SYNOPSIS

The dissertation entitled, " SYNTHESIS OF SOME NEW N^1SUBSTITUTED QUINOLINE DERIVATIVES", presented to the faculty of Science, Shivaji University, Kolhapur, in partial fulfilment of the degree of MASTER OF PHILOSOPHY in Chemistry.

The dissertation consists of three chapters. Chapter-I describes quinoline and its derivatives as an interesting class of heterocyclic compounds having a wide range of applications as drug. Most of them have antiseptic, analgesics, tryphocidal, germicidal, antitubercular, anthermintic and antiserotonin activities. In addition to these quinolines show good antibacterial, antifungal, amoebicidal, antiviral activities. Some quinolines act as antidepressants and antihypertensive agents.

The same chapter includes a brief survey of the literature on 2-quinolones and its N^1-substituted derivatives with reference to methods of synthesis, biological and industrial importance. At the end of the chapter the scope of the present work is given.

CHAPTER - II

Chapter-II is an experimental work and is divided into three parts :

Part-I : describes the details of experimental methods used for the synthesis of N^1-Hydrazido-4-methyl, quinolin-2(1H)-one derivatives. The strategy employed for the synthesis of desired compound involved the

reaction of substituted aromatic amines with acetoacetic ester in dioxane to form acetoacetanilides (Ia-c) which when cyclised in presence of sulphuric acid gave substituted quinolin-2(1H)-ones (IIa-c). The compound (IIIa-c) on N^1-carbethoxylation with ethyl chloroformate gave corresponding N^1-carbethoxy derivatives (IIIa-c). The compound (IIIa-c) undergo nucleophilic substitution with hydrazine hydrate (80%) to form their N^1-hydrazido -4-methyl-quinolin-2(1H)– ones (IVa-c). These hydrazides were further reacted with phenyl isothiocyanate yielded substituted quinolinoyl thiosemicarbazides (V a-c) as a key intermediate. These when cyclised in presence of sodium hydroxide, I_2 in KI and phosphoric acid furnished targetted 4-phenyl-2-(4'-methyl, quinolin -2'- one-1'-yl) -5-mercapto - 1,3,4-triazole (V Ia-c), 5-anilino-2-(4'-methyl, quinolin-2'-one-1'-yl)1,3,4-oxadiazole(V IIa-c) and 5-anilino-2-(4'-methyl, quinolin-2'-one-1'-yl)-1,3,4-thiadiazole (VIIIa-c) respectively (Scheme-I).

Part-IIA : deals with the synthesis of some new derivatives of N^1-Methyl hydrazido-4-methyl-quinolin-2(1H)-one.

The compounds I'a-c were synthesised as per same methodology described in the Part-I of this dissertation. The reaction of I'a-c with methyl chloro acetate in the presence of potassium carbonate in acetone gave corresponding N^1-carbmethoxymethyl, 4-methyl quinolin-2(1H)-ones (II'a-c) which when refluxed in ethanolic hydrazine hydrate gave corresponding N^1-substituted methylhydrazido-4-methyl quinolin-2(1H) ones (III'a-c). These hydrazides (III'a-c) were converted into their corresponding thiosemicarbazides (IV'a-c) by reacting them with phenylisocyanate in ethanol.

The compounds (IV'a-c) were cyclised by using different reagent such as sodium hydroxide, I_2 in KI and phosphoric acid to their N^1-substituted 4-methyl, quinolin-2(1H) ones with five membered hetero-cycles such as triazoles (V'a-c), oxadiazoles (VI'a-c) and thiadiazoles (VII'a-c). (Scheme II).

Part II.I : includes the preparation of hydrazones of N^1 substituted Hydrazides/Methyl hydrazides of 4-methyl, quinoline-2(1H)ones. (I"a-c) by reacting them with citral in methanol to form their corresponding arylidene derivatives.

The structures of these compounds have been confirmed by UV, IR, ^1H NMR, Mass spectral studies and elemental analysis. Mass spectral fragmentation patterns of some of the compounds have been reported in the Part-II of the Chapter-II (Scheme-III and IV).

CHAPTER - III

Chapter-III deals with the evaluation of the antimicrobial screening of the synthesised compounds by Agar plate diffusion method against gram +ve and gram -ve bacteria using tetracycline as standard compound.

The bacterial species selected for the antimicrobial screening were Staphylococus aureus, Staphylococus citreus (gram +ve) and Pseudomonas aerugenosa, Klebsiella pneumoniae and Escherichia coli (gram -ve) bacteria.

Most of the compounds included in the present study have exhibited moderated to good antibacterial activity against P. aerugenosa, K. pneumoniae and E. coli (Gram -ve) while they are observed to be less active against S. aureus and S. citreus (Gram, +ve). The presence of the methyl group in the phenyl ring of quinolinone nucleus and N^1-substitution with heterocyclic moiety enhances the antibacterial activity.

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