

Transformation of Penicillin Sulphoxides into Cephalosporins by Azo-compounds

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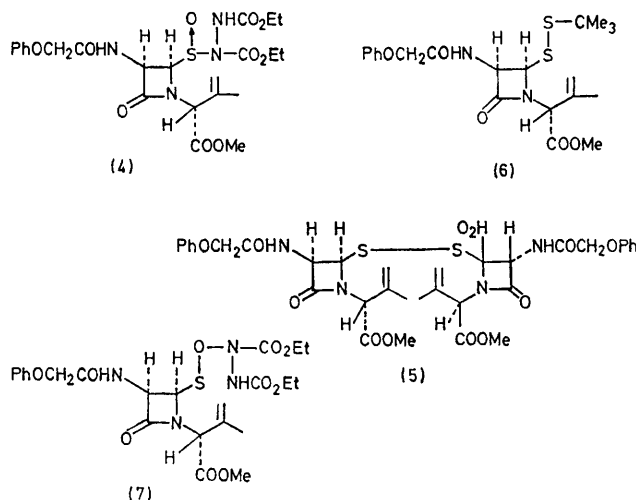
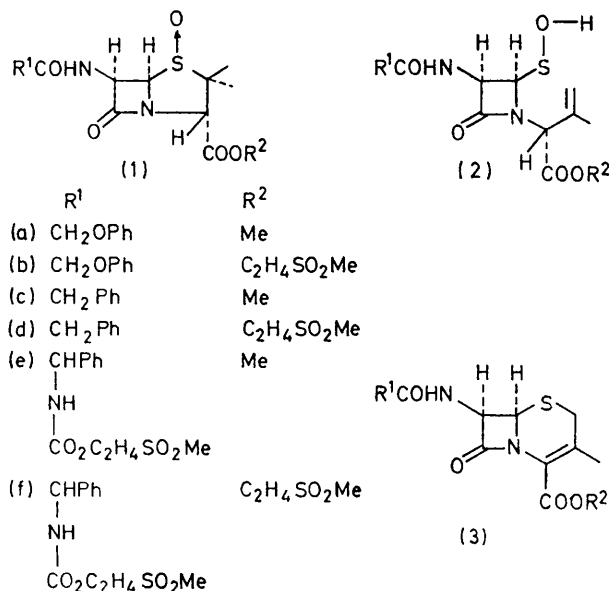
Summary Treatment of penicillin sulphoxides with azo-compounds gave cepheins (**3**) in moderate yields together with sulphinyl hydrazodicarboxylates (**4**) and thiol sulphonates (**5**).

PENICILLIN sulphoxides have been previously¹ converted into cephalosporins with acid catalysts. We have effected the same transformation under non-acidic conditions, using azo-compounds.

Treatment of the methyl ester of penicillin V sulfoxide (**1a**) with diethyl azodicarboxylate (1 mol. equiv.) in refluxing dioxan gave products which were separated by silica-gel chromatography and identified† as compound (**3a**) (25.9%), m.p. 141–142°, (**4**) (14.2%), $C_{23}H_{30}N_4O_{10}S$,

temperature, solvent, and concentration, but less affected by the species of penicillin sulfoxide.

Azo-compounds² which contain one carbonyl group ($R-N=N-COR'$, $R-N=N-COOR'$) or two carbonyl groups ($R-CO-N=N-CO-R'$, $ROCO-N=N-COOR'$) and/or one phosphono-group [$R-N=N-P(O)(OR')_2$] adjacent to the azo-group all effected similar reactions.



non-crystalline solid, (**5**) (11.3%), $C_{34}H_{38}N_4O_{12}S_2$, m.p. 58–159°, $[\alpha]_D^{25} -61.1^\circ$ (c 1.5 in $CHCl_3$), and diethyl hydrazodicarboxylate. Attempts to transform (**4**) and (**5**) into (**3**) were unsuccessful under various conditions. The reaction of (**5**) with 1,1-dimethylethanethiol gave the mixed disulphide (**6**), $C_{21}H_{28}N_2O_5S_2$, m.p. 114°, $[\alpha]_D^{25} -211.5^\circ$ (c 1.25 in $CHCl_3$).

When α,α' -azobis-(*N*-methylformamide) was used in dimethylacetamide at 100–110°, esters of penicillin sulfoxides (**1a–f**) afforded the corresponding cephem (**3a–f**) in 30–40% yields.

The reaction probably proceeds *via* intermediate (**7**) which would then be rapidly converted into (**3**), (**4**), and (**5**) along three competing reaction routes.

The optimum conditions for the conversion of (**1**) into (**3**) are now being investigated.

The yields of the products are greatly affected by the azo-compounds used and reaction conditions such as

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† The composition of all new compounds was confirmed by elemental analysis or by mass spectroscopy. Structural assignments are based on i.r. and n.m.r. spectral evidence.

‡ The disulphide (**6**) was prepared by a new disproportionation reaction of penicillin sulfoxides with disulphides, and will be published elsewhere.

¹ D. H. R. Barton and P. G. Sammes, *Proc. Roy. Soc.*, 1971, 179, 345; R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Amer. Chem. Soc.*, 1963, 85, 1896; *ibid.*, 1969, 91, 1401; D. H. R. Barton, F. Comer, D. G. T. Greig, P. G. Sammes, C. M. Cooper, G. Hewitt, and W. G. E. Underwood, *J. Chem. Soc., (C)*, 1971, 3540.

² E. Fahr and H. Lind, *Angew. Chem. Internat. Edn.*, 1966, 5, 372.