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Novel Isomerisations of a Penicillin Sulphone

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Summary Methyl benzylpenicillinate 1,1-dioxide (1) undergoes a base-induced equilibration with its 6-epimer (2), which then isomerises to (3S,4R)-1-(1-methoxycarbonyl2-methylprop-1-enyl)-3-phenylacetamido-4-oxoazetidine-2-sulphinic acid (3).

ALTHOUGH it is well established that penicillanoyl derivatives and their 1-oxides can equilibrate under basic conditions with the 6-epimers,¹ the corresponding reactions of penicillanoyl 1,1-dioxides have not been described. We now report the behaviour of methyl benzylpenicillinate 1,1dioxide (1).



When treated dropwise with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in chloroform, the sulphone (1),² m.p. 173— 174 °C, $[\alpha]_{\rm D}$ +170° (CHCl₃), rapidly afforded a 1:2 mixture of the starting material and a slightly less polar product. The new material, m.p. 124—125 °C, $[\alpha]_{\rm D}$ +161° (CHCl₃), which was isolated (37%) by silica gel chromatography, possessed *trans*-orientated β -lactam protons [δ (CDCl₃) 4·80 (d, J 1·5 Hz) and 5·15 (dd, J 1·5 and 8 Hz). That the derivative was the 6-epimer (2)† was indicated by performing the reaction in a 1:1 mixture of (CD₃)₂SO and D₂O; the n.m.r. spectrum of the purified product showed a singlet at δ 4·80 and the signal at δ 5·15 was absent. When resubjected to the reaction conditions, the 6-epimer (2) equilibrated (2:1) with the starting sulphone (1).

The equilibrium mixture of sulphones (1) and (2) was transformed into one major acidic product (80%), when treated further with DBN (> 1 mol. equiv.). The material, m.p. 136-137 °C, $[\alpha]_{\rm D}$ -176° (CHCl₃), which possessed trans-disposed β -lactam protons [δ (CDCl₃) 4.68 (d, J 2 Hz) and 5.30 (dd, J 2 and 6 Hz)], is considered to be the azetidinonesulphinic acid (3).†

Derivative (3) presumably arises from the 6-epimer (2) by a β -elimination pathway, initiated by the base-induced removal of the hydrogen atom at position 3. Such reactions are well documented for penicillanoyl derivatives and there is one report of a penicillanic ester sulphoxide behaving in an analogous manner.¹ However, β -elimination reactions of penicillanate ester sulphones have not hitherto been described.

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† The composition of new compounds was confirmed by elemental analysis. Structural assignments are based upon i.r., u.v., and n.m.r. spectroscopic evidence.

¹ R. J. Stoodley, Tetrahedron, 1975, 31, 2321.

² 'The Chemistry of Penicillin,' eds. H. T. Clarke, J. R. Johnson, and R. Robinson, Princeton University Press, Princeton, N.J., 1949, p. 177.