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Synthesis of Some Bis-(1,3,4-Oxadiazol-2-yl) Methanes of Biological and Pharamacological Interest

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The condensation of malonyl dicarbohydrazide with aldehydes yields malonyl dicarbohydrazones which underwent oxidative cyclization to give bis-(5,5′-disubstituted-1,3,4-oxadiazol-2-yl)methanes. The antibacterial, antifungal, anthelemintic and anitcatatonic activities of these compounds were studied.

INTRODUCTION

1,3,4-Oxadiazoles are associated with tuberculostatic[1], anticonvulsant[2], antiinflammatory and diuretic activities. Some bis-heterocyclic compounds are reported to display a wide spectrum of pharmacological activities.[3–5] These observations stimulated our intrest in the synthesis of bis-(5,5′-diaryl-1,3,4-oxadiazol-2-yl)methanes. Malonyl dicarbohydrazide(2) was prepared according to the method reported earlier. The condensation of hydrazide(2) with various aldehydes gave the corresponding hydrazones (3a–g). Oxidative cyclization of malonyl dicarbohydrazones with aqueous ferric chloride in acid medium afforded bis-(5-5′-disubstituted-1,3,4-oxadiazol-2-yl)methanes (4a–g) (Scheme-1).

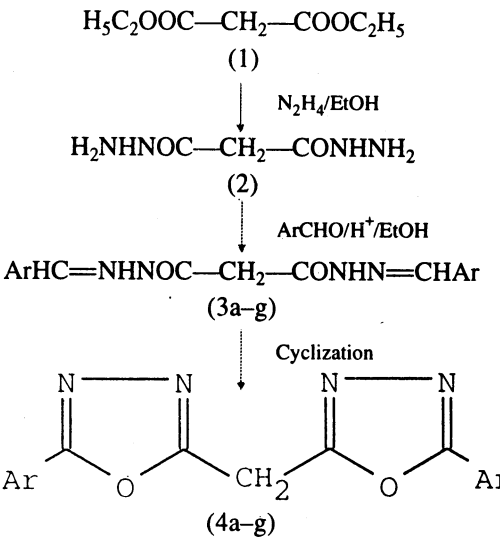
Antibacterial and Antifungal Activities

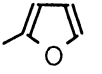
All the compounds were screened for their antibacterial activity by Cup-Plate diffusion method against *Staphylococcus aureus* and *Escherichia coli* using nutrient agar medium. *Gentamycin* was used as standard drug. Compounds 3c, 3d, 3g, 4b, 4c and 4d have shown significant activity against *E. coli* and moderate activity against *S. aureus*. The compounds were also screened for antifungal activity against *Aspergillus niger* and *Candida utelis*. Compounds 3a–g have shown weak or moderate activity against both fungi. Among bis-oxadiazoles 4c, 4b and 4f have been found to exhibit maximum activity against *A. niger*.

Pharmacological Activities

(i) *Anthelminitic Activity*—All the comounds were screened for *in vitro* anthelmintic activity on earthworms by the technique of Gaind *et al.* using piperazine citrate as standard. All compounds have shown low activity.

(ii) *Anticatatonic Activity*—The bis-heterocycles synthesised in the course of our work have been evaluated for their anticatatonic activity against rats at a concentration of 10 mg/kg body weight. Compounds 3a, 3b, 3c and 4a have shown anticatationic activity comparable to the standard drug Scopolamine.



Scheme-I. a, Ar = C_6H_5; b, Ar = $C_6H_4OCH_3(p)$; c, Ar = $C_6H_2(OCH_3)_3$; d, Ar = $C_6H_2Cl(p)$; e, Ar = $C_6H_4OH(o)$; f, Ar = $C_6H_5CH{=}CH$; g, Ar = 

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded in Nujol on Hitachi 27250 spectrophotometer.

Malonyl dicarbohydrazide (2)—A mixture of diethyl malonate (1) (0.5 M), hydrazine hydrate (10 mL, 80%) was heated under reflux in anhydrous ethanol (30 mL) for 4 h. The solid that separated after cooling was collected and crystallized from ethanol, (6.8 g, 82.50%), m.p. 160°C.

Malonyl bis-carbohydrazones (3a–g)—To a solution of malonyl dicarbohydrazide (2) (0.1 M) in ethanol (25 mL) was added freshly distilled aldehyde (0.2 M) and concentrated hydrochloric acid (3 drops) and the reaction mixture was refluxed gently for 4–5 h. The solvent was removed under reduced pressure and the solid separated was collected and crystallised from suitable solvent.

ν_{max} 3200 ν(NH), 1620 ν(C=N) and 1660 ν(C=O) cm^{-1}.

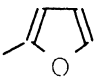
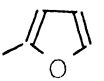
The compounds are summarized in Table-1.

Bis-(5,5'-disubstituted-1,3,4-oxadiazol-2-yl) methanes (4a–g)—Acylhydrazone (3a–g) (0.1 M) in acetic acid (0.8–1.0 mL) was treated with aqueous ferric chloride. The reaction mixture after stirring for 1 h was diluted with 100 mL of water. The contents were allowed to stand for 72 h at room temperature. The solid separated was collected and crystallized from suitable solvent.

IR: ν_{max} 1640 and 1660 ν(C=N) cm^{-1}.

The compounds were described in Table-1.

TABLE-1
PHYSICAL CHARACTERISATION DATA OF THE COMPOUNDS SYNTHESISED

Comp. No.	R	m.p. (°C)	Yield (%)	Solvent of crystallization	Molecular formula	% of nitrogen	
						Calc.	Found
3a	C_6H_5	235	62.3	acetic acid	$C_{17}H_{16}N_4O_2$	18.23	18.10
3b	$C_6H_4OCH_3(p)$	178	92.5	"	$C_{19}H_{20}H_4O_4$	15.21	15.20
3c	$C_6H_2(OCH_3)_3$	245	97.3	"	$C_{23}H_{28}N_4O_8$	11.47	11.50
3d	$C_6H_4Cl(p)$	217	74.9	"	$C_{17}H_{14}N_4O_2Cl_2$	14.85	14.80
3e	$C_6H_4OH(o)$	219	83.8	DMF	$C_{17}H_{16}N_4O_4$	16.47	16.45
3f	$CH{=}CH{\cdot}C_6H_4$	209	78.1	"	$C_{23}H_{24}N_4O_8$	15.55	15.50
3g		231	78.1	aq. DMF	$C_{13}H_{12}N_4O_4$	19.44	19.40
4a	C_6H_5	280	95.1	aq. acetic acid	$C_{17}H_{12}N_2O_2$	14.85	14.81
4b	$C_6H_4OCH_3(p)$	216	91.5	acetic acid	$C_{19}H_{16}N_4O_2$	15.38	15.35
4c	$C_6H_2(OCH_3)_3$	230	82.6	aq. DMF	$C_{23}H_{24}N_4O_8$	11.57	11.55
4d	$C_6H_4Cl(p)$	238	89.4	aq. acetic acid	$C_{17}H_{10}N_4O_2Cl_2$	15.01	15.00
4e	$C_6H_4OH(o)$	230	85.3	aq. DMF	$C_{17}H_{12}N_4O_4$	16.66	16.60
4f	$CH{=}CH{\cdot}C_6H_5$	233	93.6	DMF	$C_{21}H_{16}N_4O_2$	15.73	15.70
4g		241	82.7	aq. DMF	$C_{13}H_8N_4O_4$	19.71	19.66

All compounds gave C and H analysis satisfactorily.

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REFERENCES

1. A.E. Wilder Smith, *Arzermittel-Forsch*, **16**, 1034 (1966).
2. S.K. Choudhary, M. Choudhary, A. Choudhary and S.S. Parmar, *J. Pharm. Sci.*, **67**, 1507 (1978).
3. S.M. Kudari and S.S. Sangapure, *Curr. Sci. (India)*, **53**, 1086 (1984).
4. _____, *Karn. Univ. J.*, **32**, 101, (1987).
5. V.K. Mishra and S.C. Bahel., *J. Indian Chem. Soc.*, **66**, 867 (1983).

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