SHORT PAPER

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A convenient and efficient one-pot conversion of ketones into amides under microwave irradiation using silica gel supported $NaHSO_4$ catalyst[1†]

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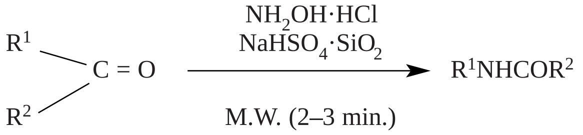
A simple and rapid conversion of ketones into the corresponding amides in high yields has been developed by treatment with hydroxylamine hydrochloride under microwave irradiation in the presence of silica gel supported $NaHSO_4$ catalyst.

The conversion of ketones into the corresponding amides is an important transformation that has been utilized for the synthesis of various bioactive natural compounds[2] as well as for the industrial production of polyamides, such as Nylon 6.[3] The ketones can be converted into oximes which then undergo Beckmann rearrangement to produce amides.[4] The alicyclic ketones give the corresponding lactams under similar reaction conditions.[4a] Some one-pot conversions of ketones into amides have also been reported[3a,5] though their numbers are limited. However, these methods suffer from certain drawbacks which include the use of corrosive reagents (*e.g.*, nitroparaffin and concentrated H_2SO_4,[5a] hydroxylamine and concentrated H_2SO_4,[5b] hydroxylamine-O-sulfonic acid and HCOOH[3a,5f]), low yields[5d] (<17% using Mexican Bentonite under microwave irradiation) and several steps involving experimental procedure[5e] (using hydroxylamine-O-sulfonic acid and SiO_2 in the presence of water under microwave irradiation). The processes using concentrated H_2SO_4 may affect the systems that are sensitive to acids.[5a–5c] Moreover, the methods which have not utilized microwave irradiation required a long reaction time.[3a,5a–5c,5f]

In continuation of our work[6] on the application of microwave irradiation for synthesis of bioactive compounds and their intermediates we have recently developed an efficient microwave assisted one-pot conversion of ketones into amides by treatment with $NH_2OH.HCl$ in the presence of silica gel supported sodium hydrogen sulfate ($NaHSO_4.SiO_2$) catalyst[7] without using any solvent (Scheme 1)



1 **2**

Scheme 1

Several ketones including cyclohexanone were conveniently converted into the corresponding amides (Table 1) in a very short period of time. The catalyst can easily be prepared[7] from the readily available materials and the experimental procedure is simple. The mechanism of the conversion could briefly be proposed as follows: the ketones at first reacted with hydroxylamine to produce ketoximes which then underwent Beckmann rearrangement to afford the amides. The major products (yields 90–96%) were formed by migration of the aryl group (except entries 8 and 9) of the intermediate ketoximes during rearrangement. However, the amides formed by alkyl migration were also the minor products (yield <5%) in each case. When the aryl group contained an electron withdrawing group, *e.g.*, $–NO_2$ (entry 8) the major product was formed by alkyl migration of the ketoxime.[8] The present method was found to be suitable for the preparation of caprolactam from cyclohexanone (entry 9). The structures of all the products were established from their analytical and spectroscopic (^1H NMR and MS) data.

In conclusion, we have developed a simple and efficient practical method for one-pot conversion of ketones into amides by applying microwave irradiation without using any solvent. The catalyst ($NaHSO_4.SiO_2$) that has been used here for the first time for such conversion is inexpensive and nonhazardous. The experimental procedure is eco-friendly.

Experimental

Acetophenone (120 mg, 1 mmol) and $NH_2OH.HCl$ (104 mg, 1.5 mmol) were mixed thoroughly with $NaHSO_4.SiO_2$ catalyst (100 mg, prepared by reported process[7]). The mixture was placed in an alumina bath inside a microwave oven (BPL, BMO, 700T, 466 watt) and irradiated for 2 min. The mixture was removed from the oven, cooled and shaken with $CHCl_3$ (10 ml). The catalyst was removed by filtration. The filtrate was concentrated and the residue was subjected to column chromatography over silica gel using hexane-EtOAc (4:1) as eluent to afford acetanilide (123 mg, 91%) and N-methylbenzamide (4 mg, 3%).

The microwave oven was operated at a half power when cyclohexanone was used for irradiation.

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References

1 Part 8 in the series "Studies on Novel Synthetic Methodologies", for part 7 see B. Das, B. Venkataiah, and P. Madhusudan, *Synlett*. 2000 (in press). IICT Communication No. 4519.

2 K. Marouka and H. Yamamoto, in *Comprehensive Organic Synthesis*, B.M. Trost, Ed. Pergamon Press 1991, Vol. 6, p.763.

3 (a) G.A. Olah and A.P. Fung, *Synthesis* 1979, 537; (b) R.E. Gawly, *Org. React*. 1988, **35**, 1.

4 (a) H.M. Meshram, *Synth. Commun*. 1990, **20**, 3253 and references cited therein; (b) A.I. Bosch, P. de la Cruz, E. Diez-Barra, A. Loupy and F. Langa, *Synlett*. 1995, 1295 and references cited therein.

5 (a) A. Novotny, *U.S. Patent* 1951, 2569114 (*Chem. Abstr*. 1952, **46**, 5078); (b) A. Novotny, *U.S. Patent* **1951**, 2579851 (*Chem. Abstr*. 1952, **46**, 6668); (c) C. Barnett, I.M. Cohn and J. Lincoln, *U.S. Patent* 1956, 2754298 (*Chem. Abstr*. 1957, **51**, 2853); (d) F. Delgado, A.C. Cano, O. Garcia, J. Alvarado, L. Velasco, C. Alvarez and H. Rudler, *Synth. Commun*. 1992, **22**, 2125; (e) A. Lavrent, P. Jacquault, J.-L. Di Martino and J. Hamelin, *J. Chem. Soc., Chem. Commun*. 1995, 1101.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Conversion of ketones into amides

Entry	R^1	R^2	Time (min.)	Isolated yield (%) of amide	M.p (°C) (reported)
1	C_6H_5	Me	2	91	112–113 (114)[9]
2	C_6H_5	C_6H_5	3	96	162–163 (162–164)[10]
3	4-(MeO)C_6H_4	Me	2.5	90	129–130 (130)[9]
4	4-(Me)C_6H_4	Me	2.5	93	144–145 (146)[9]
5	4-(F)C_6H_4	Me	2.5	94	152–153 (153)[9]
6	4-(Br)C_6H_4	Me	2.5	93	165–166 (165-166)[10]
7	4-(Cl)C_6H_4	Me	2.5	91	176–177 (177)[10]
8	4-(NO_2)C_6H_4	Me	2	18	214–216 (215)[11]
9	-$(CH_2)_5$-		3	85	67–68 (68)[10]

6 (a) B. Das, P. Madhusudhan and A. Kashinatham, *Tetrahedron Lett*. 1998, **39**, 431; *Bioorg. Med. Chem. Lett*. 1998, **8**, 1403; (b) B. Das and B. Venkataiah, *Synth. Commun*. 1999, **29**, 863.

7 G.W. Breton, *J. Org. Chem*. 1997, **62**, 8952.

8 In the entry 8 the major product 4(NO_2)C_6H_4CONHMe (yield 62%) was characterised from its spectral data: ^{1}H NMR ($CDCl_3$): δ 8.33 (2H, *d*, *J* = 9.0 Hz, Ar–H), 7.94 (2H, d, *J* = 9.0 Hz, Ar-H), 6.25 (1H, brs, -NH-), 3.06 (3H, d, *J* = 7.0 Hz, –Me); MS : *m/z* 180 ($M^{+\cdot}$), 150, 148, 132, 104.

9 *CRC Hand Book of Table for Organic Compound Identification*. The Chemical Rubber Co., Ohio, 3rd edn, 1967.

10 *Aldrich Library of NMR spectra*, Aldrich Chemical Company, USA, Vol.2, 2nd edn, 1983.

11 *CRC Hand Book of Chemistry and Physics*, CRC Press, Boca Raton, Florida, 73rd edn, 1992–1993.