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SYNTHESIS OF RACEMIC AND OPTICALLY ACTIVE β-LACTAMS DERIVED FROM ALLYL AND PROPARGYL IMINE

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Abstract: Synthesis of racemic and optically active β-lactams derived from unsaturated imines has been achieved.

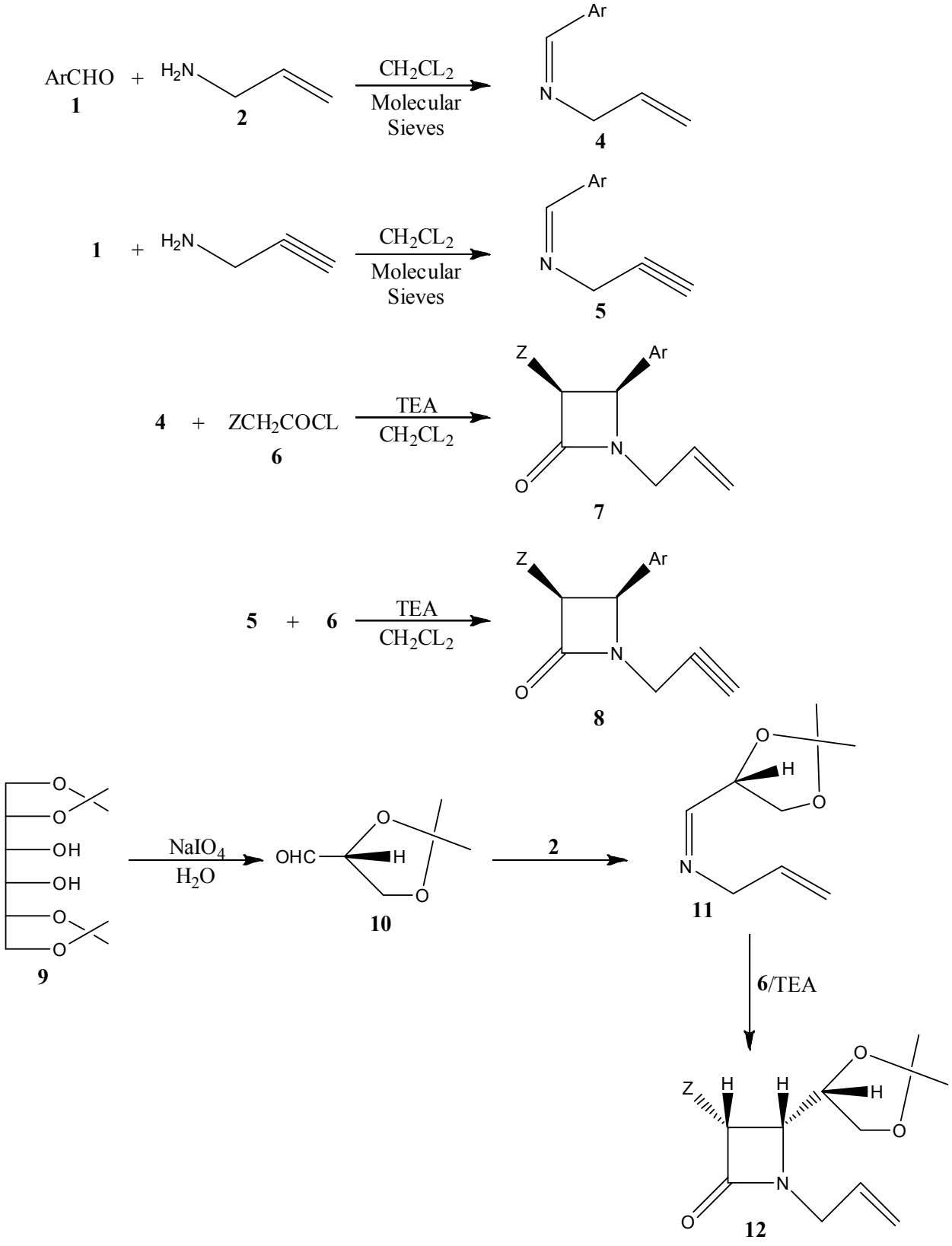
Keywords: β-Lactams, Stereospecific reaction, Allyl and Propargyl Imines.

Introduction:
Stereoselective synthesis of new of β-lactams is an emerging area because of the medicinal activities associated with these types of molecules. In this paper, synthesis of racemic and optically active β-lactams derived from allyl- and propargyl amine is described.

Results and Discussion:
Staudinger cycloaddition reaction of imines and acid chlorides (equivalent) remains the most attractive procedure for the preparation of racemic and optically active β-lactams. In general this reaction may produce *cis*-, *trans*- or a mixture of *cis* and *trans*-β-lactams depending upon the conditions of the experiments and the structure of starting materials. Unsaturated primary amines (allyl amine and propargyl amine) are highly reactive substrates. These amines easily react with aldehydes and produce imines in excellent yield. We have been engaged in the synthesis and biological evaluation of β-lactams for more than two decades. Our interests in this area have grown because of our discoveries of anticancer β-lactams. The unsatuared group present in allyl- and propargyl system can be further manipulated for advanced compounds. With this in mind, our exploration started to prepare β-lactams with these commercially available amines.
At the beginning of our study, aromatic aldehyde **1** reacted with allyl and propargyl amine (**2** and **3**) at low temperature (0^0C) using molecular sieves. The imines **4** and **5** were formed in quantitative yields. Cycloaddition reaction was then performed with these imines **4** and **5** and acid chloride **6** in the presence of triethylamine. The crude NMR showed the presence of *cis* β-lactams **7** and **8** only. No migration of the unsaturated groups could be detected in the crude reaction mixtures. This observation was then extended for the preparation optically active β-lactams. D-Glycerladehyde acetonide **10** was prepared in aqueous solution from D-nannitol derivative **9**. Allyl and propargyl amine (**2** and **3**) was reacted with this optically active aldehyde **10**. Cycloaddition reaction was then performed using the optically active imine **11** with acid chloride **6** as described for racemic imines. The reaction with optically active imine **11** produced only one *cis*-stereoisomer **12** (**Scheme 1**). This observation follows our earlier observation.

Scheme 1

Conclusion: A simple method for the preparation of racemic and chiral *cis* β-lactams with



unsaturated groups at the nitrogen of the β-lactam ring has been developed. These compounds can be used for the synthesis of polycyclic β-lactams by radical, cationic and anionic cyclization pathways.

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