SYNTHESIS AND BIOCHEMICAL STUDIES OF BIS SUBSTITUTED PHENOXYACETIC ACID HYDRAZIDES AS POTENTIAL PESTICIDE.

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Abstract

Among the various steps involved in the development of a physiologically selective pesticide, the first and the foremast step is to design a new molecule which is likely to show desired pesticidal activity. The practical exercise is then started by synthesizing the designed molecule and its congeners followed by their screening. " Structure modification of known leads", which includes recognition of a structural pattern in the lead molecule, synthesis of analogs with the recognized structural pattern, bioevaluation of each structural variant has been the guiding principle for designing and synthesis of bis substitutedphenoxyaceticacidhydrazides.

Key words

Bis Substitutedphenoxyaceticacidhydrazides, Pesticide, Lead compound, Biological Activity

INTRODUCTION

Pesticides are a group of chemical products which result in large economic and health benefits to society by crop protection and pest control. The use of pesticides enhances and stabilizes crop yields, protects the nutritional integrity of food, facilitates storage to assure round the year supplies and provides attractive and appealing agricultural products.

The economic estimates of pesticide benefits are either highly aggregate or specific to one crop and chemical. A pesticide of choice must be toxic to target pest and should have no or only minimal effects on non-target plants and animals. The potential negative aspect of pesticides include environment impacts on the quality of water and wild life habitat, pesticide resistance to targeted species, applicator's/harvestor's health and safety problems and consumer exposure to pesticide residues in food and fodder. To meet the future demands of safer pesticides efforts are needed for the development of target specific and environmentally safe pesticides. This can be achieved by carrying out modifications in the promising lead compounds of known pesticidal activity by chemical synthesis. Therefore, the synthesis and bioevaluation

of designed or structurally modified derivatives of promising lead compound(s) of natural or synthetic origin incorporated with appropriate substituents/functionalities offer a practical approach for evolving physiologically selective pesticides. Such approach is helpful to optimize the leads, provide information about structure-activity relationship (SAR) and to develop new pesticides.

The acid hydrazide derivatives are associated with wide range of biological activities such as antimicrobial, anti-tuberculosis, monoamine oxidase inhibiting activity, nematicidal etc.

RESULTS AND DISCUSSION

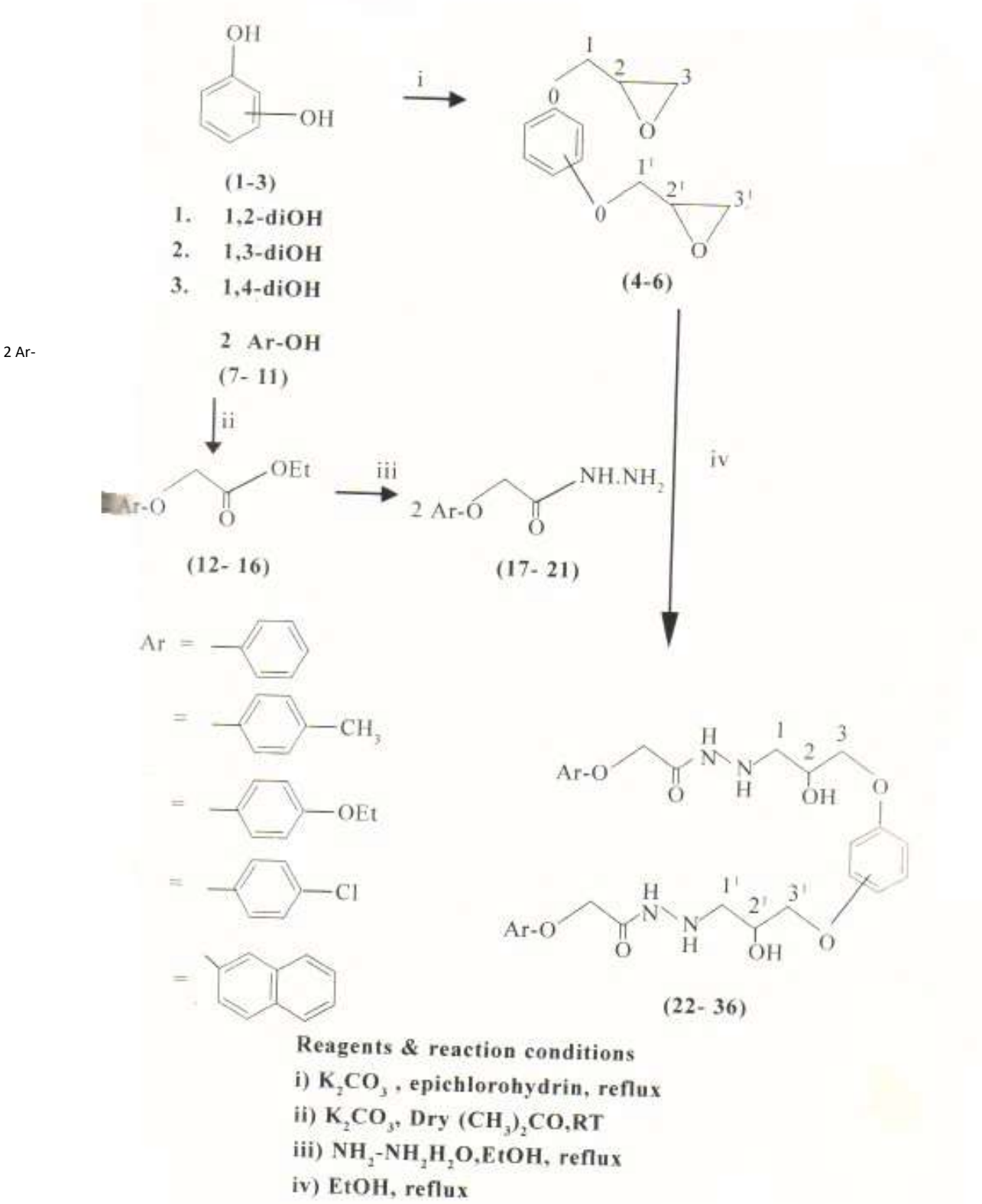
Synthesis of N, N^1 –[1,2-1,3-or 1,4-phenylene bis(oxy-2-hydroxypropyl)] bis substituted phenoxyacetic acid hydrazides (22-36).

Amond the several acid hydrazide derivatives the phenoxyacetic acid hydrazides and phenylene bix (oxyacetic acid hydrazides are associated with nematicidal and antimicrobial activities. The structural modification of the compounds are expected to exhibit enhanced biological activity pattern. The compounds incorporating phenylene bis (oxy-2- hydroxypropyl) moieties were achieved by undertaking the following sequence of synthesis Alkylation of catechol 1, resorcinol 2 and quinol 3 with excess of chloromethyloxirane in presence of anhydrous potassium carbonate gave the corresponding 1,2-,1,3- and 1, 4-bis (2,3- eposypropoxy) benzene 4, 5 and 6 in good yield. In the NMR spectrum of 5 in $CDCl_3$, the characteristic pattern of epoxypropoxy protons exhibited the splitting as already reported for such system Malik et al, (1983). Every proton in epoxypropoxy moiety was non-equivalent and showed different chemical shifts, i.e., 42 (dd,2H, 2xC_1-H, Jgem =10Hz and Jvic= 4Hz), 3,9 (dd, 2H 2xC_1 –H, Jgem = 10 Hz, Jvic = 4Hz), 3.35(m, 2H, 2xC_2-H), 2.82 (t,2H, 2xC_3-H, Jgem = Jvic =5Hz), 2.75 (dd,2H, 2xC_3 –H, Jgem = 5Hz, Jvic = 3Hz). The appearance of double doublets confirms the presence of geometrical isomerism.

The alkylation of phenol 7, 4-cresol 8, 4-ethoxyphenol 9, 4-chlorophenol 10 or β-naphthol 11 with ethyl chloroacetate in presence of potassium carbonate in acetone gave the corresponding ethyl esters of substituted phenoxyacetic acids (12-16). In the NMR spectrum of ethyl All chemical shifts in NMR are in δ ppm unit.

Phenoxyacetate 12 three protons of –CH_3 appeared as triplet at 1.3 (j=6 Hz) O-CH_2 protons showed a quarted at 4.2 (j=6 Hz). Two protons of the moiety O-CH_2-CO appeared as singlet at 4.6. IR spectrum a peak for ester group (COOEt) was assigned at 1720 cm^{-1}. The esters (12-16) were condensed with hydrazides (17-21) in good yields. (Scheme 1). In the IR spectra of acid hydrazides the peak of ester group was found disappeared and new peaks at 1650-1660 cm^{-1} were observed for CONH function. Also the characteristic bands at 3220-3300 cm^{-1} were observed for NH stretchings. The epoxides (4-6) on condensation in refluxing ethanol with the acid hydrazides (17-21) gave N, N'-[Phenylene bis (oxy-2-

hydoxypropyl)] bis phenoxyacetic acid hydrazides (22-36) in fair yields. The compounds were confirmed by the characteristic bands of –OH and C=0 stretchings at 3200 and 1620 cm^{-1} as shown in the IR spectrum of compound 36.



BIOLOGICAL ACTIVITY OF SYNTHESISED COMPOUNDS

Nematicidal Activity

All the final compounds synthesised during these studies were evaluated for the nematicidal activity second stage juveniles of root-knot nematode (*Meloidogyne javanica Treub*) and the structure activity relationship (SAR) is established. The selection of nematode species was primarily based on its geographical distribution and economic importance to agricultural crops. Aldicarb was used as a check. Aqueous gum acacia was used as control. The juvenile mortality was recorded by counting live and dead second stage juveniles under stereosocopic binocular microscope and percentage mortality was calculated. The counting of live and dead juveniles was carried out after the exposure time of 24 and 48 hours.

Antibacterial Activity

The synthesised compound were evaluated for their antibacterial activity against gram negative bacteria E. coli and gram positive bacteria B. subtills by two fold serial dilution technique using streptopenicillin as a standard and results are recorded. The perusal of the data revealed that the tested compounds exhibited differential antibacterial activity against E.coli and B. subtillis.

Antifungal Activity

All the synthesised compounds were screened for their in vitro growth inhibitory activity by two fold serial dilution technique, each concentration against Fusarium oxysporum, Alteernaria alternate and Trichoderma viride strains of phytopathogenic fungi. The perusal of the data revealed that the above compounds exhibited differential activity against these three tested fungi.

CONCLUSION:

Several heterodiazole derivatives such as oxadiazole are associated with wide range of biological activities such as antimicrobial, anti tuberculosis, monoamine oxidase inhibiting activity, nematicidal anti-inflammatory, analgesic, aniconvulsant, CNS depressant etc. These molecules need to be investigated further for their exploration for use as agrochemical with the following abjectives: -To design and synthesize new analogues by structural modification of suitable phenyloxadiazole.

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