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# AN ELEGANT USE OF GLYCINE FOR THE SYNTHESIS OF SOME NOVEL β-LACTAMS

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Regarding the structure-activity correlation in Penicillin-Cephalosporin field, it is generally believed that the presence of (i) an α-amido side chain, (ii) cis β-lactam and (iii) a free carboxy group are essential features for antibacterial activity. In view of this, we report here an elegant use of glycine for the preparation of some β-lactams having these essential features.

Syntheses of β-lactams through the annelation of imines require the preparation of a suitable acid component and an appropriate Schiff's base. We have been successful in using glycine to prepare both of these components. For example, glycine is known[1] to readily condense with ethyl acetoacetate to produce the highly stable compound (1). On the other hand we have observed that ethyl ester hydrochloride of glycine reacts readily with aromatic aldehydes in the presence of triethylamine in dichloromethane to furnish quantitatively the required imines (2).

Coupling[2] of (1) and (2) to furnish the α-enamido-β-lactams (3) was accomplished through the $POCl_3$ method[3] in yield of 30-35%. The α-amino-β-lactams (4), obtained from (3) by treatment with ethanol-HCl (2:1), were converted to the α-amido-β-lactams (5) through acylation with phenoxyacetyl chloride. The stereochemistry of these β-lactams was found to be cis through their PMR spectra. The $C_4$-H in compound (5a) appeared as doublet at $\tau$ 4.73 and at $\tau$ 4.83 in compound (5b) with the required cis coupling ($J = 5.5$ Hz). The $C_3$-H showed, as expected, a doublet of doublets having $J = 5.5$ & 9.0 Hz. Since no epimerization is involved in the formation of (5) from (3) via (4), cis stereochemistry can be assigned to these β-lactams as well.

The β-lactams (6) carrying the free carboxy function were prepared under basic conditions[4] (0.1 N NaOH in acetone) from the ester β-lactams (5) in high yield when no harm was done either to the β-lactam ring or the amide side chain. In view of the recent report[5], such compounds can serve as potential intermediates for the synthesis of fused ring β-lactams.

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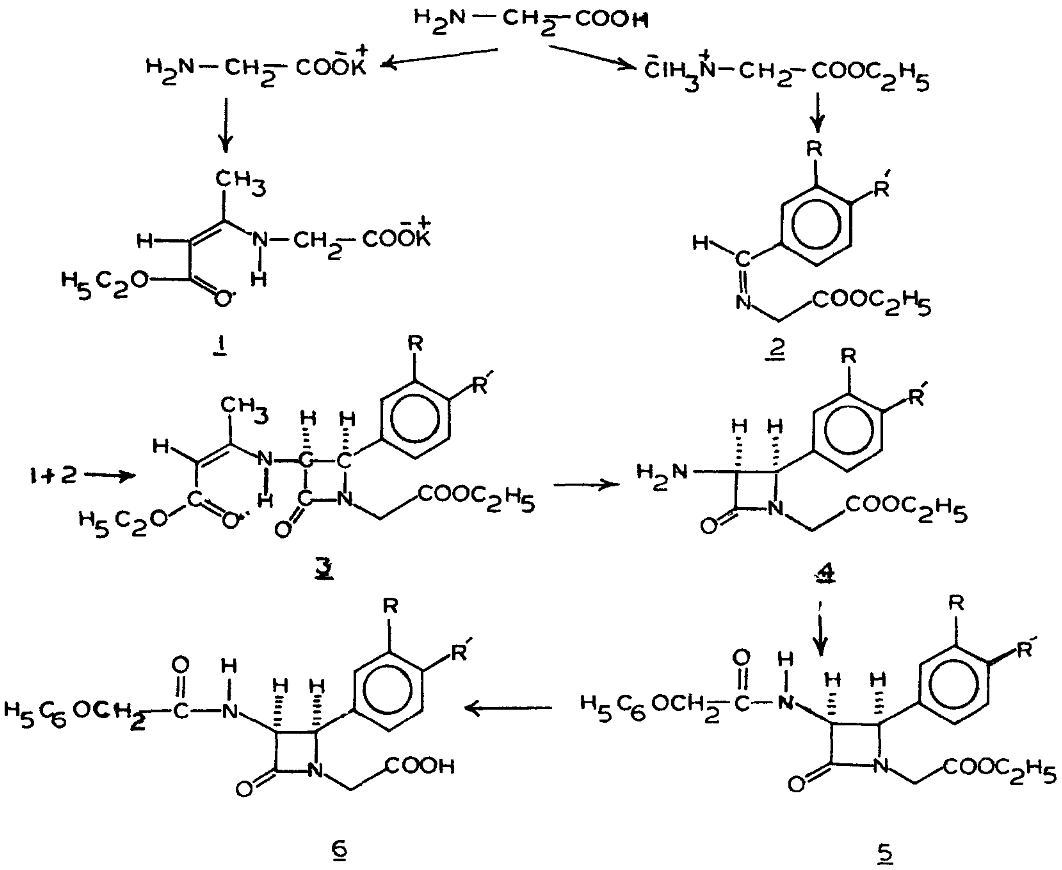

a, $R = R' = H$
b, $R = R' = OCH_3$

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