

**A MODIFIED SYNTHESIS OF AMIDES FROM KETONES VIA BACKMANN
REARRANGEMENT CATALYSED BY FERRIC CHLORIDE****M. Bakiyalakshimi^{1*}, Dr. K. L. Senthil Kumar², Dr. P. D. Gokulan³, A. Jayashree, K. Jayasurya and S. Jeevan⁴**¹Associate Professor, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri, Tamil Nadu.²Principal, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri, Tamil Nadu.³Professor & Head, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri, Tamil Nadu.⁴Student of final B.Pharm, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri, Tamil Nadu.***Corresponding Author: M. Bakiyalakshimi**

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ABSTRACT

The Beckmann rearrangement is a powerful method of a conversion of ketones into amides with the help of the catalyst ferric chloride or (CuSO₄) in the presence of acid (conc. Sulphuric acid) for an excellent yield. Additional other organic solvents are not required. This solid phase reaction is suitable for the cleavage of C-C bond and for the formation of C-N bond. Ferric chloride is inexpensive, stable, easy to handle and eco-friendly.

KEYWORDS: Beckmann rearrangement, ketones, amides, ferric chloride, organic solvent.**INTRODUCTION**

The Beckmann rearrangement, the acid-mediated isomerization of oximes to amides was discovered by Beckmann in the year of 1886.^[1] As one of the oldest and most familiar transformations in organic chemistry, it has been reviewed several times. It has become known as the Beckmann fragmentation was first observed by Wallach in 1889 but was not developed extensively until the 1960s.^[2] It has been referred to by several names over the years and also been reviewed.^[3,4] The rearrangement cyclization is the intermolecular cyclization of a nitrilium ion generated by Beckmann rearrangement from an oxime. The most prominent of these is so called phytochemical Beckmann rearrangement, first observed by De Mayo in 1963 and discussed in a several years ago.^[5]

The reaction is accelerated when C=N bond is orthogonal to the benzene ring. Thus when the C=N and aromatic groups are coplanar, a concerted sigmatropic rearrangement occurs and resonance stabilization of the developing positive charge is not possible. When the C=N and aromatic groups are forced out of coplanarity by the ortho-methyl groups, participation assists the N-O cleavage, increases the rate and affords a discrete intermediate.^[6]

In aliphatic ketoximes, the structure and solvent may play a role in the mechanism. For example, cycloalkanone oximes in acetic acid and chloroform are consistent with variable transition state geometries.^[7]

A solvent free one step conversion of ketones to amides via Beckmann rearrangement catalyzed by Ferric chloride in the presence of sulphuric acid. This is a powerful method in the organic synthesis for the preparation of amides from ketones which is often used in chemical industries. The reaction condition is milder in the liquid phase but the usage of large amount of organic solvent has made this method so critical but this reaction is also been reported in supercritical H₂O, ionic liquids and solid phase systems. Only few methods have been developed for the single step conversion of ketones to amides in the presence of ferric chloride via Beckmann rearrangement.

Various catalysts are used for the preparation of amides from ketones such as ferric chloride, NiCl₂·6H₂O, CoCl₂·6H₂O, CuSO₄·5H₂O, Fe(NO₃)₃·9H₂O, FeCl₃(anhyd), FeCl₃·6H₂O, FeCl₃·6H₂O impregnated on alumina. Therefore still exists a need to find new methodologies which are simpler, cheaper, faster and eco-friendly to facilitate these rearrangements.^[8] In view of this context and also our ongoing efforts to develop newer methodologies and we have conceived a solvent free one step conversions of ketones to amides using ferric chloride or (CuSO₄) as an eco-friendly catalyst which is suitable for the conversion of ketoximes to the corresponding amides via Beckmann rearrangement.

To begin with benzoylchloride was treated with Lewis acids such as conc. sulphuric acid, hydrogen chloride in acetic anhydride and in results of large amount of by-products. From the above results it is clear that ferric

chloride gives the best result with the satisfactory yield in ferric chloride as a solvent.

OPTIMIZATION OF CATALYST

To optimize the catalyst, a series of experiments were performed by refluxing acetone in dry toluene for 3hrs with different amounts of ferric chlorides and other catalysts to realize that 10mol% of catalyst gives the best results.

S.No	Lewis acid	Dry toluene
1.	NiCl ₂ .6H ₂ O	No reaction
2.	CoCl ₂ .6.H ₂ O	No reaction
3.	CuSO ₄ .5H ₂ O	No reaction
4.	FeCl ₃ (anhyd)	40%
5.	FeCl ₃ .6H ₂ O	80%

Next we are focusing our attention on the direct conversion of ketones to amides. Towards this, a mixture of a chemicals belonging to ketones 5ml, conc.sulphuric acid 2ml, hydrochloride in acetic anhydride 5ml, ferric chloride 1g was refluxed in dry toluene. TLC revealed that the formation of amide group.

It is worth mentioning here that it have successfully converted ketoximes into amide in the solid phase by heating (2-3hrs) using 3equiv offerric chloride. The present method is advantageous in view of catalytic usage of FeCl₃.6H₂O and direct conversion of ketones to amides. The checkthe versality of the present methodology, a variety of ketones were heated with 1.5 equiv of NH₂OH.HCl and CuSO₄ (10mol %) at 130 without any organic solvent and the results are depicted.

MATERIALS AND METHODS

Ferric chloride, ammonia, phosphorous pentachloride, benzoyl chloride, acetone, benzamide, urea, acetophenone, conc. Sulphuric acid, acetic anhydride, con hydrochloric acid, dry toluene, TLC plates, silica gel G, ethanol and water were purchased from the where of analytical grade The Best Scientific chemicals,pvt limited, Dharmapuri.

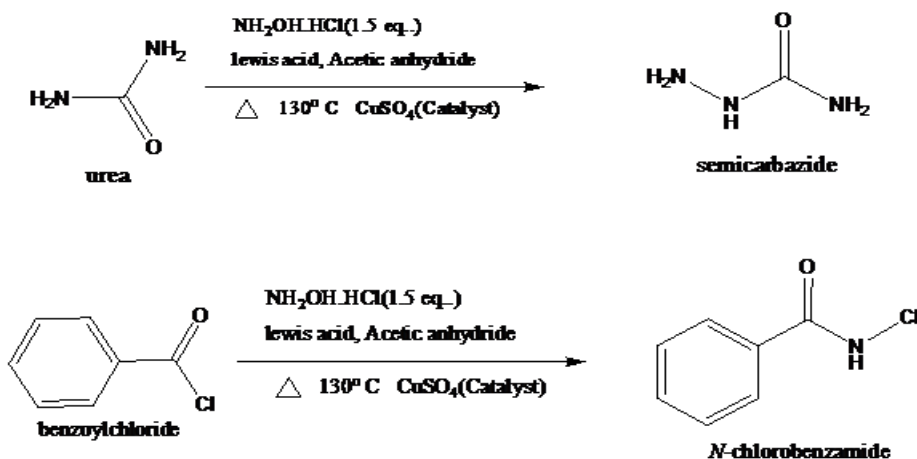
METHODOLOGY

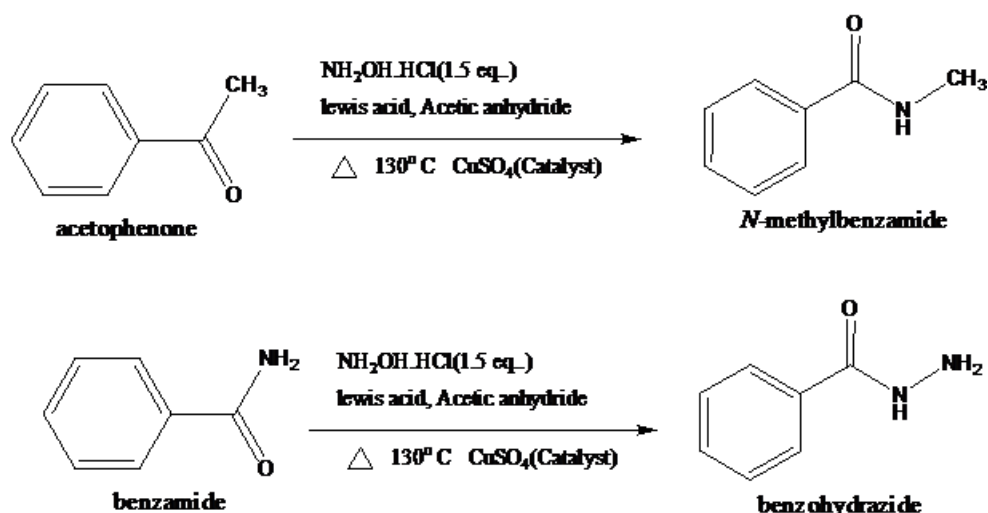
This section deals with Beckmann rearrangements that are rearrangements in the strictest terms: the functional group formula is not changed. Thus -C(=NOH)- or an derivative is converted into -C(=O)NH-. The following section deals with the reactions in which the course of the conversion is intercepted along its path and that, therefore are not a rearrangements in the same sense.

These reactions are compatible with functional groups such as carboxylic acids, esters, alcohols, ethers and alkyl halides but may not be compatible with some of the more sensitive protecting groups. Because there were fewer general methods are available for the controlled manipulation of oxime geometry. Beckmann rearrangements have not seen extensive use in complex total synthesis even though the rearrangement is spectroscopic.

Reagents such as phosphorous pentachloride continues to be a popular reagent for Beckmann rearrangement, but since numerous reagents are used. A popular medium for beckmann rearrangements of compounds that are not acid -sensitive is polyphosphoric acid. After studying the rates of rearrangements of a series of substituted acetophenone oximes, pearson noted that there is no substitution effect, that the arrangements are 12-35 times faster than in sulphuric acid, and that the rearrangement will usually occur at room temperature. The most common procedure is to heat the oxime at about 130 for a few minutes, although the recent procedure suggests the use of xylene as a cosolvent.

Next we focused our attention on the direct conversion of ketones to amides. Toward this end, a mixture of acetophenone 5ml with, ammonia and ferric chloride was refluxed in dry toluene for about 2-3 hrs at 50. TLC revealed that the formation of N-methylbenzamide and acetophenone oxime along with unreacted acetophenone. NMR of the crude product obtained after working up the reaction after 3hrs, suggested the 80% conversion of acetophenone to N-methylbenzamide.





To achieve the complete conversion of acetophenone to N-methylbenzamide, attempts such as using copper sulphate as a catalyst instead of ferric chloride, changing the mode of reaction from thermal to ultra-waves,

heating a mixture of acetophenone with sulphuric acid and acetic anhydride without any solvent at 130 resulted to our delight, incomplete conversion of acetophenone into N-methylbenzamide.

Entry	Reactant	Amide	Reaction time(min.)	Yield ^a (%)	Mp (lit.) ^b (°C)
1			90min	40%	133°C
2			120min	48%	197°C
3			180min	80%	202°C
4			150min	56%	288°C

CONCLUSION

In our studies totally 4 ketones were kept under reflux for nearly about 2-3 hrs. as the report obtained in our study is reflux of urea for 90mins at 130 resulted in the formation of 40% of semicarbazide. Reflux of benzoyl chloride for 120mins at 130 resulted in the formation of 48% of N- chlorobenzamide. Reflux of acetophenone with ferric chloride and copper sulphate for 180 mins at 130 resulted in the formation of N-methylbenzamide.

When the reaction was carried out using ferric chloride resulted in formation of 80% of N- methylbenzamide. When the reaction was carried out using copper sulphate resulted that there is no more reaction was carried out among acetophenone and copper sulphate. Reflux of benzamide with ferric chloride for 150mins at 130 resulted in the formation of 56% of benzohydrazide. In the study of Conversion of amides from ketones by Beckmann rearrangement was carried out with urea,

benzoyl chloride, acetophenone and benzamide and out of these acetophenone gives the higher yield.

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