Novel Isomerisations of a Penicillin Sulphone

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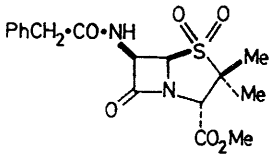
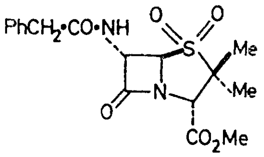
Summary Methyl benzylpenicillinate 1,1-dioxide (**1**) undergoes a base-induced equilibration with its 6-epimer (**2**), which then isomerises to (3*S*,4*R*)-1-(1-methoxycarbonyl-2-methylprop-1-enyl)-3-phenylacetamido-4-oxoazetidine-2-sulphinic acid (**3**).

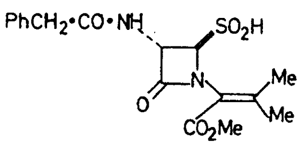
ALTHOUGH it is well established that penicillanoyl derivatives and their 1-oxides can equilibrate under basic conditions with the 6-epimers,[1] the corresponding reactions of penicillanoyl 1,1-dioxides have not been described. We now report the behaviour of methyl benzylpenicillinate 1,1-dioxide (**1**).



(1)



(2)



(3)

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, $[\alpha]_D$ +170° ($CHCl_3$), rapidly afforded a 1:2 mixture of the starting material and a slightly less polar product. The new material, m.p. 124—125 °C, $[\alpha]_D$ +161° ($CHCl_3$), which was isolated (37%) by silica gel chromatography, possessed *trans*-orientated β-lactam protons [δ ($CDCl_3$) 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 $(CD_3)_2SO$ and D_2O; 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, $[\alpha]_D$ −176° ($CHCl_3$), which possessed *trans*-disposed β-lactam protons [δ ($CDCl_3$) 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.