HOMOLYTIC CARBON-CARBON BOND FORMATION ON PYRIMIDINE DERIVATIVES

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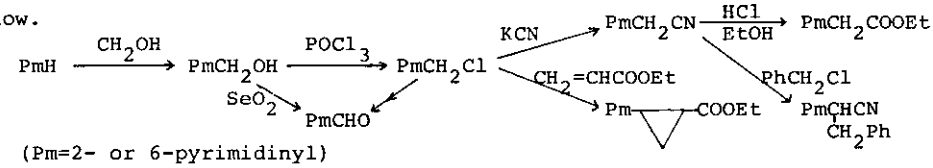
Although pyrimidine derivatives containing a carbinol or a carbonyl group at the 2- and 4-positions form relatively little explored family, they are considered to be important intermediates in making a variety of side chain on the ring. The present paper deals with the synthesis of such pyrimidines using a homolytic substitution developed by Minisci and co-workers.

The hydroxymethylation of simple pyrimidines whose 2- or 4-positions are free, with hydroxymethyl radical ($\cdot CH_2OH$) gave 2- or 4-hydroxymethylpyrimidines in good yields. The chemical property of the carbinols is similar to that of benzyl alcohol as shown below.



(Pm=2- or 6-pyrimidinyl)

Acyl radicals ($\cdot COR$) generated from aldehydes in a redox system readily react with the simple pyrimidines to give the corresponding pyrimidinyl ketones. However, a 2,5-diacetyl compound was obtained together with 2-acetyl-4,6-dimethylpyrimidine when 4,6-dimethylpyrimidine was treated with acetaldehyde in the redox system. The monoacetylpyrimidines are convertible to the pyrimidineacetic acid derivatives by the Willgerodt-Kindler reaction. Similarly, one step preparation of 2-(or 4-)pyrimidine-carboxylic esters, -amides, and -alkylamides was achieved by the reaction of the simple pyrimidine with radicals such as $\cdot COOEt$, $\cdot CONH_2$, and $\cdot CONR_2$, respectively.

During the above investigation, the favorable selectivity was observed on the substitution of 6-monosubstituted pyrimidines. Namely, the hydroxymethylation, acylation, and amidation of 6-phenylpyrimidine always gave the corresponding 6-phenyl-4-substituted pyrimidines exclusively. In contrast to our results, the acetylation of quinoline under similar conditions was reported to give 2-acetyl-, 4-acetyl-, and 2,4-diacetyl-quinoline in the ratio of 1:1:2.