REACTIONS OF ISOQUINOLINE N-OXIDE WITH CYANOACETIC ACID AND RELATED COMPOUNDS

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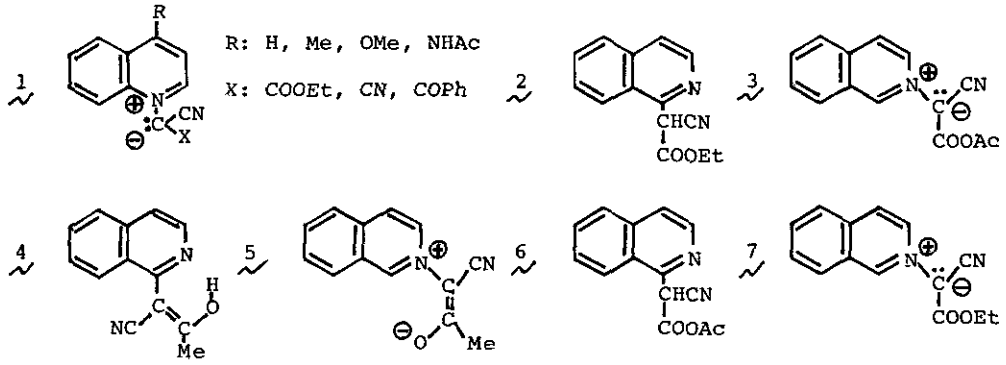
We previously reported that reactions of quinoline N-oxides with some cyanoalkanes and acetic anhydride in DMF gave quinolinium-methylides (1) as the main products[1].

Whereas the similar reaction of isoquinoline N-oxide with ethyl cyanoacetate gave no N-methylide but a 1-substituted isoquinoline (2)[1], the reaction with cyanoacetic acid was found to yield various types of 1- and N-substituted isoquinolines depending upon the reaction conditions. Treatment with cyanoacetic acid at room temperature in Ac_2O-DMF or Ac_2O-EtOH gave a N-methylide (3) or 2, respectively. On the other hand, the reaction in Ac_2O alone afforded both 1-substituted product (4) and N-methylide (5); other 1-substituted isoquinoline (6) and N-methylide (7) were also isolated, though in small amounts, on treatment of the reaction mixture with warm ethanol. The courses of the formation of these products and their chemical correlation were explored.



It was further found that isoquinoline N-oxide reacts with benzoylacetonitrile and acetic anhydride to give both 1- and N-substituted isoquinolines.

1) K. Funakoshi et al., Chem. Pharm. Bull., 26, 3504 (1978).

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