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SCREENING OF HETEROCYCLIC COMPOUNDS: INSECTICIDAL AND FUNGICIDAL ACTIVITY OF SUBSTITUTED PYRIDINES AND THEIR DERIVATIVES

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ABSTRACT

Heterocyclic compounds such as substituted pyridines and their derivatives, oxazine, carbooxyanilide and thiocarbamate were investigated for their insecticidal and antifungal activity. Some of the compounds showed moderate to good insecticidal and fungicidal activity. The compounds were already synthesized and confirmed by mass, I.R and UV visible spectra.

KEYWORDS: Oxazine, Carbooxyanilide, Thiocarbamate, Pyridines, Antifungal activity.

INTRODUCTION

Substituted pyridine are a class of heterocyclic compounds which constitute a major portion of heterocyclic chemistry. They have emerged as versatile reagents recently and have attracted considerable attention for their biological activities (Caballero *et al*., 1993; El-Sebae, 1970; Hosur *et al*., 1994). Some of these compounds exhibited activities against pathogenic organisms.

The work reported here is a continuation of our previous work on the synthesis and insecticidal and fungicidal activity of these compounds. The synthesis has been reported earlier. (Davis & Elivdge, 1953; Butt *et al*., 1967a and b; Butt *et al*., 1987) Their structures were confirmed by mass and I.R spectroscopy studies. The present work describe their insecticidal and fungicidal activity.

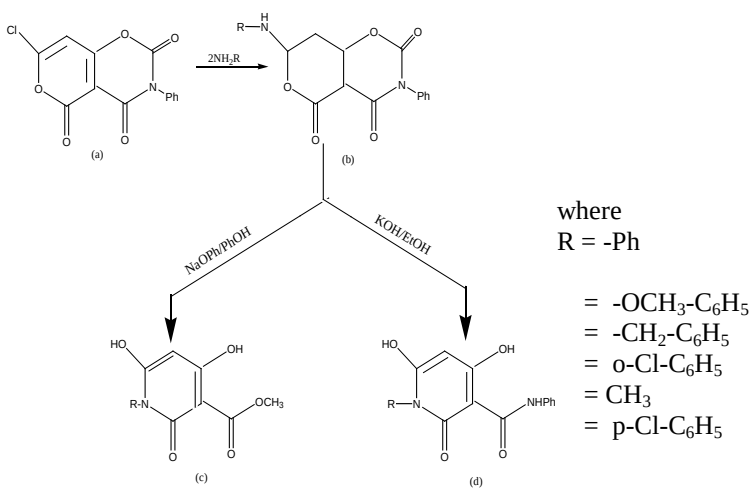
MATERIALS AND METHODS

General procedure for the synthesis of Compounds I-VIII

7-Chloro-3, 4dihydro-2, 4,5 tri oxo phenyl 2,4,5H pyrano (3,4-e)- 1,3 oxazine (0.01 mole) in 30 ml chloroform was stirred for 15min. To this mixture aniline (0.02mole) in 15 ml chloroform was added drop wise. The solution was stirred for 30 min. After completion of reaction the solid was filtered off solid compound (b) was crystallized from MeOH: Chloroform (1:1). Compound b (3.5g, 0.01 mole), sodium metal (1.2g, 4mole) in 12 ml phenol was taken in a flask and heated at 120°C for 3-5 min. The reaction mixture was diluted with water and excess of phenol was removed by shaking with ether. 2N-HCl acidified aqueous solution. The ppt of compound (c) was filtered washed and purified with MeOH: chloroform (1:1).

Compound (b) (1g) was added to 0.5g KOH in 50% aqueous EtOH. The solution was refluxed for 30min. Reaction mixture was cooled, acidified with 2N HCl, ppt of compound (d) was washed with water dried and crystallized from MeOH: Chloroform (1:1).

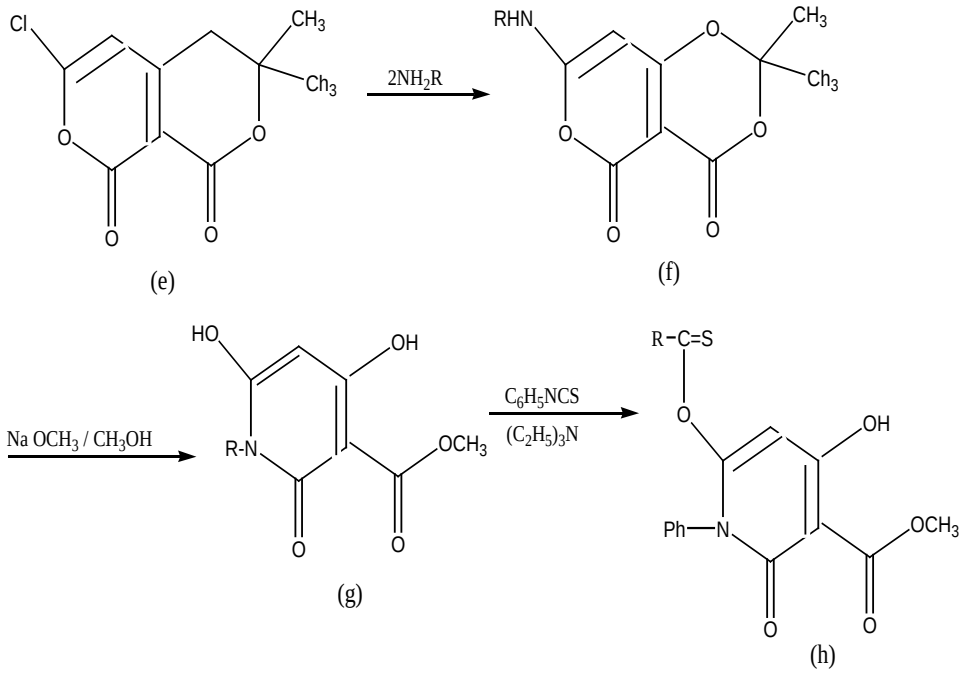
General procedure for the synthesis of compounds I-VIII



where
R = -Ph
= $-OCH_3-C_6H_5$
= $-CH_2-C_6H_5$
= o-$Cl-C_6H_5$
= CH_3
= p-$Cl-C_6H_5$

Scheme-1

General procedure for the synthesis of compounds ix-xi



Scheme-2

where
R = -NHC_6H_5
= -NHC_2H_5
= -p-$BrNHC_6H_4$

7-chloro-2, 2 dimethyl-4, 5 Dioxopyrano (4,3-d)-(1,3)-dioxin (2.35g; 0.01 mole) was taken in chloroform (30 ml), stirred and aniline (1.86g; 0.02 mole) in 15 ml chloroform was added drop wise. After complete addition stirred for another 30 min. solid compound (f) was obtained filtered, washed with water and dried.

Compound (f) (2g) was added to 40 ml MeOH containing 0.4g Sodium metal. The reaction mixture was refluxed for 30 min under anhydrous condition. Solvent was removed under vacuum. The compound was dissolved in water and aqueous solutions were acidified by 2N HCl, solid compound (g) was obtained filtered washed with water dried and crystallized from MeOH: Chloroform (1: 1).

Compound (g) (0.01 mole), phenyl iso thiocyanate (0.01 mole) triethylamine (0.01 mole) were heated on a water bath under anhydrous condition for 2 hours. Excess of triethylamine was removed under vacuum, residue was triturated with ether, solid triethylamine salt was obtained. On acidification by 2N HCl free thiocarbamate obtained (Compound h) which was crystallized from MeOH.

Compounds for insecticidel and fungicidal screening

The compounds which were studied for screening are reported with structure in Fig. 1 are:
7-Anilino-2, 4,5-trioxo-2H, 5H-pyrano-(3,4e)(1,3) oxazine (I), m.p. 190°C; (d)
6-Hydroxy-4-phenoxy-2-oxo-1-phenylpyridine-3-carboxyanilide (II), m.p. 240°C; (d)
6-Hydroxy-4-phenoxy-2-oxo-o-methylphenylpyridine-3-carboxyanilide (III), m.p. 230°C; (d)
6-Hydroxy-4-phenoxy-2-oxo-1-benzylpyridine-3-carboxyanilide (IV), m.p. 180°C; (d)
6Hydroxy-4-phenoxy-2-oxo-1-o-chlorophenyl-pyridine-3-carboxyanilide (V), m.p. 215°C; (d)
1-Methyl-1,2-hydro-2-oxo-4,6-di-hydroxy-pyridine-3-carboxy-anilide (VI), m.p. 168°C ;(d)
1-phenyl-1,2-di-hydro-2-oxo-4,6-di-hydroxy-pyridine-3-carboxyanilide (VII), m.p. 234°C; (d)
1-p-Chlorophenyl-1,2-di-hydro-2-oxo-4,6-di-hydroxypyridine-3-carboxy anilide (VIII), m.p. 197°C; (d)
1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-phenylthiocarbamate
(IX), m.p. 200°C; (d)
1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-ethylthiocarbamate
(X), m.p. 180°C ;(d)
1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-p-bromopheny thiocarbamate (XI), m.p. 184°C.

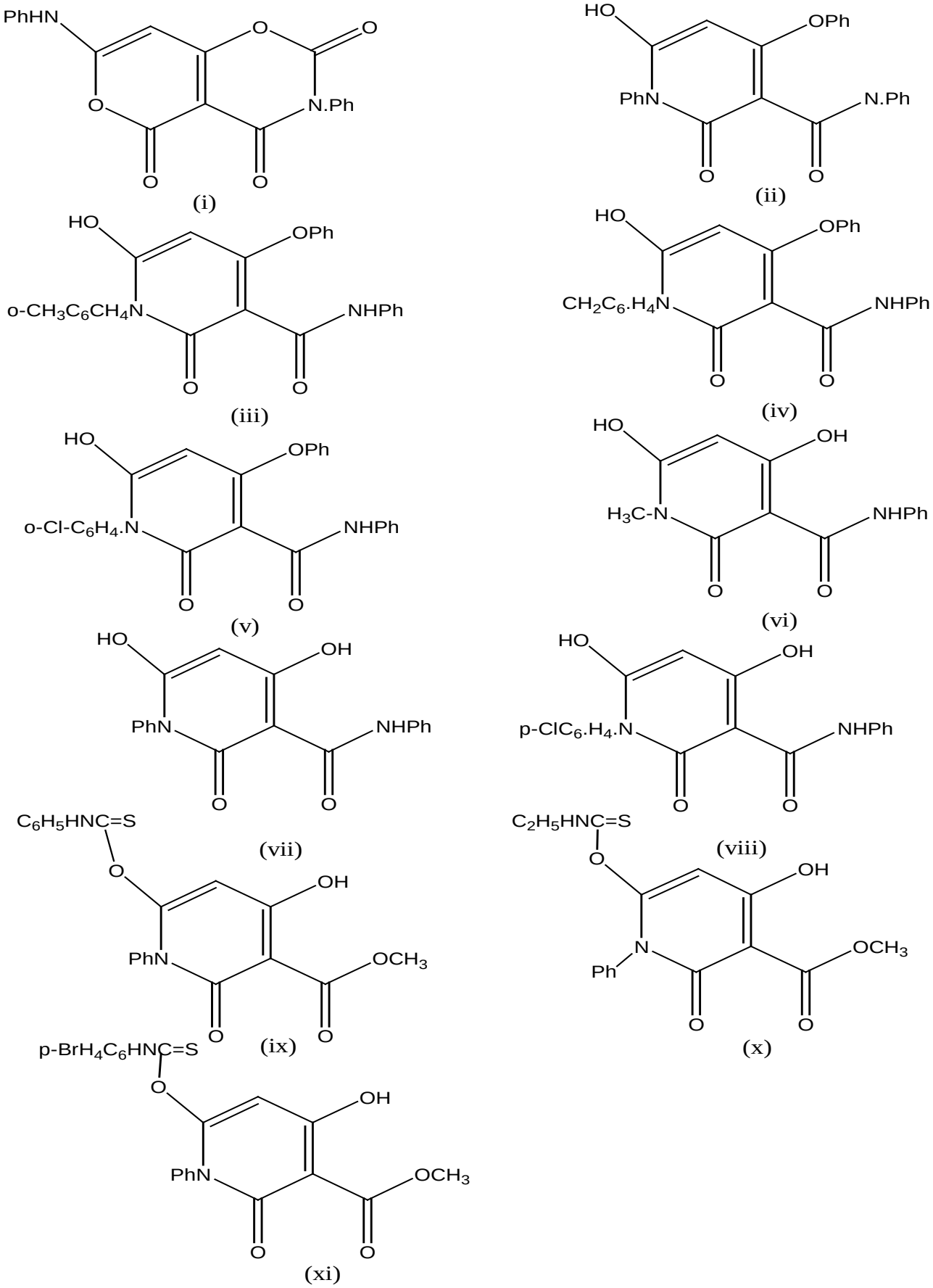


Fig. 1. Structure of substituted pyridine compounds.

RESULTS AND DISCUSSION

Some novel substituted pyridines and their derivative oxazine, carboxyanilide and thiocarbamate have been synthesized. The structures of compounds (i- xi) were confirmed on the basis of their elemental analysis and spectral data, which was reported in previous papers.

Insecticidel and fungicidal activity tests

The pyridine compounds (I-XI) were screened for insecticidal and fungicidal activity. The insecticidal activity tests were performed by contact toxicity method against *Sitophylus oryaze* and *Rhyzopertha dominica*. Commercial permethrin (coopex) was used as standard at a concentration of 235.9µg/cm^2. The antifungal activity was carried out in vitro anti fungal bioassay agar tube dilution method against fungus *Trichpophyton longifusus* by using standard drug miconazole at a concentration of 400µg/ml of DMSO. The compounds showed moderate to high activity. The results are displayed in Table 1.

Table 1. Insecticidal and fungicidal activity of substituted pyridine.

S. No.	Heterocyclic compounds	Insecticidal activity	Fungicidal activity
1.	7-Anilino-2, 4,5-trioxo-2H, 5H-pyrano-(3,4e)(1,3) oxazine	A	B
2.	6-Hydroxy-4-phenoxy-2-oxo-1-phenylpyridine-3-carboxyanilide	B	B
3.	6-Hydroxy-4-phenoxy-2-oxo-o-methylphenylpyridine-3-carboxyanilide	B	B
4.	6-Hydroxy-4-phenoxy-2-oxo-1-benzylpyridine-3-carboxyanilide	B	B
5.	6Hydroxy-4-phenoxy-2-oxo-1-o-chlorophenyl-pyridine-3-carboxyanilide	A	B
6.	1-Methyl-1,2-hydro-2-oxo-4,6-di-hydroxy-pyridine-3-carboxy-anilide	A	B
7.	1-phenyl-1,2-di-hydro-2-oxo-4,6-di-hydroxy-pyridine-3-carboxyanilide	B	B
8.	1-p-Chlorophenyl-1,2-di-hydro-2-oxo-4,6-di-hydroxypyridine-3-carboxy-anilide	B	B
9.	1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-phenylthiocarbamate	A	B
10.	1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-ethylthiocarbamate	B	B
11.	1,2-Dihydro-4-hydroxy-2-oxo-1-phenylpyridine-3-methylcarboxy-6-N-p-bromopheny thiocarbamate	B	B

A= Moderate to high activity = 60-80%

B= Slightly active = 40-60%

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