



ABSTRACT

The syntheses of Piroxicam-related heterocyclic molecules containing 1,2-benzothiazine-1,1-dioxide privileged motif, have been achieved *via* novel one-pot procedures. Cost-effective, cheaper and indigenously feasible, easy to handle synthetic route has been devised for the synthesis of Piroxicam with best yields and purity. 4-Hydroxy-2-methyl-2H-1,2-benzothiazine-3-sulfonic acid-1,1-dioxide and 4-Hydroxy-3-nitro-2-methyl-2H-1,2-benzothiazine-1,1-dioxide have been synthesized for the first time by Gabriel-Colman rearrangement from their important intermediates: saccharinmethane sulfonic acid and nitromethylsaccharin, respectively. Both of these intermediates and the target nuclei have been reported in novel one-pot reactions starting from readily available saccharin and 2-methyl-2H-1,2-benzothiazine-4-(3H)-one-1,1-dioxide, under two separate strategies.

A convenient synthesis of 4-(alkoxycarbonylmethylene)-3,4-dihydro-2H-1,2-benzothiazine-1,1-dioxide has also been achieved by the application of Wittig reagents to 2-methyl-2H-1,2-benzothiazine-4(3H)-one-1,1-dioxide that was prepared by the conventional synthetic route and by palladium-catalysed Heck cyclization methodology, as well. Derivatization of these nuclei has been carried out with un/substituted aliphatic, alicyclic, aryl and heteroaryl amino-group containing molecules to produce compounds which may act by themselves or may be used as a moiety for designing new drug molecules.

Among the newly synthesized derivatives, 3-carbamoylbenzene sulfonamides were subjected to the antimicrobial bioassay studies, both against Gram-positive and Gram-negative strains. The 3-carbamoylbenzene sulfonamides with para- and meta-benzoic acids were found most potent derivatives with lowest MICs (2.0 $\mu\text{g/ml}$ and 1.0 $\mu\text{g/ml}$) against *S. aureus* and *B. cereus*, Gram-positive bacteria, in comparison to the standard reference Penicillin G (MIC = 0.35 $\mu\text{g/ml}$). Among Gram-negative bacteria the 2,3-dimethylphenyl and 3,4-dimethylphenyl-group containing 3-carbamoylbenzene sulfonamides were found most active (MICs = 8.0 $\mu\text{g/ml}$ and 5.0 $\mu\text{g/ml}$) against *L. monocytogenes* and *E. coli*, respectively. In general, the derivatives containing lipophilic side-chains on carboxamide function produced good results, probably due to the ability to penetrate through the lipid cell membrane of Gram-negative bacteria. Further research in



this area is in progress and the newly synthesized compounds are expected to possess biological activities better than that of Piroxicam because they contain the same backbone skeleton but with certain new functionalities ever reported. X-ray crystallographic studies have also been attempted where crystals of good quality have been isolated.