BRIDGEHEAD NITROGEN HETEROCYCLES. PART IV[#]. REACTIONS OF 3-ACYL/AROYL-5-(2,4-DICHLOROPHENYL)-1,3,4-OXADIAZOL-2(3H)-ONES WITH DIAMINES

Probin C. Gogoi and Jibon C. S. Kataky*
Regional Research Laboratory, Jorhat 785 006, Assam, India

Abstract - The condensation reaction of 3-acyl/aroyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-ones (4a-f) with diamino compounds leading to the formation of fused heterocycles (7, 8 and 9) was carried out.

The work described forms a part of our general program[1] on the chemistry of oxadiazole, oxadiazole thione, azetidinones and thiadiazolidinones[1a-h] but in particular extends our studies on bridgehead nitrogen heterocycles.[2a-c] In recent years chemistry on nitrogen bridged heterocycles has made an impact in organic chemistry.[3a-c] It was reported that dicarbonyl compounds when condensed with diamino compounds e.g. hydrazine, ethylenediamine or o-phenylenediamine some new fused heterocycles were formed,[4] resulting triazepin derivative and triazolo/‾1,3,4_7oxadiazoles. These compounds are known to have wide spectrum of biological activities.[4] Our interest in the chemistry of heterocycles[1,2] and the results obtained from these studies prompted us to study the reaction of 1,3-diketones (4a-f), synthesised[5] from 1,3,4-oxadiazol-2(3H)-one (3), with diamines like hydrazine, ethylenediamine and o-phenylenediamine and to establish the structures. Exploration of the studies is principally directed towards the synthesis of new nitrogen bridged heterocycles. The results obtained during this attempt are reported in this paper.

The required 5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (3) was prepared by the reaction of ethyl chloroformate on 2,4-dichlorobenzohydrazide (1) and subsequent cyclisation in presence of phosphorus oxychloride.[6] The oxadiazolone (3) on condensation with various aliphatic and aromatic acid chlorides afforded 3-acyl/aroyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-ones (4a-f)(Scheme 1).[5] Reaction of oxadiazolone (3) with ammonia and carbon disulphide gave 3-(N-dithiocarboxy)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (5a). Oxadiazolone (3) on condensation with aroyl isothiocyanate in acetone produced 3-(N-aroylthiocarbamoyl)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-ones (5b-c) whereas with methyl iodide in presence of potassium hydroxide gives 3-methyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-

---

[#]Part III. P. C. Gogoi and J. C. S. Kataky, Heterocycles, 1991, 32, 231.

Scheme 1

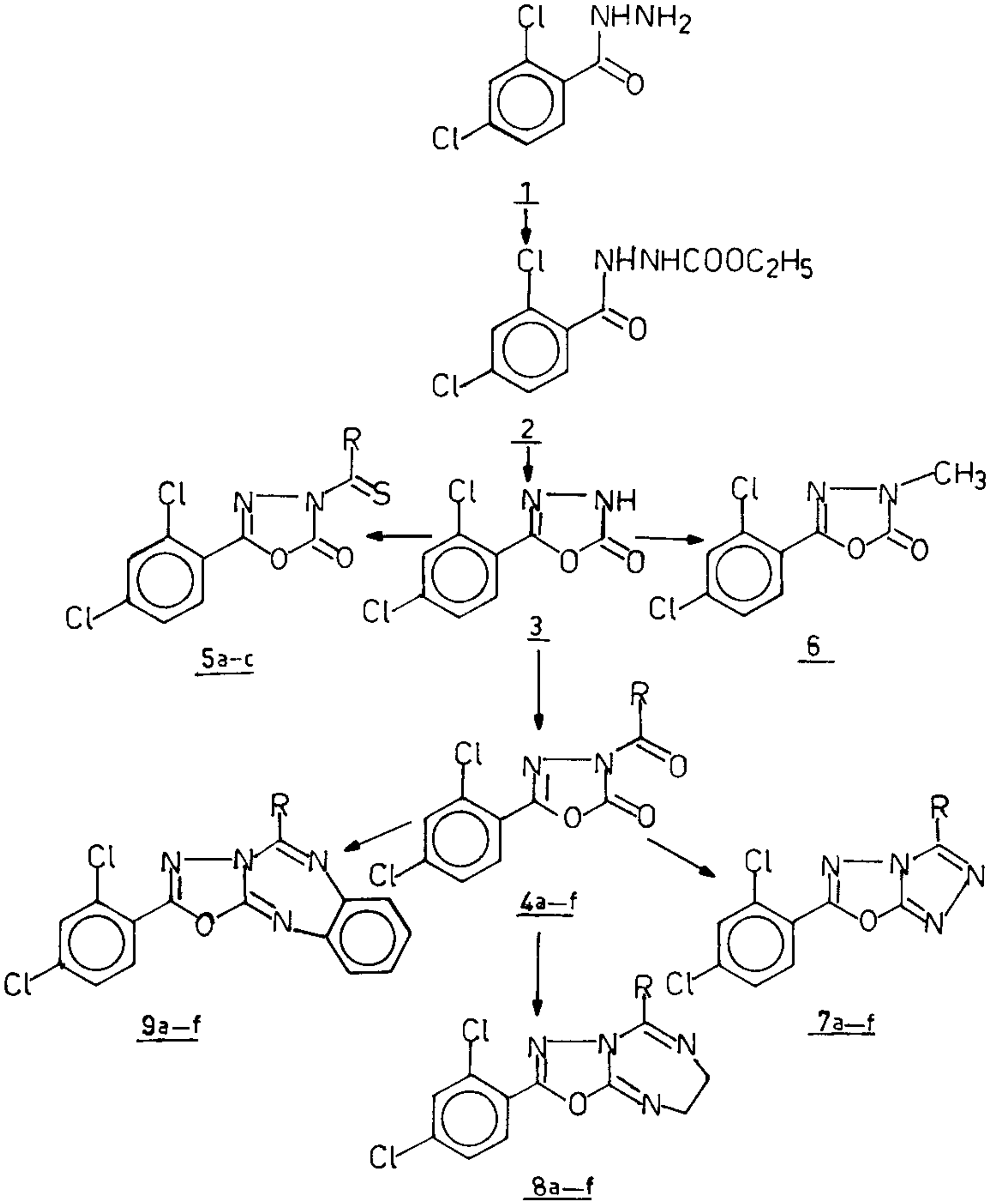

Table 1

Physical and spectral data of 5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one and derivatives (3, 4a-f, 5a-c, 6)

Compd No	R	mp (°C)	yield (%)	ir(KBr) ν cm^{-1}	^{1}H nmr (δ ppm, DMSO-d_6)	Analysis (%)					
						Found			Calcd		
						C	H	N	C	H	N
3	-	140	90	3220 (N-H) 1760 (C=O)	5.0(s,1H) 6.9-7.8(m,3H)	41.62	1.79	12.19	41.56	1.73	12.12
4a	CH_3	75	74	1840 (C=O) 1680(NC=O)	2.3(s,3H) 7.2-7.5(m,3H)	39.51	1.85	9.36	39.57	1.99	9.30
4b	n-C_4H_9	110	46	1830 (C=O) 1750(NC=O)	1.3(t,J=7 Hz,3H) 7.0-7.6(m,3H)	49.55	3.82	8.82	49.52	3.81	8.89
4c	$C_6H_3(Cl)_2$(-o,-p)	140	69	1840 (C=O) 1685(NC=O)	7.2-7.8(m,6H)	44.58	1.52	6.90	44.55	1.49	6.93
4d	C_6H_5	175	64	1840 (C=O) 1680(NC=O)	7.0-7.5(m,8H)	53.75	2.41	8.32	53.73	2.39	8.36
4e	$C_6H_4(CH_3)$(-p)	180	70	1830 (C=O) 1690(NC=O)	2.1(s,3H) 7.2-7.8(m,7H)	55.08	2.81	8.10	55.01	2.86	8.02
4f	$C_6H_5CH_2$	173	67	1830 (C=O) 1710(NC=O)	3.6(s,2H) 7.0-7.5(m,8H)	55.05	2.89	8.06	55.01	2.86	8.02
5a	SH	168	68	2560(SH) 1720(NC=O)	7.2-7.4(m,3H)	35.12	1.36	9.15	35.18	1.30	9.12
5b	C_6H_5CONH	175	60	3070(NH) 1740(NC=O)	7.2-8.0(m,8H)	48.76	2.21	10.60	38.73	2.28	10.65
5c	$C_6H_3(Cl)_2$(-o,-p)CONH	142	76	3075(NH) 1730(C=O)	7.4-8.0(m,6H)	42.81	1.40	6.62	42.86	1.43	6.67
6	CH_3	162	69	1830(C=O)	1.43(s,3H) 6.8-7.2(m,3H)	42.05	2.42	11.48	44.08	2.45	11.43

Table 2

Physical and spectral data of compounds 7a-f, 8a-f, 9a-f

Compd No	R	mp (°C)	yield (%)	ir(KBr) ν cm^{-1} C = O	^1H nmr (δ ppm, DMSO-d_6)	Analysis (%)					
						Found			Calcd		
						C	H	N	C	H	N
7a	CH_3	145	62	1640	1.3(s,3H),7.2-7.4(m,Ar-H)	44.67	2.25	20.88	44.61	2.23	20.82
7b	n-C_4H_9	156	60	1630	1.3(t,J=7 Hz,3H),7.2-7.6(m,Ar-H)	50.12	3.89	18.05	50.16	3.86	18.01
7c	$C_6H_3(Cl)_2$(-o,-p)	163	55	1640	7.0-7.4(m,Ar-H)	45.05	1.55	14.03	45.00	1.50	14.00
7d	C_6H_5	160	70	1630	7.0-7.5(m,Ar-H)	54.32	2.48	16.95	54.38	2.42	16.92
7e	$C_6H_4(CH_3)$(-p)	175	63	1640	2.1(s,3H),7.2-7.4(m,Ar-H)	55.62	2.92	16.25	55.65	2.90	16.23
7f	$C_6H_5CH_2$	160	65	1630	2.5(s,2H),7.0-7.6(m,Ar-H)	55.69	2.98	16.28	55.65	2.90	16.23
8a	CH_3	190	67	1635	1.2(s,3H),4.5(s,4H),7.0-7.5(m,Ar-H)	64.62	3.30	18.83	64.65	3.37	18.86
8b	n-C_4H_9	148	65	1640	1.3(t,J=7 Hz,3H),4.5(s,4H),7.0-7.6(m,Ar-H)	53.15	4.75	16.50	53.10	4.72	16.52
8c	$C_6H_3(Cl)_2$(-o,-p)	155	70	1640	4.6(s,4H),7.2-7.6(m,Ar-H)	47.65	2.38	13.06	47.66	2.34	13.08
8d	C_6H_5	199	75	1635	4.6(s,4H),7.0-7.5(m,Ar-H)	56.88	3.38	16.65	56.82	3.34	15.60
8e	$C_6H_4(CH_3)$(-p)	185	70	1640	4.5(s,4H),7.0-7.6(m,Ar-H)	57.98	3.78	15.09	57.91	3.75	15.01
8f	$C_6H_5CH_2$	169	75	1635	2.5(s,2H),4.5(s,4H),7.0-7.6(m,Ar-H)	57.97	3.70	15.05	57.91	3.75	15.01
9a	CH_3	165	73	1630	1.3(s,3H),7.0-7.5(m,Ar-H)	55.60	2.95	16.28	55.65	2.90	16.23
9b	n-C_4H_9	172	70	1640	1.3(t,J=7 Hz,3H),7.0-7.5(m,Ar-H)	58.95	4.15	14.42	58.91	4.13	14.47
9c	$C_6H_3(Cl_2)$(-o,-p)	189	72	1630	6.8-7.6(m,Ar-H)	52.90	2.15	11.73	52.94	2.10	11.76
9d	C_6H_5	180	65	1635	7.2-7.8(m,Ar-H)	61.95	2.90	13.70	61.92	2.95	13.76
9e	$C_6H_4(CH_3)$(-p)	178	68	1630	2.3(s,3H),6.8-7.6(m,Ar-H)	62.75	3.35	13.33	62.71	3.33	13.30
9f	$C_6H_5CH_2$	185	70	1640	2.6(s,2H),7.0-7.6(m,Ar-H)	62.75	3.38	13.34	62.71	3.33	13.30

2(3H)-one (6). Oxadiazol-5-one (4) on condensation[4] with hydrazine hydrate in ethanol gave 3-alkyl/aryl/aralkyl-6-(2,4-dichlorophenyl)-1,2,4-triazolo[3,4-b]-[1,3,4]oxadiazole (7a-f), with ethylenediamine gave 5-alkyl/aryl/aralkyl-2-(2,4-dichlorophenyl)-7,8-dihydro[1,3,4]oxadiazolo[2,3-b][1,3,5]triazepines (8a-f) and with o-phenylenediamine in dry benzene afforded 5-alkyl/aryl/aralkyl-2-(2,4-dichlorophenyl)-1,3,4-oxadiazolo[2,3-b][1,3,5]benzotriazepines (9a-f)(Scheme 1). The structure of compounds newly synthesised were deduced on the basis of analytical and spectral data (Table 2).

EXPERIMENTAL

Melting points were determined with a Büchi oil heated apparatus in open capillaries and are uncorrected. Ir spectra were recorded with a Perkin-Elmer 580B spectrophotometer using potassium bromide discs, unless otherwise stated (ν_{max} in cm^{-1}). ^1H Nmr spectra were recorded in solutions stated with TMS as the internal reference in 60 MHz and 90 MHz on a Varian T-60 and Zeol FX-90 spectrometers (chemical shifts in δ ppm). 2,4-Dichlorobenzohydrazide (1) was prepared from ethyl 2,4-dichlorobenzoate following the method of Yale et al.[7]

5-(2,4-Dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (3)

A mixture of hydrazide (1) (2.05 g, 0.01 mol) and ethyl chloroformate (20 ml) was refluxed for 2 h. After cooling the separated solid was filtered, washed with 5% aq. sodium carbonate solution and then with water. The product was dried and refluxed again with phosphorus oxychloride (25 ml) for 1 h. Excess phosphorus oxychloride was removed by distillation under reduced pressure and the residue was hydrolysed with crushed ice. The precipitate was filtered and dried and finally recrystallized from C_2H_5OH to obtain compound (3).

3-Acetyl/aroyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (4a-f)

General Procedure :

A mixture of oxadiazolone (3)(2.31 g, 0.01 mol) and aliphatic/aromatic acid chlorides (0.01 mol) was stirred for 30 min in an ice bath. Cold water (50 ml) was added and the separated solid was filtered, washed with 2% aq. sodium carbonate solution and finally crystallised from C_2H_5OH to get compounds (4a-f). The physical data of the compounds are given in Table 1.

5-(2,4-Dichlorophenyl)-2,3-dihydro-2-oxo-1,3,4-oxadiazol-3-dithiocarboxylic acid(5a)

To a mixture of oxadiazolone (3) (2.31 g, 0.01 mol) and ammonia (50 ml, sp.gr. 0.9) was added carbon disulphide (1.52 g, 0.02 mol) dropwise with stirring.After stirring at room temperature for 2 h the mixture was acidified with dilute hydrochloric acid. The precipitate formed was filtered, washed with water several times, dried and crystallised from C_2H_5OH to get compound (5a). Physical data are given in Table 1.

3-(N-Aroylthiocarbamoyl)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-ones (5b-c)

General Procedure :

To a well stirred solution of ammonium thiocyanate (1.52 g, 0.02 mol) in acetone (50 ml) was added benzoyl chloride (2.81 g, 0.02 mol). The mixture was stirred for 15 min and treated with a solution of oxadiazolone (3)(2.31 g, 0.01 mol) in acetone (50 ml) by dropwise addition. The mixture was then refluxed for 3 h, cooled to room temperature and diluted with water (50 ml). The solid appeared was filtered, washed with water and crystallised from C_2H_5OH to get compound (5b). Compound (5c) was prepared similarly using 2,4-dichlorobenzoyl chloride in place of benzoyl chloride. Physical data are given in Table 1.

3-Methyl-5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (6)

To an ice cooled solution of (3) (2.31 g, 0.01 mol) in 4% aq. potassium hydroxide solution (30 ml) was added methyl iodide (2.84 g, 0.02 mol). The mixture was stirred for 2 h. The precipitate formed was filtered, washed with water, dried and crystallised from C_2H_5OH to obtain compound (6). Physical data of the compound is given in Table 1.

3-Alkyl/aryl/aralkyl-6-(2,4-dichlorophenyl)-1,2,4-triazolo[3,4-b][1,3,4]oxadiazoles (7a-f)

General Procedure :

A mixture of compound (4) (0.001 mol) and hydrazine hydrate (99%, 0.002 mol) in ethanol (30 ml) was refluxed for 8 h. After cooling to room temperature fine crystals appeared which were filtered and crystallised from C_2H_5OH to get compounds (7a-f). The physical data of the compounds are given in Table 2.

5-Alkyl/aryl/aralkyl-2-(2,4-dichlorophenyl)-7,8-dihydro[1,3,4]oxadiazolo[2,3-b][1,3,5]triazepines (8a-f)

General Procedure :

A mixture of compound (4) (0.001 mol) and ethylenediamine (0.06 g, 0.001 mol) in ethanol (30 ml) was refluxed for 10 h. It was cooled to room temperature and the separated solid was filtered, washed with water and crystallised from C_2H_5OH to get the compounds (8a-f). The physical data are given in Table 2.

5-Alkyl/aryl/aralkyl-2-(2,4-dichlorophenyl)[1,3,4]oxadiazolo[2,3-b][1,3,5]benzotriazepines (**9a**-**f**)

General Procedure :

A mixture of compound (**4**) (0.001 mol), *o*-phenylenediamine (0.11 g, 0.001 mol) and dry benzene (20 ml) was refluxed for 12 h with a Dean-Stark apparatus. After cooling to room temperature a white solid appeared which was filtered, washed with water and crystallised from C_2H_5OH to get compound (**9a**-**f**). Physical data of the compounds are given in Table 2.

ACKNOWLEDGEMENT

The authors are grateful to Dr. J. N. Baruah, Director, Regional Research Laboratory, Jorhat, Assam, for permitting one of the authors (PCG) to carry out the research work in the laboratory. We thank the Analytical Chemistry Division of the laboratory for some of the spectral analysis.

REFERENCES

1. a) B. N. Goswami, J. C. S. Kataky, and J. N. Baruah, *J. Heterocycl. Chem*.,1984, **21**, 1225.
   b) B. N. Goswami, J. C. S. Kataky, and J. N. Baruah, *Indian J. Chem*., 1984, **23B**, 796.
   c) B. N. Goswami, J. C. S. Kataky, J. N. Baruah, and S. C. Nath, *J. Heterocycl. Chem*., 1984, **21**, 205.
   d) B. N. Goswami, J. C. S. Kataky, J. N. Baruah, S. C. Nath, and D. N. Bordoloi, *J. Indian Chem. Soc*., 1984, **61**, 530.
   e) B. N. Goswami, Ph. D. Thesis of Dibrugarh University, Assam, India, 1984.
   f) M. M. Dutta, B. N. Goswami, and J. C. S. Kataky, *J. Heterocycl. Chem*., 1986, **23**, 793.
   g) M. M. Dutta, B. N. Goswami, and J. C. S. Kataky, *J. Indian Chem. Soc*., 1990, **67**, 332.
   h) C. S. Sarma, P. C. Gogoi, and J. C. S. Kataky, *Heterocycles*, 1990, **31**, 59.
2. a) B. N. Goswami, J. C. S. Kataky, and J. N. Baruah, *J. Heterocycl. Chem*.,1986, **23**, 1439.
   b) P. C. Gogoi and J. C. S. Kataky, *Heterocycles*, 1990, **31**, 2147.
   c) P. C. Gogoi and J. C. S. Kataky, *Heterocycles*, 1991, **32**, 231.
3. a) P. C. Pradhan, B. K. Misra, and G. B. Behera, *Indian J. Chem*., 1988, **27B**, 902.
   b) E. M. Meccalli, M. D. Puppo, E. Licandro, and A. Marchesini, *J. Heterocycl. Chem*., 1981, **18**, 685.

c) R. J. Cremlin, F. J. Swinbourne, and O. Shode, J. Heterocycl. Chem., 1985, 22, 1211.

4. a) A. Burger, Medicinal Chemistry, Vol. 1, John Willy, New York, 1970, p. 668.

b) L. S. Goodman and A. Gilman, The Pharmacological Basis of Therapeutics, MacMillan, New York, 1975, p. 1009.

5. P. C. Gogoi, Ph. D. Thesis of Dibrugarh University, Assam, India, 1990.

6. J. C. Lancelot, D. Maume, and M. Robba, J. Heterocycl. Chem., 1980, 17, 625.

7. H. L. Yale, K. Losee, J. Martin, M. Holsing, F. M. Perry, and J. Bernstein, J. Am. Chem. Soc., 1953, 75, 1933.

Received, 20th August, 1990