1. NEDIT

SOME REACTIONS WITH PYRIDAZINE DERIVATIVES

A THESIS

PRESENTED BY

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SOME REACTIONS WITH PYRIDAZINE DERIVATIVES

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TO

MY PARANTS, MY WIFE AND MY SON

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VITAE

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- Infrared, U.V., N.M.R. and Mass Spectroscopy for Organic Molecules.
- (3) Free Radical Reactions.
- (4) Frontier Orbital Theory.
- (5) Organic Reactions.
- (6) Heterocyclic Chemistry.
- (7) Quantum Mechanics.
- (8) Conformational Analysis.
- (9) Polymer Chemistry.

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SUMMARY OF THE ORIGINAL WORK

SUMMARY OF THE ORIGINAL WORK

Thiazolidinone, pyrimidinedione and oxadiazoline derivatives are well known biological active compounds. In view of the varied physiological activities of these compounds, the present investigation deals with the synthesis of some pyridazine derivatives having thiazolidinone, pyrimidinedione and oxadiazoline nuclei and studying their antibacterial and antifungal activities.

The condensation of 4-carboxyhydrazide-5,6-diphenyl-3(2H)-pyridazinone (I) with aromatic aldehydes gave the corresponding arylidenehydrazide (IIa-c).

Arylidenehydrazides (IIa-c) underwent cyclization when refluxed with acetic anhydride yielding the respective oxadiazolines (IIIa-c).

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2-Phenyl-3-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-4-thiazolidinone (IVa) and 2-(p-chlorophenyl)-3-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-4-thiazolidinone (IVb) have been prepared by cycloaddition of thioglycollic acid with IIa and IIb, respectively.

a, Ar =
$$C_6H_5$$

b, Ar = C_6H_4Cl-p

The condensation of I with phenyl isothiocyanate in absolute ethanol afforded 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-4-phenyl-3-thiosemicarbazide (V), which underwent cyclization in conc. H₂SO₄ giving 2-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-yl]-5-phenylamino-1,3,4-thiadiazole (VI), whereas, cyclization of V with alkali gave 4-phenyl-5-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-yl]-1,2,4-triazoline-3-thione (VII).

Cone.
$$H_2SO_4$$

Cone. H_2SO_4
 C_6H_5
 C_6H_5

Treatment of 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcar-bonyl]-4-phenyl-3-thiosemicarbazide (V) with malonic acid and acetyl chloride gave 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbo-xamido]-3-phenyl-2,3-dihydro-2-thioxo-4,6 (1H,5H)-pyrimidinedione (VIII), which underwent condensation with p-chlorobenzaldehyde in the presence of sodium acetate and acetic acid yielding 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarboxamido]-3-phenyl-5-(p-chlorobenzylidene)-2,3-dihydro-2-thioxo-4,6 (1H,5H)-pyrimidinedione (IX). X was synthesized from V by the action of monochloroacetic acid and sodium acetate.

$$C_{6H_{5}} = C_{6H_{5}} = C_{$$

Condensation of I with \$\beta\$-dicarbonyl compounds, namely acetylacetone and benzoylacetone gave 1-[5',6'-diphenyl-3'(2H)oxopyridazin-4-ylcarbonyl]-3,5-dimethylpyrazole (XIa) and 1-(5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-5-methyl-3-phenylpyrazole (XIb), respectively.

On the other hand, I reacted with ethoxymethylenecyanoacetate in ethanol to give 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-yicarbonyi]-5-amino-4-carbethoxypyrazole (XIc).

a,
$$R = R_2 = CH_{3i}$$
; $R_1 = H$
b, $R = C_6H_5$; $R_1 = H$; $R_2 = CH_3$
c, $R = H$; $R_1 = COOC_2H_5$; $R_2 = NH_2$

I on refluxing with a mixture of acetic anhydride and ethyl cyanoacetate afforded 1-[5',6'-diphenyl-3'(2H)-oxopyridazin-4'-ylcarbonyl]-4-carbethoxy-3-methylpyrazole-5(4H)-one (XII).

Acylation of 4-carboxyhydrazide-5,6-diphenyl-3(2H)-pyridazinone (I) with different acylating agents, namely acetic anhydride, phthalic anhydride and benzoyl chloride gave the acyl derivatives XIII, XIV and XV respectively.