Asian Journal of Chemistry Vol. 19, No. 4 (2007), 3141-3144

Microwave-Assisted Synthesis and Biological Activity of 2,5-disubstituted-1,3,4-thiadiazole

YU YUYE
Normal College, Jin Hua College of Professional and Technology
Jin Hua 321017, P.R. China
E-mail: yuyeyu@gmail.com

The reaction of substitute aryl and alkyl acid with thiosemicarbazide in the presence of dehydrating agent $POCl_3$, affords a series of 2-amino-5-aryl-1,3,4-thiadiazoles under microwave irradiation. 2,5-Disubstituted-1,3,4-thiadiazoles have attracted much attention due to their diverse biological activities, such as antimicrobial, antibacterial, anesthetic, anticonvulsant and antiinflammatory activities. Compared with classical methods, this method has the advantages of high yields, short reaction time, easy preparation and mild reaction conditions. The preliminary biological test showed that the synthesized compound has weak activity to *G. zeae* Petch, *B. cinerea* Pers, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f.sp. *cucumerinum* and *Cercospora arachidicola*. The structures of compounds were characterized by melting points, ^{1}H NMR and IR.

Key Words: Microwave synthesis, Antibacterial activity, 2-Amino-5-substituted-1,3,4-thiadiazoles.

INTRODUCTION

In recent reports, it was shown that 2-amino-5-substituted-1,3,4-thiadiazoles are very useful starting materials for the synthesis of various bioactive molecules[1,2]. 2-Amino-5-substituted-1,3,4-thiadiazoles are widely applied in medicine and agriculture as pesticides[3].

Several procedures are available for the one-step synthesis of 2-amino-5-substituted-1,3,4-thiadiazoles derivative[4]. However, most the methods suffer from serious drawbacks which include the use of hazardous and expensive or commercially unavailable reagents, long reaction times, drastic reaction conditions and tedious workup procedure.

Microwave technique, meanwhile, has been widely used for a variety of organic reactions[5,6] such as Claisen, cyclization, oxidation, Diels-Alder reaction, hydrolysis, esterification, etherification and so on. Numerous reviews[7-9] have been published in favour of its considerable accelerations of the reaction rates and satisfactory yields.

EXPERIMENTAL

Melting points were determined using a Yanaco MP-241 apparatus and are uncorrected. Infrared spectra were recorded on a Bruker Equinox55 spectrophotometer as potassium bromide tablets. ^{1}H NMR spectra were measured on a Bruker AC-P500 instrument (300 MHz) using tetramethylsilane as an internal standard and dimethylsulfoxide-d_6 as solvent. Elemental analyses were performed on a Yanaco MT-3CHN elemental analyzer.

General procedure: The reactants substitute aryl and alkyl acid (0.01 mol), thiosemicarbazide (0.013 mol), $POCl_3$ (5 mL) were mixed at room temperature for 10 min. It was irradiated in a microwave oven (600 W) for 10 min. After that, the excess $POCl_3$ was removed on a rotary evaporator. Then added 40 % NaOH, up to pH = 9~10 keeping overnight the required product has been crystallized out. The products was recrystallled from DMF-EtOH. Yields are given in Table-1. All derived 2-amino-5-substituted-1,3,4-thiadiazoles are known compounds and their spectral data, as well as melting points of solids, were in agreement with those known[10-19].

TABLE-1
PHYSICAL DATA OF 2-AMINO-5-SUBSTITUTE-1,3,4-THIADIAZOLES UNDER MICROWAVE IRRADIATION

R	m.f.	Yield (%)	m.p. (Literature °C)
H-	$C_2H_3N_3S$	86	191-193 (190-192)
Me-	$C_3H_5N_3S$	83	200-201 (202-204)
Et-	$C_4H_7N_3S$	75	199-200 (196-198)
n-Pr-	$C_5H_9N_3S$	79	194 (193-195)
Iso-Pr-	$C_5H_9N_3S$	85	188-189 (187-189)
n-Bu-	$C_6H_{11}N_3S$	91	191-193 (191-193)
Cyclopropane-	$C_5H_7N_3S$	87	211-212 (210-211)
C_6H_5	$C_8H_7N_3S$	89	230-233 (230-232)
m-$CH_3C_6H_4$	$C_9H_9N_3S$	88	152-153 (153-156)
p-$OCH_3C_6H_4$	$C_9H_9N_3OS$	79	195-196 (194-198)
o-$CH_3C_6H_4$	$C_9H_9N_3S$	82	191-192 (193)
o-Cl C_6H_5	$C_8H_6N_3SCl$	85	190-193 (192-195)
p-Cl C_6H_5	$C_8H_6N_3SCl$	81	233-234 (232-233)
m-Cl C_6H_5	$C_8H_6N_3SCl$	83	207-209 (209)
p-$NO_2C_6H_5$	$C_8H_6N_4O_2S$	84	266-267 (264-265)
o-FC_6H_5	$C_8H_6FN_3S$	88	221-223 (223-225)
3-Pyridine-	$C_7H_6N_4S$	78	230-231 (230-232)
4-Pyridine-	$C_7H_6N_4S$	76	225-227 (226)
Furan-	$C_6H_5N_3OS$	90	229-230 (229-230)

Bioassay of fungicidal activities

Fungicidal activities of the present compounds against *G. zeae* Petch, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f. sp. *cucumerinum* and *Cercospora arachidicola* were evaluated using the mycelium growth rate test. The culture media, with known concentration of the test compounds. The blank test was made using acetone. The culture was carried out at 24 ± 0.5ºC. Three replicates were performed.

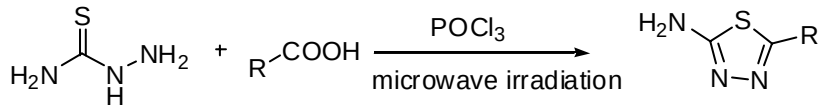
Primary bioassay (Table-2) showed that the tested compounds has weak fungicidal activity against *G. zeae* Petch, *B. cinerea* Pers, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f. sp. *cucumerinum* and *Cercospora arachidicola*.

TABLE-2
FUNGICIDAL ACTIVITY OF TESTED COMPOUNDS AT 50 ppm

R	*G. zeae* Petch	*P. infestans* (Mont.) de Bary	*B. berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma	*F. oxysporum* f.sp. *cucumerinum*	*C. arachidicola*
H-	0	38.5	0	28.9	28.5
Me-	14.3	15.4	17.8	35.1	17.9
Et-	0	15.4	11.7	0	17.9
n-Pr-	0	0	11.7	0	10.7
Iso-Pr-	11.2	22.1	10.8	15.6	11.6
n-Bu-	15.8	15.3	6.5	0	14.4
Cyclopropane-	28.2	22.1	15.6	17.8	12.3
C_6H_5	16.8	26.3	0	11.3	14.5
m-$CH_3C_6H_4$	43.2	21.3	29.8	18.9	16.3
p-$OCH_3C_6H_4$	22.9	25.5	14.5	16.6	23.3
o-$CH_3C_6H_4$	16.8	11.2	16.7	31.0	25.6
o-Cl C_6H_5	17.9	10.9	18.4	23.5	21.4
p-Cl C_6H_5	19.8	14.6	22.3	16.7	22.4
m-Cl	26.9	18.7	19.8	25.8	29.8
p-$NO_2C_6H_5$	24.3	34.5	18.3	26.4	24.1
o-FC_6H_5	45.2	36.2	26.0	11.9	10.3
3-Pyridine-	34.9	22.1	11.5	19.7	0
4-Pyridine-	43.2	11.4	41.0	25.3	18.8
Furan-	27.8	15.6	33.2	35.5	0

RESULTS AND DISCUSSION

The preparation of a new series of substituted 2-amino-5-substituted-1,3,4-thiadiazoles using a microwave technique is reported with the object of obtaining biologically active compounds. The synthetic route is shown in **Scheme-I**.



Scheme-I

REFERENCES

1. S. Ulrich and P. Plter, EP86473 (1984).
2. Z. Zhang and F. Yang, *Chin. J. Org. Chem.*, **5**, 19 (1994).
3. X. Yang and F. Chen, *Chem. Res. Chin. Univ.*, **16**, 234 (1995).
4. C.G. Le, J.H. Ding and S. Yang, *Chem. World*, 366 (2002).
5. B. Baruah, D. Prajapati, A. Boruah and J.S. Sandhu, *Synth. Commun.*, **27**, 2563 (1997).
6. S.Y. Kim, P.S. Kwon and T.W. Kwon, *Synth. Commun.*, **27**, 533 (1997).
7. H.S. Ku, F. Siu, E. Siores, J.A.R. Ball and A.S.J. Blicblau, *Mater. Pro. Tech.*, **113**, 184 (2001).
8. H.S. Ku, E. Siores, A. Taube and J.A.R. Ball, *Comp. Ind. Eng.*, **42**, 281 (2002).
9. M.S. Venkatesh and G..S.V. Raghavan, *Bio. Eng.*, **88**, 1 (2004).
10. Monsanto, US2623877 (1946).
11. S. Lawsen, *J. Chem. Soc.*, 1551 (1957).
12. BASF, DE1047600 (1948).
13. Bayer AG, DE2823636 (1979).
14. Lepetit Spa, GB815188 (1957).
15. Amer Cyanamid Co., US3705171 (1957).
16. J. Mohan, G.S.R. Anjaneyulu and Kiran, *Indian J. Chem.*, **28B**, 500 (1989).
17. T.S. Gardner, E. Wenis and J. Lee, *J. Org. Chem.*, **20**, 976 (1955).
18. P.W. Sadler, *J. Org. Chem.*, **26**, 1315 (1961)
19. R. Rao and V.R. Srinivasan, *Indian J. Chem.*, **8**, 509 (1970).

(*Received*: 12 October 2006; *Accepted*: 30 January 2007) AJC-5371