

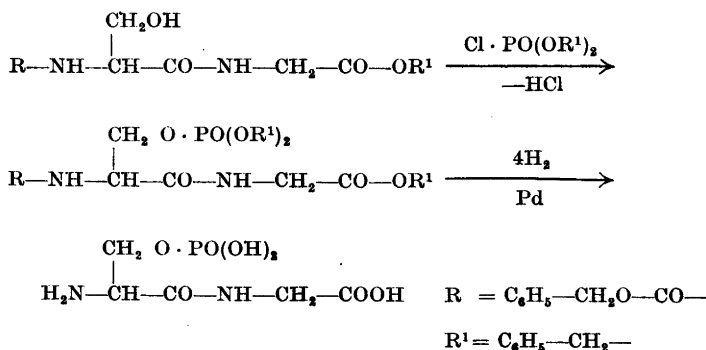
Synthesis of Phospho-Peptides. O-Phospho-DL-Seryl-Glycine

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During recent years it has been suggested that phosphorylated peptides are of great biological significance¹⁻³. A more detailed study of their properties depends partly upon the possibility of synthesising model peptides similar to the naturally occurring ones, *i. e.* peptides containing serine or threonine with phosphorylated hydroxyl groups.

Many investigations have been made on the phosphorylation of amino acids⁴⁻⁶ and, also, peptides and peptide derivatives⁷⁻⁹. Although difficulties often appeared when preparing N-phospho- and also O-phospho-amino acids⁴⁻⁶, Posternak and Grafl⁹ succeeded in synthesising four peptides, which besides glycine also contained tyrosin with the phenolic hydroxyl group phosphorylated. No synthesis of phosphopeptides containing the only two O-phosphoamino acids isolated from natural sources, O-phosphoserine and O-phosphothreonine, has, however, been reported. We have, therefore, started to synthesise such peptides and now report a synthesis of O-phospho-DL-seryl-glycine. This compound has been obtained by phosphorylation of N-benzyloxycarbonyl-DL-seryl-glycine benzyl ester (prepared by coupling benzyloxycarbonyl-DL-serin azide with glycine benzyl ester) with dibenzyl phosphoryl chloride¹⁰ at low temperature in pyridin solution, followed by removal of the benzyloxycarbonyl- and the three benzyloester-groups from the reaction product by hydrogenation in presence of palladium catalyst:



The crude phosphopeptide (20 % yield) was further purified by column chromatography on Dowex 50. M. p. 178°. On paper chromatograms (phenol-water 80:20) the phosphopeptide gives colour both with ninhydrin (brown violet) and with phosphate reagent. It has an R_F -value of 0.13 when O-phosphoserine on same chromatogram has $R_F = 0.07$. Hydrolysis (6 N HCl, 20 h, 100°) gives serine, glycine and phosphoric acid as shown by paper chromatography. (Found: N 11.3; P 13.3. Calc. for $\text{C}_8\text{H}_{11}\text{O}_7\text{N}_2\text{P}$: N 11.6; P 12.8).

By the same procedure we are now preparing phosphopeptides containing L-phosphoserine. Further details will be published later.

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