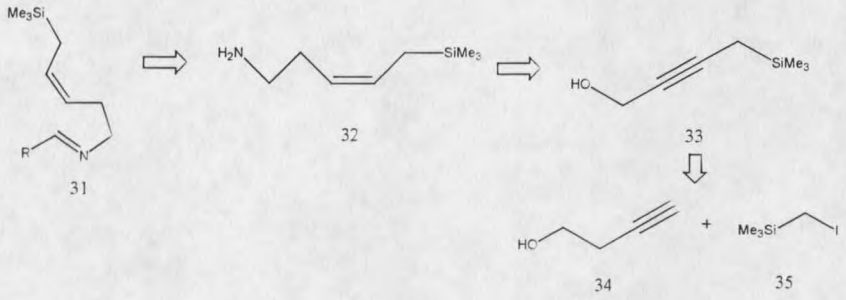


Scheme 6

CHAPTER 2

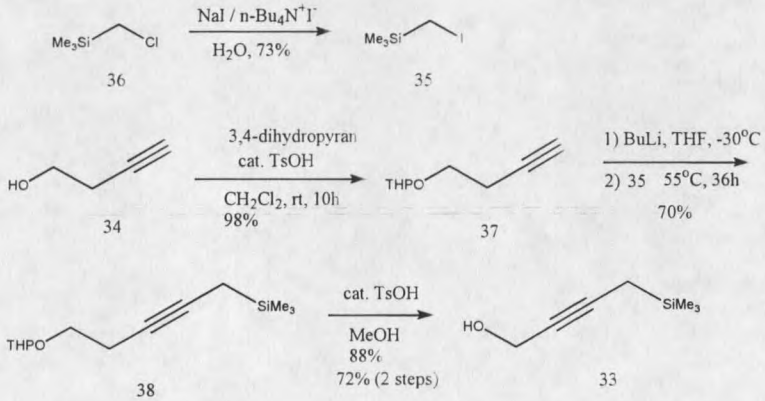
RESULTS AND DISCUSSION

The synthetic route to the allylsilane-imine precyclization substrates 31 is similar to the methods developed earlier in our laboratory and in the literature. [6,7] These imines can be conveniently prepared from amine 32 and a variety of aldehydes. (Scheme 7), while amine 32 can be prepared as shown below.



Scheme 7

The commercially available chloromethyltrimethylsilane 36 was converted to the corresponding iodide 35 by treatment with sodium iodide and tetrabutylammonium iodide in water. [8] Alkylation of the THP-protected 3-butyn-1-ol 37 [9] with iodomethyl-trimethylsilane 35 gave alkylated product 38. (Scheme 8)



Scheme 8