

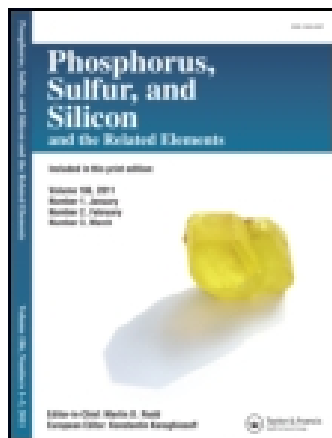
This article was downloaded by: [UQ Library]

On: 03 November 2014, At: 05:35

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



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/gpss20>

Synthesis of Thiazinobenzimidazole Derivatives in a Solventless System Under Microwave Irradiation

Majid M. Heravi^a, Navabeh Nami^a, Hossien A. Oskooie^a & Rahim Hekmatshoar^a

^a Department of Chemistry, School of Sciences, Azzahra University, Vanak, Tehran, Iran

Published online: 01 Feb 2007.

To cite this article: Majid M. Heravi, Navabeh Nami, Hossien A. Oskooie & Rahim Hekmatshoar (2005) Synthesis of Thiazinobenzimidazole Derivatives in a Solventless System Under Microwave Irradiation, *Phosphorus, Sulfur, and Silicon and the Related Elements*, 180:7, 1605-1610, DOI: [10.1080/10426500590885011](https://doi.org/10.1080/10426500590885011)

To link to this article: <http://dx.doi.org/10.1080/10426500590885011>

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>

Synthesis of Thiazinobenzimidazole Derivatives in a Solventless System Under Microwave Irradiation

Majid M. Heravi
Navabeh Nami
Hossien A. Oskooie
Rahim Hekmatshoar

Department of Chemistry, School of Sciences, Azzahra University,
Vanak, Tehran, Iran

A series of thiazino [3,2-a] benzimidazole derivatives were synthesized in a solventless system under microwave irradiation in a very short time and in excellent yields.

Keywords Benzimidazole; microwave irradiation; solventless system; thiazinobenzimidazole

Benzimidazole derivatives exhibit antibacterial activity,^{1,2} act as hypoglycaemic agents,³ and more over are indicated as being associated with a particularly wide range of biological properties, including antitumor,⁴ antiviral, and antitubercular activity.⁵ These compounds are an important class of nitrogen- and sulfur-containing heterocycles and they constitute useful intermediates in organic synthesis.⁶

The microwave-enhanced chemical reactions⁷ have gained popularity over the usual homogeneous and heterogeneous reactions as they can be conducted rapidly and pure products are obtained in high yields in a solvent-free condition. Organic solvents are not only expensive, they are also hazardous and flammable.⁸

We are interested in the chemistry of heterocyclic compounds containing nitrogen and sulfur atoms.⁹ We are also interested in microwave-assisted organic reactions in a solventless system.¹⁰ As part of a research program on the synthesis of a heterocyclic system containing nitrogen and sulfur in a solventless system under microwave irradiation and with a view to extending the synthetic utility of dialkyl

Received July 15, 2004; accepted August 10, 2004.

Address correspondence to Majid M. Heravi, Department of Chemistry, School of Sciences, Azzahra University, Vanak, Tehran, Iran. E-mail: mmh1331@yahoo.com

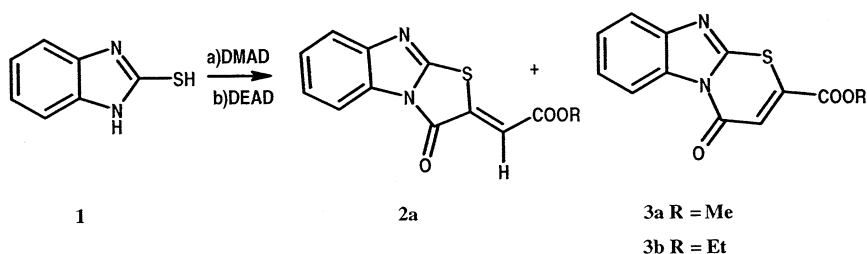
acetylendicarboxylate,¹¹ we have investigated the addition of the latter to 2-mercapto benzimidazole under microwave irradiation in a solventless system.

In 1978, McKillop and his co-workers¹² reported that benzimidazole-2-thione **1** reacted with DMAD in either methanol or acetic acid to give mixtures of two 1:1 molar-MeOH adducts. One adduct was identified as **2a** by X-ray crystallography but the other adduct, which was not isolated, was tentatively assigned structures **3a**.

In 1981, Acheson et al.¹³ have found that thione **1** and DMAD reacted in wet and dry acetonitrile to give only **2a** and in dry methanol to give only **3a**.

We have investigated the addition of DMAD or DEAD to 2-mercapto benzimidazole under microwave irradiation in solventless system.

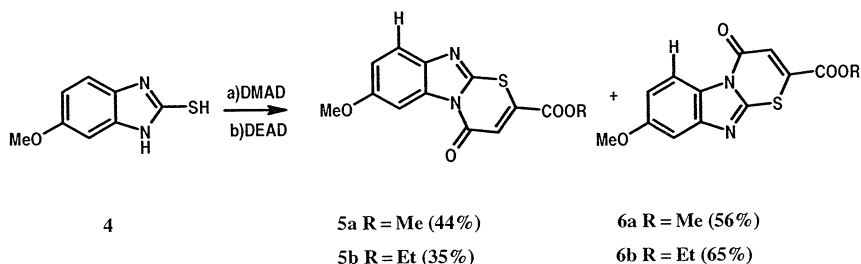
The reactions were simply conducted by mixing of **1** with dialkyl acetylenedicarboxylat (R = Me or Et) in a beaker and placing the beaker in a microwave oven for a short period of time. The progress of the reaction was monitored by TLC using ethanol and ethyl acetate as an eluent. Our product showed the same physical and spectroscopic data as given for **3a** in the literature¹³ (Scheme 1). We also used diethyl acetylene dicarboxylate to obtain the different substituted methyl-2-oxo-2H-thiazino[3, 2-a] benzimidazole-4-carboxylate. **3b**.¹³



SCHEME 1

Reaction of 5-methoxy benzimidazole-2-thione **4** with DMAD in either hot methanol or a solventless condition under microwave irradiation gave a mixture of two isomers that showed closely moving spots in TLC (ethanol: ethyl acetate) which could be separated chromatographically. These compounds were identified as methyl-7-methoxy-2-oxo-2H-thiazino[3, 2-a]benzimidazole-4-carboxylate, **5a**, and methyl-8-methoxy-2-oxo-2H-thiazino[3, 2-a]benzimidazole-4-carboxylate, **6a** (Scheme 2).

In ¹H-NMR spectra of **5a**, 9-H (7.58 δ) is more shielded than 6-H of **6a** (8.32 δ , near to C=O).



SCHEME 2

EXPERIMENTAL

The melting points were obtained using an Electrothermal IA 9100 Digital Melting Point apparatus. The IR spectra were recorded on a 4300 Shimadzu spectrometer. ^1H NMR spectra were recorded on a 500 MHz spectrometer using TMS as internal standard.

SYNTHESIS OF THIAZINO[3,2-a]BENZIMIDAZOLE

General Procedure

Compound **1** and **4** (1 mol) was mixed with DMAD or DEAD (1 mol) thoroughly in a beaker; the beaker was placed in a microwave oven for 5 min. The progress of reaction was monitored by TLC using ethanol: ethyl acetate (3:1) as an eluent. The mixture of two isomers was separated chromatographically (ethanol: ethyl acetate 3:1). **3a**, **3b**, **5a**, **5b**, **6a**, and **6b** were crystallized from a suitable solvent. The selected physical and spectroscopic data are given below.

METHYL-2-OXO-2H-THIAZINO[3,2-a]BENZIMIDAZOLE-4-CARBOXYLATE **3a**

Mp = 172°C yellow micro needles from MeOH, (Lit¹³ 172.5–173°C) yield 90%. ^1H -NMR (CDCl_3) δ 4.05 (s, 3H, OMe), 7.45 (m, 1H, benzen hydrogen), 7.52 (s, 1H, =CH), 7.55 (m, 1H, benzene hydrogen), 7.81 (d, J = 7.8, 1H, benzenhydrogen), 8.58 (d, J = 7.9, 1H, benzen hydrogen, near of CO). IR (KBr): 3035, 2910, 1731, 1691, 1580, 1470, 1430, 1354, 1256, 1184, 1108, and 755 cm^{-1} . MS, m/z; M^+ , 260 (100), 201 (25), 174 (21), 129 (15), 90 (7.2), 77 (4), 63 (5), 39 (4).

ETHYL-2-OXO-2H-THIAZINO[3,2-a]BENZIMIDAZOLE-4-CARBOXYLATE 3b

Mp = 135°C, yellow micro needles from EtOH, (Lit¹³.135–137°C) yield 87%. ¹H-NMR (CDCl₃)δ 1.45 (t, J = 7.1, 3H, Me), 4.50 (q, J = 7.1, 2H, CH₂), 7.46 (m, 2H, benzen hydrogen), 7.49 (s, 1H, =CH), 7.82 (d, J = 5.3, 1H, benzene hydrogen), 8.59 (d, J = 5, 1H, benzene hydrogen). IR (KBr): 3060, 2976, 2361, 1726, 1689, 1586, 1521, 1477, 1438, 1363, 1298, 1251, 1186, 1101, 1033, 977, 756 cm⁻¹.

METHYL-7-METHOXY-2-OXO-2H-THIAZINO[3,2-a]-BENZIMIDAZOLE-4-CARBOXYLATE 5a

Mp = 223°C, Orange micro needles, from MeOH yield 44%. ¹H-NMR (CDCl₃)δ 3.87 (s, 3H, OMe), 4.01 (s, 3H, OMe), 7.05 (d, J = 8.6, 1H, benzene hydrogen), 7.38 (s, 1H, =CH), 7.58 (d, J = 8.6, 1H, benzene hydrogen), 7.98 (s, 1H, benzene hydrogen). IR (KBr): 3060, 2923, 2853, 1733, 1691, 1617, 1477, 1433, 1366, 1292, 1249, 1194, 1148, 1114, 1020, 923, 760 cm⁻¹. MS, m/z; M⁺, 290 (100), 275 (57), 247 (7), 207 (35), 159 (11), 44 (17), 28 (92).

ETHYL-7-METHOXY-2-OXO-2H-THIAZINO[3,2-a]-BENZIMIDAZOLE-4-CARBOXYLATE 5b

Mp = 126°C, Orange powder from EtOH, yield 35%. ¹H-NMR (CDCl₃)δ 1.38 (t, J = 8.5, 3H, Me), 3.88 (s, 3H, OMe), 4.37 (q, J = 8.5, 2H, OCH₂), 6.89 (d.d, J = 8.6, 1.6, 1H, benzene hydrogen), 7.16 (d, J = 1.6, 1H, benzene hydrogen), 7.18 (s, 1H, =CH), 7.80 (d, J = 8.6, 1H, benzene hydrogen). IR (KBr): 3030, 1729, 1682, 1609, 1578, 1501, 1428, 1384, 1312, 1195, 1145, 1024 cm⁻¹. MS, m/z; M⁺, 304 (100), 298 (13), 276 (34), 261 (43.75), 203 (7), 189 (13), 159 (13), 85 (8), 69 (5), 53 (6), 32 (4).

METHYL-8-METHOXY-2-OXO-2H-THIAZINO[3,2-a]-BENZIMIDAZOLE-4-CARBOXYLATE 6a

Mp = 140°C, orange micro needles from MeOH, yield 56%. ¹H-NMR (CDCl₃)δ 3.85 (s, 3H, OMe), 4.01 (s, 3H, OMe), 6.97 (d, J = 8.6, 1H, benzen hydrogen), 7.16 (s, 1H, benzene hydrogen), 7.42 (s, 1H, =CH), 8.32 (d, 8.6, 1H, benzen hydrogen). IR (KBr): 3098, 3049, 2947, 2828, 1729, 1690, 1621, 1517, 1475, 1433, 1386, 1323, 1281, 1196, 1138, 1099, 1021, 932, 865, 752, 711, 628 cm⁻¹. MS, m/z; M⁺, 290 (100), 275 (57), 247 (7), 207 (35), 159 (11), 44 (17), 28 (92).

**ETHYL-8-METHOXY-2-OXO-2H-THIAZINO[3,2-a]-
BENZIMIDAZOLE-4-CARBOXYLATE 6b**

Mp = 139°C, orange micro needles from EtOH, yield 65%. ¹H-NMR (CDCl₃) δ 1.45 (t, J = 7.1, 3H, Me), 3.92 (s, 3H, OMe), 4.49 (q, J = 7.1, 2H, CH₂), 7.07 (d, J = 8.9, 2.2, 1H, benzene hydrogen), 7.25 (d, 2.2, 1H, benzene hydrogen), 7.5 (s, 1H, =CH), 8.43 (d, J = 8.9, 1H, benzene hydrogen). IR (KBr): 3035, 2960, 1697, 1690, 1576, 1463, 1424, 1362, 1291, 1242, 1193, 1145 cm⁻¹. MS, m/z; M⁺ 304 (100), 290 (19), 261 (25), 241 (8), 224 (35), 209 (22), 189 (12), 159 (23), 94 (5), 77 (8), 43 (9).

CAUTION

Although we did not have any accident, the use of a microwave oven in an efficient hood is highly recommended.

REFERENCES AND NOTES

- [1] G. Tennant, *Chem. Heterocycl. Compd.* **40**, 1 (1981).
- [2] a) S. T. A. Narayan, V. Kumar, and H. K. Pujari, *Indian. J. Chem. Sect. B*, **25**, 267 (1986); b) A. Chimirri, S. Grasso, G. Romeo, and M. Zappala, *Heterocycles*, **27**, 1975 (1988).
- [3] a) H. E. Alburn, R. L. Fenichel, F. G. Gregory, and P. H. L. Wei, US Pat. 4, 214, 069 (1980) Chem. Abstr. 944018a (1981); b) R. N. Hjorth, B. O. Moore, and N. H. Grant, US Pat. 4, 466, 957, 1984 (Chem., Abstr., 101, 216388i (1984).
- [4] a) R. L. Fenichel, F. J. Gregory, and H. E. Alburn, *Br. J. Cancer*, **33**, 329 (1976); b) R. M. Scholtz, J. D. Popamatheakis, J. Luetzeler, and M. A. Ghrgos, *Cancer Res.* **37**, 3338 (1977).
- [5] a) P. Schauer, M. Lkar, B. Stanovnik, and M. Fisler, *Biol. Vestn.*, **20**, 65 (1972); b) P. H. L. Wei and S. C. Bell, US Pat., 3, 704, 239 (1972) Chem. Abstr. **78**, 43482m (1973); c) P. H. L. Wei and S. C. Bell, US Pat., 3, 775, 426 (1973) (Chem. Abstr., 80, 70804u) (1974).
- [6] R. M. Acheson and N. F. Elmor, *Adv. Heterocyclic Chem.*, **23**, 263 (1978).
- [7] K. Tanaka and F. Toda, *Chem. Rev.*, **100**, 1025 (2000).
- [8] C. B. Khouw, C. B. Dartt, A. Labinger, and M. E. Davis, *J. Catal.*, **149**, 195 (1994).
- [9] a) M. M. Heravi and M. Bakavoli, *J. Chem. Res.*, **11**, 480 (1995); b) M. M. Heravi, Z. Tavaliee, and O. Sabzevari, *Indian J. Chem. Sect., B*, **37b**, 585 (1998); c) M. M. Heravi, H. A. Oskooie, and M. Mafi, *Synth. Commun.*, **27**, 1725 (1997); d) M. M. Heravi, G. H. Rajabzadeh, M. Rahimizadeh, M. Bakavoli, and M. Ghassemzadeh, *Phosphorus, Sulfur, and Silicon*, **174**, 129 (2001); e) M. M. Heravi, N. Montazeri, M. Rahimizadeh, M. Bakavoli, and M. Ghassemzadeh, *J. Chem. Res.*, 584 (2000); f) M. M. Heravi, N. Montazeri, M. Rahimizadeh, M. Bakavoli, and M. Ghassemzadeh, *Monatsh Chem.*, **132**, 1225 (2001); g) M. M. Heravi, A. Kivanloo, M. Rahimizadeh, M. Bakavoli, and M. Ghassemzadeh, *Tetrahedron Lett.*, **45**, 5747 (2004).
- [10] a) M. M. Heravi, D. Ajami, and M. Ghassemzadeh, *Synthesis*, 393 (1999); b) M. M. Heravi, D. Ajami, K. Aghapour, and M. Ghassemzadeh, *J. Chem. Soc., Chemical Communication*, 833 (1999); c) M. M. Heravi, D. Ajami, M. M. Mojtahedi, and M. Ghassemzadeh, *Tetrahedron Lett.*, **40**, 561 (1999); d) M. M. Heravi, M. Tajbakhsh,

- S. Habibzadeh, and M. Ghassemzadeh, *Phosphorus, Sulfur, and Silicon*, **177**, 2299 (2002).
- [11] a) M. M. Heravi, Y. Sh. Beheshtiha, N. Nami, and M. Ghassemzadeh, *Phosphorus, Sulfur, and Silicon*, **161**, 7 (2000); b) M. M. Heravi, Y. Sh. Beheshtiha, N. Nami, and R. Hekmatshoar, *Phosphorus, Sulfur, and Silicon*, **165**, 285 (2000).
- [12] A. Mc Killop, G. C. A. Bellinger, P. N. Preston, A. Davidson, and J. King. *Tetrahedron Lett.*, 1621 (1978).
- [13] R. M. Acheson and J. D. Wallis. *J. Chem. Soc. Perkins*, **1**, 415 (1981).