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Ji-Tai Li $^{\rm a}$, Xian-Tao Meng $^{\rm a}$ & Ying Yin $^{\rm a}$

^a College of Chemistry and Environmental Science, Hebei University, Key Laboratory of Analytical Science and Technology of Hebei Province, Key Laboratory of Medical Chemistry and Molecular Diagnosis, Ministry of Education, Baoding, China Published online: 23 Apr 2010.

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EFFICIENT PROCEDURE FOR BECKMANN REARRANGEMENT OF KETOXIMES CATALYZED BY SULFAMIC ACID/ZINC CHLORIDE

Ji-Tai Li, Xian-Tao Meng, and Ying Yin

College of Chemistry and Environmental Science, Hebei University, Key Laboratory of Analytical Science and Technology of Hebei Province, Key Laboratory of Medical Chemistry and Molecular Diagnosis, Ministry of Education, Baoding, China

The Beckmann rearrangement of a variety of ketoximes to corresponding amides catalyzed by sulfamic acid and zinc chloride was carried out in good yields at refluxing temperature in acetonitrile.

Keywords: Amides; Beckmann rearrangement; cocatalyst; ketoxime; synthesis

INTRODUCTION

The conversion of ketoxime into corresponding amide, known as the Beckmann rearrangement, is a common method used in organic chemistry and is also a topic of current interest.^[1,2] Needless to say, vapor-phase Beckmann rearrangement was a very important development, and a great number of vapor-phase Beckmann rearrangement processes^[3] have been reported. As is widely known, the reaction generally requires high temperature, strongly acidic conditions, and dehydrating media. It leads to large amounts of by-products and cannot be used with sensitive substrates. Milder conditions were tried, and investigations into clean, simple, and highly efficient processes were conducted. Liquid-phase catalytic Beckmann rearrangement usually proceeded under mild condition with high conversion and selectivity,^[4] and several methods for this rearrangement have been reported in the literature. The cyclohexanone oxime could be transformed into ɛ-caprolactam catalyzed by trialkyloxonium salts^[5] or $P_2O_5^{[6]}$ in dimethylformamide (DMF) solutions, but the yields of ε-caprolactam were unsatisfactory. Beckmann rearrangements of several ketoximes were performed in the catalytic media consisting of ionic liquid and $PCl_5^{[7a]}$ or $P_2O_5^{[7b]}$. Excellent conversion and selectivity were achieved for cyclohexanone oxime. One of the most serious shortcomings concerning the catalytic

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Address correspondence to Ji-Tai Li, College of Chemistry and Environmental Science, Hebei University, Key Laboratory of Analytical Science and Technology of Hebei Province, Key Laboratory of Medical Chemistry and Molecular Diagnosis, Ministry of Education, 071002 Baoding, China. E-mail: lijitai@hbu.cn



Scheme 1. Beckmann rearrangement of ketoximes to corresponding amides.

Beckmann rearrangement, not only in ionic liquids but also in industrial manufacturing, is that there is no an effective way to separate the ε -caprolactam product from the catalysts. Inevitably, volatile hydrogen chloride as by-product is produced.^[7c] To overcome these problems, some catalysts such as cyanuric chloride,^[8] p-toluenesulfonic acid,^[9] and BF₃ · OEt₂^[10] were used for the rearrangement to give amides in excellent yields, but a long reaction time was required. Although Beckmann rearrangement catalyzed by RuCl₃^[11] or [RhCl(cod)]₂/CF₃SO₃^[12] could give the corresponding amide in good yields, the catalyst was expensive. In addition, the Beckmann rearrangements without solvent^[13,14] and with supercritical water^[15] were developed, but high reaction temperatures were required.

Sulfamic acid (NH₂SO₃H) is a commercially available and cheap chemical that is recyclable and easy to handle as a catalyst^[16] owing to its immiscibility with common organic solvents, unique catalytic features, and intrinsic zwitterionic property that are different from conventional acidic catalysts. Recently, Wang et al. reported that Beckmann rearrangement of ketoxime catalyzed by NH₂SO₃H alone was carried out in 47–96% yield under refluxing CH₃CN, but the reactions were completed in 6–8 h.^[17] Herein we report a simple and efficient process for Beckmann rearrangement of ketoximes to amides using sulfamic acid/zinc chloride under reflux conditions in acetonitrile (Scheme 1).

RESULTS AND DISCUSSION

A large number of organic reactions can be carried out in greater yield, shorter reaction time, and milder conditions under ultrasonic irradiation than at classical conditions, and the Beckmann rearrangement using ultrasonic irradiation has been reported.^[18] Initially, we did the rearrangement of acetophenone oxime catalyzed by NH₂SO₃H under ultrasonic irradiation. No acetanilide was obtained for a long reaction time. Although the formation of acetanilide was observed when ZnCl₂ was added, the yield was still poor under ultrasonic irradiation. In the presence of sulfamic acid and zinc chloride under reflux conditions, the Beckmann rearrangement of acetophenone oxime was completely carried out within a short time.

The effect of the different catalysts on the Beckmann rearrangement of acetophenone oxime was observed. Representative results are shown in Table 1. The results suggested that $ZnCl_2$ (Table 1, entry 2) can further increase the catalytic activity of NH₂SO₃H. Some Lewis acids (Table 1, entries 3–6) were inert or less active. Therefore, less expensive $ZnCl_2$ was the best choice as a cocatalyst for NH₂SO₃H.

The effect of the solvent was also investigated. When acetonitrile and 1,2-dichloroethane were used as solvents, the acetanilide was obtained in 98% and 67%

Entry	Solvent	Catalyst	Isolated yield (%)		
1	MeCN	_	48		
2	MeCN	ZnCl ₂	98		
3	MeCN	CoCl ₂	50		
4	MeCN	FeCl ₃	41		
5	MeCN	MnCl ₂	23		
6	MeCN	MgCl ₂	7		
7	1,2-Dichloroethane	ZnCl ₂	67		
8	Toluene	ZnCl ₂	55		
9	CCl_4	$ZnCl_2$	23		
10	Dioxane	$ZnCl_2$	12		
11	THF	$ZnCl_2$	_		

Table 1. Effect of the different catalysts and solvents on the Beckmann rearrangement of acetophenone $oxime^a$

"Reaction conditions: acetophenone oxime (1 mmol), sulfamic acid (0.5 mmol), Lewis acids (0.2 mmol), solvent (3 mL), reflux, 2 h.

yields respectively (Table 1, entries 2 and 7), whereas when toluene, tetrachloromethane, dioxane, and tetrahydrofuran were used, the yields of acetanilide were very poor (Table 1, entries 8–10) or no product was found (Table 1, entry 11). It shows that solvent plays an important role in this reaction, and acetonitrile is the most suitable solvent.

The effect of the amounts of NH_2SO_3H and $ZnCl_2$ on the Beckmann rearrangement of acetophenone oxime in acetonitrile was tested. The results were summarized in Table 2. As shown in Table 2, when the amount of $ZnCl_2$ was 0.2 mmol, the rearrangement gave the acetanilide in 98% yield in the presence of 0.3 mmol NH_2SO_3H (Table 2, entry 9), whereas acetanilide was obtained in 20–81% yield by changing the amount of NH_2SO_3H from none to 0.2 mmol (Table 2, entries 6–8). Further addition of an amount of $ZnCl_2$ or NH_2SO_3H had

	Catalyst (mmol)				
Entry	NH ₂ SO ₃ H	ZnCl ₂	Time (h)	Isolated yield (%)	
1	0.5	0	2	48	
2	0.5	0.1	2	74	
3	0.5	0.15	2	82	
4	0.5	0.2	2	98	
5	0.5	0.25	2	98	
6	0	0.2	5	20	
7	0.1	0.2	3	54	
8	0.2	0.2	2	81	
9	0.3	0.2	2	98	
10	0.4	0.2	2	97	

Table 2. Effect of the ratio of NH_2SO_3H and $ZnCl_2$ on the Beckmann rearrangement of acetophenone oxime in acetonitrile^{*a*}

^aAcetophenone oxime: 1 mmol; acetonitrile: 3 mL; reflux.

Substrate	Time (h)	Product		Isolated yield (%)	Mp (°C)	Mp (°C) ^[lit.]
NOH	2		2a	98	114–116	113 ^[19]
NOH	0.75	J N N	2b	99	150-152	151 ^[19]
CI	2		2c	92	174–176	175–177 ^[20]
H ₃ CO NOH	1	H ₃ CO	2d	99	117–119	125-127 ^[20]
NOH	1		2e	96	163–165	162 ^[19]
0 ₂ N	3	O_2N	2f	30	153–155	155 ^[8]
NOH O ₂ N	3	$\mathbf{x}_{0_{2}\mathbf{N}} \xrightarrow{H} \mathbf{x}_{0}$	2g	17	211–213	214 ^[21]
HON	1.5	CH?	2h	96	154–156	153-155 ^[22]
NOH	1.5	K N N N	2i	90	128–130	132–134 ^[23]
€	2	NH O	2ј	70	39–40	40 ^[19]
NOH	2	ONHO	2k	65	69–71	72 ^[21]
	2	P _N -	21	57	29–31	30 ^[24]
	Substrate NOH OH	SubstrateTime (h)	SubstrateTime (h)Product	SubstrateTime (h)Product	SubstrateTime (h)ProductIsolated yield (%)	SubstrateTime (h)ProductIsolated yield (%)Mp (°C)

Table 3. Beckmann rearrangement catalyzed by NH₂SO₃H/ZnCl₂ under refluxing in acetonitrile

no effect on the yield of acetanilide (Table 2, entries 5 and 10). Thus, the optimum amount was NH_2SO_3H (0.3 mmol) and $ZnCl_2$ (0.2 mmol).

Compared with the reaction catalyzed by NH_2SO_3H alone, the present procedure can give greater yield in less time. For example, the Beckmann rearrangement of acetophenone oxime catalyzed by NH_2SO_3H was carried out in 96% yield under reflux for 6 h,^[17] whereas in the present procedure, treatment of acetophenone oxime under reflux for 2 h in acetonitrile afforded acetanilide in 98% yield.

From these results, the reaction conditions we chose are as follows: ketoxime (1 mmol), NH_2SO_3H (0.3 mmol), $ZnCl_2$ (0.2 mmol), and acetonitrile (3 mL) with refluxing temperature.

To explore the generality and scope of the Beckmann rearrangement catalyzed by $NH_2SO_3H/ZnCl_2$, representative ketoximes were examined (Table 3). As shown in Table 3, excellent yields were obtained with aromatic ketoximes, which contain electron-donating substituents (Table 3, entries 1a–e, 1 h, 1i). When aliphatic ketoxime was used as substrate, the rearrangement provided moderate yield (Table 3, entries 2j–l). Unfortunately, the reaction of aromatic ketoximes containing strong electron-withdrawing substituents in the benzene ring gave the desired amides in poor yield (Table 3, entries 2f, 2g). It is clear that sulfamic acid/zinc chloride has good catalytic activity for the Beckmann rearrangement of a variety of ketoximes, especially for aryl ketoximes containing electron-donating substituents.

The specific zwitterionic feature of sulfamic acid avoided the use of basic neutralization agent on the Beckmann rearrangement, and sulfamic acid and all the solvents were recyclable. The only by-product confirmed was ketone, which is derived from the deoximation of ketoxime. This procedure is significant from the viewpoint of avoiding pollution.

In summary, we have found a facile and efficient method for the Beckmann rearrangement of ketoximes to corresponding amides by using sulfamic acid/zinc chloride. The present procedure has many advantages such as mild conditions, excellent yields, and inexpensive and recyclable catalyst.

EXPERIMENTAL

The starting materials, ketoximes, were prepared according to method reported in literature,^[25] and melting points are uncorrected.

General Methods

Sulfamic acid (0.3 mmol) and zinc chloride (0.2 mmol) were added to a solution of ketoxime (1 mmol) in acetonitrile (3 mL). The mixture was heated to reflux (90 °C) for the period as indicated in Table 3. The progress of the reaction was monitored by thin-layer chromatography (TLC). After the completion of the reaction, the reaction was dispersed into 10 mL cooled diethyl ether to precipitate sulfamic acid. The resulting suspension was filtered to recycle sulfamic acid. The filtrate was evaporated, and the residue was dissolved in ethyl acetate and washed with a small amount of water. The combined organic layer was dried over anhydrous magnesium sulfate and filtered. Ethyl acetate was evaporated under reduced pressure to give the crude product, which was separated by column chromatography on silica (200–100 mesh),

eluted with petroleum ether or the mixture of petroleum ether and ethyl acetate (V/V = 3/1). The authenticity of the product was established by their melting points compared with that reported in the literature.

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