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BANIK'S RULE: RAPID HEATING FORMS TRANS BETA LACTAMS WITH DIARYLIMINES

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Abstract:
Cycloaddition of Schiff base with acid chloride or its equivalent in the presence of a tertiary base gives β-lactams. This reaction may produce cis, trans or a cis-trans isomeric mixture of β-lactams. depending upon the structures of the imine and acid chloride as well as on the condition of the experiment. No generalization of the stereochemistry of the β-lactams from cycloaddition is possible. However, based upon our significant studies in this area, the author has identified a fundamental rule. It is named: Banik's Rule. The author has found rapid heating of the reactants form trans β-lactams with diarylimines irrespective of the nature of the acid chlorides.

Key words: Beta Lactams, Rule, Ketenes, Imines, Cycloaddition, Stereochemistry, Mechanisms

Introduction:

Synthesis and biological evaluation of *β*-lactams are the subjects of intense investigations [1]. The most attractive method for the synthesis of the *β*-lactam is called cycloaddition known as the Staudinger reaction. This method produces cis, trans or a mixture of cis-trans *β*-lactams depending upon the structures of the imines and acid chlorides. The condition of the experiments dictates the stereochemistry of the products. The author's independent work on *β*-lactams for the past more than three decades has culminated a rule on the preparation of these crucial molecules. On this basis, this paper describes the Banik's Rule: "rapid heating of the reactants form trans β-lactams with diarylimines" irrespective of the nature of the acid chlorides.

Results and Discussion:

Synthesis of diverse *β*-lactams with defined stereochemistry was performed by reaction with imines and acid chlorides or its equivalents in the presence of triethylamine or another tertiary amine. Diverse types of imines obtained from carbonyl compounds and primary amines are used. The primary amines can be any of these aromatic, heteroaromatic, aliphatic, arylaliphatic,

alkenyl and alkynyl compounds. The carbonyl compounds can be any of these aliphatic, aromatic, and aromatic-aliphatic compounds. Acid chlorides or its equivalents are carbon, oxygen, nitrogen, and sufur-derived molecules.

Notably, these acid chlorides form cis as well as trans *β*-lactams. Lower temperature (zero degree to room temperature) favors the formation of cis and high temperature helps to form trans compound with diaryl imines except with sulfur-acid chloride. In contrast, the product distribution changes depending upon the temperature of the reaction and the way the reaction mixture was heated. If the temperature of the reaction increases, the ratio of trans *β*-lactam in the mixture increases. For example, the reaction of acetoxyacetyl chloride and diphenyl imine in dichloromethane produces exclusively cis *β*-lactams after 6h at 0^0C. At reflux temperature, the reaction gives a mixture of cis and trans *β*-lactams in equal proportions within an hour (the increase of temperature is done slowly from room temperature using the controller of the heater). If the same reactants are allowed to heat in a preheated oil bath, the reaction undergoes completion within 30 minutes and 90% of the trans isomer is formed. The reaction follows an identical pattern when dichloroethane, toluene, chlorobenzene and DMF are used as solvents. The reaction produces trans compound more readily in solvents with high boiling point and if the reaction mixture is exposed to a preheated system (oil bath, sand bath). An identical result is found when the reactions are conducted in a microwave oven [2]. A rapid heat is applied in a microwave and the reaction is completed within 4-5 minutes. Similarly, high boiling solvents chlorobenzene produces more trans compound than dichloromethane. These observations suggest that rapid heat is responsible for the formation of trans *β*-lactams. No isomerization of the cis lactam to the tarns compound is noted. An identical observation is seen when other oxygen-containing acid chlorides (benzyloxyacetyl chloride, methoxyacetyl chclorde and phenoxyacetyl chloride) are used.

Following an identical approach, phthalimido acetyl chloride produces a higher proportion of trans β-lactams if it is added to a preheated diarylimine solution. The same reaction produces a mixture of two isomers at cold condition. Crotonyl chloride and propionyl chloride follow the same rule. Phenylthioacetyl chloride however, always produces trans β-lactam regardless of the temperature of the process.

The *trans-β*-lactams are formed by an isomerization of transition state. This is occurred by a conrotatory cyclic system formation route [3].

Conclusions: In summary, the synthesis of trans *β*-lactams from diarylimines by cycloaddition method depends on the way heat is delivered to the reaction mixture.

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