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p-Toluenesulfonic acid mediated zinc chloride: highly effective catalyst for the Beckmann rearrangement

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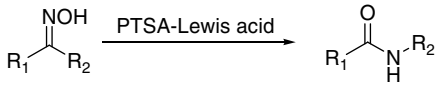
Abstract—PTSA–$ZnCl_2$ has been proved to be an excellent catalyst for liquid-phase Beckmann rearrangement of ketoximes in acetonitrile. The satisfactory yields of amides were obtained in the present of this catalyst system.

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. It accomplishes both the cleavage of carbon–carbon bond and the formation of a carbon–nitrogen bond, and represents a powerful method particularly for manufacture of ε-caprolactam in the chemical industry. This reaction, however, generally requires high reaction temperature and a large amount of a strong Brønsted acid and dehydrating media, causing large numbers of byproducts and serious corrosion problems.[1] Although a great number of the vapor-phase Beckmann rearrangement processes have been reported, low selectivity for ε-caprolactam and rapid decay of activity generally resulted under very high reaction temperatures.[2] Liquid-phase catalytic Beckmann rearrangement under mild condition, on the contrary, can be obtained with high conversion and selectivity.[3] On these basis, mild conditions were tried and several interesting variants were developed, for example, using ionic liquid at room temperature,[4] trifluoromethanesulfonic acid,[5] chlorosulfonic acid,[6] sulfamic acid,[7] cyanuric chloride,[8] chloral,[9] anhydrous oxalic acid,[10] *O*-alkyl-*N*,*N*-dimethylformamidium salt,[11] ethyl chloroformate/boron trifluoride etherate,[12] P_2O_5,[13] bis(2-oxo-3-oxazolidinyl)phosphinic chloride[14] and diethyl chlorophosphate.[15] However, these methods currently suffer from the use of toxic solvent, expensive reagents and low yields. Therefore, it is necessary to develop a simple, clean and no expensive catalyst system for the Beckmann rearrangement of ketoxime.

p-Toluenesulfonic acid (PTSA) is commercially available and is a very cheap chemical with stability. Recently, it is shown that PTSA has the prospect to be used as a substitute for conventional acidic catalytic materials. Last year, it has been used as an efficient acid catalyst for the synthesis of 4(3H)-quinazolinones,[16] the regiospecific nitration of phenols[17] and the carbonylation of formaldehyde.[18] Herein we wish to report our preliminary results on the first highly effective *p*-toluenesulfonic acid (PTSA) mediated zinc chloride catalyzed the Beckmann rearrangement of ketoxime to produce corresponding amides without producing any waste (Scheme 1).

Initially, acetophenone oxime has been used as a substrate to test the feasibility of PTSA/$ZnBr_2$ used as a catalyst for the Beckmann rearrangement. The results are summarized in Table 1. Scarcely any reaction occurred when PTSA and $ZnBr_2$ were used as a sole catalyst (Table 1, entries 1 and 2). While the reaction was conducted with PTSA mediated zinc bromide, the 93% yield of acetanilide was obtained (Table 1, entry 3). The only by-product being confirmed is acetophenone, which is derived from the deoximation of acetophenone oxime.



Scheme 1.

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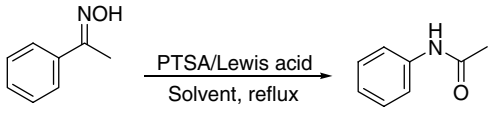
Table 1. Effects of reaction conditions on the Beckmann rearrangement of acetophenone oxime[a]



Entry	Catalyst I	Catalyst II	Solvent	Reaction time [h]	Yield[e] (%)
1	—	$ZnBr_2$	MeCN	5.0	—
2	PTSA	—	MeCN	5.0	—
3	PTSA	$ZnBr_2$	MeCN	5.0	93
4	Acetic acid	$ZnBr_2$	MeCN	5.0	68
5	Benzoic acid	$ZnBr_2$	MeCN	5.0	41
6	PTSA	$ZnCl_2$	MeCN	5.0	93
7	PTSA	$SnCl_4$	MeCN	5.0	67
8	PTSA	$FeCl_3$	MeCN	5.0	51
9	PTSA	$Zn(OAc)_2$	MeCN	5.0	—
10	PTSA	$ZnCl_2$	$MeNO_2$	5.0	82
11	PTSA	$ZnCl_2$	Toluene	5.0	—
12	PTSA	$ZnCl_2$	1,4-Dioxane	5.0	—
13[b]	PTSA	$ZnCl_2$	MeCN	5.0	51
14[c]	PTSA	$ZnCl_2$	MeCN	5.0	98
15[d]	PTSA	$ZnCl_2$	MeCN	5.0	99
16	PTSA	$ZnCl_2$	MeCN	2.0	75
17	PTSA	$ZnCl_2$	MeCN	3.0	90
18	PTSA	$ZnCl_2$	MeCN	4.0	95

[a] Reaction and conditions: catalyst I (0.10 mmol), catalyst II (0.10 mmol), acetophenone oxime (1.0 mmol), solvent 5 mL.
[b] $ZnCl_2$ 0.05 mmol.
[c] $ZnCl_2$ 0.12 mmol.
[d] $ZnCl_2$ 0.15 mmol.
[e] GC yield.

The effects of the various organic acid on the Beckmann rearrangement of acetophenone oxime were also investigated (Table 1). When using acetic acid or benzoic acid as a substitute, the yield of acetanilide is only 68% and 41%, respectively (Table 1, entries 4 and 5). This was probably due to the different acidities of the various organic acid.

Next, we examined the effect of the different Lewis acids on the Beckmann rearrangement of acetophenone oxime. From Table 1, it is clear that $ZnCl_2$ and $ZnBr_2$ showed the best co-catalytic effects (Table 1, entries 3, 6–9). $ZnCl_2$ is chosen as the co-catalyst for the Beckmann rearrangement because it is much cheaper than $ZnBr_2$ and has satisfactory activity. At the same time, the effect of the amount of $ZnCl_2$ was investigated. The results suggested that increasing the amount of $ZnCl_2$ had a pronounced positive effect on the catalytic activity (Table 1, entries 6, 13–15). However, the enhancement of $ZnCl_2$ beyond 0.12 mmol gave only a slight increase in the yield of acetanilide.

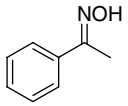
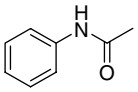
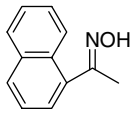
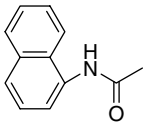
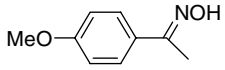
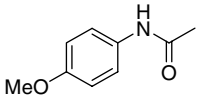
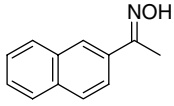
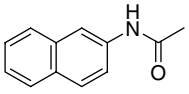
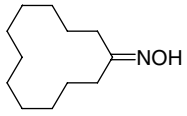
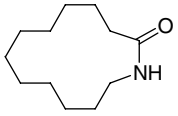
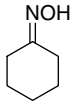
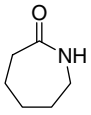
In order to established the optimized reaction conditions, we examined the effect of the solvent. Polar and nucleophilic solvents, such as acetonitrile and nitromethane, were suitable for this catalyst (Table 1, entries 6 and 10). When using toluene and 1,4-dioxane as solvent, the product of the Beckmann rearrangement was not found (Table 1, entries 11 and 12). It shows that solvent plays an important role in this reaction. The reaction time effect was also investigated. It has shown that the increase of the reaction time is propitious for the increasing yield of acetanilide (Table 1, entries 16–18).

To explore the generality and scope of the Beckmann rearrangement catalyzed by PTSA/$ZnCl_2$, respective ketoximes as substrates were examined under reflux condition in acetonitrile for 5 h (Table 2). The results showed that excellent yields were obtained with aromatic ketoximes (Table 2, entries 1–4) in this PTSA/$ZnCl_2$ catalytic system. Cyclododecanone oxime was also very reactive and converted to the corresponding amide in 93% of yield (Table 2, entry 5), which was useful as a staring material for nylons. When cyclohexanone oxime was used as substrate, the ε-caprolactam provided moderate yield (Table 2, entry 6). Unfortunately, acetone oxime was extremely unreactive to the corresponding amide (Table 2, entry 7).

In summary, the Beckmann rearrangement of aromatic ketoximes can be conducted with PTSA/$ZnCl_2$ as a catalyst under mild condition, excellent yield of corresponding amides was obtained and the results strongly depended on the nature of the solvents used. This offers an attractive catalytic system for the Beckmann rearrangement. Further studies are in progress in our laboratories to clarify the catalytic mechanism and to explore more versatile mediate catalytic system for the Beckmann rearrangement.

General procedure: For each reaction, the oxime (1.0 mmol), PTSA (0.1 mmol), $ZnCl_2$ (0.12 mmol) and acetonitrile (5.0 mL) were charged into 50 mL round bottom flask equipped with a magnetic stirrer and condenser. The mixture was refluxed for 5.0 h and cooled to room temperature. Qualitative analyses were conducted with HP6890/5973 GC–MS and quantitative analyses

Table 2. The effects of the different oxime on the Beckmann rearrangement[a]

Entry[a]	Substrate	Product	Yield[b] (%)
1			97
2			92
3			97
4			90
5			93
6			40
7			—

[a] Reaction and conditions: PTSA (0.10 mmol), $ZnCl_2$ (0.12 mmol), oxime (1.0 mmol), acetonitrile 5 mL, reaction time 5.0 h.
[b] Isolated yield.

were conducted with Agilent 6820 equipped with FID detector.

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References and notes

1. Smith, M. B.; March, J. In *Advanced Organic Chemistry*, 5th ed.; John Wiley and Sons: New York, 2001; p 1415.
2. (a) Heitmann, G. P.; Dahlhoff, G.; Niederer, J. P. M.; HÖlderich1, W. F. *J. Catal.* **2000**, *194*, 122; (b) Mao, D.; Chen, Q.; Lu, G. *Appl. Catal. A* **2003**, *244*, 273; (c) Tsai, C.; Zhong, C.; Wang, I.; Liu, S.; Chen, W.; Tsai, T. *Appl. Catal. A* **2004**, *267*, 87; (d) Ishida, M.; Suzuki, T.; Ichihashi, H.; Shiga, A. *Catal. Today* **2003**, *87*, 187; (e) Ichihashi, H.; Kitamura, M. *Catal. Today* **2002**, *73*, 23; (f) Dongare, M. K.; Bhagwat, V. V.; Ramana, C. V.; Gurjar, M. K. *Tetrahedron Lett.* **2004**, *45*, 4759; (g) Forni, L.; Fornasari, G.; Tosi, C.; TrifirÒ, F.; Vaccari, A.; Dumeignil, F.; Grimblot, J. *Appl. Catal. A* **2003**, *248*, 47; (h) Ko, Y.; Kim, M. H.; Kim, S. J.; Seo, G.; Kim, M.-Y.; Uh, Y. S. *Chem. Commun.* **2000**, 829; (i) Mao, D.; Lu, G.; Chen, Q. *J. Mol. Catal. A: Chem.* **2005**, *240*, 164; (j) Ghiaci, M.; Abbaspur, A.; Kalbasi, R. *J. Appl. Catal. A: Gen.* **2005**, *287*, 83; (k) Palkovits, R.; Yang, C.; Olejnik, S.; Schüth, F. *J. Catal.* **2006**, *243*, 93; (l) Bu, Y.; Wang, Y.; Zhang, Y.; Wang, L.; Mi, Z.; Wu, W.; Min, E.; Fu, S. *Catal. Commun.* **2007**, *8*, 16.
3. (a) Nguyen, M. T.; Raspoet, G.; Vanquickenborne, L. G. *J. Am. Chem. Soc.* **1997**, *119*, 2552; (b) Elgue, S.; Prat, L.; Coget, P. *Separat. Purific. Technol.* **2004**, *34*, 273.
4. (a) Peng, J.; Deng, Y. *Tetrahedron Lett.* **2001**, *42*, 403; (b) Gui, J.; Deng, Y.; Hu, Z.; Sun, Z. *Tetrahedron Lett.* **2004**, *45*, 2681; (c) Du, Z.; Li, Z.; Gu, Y.; Zhang, J.; Deng, Y. *J. Mol. Catal. A: Chem.* **2005**, *237*, 80; (d) Guo, S.; Du, Z.; Zhang, S.; Li, D.; Li, Z.; Deng, Y. *Green Chem.* **2006**, *8*, 296.
5. (a) Zumi, Y. *Chem. Lett.* **1990**, 2171; (b) Narasaka, K.; Kusama, H.; Yamashita, Y.; Sato, H. *Chem. Lett.* **1993**, 489.
6. Li, D.; Shi, F.; Guo, S.; Deng, Y. *Tetrahedron Lett.* **2005**, *46*, 671.

7. Wang, B.; Gu, Y.; Luo, C.; Yang, T.; Yang, L.; Suo, J. *Tetrahedron Lett.* **2004**, *45*, 3369.
8. (a) De, L. L.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272; (b) Furuya, Y.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 11240.
9. Chandrasekhar, S.; Gopalaiah, K. *Tetrahedron Lett.* **2003**, *44*, 755.
10. Chandrasekhar, S.; Gopalaiah, K. *Tetrahedron Lett.* **2002**, *43*, 2455.
11. Izumi, Y. *Chem. Lett.* **1990**, 2171.
12. Antikumar, S.; Chandrasekhar, S. *Tetrahedron Lett.* **2000**, *41*, 5427.
13. Ren, R. X.; Zueva, L. D.; Ou, W. *Tetrahedron Lett.* **2001**, *42*, 8441.
14. Zhu, M.; Cha, C.; Deng, W.; Shi, X. *Tetrahedron Lett.* **2006**, *47*, 4861.
15. Sardarian, A. R.; Shahsavari-Fard, Z.; Shahsavari, H. R.; Ebrahimi, Z. *Tetrahedron Lett.* **2007**, *48*, 2639.
16. Narasimhulu, M.; Mahesh, K. C.; Reddy, T. S.; Rajesh, K.; Venkateswarlu, Y. *Tetrahedron Lett.* **2006**, *47*, 4381.
17. Anuradha, V.; Srinivas, P. V.; Aparna, P.; Rao, J. M. *Tetrahedron Lett.* **2006**, *47*, 4933.
18. Li, T.; Souma, Y.; Xu, Q. *Catal. Today* **2006**, *111*, 288.