Removal of Protected Peptides from an *ortho*-Nitrobenzyl Resin by Photolysis

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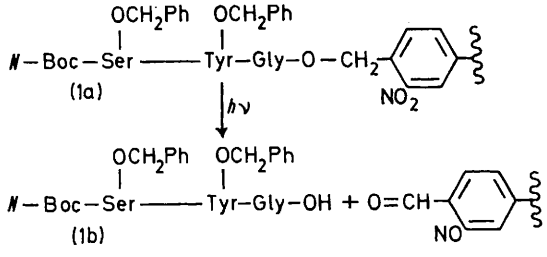
Summary Protected peptides can be removed from an *ortho*-nitrobenzyl resin by photolysis.

RECENTLY several modified resins suitable for the solid-phase synthesis of protected peptide fragments have been developed.[1] We report a method for the preparation of *N*-t-butoxycarbonylpeptide free acids by solid-phase peptide synthesis. The protected peptides are synthesized stepwise on an *ortho*-nitrobenzyl resin then removed from the resin by photolysis under conditions which do not cleave acid-labile protecting groups nor decompose aromatic amino-acids. The use of the photolabile *o*-nitrobenzyl group for protection of aldehyde, amino-, and carboxy-groups has been reported.[2]



An *o*-nitrochloromethyl resin was prepared by nitration of chloromethylated polystyrene beads (1% divinylbenzene) according to the procedure of Merrifield.[3] *N*-t-Butoxycarbonylamino-acids were attached to the nitro-resin by heating under reflux with triethylamine in ethyl acetate.[4]

To remove the *N*-protected amino-acids from the nitro-resin, the *N*-t-butoxycarbonylamino-acid nitro-resins were suspended in methanol, and irradiated under anaerobic conditions for 12—17 h with stirring in an RPR-100 apparatus (Rayonet, The Southern Co., Middletown, Conn.) equipped with RPR-3500 Å lamps. Wavelengths below 3200 Å were filtered out.[5] The resin was removed by filtration and the solvent evaporated. After purification by chromatography followed by crystallization, the *N*-t-butoxycarbonylamino-acids were isolated in good yield (see Table). No racemization of the amino-acids was detected, and no *N*-t-butoxycarbonylamino-acid remained on the resin.

TABLE

Photolysis of N-*t-butoxycarbonylamino-acid* o-*nitrobenzyl resins in methanol*

N-Protected amino-acid on resin	Yield of *N*-protected amino-acid (%)	M.p. (°) (reported)[7]	Photolysis time (h)
Gly	71·2	88—90 (89—90)	12
Leu	64·7	86—87 (86—87)	14
Phe (D,L)	66·4	145—147	17
Phe (L)	59·6	87—89 (88—88·5)	15
Tyr-OCH_2Ph	52·7	108—110	15
Trp	57·3	137—138 (138·5—139·5)	17

N-t-Butoxycarbonyl-*O*-benzyl-L-seryl-*O*-benzyl-L-tyrosylglycyl-*o*-nitrobenzyl resin (**1a**) was synthesized using *N*-t-butoxycarbonylglycyl-*o*-nitro-resin (1·05 mmol/g)

according to the general procedure of Merrifield.[3,6] Deblocking was achieved by treatment with 50% trifluoroacetic acid in methylene chloride. Dicyclohexylcarbodiimide was used as the coupling reagent. The tripeptide (**1b**) was removed from the *o*-nitro-resin by irradiation at 3500 Å for 12 h as described and was isolated in 62% yield.† The tripeptide (**1b**) prepared in this way was identical to a sample prepared by solution procedures.†

Removal of protected peptides from the *o*-nitrobenzyl resin by irradiation provides a method for the synthesis of protected peptide fragments suitable for coupling in solution or on a solid support.

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† Satisfactory amino-acid analysis, microanalysis, t.l.c., n.m.r., and i.r. data were obtained.

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