SYNTHESIS AND REDUCING ABILITIES OF 1-SUBSTITUTED DIHYDROPYRIMIDINES

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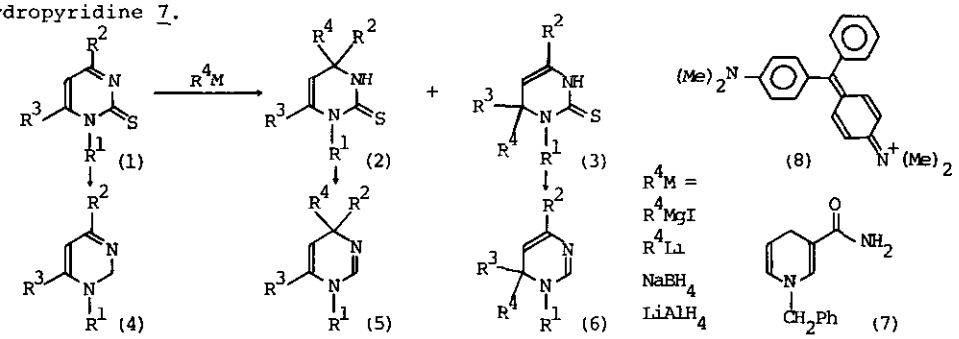
N-Substituted pyridines have been extensively investigated as model compounds of NAD(P)H. In spite of being aza-analogues of dihydropyridines, little attention has been paid for the synthesis and properties of dihydropyrimidines, especially 1-substituted dihydropyrimidines. First we tried to synthesize 1-substituted dihydropyrimidines by desulfuration of pyrimidine-2(1H)-thiones or their dihydro-derivatives with Raney nickel.

3,4-Dihydropyrimidine-2(1H)-thiones (2) were treated with Raney nickel in MeOH at 50 °C for 1 h, then refluxed for 2 h to afford 1,4-dihydropyrimidines (5). 1,6-Dihydropyrimidines (6) were also obtained by the same treatment of 3,6-dihydropyrimidine-2(1H)-thiones (3) with Raney nickel. Furthermore, pyrimidine-2(1H)-thiones (1) were treated with Raney nickel for 3 h at room temperature under hydrogen atmosphere to give 1,2-dihydropyrimidines (4).

Since dihydropyrimidines are aza-analogues of dihydropyridines, they are expected to exhibit reducing abilities. Therefore, reducing abilities of dihydropyrimidines are compared with those of 1-benzyl-1,4-dihydronicotinamide (7) in the following points: (a) the measurement of oxidation potentials; (b) the measurement of rate constant for reduction by the decrease of the absorbance of malachite green (8); (c) the solvent effect. As a result, dihydropyrimidines show reducing abilities similarly to dihydropyridine 7.



In conclusion, the selective synthesis of three types of dihydropyrimidine isomers is established. Further, these dihydropyrimidines exhibit reducing abilities similarly to dihydropyridines. The detailed studies on mechanism are now in progress.