Synthesis of 10-Thiaisoalloxazines

By T. HIRAMITSU and Y. MAKI*

(*Gifu College of Pharmacy*, 6-1, *Higashi-5-Chome, Mitahora, Gifu* 502, *Japan*)

Summary Irradiation of 6-(2-azidophenylthio)uracils (**2**) with a high-pressure mercury arc lamp resulted in the almost exclusive formation of dihydro-10-thiaisoalloxazines (**3**), while thermolysis of (**2**) gave a mixture of (**3**) and dihydro-5-thiaisoalloxazine (**4**).

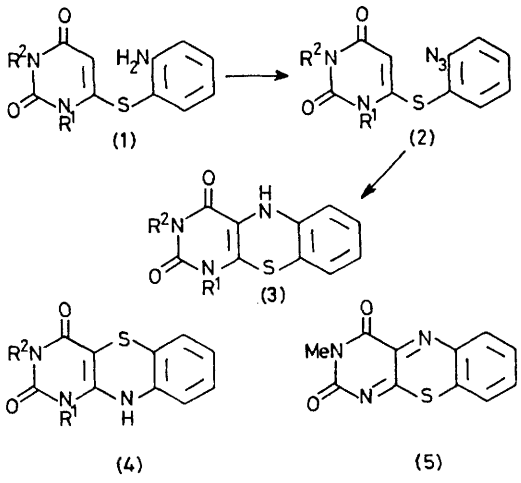
RECENTLY 5-deazaisoalloxazines[1] and dihydro-5-thiaisoalloxazines[2] have been used as flavin analogues in an attempt to elucidate the mechanism of flavin redox-reactions. In view of their structural similarities to these systems, the 10-thiaisoalloxazines (**3**) and (**5**) may also serve as models for flavins. We report here the synthesis of the hitherto unknown 10-thiaisoalloxazines (**3**) and (**5**) which involves a novel photochemical thiazine-cyclization of the corresponding azides (**2**).

The 6-(2-azidophenylthio)uracils (**2a**—**c**) were prepared in high yields by diazotisation of the 6-(2-aminophenylthio)-uracils (**1a**—**c**) followed by treatment with sodium azide and recrystallisation from EtOH.† The azide (**2a**) (m.p. 163 °C decomp.) (0·001 mol) was irradiated in methanol (200 ml) with a 100 W high-pressure mercury arc lamp through a Pyrex filter under nitrogen for 3 h at room temperature. After removal of the solvent and recrystallisation from acetone, dihydro-10-thiaisoalloxazine (**3a**) (m.p. 228 °C decomp.) was obtained in 70% yield. The n.m.r. spectrum of the reaction mixture did not show detectable amounts of the isomeric dihydro-5-thiaisoalloxazine (**4a**)[3] or the amine (**1a**). Analogous irradiation of (**2b**) (m.p. 182 °C decomp.) and (**2c**) (m.p. 175 °C decomp.) gave (**3b**) (m.p. 262 °C decomp.) and (**3c**) (m.p. 267 °C

† Satisfactory analytical and spectral data were obtained for all new compounds.

decomp.) in 57 and 45% yields, respectively; both were recrystallised from MeOH.

To our knowledge, this is the first example of the photochemical cyclisation of azides to the corresponding fused 1,4-benzothiazines.



a; R^1, R^2 = Me
b; R^1 = H, R^2 = Me
c; R^1, R^2 = H

SCHEME

Although details of the mechanism are not clear at present, the formation of (**3a**—**c**) could be explained in terms of the insertion of a nitrene intermediate[4] into the C(5)–H bond of the uracil ring.

It is of interest to compare this photochemical reaction with thermolysis of the azides (**2a**—**c**); *e.g.*, when (**2a**) in $(CD_3)_2SO$ was heated at 140—150 °C for 3·5 h, the rearranged product (**4a**) was formed together with (**3a**) (2 : 1 ratio by n.m.r. spectroscopy).

Cadogan *et al.*[5] have shown that photolysis of 2-azidodiphenyl sulphides gives the corresponding 2-aminodiphenyl sulphides, whereas thermolysis leads to the exclusive formation of phenothiazines in high yields *via* an intramolecular rearrangement. The present results are in contrast with these previous observations.

As expected, (**3b**) and (**3c**) are sensitive to oxidation. Treatment of (**3b**) with an equimolar amount of 1,4-benzoquinone in acetonitrile at room temperature gave 10-thiaisoalloxazine (**5**) (m.p. 270 °C decomp.) in 70% yield. The u.v. spectrum of (**5**) ($CHCl_3$: λ_{max} 286, 358, and 460 nm) is quite similar to that of 3,10-dimethylisoalloxazine ($CHCl_3$: λ_{max} 271, 333, and 436 nm) except for the bathochromic shift of the former absorptions. In a manner similar to flavins,[6] (**5**) was smoothly reduced to (**3b**) by the action of 1,3-propanedithiol.

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