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REMOVAL OF PEPTIDES FROM "MERRIFIELD SOLID PHASE" BY TRANSESTERIFICATION WITH AN ANION EXCHANGE RESIN

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In connection with another study, we have recently observed that amino acid and peptide benzyl esters can be transesterified with methanol or ethanol in the presence of a strong anion exchange resin at room temperature (1). Since in the "Merrifield solid phase" peptide system (2), the peptides are covalently bound to the polymer by a benzyl ester linkage, we have applied the transesterification procedure to the cleavage of peptides from the resin support.

In a typical experiment t-Boc-val-phe-o-Resin (1g, 0.43 mM) (3) was suspended in methanol (10 ml) and Bio-Rad AG1-X8 (1g, hydroxide form, washed with anhydrous methanol) (4) was added. The formation of the product t-Boc-val-phe-OMe was followed by gas liquid chromatography (5' x 1/8" column packed with 5% QF1 on DMCS treated Gas Chrom P at 245°). After 2 hours at room temperature the resins were filtered off and the methanol solution evaporated to dryness in vacuum. The crystalline residue (100 mg, 61% yield) was homogeneous (t.l.c., g.l.c.) and its structure was confirmed by mass spectrometry (M^+ 378) and direct comparison with an authentic specimen. Since diastereoisomeric t-Boc-L-pro-DL-amino acid methyl esters can be resolved by g.l.c. (5),

we could confirm the steric homogeneity (< 1% of LD dipeptide) of the isolated t-Boc-dipeptide methyl esters obtained from t-Boc-pro-ala Resin, t-Boc-pro-val Resin, t-Boc-pro-phe Resin and t-Boc-pro-leu Resin. Transesterifications with larger peptide resin esters (up to octapeptides have been tried), show that the commonly used protecting groups remain intact, but that the ω-carboxyl functions of aspartic and glutamic residues are also transesterified. The isolated t-Boc-peptide esters (50-70% yield) are homogeneous (t.l.c., M.S.) and often crystalline and even tryptophan containing peptides such as t-Boc-try-ala Resin could be cleaved with a 60% recovery of the methyl ester (MS, M+ 389).

The very mild conditions of the transesterification with another resin, avoiding racemization, make it an attractive candidate for use in solid phase peptide synthesis.

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