RING TRANSFORMATIONS OF 1,3-OXAZIN-4-ONE DERIVATIVES

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Previously, we have reported the reaction of imidates with diketene to give 6-methyl-2-substituted 1,3-oxazin-4-one and its 2,3-dihydro derivatives. The present paper reports ring transformations of such 1,3-oxazin-4-one derivatives to afford pyridone and pyrimidine derivatives.

Refluxing 2-ethoxy-2,3-dihydro-6-methyl-2-phenyl-4H-1,3-oxazin-4-one in organic solvents such as benzene results in the elimination of ethanol to give 6-methyl-2-phenyl-1,3-oxazin-4-one. However, heating the aliphatic homologue, 2-alkyl(aralkyl)-2-ethoxy-2,3-dihydro-6-methyl-4H-1,3-oxazin-4-ones give rise to ring transformed compounds, 5-acetyl-2,6-dialkyl(or aralkyl)-4-hydroxypyridines.

2-Ethoxycarbonylmethylene-2,3-dihydro-6-methyl-4H-1,3-oxazin-4-one and 2,3-dihydro-2-methoxy-6-methyl-2-(2-pyridyl)-4H-1,3-oxazin-4-one are transformed into ethyl 6-hydroxy-4-methyl-2(1H)-pyridone-5-carboxylate and 6-hydroxy-4-methyl-5-(2-pyridyl)-2(1H)-pyridone respectively.

6-Methyl-2-phenyl-4H-1,3-oxazin-4-one reacts with active methylene compounds to give the pyridine derivatives. For instance, reaction with ethyl malonate and ethyl cyanoacetate gives rise to ethyl 3-acetyl-4-hydroxy-6-phenyl-2(1H)-pyridone-5-carboxylate and 3-acetyl-5-cyano-4-hydroxy-6-phenyl-2(1H)-pyridone, respectively. Similarly, acetylacetone, cyclohexan-1,3-dione, ethyl acetoacetate, and benzoylacetonitrile react with the oxazine to give 3,5-diacetyl-4-methyl-6-phenyl-2(1H)-pyridone, 4-acetyl-5,6,7,8-tetrahydro-1-phenyl-3H-isoquinolin-3,8-dione, 3-acetyl-5-ethoxycarbonyl-4-methyl-6-phenyl-2(1H)-pyridone, and 3-acetyl-5-cyano-4-hydroxy-6-diphenyl-2(1H)-pyridone, respectively. Reaction with malononitrile gives rise to 3-acetyl-4-amino-5-cyano-6-phenyl-2(1H)-pyridone. Similar reactions are carried out using the 2,3-dihydro-oxazines such as 2-ethoxy-2,3-dihydro-2,6-dimethyl-4H-1,3-oxazin-4-one.

6-Methyl-2-phenyl-4H-1,3-oxazin-4-one reacts with enamines, such as 1-(1-cyclopenten-1-yl)pyrrolidine and 1-(1-cyclohexen-1-yl)pyrrolidine to give 4-acetyl-6,7-dihydro-3-hydroxy-1-phenyl-5H-2-pyrindine and 4-acetyl-5,6,7,8-tetrahydro-3-hydroxy-1-phenyl-isoquinoline, respectively. Similarly, the 2,3-dihydro-4H-type oxazine such as 2-alkyl-2-ethoxy-2,3-dihydro-6-methyl-4H-1,3-oxazin-4-ones reacts with enamine to give the corresponding ring transformed products.