Reaction of β-Hydroxyethanesulphenyl Chlorides with Phosphines; a Route to Episulphides

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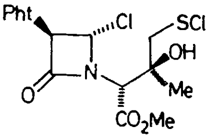
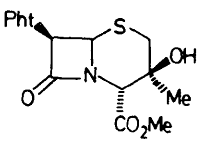
Summary A cephalosporin-derived β-hydroxyethane-sulphenyl chloride reacted smoothly with triphenylphosphine to produce an episulphide; this is a mild method for obtaining such a functionality.



(1)



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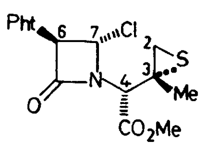
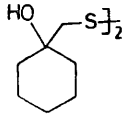
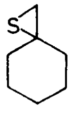


(3)

[Pht = phthalimido]



(4)



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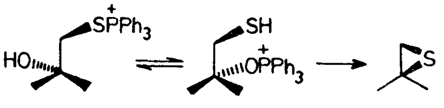

(6) (7) (8)

During a study of the sulphenyl chloride (**1**), derived by direct chlorination of the cephalosporin derivative (**2**) we observed a remarkably ready reaction of this substance with triphenylphosphine. Thus chlorination of (**2**) at $-30\ ^\circ C$ (CH_2Cl_2) with 1 mol. equiv. of chlorine gave (**1**)[1] which was treated at $-30\ ^\circ C$ with triphenylphosphine (1 mol. equiv. in CH_2Cl_2). Upon warming to room temperature there was isolated, after chromatography, the episulphide (**3**) (50%) as an oil, ν_{max} 1790 cm^{-1}; δ ($CDCl_3$), 1·80 (s, Me), 2·56 and 3·01 (2 × d, J 2·5 Hz, H-2), 3·81 (s, Me), 4·35 (s, H-4), 5·52 (d, J 1·5 Hz, H-7), and 6·13 (d, J 1·5 Hz, H-6); M^+ 394.† In order to check the utility of this reaction, we treated the β-hydroxydisulphide (**4**) with chlorine (1 mol equiv., 25 °C, CH_2Cl_2), added triphenylphosphine [2 mol equiv., based on (**4**)] and stirred the mixture at 25 °C for 1 h. Evaporation and chromatography (silica gel, pentane) gave the episulphide (**5**) (60%) as an oil identical (i.r. and n.m.r. spectra) to authentic material;[2] ν_{max} (film) 2940 cm^{-1}; δ ($CDCl_3$), 1·6 (m, cyclohexyl) and 2·41 (s, CH_2S).

Presumably the mechanism of this conversion involves initial formation of a phosphonium salt, *e.g.*, as (**6**), exchange to the oxyphosphonium species (**7**), followed by displacement. For this reason we assign the inverted stereochemistry at C-3 in the episulphide (**3**). A similar process has been observed[3] when β-hydroxyethyldisulphides were heated with triphenylphosphine. However, the more vigorous conditions required to break the S–S bond led to poorer yields of episulphides and of course an equivalent reduction in the yield of the β-hydroxyethanethiol.

The reaction of β-hydroxyethanesulphenyl chlorides and phosphines appears to be a useful and mild method for preparation of episulphides, and within the cephalosporin system may be of utility in the synthesis of nuclear analogues.

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† All new substances have given adequate combustion analyses.

[1] S. Kukolja, *J. Amer. Chem. Soc.*, 1971, **93**, 6267.

[2] R. A. Y. Jones, A. R. Katritzky, A. C. Richards, and R. Scattergood, *J.C.S. Perkin II*, 1972, **41**; the yield found in this case was 13·5%.

[3] L. E. Overman and E. M. O'Connor, *J. Amer. Chem. Soc.*, 1976, **98**, 771; M. Grayson and C. E. Farley, *Chem. Comm.*, 1967, 831.