

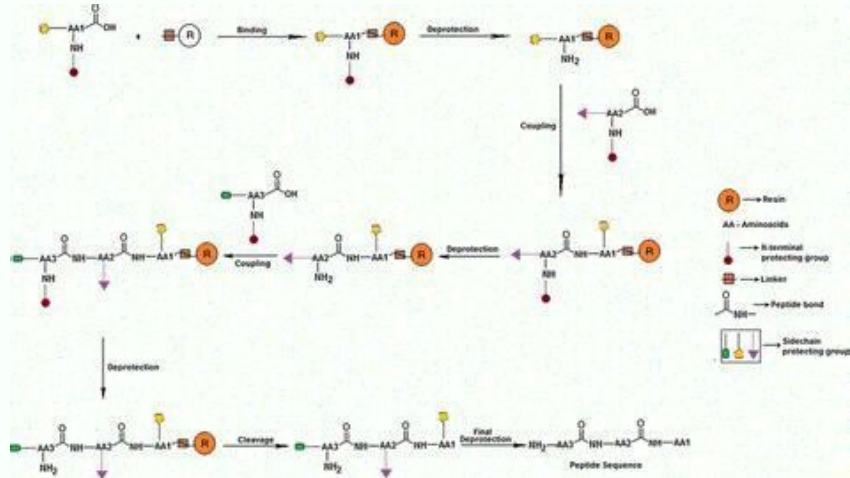
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AAPTec's Guide to Solid Phase Peptide Synthesis is an introduction to solid phase peptide synthesis It discusses how solid phase peptide synthesis is performed, the amino acid derivatives, resin and reagents used in peptide synthesis, and some of the common problems in solid phase peptide synthesis and how to avoid them, plus also suggested procedures and guides to choosing resins and planning a successful peptide synthesis.Click on the section you want to go to or download the guide as a pdf file.CLICK HERE TO DOWNLOAD GUIDE TO SOLID PHASE PEPTIDE SYNTHESIS (pdf)I. Introduction - PublicationsII. Brief Outline and History of Solid Phase Peptide SynthesisA. HistoryB. Overview of Solid Phase Peptide Synthesis1. General Solid Phase Peptide Synthesis Scheme2. Selective Deprotectiona. Boc/Bzl Protectionb. Boc Deprotection Mechanismc. Fmoc/tBu Protectiond. Fmoc Deprotection Mechanisme. Ligation and Fragment CondensationIII. Equipment for Solid Phase Peptide SynthesisA. Manual SynthesisB. Automated SynthesizersIV. Resins for Solid Phase SynthesisA. Core Resins1. Polystyrene 2. Merrifield Resin 3. Hydroxymethyl Resin 4.



Boc Deprotection Mechanismc. Fmoc/tBu Protectiond. Fmoc Deprotection Mechanisme. Ligation and Fragment CondensationIII. Equipment for Solid Phase Peptide SynthesisA. Manual SynthesisB. Automated SynthesizersIV. Resins for Solid Phase SynthesisA. Core Resins1. Polystyrene 2. Merrifield Resin 3. Hydroxymethyl Resin 4.

Supplementary Material (ESI) for Chemical Communications

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Selective hydrolysis of peptides promoted by metal ions: a positional scanning approach

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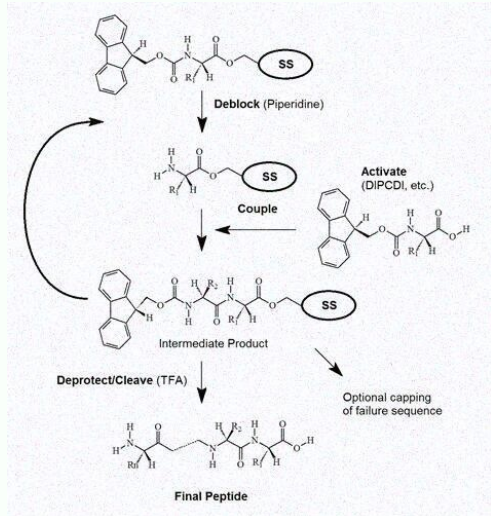
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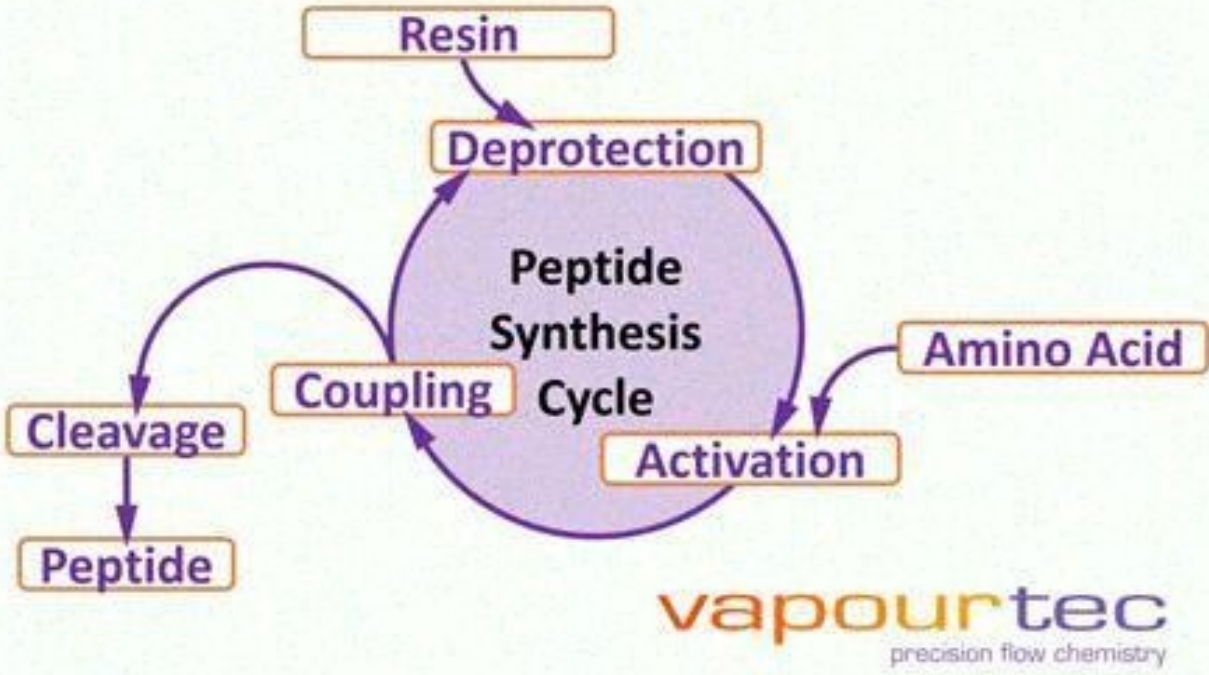
Solid phase peptide synthesis

Individual acetylated dipeptides and positional scanning library samples were prepared from 2-chlorotrityl chloride resin (1.08 mmol/g) by established manual solid phase synthesis protocols using activated Fmoc-glycine, Fmoc-leucine, and Fmoc-methionine monomer units.¹ All coupling, Fmoc deprotection, and acetylation reactions proceeded to greater than 99.5% completion as accessed by ninhydrin and/or chloranil tests.^{1a,d,e} Coupling and Fmoc deprotection were further confirmed by derivatization of peptides with dansyl chloride and subsequent reversed-phase HPLC analysis.² The procedures employed for preparation of the individual acetylated dipeptides AcMet-Gly, AcMet-Leu, AcMet-Met, AcLeu-Met, AcGly-Gly, AcGly-Met, AcLeu-Leu, AcLeu-Gly, and AcGly-Leu are as follows.

Boc/Bzl Protectionb. Boc Deprotection Mechanismc. Fmoc/tBu Protectiond.



Ligation and Fragment CondensationIII.



Boc/Bzl Protectionb. Boc Deprotection Mechanismc. Fmoc/tBu Protectiond. Fmoc Deprotection Mechanismf. Ligation and Fragment CondensationIII. Equipment for Solid Phase Peptide SynthesisA. Manual SynthesisB. Automated SynthesizersIV. Resins for Solid Phase SynthesisA. Core Resins1. Polystyrene 2. Merrifield Resin 3. Hydroxymethyl Resin 4. Amino Core ResinsB. Linked Resins1. Linkers 2. PAM Resin 3.

Table 1. The eleven probes used in this study.			
Probe	Putative Target	Original Protein Source	Sequence ³
P1	SHP1	Sgnc	RH-GDEGKHSELLNNH ₂
P2	PTP1B/PTP	Sad	RHGGSAAPKLRKNNH ₂
P3	PTP1B	Stat5b	RH-GGKAVGGKQKQNNH ₂
P4	LWPTP	Zap70	RH-GGLNSGGKTPKNNH ₂
P5	SHP2	Plab2	RH-GGLPREGKVVVNNH ₂
P6	SHP1/SHP2	CD31	RH-GGSEGVGKTKVQNNH ₂
P7	PTP1B	Tyk2	RH-GGPEGEKQVYKNNH ₂
P8	SHP2/PTP1B	Janus	RH-GGPGQGEKQVYKNNH ₂
P9	SHP2/PTP1B	EGFR	RH-GGVGADGKLPQNNH ₂
P10	PTP1B	Zwang ⁴	RH-GGLEKESKNNH ₂
P11	PTP1B	Stat5b	RH-KBGRVH-KAVGQKQVQKQNNH ₂

¹ Obtained from www.sbc.edu. ² Obtained from reference 30. ³ X = 2-FMPT.

Ligation and Fragment CondensationIII. Equipment for Solid Phase Peptide SynthesisA. Manual SynthesisB. Automated SynthesizersIV. Resins for Solid Phase SynthesisA. Core Resins1. Polystyrene 2. Merrifield Resin 3. Hydroxymethyl Resin 4. Amino Core ResinsB. Linked Resins1. Linkers 2. PAM Resin 3. Wang Resin 4. Amide/Amine Forming Resins for Fmoc/tBu 5. MBHA Resin 6. Trityl and 2-Cl-Trityl Resin 7. Nucleophile Labile Resins 8. DHP Resins 9. Weinreb Resin 10. Substrate-Attached ResinsV. Solvents for Solid Phase Peptide SynthesisVI. Amino Acid DerivativesA. ArginineB. Aspartic Acid and Glutamic AcidC. Asparagine and GlutamineD. Cysteine and PenicillamineE. HistidineF.

Lysine, Ornithine, 2,4-Diaminobutanoic Acid and 2,3-Diaminopropanoic AcidG. MethionineH. Serine, Threonine, and 4-HydroxyprolineI. TryptophanJ. TyrosineVII. Coupling ReagentsA. CarbodiimidesB. BOP, PyBOP, PyAOP, PyBrOP, BOP-ClC. HATU, HBTU, HCTU, TATU, TBTD, TOTU, COMUE, TDBTU, TSTU, TNTU, TPTUF. Other Coupling ReagentsVIII. Monitoring of Coupling and CappingIX. Aggregation, Difficult Sequences, and Side ReactionsA. AggregationB. RacemizationC. Side Reactions1. Diketopiperidine Formation 2. Aspartamide Formation 3. Pyroglutamate Formation 4. 3-(1-Piperidinyl)alanine Formation 5. Guanidinylation 6. Transfer of Sulfonyl Protecting Groups 7. Oxidation of Methionine 8. N->O ShiftD. Side Reactions During HF Cleavage1. Homoserine Lactone Formation 2. Glutamic Acid Side Reactions 3. Asp-Pro CleavageX. Peptide ModificationA. CyclizationB. Stapled PeptidesC. N-Methylation of Peptide BackboneD. PhosphorylationE. Myristylation/PalmitylationF. GlycosylationG. IsoprenylationH. PEGylationI. BiotinylationJ. Fluorescent LabelingK. Caged PeptidesL. MAP PeptidesM. ThioestersXI. Planning a Peptide SynthesisA. N- and C-Terminal FunctionalityB.

Boc vs FmocC. Selecting a Resin for Peptide SynthesisD. Selecting Amino Acid DerivativesE. Planning the Synthesis of Peptides Containing Multiple Disulphide BondsF. Storing and Using Amino Acid SolutionsXII. Technical NotesA. Attaching the First Residue to Resin1. Merrifield Resin 2. Activation of Trityl Resins 3. Attachment of Amino Acids to Trityl Resins 4. Attachment of Carboxylic Acids to Hydroxy-Substituted Resins 5. Attachment of Amino Acids to Fmoc-Protected Amide Forming Resins 6. Attachment of Boc-Amino Acids to BHA or MBHA Resins 7. Alcohol Coupling to CarboxypolystyreneB. Measuring Substitution of Fmoc-Amino Acid ResinsC. Standard Coupling Procedures1. N-Terminal Deprotectiona. Boc Deprotectionb. Fmoc Deprotectionc. Fmoc Deprotection with DBU2. Converting CHA and DCHA Salts to Free Acids3. Couplinga. DIC/HOBt Couplingb. EDC Couplingc. BOP Couplingd. PyBOP Couplinge. HBTU/HATU/HCTU/TBTU Couplingf. Fast Boc Deprotection with In Situ Couplingg. N-Methyl Amino Acid Coupling with PyBrOPh. TSTU Coupling in Aqueous SolventsI.

Fragment Coupling with TBTDJ. Solid Phase Coupling with DEPBTk. Solution Phase Coupling with DEPBTk. Head to Tail Coupling with DEPBT4. Coupling Testsa. Kaiser Test (Ninhydrin Test)b. Isatin Testc. Chloranil Test5. Capping ProcedureD. Cleavage1. Cleavage from Merrifield Resina. Standard HF Cleavageb. Low-High HF Cleavagec. Standard Trifluoromethanesulfonic Acid Cleavagee. Low-High Trifluoromethanesulfonic Acid Cleavagee. TMSOTf Cleavage2. Wang Resin Cleavagea. TFA Cocktail Procedureb. TMSBr Procedure3. HMPA Resin Cleavage4. Rink Amide Resin Cleavage5. Cleavage from Sieber Amide Resin6. Cleavage of Protected Peptides from 2-Chlorotrityl Resin7. Cleavage from Oxime Resina. Cleavage to Peptide Acidb. Cleavage to Peptide Esterc. Cleavage to Peptide Amide8. HMBA-MBHA Resin Cleavagea. Cleavage to Peptide Acidb. Cleavage to Peptide Esterc. Cleavage to Peptide Amide9. Weinreb Resin Cleavage to Aldehydes9. Alcohol Cleavage from DHP Resin11. Alcohol Cleavage from Carboxypolystyreneaa. Sodium Carbonate Cleavageb. Sodium Methoxide CleavageE. Cleavage Cocktails1. "Odorless" Reagent B2. Reagent H for Methionine Containing Peptides3. Reagent K for Peptides Containing Cys, Trp, Met, or Tyr4. Low Odor Reagent L5. Reagent R for Arginine Containing PeptidesF. Side-chain Deprotection1. Arg(Mtr)2. Arg(Pbf) and Arg(Pmc)3. Cys(Acm)4. Cys(tBu)5.

Cys(Trt)6. His(DNP)7. Allyl and Alloc8. Dde and ivDde9. Trp(CHO)10. Met(OX)11. Post Cleavage Purification and AnalysisA. Precipitation and IsolationB. Yield CalculationC. HPLC AnalysisD. HPLC PurificationE. Removal of TFAIV. Storage and Handling of PeptidesXV. Dissolving Peptides Fischer, E. & Otto, E. Synthesis of the derivatives of some dipeptides. Ber. Deutsch. Chem. Ges.36, 2106-2116 (1903). Bergmann, M. & Zervas, L. A general procedure of the peptide synthesis. Ber. Deutsch. Chem. Ges.65, 1192-1201 (1932).

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