Iranian Journal of Organic Chemistry 2 (2009) 76-79

Silica sulfuric acid: an eco-friendly and reusable catalyst for synthesis of amides via Ritter reaction

Bi Bi Fatemeh Mirjalili[a*] and Bahareh Sadeghi[b]
[a]*Department of Chemistry, College of Science, Yazd University, Yazd. P.O.Box 89195-741, Iran*
[b]*Department of Chemistry, Islamic Azad University, Yazd Branch, P.O. Box 89195-155, Yazd, Iran*

Abstract: Silica sulfuric acid (SiO_2-OSO_3H) as an eco-friendly, readily available and reusable catalyst was applied for the synthesis of N-alkyl amides from nitriles and alcohols in Ritter reaction. This solvent free procedure is very simple with excellent yields and easy workup.

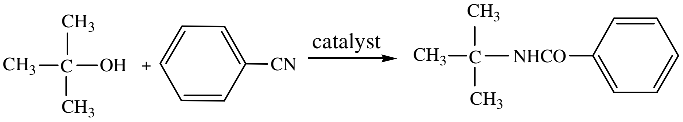
Keywords: Ritter reaction; Silica sulfuric acid; Amide, Nitrile; Alcohol; Solvent-free conditions

Introduction

The Ritter reaction has been known as an important methodology for amide synthesis via reaction of a nitrile with an alcohol [1]. This reaction is especially useful for the preparation of bulky amides from tertiary alcohols and various nitriles. The product *N-tert*-butyl amides are pharmaceutically important [2,3] and also serve as precursors of the corresponding amines. The method has also been beneficent for the syntheses of amides under the influence of certain catalysts such as $Ca(HSO_4)_2$ [4], P_2O_5/SiO_2 [5], $Bi(OTf)_3$ [6], $H_3PW_{12}O_{40}$ [7], Heteropoly acids [8], PMA/SiO_2 [9], Nafion® NR 50 [10] and MFI zeolites [11]. However, in some cases, the reuse of catalysts is not possible [4-6]. Silica sulfuric acid (SiO_2-OSO_3H), a solid acid, is a versatile catalyst that makes many reaction processes more convenient, more economic and environmentally benign. Owing to the numerous advantages associated with this cheap and non-hazardous catalyst, Silica sulfuric acid has been explored as a powerful catalyst for various organic transformations [12,13]. This solid acid has also been used in synthesis of oxazolines and imidazolines [14], synthesis of 2,3-dihydroquinazolin-4(1H)-ones [15], aromatization of 1,2-dihydroquinolines with $NaNO_2$ [16], chemoselective detritylation of 5'-tritylated nucleosides [17] and synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones [18]. In this research, we wish to report an efficient and versatile procedure for the preparaton of amides via Ritter reaction in the presence of silica sulfuric acid as catalyst.

Results and discussion

In continuation of our efforts to use solid acids in organic synthesis [13, 19-26], we herein report a simple and efficient protocol for Ritter reaction using a cheap and readily available SiO_2-OSO_3H catalyst. To become familiar with the efficacy of silica sulfuric acid, we selected some comparative experiments with some solid acids and the results are summarized in Table 1. These results clearly show the advantages of our methodology over other protic or Lewis acid catalyzed Ritter reactions. To optimize the reaction conditions, the reaction of *tert*-amyl alcohol and benzonitrile was used as a model reaction.



---

*Corresponding author. Fax: (+98) 351 8210644 Tel: (+98) 351 8211670-9 E-Mail: *fmirjalili@yazduni.ac.ir*

Table 1. Acid-catalyzed synthesis of *N*-(*tert*-butyl) benzamide

Entry	Catalyst(g) ((mmol))	Alcohol/Nitrile (mmol)	Condition/solvent	Time(h)/Yield(%)	Ref.
1	$Ca(HSO_4)_2$((1))	1/30.76	100^{o}C/nitrile	2/91	[4]
2	60%P_2O_5/SiO_2(0.2)	1/1	100^{o}C/-	2.5/92	[5]
3	$Bi(OTf)_3$((0.16))	0.8/3.9	100^{o}C/H_2O	17/85	[6]
4	PMA/SiO_2(2.9)	2.9/2.6	80^{o}C/-	6/95	[9]
5	$H_3PW_{12}O_{40}$ ((0.05))	1/3	reflux/H_2O	10/99	[7]
6	SiO_2-OSO_3H(0.05)	1/1	100^{o}C/-	2/78	-
7	SiO_2-OSO_3H(0.1)	1/1	100^{o}C/-	2/96	-
8	SiO_2-OSO_3H(0.15)	1/1	100^{o}C/-	2/97	-
9	SiO_2-OSO_3H(0.1)	1/1	50^{o}C/-	2/85	-
10	SiO_2-OSO_3H(0.1)	1/1	150^{o}C/-	2/90	-
11	SiO_2-OSO_3H(0.1)	1/1	reflux/DCM	4/63	-
12	SiO_2-OSO_3H(0.1)	1/1	reflux/EtOH	4/65	-
13	SiO_2-OSO_3H(0.1)	1/1	reflux/H_2O	4/78	-
14	SiO_2-OSO_3H(0.1), ^{2}nd run	1/1	100^{o}C/-	2/90	-
15	SiO_2-OSO_3H(0.1), ^{3}rd run	1/1	100^{o}C/-	2/87	-

Reactions at different temperatures and various molar ratios of substrates in the presence of SiO_2-OSO_3H revealed that the best conditions were solvent-free at 100°C and the best optimum molar ratio of alcohol (mmol):nitrile (mmol):SiO_2-OSO_3H (g) was 1:1:0.1. The reusability of the SiO_2-OSO_3H catalyst was also examined. After each run, $CHCl_3$ was added and the product was filtered, the solvent evaporated and the residue (catalyst) was washed with $CHCl_3$ and reused. Apparently, treatment with $CHCl_3$ removes tars more efficiently from the catalyst surface (Table 1, entries 14 and 15). This catalyst was reusable, although a gradual decline in activity was observed. The scope and generality of this protocol was demonstrated by subjecting a broad range of secondary and primary benzylic alcohols, secondary and tertiary aliphatic alcohols, ethanol and allyl alcohol to the reaction with acetonitrile, benzylic and aromatic nitriles in the presence of silica sulfuric acid (Table 2).

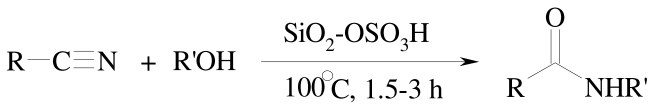


Table 2. Preparation of amides from alcohols and nitriles in the presence of SiO_2-OSO_3H under heterogeneous conditions

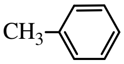
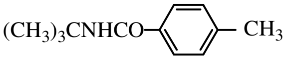
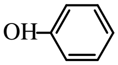
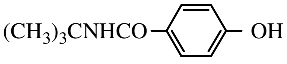
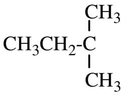
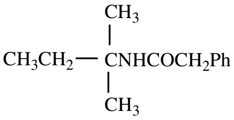
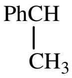
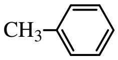
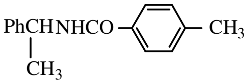
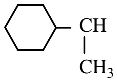
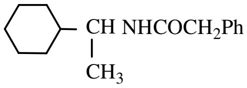
Entry	R'	R	Product^a	Time(h)/Yield (%)	Ref.
1	$(CH_3)_3C$	CH_3	$(CH_3)_3CNHCOCH_3$	1.5/90	[4]
2	$PhCH_2$	CH_3	$PhCH_2NHCOCH_3$	2/91	[28]
3	$PhCH_2$	Ph	$PhCH_2NHCOPh$	2.5/90	[4]
4	$(CH_3)_3C$	$PhCH_2$	$(CH_3)_3CNHCOCH_2Ph$	1.5/90	[28]
5	$(CH_3)_3C$	$CNCH_2$	$(CH_3)_3CNHCOCH_2CONHC(CH_3)_3$	3/74	[5]
6	$(CH_3)_3C$	C=C	$(CH_3)_3CNHCOCH=CH_2$	3/89	[28]
7	$CH_3CH_2C(CH_3)_2$	Ph	$CH_3CH_2C(CH_3)_2NHCOPh$	2/95	[6]
8	$(CH_3)_3C$			1.5/90	[27,28]

Table 2. Continued

9	$(CH_3)_3C$			2/89	[7]
10	$(CH_3)_3C$	Ph	$(CH_3)_3CNHCOPh$	2/96	[9]
11	$PhCH_2$	$PhCH_2$	$PhCH_2NHCOCH_2Ph$	2.5/89	[28]
12	 $CH_3CH_2\text{-}\overset{CH_3}{\underset{CH_3}{C}}$	$PhCH_2$	 $CH_3CH_2-\overset{CH_3}{\underset{CH_3}{C}}NHCOCH_2Ph$	1.5/91	[28]
13	 $\underset{CH_3}{PhCH}$			2/94	[28]
14	CH_3CH_2	$PhCH_2$	$CH_3CH_2\ NHCOCH_2Ph$	3/0	-
15	$CH_2{=}CHCH_2$	$PhCH_2$	$CH_2{=}CH-CH_2NHCOCH_2Ph$	3/85	-
16		$PhCH_2$		1.5/84	-

[a]Almost all products are known and were identified by their melting point, IR and ^{1}H-NMR spectra according to literature

In most cases, the reactions proceeded cleanly and the desired amides were obtained in excellent yields. Ritter reaction of simple allyl alcohol and secondary alcohols with nitriles in the presence of silica sulfuric acid afforded the corresponding amides in good yields. No Ritter reaction took place with ethanol as a primary alcohol. The efficiency of the present procedure was examined with 60 mmol of *tert*-butyl alcohol and acetonitrile which gave *N-tert*-butyl acetamide in 85% yield.

In summary, a general procedure for the conversion of nitriles into amides has been developed using a catalytic amount of silica sulfuric acid instead of corrosive acids. Under solvent-free conditions, silica sulfuric acid is a reusable, efficient, cheap, eco-friendly, readily available and heterogeneous catalyst for this reaction. Secondary, allylic and benzylic alcohols as well as tertiary alcohols react efficiently in Ritter reaction with some advantages such as selectivity, generality, simplicity, clean reactions, easy work up, scale up and improved yields.

Experimental

Alcohols, nitriles, silica gel, chlorosulfonic acid and other necessary chemical compounds were purchased from Fluka and Merck companies. Silica sulfuric acid was prepared according to literature [29]. The products were known and were characterized by IR and ^{1}H-NMR spectra and by comparing their physical properties with those reported in the literature. IR spectra were run on a Shimadzu IR-470 spectrometer. ^{1}H-NMR was obtained using a Bruker Avans 300 MHz spectrometer. Melting points were determined with a Barnstead Electrothermal Melting Point apparatus.

General Procedure for the Synthesis of Amides

A mixture of alcohol (3 mmol), nitrile (3 mmol), and silica sulfuric acid (0.3 g) was placed in a round bottom flask. The materials were mixed and heated at 100ºC for the given time (Table 2). The progress of the reaction was followed by TLC. After the completion of the reaction, the resulting mixture was cooled to room temperature and extracted with EtOAc (2 × 20 mL). The organic layer was washed with 10% $NaHCO_3$ and water, dried with Na_2SO_4 and concentrated to give the products in 74–96% yields. The solid was then crystallized with H_2O.

Acknowledgments

Financial support for this work by the Research Council of Yazd University and Islamic Azad University, Yazd Branch, is gratefully acknowledged.

References

[1] Ritter, J. J.; Minieri, P. P.; *J. Am. Chem. Soc.* **1948**, *70*, 4045.
[2] Benson, F. R.; Ritter, J. J.; *J. Am. Chem. Soc.* **1949**, *71*, 4128.
[3] Samguigni, J.A.; Levins, R.; *J. Med. Chem.* **1964**, *7*, 573.

[5] Niknam, K.; Zolfigol, M. A.; Sadabadia, T.; *J. Iran. Chem. Soc*. **2007**, *4*, 199.

[6] Tamaddon, F.; Khoobi, M.; Keshavarz, E.; *Tetrahedron Lett*. **2007**, *48*, 3643.

[7] Callens, E.; Burton, A. J.; Barrett, A. G. M.; *Tetrahedron Lett*. **2006**, *47*, 8699.

[8] Firouzabadi ,H.; Iranpoor, N.; Khoshnood, A.; *Catal.Commun*. **2008**, *9*, 529.

[9] Okuhara, T.; Chen, X.; Matsuda, H.; *Appl. Catal. A: Gen.* **2000***, 200,* 109.

[10] Yadav, J. S.; Subba Reddy, B. V.; Pandurangam, T.; Jayasudan Reddy, Y.; Gupta, M. K.; *Catal. Commun*. **2008**, *9*, 1297.

[10] Polshettiwar, V.; Varma, R. S.; *Tetrahedron Lett*. **2008**, *49*, 2661.

[11] Okuhara, T.; Chen, X.; *Microporous and Mesoporous Materials* **2001**, *48*, 293.

[12] Salehi, P.; Zolfigol, M. A.; Shirini, F.; Baghbanzadeh M.; *Curr. Org. Chem*. **2006,** *10*, 2171.

[13] Bamoniri, A.; Zolfigol, M. A.; Mohammadpoor-Baltork, I.; Mirjalili, B. F.; *J. Iran. Chem. Soc.* **2006**, *3,* 85.

[14] Mohammadpoor-Baltork, I.; Mirkhani, V.; Moghadam, M.; Tangestaninejad, Sh.; Zolfigol, M. A.; Abdollahi-Alibeik, M.; Khosropour, A. R.; Kargar, H.; Hojati, F.; *Catal. Commun*. **2008**, *9*, 894.

[15] Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Zolfigol, M. A.; Agheb, M.; Heydari, S.; *Catal.Commun*. **2008**, *9*, 785.

[16] Niknam, K.; Karami, B.; Zolfigol, M. A.; *Catal. Commun*. **2007**, *8*, 1427.

[17] Khalafi-Nezhad, A.; Parhami, A.; Soltani Rad, M. N.; Zolfigol, M. A.; Zare, A.; *Tetrahdron Lett*. **2007**, *48*, 5219.

[18] Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Bodaghi Fard, M. A.; *Tetrahdron Lett*. **2003**, *44*, 2889.

[19] Hajipour, A. R.; Zarei, A.; Khazdooz, L.; Mirjalili, B. F.; Sheikhan, N.; Zahmatkesh, S.; Ruoho, A. E.; *Synthesis* **2005**, *20*, 3644.

[20] Sadeghi, B.; Mirjalili, B. F.; Hashemi, M. M.; *Tetrahedron Lett*. **2008**, *49*, 2575.

[21] Hajipour, A. R.; Mirjalili, B. F.; Zarei, A.; Khazdooz, L.; Ruoho, A. E.; *Tetrahedron Lett.* **2004**, *45, 6607.*

[22] Bamoniri, A.; Zolfigol, M. A.; Mohammadpoor-Baltork, I.; Mirjalili, B. F.; *J. Iran. Chem. Soc.* **2006***, 3, 85.*

[23] Shirini, F.; Zolfigol, M. A.; Safari, A.; Mohammadpoor-Baltork, I.; Mirjalili, B. F.; *Tetrahedron Lett.* **2003**, *44*, 7463.

[24] Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Karimi-Zarchi, M. A.; Zaghaghi, Z. Parvaideh, M.; *J. Iran. Chem. Soc.*, **2007**, *4*, 340.

[25] Bamoniri, A.; Mirjalili, B. F.; Zolfigol, M. A.; Mohammadpoor-Baltork, I.; *J. Iran. Chem. Soc*. **2007**, *4*, 332.

[26] Sadeghi, B.; Mirjalili, B. F.; Hashemi, M. M.; *J. Iran. Chem. Soc.* **2008**, *5,* 694.

[27] Reddy, K. L.; *Tetrahedron Lett.* **2003**, *44*, 1453.

[28] (a) http://www.aist.go.jp/RIODB/SDBS/cgi-bin/cre_index.cgi, (b) http://www. Sigmaaldrich.com.

[29] Zolfigol, M. A.; *Tetrahedron* **2001**, *57*, 9509.