# Concentration-dependent Photoreaction of Benzothiazolyldithioazetidinones: Novel Photochemical Formation of Penam Derivatives

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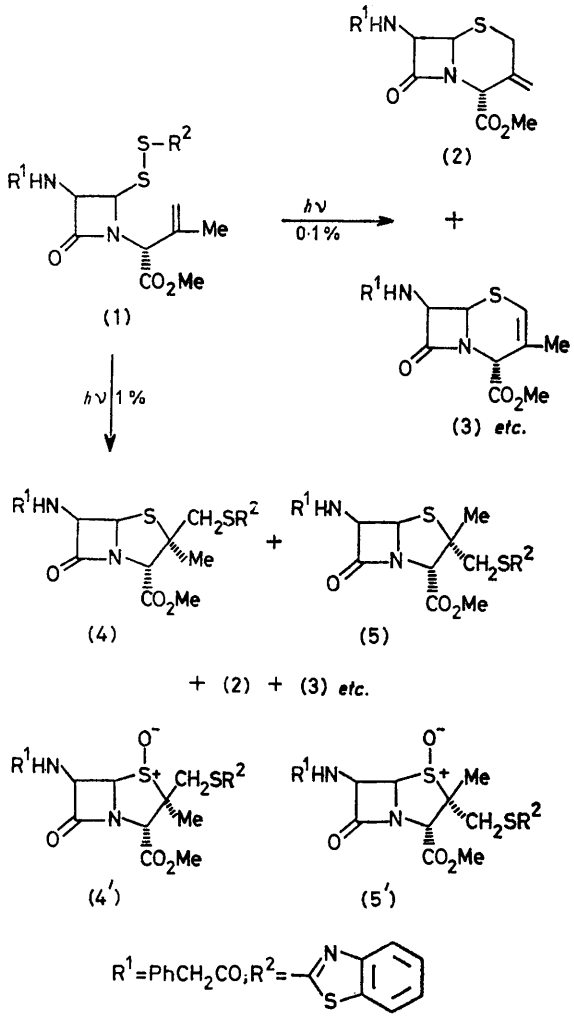
*Summary* The photoreaction of benzothiazolyl dithioazetidinones is concentration dependent; at low concentrations cepham derivatives are formed almost exclusively, whereas at high concentrations penam derivatives predominate.

A HIGHLY regioselective photocyclisation of the benzothiazolyl dithioazetidinone (**1**)[1] leading to the 2-methylenecepham (**2**) and 2-cephem (**3**) derivatives has been reported by us,[2] and Gordon and Cimarusti have confirmed and extended our previous observations.[3]

We now report that the photoreaction of the dithioazetidinone (**1**) is significantly concentration dependent; irradiation of (**1**) at higher concentrations than used before resulted in the predominant formation of $\beta$- and $\alpha$-(benzothiazolylthiomethyl)penam derivatives (**4**) and (**5**) rather than the cepham and cephem derivatives (**2**) and (**3**)

(Scheme 1). The present observations provide a novel example of the photochemical formation of penams and have mechanistic implications.



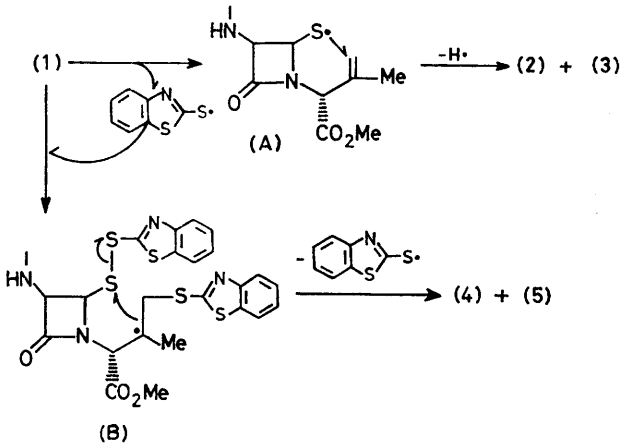
SCHEME 1

When a 0·1% solution of the dithioazetidinone (**1**) in acetonitrile was irradiated by a high-pressure mercury arc lamp through a Pyrex filter under nitrogen, compounds (**2**) and (**3**) and 2-mercaptobenzothiazole were isolated in 45, 11, and 10% yields, respectively. T.l.c. of the mixture did not show the presence of a detectable amount of the penam derivatives (**4**) or (**5**). Upon irradiation of a 1% solution of (**1**) in acetonitrile under analogous conditions, however, a mixture of several photoproducts was obtained. Careful silica gel chromatography (solvent: benzene–ethyl acetate, 5:1) led to separation of a mixture of the isomeric benzothiazolylthiomethyl penams (**4**) and (**5**), and compounds (**2**) and (**3**) in 30 [(**4**) + (**5**)], 19, and 5% yields, respectively. The $^1$H n.m.r. spectrum of the mixture of (**4**) and (**5**) indicated that they were present in a ratio of *ca.* 2:1. Two unidentified products were also obtained in small quantities together with 2-mercaptobenzothiazole, its disulphide, and bis-(4-oxoazetidin-2-yl) disulphide.[1]

Difficulty in chromatographic separation of the isomeric penams (**4**) and (**5**) was overcome by their quantitative oxidation to the corresponding sulphoxides (**4′**) and (**5′**) (*m*-chloroperbenzoic acid; $CHCl_3$, 0 °C).† The major sulphoxide (**4′**) was identical in every respect with an authentic sample prepared by reaction of β-bromomethylpenams[4] with 2-mercaptobenzothiazole followed by oxidation.

Differences between the $^1$H n.m.r. chemical shifts of the sulphoxides (**4′**) and (**5′**) are parallel to those observed in β- and α-acetoxymethylpenam β-sulphoxides;[5] *e.g.*, the methyl signal of (**5′**) (δ 1·80) is more deshielded than that of (**4′**) (δ 1·27). This marked difference of the methyl signal position can be ascribed to the screening effect of the β-sulphoxide bond,[6] indicating that the benzothiazolylthiomethyl group in (**4′**) and (**5**) adopts the β- and α-configuration, respectively. Thus, the stereochemistry of the isomeric penams (**4**) and (**5**) is β and α respectively.

These results of irradiation of the dithioazetidinone (**1**) at high concentrations may be rationalized in terms of competitive occurrences of intra- and inter-molecular radical reactions as outlined in Scheme 2.



SCHEME 2

Homolytic cleavage of the S–S bond of (**1**) in an excited state could give a thiyl radical (A) and a benzothiazolylthiyl radical. As proposed previously,[2] intramolecular attack of the thiyl radical (A) on the terminal olefinic carbon atom leads to formation of the cepham derivatives (**2**) and (**3**). At high concentrations of (**1**), however, intermolecular attack of the initially formed benzothiazolylthiyl radical on the olefinic bond of the remaining (**1**) could occur competitively to produce the carbon-centred radical intermediate (B). Intramolecular radical substitution on

† Mechanistic considerations mainly based on control of reagent approach by the 6β-amide group together with spectral data support the preferred oxidation of the more hindered thiazoline sulphur and the β-configuration of the sulphoxide grouping (for a review, see ref. 6, p. 203).

the S–S bond in (B) could afford the penam derivatives (**4**) and (**5**). Although other mechanisms involving an ionic process may be possible, the nonstereoselectivity of the reaction is compatible with this reaction sequence.

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