THE REGIOSELECTIVE SYNTHESIS OF ISOXAZOLES FROM ENONES WITH HYDROXYLAMINE

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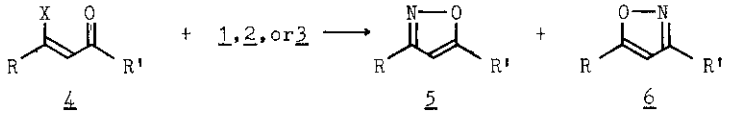
Many papers have been reported on the synthetic utility of isoxazoles. Although the preparation of unsymmetric isoxazoles was examined under various conditions, the regioselective synthesis had been limited to the special case.

Considering the pka values of hydroxylamine, there are three hydroxylamine species 1, 2, and 3. The reaction of β-substituted enones 4 with 2 gave isoxazole

$$\underset{\underline{1}}{{}^{+}NH_3OH} \rightleftharpoons \underset{\underline{2}}{NH_2OH} \rightleftharpoons \underset{\underline{3}}{NH_2O^{-}}$$

5 in good yield. On the contrary, in the reaction of 1 and 3, the product ratio of 5 and 6 was depend on the property of β-substituent groups of enones 4. Though enones having the amino groups gave isoxazole 5, enones having the alkoxy or thioxy groups gave isoxazole 6.



From the further studies of the formation of isoxazoles, the reaction mechanism was postulated. Hydroxylamine species 1, 2, and 3 mainly attacked β-carbon of β-substituted enones 4 under any condition. After attack of hydroxylamine species, the cyclization proceeded in considerbly fast reaction rate to form the isoxazoline intermediates which were detected by CMR. In the last step, isoxazoles were formed by the elimination reaction. The regioselectivity in the formation of unsymmetric isoxazoles was governed by the nucleophilicity of hydroxylamine species, and the properties of β-substituent groups.