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Highly efficient Beckmann rearrangement and dehydration of oximes

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Abstract—Under mild conditions, Beckmann rearrangement of a variety of ketoximes could proceed in the presence of chlorosulfonic acid using toluene as a solvent with excellent conversion and selectivity. This procedure could also be applied in the dehydration of aldoximes for obtaining the corresponding nitriles.

1. Introduction

A great effort has been made to know, to lucubrate, and to manufacture the amides and the transformation of ketoximes to corresponding amides, known as the Beckmann rearrangement, is a common method, and is a topic of current interest. As it is widely known, the reaction generally requires relatively high reaction temperature, strong acid, for example, concentrated sulfuric acid, which usually lead to large amounts of waste.[1] On these bases, milder conditions were tried and investigations on clean, simple, and highly efficient processes became the chemists interesting undertaking. Needless to say, vapor-phase Beckmann rearrangement was a very important direction and many catalyst systems such as boria-hydroxyapatite,[2] metal ilerite,[3] supported oxide,[4] and zeolites including MCM-41,[5] MCM-22,[6] SAPO-11,[7] and MgCoAlPO-36[8] were reported. However, these processes were mainly concentrated on the synthesis of caprolactam and low selectivity or rapid decay of activity was generally resulted partially because of the high reaction temperature. As for the liquid-phase process, it usually proceeded under milder conditions and could afford various amides, and good results have been obtained by using $AlCl_3{\cdot}6H_2O/KI/H_2O/CH_3CN$,[9] cyanuric chloride/DMF,[10] sulfamic acid,[11] chloral,[12] anhydrous oxalic acid,[13] solid metaboric acid,[14] boron trifluoride etherate,[15] *O*-alkyl-*N*,*N*-dimethylformamidium salt,[16] tetrabutylammonium perrhenate,[17] chlorosulfonic acid–dimethyl formamide reagent,[18] and antimony(V) salt,[19] etc., as catalysts. Recently, the Beckmann rearrangement in supercritical water[20] and ionic liquids[21] were also reported, however, the yield in supercritical water was very low and the ionic liquid catalytic system was very complicated. Therefore, the development of simple, highly efficient, and highly selective Beckmann rearrangement process was still highly demanded.

At the same time, dehydration of oximes to nitriles is also an important transformation in organic syntheses and a number of methods have been developed[22] although the methods developed so far have their own limitations. For example, the use of extremely anhydrous reaction conditions, toxic, and hazardous chemicals and the need of cumbersome work-up procedures.[23–25] Therefore, the search for a more convenient method is still continuing.

We now wish to report a simple and efficient process for Beckmann rearrangement of ketoximes to amides or dehydration of aldoximes to nitriles using chlorosulfonic acid in toluene, in which the mole ratio of chlorosulfonic acid and oxime was 1:2 and it should be greener than the sulfuric acid system currently used.

2. Results and discussion

The Beckmann rearrangement of a series of alkyl and aryl ketoximes to corresponding amides was firstly conducted (Scheme 1).

Keywords: Beckmann rearrangement; Oxime; Dehydration; Chlorosulfonic acid; Catalysis.
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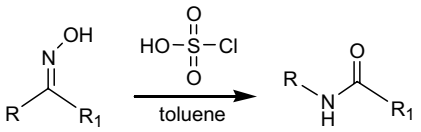

Scheme 1.

As it was shown in Table 1, moderate to good results were obtained over Beckmann rearrangement of acetone oxime, cyclopentanone oxime, and cyclohexanone oxime (entries 1–3). The conversion of these oximes all nearly 100%, however, the selectivities were only 43%, 64%, and 72%, respectively. Based on the qualitative analysis by GC–MS, it could be known that their main byproducts were the corresponding ketones and only trace amounts of dimeric oxime were observed (~0.1%). Much better results could be obtained if aryl ketoximes were used as substrates in Beckmann rearrangement reaction. The conversions of acetophenone oxime and its derivatives, for example, *p*-methyl acetophenone oxime, *p*-methoxyl acetophenone oxime, *m*(*p*)-amino acetophenone oxime, and *m*(*p*)-nitro acetophenone oxime, all nearly 100% with selectivities >98% (entries 4–10). No obvious different activities exhibited between *m*-amino (nitro) acetophenone oxime and *p*-amino (nitro) acetophenone oxime although it was reported previously that acetophenone oxime with *p*-position

Table 1. Results of Beckmann rearrangement of ketoximes to amides in toluene

Entry	Oximes	Products	Conversion (%)	Selectivity (%)
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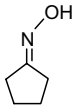
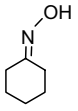
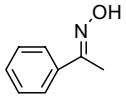
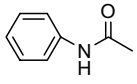
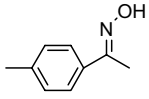
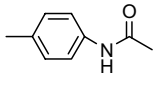
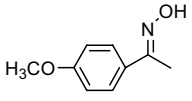
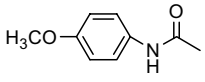
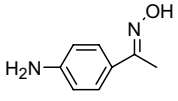
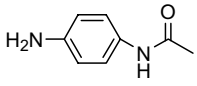
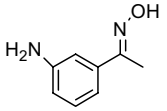
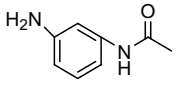
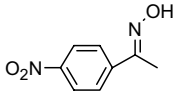
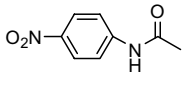
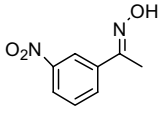
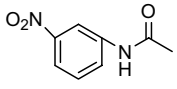
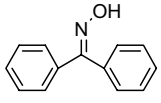
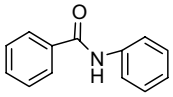
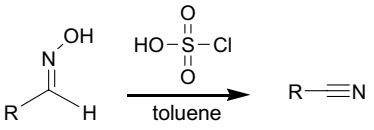
2			~99	64
3			~99	72
4			~99	98
5			~99	99
6			~99	99
7			~99	98
8			~99	98
9			~99	99
10			~99	98
11			~99	~100

substitutes were more active than that with *m*-position substitutes.[10] As to the Beckmann rearrangement of benzophenone oxime, a symmetrical oxime, its conversion reached to ~100% and no by-product was detected after reaction except the desired amide (entry 11).

The chlorosulfonic acid in toluene was also an efficient and versatile alternate system for the dehydration of aldoximes to nitriles (Scheme 2).

Under the same conditions, treatment of the aldoximes with chlorosulfonic acid in toluene afforded the corresponding nitriles rapidly and quantitatively (Table 2). Excellent results over aryl aldoximes with different substituted groups, for example, methoxyl, nitro, and hydroxyl, were obtained, which conversions and selectivities all nearly 100% (entries 1–6). Not as the low selectivities obtained in Beckmann rearrangement reaction of alkyl ketoximes, nearly 100% of conversion and selectivity were achieved for the dehydration of heptaldehyde oxime (entry 7).



Scheme 2.

3. Conclusions

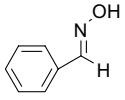
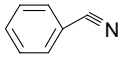
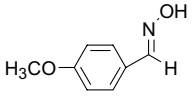
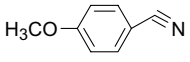
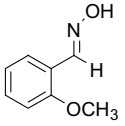
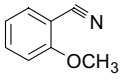
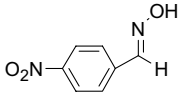
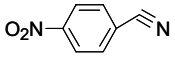
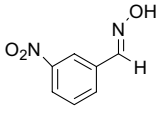
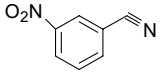
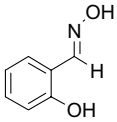
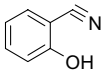
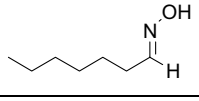
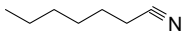
In conclusion, a simple and easily reproducible technique was developed for the Beckmann type or dehydration reaction of oximes, especially for aryl oximes, to corresponding amides and nitriles. The method seems to be convenient with respect to other reports and could be used as a valid alternative.

4. Experimental

All solvents and reagents were A.R. and the aryl oximes were recrystallized by ethanol/water before using to remove the ketones/aldehydes because the hydrolysis of aryl oximes usually occurred.

General procedure: for each reaction, the oxime (12 mmol, 0.88 g ~ 2.36 g) and toluene (3 ml) were charged into a 50 ml two mouth round-bottom flask equipped with a magnetic stirrer and condenser. Then the reactor was heated to 90 °C and chlorosulfonic acid (0.4 ml, 6 mmol) was added drop-wise to the mixture from the other mouth of the round-bottomed flask. The reaction was further reacted for 0.5 h and then the resulted mixture was cooled to room temperature. In order to achieve the isolated yields, 12 mmol of sodium hydroxide was added to the resulted mixture to neutralize the acid. Then adequate toluene was added to completely dissolve the product for analysis. Quantitative

Table 2. Results of dehydration of aldoximes to nitriles in toluene

Entry	Oximes	Products	Conversion (%)	Selectivity (%)
1			99	98
2			99	99
3			99	99
4			99	99
5			99	99
6			99	99
7			99	99

analyses were conducted with a HP 6890 GC equipped with a FID detector. Qualitative analyses were conducted with a HP 6890/5973 GC–MS with a chemstation containing a NIST mass spectral database.

Acknowledgements

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References and notes

1. (a) Gawly, R. E. *Org. React.* **1988**, *35*, 1; (b) Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; John Wiley & Sons: New York, 2001; p 1415.
2. Izumi, Y.; Sato, S.; Urabe, K. *Chem. Lett.* **1983**, 1649.
3. (a) Kim, S. J.; Jung, K. D.; Joo, O. S.; Kim, E. J.; Kang, T. B. *Appl. Catal. A: Gen.* **2004**, *266*, 173; (b) Ko, Y.; Kim, M. H.; Kim, S. J.; Seo, G.; Kim, M. Y.; Uh, Y. S. *Chem. Commun.* **2000**, 829.
4. (a) Dongare, M. K.; Bhagwat, V. V.; Ramana, C. V.; Gurjar, M. K. *Tetrahedron Lett.* **2004**, *45*, 4759; (b) Mao, D.; Chen, Q.; Lu, G. *Appl. Catal. A: Gen.* **2003**, *244*, 273.
5. (a) Dai, L. X.; Hayasaka, R.; Iwaki, Y.; Koyano, K. A.; Tatsumi, T. *Chem. Commun.* **1996**, 1071; (b) Dai, L. X.; Koyama, K.; Miyamoto, M.; Tatsumi, T. *Appl. Catal. A: Gen.* **1999**, *189*, 237; (c) Maheswari, R.; Sivakumar, K.; Sankarasubbier, T.; Narayanan, S. *Appl. Catal. A: Gen.* **2003**, *248*, 291; (d) Chaudhari, K.; Bal, R.; Chandwadkar, A. J.; Sivasanker, S. *J. Mol. Catal. A: Chem.* **2002**, *177*, 247.
6. (a) Dahlhoff, G.; Barsnick, U.; Hölderich, W. F. *Appl. Catal. A: Gen.* **2001**, *210*, 83; (b) Tsai, C. C.; Zhong, C. Y.; Wang, I.; Liu, S. B.; Chen, W. H.; Tsai, T. C. *Appl. Catal. A: Gen.* **2001**, *267*, 87.
7. Singh, P. S.; Bandyopadhayay, R.; Hegde, S. G.; Rao, B. S. *Appl. Catal.* **1996**, *136*, 249.
8. Raja, R.; Sankar, G.; Thomas, J. M. *J. Am. Chem. Soc.* **2001**, *123*, 8153.
9. Boruah, M.; Konwar, D. *J. Org. Chem.* **2002**, *67*, 7138.
10. Luca, L. De.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272.
11. Wang, B.; Gu, Y.; Luo, C.; Yang, T.; Yang, L.; Suo, J. *Tetrahedron Lett.* **2004**, *45*, 3369.
12. Chandrasekhar, S.; Gopalaiah, K. *Tetrahedron Lett.* **2003**, *44*, 755.
13. Chandrasekhar, S.; Gopalaiah, K. *Tetrahedron Lett.* **2003**, *44*, 7437.
14. Chandrasekhar, S.; Gopalaiah, K. *Tetrahedron Lett.* **2002**, *43*, 2455.
15. Anilkumar, R.; Chandrasekhar, S. *Tetrahedron Lett.* **2000**, *41*, 5427.
16. Izumi, Y. *Chem. Lett.* **1990**, 2171.
17. Narasaka, K.; Kusama, H.; Yamashita, Y.; Sato, H. *Chem. Lett.* **1993**, 489.
18. Kira, M. A.; Shaker, Y. M. *Egypt. J. Chem.* **1973**, *6*, 551.
19. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1991**, 1953.
20. (a) Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama, T.; Arai, M. *J. Am. Chem. Soc.* **2000**, *122*, 1908; (b) Sato, O.; Ikushima, Y.; Yokoyama, T. *J. Org. Chem.* **1998**, *63*, 9100; (c) Boero, M.; Ikeshoji, T.; Liew, C. C.; Terakura, K.; Parrinello, M. *J. Am. Chem. Soc.* **2004**, *126*, 6280; (d) Ikushima, Y.; Sato, O.; Sato, M.; Hatakeda, K.; Arai, M. *Chem. Eng. Sci.* **2003**, *58*, 935.
21. (a) Peng, J.; Deng, Y. *Tetrahedron Lett.* **2001**, *42*, 403; (b) Ren, R. X.; Zueva, L. D.; Ou, W. *Tetrahedron Lett.* **2001**, *42*, 8441; (c) Gui, J.; Deng, Y.; Hu, Z.; Sun, Z. *Tetrahedron Lett.* **2004**, *45*, 2681.
22. (a) Konwar, D.; Boruah, R. C.; Sandhu, J. S. *Tetrahedron Lett.* **1990**, *34*, 1063; (b) Kato, Y.; Ooi, R.; Asano, Y. *J. Mol. Catal. B: Enzym.* **1999**, *6*, 249.
23. Sosnovsky, G.; Krogh, J. A. *Synthesis* **1978**, 703.
24. Ho, T. L.; Wong, C. M. *Synth. Commun.* **1975**, *5*, 423.
25. Dulcere, J. P. *Tetrahedron Lett.* **1981**, *22*, 1599.