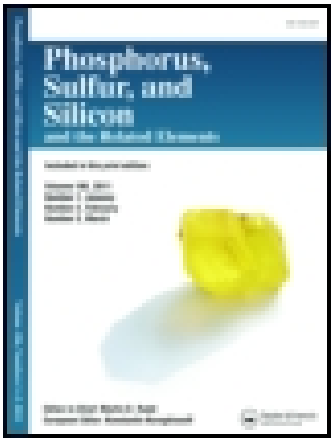
This article was downloaded by: [Northeastern University]
On: 27 November 2014, At: 01:01
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954
Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Microwave-Assisted Synthesis of Spiro(cycloalkane thiazolo-s-tetrazine)

Rajani K. Behera [a] , Anita Pati [b] , Manabendra Patra [a] & Ajay K. Behera [a]

[a] Organic Synthesis Laboratory, Department of Chemistry , Sambalpur University , Burla, Orissa, India

[b] National Institute of Science & Technology , Berhampur, Orissa, India

Published online: 03 Nov 2009.

To cite this article: Rajani K. Behera , Anita Pati , Manabendra Patra & Ajay K. Behera (2009) Microwave-Assisted Synthesis of Spiro(cycloalkane thiazolo-s-tetrazine), Phosphorus, Sulfur, and Silicon and the Related Elements, 184:11, 2827-2834, DOI: 10.1080/10426500802590038

To link to this article: http://dx.doi.org/10.1080/10426500802590038

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

Downloaded by [Northeastern University] at 01:01 27 November 2014

Phosphorus, Sulfur, and Silicon, 184:2827–2834, 2009
Copyright © Taylor & Francis Group, LLC
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500802590038

Taylor & Francis
Taylor & Francis Group

Microwave-Assisted Synthesis of Spiro(cycloalkane thiazolo-*s*-tetrazine)

Rajani K. Behera,[1] Anita Pati,[2] Manabendra Patra,[1] and Ajay K. Behera[1]
[1]Organic Synthesis Laboratory, Department of Chemistry, Sambalpur University, Burla, Orissa, India
[2]National Institute of Science & Technology, Berhampur, Orissa, India

Microwave irradiation of cyclic ketones with thiocarbohydrazide furnish the corresponding s*-tetrazine derivatives* ***1a–d****, which upon irradiation with chloroacetic acid and sodium acetate in acetic acid, give the corresponding thiazolidinone derivatives* ***2a–d****. These derivatives* ***2a–d*** *upon condensation with benzaldehyde afford the benzylidine derivatives* ***3a–d****. The* s*-tetrazine derivatives* ***1a–d*** *and 1,2-dibromoethane upon irradiation gives the thiazolo-*s*-tetrazine derivatives* ***4a–d****. The structures of* ***1–4*** *were established by IR,* ^{1}H *NMR, and* ^{13}C *NMR data.*

Keywords Irradiation; microwave assisted; spiro; tetrazine

Downloaded by [Northeastern University] at 01:01 27 November 2014

INTRODUCTION

Sometimes, in a chemical reaction, starting materials as well as products decompose or unwanted products are formed because of a long reaction time and high temperature, which invariably reduce the percentage of yield. Thus the production of a large amount of waste from a reaction is undesirable both from economic and an environmental point of view. Green technologies form an alternative method to allow a more clean and efficient chemical syntheses. Microwave energy is fast becoming the method of choice for both industrial and academic chemists for driving reactions to completion, as it offers the safest, most effective way to increase reaction rates and improve product yields, while promoting green chemistry ideas. Reactions that previously took hours, or

Received 12 June 2008; accepted 20 October 2008.
The authors thank to the Department of Science & Technology, Govt. of India, and University Grant Commission, New Delhi, for FIST and DRS support. One of the authors (A.P.) thanks Sambalpur University for the Sir J.J. Ghandy fellowship.
Address correspondence to Rajani K. Behera, Organic Synthesis Laboratory, Department of Chemistry, Sambalpur University, Jyoti Vihar, Burla 768 019, Orissa, India. E-mail: rajanibehera@yahoo.co.in

Downloaded by [Northeastern University] at 01:01 27 November 2014

even days, to complete can now be performed in minutes.[1–8] In the last decade, some of the first examples yielded interesting results, which led to much research in this novel technique.[9–19] Dandia et al.[20] reported a one-pot synthesis of novel spiro[pyrazolo[4,3-*c*][1, 5]benzothiazepines] with a 71% yield within 6–8 min using microwave irradiation. They also reported the synthesis of novel spiro[indole-pyrido[2,3-d]pyrimidines] by the reaction of in situ generated spiro[indole-dihydropyridine] and urea/CS_2 using basic alumina as a solid support or a few drops of DMF as a homogenizer under microwave irradiation for 3–4 min in 85–89% yield.[21] Spiro-(indoline-isoxazolidines) were prepared in modest yields, by the cycloaddition reaction between ethyl(3-indolylidene)-acetate and various substituted α, *N*-diphenylnitrones under solvent-free conditions using a microwave method.[22] The reaction conducted under conventional heating in an oil bath did not proceed even after 20 h, especially when it was carried out without solvent. The 4′-(2-butyl-4-oxo-1,3-diaza-spiro[4.4]non-1-en-3-ylmethyl)-biphenyl-2-carbonitrile was synthesized by irradiating methyl 1-amino-1-cyclopentanecarboxylate and valeric acid in anhydrous pyridine, with triphenyl phosphate (neat).[23]

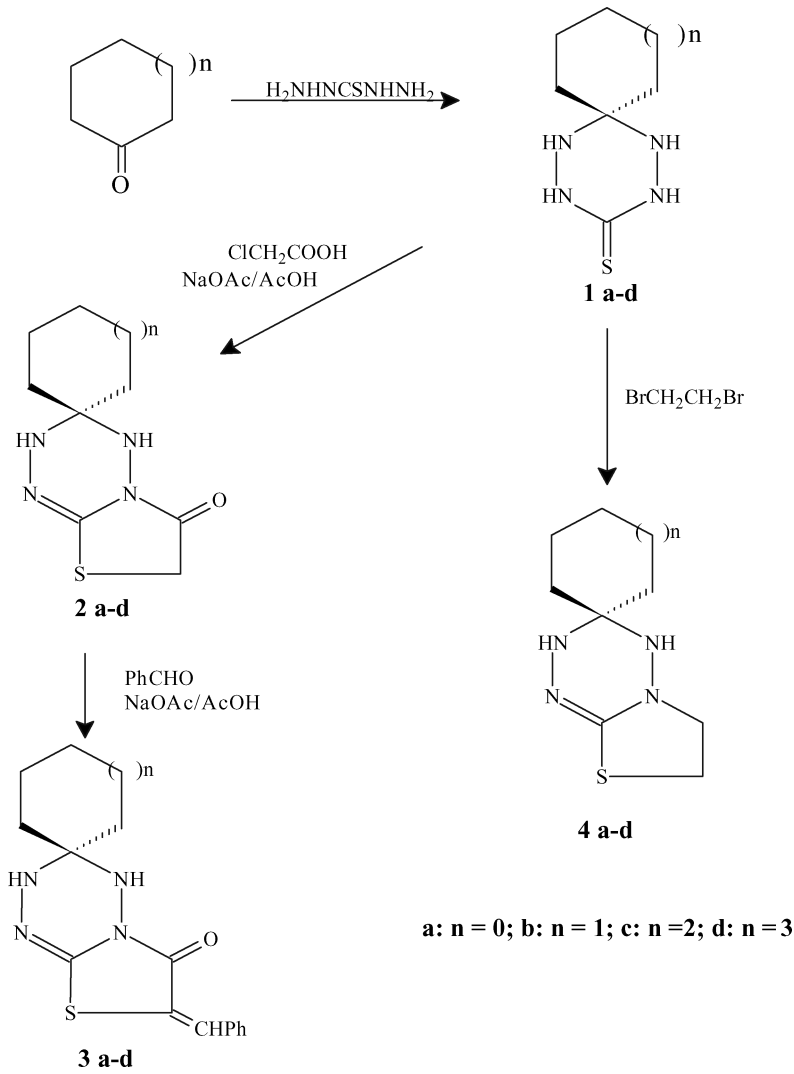
In our ongoing research program on the development of spiroheterocycles, we became interested in the efficient and microwave-assisted syntheses of the spirotetrazines into which thiazole and thiazolidinone moieties were incorporated. Pujari and colleagues[24–27] reported the syntheses of spirotetrazines derivatives (**1–4**) by conventional methods that required long reaction times and only moderate yields. Therefore, we have investigated the syntheses of these compounds (**1–4**) in microwave conditions.

RESULTS AND DISCUSSION

Cycloalkanones of different sizes undergo condensation with thiocabohydrazide under microwave condition to yield corresponding s-tetrazine derivatives **1a–d**. Thiazolidinone derivatives **2a–d** are obtained upon irradiation of a mixture of s-tetrazine derivatives **1a–d** and chloroacetic acid in acetic acid in the presence of sodium acetate. These thiazolidinone derivatives **2a–d** containing active methylene groups are subjected to condensation with benzaldehyde to form respective benzylidine compounds **3a–d**. Thiazolo-s-tetrazine derivatives **4a–d** are also obtained by the reaction of the s-tetrazine derivatives **1a–d** with dibromoethane. These reactions are depicted in Scheme 1.

The IR spectral data of the compounds synthesized by microwave irradiation were identical to those reported earlier.[24–27] The ^{1}H NMR

Downloaded by [Northeastern University] at 01:01 27 November 2014



SCHEME 1

spectral data of compounds **2–4** revealed some interesting results, which were not observed by Pujari and colleagues.[24–27] It was reported that the methylene protons of cycloalkane ring adjacent to the spiro carbon in compounds **2** appeared as one multiplet at δ 2.46–2.62 in their ^{1}H NMR spectra. In the case of these compounds synthesized by microwave irradiation, two clear multiplets were observed in the ^{1}H

NMR spectra at δ 2.54–2.57 and at δ 2.68–2.71. This is because these compounds have a thiazolidinone moiety on one side of the spirotetrazine structure, which makes the methylene proton of cycloalkane ring adjacent to spiro carbon slightly different. The downfield shift experienced by one of the methylene protons is due to the carbonyl group of thiazolidinone ring in **2**, which is evident from the fact that in case of compound **4**, where there is no carbonyl group, only one multiplet has been observed at δ 2.42–2.52.

The ^{1}H NMR data of compounds **3c** and **4c** and the ^{13}C NMR data of compounds **1c–4c** are also given in the appropriate places in the Experimental section, which were not reported earlier.[25] The ^{13}C NMR spectral data provides strong evidence in favor of the formation of the products as mentioned and also confirm the proposed structures.

We have synthesized 16 novel spiro compounds. The IR and ^{1}H NMR data of all the compounds synthesized by microwave irradiation were found to be almost identical with those reported earlier.[24–27] The analytical and spectral data of compounds **3b**, **3d**, **4a**, **4c**, and **4d** synthesized by the microwave method are given in the Experimental section, as these were not reported earlier. The reaction times, yields of the products (**1–4**) under microwave condition and from the classical heating method, and also the melting points of these compounds are given in the Table I.

EXPERIMENTAL

The melting points were determined on a Zenith apparatus and are uncorrected. IR spectra were recorded on a Perkins Elmer FT-IR spectrophotometer using KBr disc. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz FT NMR spectrometer and were recorded in $CDCl_3$. Purity of the products was checked by TLC, using silica gel G (BDH) and toluene:ethyl acetate (1:1) as eluent. The reactions were done in a domestic microwave oven (LG make) operated at 700 Watt generating 2450 MHz frequency. Thiocarbohydrazide was prepared according to the reported procedure.[28]

1,2,4,5-Tetraazaspiro[5.6]dodecane-3-thione (1c)

A mixture of thiocarbohydrazide (1.06 g, 0.01 mol) and cycloheptanone (1.18 mL, 0.01 mol) in water:ethanol (1:1, 2 mL) was taken in a beaker (25 mL). Then the mixture was irradiated in a microwave oven for 50 sec. The cream-colored precipitate obtained was washed well with hot water (25 mL) and finally crystallized from ethanol to obtain needle-shaped crystals. Mp 155°C, Yield 95%, (Found S, 15.89, $C_8H_{16}N_4S$

Downloaded by [Northeastern University] at 01:01 27 November 2014

TABLE I Physical and Analytical Data

Comp. No.	n	Molecular formula	Microwave method Mp (°C)	Yield (%)	Time (Sec)	Conventional method Mp (°C)	Yield (%)	Time (h)	S% Cal. (Found)
1a	0	$C_6H_{12}N_4S$	167	92	50	179[a]	89[a]	24[a]	21.62 (21.55)
1b	1	$C_7H_{14}N_4S$	168	93	40	169[b]	81[b]	24[b]	17.20 (17.16)
1c	2	$C_8H_{16}N_4S$	155	95	50	150[c]	85[c]	24[c]	16.00 (15.89)
1d	3	$C_9H_{18}N_4S$	175	90	45	180[d]	84[d]	24[d]	14.95 (14.90)
2a	0	$C_8H_{12}N_4SO$	140	70	40	144[e]	59[e]	6[e]	15.09 (14.96)
2b	1	$C_9H_{14}N_4SO$	129	75	40	130[b]	53[b]	5[b]	14.16 (13.99)
2c	2	$C_{10}H_{16}N_4SO$	133	77	40	135[c]	66[c]	5[c]	13.33 (13.18)
2d	3	$C_{11}H_{18}N_4SO$	125	75	40	120[d]	63[d]	5[d]	12.60 (12.54)
3a	0	$C_{15}H_{16}N_4SO$	180	62	40	177[e]	40[e]	3[e]	10.67 (10.61)
3c	2	$C_{17}H_{20}N_4SO$	235	70	40	240[c]	50[c]	3[c]	9.76 (9.68)
4b	1	$C_9H_{16}N_4S$	176	60	35	179[b]	44[b]	6[b]	15.09 (14.95)

[a]Ref.[29]
[b]Ref.[24]
[c]Ref.[26]
[d]Ref.[27]
[e]Ref.[25]

Downloaded by [Northeastern University] at 01:01 27 November 2014

requires S, 16.0%). IR (KBr) in cm^{-1}: 1231 (C=S), 3155–3205 (N−H). ^{1}H NMR ($CDCl_3$): δ1.64 (m, 8H, 4 × C***H***$_2$), 2.35 (m, 4H, 2 × C***H***$_2$), 4.35 (bs, 2H, 2 × N***H***), 8.44, 8.50 (bs, 2H, 2 × N***H***CS). ^{13}C NMR ($CDCl_3$): δ 24.23, 27.50, 30.10, 36.88, 179.72 (**C**=S).

6′(7′H)-Oxospiro[cycloheptane-1,3′(4′H)-[2H]thiazolo[3,2-b]-s-tetrazine] (2c)

To a mixture of **1c** (2.00 g, 0.01 mol), chloroacetic acid (0.95 g, 0.01 mol), and fused sodium acetate (0.82 g, 0.01 mol), a few drops of glacial acetic acid were added and the mixture was irradiated in a microwave oven for 40 sec. Then the reaction mixture was poured into ice cold water, and the precipitate obtained was filtered, washed well with water (50 mL), and crystallized from ethanol. Mp 133°C, Yield 77%, (Found S, 13.18, $C_{10}H_{16}N_4SO$ requires S, 13.33%). IR (KBr) in cm^{-1}: 1613(C=N), 1738(C=O), 3209–3318 (N−H). ^{1}H NMR ($CDCl_3$): δ 1.64 (m, 8H, 4 × C***H***$_2$), 2.56 (m, 2H, C***H***$_2$), 2.71 (m, 2H, C***H***$_2$), 3.74 (s, 2H, S-C***H***$_2$), 4.59 (bs, 2H, 2 × N***H***). ^{13}C NMR ($CDCl_3$): δ 24.24, 27.50, 30.12, 32.49 (Thiazolidinone ***C***H_2), 36.88, 149.5 (N = ***C***=S), 171.3 (***C***=O).

Downloaded by [Northeastern University] at 01:01 27 November 2014

7′-Benzylidine-6′(7′H)-oxospiro[cycloheptane-1,3′(4′H)-[2H]thiazolo[3,2-b]-s-tetrazine] (3c)

To a mixture of **2c** (0.24 g, 0.001 mol), benzaldehyde (0.1 mL, 0.001 mol), and sodium acetate (0.16 g, 0.002 mol), a few drops of glacial acetic acid were added and the mixture was irradiated in a microwave oven for 40 sec. The yellow-colored precipitate obtained was washed well with water (50 mL) and then crystallized from glacial acetic acid. Mp 235°C, Yield 70%, (Found S, 9.68, $C_{17}H_{20}N_4SO$ requires S, 9.76%). IR (KBr) in cm^{-1}: 1615 (C=N), 1705 (C=O), 3201–3315 (N−H). ^{1}H NMR ($CDCl_3$): δ1.64 (m, 8H, 4 × C***H***$_2$), 2.54 (m, 2H, C***H***$_2$), 2.73 (m, 2H, C***H***$_2$), 4.57 (bs, 2H, 2 × N***H***), 7.71 (m, 6H, Ar-*H* & = C***H***). ^{13}C NMR ($CDCl_3$): δ 24.22, 27.49, 30.12, 36.88, 122.2 (Thiazolidinone ***C*** = CH), 127.1, 128.6, 129.4, 132.5 (=***C***H), 136.8, 149.4 (N = ***C***−S), 166.22 (***C***=O).

7′-Benzylidene-6′(7′H)-oxospiro[cyclohexane-1,3′(4′)H-[2H]thiazole[3,2-b]-s-tetrazine] (3b)

It was prepared from **2b** by the same method as above in 40 sec. Mp 215°C, Yield 65%, (Found S, 10.19, $C_{16}H_{18}N_4SO$ requires S, 9.99%). IR (KBr) in cm^{-1}: 1565, 1630, 1705, 3240, 3300. ^{1}H NMR ($CDCl_3$): 1.55 (m, 6H, 3 × C***H***$_2$), 2.52 (m, 4H, 2 × C***H***$_2$), 4.59 (bs, 2H, 2 × N***H***), 7.74 (m, 6H, Ar-***H*** & = C***H***). ^{13}C NMR ($CDCl_3$): 24.22, 27.49, 30.12, 36.88, 122.2, 127.1, 128.6, 129.4, 132.5, 136.8, 149.4, 166.2.

7′-Benzylidene-6′(7′H)-oxospiro[cyclooctane-1,3′(4′)H-[2H]thiazole[3,2-b]-s-tetrazine] (3d)

It was prepared from **2d** by the same method as above in 60 sec. Mp 225°C, Yield 64%, (Found S, 9.36, $C_{18}H_{22}N_4SO$ requires S, 9.24%). IR (KBr) in cm^{-1}: 1570, 1635, 1708, 3245, 3310. ^{1}H NMR ($CDCl_3$): 1.58 (m, 10H, 5 × C***H***$_2$), 2.46 (m, 4H, 2 × C***H***$_2$), 4.60 (bs, 2H, 2 × N***H***), 7.69 (m, 6H, Ar-***H*** & = C***H***). ^{13}C NMR ($CDCl_3$): 23.60, 24.34, 27.55, 30.28, 37.10, 122.8, 127.4, 128.8, 130.2, 133.0, 137.4, 150.6, 167.1.

6′,7′-Dihydrospiro[cycloheptane-1,3′(4′H)-[2H]thiazolo[3,2-b]-s-tetrazine] (4c)

To a mixture of **1c** (2.00 g, 0.01 mol) and 1,2-dibromoethane (1.88 g, 0.01 mol), a few drops of glacial acetic acid were added and the mixture was irradiated in a microwave oven for 35 sec. Then the reaction mixture was cooled, ice cold water was added, and the precipitate obtained was filtered, dried, and crystallized from ethanol. Mp 170°C, Yield 74%,

(Found S, 14.09, $C_{10}H_{18}N_4S$ requires S, 14.16%). IR (KBr) in cm^{-1}: 1610 (C=N), 3160–3250 (N−H). ^1H NMR ($CDCl_3$): δ1.67 (m, 8H, 4 × C***H***$_2$), 2.50 (m, 4H, 2 × C***H***$_2$), 3.16 (t, 2H, S-C***H***$_2$), 3.85 (t, 2H, -N-C***H***$_2$), 4.45 (bs, 2H, 2 × N***H***). ^{13}C NMR ($CDCl_3$): δ 24.24, 27.48, 30.12, 36.12 (S- ***C***H_2), 36.88, 55.64 (N-***C***H_2), 149.4 (N=***C***-S).

6′,7′-Dihydrospiro[cyclopentane-1,3′(4′H)-[2H]thiazolo[3,2-b]-s-tetrazine] (4a)

It was prepared from **1a** by the same method as above in 35 secs. Mp 175°C, Yield 62%, (Found S, 16.02, $C_8H_{14}N_4S$ requires S, 16.16%). IR (KBr) in cm^{-1}: 1530, 1600, 3080, 3160. ^1H NMR ($CDCl_3$): δ 1.72 (m, 4H, 2 × CH_2), 2.55 (m, 4H, 2 × CH_2), 3.20 (t, 2H, S-CH_2), 3.88 (t, 2H, -N-CH_2), 4.52 (bs, 2H, 2 × N*H*). ^{13}C NMR ($CDCl_3$): δ 27.60, 30.38, 36.44, 37.15, 55.74, 150.10.

6′,7′-Dihydrospiro[cyclooctane-1,3′(4′H)-[2H]thiazolo[3,2-b]-s-tetrazine] (4d)

It was prepared from **1d** by the same method as above in 35 sec. Mp 171°C, Yield 69%, (Found S, 13.33, $C_{11}H_{20}N_4S$ requires S, 13.14%). IR (KBr) in cm^{-1}: 1560, 1610, 3160–3250. ^1H NMR ($CDCl_3$): δ1.58 (m, 10H, 5 × CH_2), 2.52 (m, 4H, 2 × CH_2), 3.18 (t, 2H, S-CH_2), 3.86 (t, 2H, -N-CH_2), 4.64 (bs, 2H, 2 × N*H*). ^{13}C NMR ($CDCl_3$): δ 23.58, 24.44, 27.56, 30.32, 36.12, 36.90, 55.70, 149.8.

REFERENCES

[1] R. S. Verma, A. K. Chatterji, and M. Varma, *Tetrahedron Lett.*, **34,** 46303 (2000).
[2] M. Kidwai, *Chem. Edu. Rev.*, **15,** 77 (2001).
[3] D. Michael, *Chem. Soc. Rev.*, **20,** 1 (1991).
[4] K. Mogiluidh, N. V. Reddy, and P. R. Reddy, *Indian J. Heterocycl. Chem.*, **10,** 267 (2001).
[5] S. A. Gale, *Chem. Soc. Rev.*, **26,** 233 (1997).
[6] P. Lidstrom, J. Tierney, B. Wathey, and J. Westman, *Tetrahedron*, **57,** 9225 (2007).
[7] D. H. More, N. S. Pawar, P. M. Dewang, S. L. Patil, and P. P. Mahulikar, *Russ. J. Green Chem.*, **74,** 2244 (2004).
[8] D. H. More, N. S. Pawar, and P. P. Mahulikar, *J. Sci. Ind. Res.*, **62,** 1024 (2003).
[9] A. R. Katritzky, C. Cai, and S. K. Singh, *J. Org. Chem.*, **71,** 3375 (2006).
[10] W. Solodenko, P. Bröker, J. Messinger, U. Schön, and A. Kirschning, *Synthesis*, 461 (2006).
[11] R. E. Tundel, K. W. Anderson, and S. L. Buchwald, *J. Org. Chem.*, **71,** 430 (2006).
[12] H. Lipshutz, B. A. Frieman, T. Butler, and V. Kogan, *Angew. Chem. Int. Ed.*, **45,** 800 (2006).
[13] C.-S. Jia, Z. Zhang, S.-J. Tu, and G.-W. Wang, *Org. Biomol. Chem.*, **4,** 104 (2006).

Downloaded by [Northeastern University] at 01:01 27 November 2014

[14] G. W. Kabalka and M. Al-Masum, *Org. Lett.*, **8,** 11 (2006).
[15] G. Minetto, L. F. Raveglia, A. Sega, and M. Taddei, *Eur. J. Org. Chem.*, 5277 (2005).
[16] U. Kazmaier and S. Ackermann, *Org. Biomol. Chem.*, **3,** 3184 (2005).
[17] C. Kuang, Q. Yang, H. Senboku, and M. Tokuda, *Synthesis*, 1319 (2005).
[18] A. Porcheddu, G. Giacomelli, and M. Salaris, *J. Org. Chem.*, **70,** 2361 (2005).
[19] M. Follmann, F. Gaul, T. Schäfer, S. Kopec, and P. Hamley, *Synlett*, 1009 (2005).
[20] A. Dandia, M. Sati, K. Arya, P. Sarawgi, and A. Loupy, *Arkivoc*, **i,** 105 (2005).
[21] A. Dandia, K. Arya, S. Khaturia, and P. Yadav, *Arkivoc*, **xiii,** 80 (2005).
[22] K. V. Raunak, S. Mukherjee, Poonam, A. K. Prasad, C. E. Olsen, S. J. C. Schäffer, S. K. Sharma, A. C. Watterson, W. Errington, and V. S. Parmar, *Tetrahedron*, **61,** 5687 (2005).
[23] P. Ye, K. Sargent, E. Stewart, J. F. Liu, D. Yohannes, and L. Yu, *J. Org. Chem.*, **71,** 3137 (2006).
[24] G. D. Gupta and H. K. Pujari, *Indian J. Chem.*, **20B,** 296 (1981).
[25] V. Bindal and H. K. Pujari, *Indian J. Chem.*, **24B,** 1227 (1985).
[26] K. K. Jain and H. K. Pujari, *Indian J. Chem.*, **21B,** 315 (1982).
[27] B. V. Satnarayan, B. R. Sharma, R. Dahiya, G. D. Gupta, K. K. Jain, R. N. Handa, and H. K. Pujari, *Indian J. Chem.*, **26B,** 739 (1987).
[28] I. F. Audrieth, E. S. Scottm, and P. S. Kippur, *J. Org. Chem.*, **19,** 733 (1954).
[29] R. W. Lamon, *J. Org. Chem.*, **34,** 756 (1969).

Downloaded by [Northeastern University] at 01:01 27 November 2014