Silica sulfuric acid as a reusable catalyst for the conversion of ketones into amides by a Schmidt reaction under solvent-free conditions

Hossein Eshghi,[a,b]* Asadollah Hassankhani[b] and Elaheh Mosaddegh[b]

[a]Department of Chemistry, Ferdowsi University of Mashhad, Mashhad 91775-1436, Iran

[b]Department of Chemistry, Sistan and Baluchestan University Zahedan 98135-674 Iran

Silica sulfuric acid is a highly efficient reagent for the conversion of a variety of ketones into the corresponding amides by a Schmidt reaction under solvent-free conditions. Cyclic, aliphatic and aromatic ketones with electron-donating or withdrawing substituents may be converted easily in excellent yield. The major advantages of this method are: operational simplicity, the ready availability of the reagent, selectivity, general applicability, mild reaction conditions, short reaction times and high yields. The recovered catalyst could be used in new attempts without any purification.

Keywords: silica sulfuric acid, ketones, amides, schmidt reaction, solvent-free

The reaction of hydrazoic acid with carbonyl compounds, known as the Schmidt reaction,[1] is a convenient method for the synthesis of a wide variety of nitrogen-containing materials.[2] The traditional methods generally involve the use of excess or stoichiometric amounts of strong Brønsted or Lewis acids such as concentrated sulfuric acid,[3,4] polyphosphoric acid,[5] $POCl_3$,[6] HBr,[6] HCl,[6] $AlCl_3$[6] and solvents such as benzene,[3,6] concentrated sulfuric acid,[3,6] molten trichloroacetic acid,[6,7] glacial acetic acid[3] and nitrobenzene.[6] Until now there has been no report of reactions under solvent-free conditions. There is, therefore, a need to develop a convenient and mild procedure for the preparation of amides and lactams from ketones by the Schmidt reaction. The main disadvantages associated with classical procedures include the use of hydrazoic acid which presents considerable experimental difficulties due to its toxicity and tendency to explode. Replacement of hydrazoic acid by inorganic azides, which are poorly soluble in organic solvents, causes an increase in reaction time and decrease in product yield. In order to minimise this problem we have recently reported the synthesis of 1,5-fused tetrazoles by a Schmidt reaction under solvent-free conditions.[8]

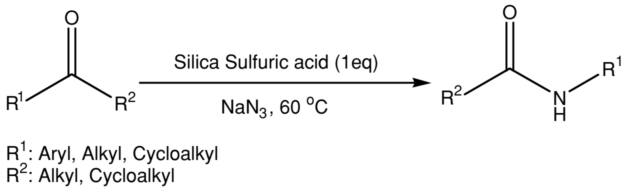
Recently, there has been a growing interest in the use of silica sulfuric acid in organic synthesis.[9-11] Silica sulfuric acid is an excellent candidate for sulfuric acid replacement in organic reactions as it does not lead to the destruction of acid sensitive functional groups.[11] Silica sulfuric acid can be easily prepared from commercially available starting materials.[9]

Following of our ongoing research programme to develop new synthetic methodologies for the Schmidt reaction of carbonyl compounds under solvent-free conditions, we have found that silica sulfuric acid can be used as a reagent for the reaction in dry media (see Scheme 1 and Table 1).

Results and Discussion

The general reaction is illustrated in the Scheme 1 and the results are reported in Table 1. All reactions were carried out by simple stirring of the reagents at 60 °C without solvent for 20–45 min (see Caution in Experimental Section). Cyclic, aliphatic and aromatic ketones with electron-donating or withdrawing substituents can be easily converted into the corresponding amides in excellent yield. The rearrangement products were identified in all cases by comparison with authentic samples prepared by reported procedures.[12]

Several cyclic ketones undergo the Schmidt reaction upon treatment with this catalyst to afford the corresponding lactams (entries 3–5). In some cases only one of the two possible amides and lactams is obtained (entries 1, 2, and 4). In the other cases, the major product is the one where the bulkier group has migrated (entries 6–9). Generally, migration of an aryl group predominates over that of an alkyl group (entries 1, 2, 6 and 7).



Scheme 1

In summary, we have developed a novel and efficient method for the synthesis of amides and lactams by the Schmidt reaction of ketones with sodium azide using silica sulfuric acid as a reusable catalyst. This method offers several advantages including mild reaction conditions, solvent-free media, operational simplicity, short reaction times, high yields, and high selectivity without formation of by-products[13, 14] such as tetrazoles, amino tetrazoles, nitriles and ureas.

Experimental

All melting points recorded are uncorrected open capillary measurements. IR spectra were recorded on a Shimadzu -IR 470 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker-80 and 100 MHz instruments using tetramethylsilane (TMS) as an internal standard. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instrument at 70 eV. Columns chromatography was carried out on short columns of silica gel 60 (230–400 mesh) in glass columns (2–3 cm diameter) using 15–30 g of silica gel per 1 g of crude mixture. Silica sulfuric acid was obtained according to the literature procedure.[9]

Caution: In our procedure, we added silica sulfuric acid to a mixture of the ketone and sodium azide and we have not observed any explosion or hazardous vapours by heating the reaction mixture at 60 °C. However, due care should be taken particularly in any reverse addition of sodium azide to a mixture of silica sulfuric acid and ketone.

Conversion of ketones to amides

General procedure: Silica sulfuric acid (2 mmol) was added to a mixture of the ketone (2 mmol), and NaN_3 (4 mmol) in a round-bottom flask (10 ml). The mixture was stirred and heated in an oil bath at 60 °C for 20–45 min. The progress of the reaction was monitored by TLC. After the reaction was complete, ethyl acetate (15 ml) was added to the reaction mixture and silica sulfuric acid was removed by filtration. The filtrate was then washed with water (10 ml), dried over anhydrous $CaCl_2$ and the solvent evaporated in a vacuum to give the crude product. Purification of the solid products was achieved by crystallisation from a suitable solvent such EtOH.

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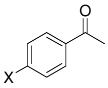
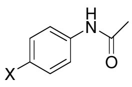
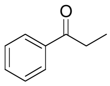
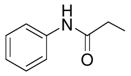
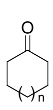
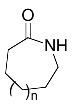
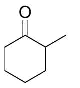
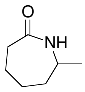
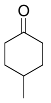
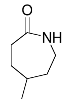
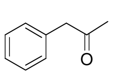
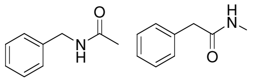
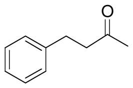
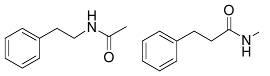
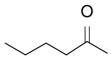
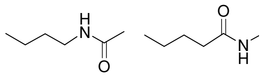
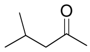
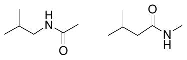
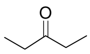
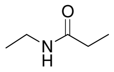
* Correspondent. E-mail: heshghi@ferdowsi.um.ac.ir

Table 1 Preparation of amides and lactams from ketones and sodium azide using silica sulfuric acid under solvent-free conditions[a]

Entry	Substrate	Products	Time/min	Yield/%[b]	B.p./°C (Torr) or M.p./°C	
					Found	Reported[ref]
1	 a) X = H b) X = Cl c) X = Me d) X = NO_2	 a) X = H b) X = Cl c) X = Me d) X = NO_2	25 35 25 45	95 92 91 90	115 179 151 213	115[12a] 179[12b] 154[12b] 216[12b]
2			30	95	101–102	101–103[12a]
3	 a) $n = 0$ b) $n = 1$ c) $n = 2$ d) $n = 3$ e) $n = 7$	 a) $n = 0$ b) $n = 1$ c) $n = 2$ d) $n = 3$ e) $n = 7$	25 35 35 30	95 92 92 92	38–39 68–69 69–70 195(760)	38.5–39.5[5a] 68–69[12a] 69[16] 138(4)[17]
4			30	95	148–149	148–149[17]
5			25	95	89–90	90–91[5a]
			35	93	68	68–69[18]
6		 3 : 1	25	91	58–60	58–59[12a]
7		 5 : 1	25	93	50–51	50–51[12a]
8		 3 : 1	20	92	228(760)[c]	229(760)[18]
9		 2.5 : 1	20	92	225(760)[c]	227(760)[19]
10			20	92	220(760)[c]	222(760)[18]

[a]Products were characterised by their physical constants, comparison with authentic samples and IR and NMR spectroscopy.[12,15-19] [b]Isolated yields. [c]Corresponded to the major product after column chromatography.

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