ABSTRACT

During the course of this research work, a number of 2,1-benzothiazine 2,2-dioxide related novel heterocyclic molecules were synthesized. Starting with the synthesis of precursor 2,1-benzothiazine 2,2-dioxide molecules, novel 2,1-benzothiazine 2,2-dioxide related heterocyclic molecules with good biological potential like antibacterial, antifungal and antioxidant were synthesized with best possible yields and purity. The precursor molecules were initially synthesized by already reported procedures which were later improved to get better yields. The influence of bromine atom at position 5 of the benzene ring, on the reactivity of 2-Amino-5-bromo-benzoic acid methyl ester starting material towards the nucleophilic reactions was explored. It was observed that 2-Amino-5-bromo-benzoic acid methyl ester exhibited poor reactivity as compared with 2-Amino-benzoic acid methyl ester. Mainly the reactivity of the carbon atom bearing two acidic hydrogen atoms at position 3 of thiazine ring has been explored to be replaced with halogen like atoms. Similarly, the carbonyl function of thiazine ring at position 4 was converted to imine by reacting it with hydrazine and this resultant imine was treated with aldehydes/ketones to get di-imine derivatives of 2,1-benzothiazine molecule. Finally, a few of these di-imine derivatives were then subjected to halogenation at position 3 of thiazine ring.

In first methodology, a novel series of biologically active 3,3-dihalo-1-alkyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-one derivatives were synthesized from the un/substituted 2,1-benzothiazine 2,2-dioxide nuclei with variously substituted *N*-alkyl moieties. 2,1-benzothiazine 2,2-dioxide nuclei were subjected to halogenations using *N*-bromo-/*N*-chloro-succinimide under free radical conditions in the presence of dibenzoyl per oxide. Both of the two acidic hydrogen atoms at position three of thiazine ring were replaced to give 3,3-dihalo substituted derivatives. Antifungal and antioxidant activities were then evaluated. Some derivatives from this series shown promising results for their antifungal activity against selected five fungal strains. It was observed that the halogen atoms at position three has created excellent fungicidal activity to the previously non-antifungal 2,1-benzothiazine 2,2-dioxide derivatives.

In the next methodology, a biologically active series of *N*-Benzylidene-*N'*-(1-alkyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines was

synthesized and screened for their antibacterial and antioxidant potential. 2,1-benzothiazine 2,2-dioxide moieties with various substitutions were converted to 1-alkyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines by their reaction with hydrazine hydrate in alcoholic solvent. This monocyclic imine was then reacted with different aldehydes and ketones under the conditions of reflux and ultrasonic bath to get di-imine derivatives. It was observed that reactions in ultrasonic bath were accomplished with highly reduced reaction times and improved yields. One of the series of di-imine derivatives was evaluated for bactericidal activity against gram positive and gram negative bacteria with moderate to good results. Similarly, other di-imine series was evaluated for their anti-oxidant potential with positive results.

A few of the above di-imine derivatives were then subjected to halogenation at position three of thiazine ring to get a novel series of 3-monohalo-1-methyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ones. Only one of the two acidic hydrogen atoms at position three of thiazine ring was replaced to give 3-monohalo substituted molecules. Derivatives from this series were evaluated for bactericidal activity against Gram-positive and Gram-negative bacteria with moderate to excellent results.

The newly synthesized molecules were characterized by spectroscopic techniques like IR, ^{1}H and ^{13}C NMR, Mass spectrometry and elemental analysis. Many of the representative compounds from all the series were re-crystallized in suitable solvents and characterized by CCD diffractometer for characterization and crystal structure analysis. The stereochemistry of some of these compounds is also discussed briefly.