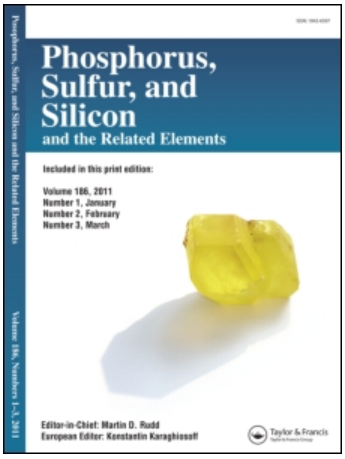

Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Wang, Xicun , Liu, Juan and Li, Zheng(2006) 'Synthesis of Substituted 1,3,4-Oxadiazoles Under Microwave Irradiation', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 3, 627 — 630
To link to this Article: DOI: 10.1080/10426500500269877
URL: http://dx.doi.org/10.1080/10426500500269877

Phosphorus, Sulfur, and Silicon, 181:627–630, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500500269877

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Synthesis of Substituted 1,3,4-Oxadiazoles Under Microwave Irradiation

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A series of substituted 1,3,4-oxadiazoles were synthesized by the cyclization of 2,6-pyridine dicarboxylic acid, 5-(4′-carboxyl-phenyl)-2-furanylcarboxylic acid, or p-*phthalic acid, and aryl hydrazines in the presence of phosphorus oxychloride under the condition of microwave irradiation.*

Keywords 1,3,4-oxadiazoles; microwave irradiation; synthesis

INTRODUCTION

Substituted 1,3,4-oxadiazoles are widely applied in medicine and agriculture; for example, they are used as psychotropic drugs,[1] antiinflammatory[2] reagents, pesticides, and insecticidal,[3] fluorescence,[4] and plant growth reagents[5] etc. Meanwhile, pyridine and furan derivatives[6] also have attracted much attention due to their anticancer,[2] antihypertension,[5] and antifungal[7] activity.

The conventional methods of the synthesis of 1,3,4-oxadiazloes are as follows: (1) the cyclization of 1,4-disubstituted thiosemicarbazide in the presence of either I_2/NaOH[8] or dicyclohexycarbodiimide (DCC),[9,10] and (2) the condensation of acid hydrazide with aromatic acids or cyanogen bromide under a severe condition. These methods are inconvenient as

Received February 15, 2005; accepted May 24, 2005.

The authors thank the Scientific and Technological Innovation Engineering department of the Northwest Normal University (NWNU-KJCXGC-02-08); Natural Science Foundation of Gansu Province (ZS021-A25-006-Z); Environmental Protection Foundation of Gansu Province (GH-2003-19), and Youth Foundation of Northwest Normal University (NWNU-03-01) for financial support of this work.

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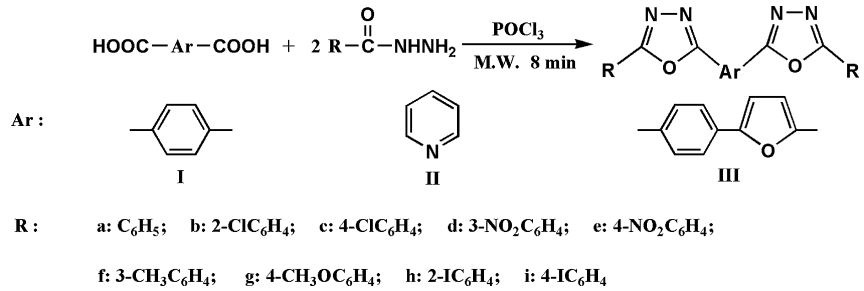
they require heating of the reactants for an extended period of time. Moreover, the yield is frequently only moderate or low.

Microwave technique, meanwhile, has been widely used for a variety of organic reactions,[11,12] such as Claisen, cyclization, oxidation, Diels-Alder reaction, hydrolysis, esterification, etherification, and so on. Many reviews[13–15] have been published in favor of its considerable accelerations of the reaction rates and satisfactory yields.

RESULTES AND DISCUSSION

In view of this, we report herein the preparation of a new series of substituted 1,3,4-oxadiazoles using a microwave technique with the objective of obtaining new biologically active compounds. The synthetic route is shown in Scheme 1.



SCHEME 1

The reaction of 2,6-pyridine dicarboxylic acid, *p*-phthalic acid, and 5-(4′-carboxyl-phenyl)-2-furanylcarboxylic acid with aryl hydrazines catalyzed by pyridine on exposure to microwave irradiation in the presence of phosphorus oxychloride resulted in a series of substituted 1,3,4-oxadiazoles. The results are shown in Tables I and II.

EXPERIMENTAL

Melting points were determined on a XT-4 thermal apparatus and the m.p. are uncorrected. ^{1}H NMR spectra were obtained on a Avanci-D2X-200 instrument using DMSO-d_6 as a solvent and TMS as internal standard. IR spectra were recorded using KBr pellets on a Nicolet AVATAR 360 FT-IR. Elemental analyses were performed on a Carlo-Erba 1106 Elemental Analysis instrument. The acids and aroyl hydrazines[16] were prepared according to literature methods.

TABLE I The Physical Data of 1,3,4-Oxadiazoles Under Microwave Irradiation

	Ar	Mol. formula	Yield (%)	M.P. (°C)	Elemental Analysis % (Found) C	H	N
Id	$3\text{-}O_2NC_6H_4$	$C_{22}H_{12}N_6O_6$	86	>300	57.86(57.90)	2.74(2.65)	18.31(18.41)
Ig	$4\text{-}OCH_3C_6H_4$	$C_{24}H_{18}N_4O_4$	83	>300	67.66(67.60)	4.13(4.25)	13.19(13.14
Ih	$2\text{-}IC_6H_4$	$C_{22}H_{12}N_4O_2I_2$	75	>300	42.58(42.75)	2.01(1.96)	9.13(9.06)
Ii	$4\text{-}IC_6H_4$	$C_{22}H_{12}N_4O_2I_2$	79	>300	42.79(42.75)	1.84(1.96)	8.99(9.06)
IIb	$2\text{-}ClC_6H_4$	$C_{21}H_{11}N_5O_2Cl_2$	85	>300	57.68(57.82)	2.47(2.54)	16.16(16.05)
IId	$3\text{-}NO_2\ C_6H_4$	$C_{21}H_{11}N_7O_6$	91	>300	55.03(55.15)	2.35(2.42)	21.58(21.44)
IIg	$4\text{-}OCH_3C_6H_4$	$C_{23}H_{17}N_5O_4$	87	>300	64.71(63.64)	3.98(4.01)	16.26(16.39)
IIIa	C_6H_5	$C_{26}H_{16}N_4O_3$	89	269–271	72.38(72.22)	3.70(3.73)	13.05(12.96)
IIIc	$4\text{-}ClC_6H_4$	$C_{26}H_{14}N_4O_3Cl_2$	72	>300	62.15(62.29)	2.69(2.81)	11.34(11.18)
IIIe	$4\text{-}NO_2\ C_6H_4$	$C_{26}H_{14}N_6O_7$	74	279–281	59.63(59.78)	2.61(2.70)	16.14(16.09)
IIIf	$3\text{-}CH_3C_6H_4$	$C_{28}H_{20}N_4O_3$	78	223–225	73.19(73.03)	4.35(4.38)	12.03(12.17)

General Procedure for the Preparation of 1,3,4-Oxadiazoles

A mixture of 5-(4′-carboxyphenyl)-2-furanylcarboxylic acid (1 mmol) or 2,6-pyridine dicarboxylic acid (1 mmol), aryl hydrazines (2 mmol), phosphorus oxychloride (6 mL), and 2 drops of pyridine was irradiated in a microwave oven (490 W) for 8 min. When it was cooled to r.t., some pieces of ice were added and the mixture stood for 2–4 h. The precipitate was

TABLE II The IR and ^{1}H NMR Data of 1,3,4-Oxadiazoles Under Microwave Irradiation

Entry	IR/cm^{-1} C=N–N=C–O	^{1}HNMR (DMSO-d_6) δ
I-d	1623 1546 1487 1091	7. 62–8.31 (m, 12H, Ar-H)
I-g	1614 1530 1446 1074	3.93 (s, 6H, CH_3) 7.41–8.12 (m, 12H, Ar-H)
I-h	1619 1534 1476 1083	7.54–8.17 (m, 12H, Ar-H)
I-i	1617 1538 1479 1085	7.52–8.19 (m, 12H, Ar-H)
II-b	1603 1530 1479 1095	8.32–8.51 (m, 3H, C_5H_3N) 7.63–8.24 (m, 8H, Ar-H)
II-d	1612 1533 1485 1091	8.37–8.65 (m, 3H, C_5H_3N) 7.75–8.37 (m, 8H, Ar-H)
II-g	1607 1529 1468 1089	3.86 (s, 6H, CH_3) 8.39–8.52 (m, 3H, C_5H_3N) 7.58–8.18 (m, 8H, Ar-H)
III-a	1608 1537 1469 1087	7.24–8.30 (m, 16H, Ar-H, and Fu-H)
III-c	1613 1541 1457 1086	7.25-8.23 (m,14H, Ar-H, and Fu-H)
III-e	1607 1534 1466 1080	7.33-8.41 (m,14H, Ar-H, and Fu-H)
III-f	1612 1537 1465 1075	2.44 (s, 6H, CH_3) 7.24–8.21 (m, 14H, Ar-H, and Fu-H)

collected by filtration and washed with a saturated sodium carbonate solution (2 × 10 mL) and water (3 × 10 mL). The product was recrystallized from DMF and EtOH.

REFERENCES

[1] H. Liszkiewicz, T. Glowiak, M. W. Kowalska, M. Rutkowska, and A. Szelag, *Pol. J. Chem.*, **73,** 321 (1999); *Chem. Abstr.*, **130,** 237520 (1999).
[2] F. A. Omar, N. M. Mahfouz, and M. A. Rahman, *Eur. J. Med. Chem. Chim. Ther.*, **31,** 819 (1996).
[3] S. Gao, X. H. Qian, G. H. Song, and Q. C. Huang, *J. Fluoric Chem.*, **117,** 63 (2002).
[4] J. L. Zhang, M. Matsuoka, H. Yamashita, and M. Anpo, *Langmuir.*, **15,** 17 (1999).
[5] S. Perez, B. Lasheras, C. Oset, and A. J. Carmen, *J. Heterocycl. Chem.*, **34,** 1572 (1997).
[6] M. Y. Li, P. Z. Hu, W. R. Zhu, and K. X. Xu, *Chin. Chem. Let.*, **14,** 572 (2003).
[7] K. Kawasaki, M. Masubuchi, K. Morikami, S. Sogabe, T. Aoyama, H. Ebiike, S. Niizuma, M. Hayase, T. Fujii, K. Sakata, H. Shindoh, Y. Shiratori, Y. Aoki, T. Ohtsuka, and N. Shimma, *Bioorg. & Med. Chem. Let.*, **13,** 87 (2003).
[8] B. S. Vashi, D. S. Mehta, and V. H. Shah, *Indian J. Chem. Sect., B*, **35,** 111 (1996).
[9] X. M. Wu, X. H. Wu, J. Y. Xu, W. Y. Hua, *J. Chin. Pharm. Univers.*, **27,** 641 (1996).
[10] A. H. Mandour, N. M. Fawzy, T. H. El-Shihi, and Z. E. El-Bazza, *Pak. J. Sci. Ind. Res.*, **38,** 402 (1995); *Chem. Abstr.*, **127,** 135773 (1996).
[11] B. Baruah, D. Prajapati, A. Boruah, and J. S. Sandhu, *Synth. Commun.*, **27,** 2563 (1997).
[12] S. Y. Kim, P. S. Kwon, and T. W. Kwon, *Synth. Commun.*, **27,** 533 (1997).
[13] H. S. Ku, F. Siu, E. Siores, J. A. R. Ball, and A. S. J. Blicblau, *Mater. Pro. Tech.*, **113,** 184 (2001).
[14] H. S. Ku, E. Siores, A. Taube, and J. A. R. Ball, *Comp. & Indus. Engine.*, **42,** 281 (2002).
[15] M. S. Venkatesh and G. S. V. Raghavan, *Bio. Engine.*, **88,** 1 (2004).
[16] G. Y. Ding, M. Y. Xie, and G. F. Zhao, *Chin. J. Appl. Chem.*, **12,** 99 (1995); *Chem. Abstr.*, **124,** 146278 (1995).