THIA AND RING-OPENING ANALOGUES OF ISOALLOXAZINES

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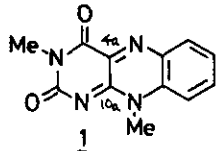
The use of flavin mimics such as isoalloxazines and deazaisoalloxazines has been enlightening in the development of chemical insight in the flavin-catalyzed redox reactions. Our special attention has been paid to an alternation of the reactivity of the conjugated diimine moiety in the isoalloxazine ring by virtue of chemical manipulation.



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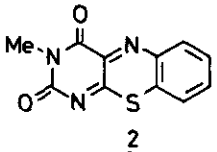

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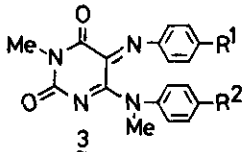

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Along this line, we examined the reaction of 10-thiaisoalloxazine 2 and 5-anilidene-6-(N-methylanilino)pyrimidinedione derivatives 3 with alcohols and dithiols.

The most striking effect of the sulfur on the conjugated diimine of 2 is the increased susceptibility to the nucleophilic addition, the enhanced oxidation capacity and the change of the initial reaction site (4a⟶10a).

For example, the reaction of 2 with primary alcohols gave 4a,10a-diadducts across the conjugated diimine moiety, whereas 2 was reduced to dihydro-10-thiaisoalloxazine by secondary alcohols. The 10-thiaisoalloxazine 2 reacted with 1,2-ethanedithiol and 1,3-propanedithiol in the neutral medium to give the 4a,10a-cyclic adducts and the dihydro-10-thiaisoalloxazine, respectively. Under similar conditions, the isoalloxazine 1 did not react with alcohols and dithiols. An initial reaction site of 2 was proved to be the 10a-position on the basis of X-ray crystalographic analysis of the cyclic adduct obtained by the reaction of 2 with 2-mercaptoethanol.

The pyrimidinedione derivatives 3 underwent ring-contraction when reacted with methanol and ethanol. The reaction of 3 with dihydrolipoamide in the basic medium caused oxidation to give lipoamide and the corresponding uracil derivative quantitatively. Under analogous conditions, oxidation of dihydrolipoamide by 1 proceeded only in low yield. This fact shows that 3 possesses the enhanced oxidation capacity comparing with the parent isoalloxazine 1.