SYNTHESIS OF PYRIMIDINYLMETHYL KETONES FROM CHLOROPYRIMIDINES

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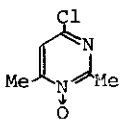
In order to open a way to a simple procedure for the introduction of acylmethyl groups into pyrimidine nuclei, the reaction of 2- and 4-chloropyrimidines with various carbanion-type reagents was investigated.

2,6-Dimethyl-4-chloropyrimidine N-oxide (3) reacted with ethyl cyanoacetate and malononitrile to give the expected products (4a,b) in good yield, while the reaction of the N-oxide (3) with methyl ketones failed. The use of 4-benzenesulfonyl-2,6-dimethylpyrimidine (6) instead of the N-oxide (3), appeared to remove the above restriction. Namely, 6 reacted readily not only with active methylene compounds but with acetone, acetophenone and cyclohexanone to give the pyrimidines (7a,b & 8) with a carbonyl function in satisfactory yields.



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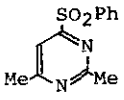

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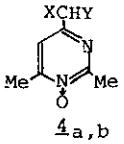
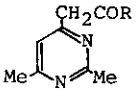
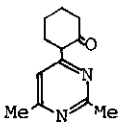


4a,b



7a,b



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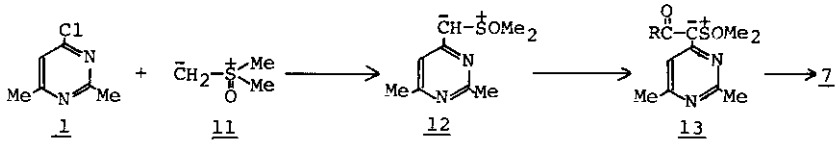
Futher investigation was made to find reactions with wider applicability. Consequently, the reaction of simple chloropyrimidines with dimethyloxosulfonium methylide (11) was concluded to be fitted for our subject. For example, 2,6-dimethyl-4-chloropyrimidine (1) reacted with 11 to give the pyrimidinylmethylide (12), which was smoothly acylated with various acylating agents. Raney Ni desulfurization of the acylmethylides (13) thus obtained afforded the 4-acylmethylpyrimidines (7) in satisfactory yields.



1 11 12 13

The synthesis of the corresponding 2-isomers was also achieved by the application of this method.