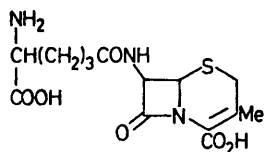


## Deacetoxycephalosporin C from *Streptomyces* and Fungi

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*Summary* A new metabolite produced by two species of *Streptomyces* and twenty two strains of fungi, is identified as deacetoxycephalosporin C. SEVERAL new cephalosporin antibiotics have been isolated recently from *Streptomyces* species.<sup>1,2</sup> In addition to the three new  $\beta$ -lactam antibiotics produced by two species of

*Streptomyces*<sup>1</sup> a minor metabolite was isolated from both species. It was identified as deacetoxycephalosporin C (1). This antibiotic was also produced by twenty two strains of fungi from our collection.<sup>3</sup> Deacetoxycephalosporin C has



(1)

been postulated to be an intermediate in the biosynthesis of cephalosporin C.<sup>4</sup> Cephalosporin C has been converted into deacetoxycephalosporin C by hydrogenolysis.<sup>5</sup>

The new metabolite crystallized as  $C_{14}H_{13}N_3O_6SLi \cdot 2H_2O$  i.r. (mull):  $1755\text{ cm}^{-1}$  ( $\beta$ -lactam). u.v. ( $H_2O$ ):  $\lambda$  260 nm ( $\epsilon$  8800). c.d. ( $H_2O$ ): two Cotton effects, 256 ( $\Delta\epsilon + 8.05$ ), 221 nm ( $\Delta\epsilon - 10.1$ ). Potentiometric titration (66% DMF): initial pH 5.0,  $pK_a$ 's 4.0, 5.8, and 10.6. Amino-acid

analysis:  $2.33\ \mu\text{mol/mg}$  of  $\alpha$ -amino adipic acid and  $1.13\ \mu\text{mol/mg}$  of glycine. The antibiotic was converted into its *N*-chloroacetyl derivative with chloroacetyl chloride, and then methylated with diazomethane. Crystallization afforded its *N*-chloroacetyl methyl ester derivative, m.p.  $209\text{--}210^\circ$ . i.r. (mull):  $1760\text{ cm}^{-1}$  ( $\beta$ -lactam). u.v. (EtOH): 250 nm ( $\epsilon$  6800). Amino-acid analysis:  $2.20\ \mu\text{mol/mg}$  of  $\alpha$ -amino adipic acid and  $1.49\ \mu\text{mol/mg}$  of glycine.

Cephalosporin C was converted into deacetoxycephalosporin C<sup>5</sup> (1) and then into its *N*-chloroacetyl dimethyl ester. The i.r. and u.v. spectra of authentic deacetoxycephalosporin C obtained by hydrogenolysis of cephalosporin C, and the minor metabolite of the two *Streptomyces* species were identical. The identity was further confirmed by comparison of the *N*-chloroacetyl dimethyl esters. The occurrence of deacetoxycephalosporin C as a metabolite in *Streptomyces* fermentation offers new avenues of research in biosynthesis of  $\beta$ -lactam antibiotics.

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