

황산-실리카에 의해 촉진된 Ketone의 효율적인 One-Pot 베크만 자리옮김 반응

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One-Pot Efficient Beckmann Rearrangement of Ketones Catalyzed by Silica Sulfuric Acid

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요 약. Microwave irradiation하에서 황산 실리카를 사용한 케톤에서 아미드의 합성을 관한 one-pot Beckmann 자리옮김 반응에 대한 보고이다. 산과 케톤의 몰비율이 1:2인 이 방법의 장점은 간단한 조작과 짧은 반응시간으로 높은 수율을 가진 위치선택적 반응이고, 최근에 사용되었던 방법보다 더 친환경적이다.

주제어: 황산-실리카, 케톤, 아미드, Microwave irradiation, Beckmann 자리옮김 반응

ABSTRACT. A one-pot Beckmann rearrangement for the preparation of amides from ketones is described using the silica sulfuric acid under Microwave irradiation. Advantages of this method are regioselectivity with high yields in a simple operation and short reaction time, in which the mole ratio of acid and ketone was 1:2 and it should be greener than the currently used systems.

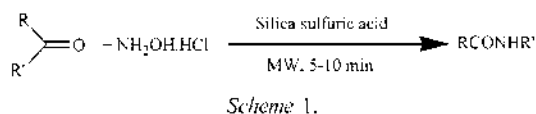
Keywords: Silica Sulfuric Acid, Ketones, Amides, Microwave Irradiation, Beckmann Rearrangement

INTRODUCTION

The rearrangement of ketoximes to the amides, known as the Beckmann reaction, is a common method in organic chemistry, and is a topic of current interest.^{1,2} The classical Beckmann rearrangement³ requires excess or stoichiometric amounts of strong protic acids such as concentrated sulfuric acid or phosphoric acid which cause a large amount of by-products and serious corrosion problems.¹ The reaction generally requires relatively high reaction temperature for long reaction times. On these bases, milder conditions were tried and investigations on clean, simple, environmentally benign, and highly

efficient processes became the chemists interesting undertaking.^{4,5} Several improved procedures have been reported using modified reagents⁶ and solid acids like clay⁷ and zeolites.⁸ However, most of these procedures involve vapor phase reactions⁹. Low selectivity of the migrating group and rapid decay of catalyst activity, generally resulted because of high reaction temperature.^{3,9} Furthermore, the reactions are sluggish when they are performed in the liquid phase.^{5a,10} Relatively few solid phase methods have been developed¹¹ and fewer methods are available for one-pot Beckmann rearrangement of ketones.¹²⁻¹⁵

We now wish to report a simple and efficient pro-



cess for one-pot Beckmann rearrangement of ketones to amides using silica sulfuric acid in solvent-free conditions, in which the mole ratio of acid and ketone was 1:2 and it should be greener than the sulfuric acid and chlorosulfonic acid systems which currently used¹⁶ in organic solvents (Scheme 1).

RESULTS AND DISCUSSION

Silica sulfuric acid is an excellent candidate for sulfuric acid or chlorosulfonic acid replacement in organic reactions without any limitation such as destruction of acid sensitive functional groups, use of rather toxic solvents and expensive reagents or solvents. Silica sulfuric acid can be easily prepared from commercially available starting materials.¹⁷ Chlorosulfonic acid was used as a catalyst in the Beckmann rearrangement¹⁶ of ketoximes to the corresponding amides in solvents such as DMF and toluene. However, a relatively large amount of these solvents was needed which are expensive and would cause environmental problems. Moreover, in the cases of aliphatic and cyclic ketones selectivity was decreased.

In order to prepare amides, various types of ketones were mixed with hydroxylamine hydrochloride and 0.5 equivalent of silica sulfuric acid in a mortar and pestle. The reaction mixture was irradiated in microwave oven for 5-10 minutes. The corresponding amide was obtained in high yields. The experimental results are summarized in Table 1.

As shown in the Table 1 several structurally varied ketones undergo clean, remarkably fast and direct nitrogen insertion reactions by a one-pot Beckmann-type reaction to the corresponding amides. This mild and versatile method can also be applied for both aromatic and aliphatic ketones. The Beckmann rearrangement of cyclic ketones proceeds effectively to afford the corresponding lactams in good to excellent yields (entries 1a-e and 2). In the

cases of unsymmetrical ketones the reaction was selective and one of the two possible amides produced (entries 3-5). Generally, migration of an aryl group predominates over that of an alkyl group. In the other cases, the major product being the one where the more bulky group has migrated (entries 6 and 7). Products were characterized by their physical constants, comparison with authentic samples, and IR and NMR spectra.^{4,13,14,18-21} In all ¹H-NMR spectra (CDCl₃, 25 °C) the NH group of amides appeared around 6-8 as a broad singlet and the ¹H chemical shifts and respective relative integrations of α -hydrogens are given in Table 1. In IR spectra the NH and C=O groups were observed around 3250-3350 and 1640-1680 cm⁻¹ respectively.

In conclusion, an environmentally benign method for synthesis of amides and lactams has been developed, which involves the one-pot Beckmann rearrangement of ketones using silica sulfuric acid as a reusable catalyst. In addition, it offers high yields, ease of work-up and high selectivity without formation of by-products such as tetrazoles, amino tetrazoles, nitriles and ureas.

EXPERIMENTAL SECTION

All melting points recorded are uncorrected open capillary measurements. IR spectra were recorded on a Shimadzu -IR 470 spectrophotometer. ¹H-NMR spectra were recorded on a Bruker-80 and 100 MHz instrument using tetramethylsilane (TMS) as an internal standard. Silica gel 60 (230-400 mesh) was purchased from Fluka and was dried in an oven at 120 °C for 2 h. Irradiation was carried out in a domestic microwave oven (Electra, 2450 MHz, 400 W) for optimized time. Silica sulfuric acid was obtained according to literature.¹⁷

Conversion of Ketones to Amides

General procedure: A mixture of ketone (2 mmol), hydroxylamine hydrochloride (4 mmol) and silica sulfuric acid (0.4 g, 1mmol) was grounded thoroughly in a mortar. The mortar was covered with a watch glass and put inside a domestic Microwave oven (2450 MHz, 400 W). The mixture was irradi-

Table 1. One-pot Preparation of Amides and Lactams from Ketones by Using Silica Sulfuric Acid.^a

Entry	Substrate	Products	Time (min)	Yield (%) ^b	B.p. °C (Torr) or M.p. °C		Selected ¹ H chemical shift ^c			
					Found	Reported[ref]	NH	U ₂ -N ⁻	U ₂ -CO	
1			a) n=0	5	72	38-9	38.5-39.5 [18]	6.5 (1)	3.3 (2)	2.3 (2)
			b) n=1	7	75	68-9	68-9 [14]	6.5 (1)	3.2 (2)	2.3 (2)
			c) n=2	7	72	69-70	69 [13a]	6.8 (1)	3.3 (2)	2.4 (2)
			d) n=3	7	68	195(760)	138(4) [19]	6.6 (1)	3.3 (2)	2.4 (2)
			e) n=7	7	75	143-9	143-9 [19]	6.1 (1)	3.2 (2)	2.4 (2)
2			7	78	68	68-9 [20]	6.4 (1)	3.2 (2)	2.5 (2)	
3			8	92	115	115 [14]	8.2 (1)	-	2.1 (3)	
4			10	85	179	179 [21]	7.4 (1)	-	2.2 (3)	
5			8	88	151	154 [21]	7.6 (1)	-	2.2 (3)	
6			10	73 ^d	213	216 [21]	6.2 (1)	-	2.2 (3)	
7			8	90 ^d	101-2	101-3 [14]	7.9 (1)	-	2.3 (2)	

^aProducts were characterized by their physical constants, comparison with authentic samples and IR and ¹H-NMR spectra^{4,13,14,18-21}. ^bIsolated yields. ^cThe numbers within the parentheses are the respective relative areas. ^dRatio of the products were determined from ¹H-NMR spectra of the crude product.

ated for the time indicated in Table 1. The progress of the reaction was monitored by TLC. After the reaction was complete, ethyl acetate (15 cm³) was added to the reaction mixture and silica sulfuric acid was removed by filtration. It was then washed with water (10 cm³) and dried over anhydrous CaCl₂ and the solvent evaporated in vacuum to give the crude product. Purification of solid products was achieved by crystallization from suitable solvent such EtOAc. Products are known compounds and were characterized by comparison of their spectral data (IR, ¹H-NMR) and physical properties with those reported in the literature.^{4,13,14,18-21}

REFERENCES

- (a) Gawly, R. E.; *Org. React.* **1988**, *35*, 1; (b) Donaruma, L. G.; Heldt, W. Z. *Org. React.* **1960**, *11*, 1.
- Smith, M. B.; March, J. *Advanced Organic Chemistry*; John Wiley & Sons: New York, U. S. A., 2001, 5th ed., p 1415 and references therein.
- (a) Beckmann, E. *Chem. Ber.* **1886**, *19*, 988; (b) Izumi, Y.; Sato, S.; Urabe, K. *Chem. Lett.* **1983**, 1649.
- (a) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *J. Org. Chem.* **2002**, *67*, 6272; (b) Yadav, J. S.; Reddy, B. V. S.; Madhavi, A. V.; Ganesh, Y. S. *J. Chem. Res. (S)* **2002**, 236; (c) Arisawa, M.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 311; (d) Kikugawa, Y.; Tsuji, C.; Miyazawa,

- E.; Sakamoto, T. *Tetrahedron Lett.* **2001**, *42*, 2337; (e) Anilkumar, R.; Chandrasekhar, S. *Tetrahedron Lett.* **2000**, *41*, 5427; (f) Thakur, A. J.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Synth. Commun.* **2000**, *30*, 2105.
5. (a) Sato, H.; Yoshioka, H.; Izumi, Y. *J. Mol. Catal. A: Chemical*, **1999**, *149*, 25; (b) Laurent, A.; Jacquault, P.; Di Martino, J. L.; Hamelin, J. *J. Chem. Soc., Chem. Commun.* **1995**, 1101.
6. (a) Imamoto, T.; Yokoyama, H.; Yokoyama, M. *Tetrahedron Lett.* **1981**, *22*, 1803; (b) Jung, M. E.; Zeng, L. M. *Tetrahedron Lett.* **1983**, *24*, 4533; (c) Kamijū, T.; Harada, H.; Lizuka, K. *Chem. Pharm. Bull.* **1984**, *32*, 2560; (d) Pai, S. G.; Bajpai, A. R.; Deshpande, A. B.; Samant, S. D. *Synth. Commun.* **1997**, *27*, 379.
7. (a) Bosch, A. I.; De la Cruz, P.; Diez-Barra, E.; Loupy, A.; Langa, F. *Synlett*, **1995**, 1259; (b) Meshram, H. M. *Synth. Commun.* **1990**, *20*, 3253.
8. (a) Reddy, J. S.; Ravishankar, R.; Sivasankar, S.; Ratnaswamy, P. *Catal. Lett.* **1993**, *17*, 139; (b) Bhawal, B. M.; Mahabate, S. P.; Likhite, A. P.; Deshmukh, A. R. A. S. *Synth. Commun.* **1995**, *25*, 3315.
9. (a) Ko, Y.; Kim, M. H.; Kim, S. J.; Seo, G.; Kim, M. Y.; Uh, Y. S. *Chem. Commun.* **2000**, 829; (b) Dai, L. X.; Koyama, K.; Miyamoto, M.; Tatsumi, T. *Appl. Catal. A: Gen.* **1999**, *189*, 237; (b) Ushikubo, T.; Wada, K. *J. Catal.* **1994**, *148*, 138.
10. Izumi, Y. *Chem. Lett.* **1990**, 2171.
11. (a) Khodaei, M. M.; Meybodi, F. A.; Rezaei, N.; Salehi, P. *Synth. Commun.* **2001**, *31*, 941; (b) Ghiaci, M.; Imanzadeh, H. *Synth. Commun.* **1998**, *28*, 2275.
12. Ganboa, I.; Palomo, C. *Synth. Commun.* **1983**, *13*, 941.
13. (a) Sharghi, H.; Hosseini, M. *Synthesis* **2002**, 1057; (b) Sharghi, H.; Hosseini, M. *J. Chem. Research (S)*, **2003**, 176.
14. Eshghi, H.; Gordi, Z. *Synth. Commun.* **2003**, *33*, 2971.
15. Gopalakrishnan, M.; Sureshkumar, P.; Kanagarajan, V.; Thanusu, J. *Lett. Org. Chem.* **2005**, *2*, 444.
16. (a) Kira, M. A.; Shaker, Y. M. *Egypt. J. Chem.* **1973**, *6*, 551; (b) Li, D.; Shi, F.; Guo, S.; Deng, Y. *Tetrahedron Lett.* **2005**, *46*, 671.
17. Zolfigol, M. A. *Tetrahedron* **2001**, *57*, 9509.
18. Conly, R. T. *J. Org. Chem.* **1958**, *23*, 1330.
19. Olah, G. A.; Fung, A. P. *Synthesis*, **1979**, 537.
20. R. C. Weast and J. G. Grasselli, *Handbook of Data on Organic Compounds*, 2nd Ed.; 1989.
21. A. I. Vogel. *Text Book of Practical Organic Chemistry*; 4th Ed.; Longman: London, U. K., 1986.