V

SUMMARY

CHAPTER - V

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Arylheterodiazoles such as oxadiazoles, thiadiazoles and triazoles are well known for their antifungal activity. This prompted us to synthesize and evaluate p-tert-butylphenoxymethyloxadiazoles, triazolothiadiazoles and triazolothiadiazines.

Hydrazinolysis of ethyl p-tert-butylphenoxy acetate (II) with hydrazine hydrate provided p-tert-butylphenoxyacetic acid hydrazide (III). The ester (II) on reaction with methanolic sodium hydroxide gave p-tert-butylphenoxyacetic acid (V). Cyclisation of hydrazide (III) with substituted aromatic acid furnished 5-(p-tert-butylphenoxymethyl)-2-substituted phenyl-1,3,4-oxadiazoles (VII a-c). The conversion was found to take place via the formation of N^2-benzoyl-p-tert-butylphenoxyacetic acid hydrazide (VIII). Cyclisation of p-tert-butylphenoxyacetic acid hydrazide (III) with p-tert-butylphenoxyacetic acid (IV) and chloroacetic acid gave symmetrical 2,5-bis(p-tert-butylphenoxymethyl)-1,3,4-oxadiazole (V) and 5-(p-tert-butylphenoxymethyl)-2-chloromethyl-1,3,4-oxadiazole (VI) respectively.

The hydrazide III on treatment with carbon disulphide and potassium hydroxide resulted in the formation of p-tert-butylphenoxyacetic acid 2-(dithiocarboxy)hydrazide monopotassium salt (IX) which on cyclisation with hydrazine hydrate gave 4-amino-5-(p-tert-butylphenoxymethyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (X).

Condensation of X with substituted aromatic acid; p-tert-butylphenoxyacetic acid, carbon disulphide and substituted aromatic benzaldehydes gave 3-(p-tert-butylphenoxymethyl)-6-substituted phenyl-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole (XIa-c); 3,6-bis(p-tert-butylphenoxymethyl)-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole (XII); 3-(p-tert-butylphenoxymethyl)-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole-6(5H)-thione (XIII) and 3-(p-tert-butylphenoxymethyl)-5,6-dihydro-6-substituted phenyl-1,2,4-triazolo[3,4-b][1,3,4]thiadiazole (XIVa-g) respectively.

Cyclisation of X with chloroacetic acid and benzoin furnished 3-(p-tert-butylphenoxymethyl)-5H-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine-6(7H)-one (XV) and 3-(p-tert-butylphenoxymethyl)-5H-6,7-diphenyl-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (XVII). XV on condensation with substituted aromatic benzaldehydes gave 3-(p-tert-butylphenoxymethyl)-7-(4-methoxyphenyl)methylene-5H-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine-6-one (XVIa-d).

Condensation of III with substituted benzaldehydes/acetophenones gave Schiff's base XVIIIa-c; XIXa-i, which were further cyclised with mercaptoacetic acid to give 3-(p-tert-butylphenoxyacetamido)-2,3,4,5-tetrahydro-2-(substituted phenyl)-4-oxothiazole (XXa-h).

Treatment of III with potassium thiocynate in acidic medium furnished p-tert-butylphenoxyacetic acid(2-aminothioxomethyl)hydrazide (XXI), which on condensation with substituted aromatic benzaldehydes gave p-tert-butylphenoxyacetic acid-2-[{(substituted phenyl)methyleneamino}thioxomethyl] hydrazide (XXIIa-g).

The conversions were monitored by concomitant expected change in the IR and ^1H NMR spectra of the products and further corroborated by N and S analytical data.

The compounds were tested for in vitro growth inhibitory activity against Fusarium oxysporum and Rhizoctonia solani by two fold serial dilution technique. The activity results were compared with a standard fungicide, bavistin. Some compounds were found active at concentration varying from 25-50 $\mu g\ ml^{-1}$. XIb was active at 12.5 $\mu g\ ml^{-1}$ of concentration against F. oxysporum and XIII at 6.25 $\mu g\ ml^{-1}$ against R. solani

In general, triazolothiadiazoles and their dihydro analogs showed better pattern of activity as compared to triazolothiadiazines and oxadiazoles.