SYNTHESIS OF 3-SUBSTITUTED 4H-1-BENOTHIOPYRANS AND RELATED HETEROCYCLIC COMPOUNDS

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The introduction of specific substituent group into the 3-position of 2-phenyl 4H-1-benzothiopyran-4-ones (thioflavones) 1 has been examined, because the introduction of a chloromethyl and acetoxymethyl group into the corresponding position of 1,4-naphthoquinones and 4H-1-benzothiopyran-4-one 1,1-dioxides is required for bioactivation. 3-(Formyl)thioflavone 3 was prepared by the Sarett oxidation of 3-(hydroxymethyl)thioflavone 2a with chrominium trioxide. A formyl group of 3 was also converted into cyano, acryl and carboxyl group in good yields. The Meerwein reaction of thiochromone as well as chromone with p-nitrobenzenediazonium ion gave only 3-(4'-nitrophenyl)thiochromone (isothioflavone). It was found that 3-(amino)-thiochromone was easily prepared by reaction of 3-(bromo)thiochromen-4-one with sodium azide.

Condensation of 3-(amino)thiochromone with diethyl ethoxymethylenemalonate and with dimethyl acetylenedicarboxylate gave intermediates, which were theremally cyclized to give 4,10-dihydro-4,10-dioxo-1H-[1]-benzothiopyrano[3,2-b]pyridinecarboxylates. 3-(Formyl)thiochromone was condensed with o-phenylenediamine to give 7-oxo-7,13-dihydro-[1]-benzothiopyrano[2,3-b]-1,5-benzodiazepine. The *in vitro* antimicrobial activity and *in vivo* antitumor activity (lymphocytic leukemia P-388) of 3-substituted thioflavones have been also examined.