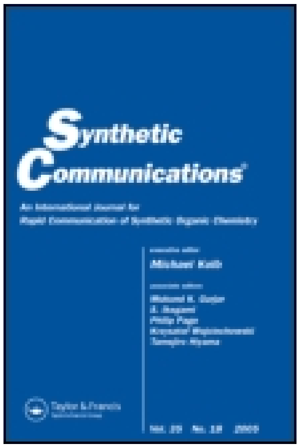
This article was downloaded by: [University of Arizona]
On: 27 August 2013, At: 20:56
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Microwave-Assisted Conversion of Nitriles to Thioamides in Solvent-Free Condition

Firouz Matloubi Moghaddam [a], Leila Hojabri [a] & Mohammad Dohendou [a]
[a] Sharif University of Technology, Department of Chemistry, Tehran, Iran

Published online: 21 Aug 2006.

To cite this article: Firouz Matloubi Moghaddam, Leila Hojabri & Mohammad Dohendou (2003) Microwave-Assisted Conversion of Nitriles to Thioamides in Solvent-Free Condition, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:24, 4279-4284, DOI: 10.1081/SCC-120026857

To link to this article: http://dx.doi.org/10.1081/SCC-120026857

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 24, pp. 4279–4284, 2003

Microwave-Assisted Conversion of Nitriles to Thioamides in Solvent-Free Condition

**Firouz Matloubi Moghaddam,* Leila Hojabri,
and Mohammad Dohendou**

Sharif University of Technology,
Department of Chemistry, Tehran, Iran

ABSTRACT

Nitriles are efficiently transformed to thiomorpholides via the Willgerodt-Kindler reaction under microwave irradiation in solvent-free conditions.

Key Words: Nitriles; Thiomorpholides; Willgerodt-Kindler reaction; Microwave irradiation.

---

*Correspondence: Firouz Matloubi Moghaddam, Sharif University of Technology, Department of Chemistry, P.O. Box 11365-9516, Tehran, Iran; E-mail: matloubi@sharif.edu.

DOI: 10.1081/SCC-120026857 0039-7911 (Print); 1532-2432 (Online)

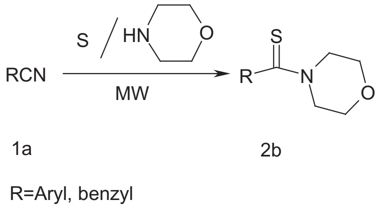
www.dekker.com

Thioamides have widespread uses such as versatile intermediates in organic synthesis,[1] pesticides,[2,3] anti inflammatory,[2] and antiulcer agents.[4] A recent review published in the literature, also shows the importance of these compounds for the preparation of heterocyclic compounds.[5]

Many different methods to prepare thioamides have been reported in the literature.[6] The classical route for their synthesis is the Willgerodt-Kindler reaction of aryl alkyl ketones, already has been extended from the original forms to many other functional groups such as aldehydes, unsaturated hydrocarbons, nitriles, amines, imines, epoxides, and alcohols.[7] High temperature (120°C) and long refluxing time (6 h) are required in the classical route.[8] Recently, we and others have shown the efficiency of microwave-heating for the synthesis of thioamides from styrenes,[9] aldehydes, and ketones.[10,11] In the present work, we wish to report the preparation of thioamides from nitriles via Willgerodt-Kindler reaction assisted by microwave irradiation in solvent-free conditions (Sch. 1). Morpholine as an inexpensive and readily available secondary amine was used and found to be most suitable in the reaction conditions. The reaction conditions were optimized by examination of different parameters, such as time of irradiation, the ratio of sulfur to morpholine and nitriles. After performing several experiments, the optimum molar ratio of nitrile:sulfur:morpholine was found to be 1:2.5:5.

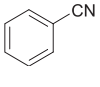
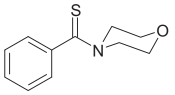
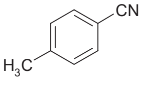
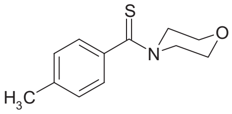
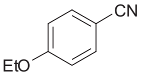
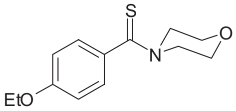
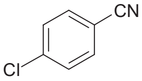
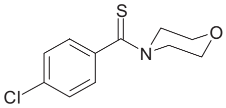
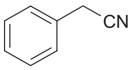
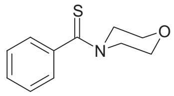
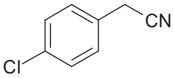
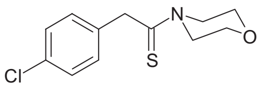
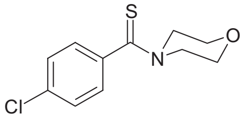
In a typical procedure, nitrile (3 mmol), elemental sulfur (7.5 mmol), and morpholine (15 mmol) were mixed and placed in a closed teflon vessel (~10 mL) and subjected to microwave irradiation for a given time (see Table 1). After conventional work-up the thiomorpholides were obtained in good to excellent yields. The results are summarized in Table 1.

When benzylnitriles were used as starting materials, the same products were obtained as with benzonitriles (Table 1, Entries 1,5). In general, there is no proven mechanism for Willgerodt reaction, especially for the nitriles as starting materials, which has received little attention.



Scheme 1.

Table 1. Microwave-assisted conversion of nitriles to thiomorpholides.

Entry	Substrate(a)	Product(b)	Time (min)	Yield (%)[a]
1		 **1b**	4.5	70
2		 **2b**	2.5	95
3		 **3b**	3	80
4		 **4b**	4.5	30
5		 **5b**	1	83
6		 **6b** I +  II	1	I = 20 II = 60

[a] All yield refer to isolated products.

However, our results are in accordance with the reported literature results.[8,12] *p*-Chlorobenzylnitrile (Table 1, Entry 6) produces the respected compound in 20% yield along with *p*-chlorobenzothiomorpholide (60%). To the best of our knowledge, the case of nitriles has not been studied yet by this methodology. It is a convenient method for rapid and high-yielding production of thioamides from nitriles by microwave activation. Further investigations of this reaction and its mechanism are now in progress in our laboratory.

In conclusion, the reaction described herein represents a simple entry into the synthesis of thiomorpholides from nitriles. The method has advantages, of being completed within few minutes, while it produces thiomorpholides in good to excellent yields.

EXPERIMENTAL

Melting points were measured on a Buchi Melting Point B-540 and are uncorrected. ^{1}H NMR spectra were measured ($CDCl_3$ solution) with a Brüker DRX-500 AVANCE spectrometer at 500.1 MHz. Infrared spectra were recorded on a Mattson 1000 FT-IR spectrometer (Unicam).

General Procedure for Willgerodt-Kindler Reaction of Nitriles

A mixture of nitrile (5 mmol), sulfur (12.5 mmol), and morpholine (25 mmol) were mixed in a teflon flask (~10 mL) and was allowed to be exposed to microwave[13] irradiation for given time (Table 1). The cooled reaction mixture was taken up in acetone. After filtration, the solvent was removed under reduced pressure and the residue was washed with dilute hydrochloric acid and chloroform. The chloroform portion was separated and solvent was removed under reduced pressure and the residue was purified by column chromatography using hexane, ethylacetate (2:1) as eluent. Further purification of the compounds were performed by recrystallization from ethanol. All products were identified by their melting points, IR and ^{1}H NMR spectra and their physical data are in agreement with the literature **1b**,[8,12,14] **4b**,[15] **5b**,[16–18] **6b**.[19,20]

Spectroscopic Data

1b. Pale yellow crystal. M.p.: 137–139°C. IR (KBr) (ν_{max}, cm^{-1}): 1115 (C=S), ^{1}H NMR: δ 3.62 (2H, t, $J = 4.6$ Hz, CH_2), 3.66 (2H, t, $J = 4.6$ Hz, CH_2), 3.90 (2H, t, $J = 4.8$ Hz, CH_2), 4.46 (2H, t, $J = 4.8$ Hz, CH_2), 7.29–7.40 (5H, m CH).

2b. Pale yellow crystal. M.p.: 126–128°C. IR (KBr) (ν_{max}, cm^{-1}): 1115 (C=S), ^{1}H NMR: δ 2.37 (3H, s, CH_3), 3.66 (4H, bs, CH_2), 3.90 (2H, t, $J = 4.8$ Hz, CH_2), 4.45 (2H, t, $J = 4.8$ Hz, CH_2), 7.20 (4H, ABquarted, $J = 8.3$ Hz, CH).

3b. Pale yellow crystal. M.p.: 120–122°C. IR (KBr) (ν_{max}, cm^{-1}): 1115 (C=S), ^{1}H NMR: δ 1.43 (3H, t, $J = 7.0$ Hz, CH_3), 3.67 (4H, bs,

CH_2), 3.89 (2H, bs, CH_2), 4.06 (2H, q, $J = 7.0$ Hz, CH_2), 4.43 (2H, bs, CH_2), 6.87 (2H, d, $J = 8.9$ Hz, CH), 7.27(2H, d, $J = 8.9$ Hz, CH).

4b. Pale yellow crystal. M.p.: 138–140°C. IR (KBr) (ν_{max}, cm^{-1}): 1115 (C=S), ^{1}H NMR: δ 3.64 (4H, m, CH_2), 3.91 (2H, t, $J = 4.8$ Hz, CH_2), 4.45 (2H, t, $J = 4.8$ Hz, CH_2), 7.25 (2H, d, $J = 8.9$ Hz, CH), 7.36 (2H, d, $J = 8.9$ Hz, CH).

5b is similar to **1b**.

6b. Yellow crystal. M.p.: 102–104°C. IR (KBr) (ν_{max}, cm^{-1}): 1115 (C=S), ^{1}H NMR: δ 3.45 (2H, t, $J = 5.0$ Hz, CH_2), 3.62 (2H, t, $J = 4.6$ Hz, CH_2), 3.75 (2H, t, $J = 4.6$ Hz, CH_2), 4.32 (2H, s, CH_2), 4.36 (2H, t, $J = 5.0$ Hz, CH_2), 7.30 (4H, ABquarted, $J = 8.4$ Hz, CH).

REFERENCES

1. Metzner, P. Synthesis **1992**, 1185.
2. Herbert Haller, L.J.; Barthel, Wm. F. U.S. Pat. 2,358,925, Sept. 1994.
3. Leresque, C.L. U.S. Pat. 2,560,296, July 10, 1951.
4. Kureha Chemical Industry Co. Ltd. Jpn. Kokai Tokyo 81 12 315, 6 Feb. 1981.
5. Tadeusz S. Jagodzinski. Chem. Rev. **2003**, *103*, 197–227.
6. Schaumann, E. In *Comprehensive Organic Synthesis*; Trost, B.M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, 419–434 pp.
7. Brown, E.V. Synthesis **1975**, 358–373.
8. Purrello, G. Gazz. Chim. Ital. **1965**, *95*, 1089.
9. Matloubi Moghaddam, F.; Ghaffarzadeh, M.; Dekamin, M.G. J. Chem. Research(s) **2000**, 228–229.
10. Matloubi Moghaddam, F.; Ghaffarzadeh, M. Synth. Commun. **2001**, *31*, 317–321.
11. Nooshabadi, M.; Aghapoor, K.; Darabi, H.R.; Mojtahedi, M.M. Tetrahedron Letters **1999**, *40*, 7549–7552.
12. Bruno, G.; Purrello, G. Gazz. Chim. Ital. **1966**, *96*, 986.
13. A domestic microwave oven AEG (650 W) at 2450 MHz with full power was used for this work.
14. Carayon-Gentil, A.; Minot, M.; Charbrier, P. Bull. Soc. Chim. France **1964**, 1420.
15. Kulganek, V.V.; Yanovskaya, L.A. Izv. Akad. Nauk. SSSR, Ser. Khim. **1979**, *11*, 2585–2586.
16. Carmack, M.; Detar, D.F. U.S. Pat 2,495,567, Jan., 1950.
17. Detar, D.F.; Carmack, M. J. Amer. Chem. Soc. **1946**, *68*, 2025.

18. Purrello, G. Gazz. Chim. Ital. **1961**, *91*, 1373.
19. Carlson, R.; Lunstedt, T.; Shabana, R. Acta. Chem. Scand., Ser. B **1986**, *40*, 534–544.
20. Claus, A.; Wehr, R. J. Prakt. Chem(2) **1891**, *85*, 44.

Received in the UK July 24, 2003