ON THE REACTION OF 5-AMINOISOXAZOLES AS AMBIDENT NUCLEOPHILES: SYNTHESIS OF 4,7-DIHYDROISOXAZOLO[5,4-b]PYRIDINES

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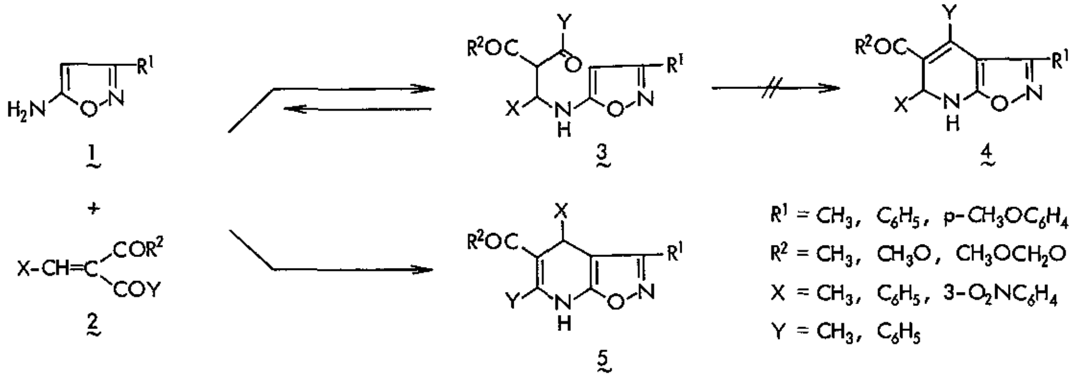
In a continuing program of studies on the chemistry and utilization of isoxazole derivatives, we attempted the reaction of 5-aminoisoxazoles (1), which have the properties of both aromatic amines and enamines, with α,β-unsaturated ketones (2). Treatment of 1 with 2 in ethylene glycohol (EG) at room temperature afforded the corresponding amino-adducts (3), shown in the Figure, in good yields. On the other hand, when the reactions were carried out using t-butanol as the solvent with heating, the 4,7-dihydroisoxazolo[5,4-b]pyridines (5) were obtained in excellent yields. Reaction of 1 with m-nitrobenzaldehyde also afforded the products 6 and 7. Conversion of the amino-adducts (3) into the cyclized products by heating did not afford the Skraup-type products (4) but gave 5. These results suggest that 3 and 5 are kinetically and thermodynamically controlled products, respectively, and the formation of 5 from 3 may result via the retro "Michael" reaction of 3 to the starting 1 and 2.



$R^1 = CH_3,\ C_6H_5,\ p\text{-}CH_3OC_6H_4$
$R^2 = CH_3,\ CH_3O,\ CH_3OCH_2O$
$X = CH_3,\ C_6H_5,\ 3\text{-}O_2NC_6H_4$
$Y = CH_3,\ C_6H_5$