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Synthesis of some novel 1, 3, 4-oxadiazole and its anti-bacterial and anti-fungal activity

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ABSTRACT

Research on 1, 3, 4-oxadiazole and their synthetic analogs have revealed a variety of pharmacological activities including anti-microbial, anti-tubercular and insecticidal agents. Some of these compounds have also analgesic, anti-inflammatory, anti-cancer, anti-HIV agent, anti-parkinsonian and anti-proliferative agent. It was our interest to make novel derivatives of the titled compounds and evaluate the anti-bacterial and anti-fungal activities. 1, 3, 4-oxadiazole and its derivatives were obtained from 6-phenyl-2-substituted quinoline-4-carbohydrazide and a mixture of carbon disulphide and potassium hydroxide. Elemental analysis, IR, 1H-NMR, and mass spectral data established identification of the compounds. Products were evaluated for their antimicrobial activity using cup plate method1. Some of the obtained compounds
showed the interesting antimicrobial activity.

Keywords: 1, 3, 4-oxadiazole, Anti-Bacterial, Anti-Fungal, Anti-inflammatory, Anti-cancer

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INTRODUCTION

Due to the interesting activity of 2, 5-disubstituted 1, 3, 4-oxadiazole as biological agent's considerable attention has been focused on this class. The pharmaceutical importance of these compounds lies in the fact that they can be effectively utilizing as antibacterial, antitubercular and insecticidal agents [1, 2, 3, 4]. Some of these compounds have also analgesic, anti-inflammatory, anticancer, anti-HIV agent, anti parkinsonian and antipriliferative agent [5, 6, 7, 8, 9]. In addition, 1, 3, 4-oxadiazole has played a crucial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis [10, 11]. In continuation of our research in the chemistry of oxadiazoles, we now report here in the synthesis of novel 1,3,4-oxadiazole and its anti-bacterial and anti-fungal activity.

MATERIALS AND METHODS

All the melting points were determined routinely in an open capillary tube and are uncorrected. Completion of reaction was routinely checked by TLC on silica gel-G plates of 0.5mm thickness and the spots were located by iodine. The PMR spectra were recorded in $CDCl_3$ on a Brucker DRX-300 at 300 MHz. The IR spectra were recorded on a Shimadzu-8400 FT-IR spectrometer in KBr (γ in cm^{-1}). Elemental analyses of the newly synthesized compounds were carried out on a Carlo Erba-1108 analyzer and result within the range of the theoretical value was found. Mass spectra were scanned on a GCMS-QP200 instrument.

General procedure for the synthesis of Quinoline-4-carboxylic acid (1)
A mixture of Aldehyde (0.01 mol), freshly distilled pyruvic acid (0.01 mol) and absolute ethyl alcohol (25 ml) was refluxed to the boiling point on a water bath and a solution of Amine (0.01 mol) in absolute ethyl alcohol (25 ml) was added slowly with frequent shaking. The content was refluxed for 3 hours and allowed to stand overnight. The product was filtered and recrystallised from ethanol.

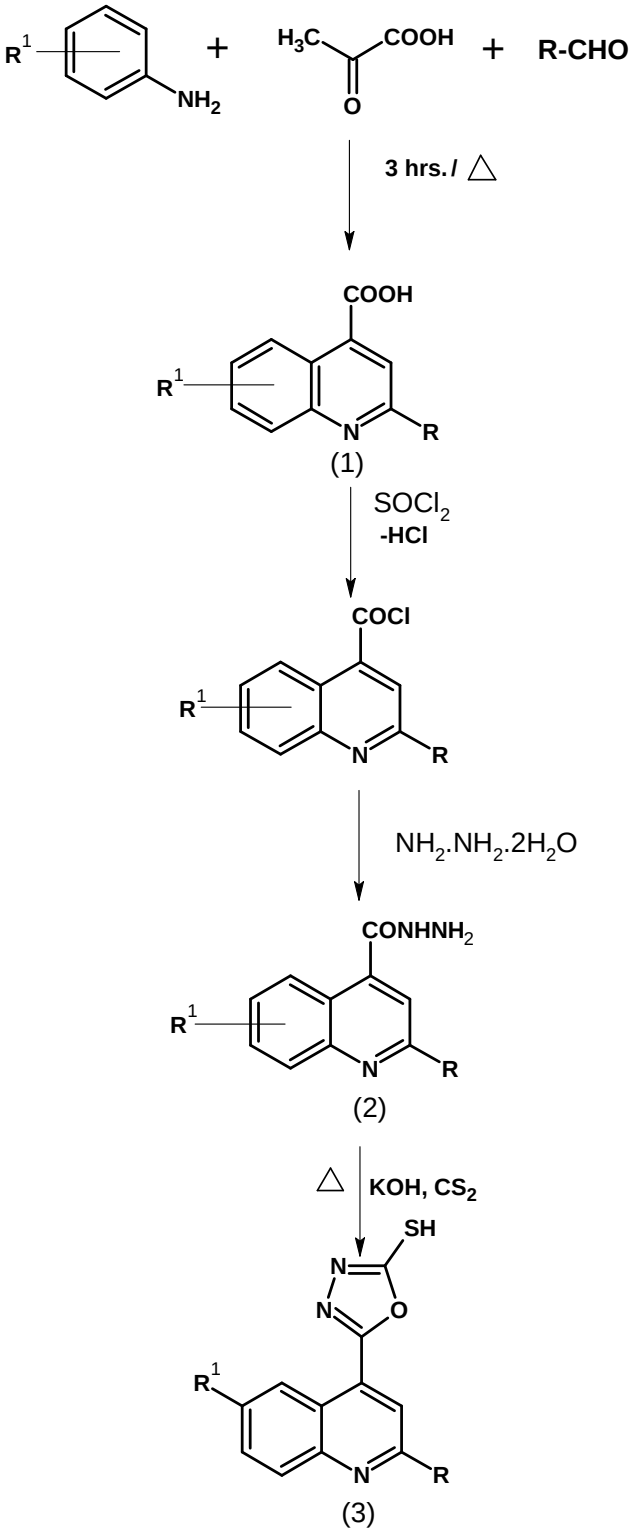
General procedure for the synthesis of Quinoline-4-carbohydrazide (2)
A mixture of (1) (0.01 mol) in dioxan (40 ml) in and thionyl chloride (10 ml) was refluxed at 60-70^{0}C for 3 hours. Excess of thionyl chloride was removed by distillation and product obtained was kept at 0^{0}C, add 2 to 3 drops of pyridine and further refluxed with hydrazine hydrate 99% (0.1 mol) for 6 hours. The contents were poured in to ice-cold water. The resulting product was filtered, dried and crystallised from dimethyl formamide.

General procedure for the synthesis of 1,3,4-Oxadiazole (3)
A mixture of (2) (0.01 mol), potassium hydroxide (0.01 mol), carbon disulphide (4 ml) and ethanol (15 ml) was heated under reflux until the evolution of H_2S ceases. The reaction mixture was concentrated, dissolved in water and acidified with HCl. The resulting product was recrystallised from methanol. Similarly the other compounds were prepared.

Table No. 1: Physical constants of 1, 3, 4-Oxadiazole (3_{a-i}).

Comp. No.	R	R^1	Molecular Formula	M.W.	Yield %	M.P. ^{0}C	R_f Value Rf_1/Rf_2	% of Nitrogen Calcd./Found
3_a.	4-Cl-C_6H_4	4-F	$C_{17}H_9ClFN_3OS$	316	60	198	0.49/0.52	13.31/13.28
3_b.	4-Cl-C_6H_4	4-Cl	$C_{17}H_9Cl_2N_3OS$	332	58	174	0.50/0.53	12.65/12.60
3_c.	4-Cl-C_6H_4	4-NO_2	$C_{17}H_9ClN_4O_3S$	343	61	169	0.51/0.54	16.35/16.30
3_d.	4-F-C_6H_4	4-F	$C_{17}H_9F_2N_3OS$	299	59	138	0.45/0.53	12.31/12.27
3_e.	4-F-C_6H_4	4-Cl	$C_{17}H_9ClFN_3OS$	316	68	178	0.51/0.50	13.31/13.27
3_f.	4-F-C_6H_4	4-NO_2	$C_{17}H_9FN_4O_3S$	326	63	133	0.44/0.49	17.17/17.12
3_g.	4-CH_3-C_6H_4	4-F	$C_{17}H_{14}FN_3O$	337	60	153	0.47/0.50	12.46/14.42
3_h.	4-CH_3-C_6H_4	4-Cl	$C_{17}H_{14}ClN_3O$	354	59	155	0.51/0.58	11.88/11.83
3_i.	4-CH_3-C_6H_4	4-NO_2	$C_{17}H_{14}N_4O_3$	347	56	161	0.46/0.51	15.38/15.32

Reaction Scheme



RESULTS AND DISCUSSION

The physical data for compound **(1)** are as follows; Yield: 70%, m.p. 148^{0}C, Anal. Calculated for $C_{16}H_9F_2O_2$; Required: C (67.37%), H (3.18%), N (4.91%); Found: C (67.32%), H (3.11%), N (4.86%); IR (KBr) Vmax Cm-1: 2956 (C-H str., asym.), 2852 (C-H str., sym.), 3178, 1462, (C=C-H, C=C), 1656 (C=O sym., str.).

The physical data for compound (2) are as follows; Yield: 68%, M.P.: 217^{0}C, Anal. Calculated for $C_{16}H_{11}F_2N_3O$; Required: C (64.21%), H (3.70%), N (14.04%); Found: C (64.16%), H (3.66%), N (13.99%); IR (KBr) Vmax Cm-1: 3420 (N-H str.), 2956 (C-H str., asym.), 2852 (C-H str., sym.), 1336, 3178, 1462, (C-N str., C=C-H, C=C), 1656 (C=O sym., str.).

The physical data for compound (3_d) are as follows; Yield: 59%, M.P.: 138^{0}C, Anal. Calculated for $C_{17}H_9F_2N_3OS$; Required: C (59.82%), H (2.66%), N (12.31%); Found: C (59.76%), H (2.61%), N (12.27%); IR (KBr) Vmax Cm-1: 2956 (C-H str., asym.), 2900 (C-H str., sym.), 1305, 3178, 1458, (C-N str., C=C-H, C=C), 1207 (C-O-C asym., str.), 644 (C-S sym., str.) PMR δ/ppm (DMF) : 3.1 (s,1H,-SH), 6.8 (d,2H, Ar-H), 6.8 (s, 1H, Ar-H), 6.9 (m,1H, Ar-H), 7.0 (s,1H, Ar-H), 7.5 (m, 3H, Ar-H) ; Mass spectrum of the compound exhibited a molecular ion peak at m/z 341.

Antimicrobial activity

The purified products were screened for its antibacterial activity. The nutrient agar broth prepared by the usual method was inoculated especially with 0.5 ml for 24 hrs. Old subculture of *S.aureus, S.pyogens, E.coli,* and *P.aeruginosa* in separate conical flask at 40-50$_0$C and mixed well by gentle shaking. About 25 ml of the contents of the flask were poured and evenly spread in a petridish (13 cm in diameter) and allowed to set for two hrs. The cups (10 mm in diameter) were formed by the help of borer in agar medium and filled with 0.10 ml (1 mg/ml) solution of a sample in dimethyl formamide. The plates are incubated at 37°C for 24 hrs and the control was also maintained with 0.1 ml of dimethyl formamide in similar manner, and the zones of inhibition of the bacterial growth are measured in mm diameter and are recorded in table 2.

Antifungal activity

A.niger was employed for testing fungicidal activity using cup-plate method. The cultures were maintained on Sabourauds agar slants. Purified compounds were used for testing the fungicidal activity. Sterilized Sabourauds agar medium was inoculated with 72 hrs old, 0.5 ml suspensions of fungal spores, in separate flask. About 25 ml of the inoculated medium was evenly spreaded in a sterilized petri-dish and allowed to set for 2 hrs. The cups (10 mm in diameter) were punched in petri-dish and loaded with 0.1 ml (1.0 mg/ml) of solution of a sample in dimethyl formamide.

The plates were incubated at room temperature (30°C) for 48 hrs. After the completion of incubation period the zones of inhibition of growth in the form of diameter in mm was measured. Along the test solution in each petridish one cup was filled up with solvent, which acts as a control. The zones of inhibition are recorded in table 2.

Table No. 2: Comparative antimicrobial activity OF 1, 3, 4-Oxadiazole (3_{a-i}). (Different Inhibition Concentration in µg/ml)

Com. No.	R	R^1	Antibacterial activity (Zones of inhibition in m.m.)									
			E.coli MTCC-443					*P.aeruginosa MTCC-424*				
			5	25	50	100	250	5	25	50	100	250
3_a	4-Cl-C_6H_4	4-F	-	15	17	20	21	-	12	13	14	15
3_b	4-Cl-C_6H_4	4-Cl	-	12	13	17	19	-	13	15	18	19
3_c	4-Cl-C_6H_4	4-NO_2	-	14	16	17	21	-	10	12	13	15
3_d	4-F-C_6H_4	4-F	-	11	12	15	21	-	10	13	15	17
3_e	4-F-C_6H_4	4-Cl	-	12	15	19	21	-	12	14	16	19
3_f	4-F-C_6H_4	4-NO_2	-	14	16	17	18	-	11	15	16	18
3_g	4-CH_3-C_6H_4	4-F	-	12	13	15	17	-	12	14	16	18
3_h	4-CH_3-C_6H_4	4-Cl	-	15	17	18	20	-	11	14	16	19
3_i	4-CH_3-C_6H_4	4-NO_2	-	15	17	19	22	-	10	12	16	17
Comparative activity of (3_{a-i}) with known chosen standard drugs												
Standard drug			Antibacterial activity									
Amplicilline			14	15	16	19	20	14	15	15	18	20
Chloramphenicol			14	17	23	23	23	14	17	18	19	21
Ciprofloxacin			20	23	28	28	28	20	23	24	26	27
Norfloxacin			22	25	26	27	29	18	19	21	23	23

Table No.2: comparative antimicrobial activity of 1, 3, 4-Oxadiazole (3_{a-i}). (Different Inhibition Concentration in µg/ml).

Com. No.	R	R^1	Antibacterial activity (Zones of inhibition in m.m.)									
			S.pyogens MTCC-442					*S.aureus MTCC-96*				
			5	25	50	100	250	5	25	50	100	250
3_a	4-Cl-C_6H_4	4-F	-	09	14	17	19	-	13	14	15	19
3_b	4-Cl-C_6H_4	4-Cl	-	10	13	15	17	-	10	12	16	18
3_c	4-Cl-C_6H_4	4-NO_2	-	10	12	14	16	-	11	13	14	17
3_d	4-F-C_6H_4	4-F	-	11	13	14	17	-	11	13	16	17
3_e	4-F-C_6H_4	4-Cl	-	09	11	14	19	-	10	13	15	16
3_f	4-F-C_6H_4	4-NO_2	-	10	13	14	18	-	12	13	16	17
3_g	4-CH_3-C_6H_4	4-F	-	11	13	15	18	-	09	11	14	19
3_h	4-CH_3-C_6H_4	4-Cl	-	10	14	17	20	-	10	13	14	18
3_i	4-CH_3-C_6H_4	4-NO_2	-	11	14	18	20	-	09	14	17	20
Comparative activity of (3_{a-i}) with known chosen standard drugs												
Standard drug			Antibacterial activity									
Amplicilline			11	14	16	18	19	10	13	14	16	18
Chloramphenicol			10	13	19	20	20	12	14	19	20	21
Ciprofloxacin			16	19	21	21	22	17	19	21	22	21
Norfloxacin			18	19	20	21	21	19	22	25	26	28

Table no. 2: comparative antimicrobial activity of 1, 3, 4-Oxadiazole (3_{a-i}). (Different Inhibition Concentration in µg/ml).

Com. No.	R	R^1	Antifungal activity (Zones of inhibition in m.m.)									
			A.niger MTCC-282					*A.clavatus MTCC-1323*				
			5	25	50	100	250	5	25	50	100	250
3_a	4-Cl-C_6H_4	4-F	-	19	21	24	25	-	19	21	22	24
3_b	4-Cl-C_6H_4	4-Cl	-	18	20	23	24	-	18	20	22	23
3_c	4-Cl-C_6H_4	4-NO_2	-	20	22	23	25	-	18	19	22	24
3_d	4-F-C_6H_4	4-F	-	16	17	20	23	-	10	20	21	24
3_e	4-F-C_6H_4	4-Cl	-	18	19	22	25	-	18	20	22	24
3_f	4-F-C_6H_4	4-NO_2	-	17	19	22	24	-	21	22	23	25
3_g	4-CH_3-C_6H_4	4-F	-	19	22	23	24	-	21	22	23	25
3_h	4-CH_3-C_6H_4	4-Cl	-	18	21	22	24	-	19	20	22	24
3_i	4-CH_3-C_6H_4	4-NO_2	-	19	20	21	23	-	18	18	21	22
Comparative activity of (3_{a-i}) with known chosen standard drugs												
Standard drug			Antifungal activity									
Griseofulvin			19	23	25	25	28	18	21	22	22	24
Nystatin			18	19	24	29	29	18	21	24	25	26

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REFERENCES

[1] G.Grover, S.G.Kini. *Indian Journal of Heterocyclic Chemistry*., **2003**, 12, 289.
[2] J.Hazarika , J.C.S Kataky. *Indian Journal of Heterocyclic Chemistry*. **1997**; 7: 47.
[3] P.R.Kagthara, N.S.Shah, R.K.Doshi, H.H.Parekh,. *Indian. Journal of Chemistry*.**1999**; 38B: 572.
[4] B.Shivarama Holla, C.S.Prasanna, Boja Poojary, K.S. Rao, K.Shridhara, U.Ganesha Bhat. *Indian Journal of Chemistry*. **2004**; 43B: 864.
[5] Zheng Li & Xicum Wang. *Indian Journal of Chemistry*.**2003**; 42B: 941.
[6] M.Amir, S. Shahani. *Indian Journal of Heterocyclic Chemistry*.**1998**; 8:107.
[7] H.P.Shah, B.R.Shah, J.J.Bhatt, N.C.Desai, P.B.Trivadi, N.K.Undavia. *Indian Journal of Chemistry*.**1996**; 37B: 180.
[8] J.Hazarika, J.C.S.Kataky, *Indian Journal of Heterocyclic Chemistry*.**1998**; 7: 83.
[9] H. Liszkiewicz, M. W. Kowalska, J. Wietrzyk A. Opolski. *Indian Journal of Chemistry*.**2003**; 42B:2846.
[10] K.Mogilaiah, N.Vasudeva Reddy,.*Indian Journal of Chemistry*.**2003**; 42B:2124.
[11] M.S.Chande, A.A.Godbole, E.Coutinho, P.Desai *Indian Journal of Chemistry* **2003**;42B: 397.