

7 α -HYDROXYCEPHALOSPORIN C, AN INTERMEDIATE IN THE METHOXYLATION
OF CEPHALOSPORIN C BY A CELL-FREE EXTRACT OF *S. CLAVULIGERUS*

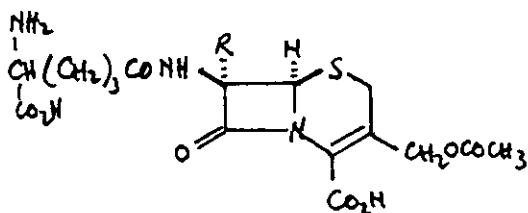
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One of the β -lactam antibiotics produced by *Streptomyces clavuligerus* is cephamycin C (1). Abraham and co-workers have reported ¹ that cell-free extracts of *S. clavuligerus* convert cephalosporin C (2) and the O-carbamoyl analogue (3) into the corresponding cephamycins (4) and (1). It was suggested that methoxylation was a two stage process involving molecular oxygen and a methyl transfer from methionine. ^{1,2}

A detailed examination of this methoxylation stage in cephamycin biosynthesis has been undertaken. Cephalosporin C (2) was incubated with a cell free preparation from *S. clavuligerus*, and h.p.l.c. analysis indicated the formation of 7 α -hydroxycephalosporin (5) together with 7 α -methoxycephalosporin C (4); (5) was isolated and fully characterised spectroscopically and by comparison with synthetic material. 7 α -hydroxycephalosporin C (5) was treated in a similar manner with the same enzyme preparation including added S-adenosylmethionine and 7 α -methoxycephalosporin C (4) detected by h.p.l.c.

This evidence confirms that the methoxylation of cephalosporin C is a two stage process, oxygenation of the cephalosporin yielding a 7 α -OH intermediate which is subsequently methylated.



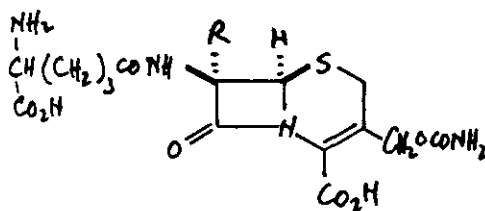
(2) R = H

(4) R = OMe

(5) R = OH

(1) R = OMe

(3) R = H



1. Biochem. J., 1979, 179, 47; 1980, 186, 613.
2. Antimicrob. Agents. Chemother., 1972, 1, 247.