

Rearrangements of a Penicillin-derived Ylide

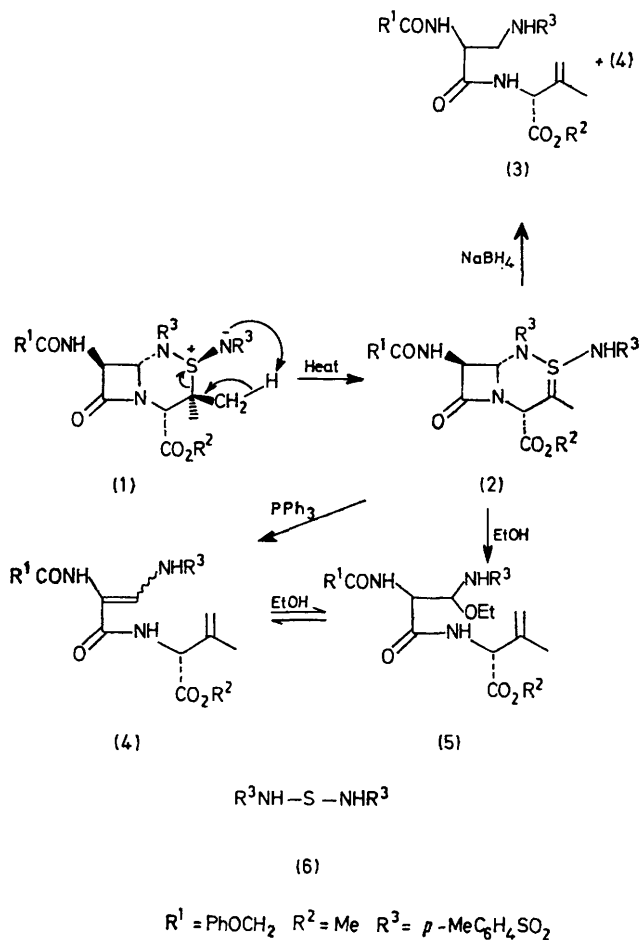
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Summary The β -lactam fused thiadiazine ylide (1) undergoes quantitative thermal rearrangement to the thiadiazine ring-opened β -lactam (2), which can then undergo

β -lactam cleavage reactions with a variety of nucleophilic reagents to give dipeptides [(3)—(5)].

PREVIOUSLY we have described¹ 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 postulated² intermediates in the biosynthesis of penicillins.



SCHEME

Thermolysis of (1) in refluxing toluene followed by removal of solvent afforded quantitatively a β -lactam as a solid foam $[\alpha]_{\text{D}}^{20} - 112^\circ$ ($c = 1.00$, 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 (τ 4.23 and 4.62, J 2 Hz), a $\beta\gamma$ -dehydrovalinyl 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. $124\text{--}126^\circ$, $[\alpha]_{\text{D}}^{20} - 44^\circ$ ($c = 1.00$, 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 deuterio-pyridine 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. $156\text{--}157^\circ$, $[\alpha]_{\text{D}}^{20} - 41^\circ$ ($c = 1.00$, 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)† $[\alpha]_{\text{D}}^{20} - 60^\circ$ ($c = 1.00$, 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.

We thank the S.R.C. for a CAPS award to G.J. and a grant towards an MS30 mass spectrometer, Beecham Research Laboratories for starting materials, and PCMU, Harwell for n.m.r. and mass spectra.

(Received, 23rd September 1974; Com. 1198.)

† 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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