SYNTHESIS OF 2-SUBSTITUTED DIHYDROPYRIMIDINES AND THEIR PROPERTIES

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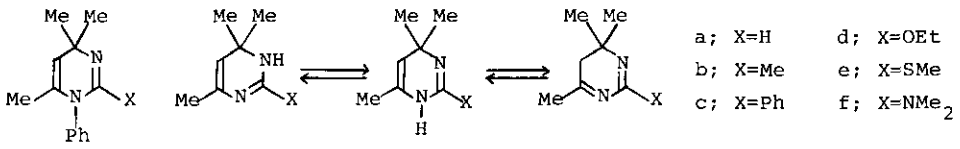
Dihydropyridines have been extensively investigated as model compounds of NAD(P)H. Although dihydropyrimidines are aza-analogs of dihydropyridines, little attention has been paid for their synthesis and properties. We previously reported that three types of dihydropyrimidine isomers were synthesized by the desulfurization of pyrimidine-2(1H)-thiones and their dihydro-derivatives. However, this method was limited to the preparation of 2-unsubstituted dihydropyrimidines. In the course of investigation of dihydropyrimidine properties, we tried to synthesize dihydropyrimidines which have various substituents on C-2, and to compare their properties each other.

2-Substituted 1,4-dihydro-1-phenylpyrimidines (1b,d,e) were synthesized from N-phenylation of N-unsubstituted 3,4-dihydropyrimidine, and from the O, S-selective alkylation of 3,4-dihydro-1-phenylpyrimidine-2(1H)-one and -thione, respectively.

It was reported that 3,4-dihydro-4,4,6-trimethylpyrimidines existed as a mixture of 1,4- and 3,4-dihydro forms. Actually, N-unsubstituted dihydropyrimidines which have a C-substituent on C-2 (2a,b,c) existed as a mixture of 1,4- and 3,4-dihydro forms, while 2-hetero-substituted dihydropyrimidines (2d, e,f) were a mixture of 3,4- and 4,5-dihydropyrimidines. This is the first example that 2d,e,f existed in tautomeric equilibrium between two dihydro forms. Further, the amino group on C-2 lowered the oxidation potential.

It was concluded that the substituents on C-2 of N-unsubstituted dihydropyrimidines have large influence on their properties.



1 2 3(a-c) 4(d-f)

a; X=H d; X=OEt
b; X=Me e; X=SMe
c; X=Ph f; X=NMe_2