

PENICILLIN-CEPHALOSPORIN CONVERSION WITH COMPLETE UTILIZATION
OF ALL THE FRAMEWORK ELEMENTS

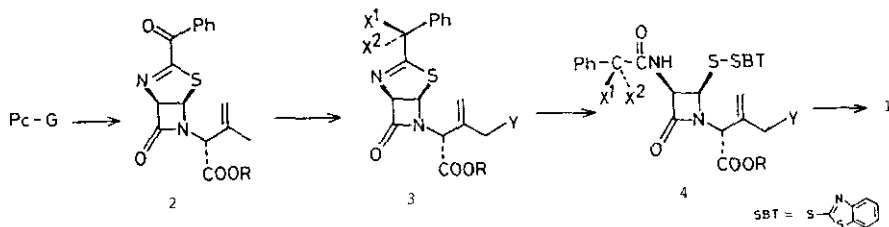
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Recently, successful conversion of penicillins to useful cephalosporin antibiotics has been developed by several groups. In the final stage, the C(7)-acylamino groups, derived from the C(6)-substituents of natural penicillins, have been replaced with the desired acylamino groups. On the other hand, some of cephalosporins of newer generation, e.g., 1a-c, possess α -substituted phenacylamino groups at the C(7)-position.

This paper describes an efficient synthesis of cephalosporins 1a-c from penicillin G without discarding any of the framework elements as outlined in the following scheme.

Thiazoline-azetidinones 3 ($C \begin{smallmatrix} X^1 \\ X^2 \end{smallmatrix} = C=O$; $Y = Cl$) were obtained by the electrolytic ene-type chlorination of thiazoline-azetidinones 2 derived from penicillin G [Tetrahedron Lett., 22, 3193 (1981)]. Replacement of the allylic chlorine atom with STZ was performed by two-step operation: NaI/acetone (Δ); NaSTZ/acetone. Reduction of 3 ($C \begin{smallmatrix} X^1 \\ X^2 \end{smallmatrix} = C=O$; $Y = STZ$) with $Zn/AcOH/CH_2Cl_2$, BH_3NH_3/CH_2Cl_2 , or $+e^-$ afforded the corresponding alcohols 3 ($X^1 = H$, $X^2 = OH$ / $X^1 = OH$, $X^2 = H$: 3/2 1/2). Transformation of 3 to dithioazetidinones 4 was achieved by the hydrolytic ring-opening of the thiazoline moiety and simultaneous trapping of the thiol group with BTS $\rightarrow$ in aq. HCl/THF. Cyclization of 4 with NH_3/DMF and/or modification of the benzylic C=O group yielded 1a-c, respectively.



	R	Y
a Cefamandole		STZ
b SKR-80000		STZ
c Lafargulm AL-226		H