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Synthesis and fungicidal activities of some 2- aryl-5-[phthalimido substituted methyl] 2, 5-bis [phthalimido substituted methyl]-1,3,4-oxadiazoles

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ABSTRACT

Several 2-aryl-5-[phthalimido substituted methyl]-1,3,4-oxadiazoles have been synthesised by the stirring of 2-[phthalimido] alkanoyl aryl hydrazone with bromine in presence of fused sodium acetate and 2,5-bis [phthalimido substituted methyl]-1,3,4-oxadiazoles have been synthesised by the cyclisasation of 1,2-bis [phthalimido] alkanoyl hydrazine with conc. H_2S0_4 with constant stirring in cold and screened for their anti fungal activities against Pyricularia oryzae, Pseudoperonospora cubensis, Sphaerotheca fuliginea and Phytophthora infestans.

Keywords: Phthalimido substituted methyl, 1,3,4-oxadiazoles, fungicidal activity.

INTRODUCTION

In continuation of our work on fused hetero cycles [1-3] and in view of the activities exhibited by 1, 3, 4-oxadiazole compounds with improved biological activities[4-6]. Thus synthesis of 2-aryl-5- [phthalimido substituted methyl]-1,3,4-oxadizoles [5] and 2,5-bis [phthalimido substituted methyl]-1,3,4-oxadiazoles [7] was undertaken with a view to getting compounds of better biological activities. The structure of these compounds was established by the IR, ^{1}HNMR spectral data and elemental analysis.

MATERIALS AND METHODS

Melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer-881 spectrophotometer and ^{1}HNMR spectra on a Perkin Elmer R-32 spectrometer at 60 MHz. Procedure for one typical case for each step has been described.

2-[Phthalimido] alkanoic acid 1 (R=H, n=1) : 2-[Phthalimido] alkanoic acid was prepared according to the method of Billman and Harting [7] by heating a mixture of glycine (18.75g; 0.25M) and phthalic anhydride (37.0g; 0.25M) at 180-185^{0}c on oil bath for 30 minutes. The solid compounds thus obtained were cooled and filtered. The compounds separated were recrystallised from aq. ethanol (m.p. 190^{0}c, literature [7] reports the m.p. 191^{0}c).

2-[Phthalimido] alkanoyl chloride 2. (R=H, n=1): The required 2-[phthalimido] alkanoyl chloride were prepared by refluxing 2- [phthalimido] alkanoic acid (36.9 g; 0.18M) and thionyl chloride (23.4 ml; 0.20M) for 1 hour[8]. The excess of thionyl chloride was removed the residue was dried and recrystallised from acetone m.p. 85^0c, literature[8] reports the same m.p.

2-[Phthalimido] alkanoyl hydrazine 3. (R=H, n=1): A mixture of 2-[Phthalimido] alkanoyl chloride (23.7g; 0.1M), hydrazine hydrate (5.0ml) was refluxed in dichloro methane (50 ml) for 1 hour, the residue poured in to cold water. The compound thus obtained was filtered, washed, dried and recrystallised from aq. ethanol m.p. 139^0c, literature[8] reports the same m.p.

2-[Phthalimido alkanoyl] aryl hydrazones 4a. (R=H, n=1; R=2-CH3) : A mixture of 2- [phthalimido] alkanoyl hydrazine (4.38 g; 0.02M) and benzaldehyde (2.4 ml; 0.02M) with few drops of gl. acetic acid was refluxed in methanol for 4 hours. Excess of solvent was removed and the residue poured in to cold water. The compound thus obtained was filtered, washed, dried and recrystallised from aq. ethanol m.p. 121^0c yield 65% IR (KBr) : 3402 (-NH) 1737, 1668 (>C=0) 1593, 1500 and 1460 cm^{-1} (aromatic ring); ^{1}HNMR (DMSO-d6); δ 2.4 (s, 3H, CH_3); 3.3 (s, 2H, NCH_2) 7.7-8.5 (m.8H+1H, Ar-H+CH); 8.7 (s, 1H, NH).

2-Aryl-5-[phthalimido substituted methyl]-1,3,4- oxadiazoles 5a.(R=H, n=1; R=2 CH3): It was prepared by stirring 2-[phthalimido] alkanoyl aryl hydrazone (4.38g, 0.02M), bromine (2.4ml, 0.02M) and fused sodium acetate(1.64g; 0.02M) in acetic acid on ice bath for 30 minutes, poured in to water and neutralised by sodium carbonate. The solid mass was filtered washed with water, dried and recrystallised from aq. ethanol. m.p. 137^0c yield 66% IR (KBr); 3398 (-NH), 1688 (>C=0), 1618 (>C=N), 1564, 1490, 1417 (aromatic ring) and 1132 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 2.3 (s, 3H, CH_3), 3.2 (s, 2H, NCH_2), 7.1-7.9 (m, 8H, Ar-H)

5b IR (KBr); 3392 (-NH), 1680 (>C=0), 1616 (>C=N), 1560, 1492, 1411 (aromatic ring) and 1130 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 3.1 (s, 2H, NCH_2), 7.2-7.6 (m, 9H, Ar-H)

5c IR (KBr); 3396 (-NH), 1684 (>C=0), 1611 (>C=N), 1564, 1494, 1421 (aromatic ring) and 1136 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 2.3 (s, 3H, CH_3), 3.2 (s, 2H, NCH_2), 7.4-8.0 (m, 8H, Ar-H)

5d IR (KBr); 3396 (-NH), 1684 (>C=0), 1611 (>C=N), 1564, 1494, 1421 (aromatic ring) and 1136 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 3.2 (s, 2H, NCH_2), 3.8 (s, 3H, OMe), 7.4-8.0 (m, 8H, Ar-H).

5e IR (KBr); 3398 (-NH), 1690 (>C=0), 1620 (>C=N), 1563, 1496, 1414 (aromatic ring) and 1138 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 2.7 (t, 2H, CH_2), 3.1 (t, 2H, $CONCH_2$), 7.1-7.9 (m, 8H, Ar-H).

5f IR (KBr); 3396 (-NH), 1681 (>C=0), 1616 (>C=N), 1560, 1490, 1422 (aromatic ring) and 1136 cm^{-1} (C-0-C); ^{1} HNMR (DMSO-d_6): δ 2.7 (t, 2H, CH_2), 3.2 (t, 2H, $CONCH_2$), 3.8 (s, 3H, OMe), 7.4-8.0 (m, 8H, Ar-H).

1,2-Bis [phthalimido] alkanoyl hydrazine 6a. (R=H, n=2) : It was prepared by refluxing a mixture of 2-[phthalimido] alkanoyl chloride (9.48g; 0.04M), hydrazine hydrate (5.0 ml) and triethyl amine (1.5ml, 0.01 M) in dichloro methane (20 ml) for 30 minutes. The reaction mixture was cooled, filtered washed with water, dried and recrystallised from aq. ethanol. m.p. 152^0c yield 54%. IR (KBr) : 3408, 3389 (-NH), 1710, 1689 (>C=0), 1562, 1500 and 1462 cm^{-1} (aromatic ring), ^{1}HNMR (DMSO-d_6) : δ 2.6-2.7 (t, 4H, 2 x CH_2CO), 3.8-3.9 (t,4H, 2 x NCH_2), 7.6-7.9 (m, 8H, Ar-H), 8.1 (s, 1H, NH).

2, 5- Bis [phthalimido substituted methyl]-1, 3, 4- oxadiazoles 7 a. (R=H, n=2) : The 1,2-bis [phthalimido] alkanoyl hydrazine (2.17g ; 0.005M) was cyclodehydrated by conc H_2SO_4 (2.5ml) in cold with constant stirring. When addition is completed the residue was left at room temperature for over night and poured in to cold water and neutralised with ammonia, the desired product precipitated out, It was filtered, washed and recrystallised from aq. ethanol, m.p. 147^0c yield 61% IR. (KBr) : 1702, 1682 (>C=0), 1642, 1636 (>C=N), 1558, 1488, 1448 (aromatic ring) and 1149 cm^{-1} (C-O-C); ^{1}HNMR (DMSO-d_6) ; δ 2.5-3.0 (t, 4H, 2 x CH_2), 3.8-41 (t, 4H, 2 x NCH_2) 7.7-8.0 (m.8H, Ar-H).

7b IR. (KBr) : 1708, 1690 (>C=0), 1631, 1638 (>C=N), 1553, 1484, 1450 (aromatic ring) and 1146 cm^{-1} (C-O-C); ^{1}HNMR (DMSO-d_6) ; δ 4.6 (s, 4H, CH_2) 7.7-8.0 (m.8H, Ar-H).
7c IR. (KBr) : 1710, 1686 (>C=0), 1630, 1634 (>C=N), 1550, 1484, 1451 (aromatic ring) and 1146 cm^{-1} (C-O-C); ^{1}HNMR (DMSO-d_6) ; δ 1.50 (d, 6H, CH_3), 4.0 (q, 2H, CH), 7.7-8.0 (m.8H, Ar-H).
Other such compounds were also prepared in a similar way.

RESULTS AND DISCUSSION

The characterization data of the prepared compounds are given in table 1.

Table 1. Characterization data of Compounds 5a-e and 7a-g

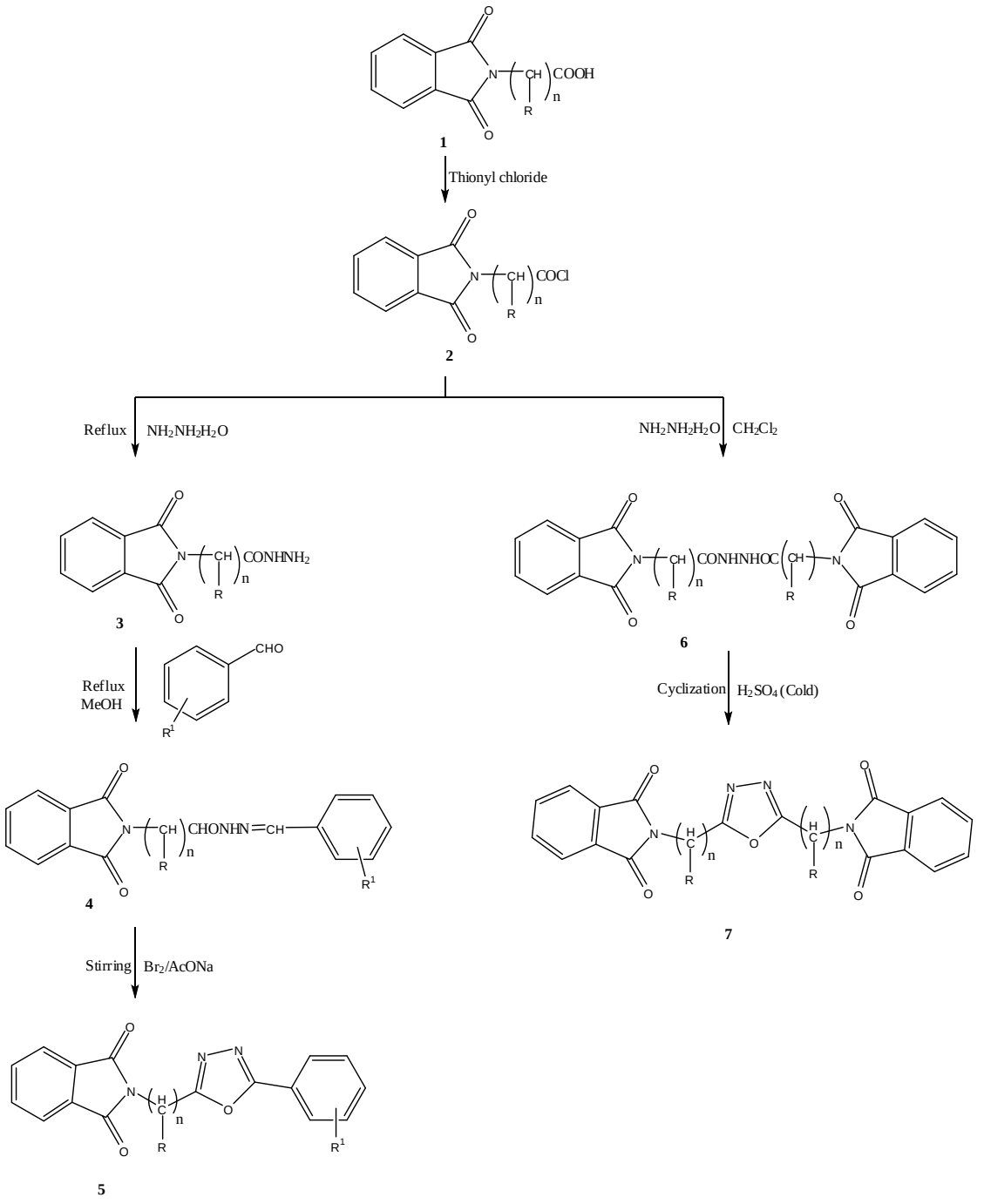
Compd.	M.P. (oc)	Yield (%)	Mol. formula	Found C	(%) H	(Calcd.) N
5a	137	66	$C_{18}H_{13}O_3N_3$	(67.71) 67.31	(4.10) 4.19	(13.16) 13.56
5b	83	60	$C_{17}H_{11}O_3N_3$	(66.88) 66.81	(3.63) 3.51	(13.76) 13.58
5c	132	66	$C_{18}H_{13}O_3N_3$	(67.71) 67.33	(4.10) 4.17	(13.16) 13.56
5d	139	61	$C_{18}H_{13}O_4N_3$	(64.47) 64.40	(3.91) 3.81	(12.53) 12.59
5e	123	58	$C_{18}H_{12}O_3N_3Cl$	(61.11) 61.08	(3.42) 3.21	(11.88) 11.80
5f	121	86	$C_{19}H_{15}O_4N_3$	(65.32) 65.30	(4.33) 4.39	(12.03) 12.33
7a	147	51	$C_{22}H_{16}O_5N_4$	(63.46) 63.40	(3.87) 3.81	(13.46) 13.38
7b	151	56	$C_{20}H_{12}O_5N_4$	(61.86) 61.89	(3.11) 3.01	(14.43) 14.49
7c	137	48	$C_{22}H_{16}O_5N_4$	(63.46) 63.32	(3.87) 3.81	(13.46) 13.39

The results of Fungicidal activity of compounds are presented in table 2.

Table 2. Fungicidal activity of compounds 5 a-f and 7a-c.

Compound	**Mean% inhibition after 7 days**							
	P.oryzae		***P.cubensis***		***S.fulginea***		***P.infestans***	
	500ppm	**100ppm**	**500ppm**	**100ppm**	**500ppm**	**100ppm**	**500ppm**	**100ppm**
5a	39	22	40	23	39	22	40	23
5b	36	19	37	20	38	20	38	21
5c	91	76	89	73	88	70	90	74
5d	89	74	88	72	87	70	88	73
5e	93	74	90	71	89	69	90	70
5f	86	69	84	66	84	65	85	67
7a	42	26	41	24	40	22	41	23
7b	39	25	40	23	39	25	40	23
7c	88	73	87	72	86	69	87	72
Carbendazim	100	88	100	89	100	88	100	90

We have synthesised 2-aryl-5- [phthalimido substituted methyl]-1, 3, 4-oxadiazoles and 2, 5 bis-[phthalimido substituted methyl]-1, 3, 4-oxadiazoles. All these compounds have been assayed for their fungicidal activities against *pyricularia oryzae, pseudoperonospora cubensis, sphaerotheca fuliginea, and phytophthora infestans.* Some of them have shown excellent fungicidal activity. The Scheme is shown in figure 1.



5a, R = H, n = 1, R^1 = 2-CH_3

5b, R = H, n = 1, R^1 = 2-H

5c, R = H, n = 1, R^1 = 4-CH_3

5d, R = H, n = 1, R^1 = 4-OCH_3

5e, R = H, n = 2, R^1 = 4-Cl

5f, R = H, n = 2, R^1 = 4-OCH_3

7a, R = H, n = 2

7b, R = H, n = 1

7c, R = CH_3, n = 1

Fig.1 Scheme

APPLICATIONS

Fungicidal Activity

Compound 5a-f and 7a-c were screened for theirs antifungal activity against *Pyricularia oryzae, Pseudoperonospora cubensis, Sphaerotheca fuliginea, Phytophthora infestans* by agar growth technique[9] at 500 ppm and 100 ppm concentration. The results were compared with commercial fungicide carbendazim tested under similar conditions. Amongst these the most active compound **5c**, **5d**, **5e**, **5f** and **7c** showed activity nearly comparable 89-91% to that of carbendazim 100% as shown in Table 2**.**

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