

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.

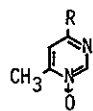
1) Reaction of A_1 with active methylene compounds e.g. malononitrile in acetic anhydride afforded an adduct (B) instead of the expected 2-pyrimidinemalononitrile. Acid hydrolysis of the adduct leading to aminomethylenemalononitrile exhibited that the adduct did not contain any aromatic ring. Reaction of A_1 with ethyl α -ethoxycarbonylacetimide 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 oxaloylaceta moiety at the 2-position.

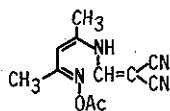
4) Although the cycloaddition of phenyl isocyanate with A_2 gave the 2-anilinopyrimidines (F) as expected, phenyl isothiocyanate afforded an abnormal product (G) whose structure was confirmed by converting it to 4-anilino-5-hydroxy-6-methylpyrimidine. The reaction pathway was assumed to involve the 1,3-sigmatropic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

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

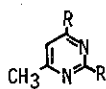


A_1 : R=methyl

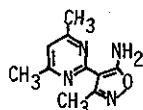
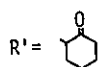
A_2 : R=alkoxyl



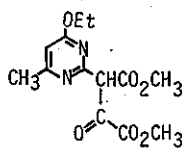
B



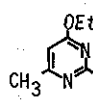
C



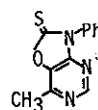
D



E



F



G