

REACTION OF PYRIMIDINE N-OXIDES ON THE CARBON-CARBON BOND FORMATION

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In order to examine the synthetic utility, 4,6-dimethyl- ( $A_1$ ) and 4-alkoxy-6-methylpyrimidine 1-oxides ( $A_2$ ) were treated with following nucleophilic reagents.

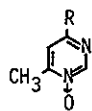
1) Reaction of  $A_1$  with active methylene compounds e.g. malononitrile in acetic anhydride afforded an adduct (B) instead of the expected 2-pyrimidinemalononitrile. Acid hydrolysis of the adduct leading to aminomethylenemalononitrile exhibited that the adduct did not contain any aromatic ring. Reaction of  $A_1$  with ethyl  $\alpha$ -ethoxy-carbonylacetimide gave rise to the similar result.

2) On the contrary, morpholine enamines such as morpholinocyclohexene, morpholinocycloheptene and morpholinoisobutene reacted with  $A_{1,2}$  to give the pyrimidine derivatives (C) possessing a carbonyl side chain at the 2-position. The reaction of 5-amino-3-methylisoxazole also gave the corresponding product (D). These results suggested that the ring fission of pyrimidine N-oxides might be caused by an active methylene group on the attacking reagents.

3) The 1,3-dipolar cycloaddition of dimethyl acetylenedicarboxylate to  $A_2$  afforded the pyrimidine-2-acetate via the intermediate (E) containing an oxaloylacetate moiety at the 2-position.

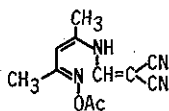
4) Although the cycloaddition of phenyl isocyanate with  $A_2$  gave the 2-anilinopyrimidines (F) as expected, phenyl isothiocyanate afforded an abnormal product (G) whose structure was confirmed by converting it to 4-anilino-5-hydroxy-6-methylpyrimidine. The reaction pathway was assumed to involve the 1,3-sigmatropic rearrangement.

Comparing with the reactions of quinoline 1-oxide already shown in literatures, the above results (1-4) will be discussed in detail.

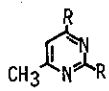


$A_1$ : R=methyl

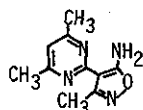
$A_2$ : R=alkoxyl



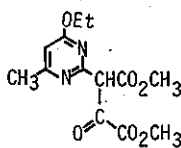
B



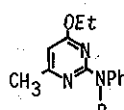
C



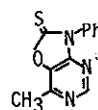
D



E



F



G