# Rearrangements of a Penicillin-derived Ylide

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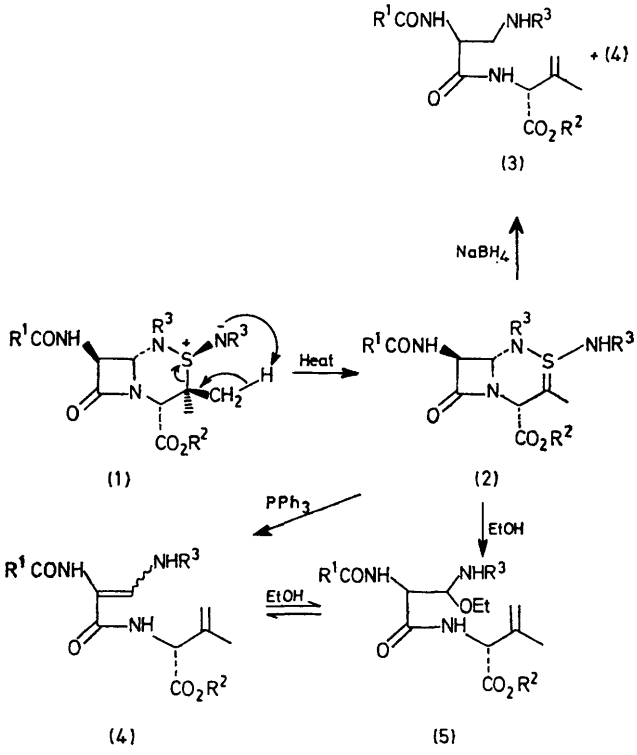
*Summary* The β-lactam fused thiadiazine ylide (**1**) undergoes quantitative thermal rearrangement to the thiadiazine ring-opened β-lactam (**2**), which can then undergo β-lactam cleavage reactions with a variety of nucleophilic reagents to give dipeptides [(**3**)—(**5**)].

Previously we have described[1] the formation and structure determination of penicillin-derived ylides (**1**). We now report the transformations of (**1**) into another new β-lactam (**2**) and reactions of (**2**) which lead to dipeptides structurally related to recently postulated[2] intermediates in the biosynthesis of penicillins.




$R^3NH-S-NHR^3$

(6)

$R^1 = PhOCH_2$ $R^2 = Me$ $R^3 = p\text{-}MeC_6H_4SO_2$

Scheme

Thermolysis of (**1**) in refluxing toluene followed by removal of solvent afforded quantitatively a β-lactam as a solid foam $[\alpha]_D^{20°} -112°$ ($c$ = 1·00, $CHCl_3$). The i.r. spectrum indicated β-lactam (1783 $cm^{-1}$) and also loss of the S=N ylide functional group of (**1**). The n.m.r. spectrum was in accord with structure (**2**)† showing *trans*-oriented β-lactam protons ($\tau$ 4·23 and 4·62, $J$ 2 Hz), a βγ-dehyrovalinyl group and two tosyl units. The mechanism of formation of (**2**) presumably involves β-elimination leading to the ring-opened structure (Scheme).

Treatment of (**2**) with triphenylphosphine under ambient conditions gave a white crystalline non-β-lactam, m.p. 124—126°, $[\alpha]_D^{20°} -44°$ ($c$ = 1·00, dioxan), together with triphenylphosphine sulphide. The reaction product was characterised as the enamine (**4**) by elemental analysis and i.r. and n.m.r. spectroscopy. It was noted [by n.m.r. spectroscopy (220 MHz)] that (**4**) existed in deuteriopyridine solution as an equilibrium mixture of the (*E*)- and (*Z*)- acryloyl isomers. In dry deuteriochloroform, only one isomer was observed. In the u.v. spectrum (EtOH), compound (**4**) exhibited absorption at 220, 262, 268 and 275 nm which compared favourably with data recently reported for related enamines.[2d,3] Addition of base resulted in generation of a new chromophore at 298 nm ($\epsilon$ = 17,900). Subsequent addition of acid regenerated the original chromophores.

Both the β-lactam (**2**) and the enamine (**4**) on standing in ethanol deposited white crystals, m.p. 156—157°, $[\alpha]_D^{20°} -41°$ ($c$ = 1·00, dioxan), shown to be the homogeneous ethanolamine (**5**).† Extensive n.m.r. decoupling experiments at 220 MHz conclusively established the structure. An interesting by-product from (**2**) in this reaction was the bis-(toluene-*p*-sulphonylamino)sulphide (**6**).† Compound (**5**) could be equilibrated in certain solvents with the enamine (**4**). It was also noted that the β-lactam (**2**), when treated with other nucleophiles such as acetate and thiocyanate, rapidly afforded complex mixtures of β-lactam cleaved products from which (**4**) was isolated.

Sodium borohydride reduction of (**2**) gave as the major product, (**3**)† $[\alpha]_D^{20°} -60°$ ($c$ = 1·00, dioxan), together with hydrogen sulphide and toluene-*p*-sulphonamide. A small amount of (**4**) was also isolated. Further borohydride reduction of (**4**) gave (**3**), together with the primary alcohol‡ resulting from reduction of the ester.

The transformation of penicillins into enamines such as (**4**) *via* the readily accessible ylides (**1**) represents a novel method of unzipping the penam nucleus, and affords an attractive route for degradation studies of isotopically-labelled penicillins.

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† New compounds gave satisfactory elemental analyses and/or high resolution mass measurement.

‡ Structure determined by i.r. and n.m.r. spectroscopy.

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