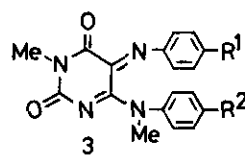
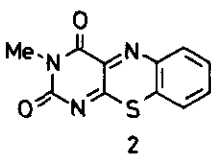
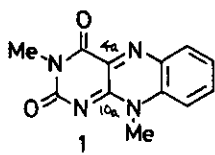


THIA AND RING-OPENING ANALOGUES OF ISOALLOXAZINES

Magoichi Sako, Yutaka Kojima, Kosaku Hirota, and Yoshifumi Maki

Gifu College of Pharmacy, Mitahora-higashi, Gifu, 502, Japan

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.



Along this line, we examined the reaction of 10-thiaisoalloxazine 2 and 5-anilidene-6-(N-methylanilino)pyrimidin-2(1H)-one 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 crystallographic analysis of the cyclic adduct obtained by the reaction of 2 with 2-mercaptoethanol.

The pyrimidin-2(1H)-one 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.