SYNTHESIS AND REACTION OF 3,4-DIHYDROTHIENO[2,3-d]PYRIMIDINE DERIVATIVES

Fumiyoshi Ishikawa and Hitoshi Yamaguchi
Research Institute, Daiichi Seiyaku, Co. Ltd.,
Edogawa-ku, Tokyo 132, Japan

Reaction of 2,4-dichloro-5,6,7,8-tetrahydro[1]benzothieno[2,3-d]pyrimidine (1) with sodium borohydride gave 2-chloro-3,4,5,6,7,8-hexahydro[1]benzothieno[2,3-d]pyrimidine (2). Compound 2 was reacted with some nucleophiles to yield the corresponding 2-substituted products (3) such as 2-amino-, oxo-, thioxo-, ethoxy- and methylthio-3,4-dihydro derivatives. Compounds 3 were readily oxidized under various conditions to 2-substituted thieno[2,3-d]pyrimidine derivatives (4). Alkylation of 2 gave predominantly 2-chloro-1- or 3-alkyl derivatives depending upon the nature of alkylating reagents. New heterocycles (1,5-dihydroimidazo[1,2-a]thieno[2,3-d]pyrimidine, 1,2,3,5-tetrahydroimidazo[1,2-a]thieno[2,3-d]pyrimidin-2-one and 2,3-dihydro-5H-oxazolo[3,2-a]thieno[2,3-d]pyrimidine) were obtained by use of the reactions described above.

Reductions of 4-chloro and 4-unsubstituted thieno[2,3-d]pyrimidines having a functional group, *eg* hydrogen, methyl, phenyl, amino, ethoxy, methylthio, methylsulfinyl and methylsulfonyl, at position 2 with sodium borohydride were stimulated by the electron withdrawing group at position 2. Furthermore, some 2,4-dichloro derivatives of quinazoline and thieno-[3,2-d]- and -[3,4-d]-pyrimidine were reduced with the same reagent to give the corresponding 2-chloro-3,4-dihydro derivatives.