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# Chloramine-T mediated synthesis of 1, 3, 4-oxadiazoles

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**ABSTRACT**

A new series of 1, 3, 4-oxadiazole (4a-4j) derivatives have been synthesized by oxidative cyclization of various INH hydrazones with chloramine – T as a powerful oxidizing agent. The INH hydrazones (3a-3j) in turn are obtained by the reaction of INH, with substituted aromatic aldehydes. The new products were characterized by special and analytical data. All the final synthesized compounds have been evaluated for their in-vitro antibacterial and antifungal activity. Some of the compound showed promising activity.

**Key words**: 1, 3, 4-oxadiazoles, chloramine-T, hydrazones, antibacterial and antifungal activity.

## INTRODUCTION

1, 3, 4-oxadiazoles represent one of the most active class of compounds possessing a wide spectrum of biological activities like antibacterial[1], antifungal[2], analgesic[3], anti-inflammatroy[4], pestisidal[5], CNC stimulant[6] activities. INH is a well known antitubercular drug[7]. In view of these observations it was thought of interest to synthesize some 1, 3, 4-oxadiazoles by a new synthetic route.

The reaction sequence leading to the formation of title compounds is outlined in Scheme-01. INH upon reaction with substituted aromatic aldehydes in presence of few drops of glacial acetic acid will yields the intermediate hydrazones (3a-3j). Oxidative cyclization of hydrazones with chloramine – T in ethanol medium under reflux will yields the title compounds (4a-4j). The final synthesized compounds were assigned on the basis of IR, MASS and $^1$H NMR spectral data.

## EXPERIMENTAL

Melting points were determined using open capillary tube method and are uncorrected. TLC was monitored to check the purity. IR spectra were recorded using KBr disk on a Shimadzu Perkin-Elmer 8201 FT-IR spectrophotometer. The $^1$H NMR spectra were recorded on BRUKER AVANCE II 400 NMR SPECTROMETER in $CDcL_3$ and DMSO-$d_6$ using TMS as internal reference (chemical shifts in ä ppm). The FAB mass spectra were recorded on JEOL SX-102/DA-6000 Mass spectrometer operating at 70ev.

### Synthesis of hydrazones

A mixture of hydrazide (0.01 mol) and substituted aromatic aldehydes (0.01 mol) in absolute alcohol (35 ml), in presence of catalystic amount of glacial acetic acid was refluxed for about 6-7 hrs. The reaction mixture was cooled and poured into the crushed ice. The precipitated compound

was filtered and washed with water and recrystallized from absolute alcohol, The physical data of hydrazones (3a-3j) is given in table-1.

**3a: IR (KBr) ($cm^{-1}$)**

3218 (CH-Ar), 3061 (C-H), 1676 (C=O), 1593 (C = C)

**$^1$H-NMR ($CDCl_3$) δ ppm**

3.82 (s, 3H, OCH3), 6.87 – 9.1 (m, 9H, Ar-H, Ar-CH),11.86 (s, 1H, CONH), MS : m/z: 255[$M^+$].

**3a: IR (KBr) ($cm^{-1}$)**

3059 (CH-Ar), 2904 (C-H), 1656 (C=O), 1601 (C = C).

**$^1$H-NMR ($CDCl_3$) δ ppm**

6.8 - 9.1 (m, 9H, Ar-H, Ar-CH) 11.4 (s, 1H, OH), 12.0 (s, 1H, CONH). MS : m/z: 241[$M^+$].

Similarly other derivatives (3a-3j) were synthesized and their physical data is given in table 1.

**Synthesis of 1, 3, 4-oxadiazoles[8]**

A mixture of Schiff base (0.01 mol) and chloramine – T (0.01 mol), in absolute alcohol (50 ml) was refluxed for about 6 hrs. The reaction mixture was cooled and the solid sodium chloride which is separated was filtered out and the filtrate is concentration on a water bath and the compound which is obtained is recrystallized from alcohol. The physical data of oxadiazoles (4a-4j) is given in table 2.

**4f: IR (KBr) ($cm^{-1}$)**

1640 (C=N), 1559 (C=C), 1165 (C-O-C), 1039 (N-N).

**$^1$H-NMR ($CDCl_3$) δ ppm**

7.72 – 8.84 (m, 9H, Ar-H) MS: m/z: 223 [$M^+$].

**4f: IR (KBr) ($cm^{-1}$)**

1649 (C=N), 1597 (C=C), 1159 (C-O-C), 1097 (N-N).

**$^1$H-NMR ($CDCl_3$) δ ppm**

6.36 – 8.75 (m, 7H, Ar-H) MS: m/z: 223 [$M^+$].

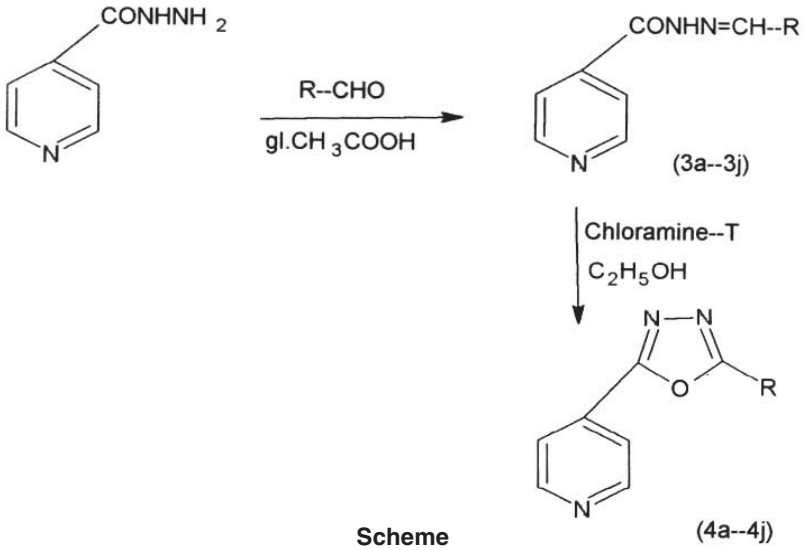
**4f: IR (KBr) ($cm^{-1}$)**

1660 (C=N), 1579 (C=C), 1162 (C-O-C), 1096 (N-N).

**$^1$H-NMR ($CDCl_3$) δ ppm**

2.41 (s, 3H, $CH^3$), 7.21-8.84 (m, 8H, Ar-H) MS: m/z: 237 [$M^+$].

Similarly other derivatives (4a-4j) were synthesized and their physical data is given in table 2.




**Scheme**

**Antibacterial and antifungal activity**

sAll the compounds were screened for their in *vitro antibacterial and antifungal activity*. Antibacterial activity was carried out against *S. aureus, P. aeruginosa, E. coli and B. subtilis* by the cup plate method[9] at a conc. of 100 µg/ml (table 3). The standard drug used was Streptomycin and DMF was kept as solvent control. The antifungal studies were carried out against fungus *C. albicans and A. niger* using Flucanazole as standard.

## RESULTS AND DISCUSSION

The antibacterial activity of the newly synthesized compounds in the present investigation was assessed by the cup-plate method. The results of the antibacterial studies are shown in table-3. Among the compounds tested 4e, 4f, 4i showed good activity against both the gram positive and gram negative pathogenic organisms. But most of the compounds are active against S. aureus and P. aeruginosa. The rest of the compounds showed moderate activity against all the four organism.

In the antifungal activity, the compounds 4g and 4g showed highest activity against both the fungal organisms. The other compounds showed moderate activity.

**Table 1: Physical data of hydrazones (3a-3j)**

| S. No. | R-CHO | Molecular weight | Molecular formula | Melting Point (°C) | % yield |
|---|---|---|---|---|---|
| 3a | 4-$OCH_3$ | 225 | $C_{14}H_{13}N_3O_2$ | 139 | 66 |
| 3b | 4Cl | 259.5 | $C_{13}H_{10}N_3OCl$ | 178 | 56 |
| 3c | 3-$NO_2$ | 270 | $C_{13}H_{10}N_4O_3$ | 195 | 65 |
| 3d | 4-$NO_2$ | 270 | $C_{13}H_{10}N_4O_3$ | 177 | 70 |
| 3e | $N(CH_3)_2$ | 268 | $C_{15}H_{16}N_4O$ | 163 | 59 |
| 3f | $C_6H_5$ | 225 | $C_{13}H_{11}N_3O$ | 110 | 60 |
| 3g | 2-furyl | 215 | $C_{11}H_9N_3O_2$ | 157 | 63 |
| 3h | $(2,5\text{-}OCH_3)_2$ | 305 | $C_{15}H_{15}N_3O_2$ | 166 | 69 |
| 3i | 2-OH | 241 | $C_{13}N_{11}N_3O_2$ | 170 | 73 |
| 3j | 4-$CH_3$ | 239 | $C_{14}N_{13}N_3O$ | 183 | 60 |

**Table 2: Physical data of 1, 3, 4-oxydiazoles (4a-4j)**

| Comp | R-CHO | Molecular weight | Molecular formula | Melting Point (°C) | Yield (%) |
|---|---|---|---|---|---|
| 4a | 4-$OCH_3$ | 253 | $C_{14}H_{13}N_3O_2$ | 176 | 45 |
| 4b | 4Cl | 257 | $C_{13}H_8N_3OCl$ | 184 | 58 |
| 4c | 3-$NO_2$ | 268 | $C_{14}H_8N_4O_3$ | 154 | 71 |
| 4d | 4-$NO_2$ | 268 | $C_{14}H_8N_4O_3$ | 136 | 68 |
| 4e | 4-$N(CH_3)_2$ | | | Viscous mass | |
| 4f | $C_6H_5$ | 223 | $C_{13}H_9N_3O$ | 170 | 60 |
| 4g | 2-furyl | 213 | $C_{11}H_7N_3O_2$ | 121 | 58 |
| 4h | $(2,5\text{-}OCH_3)_2$ | | | Viscous mass | |
| 4i | 2-OH | 239 | $C_{13}N_9N_3O_2$ | 160 | 70 |
| 4j | 4-$HC_3$ | 237 | $C_{14}N_{11}N_3O$ | 109 | 68 |

**Table 3: Antimicrobial and antifungal activities of compounds 4a-j**

| Comp. | Diameter of zone of inhibition (mm) at 10µgmml concentration | | | | | A.niger |
|---|---|---|---|---|---|---|
| | *S. aureus* | *B. subtilis* | *E. coli* | *P. aeruginosa* | *C. albicans* | |
| 4a | 11 | 09 | 10 | 12 | 10 | 11 |
| 4b | 12 | 08 | 11 | 13 | 13 | 12 |
| 4c | 10 | 09 | 10 | 12 | 11 | 10 |
| 4d | 11 | 10 | 09 | 12 | 11 | 10 |
| 4e | 11 | 13 | 12 | 13 | 11 | 09 |
| 4f | 11 | 10 | 12 | 13 | 10 | 10 |
| 4g | 12 | 12 | 10 | 11 | 11 | 12 |
| 4h | 12 | 11 | 11 | 09 | 11 | 11 |
| 4i | 13 | 12 | 10 | 11 | 10 | 10 |
| 4j | 11 | 12 | 10 | 11 | 10 | 10 |
| Streptomycin | 20 | 21 | 21 | 22 | - | - |
| Flucanazole | - | - | - | - | 21 | 22 |
| Control (DMF) | - | - | - | - | - | - |

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