SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 2-PHENYL-4H-BENZO[b]-THIOPYRAN-4-ONES (THIOFLAVONES) AND RELATED COMPOUNDS

H. Nakazumi, T. Ueyama, T. Kitaguchi and T. Kitao
Department of Applied Chemistry, College of Engineering
University of Osaka Prefecture, Sakai, Osaka 591, Japan

2-Phenyl-4H-benzo[b]thiopyran-4-ones (thioflavones)are compounds of pharmacologically interest as the thio analogs of flavones which are an important group of naturally occurring bioactive compounds. Few connections between chemical structures of thioflavones and pharmacological effects have so far studied. We recently initiated a program to prepare and evaluate new thioflavones as biologically and pharmacologically effective compounds. We now report our results on the synthesis and antibacterial activity of 3-substituted thioflavones and some related compounds. 3-(Chloromethyl)thioflavone 2 could be obtained by chloromethylation of thioflavone 1 with chloromethyl methyl ether and 60% fuming H_2SO_4 at 55-60 °C for one day (yield 22%). New 3-substituted thioflavones (3) could be derived easily from 2 using aniline, morpholine and sodium alkoxide as nucleophilic reagents. Thioflavone 1,1-dioxide 4 and thioflavone 1-oxide 5 designed as analogs of 1,4-naphthoquinones were also prepared by oxidation of the corresponding thioflavones with 30% H_2O_2 in AcOH.

These compounds were screened via in vitro antibacterial activity. We now found that an introduction of a substituted-methyl group at the 3 position of thioflavone resulted in an unique antibacterial activity against P. crustosum, whereas the parent compound 1 exhibited no antibacterial activity. The substituent effect on the antibacterial activity of 4 and 5 will also be discussed.