Ultra Chemistry Vol. 8(3), 409-414 (2012).

Synthesis and Characterization of 5-{2-[(4-substituted phenyl) amino] ethyl}-N-(4-substituted phenyl) 1,3,4-oxadiazole-2-amine as possible fungicides

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(Acceptance Date 29th December, 2012)

Abstract

3-(4-Bromo anilino) methyl propionate (Ia-f) obtained from 4-bromo aniline and methylacrylate. These compounds further treating with hydrazine hydrate (99%) in ethanol yielded 3-(4-bromo anilino) propionic acid hydrazine (IIa-f), which on further treating with aryl isothiocyanate (0.01 moles) in the presence of ethanol gives the title compounds 5-{2-[(4-substituted phenyl amino) ethyl]-N-(4-substituted phenyl) 1,3,4-oxadiazole-2-amine (IIIa-r). All the synthesize compounds were well characterized by their elemental and spectral studies. The fungitoxicity of the synthesized compounds were evaluated against *Phytophthora infestans* and *Helminthosporium oryzae*.

Key words : 4-Bromo aniline, Methyl acrylate, Hydrazine hydrate, Aryl isothiocyanate, *Helminthosporium oryzae* and *Phytophthora infestans*

Introduction

Five membered Heterocyalic compounds present in the living beings where these performs important biological functions. 1,3,4-oxadiazole derivatives are known to exhibit various useful biological activities including herbicidal[1-5], fungicidal[6-8], bactericidal[9-12], insecticidal[13-16] & viricidal[17] and to show a broad spectrum of medicinal properties[18-22].

Experimental

3-(4-Bromo anilino) methyl propionate (Ia-f):

Equimolar quantities of 4-bromo aniline and methyl acrylate were refluxed on a heating mantle for 15 hours in the presence of glacial acetic acid. The contents were concentrated, cooled and poured on to crushed ice. The resulting solid which separated out was

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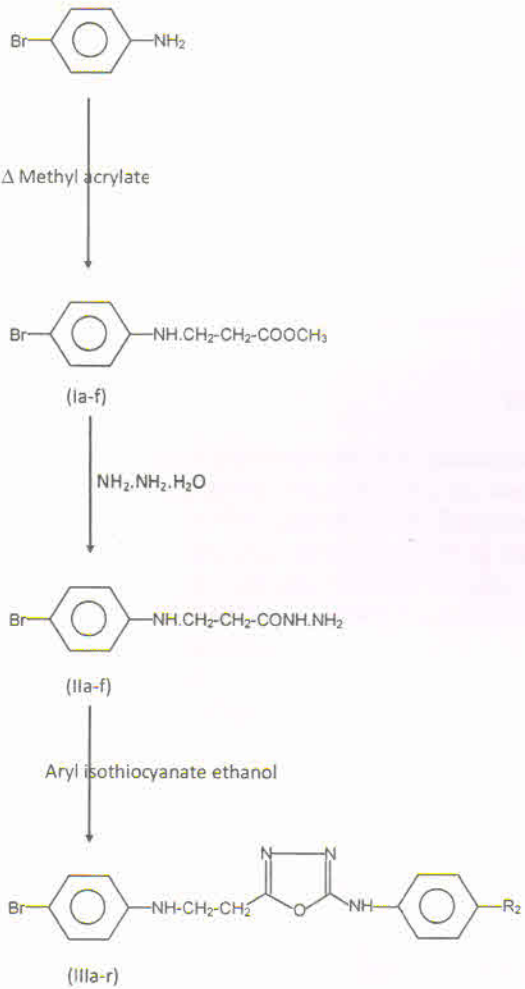

Scheme-I

filtered washed with H_2O, dried and recrystallized from ethanol, M.P. 137^{0}C, yield 80% of theory.

Analysis : Found C, 46.5; N, 5.4%.

IR (KBr) 2838 (-NH-), 1735 (-C-O-), 970, 913 (Aromatic region) cm^{-1}

^{1}HNMR ($CDCl_3$) δ : 2.03 (2H, t, CH_3), 2.54 (2H, t-CH_2-CO),

3.2 (3H, s, -$COOCH_3$), 5.82 (1H, s, NH)

6.5-7.4 (4H, m, Ar-H)

Similarly other 3-(substituted anilino) methyl propionate, where synthesized which are given below-

(a) 3-(2-Bromo anilino) methyl propionate, M.P. 135^{0}C, yield 77% of the theory.

(b) 3-(2-Chloro anilino) methyl propionate, M.P. 138^{0}C, yield 75% of the theory.

(c) 3-(4-Chloro anilino) methyl propionate, M.P. 141^{0}C, yield 78% of the theory.

(d) 3-(2-Methyl anilino) methyl propionate, M.P. 145^{0}C, yield 74% of the theory.

(e) 3-(4-Methyl anilino) methyl propionate, M.P. 150^{0}C, yield 75% of the theory.

3-(4-Bromo anilino) methyl propionic acid hydrazide (IIa-f) :

To an ethanolic solution of 3-(4-bromo anilino methyl propionate (0.01 mol), hydrazine hydrate (99%) was added. The resulting reaction mixture was refluxed on a steam bath for 10-12 hours. The excess of the ethanol with cold water dried and recrystallized from ethanol, M.P. 130^{0}C, yield 72% (of the theory).

Analysis : Found C, 42.5; N, 16.3%, M.F. $C_8H_{12}N_3OBr$.

Requires C, 41.8; N, 16.2%

IR (KBr) : 3316 (-NH_2), 3095 (-NH-CH_2), 9650 (>C=O)) cm^{-1}

^{1}HNMR (DMSO-d_6) δ : 2.2 (2H, m, NCH_2), 3.2 (2H, m, -CH_2CO-),

4.1 (2H, s, NH_2), 5.8 (1H, s, NH)

6.2-7.3 (4H, m, Ar-H), 9.0 (1H, s,-CONH)

Table 1. Characterization data of 5-(2-[(substituted phenyl) amino] ethyl}-N-(substituted phenyl)-1,3,4-oxadiazole-2-amine.

Compd. No.	R_1	R_2	Molecular formula	M.P. (^{0}c)	Yield %	Analysis, Found (Calcd.)%	
						C	N
a	2-Br	H	$C_{16}H_{15}N_4OBr$	145	74	53.47 (53.48)	15.60 (15.59)
b[a]	4-Br	H	$C_{16}H_{15}N_4OBr$	152	78	53.46 (53.48)	15.57 (15.59)
c	2-Cl	H	$C_{16}H_{15}N_4OCl$	149	72	61.05 (61.04)	17.79 (17.80)
d	4-Cl	H	$C_{16}H_{15}N_4OCl$	154	73	61.3 (61.04)	17.81 (17.80)
e	2-CH_3	H	$C_{17}H_{18}N_4O$	156	77	68.36 (69.38)	19.03 (19.04)
f	4-CH_3	H	$C_{17}H_{18}N_4O$	154	78	69.36 (69.38)	19.05 (19.04)
g	2-Br	4-CH_3	$C_{17}H_{17}N_4OBr$	152	80	55.71 (54.69)	15.03 (15.01)
h	4-Br	4-CH_3	$C_{17}H_{17}N_4OBr$	148	82	54.70 (54.69)	15.02 (15.01)
i	2-Cl	4-CH_3	$C_{17}H_{17}N_4OCl$	151	81	62.12 (62.10)	17.02 (17.04)
j	4-Cl	4-CH_3	$C_{17}H_{17}N_4OCl$	153	80	62.08 (62.10)	17.05 (17.04)
k	2-CH_3	4-CH_3	$C_{18}H_{20}N_4O$	155	76	70.10 (70.12)	18.16 (18.18)
l	4-CH_3	4-CH_3	$C_{18}H_{20}N_4O$	156	81	70.13 (70.12)	18.17 (18.18)
m	2-Br	4-Cl	$C_{16}H_{14}N_4OClBr$	149	76	48.78 (48.79)	14.25 (14.23)

n	4-Br	4-Cl	$C_{16}H_{14}N_4OClBr$	147	75	48.80 (48.79)	14.21 (14.23)
o	2-Cl	4-Cl	$C_{16}H_{14}N_4OCl_2$	144	78	55.00 (55.01)	16.05 (16.04)
p	4-Cl	4-Cl	$C_{16}H_{14}N_4OCl_2$	148	76	55.03 (55.01)	16.06 (16.04)
q	2-CH_3	4-Cl	$C_{17}H_{14}N_4OCl$	150	74	62.12 (62.10)	17.05 (17.04)
r	4-CH_3	4-Cl	$C_{17}H_{17}N_4OCl$	152	75	62.09 (62.10)	17.03 (17.04)

a. IR (KBr) : 3220 (–NH), 2368 (>C–NH–C<) cm^{-1}
^{1}HNMR (DMSO-d_6) δ : 4.5 (1H, s ,NH), 2.3 (2H, t, CH_2), 7.2 - 7.8 (8H, m, Ar–H)

Other five hydrazine were prepare following the some procedure which are given below-

(a) 3-(2-Bromo anilino) propionate acid hydrazide, M.P. 132^{0}C, yield 71% of the theory.

(b) 3-(2-Chloro anilino) propionate acid hydrazide, M.P. 135^{0}C, yield 71% of the theory.

(c) 3-(4-Chloro anilino) propionate acid hydrazide, M.P. 146^{0}C, yield 75% of the theory.

(d) 3-(2-Methyl anilino) propionate acid hydrazide, M.P. 148^{0}C, yield 72% of the theory.

(e) 3-(4-Methyl anilino) propionate acid hydrazide, M.P. 135^{0}C, yield 73% of the theory.

5-{2-[4-Substituted phenyl amino] ethyl}-N-(substituted phenyl)-1,3,4-oxadi- azole-2-amine:

3-(Substituted anilino) propionic acid hydrazide (0.01 mol) and aryl isothiocyanate (0.01 mol) in ethanol was refluxed for 3 hours. The content were concentrated and poured on the crushed ice, the solid product was filtered and dried to give thiosemicarbazide. To the crude thiosemicarbazide (0.03 mol) in ethanol (30 ml) aqueous NaOH (6 N, 5 ml) was added dropwise and the reaction mixture was refluxed for 4 hours on cooling, the separated solid was washed thoroughly with H_2O and recrystallized from ethanol.

Eighteen such titled compounds were synthesized following the above procedure. All the synthesized compounds were crystallized from ethanol and with their characterization data, M.P. yield, molecular formula, elemental analysis and spectral data are recorded in Table 1. Special data IR (KBr) and ^{1}HNMR (DMSO-d_6) of the representative compounds is given as footnote in the table.

Results and Discussion and Fungitoxicity

The screening data indicate that all the compounds were more active against *Helmintosporium oryzae* as compared with *Phytophthora infestans* but the difference was marginal. Most of the compounds showed the significant antifungal activity of 100 ppm against both the fungal species but their fungitoxicity decreased markedly on dilution (100 and 10 ppm) concentration out of these the compounds *d, j & o* exhibited fungitoxicity of the order of **Dithane M-45** at 1000 ppm against both the test fungi. However their activity decreased markedly at lower conc. (100 and 10 ppm) except in the compounds d, *j & o* which exhibited 50-53% growth of the both the fungi species even at 100 ppm.

It is however noteworthy that the introduction of chloro and methoxy group in the aryl moiety of these compounds tends to arguments the fungitoxicity and that the introduction of chloro group of ortho position is more effective than that at para position. Likewise, the introduction of methoxy group at ortho position is more effective than para position. The overall results are not so encouraging as one would expect from combined performance of the two biolable nuclei *viz.* 4-bromo aniline and aryl isothocynate.

Acknowledgement

The authors are thankful to the Principal and Head, Department of Chemistry, S.C. Post Graduate College, Ballia for providing laboratory facilities and Director CDRI, Lucknow of recording IR and NMR spectra.

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