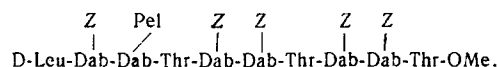


# SOLID-PHASE SYNTHESIS OF A DECAPEPTIDE CONTAINING L- $\alpha,\gamma$ -DIAMINO BUTYRIC ACID

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In connection with investigations on the synthesis and biological action of peptides related to the antibiotics, the polymyxins obtained by Merrifield's solid-phase method [1], a decapeptide has been obtained which contains the same set of amino acids as the natural antibiotic polymyxin M: six residues of L- $\alpha,\gamma$ -diaminobutyric acid (Dab), one of which is acylated with pelargonic acid (Pel), three L-threonine residues, and one D-leucine residue.



As the polymeric support we used a chloromethylated copolymer of styrene with 1% of divinylbenzene which contained 8% of chlorine. The growth of the peptide chain was effected by the stepwise addition of amino acids to the BOC-threonyl-polymer. The L- $\alpha,\gamma$ -diaminobutyric acid was blocked at the  $\alpha$ -amino group by o-nitrophenylsulfonyl protection and at the  $\gamma$ -amino group by benzyloxycarbonyl protection (Z) [3]. The D-leucine and L-threonine were introduced into the synthesis in the form of the BOC derivatives. The BOC-threonyl-polymer obtained contained 0.6 mmole of threonine per gram of polymer. The tert-butyloxycarbonyl group was eliminated with a 4 N solution of HCl in dioxane for 30 min, and the o-nitrophenylsulfonyl group with a 1 N solution of HCl in acetic acid for 10 min [4]. Condensation was carried out by means of dicyclohexylcarbodiimide (DCHC) in methylene chloride with 2.5-fold excesses of amino acids and DCHC. The addition of each amino acid was checked with the aid of an automatic amino-acid analyzer. The peptide was separated off from the polymer by transesterification with a 1 N solution of triethylamine in methanol [5]. The decapeptide was obtained in the pure state (71%) after two recrystallizations from methanol-ether and purification on a column of Sephadex LH-20. Mp 142-143°C,  $[\alpha]_D^{20} -27.1^\circ$  (c 0.5; acetic acid). Amino-acid analysis: Dab 6.0, Thr 2.8, Leu 0.72.

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