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Microwave-Induced Synthesis of *Bis*-β-Lactams from Hydrobenzamide

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ABSTRACT

Microwave-induced synthesis of *bis*-β-lactams is performed by Staudinger cycloaddition reaction of acid chloride and hydrobenzamide.

KEYWORDS

Cycloaddition, Hydrobenzamide, Bis-β-Lactams, Diastereospecific.

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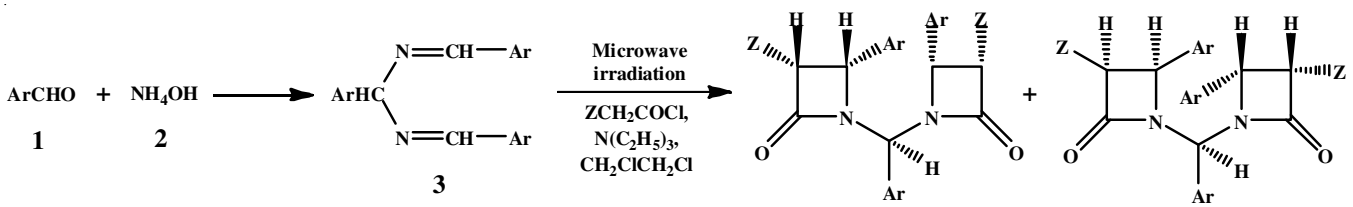
INTRODUCTION

Our research group has been conducting the synthesis and biological evaluation of diverse β-lactams for the past many years. It is widely recognized that β-lactams are clinically active drugs for the cure of infectious diseases. However, these are also used for different types of medical disorders [1-8]. A number of effective strategies were discovered for the synthesis of 2-azetidinone core ring present in all β-lactams [1-8]. Perhaps, the most important reaction for the synthesis of β-lactams is Staudinger cycloaddition reaction between imines and activated acids in the presence of a tertiary base. The imines are prepared by a condensation reaction between aldehydes or ketones and primary amines. The use of ammonia as the equivalent of amine (ammonium hydroxide) was not exploited in the synthesis of β-lactams under microwave irradiation [9-17].

Our work on β-lactam chemistry and microwave-induced reactions is suited for the preparation of *bis*-β-lactams from hydrobenzamide. Reaction of acid chloride with hydrobenzamide under microwave irradiation in the presence of a tertiary base would be a topic of current interest since nothing is known about the stereoselectivity of this process. Microwave-induced reactions are very useful in the synthesis of biologically active molecules including in the stereoselective preparation of diverse β-lactams as well. We describe here a microwave-induced method for the synthesis of diastereoselective β-lactams starting from hydrobenzamide.

EXPERIMENTAL

Hydrobenzamide (**3**) was prepared by reaction of strong ammonia (**2**) and various aldehydes (**1**) [18]. This molecule has two C=N bonds and, therefore, it is expected to form *bis*-β-lactams under forcing conditions. Microwave-induced (domestic and automated) reaction of hydrobenzamide **3** with different



	Z	Ar	Ratio
4 & 5	OCH_3	Phenyl	50:50
4 & 5	OBn	Phenyl	45:55
4 & 5	OBn	*p*-Methoxyphenyl	50:50
4 & 5	OCH_3	*p*-Methoxyphenyl	50:50

Scheme-I: Microwave-induced synthesis of β-lactams

acid chlorides in the presence of triethylamine afforded a mixture of two *cis bis*-β-lactams **4** and **5** in different proportions. In contrast to earlier observation, no *trans*-isomers were formed [18-22] (**Scheme-I**). It was found that 1,2-dichloroethane works as the best solvent. The reaction was completed within 5 to 7 min in a domestic microwave or automated microwave oven [18-22]. The diastereomers were separated by column chromatography. The m.p. and the NMR data of these compounds were identical to the compounds prepared by the conventional method [18]. It was important to note that the compounds **6** and **7** are formed in almost equal amounts by the microwave method. However, compound **6** was the major isomer under classical method (**Scheme -I**).

RESULTS AND DISCUSSION

Preparation of unique *bis*-β-lactams by the microwave irradiation method using hydrobenzamide is very fast. An easy separation of the diastereomers can be done. The structure of these molecules would permit one to perform several chemical manipulations. This method can be used for the preparation of optically active *bis*-β-lactams with defined stereochemistry.

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