

Sulfamic acid as a cost-effective and recyclable catalyst for liquid Beckmann rearrangement, a green process to produce amides from ketoximes without waste

Bo Wang, Yanlong Gu, Cheng Luo, Tao Yang, Liming Yang* and Jishuan Suo

*State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics,
Chinese Academy of Sciences, Lanzhou 730000, China*

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Abstract—Sulfamic acid ($\text{H}_2\text{NSO}_3\text{H}$) has been proved to be an efficient and green catalyst for liquid Beckmann rearrangement of ketoxime in dried acetonitrile. The use of basic neutralization agent has been avoided in this system due to its intrinsic zwitterionic property. Thus it is a green process for preparation of amide from ketoxime without producing any waste.

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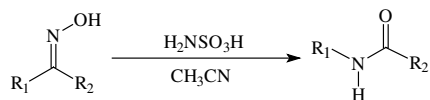
The conversion of ketoxime into corresponding amide, known as the Beckmann rearrangement, is a common method used in organic chemistry¹ and is also a topic of current interest. It accomplishes both the cleavage of a carbon–carbon bond and the formation of a carbon–nitrogen bond, and represents a powerful method particularly for manufacturing ϵ -caprolactam in the chemical industry. The reaction generally requires high reaction temperature and strong acidic and dehydrating media,¹ thus, the application of sensitive substrates is usually impeded in this reaction. On these basis, mild conditions were tried and several interesting variants were developed.^{2,3} Recently, the Beckmann rearrangement was reported to be accomplished in ionic liquids at room temperature.⁴ Nevertheless, until now the occurrence of mild conditions was only related to the use of rather toxic solvents and expensive reagents. On the other hand, the problem, which is almost common to all conventional catalytic systems, is that it is very difficult to separate the product from the solution containing catalyst, because there exists on the inevitable interaction of acidic catalyst with basic substrates (including ketoximes and amides), and as a result, a large amount of basic neutralization agent has to be used to obtain a

neat desired product, so that the reaction can lead to large amounts of byproducts. Therefore, it is necessary to develop a green, simple, and cost-effective catalytic system for Beckmann rearrangement of ketoxime.

Sulfamic acid ($\text{NH}_2\text{SO}_3\text{H}$, SA) is a dry, nonvolatile, nonhygroscopic, odorless, and white crystalline solid with an outstanding physical property and stability. The crystal can be kept in the laboratory for many years without change. It is commercially available and is a very cheap chemical. Recently, it is shown that SA has the prospect to be used as a substitute for conventional acidic catalytic materials. Last year, it has been used as an efficient heterogeneous acid catalyst for ketal formation or acetalation⁵ and deprotection of acetals.⁶ Subsequently, we reported sulfamic acid catalyzed tetrahydropyranylation of hydroxy compounds,⁷ esterification of cyclic olefins with aliphatic acids under solvent-free conditions,⁸ and transesterification of β -ketoesters in ionic liquids.⁹ In those homogeneous liquid reactions, SA is recyclable and is easy to handle as a catalyst owing to its immiscibility with common organic solvents, and the unique catalytic features and intrinsic zwitterionic property of SA is very different from the conventional acidic catalyst, which prompted us to explore further applications of $\text{NH}_2\text{SO}_3\text{H}$ as an acidic catalyst in other carbon–carbon and carbon–heteroatom forming reactions. We report herein, for the first time, sulfamic acid catalyzed liquid Beckmann rearrangement of ketoximes to produce corresponding amides without producing any waste (Scheme 1).

Keywords: Beckmann rearrangement; Sulfamic acid; Ketoxime; Amide; Green synthesis.

* Corresponding author. Tel.: +86-931-8277635; fax: +86-931-82770-88; e-mail: limy@ns.lzb.ac.cn

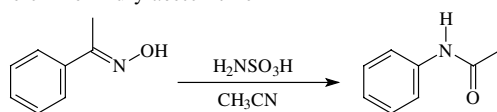


Scheme 1. Sulfamic acid catalyzed liquid Beckmann rearrangement of ketoximes.

Initially, acetophenone oxime has been used as a substrate to test the feasibility of sulfamic acid used as a catalyst for Beckmann rearrangement. Thus, treatment of acetophenone oxime with sulfamic acid at 90 °C in dried acetonitrile afforded a 96% yield of acetanilide after 6 h of reaction. Better catalytic activity of sulfamic acid was obtained with 10% of catalyst than with 5% or without any catalyst (Table 1, entries 1–3). The only by-product being confirmed is acetophenone, which is derived from the deoxygenation of acetophenone oxime. Subsequent experiments revealed that both 6 h and 90 °C are necessary to complete the reaction. When 4 h or 60 °C is used, the yield of acetanilide is only 34.0% and 30.0%, respectively (entries 4 and 5).

Table 2 shows the effects of different solvents on the reaction of acetophenone oxime catalyzed by sulfamic acid at 90 °C. In CCl₄, the conversion of the substrate proves to be quite high, almost 90%, but the selectivity to acetanilide is only 4% after 6 h (entry 1). In contrast to nonpolar organic solvents, high reaction rate and improved selectivity are the features obtained in polar

Table 1. Sulfamic acid catalyzed Beckmann rearrangement of acetophenone oxime in dry acetonitrile



Entry	Cat./oxime (%)	Temperature (°C)	Time (h)	Yield ^a
1	10	90	6	96
2	5	90	6	27
3 ^b	—	90	6	0
4	10	60	6	30
5	10	90	4	34

^a GC yield.

^b Without catalyst.

Table 2. Sulfamic acid catalyzed Beckmann rearrangement of acetophenone oxime in different solvents^a

Entry	Solvent	Conversion (%) ^b	Selectivity (%) ^c
1	CCl ₄	90	4
2	Toluene	60	25
3	CH ₃ CN	99	98
4	NMP	85	76
5	DMF	92	50
6	DEC	70	25
7	[BMIm]Cl	—	—

^a Reaction conditions: 0.6 g (4.42 mmol) acetophenone oxime, 0.042 g (0.44 mmol) sulfamic acid, 90 °C, 6 h.

^b Conversion of acetophenone oxime.

^c Selectivity to acetanilide.

organic solvents. For example, the treatment of acetophenone oxime with sulfamic acid in acetonitrile afforded the acetanilide in a selectivity of 98% with a nearly complete conversion whereas the same reaction in toluene give a mixture of acetophenone and acetanilide in a ratio of 3:1 with a conversion of 60% of oxime (entries 2 and 3). Although all other polar organic solvents are effective media for sulfamic acid catalyzed Beckmann rearrangement, acetonitrile is proved to be the best (entries 4–6). Chloride based imidazolium ionic liquids, such as 1-butyl-3-methylimidazolium chloride ([BMIm]Cl), has been used as a novel solvent for sulfamic acid catalyst in our previous work.⁹ Unfortunately, Beckmann rearrangement of acetophenone oxime does not effectually proceed in [BMIm]Cl (entry 7).

Since avoiding the production of waste in the product separation procedure was the aim for developing a new catalytic system, the isolation of acetanilide was also attempted. It has already been manifested that sulfamic acid was comprised not of the aminosulfonic acid form, but rather of ⁺H₃NSO₃⁻ zwitterionic units by both X-ray and neutron diffraction techniques.¹⁰ So, sulfamic acid is immiscible with diethyl ether, and it can be precipitated from the reaction mixture by dispersing it in a large amount of diethyl ether. After filtration, a neat product can be obtained by concentrating the filtrate and followed by the elution of acetone using a chromatographic column. Most importantly, no interaction was happening between the ketoximes and amides with sulfamic acid catalyst, as a result, the neutralizing agent that is absolutely necessarily, can be avoided. This procedure is significant from the viewpoint of avoiding pollution. The separation procedure is shown schematically in Figure 1. It appears that all solvents and catalyst are recyclable and no waste is produced in Beckmann rearrangement of acetophenone oxime over the sulfamic acid catalytic system. Thus, the sulfamic acid/dried acetonitrile system represents a substantial improvement over previous methods,¹¹ wherein an excess of bases (such as ammonia water, Na₂CO₃, etc.) is required to affect the product separation would produce a large amount of wastes at the same time.

Table 3 shows the results of Beckmann rearrangement of various ketoximes over H₂NSO₃H in dried acetonitrile. It has shown that aryl ketoximes have higher activity than the others, and acetophenone oxime has the best result among the oximes in this sulfamic acid system (entry 1–4). Cyclohexanone oxime and cyclopentanone oxime also provide moderate yields (entries 5 and 6). Using short chain aliphatic ketoximes, acetone oxime, and butanone oxime, 47% and 53% of yields of product is achieved by this method (entries 7 and 8). It is seen that the sulfamic acid/dried acetonitrile system has good activity for the Beckmann rearrangement of a variety of ketoximes, especially for aryl ketoximes.

The reuse ability of H₂NSO₃H was studied in this system. The catalyst can be so easily separated by dispersing the reaction mixture in diethyl ether, that the recovery and reuse of H₂NSO₃H could be very

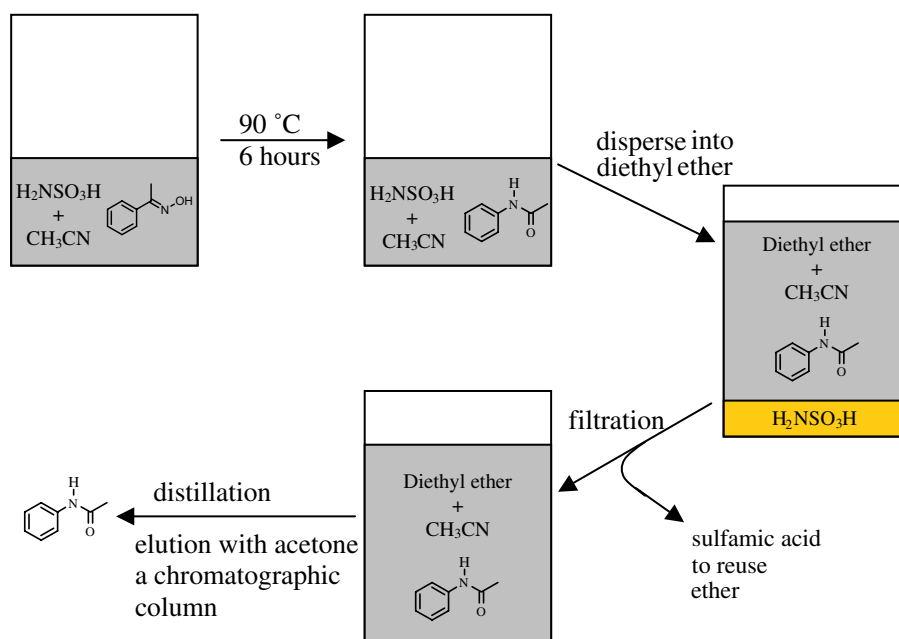


Figure 1. Procedure of product separation in sulfamic acid catalyzed Beckmann rearrangement.

Table 3. Beckmann rearrangement of various ketoximes over sulfamic acid in dried acetonitrile^a

Entry	Substrate	Time (h)	Product	Yield (%) ^b
1		6		96
2		8		95
3		8		88
4		8		85
5		6		40
6		6		59
7		6		53
8		6		47
9 ^c		6		85

^a Reaction conditions: 4.42 mmol ketoxime, 0.042 g (0.44 mmol) sulfamic acid, 90°C .

^b Yields of products of rearrangement.

^c Reuse for four time.

convenient. As shown in entry 9, the yield of acetophenone oxime only decreases a little after the reuse of $\text{H}_2\text{NSO}_3\text{H}$ for four times.

The specific zwitterionic feature of sulfamic acid has been proved to provide an efficient route for separating corresponding products of Beckmann rearrangement of ketoximes, and the sulfamic acid/dried acetonitrile system also has made an improvement over previous methods for producing corresponding amides in dried acetonitrile. The use of basic neutralization agent has been avoided, and all the solvents and catalyst are recyclable and no waste is produced. Thus it is a green process for the preparation of amide from ketoxime without producing any waste.

A representative procedure as follows: To acetophenone oxime (4.42 mmol) in dried acetonitrile (5 mL), was added sulfamic acid (0.42 g, 0.44 mmol) and the mixture was heated at 90 °C for 6 h. And then the reaction content was dispersed into 15 mL cooled diethyl ether, so that the catalyst of sulfamic acid could be precipitated out. After filtrating, the liquid content could be analyzed by GC. The concentration of reactant and product was directly given by the system of GC chemstation according to the area of each chromatograph peak. The pure products could be obtained by the distillation and then separating it on silica gel column using acetone as eluent.

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