Chapter 5

Conclusion

The new heterocyclic fuse-ring 2-Thiooxpyrimido-[4,3-d]-quinoline-4-one derivatives were synthesized by the modification of Pyrazolo-[4,3-c]-quinoline-3-(5H)-one derivatives which are supposed to be the ligands of benzodiazepine receptors.

The synthetic route of 2-Thiooxopyrimido-[4,3-d]-quinoline-4-one and its derivatives proceeded through 4 step. Firstly, 4-Hydroxyquinolines were prepared by condensation of diethyl ethoxymethylenemalonate and aniline or its derivatives followed by cyclization to 3-Carboethoxy-4-hydroxyquinolines at high temperature. Then, 4-Hydroxy substituted of quinolines were chlorinated with thionyl chloride or phosphorous oxychloride to afford 4-Chloroquinoline intermediates which were then transformed to 4-Isothiocyanato-quinolines by nucleophilic substitution of potassium thiocyanate in toluene. Finally, the desire products were suceeded by cyclization reaction of isothiocyanate group and ester group with ammonia gave two derivatives of 2-Thiooxopyrimido-[4,3-d]-quinoline-4-(3,6-H)-one and 8-Chloro-9-fluoro-2-thiooxopyrimido-[4,3-d]-quinoline-4-(3,6-H)-one. The N-3 substituted Thiooxopyrimidoquinolone derivatives were carried *via* either alkylation of 2-Thiooxopyrimido-[4,3-d]-quinoline-4-(3,6-H)-one derivative in alkali medium or reaction of amine derivatives with 4-Isothiocyanatoquinolines. Five Thiooxopyrimidoquinolone derivatives were obtained by the above mentioned route, namely, 3-Phenyl-2-thiooxo pyrimido-[4,3-d]-quinoline-4-(6H)-one, 8-Chloro-9-fluoro-3-phenyl-2-thiooxopyrimido-[4,3-d]-quinoline-4-(6H)-one, 8-Chloro-3-(4'-chloro phenyl)-9-fluoro-2-mercapto-pyrimido-[4,3-d]-quinoline-4-one, 8-Chloro-9-fluoro-2-mercapto-3-(4'-methyl phenyl)-pyrimido-[4,3-d]-quinoline-4-one and 8-Chloro-3-ethyl-9-fluoro-2-mercapto-pyrimido-[4,3-d]-quinoline-4-

one. Oxidation reaction of 8-Chloro-9-fluoro-3-phenyl-2-thiooxopyrimido-[4,3-d]-quinoline-4-(6H)-one by peroxide or peracid gave 2,4-pyrimidinedione fused to quinoline ring, 3-Chloro-9-fluoro-3-phenyl-pyrimido-[4,3-d]-quinoline-2,4-(6H)-dione.

The molecular structure of 2-Thiooxopyrimido-[4,3-d]-quinoline-4-one derivatives can exist in several isomeric form due to electron delocalize in the molecule. The products and major forms of them were identified by IR, NMR and MS technique.