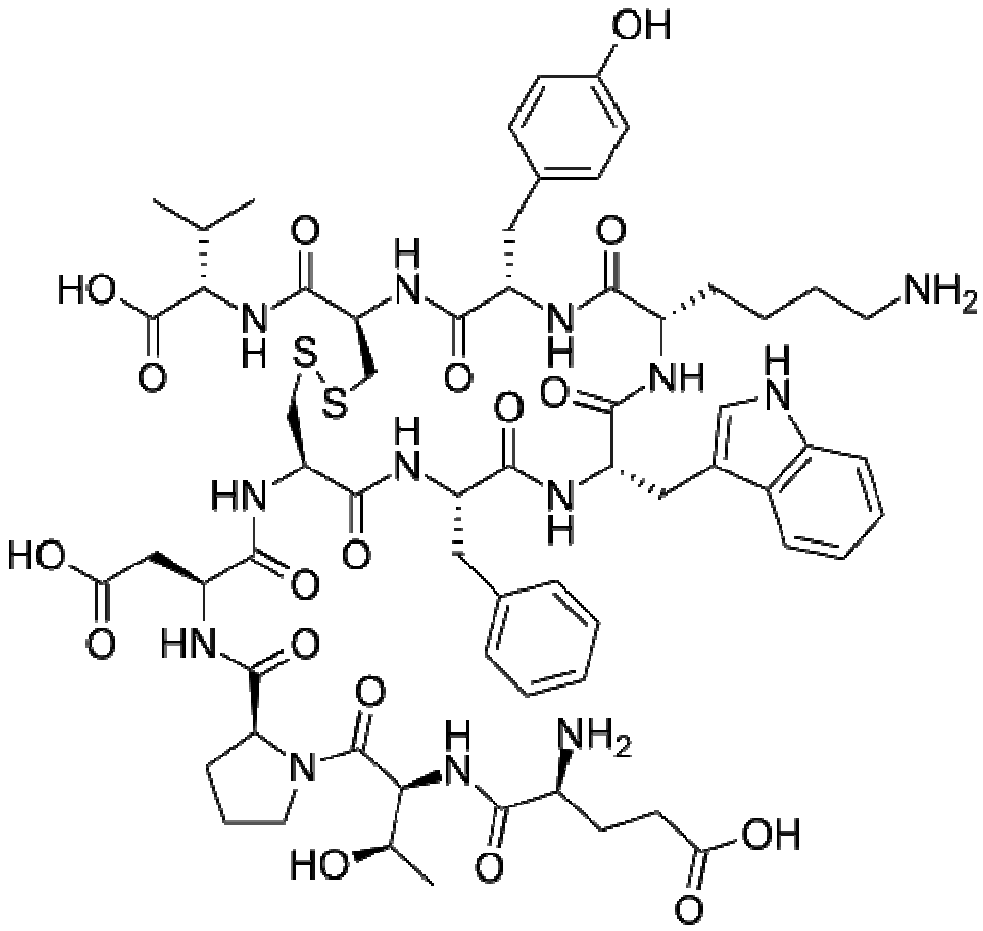
Urotensin-II



In mammals, it is involved in the regulation of the cardiovascular system

Urotensin-II Analogues

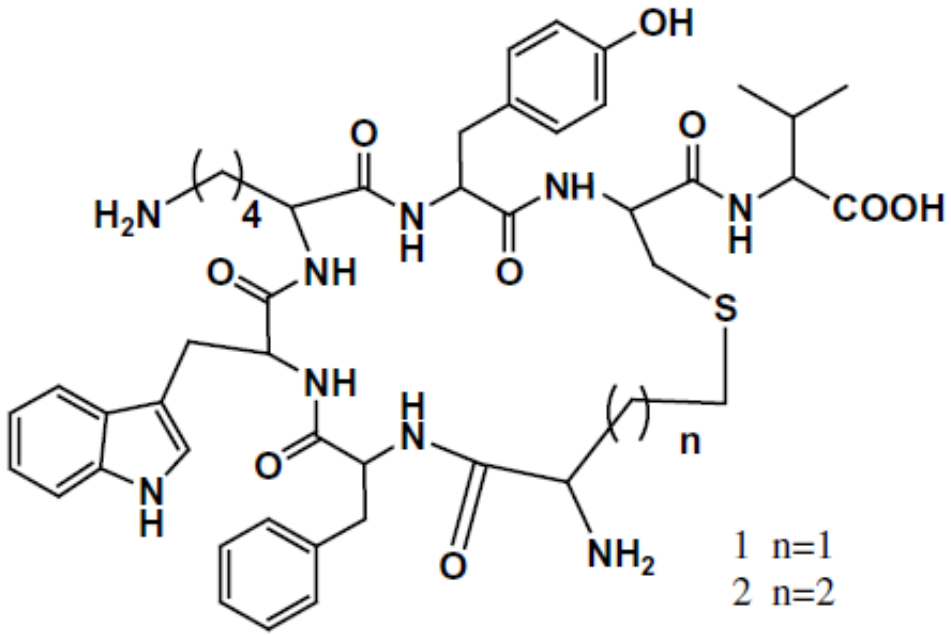
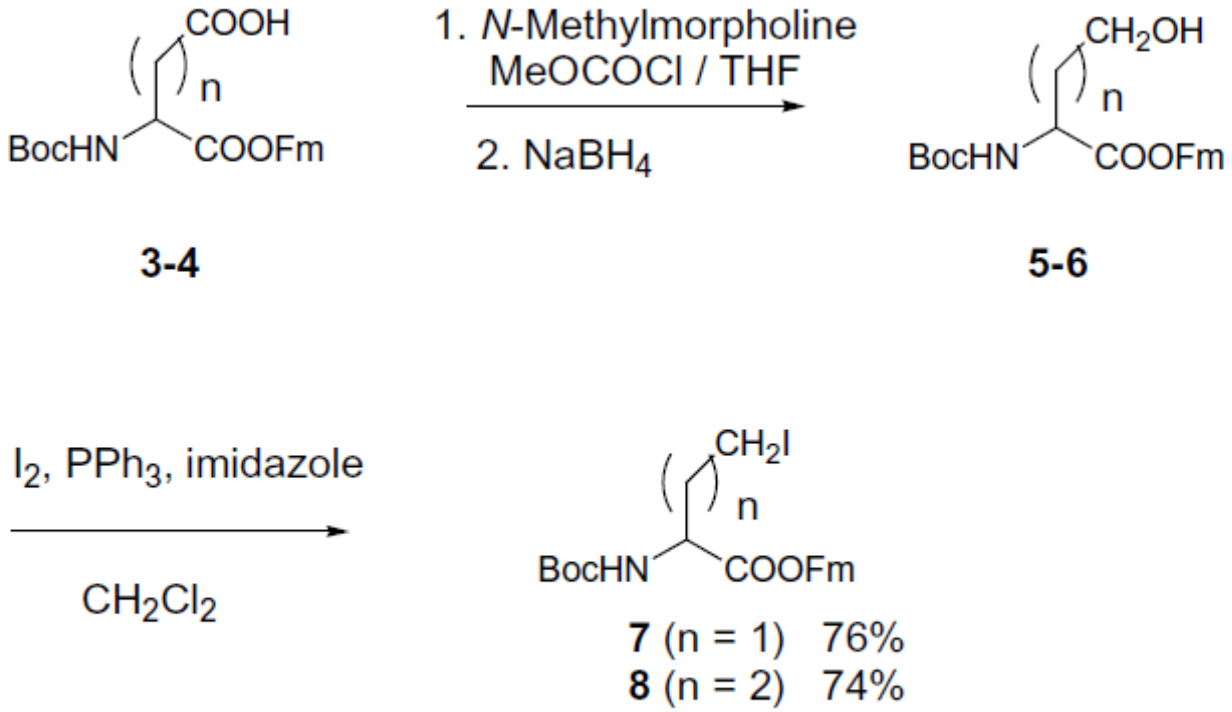


Figure 1. Urotensin-II analogues with monosulfide bridges.

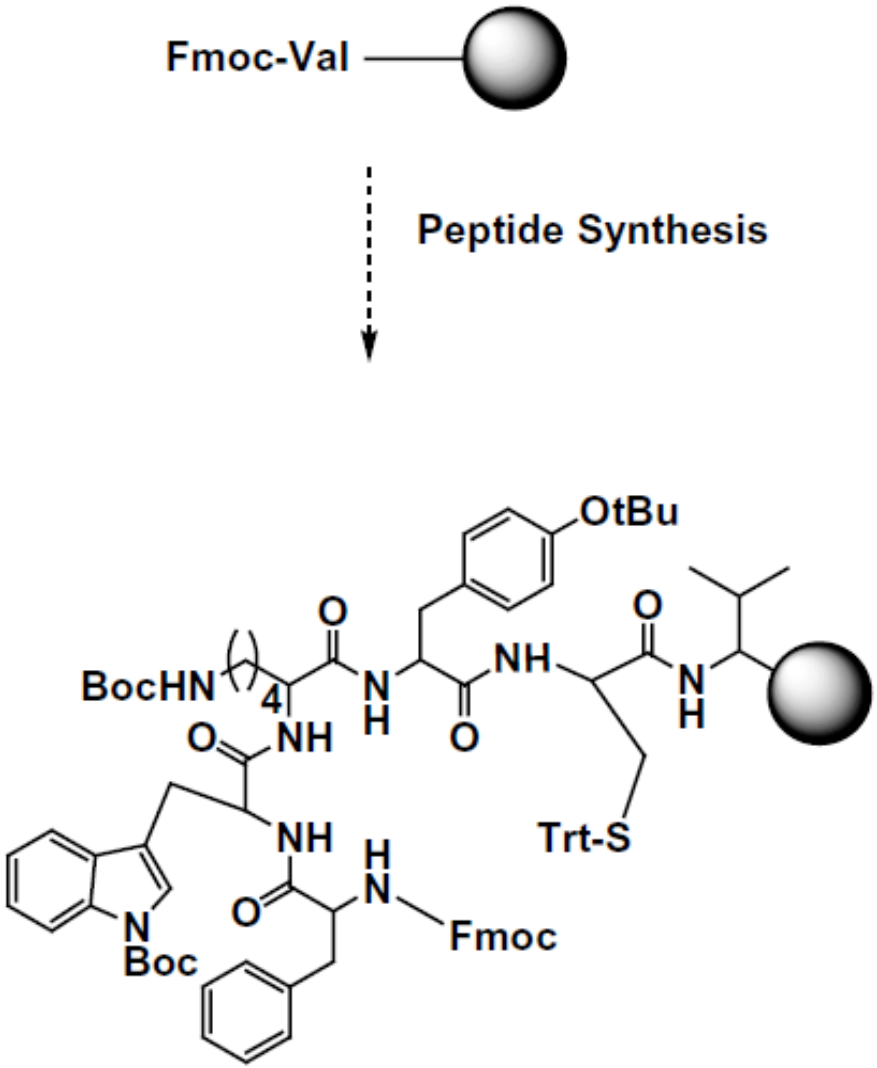
Tetrahedron Letters 45 (2004) 1453–1456

Urotensin-II Analogues

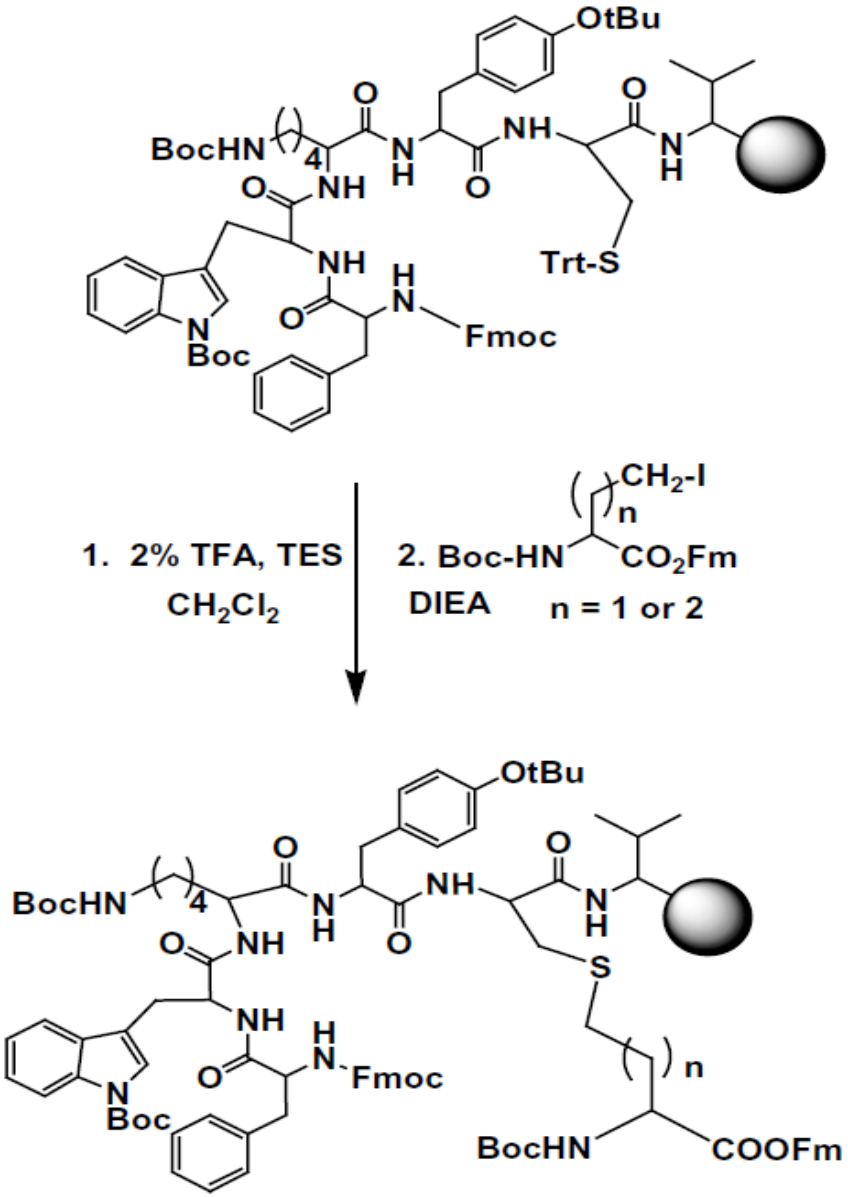


Scheme 1. Synthesis of iodide derivatives.

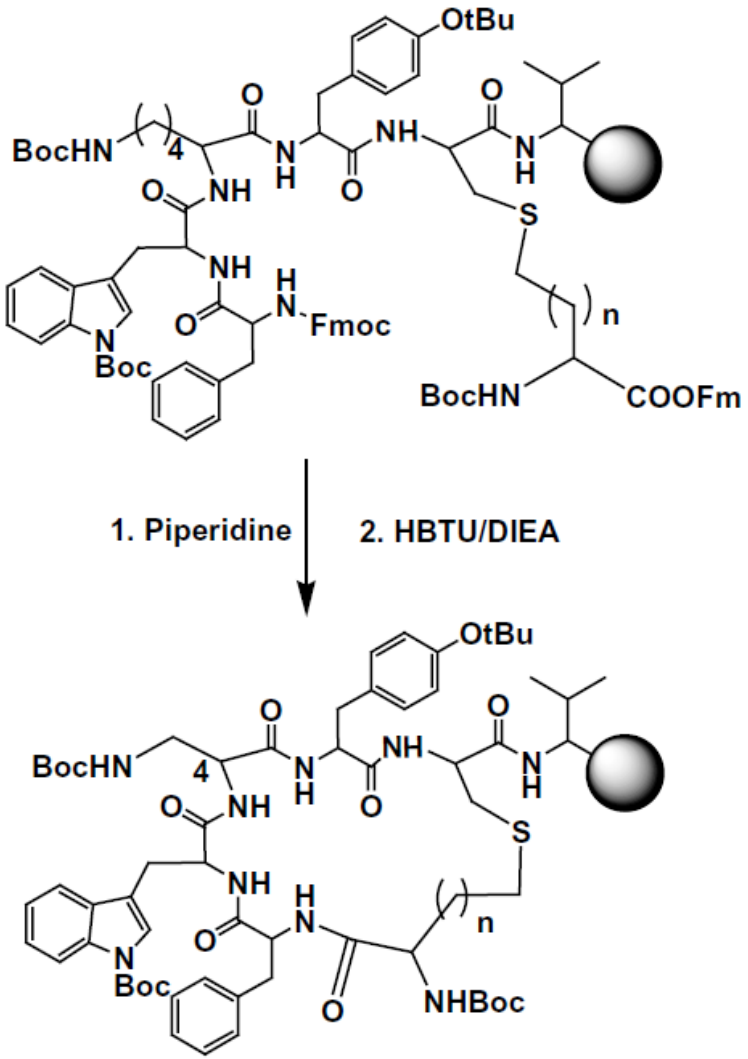
Urotensin-II Analogues



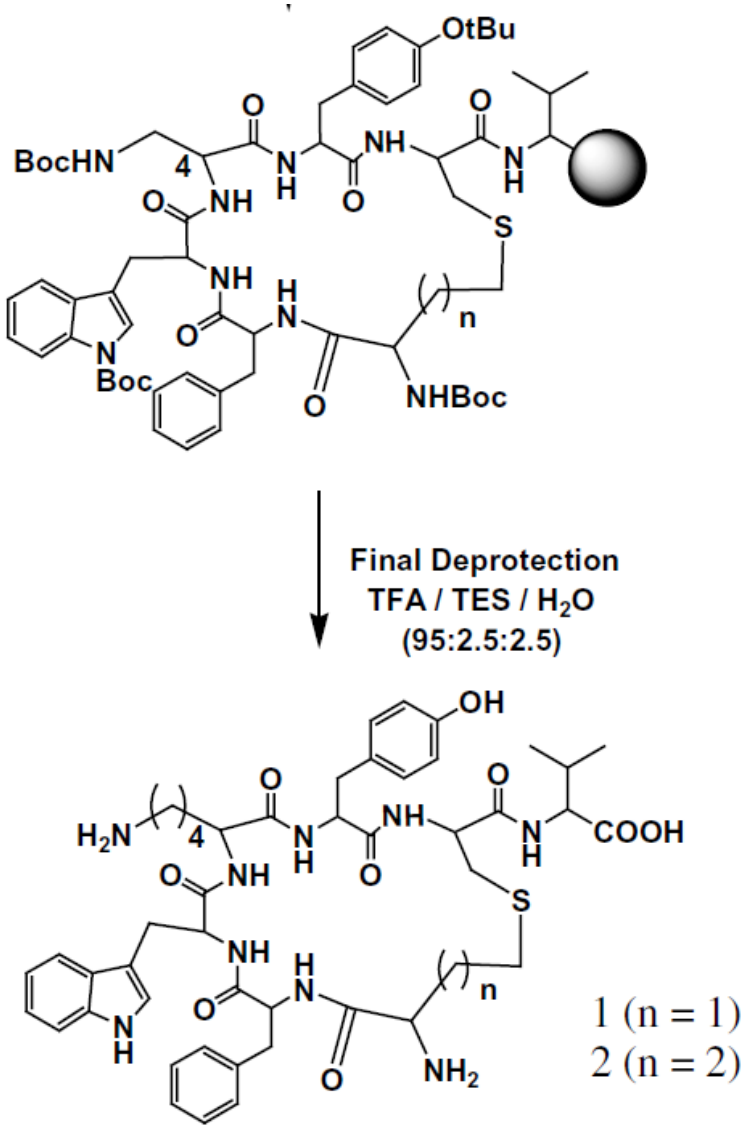
Urotensin-II Analogues



Urotensin-II Analogues



Urotensin-II Analogues



Urotensin-II Analogues

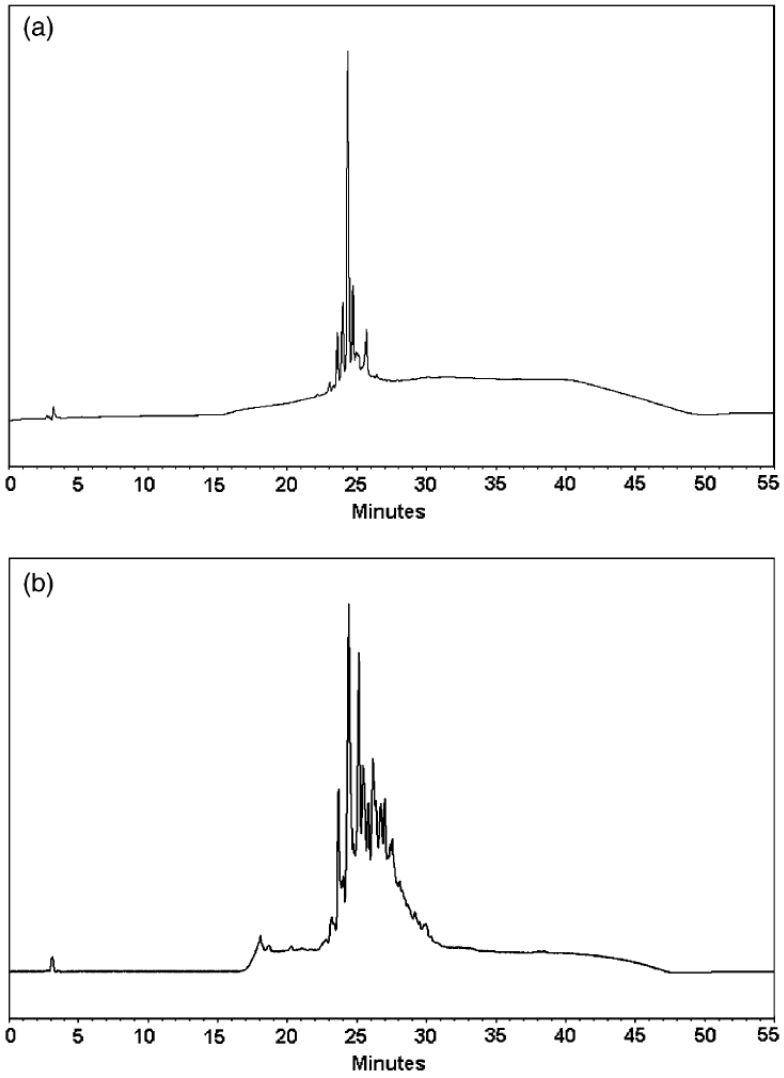
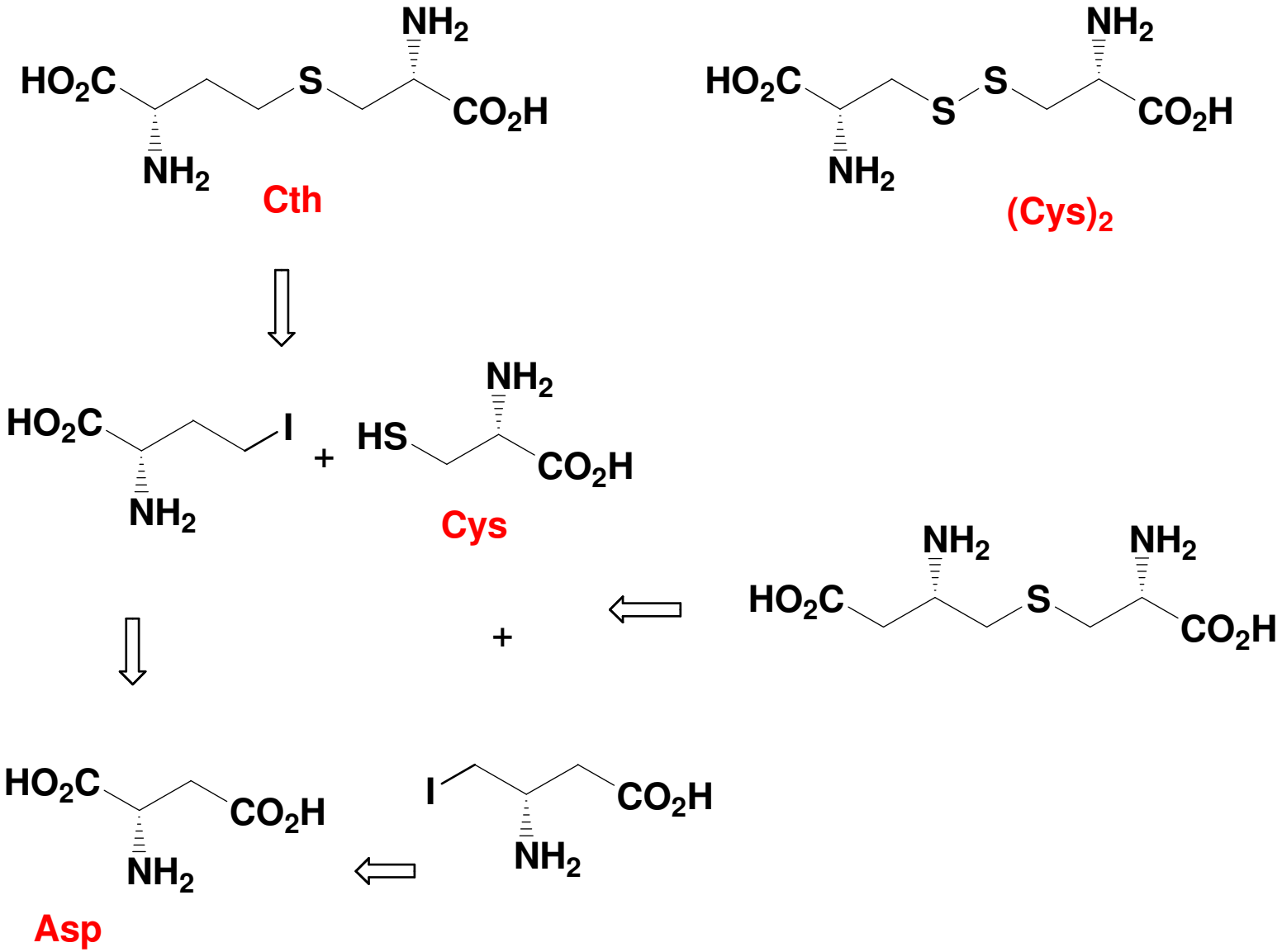
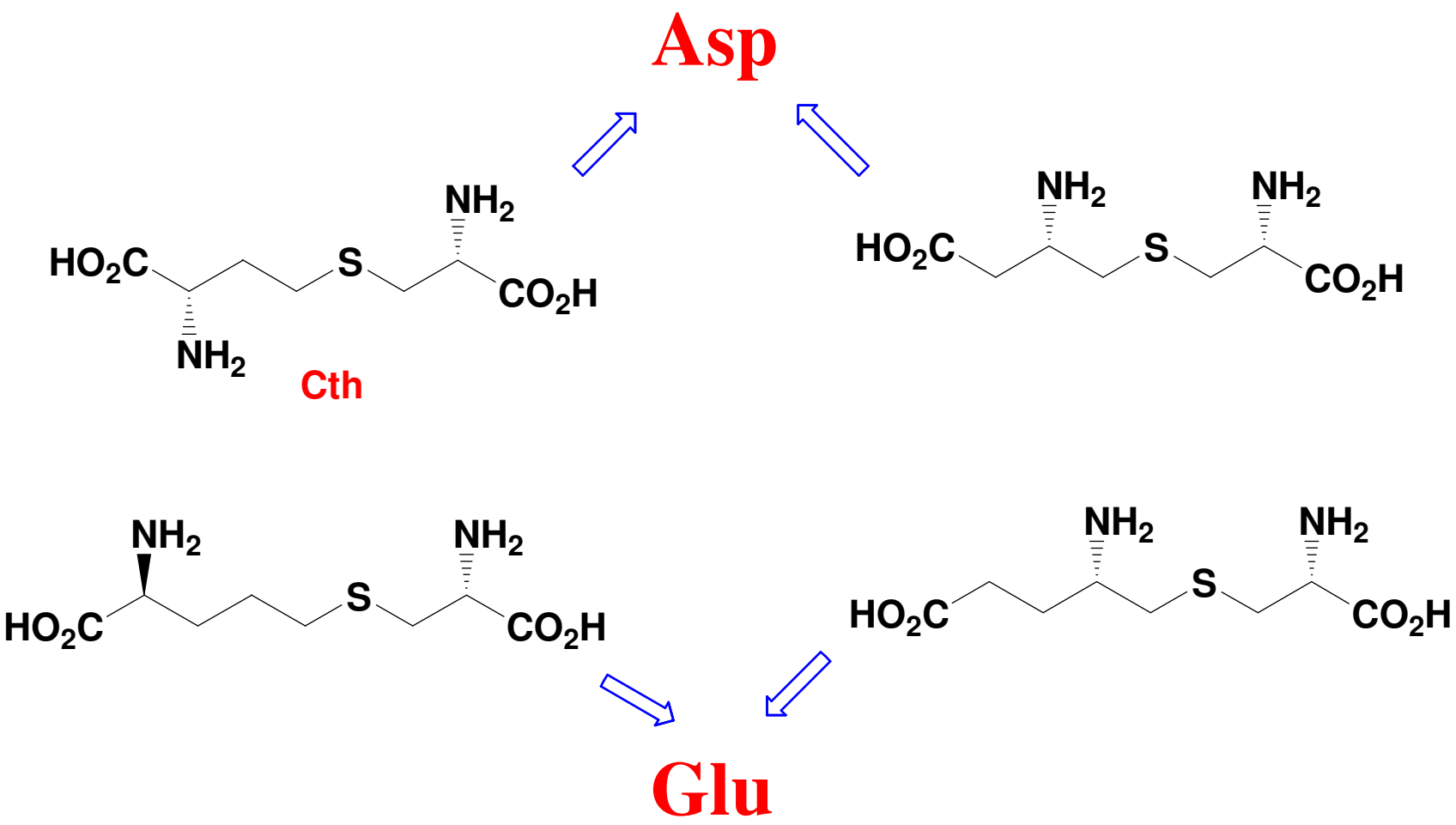


Figure 2. Reverse-phase HPLC profile of the final crude compound **1** obtained by microwave-assisted synthesis (a) and by the conventional method (b) (C_{18} column, linear gradient 10–90% MeCN/H_2O in 40 min, flow rate of 1.0 mL/min) after cleavage from the resin.

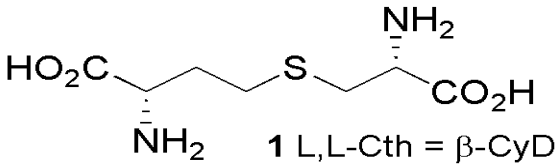
Cystathionine family



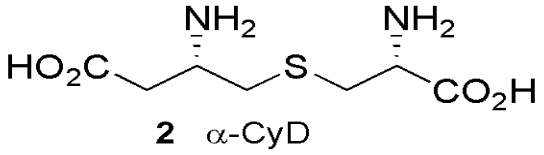
Cystathionine family



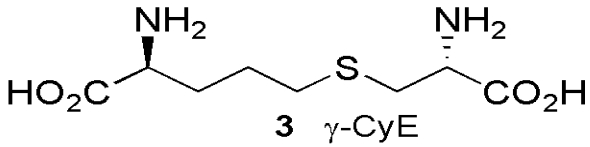
Cystathionine family



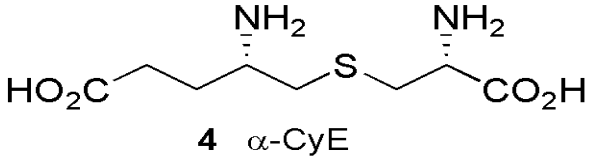
1 L,L-Cth = β-CyD



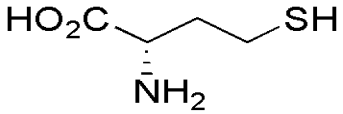
2 α-CyD



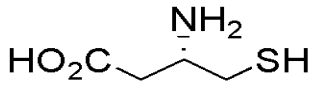
3 γ-CyE



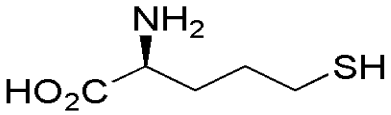
4 α-CyE



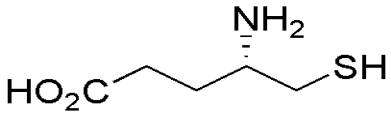
5 L-Hcy



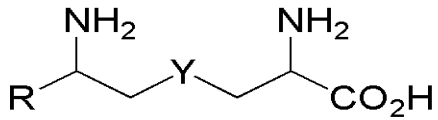
6 β^3-L-Cys



7 L-5-mercapto-Nva



8 γ^3-L-Cys



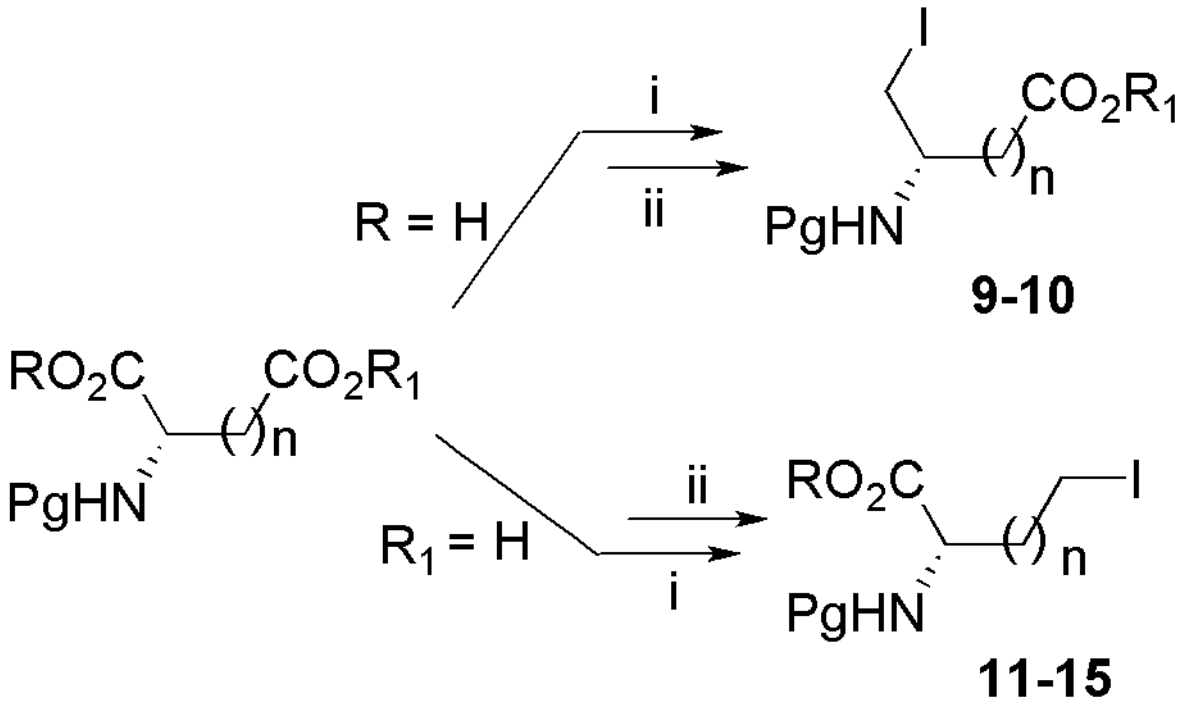
R= proteinogenic side chains

Y = S, CyX amino acids

Y = Se, SeX amino acids

Amino Acids 2012 in press

Cystathionine family



i: NMM, MeOCOCl, THF, 0°C, 15 min, then $NaBH_4$ (or $NaBD_4$), H_2O
ii: TPP-I_2, ImH, THF, reflux, 1 h

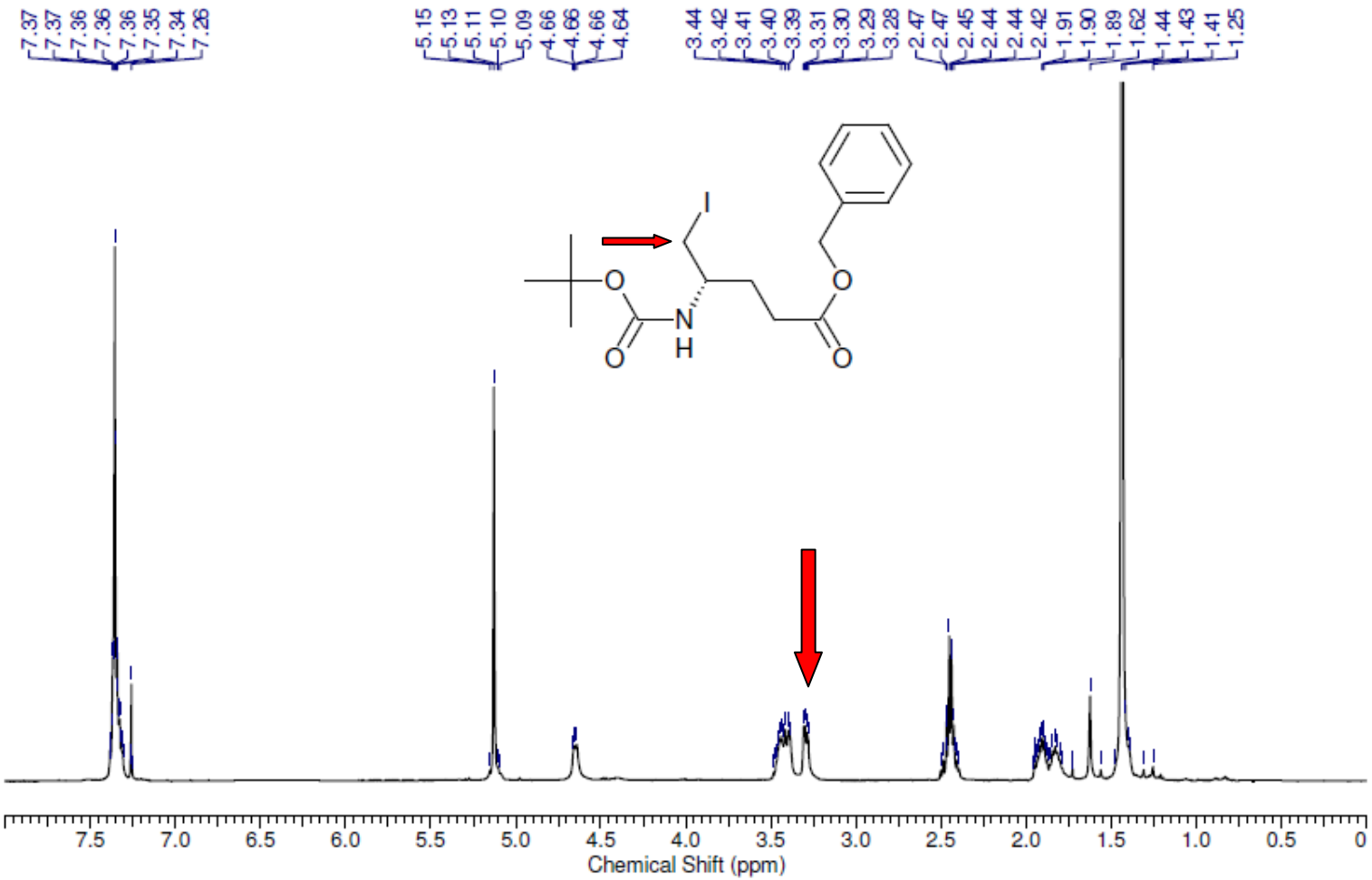
Cystathionine family

Table: N,C-Protected ω-Iodoamino Acids

Iodide	n	R	R_1	Pg	Yield (%)[a]
9	1	H	Bn	Boc	80
10	2	H	Bn	Boc	77
10-d_2	2	H	Bn	Boc	84
11	1	Allyl	H	Boc	79
12	1	Fm	H	Boc	76
13	1	t-Bu	H	Boc	81
14	2	Bn	H	Boc	83
15	2	Allyl	H	Fmoc	90

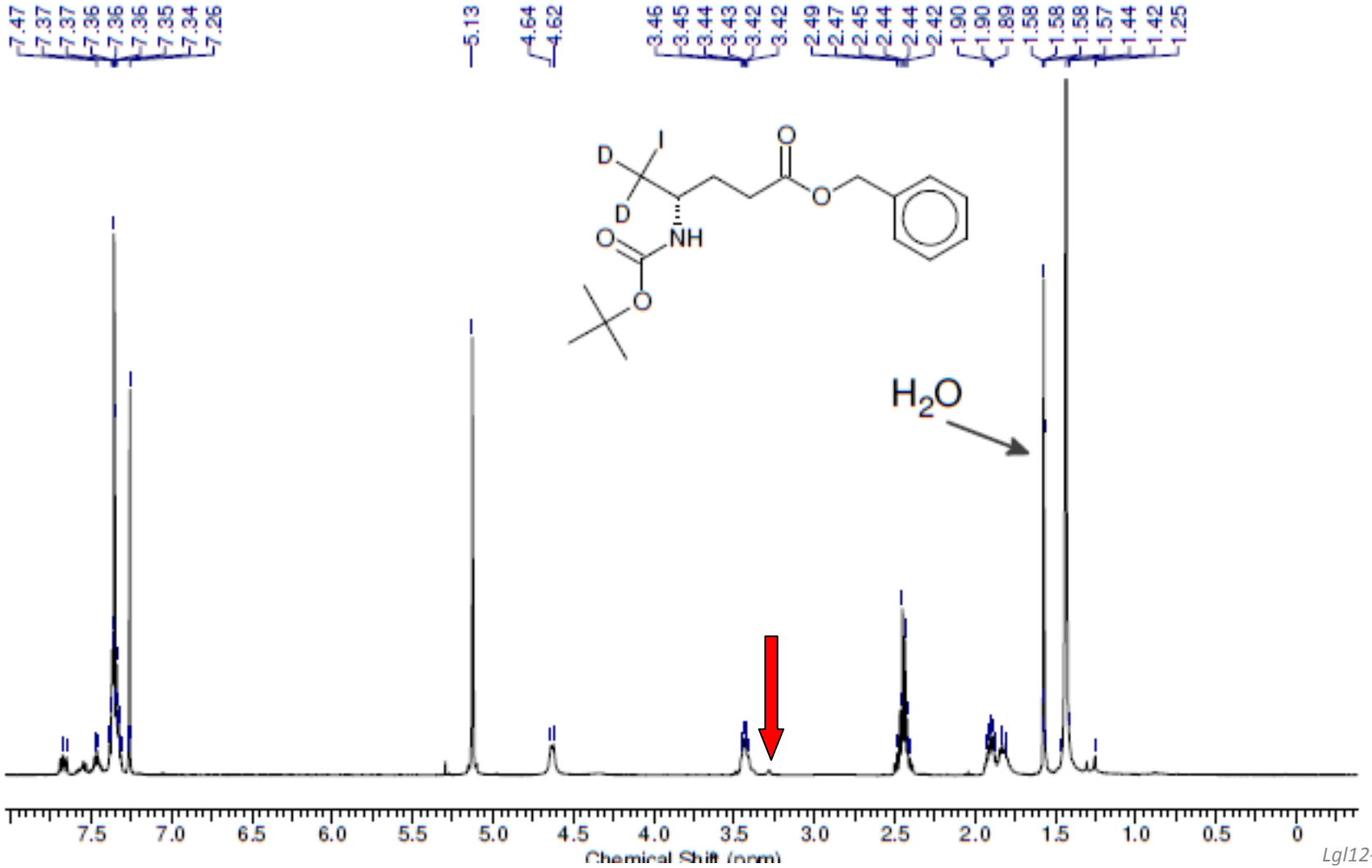
Cystathionine family

benzyl (4S)-4-[(tert-butoxycarbonyl)amino]-5-iodopentanoate (**10**):

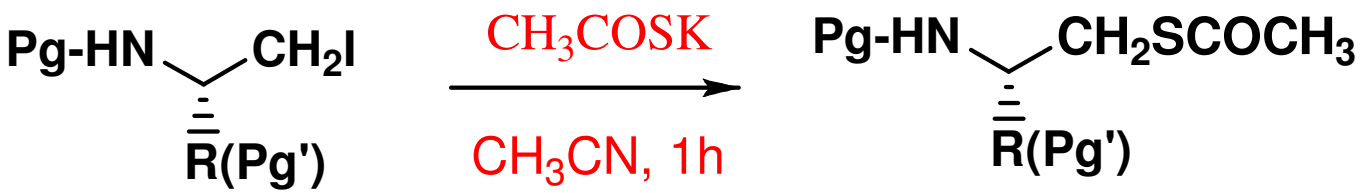


Cystathionine family

benzyl (4S)-4-[(tert-butoxycarbonyl)amino]-5-iodo(5,5-$^2H_2$)pentanoate (**10-d$_2$**):

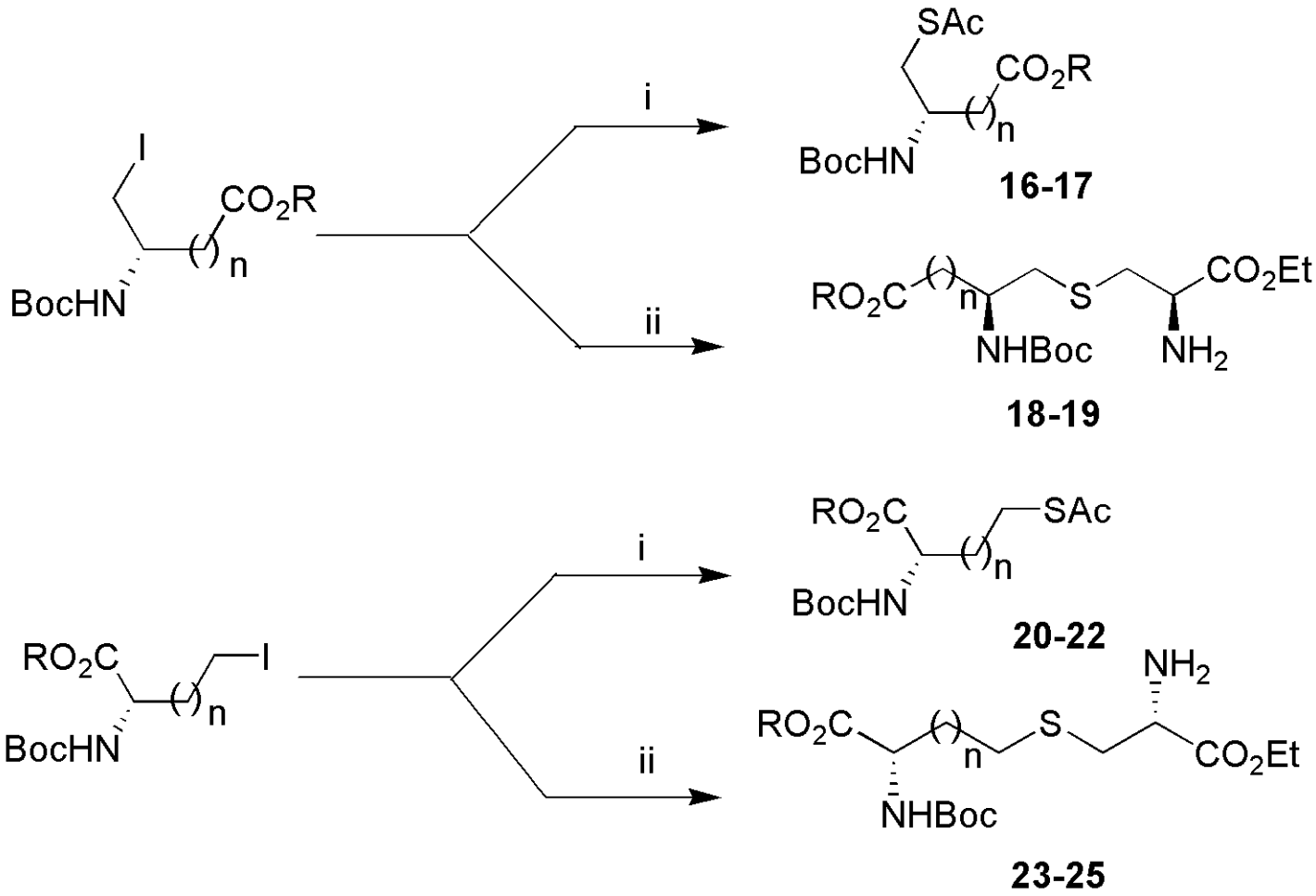


Thioalkylation: Potassium thioacetate



91-96%

Cystathionine family



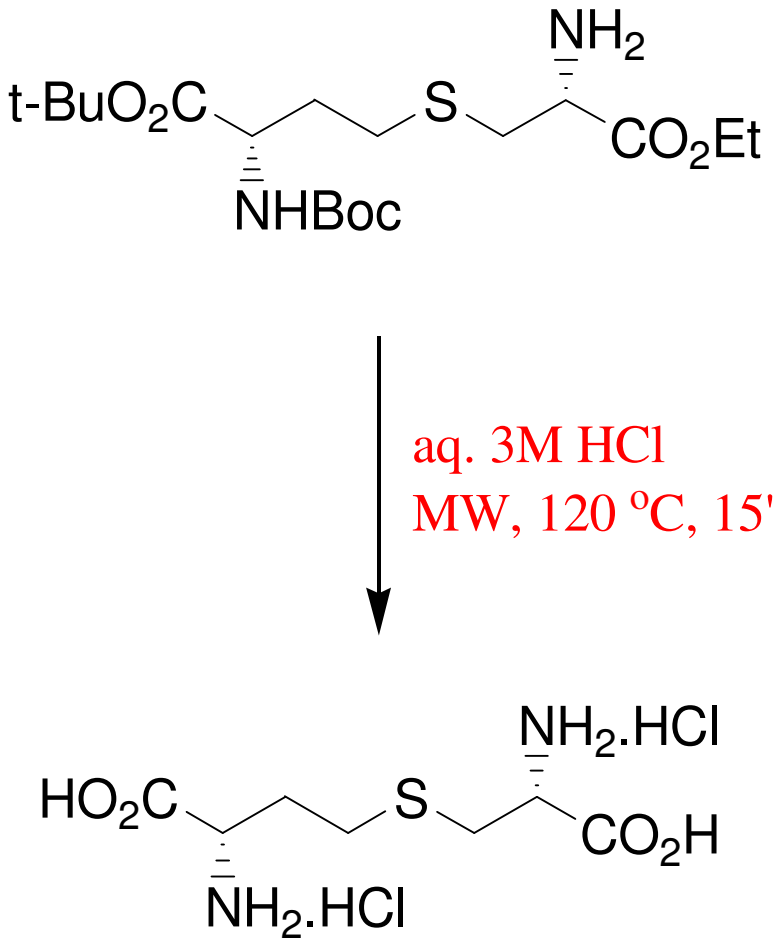
i:) AcSK, CH_3CN, r.t, 1 h; ii:) HCl·L-Cys-OEt, Cs_2CO_3, DMF, r.t., 3 h

Cystathionine family

Table: Protected Cystathionine and Homocysteine

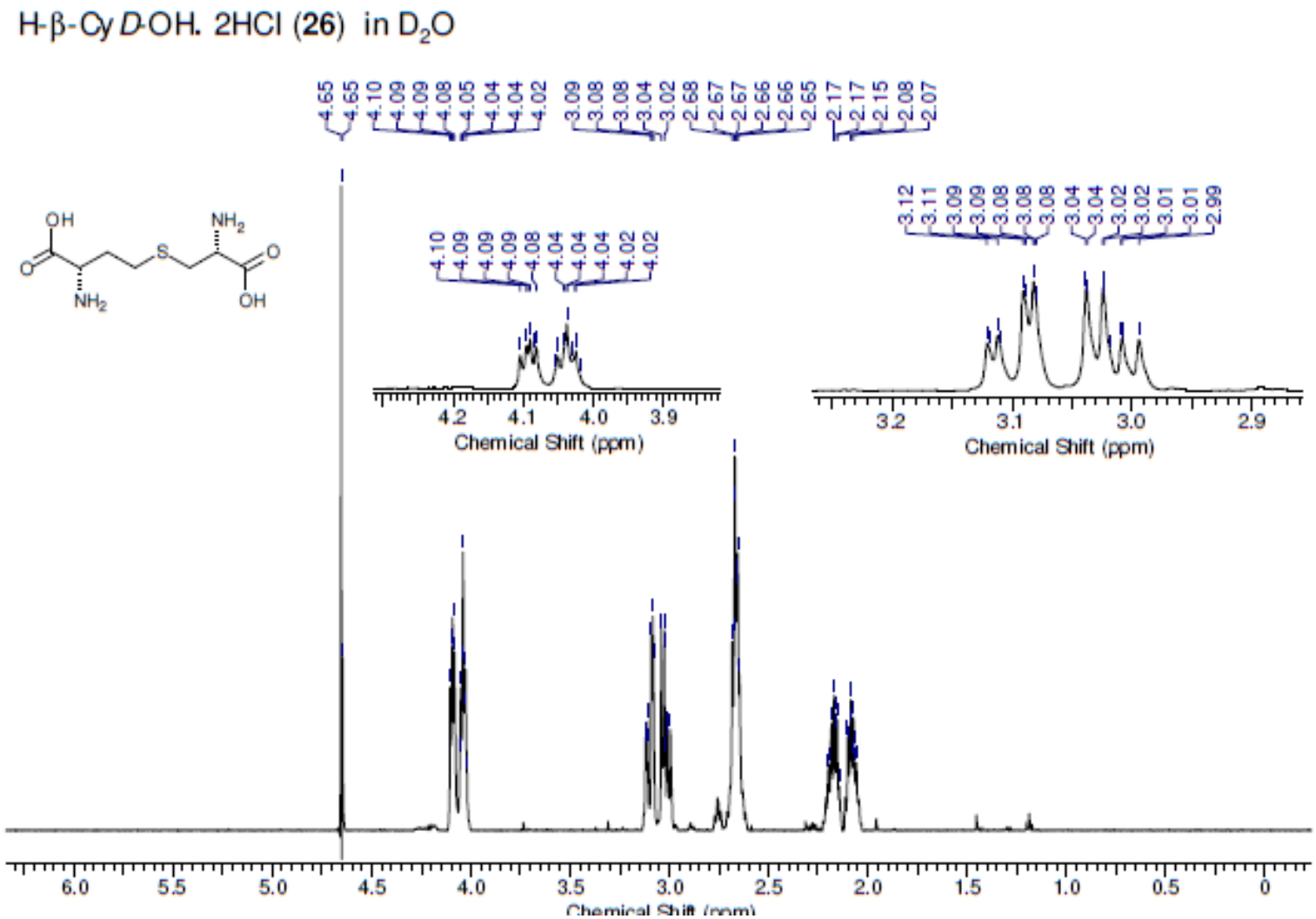
Amino Acids	n	Three-letter symbols	R	Yield (%)[a]
16	1	Boc-β^3-Cys(Ac)-OBn	Bn	95
17	2	Boc-γ^3-Cys(Ac)-OBn	Bn	93
17-d_2	2	Boc-γ^3-Cys(Ac)-OBn-d_2	Bn	96
18	1	H-α-Cy*D*(Boc,OBn)-OEt	Bn	85
19	2	H-α-Cy*E*(Boc,OBn)-OEt	Bn	88
20	1	Boc-Hcy(Ac)-OFm	Fm	92
21	1	Boc-Hcy(Ac)-OtBu	t-Bu	94
22	2	Boc-Nva(5-SAc)-OBn	Bn	91
23	1	H-β-Cy*D*(Boc,OAll)-OEt	Allyl	82
24	1	H-β-Cy*D*(Boc,OtBu)-OEt	t-Bu	87
25	2	H-γ-Cy*E*(Boc,OBn)-OEt	Bn	84

β-CyD Hydrolysis

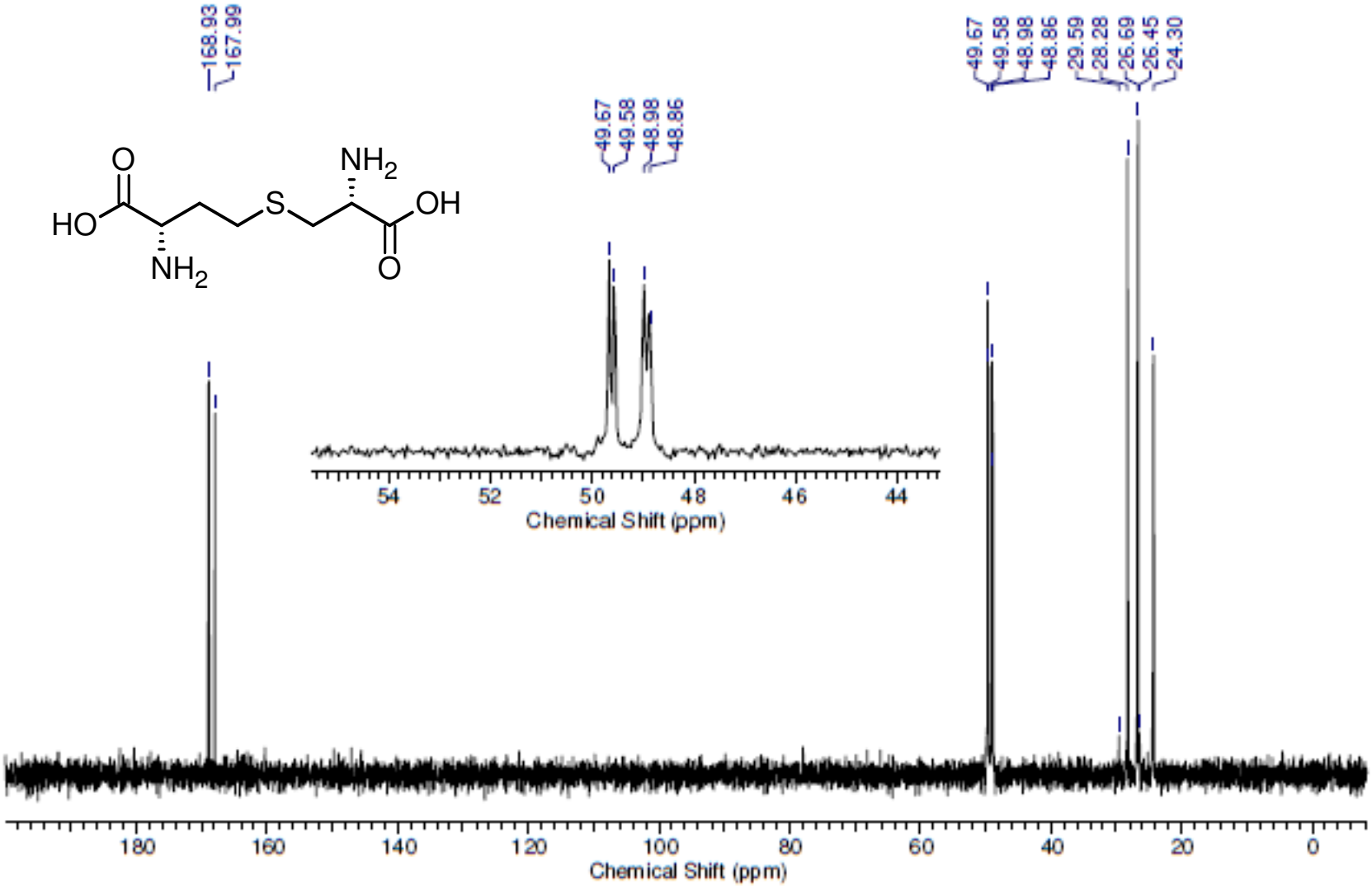


quantitative

Cystathionine family

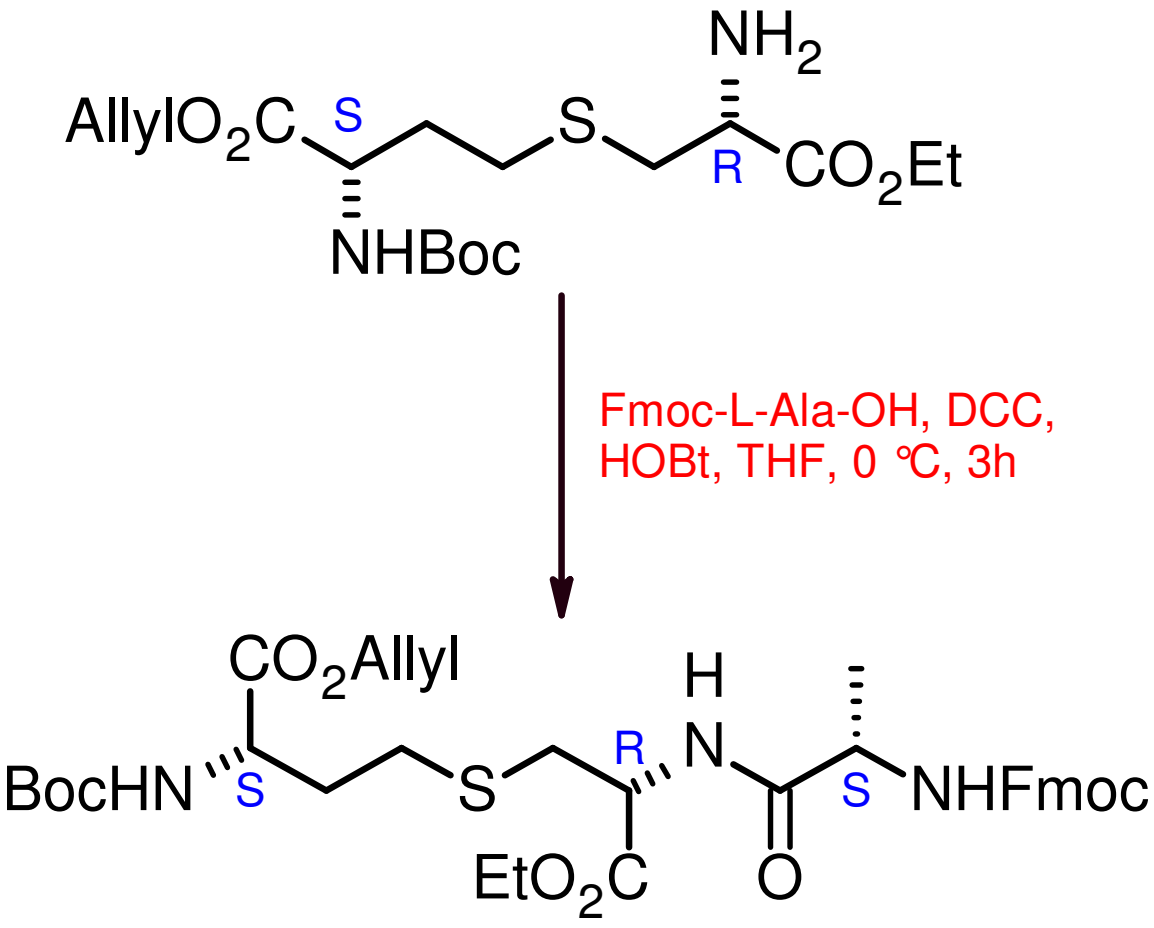


Cystathionine family



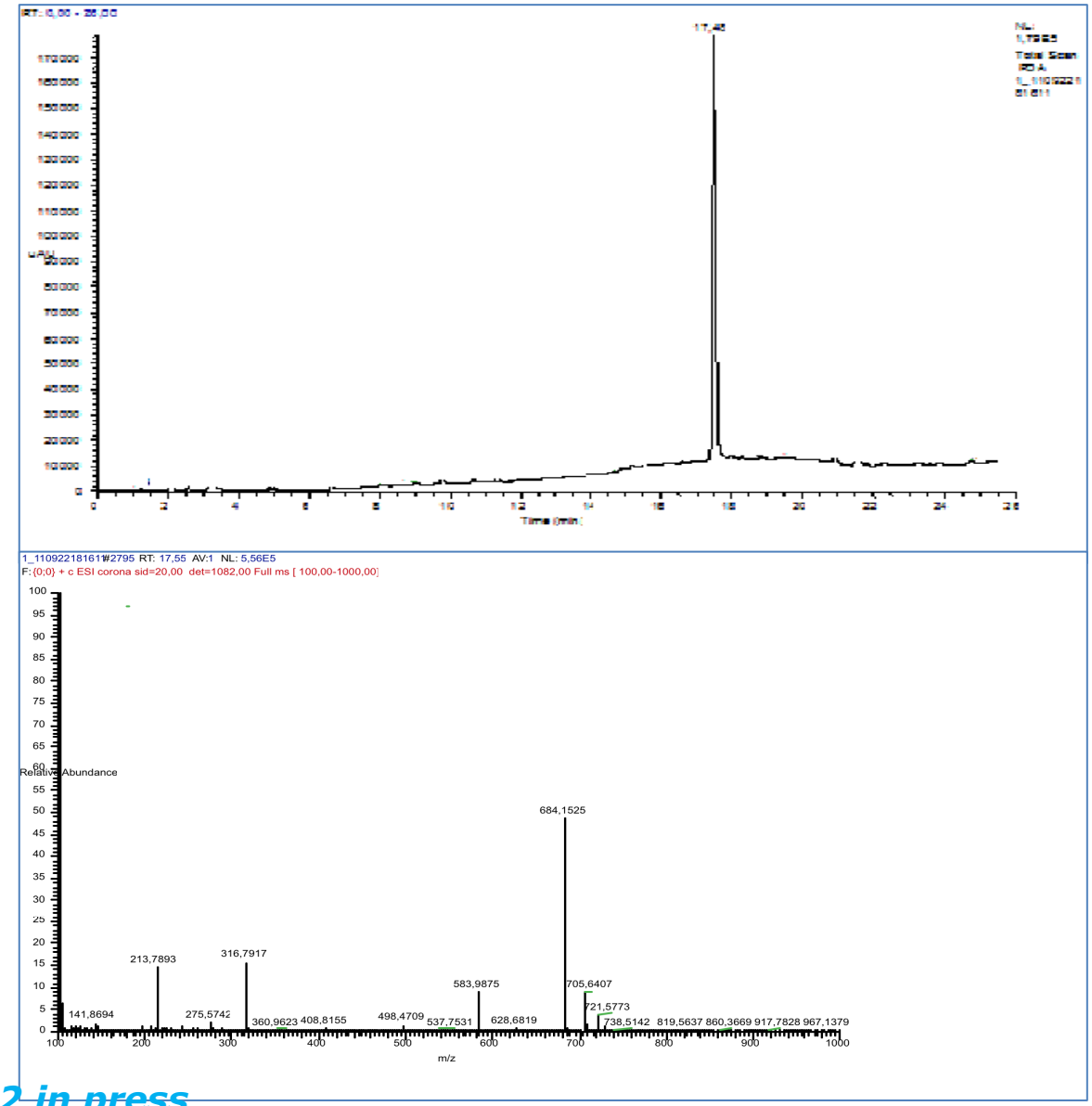
Amino Acids 2012 in press

Peptide Coupling



95%

HPLC and MS di Fmoc-Ala-β-CyD(Boc,OBn)-OEt



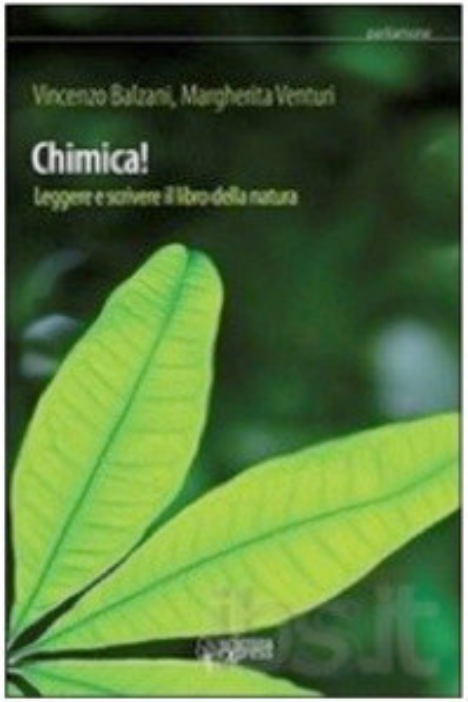
Amino Acids 2012 in press

Amino acids chemistry

Navigazione articolo
← Precedente

Recensione: “CHIMICA! Leggere e scrivere il libro della natura.”

CHIMICA! Leggere e scrivere il libro della Natura.di Vincenzo Balzani e Margherita Venturi	Ed. ScienzaExpress Collana:Parliamone. Trieste, 2012, 135p. 12 euro



Come sicuramente ricorderete Galileo sostenne ne “Il Saggiatore” che il libro della Natura era scritto in lingua matematica e i suoi caratteri erano le figure geometriche; una posizione fortemente innovativa rispetto ai canoni del suo tempo.
In questo agile libretto Balzani e Venturi, due colleghi dell’Università di Bologna che tutti noi conosciamo, fortemente impegnati nella ricerca ma anche nella divulgazione, fanno un passo ulteriore; il libro della Natura è scritto in un linguaggio chimico, dove gli atomi corrispondono alle lettere e le molecole alle parole. Si tratta di un linguaggio che ci permette non solo di leggere la Natura ma anche di scriverci, inventando nuove parole, ossia nuove molecole.
E quindi sia “Chimica!” con tanto di punto esclamativo, una esclamazione che riflette l’entusiasmo di chi comprende la incredibile potenza di questo linguaggio.

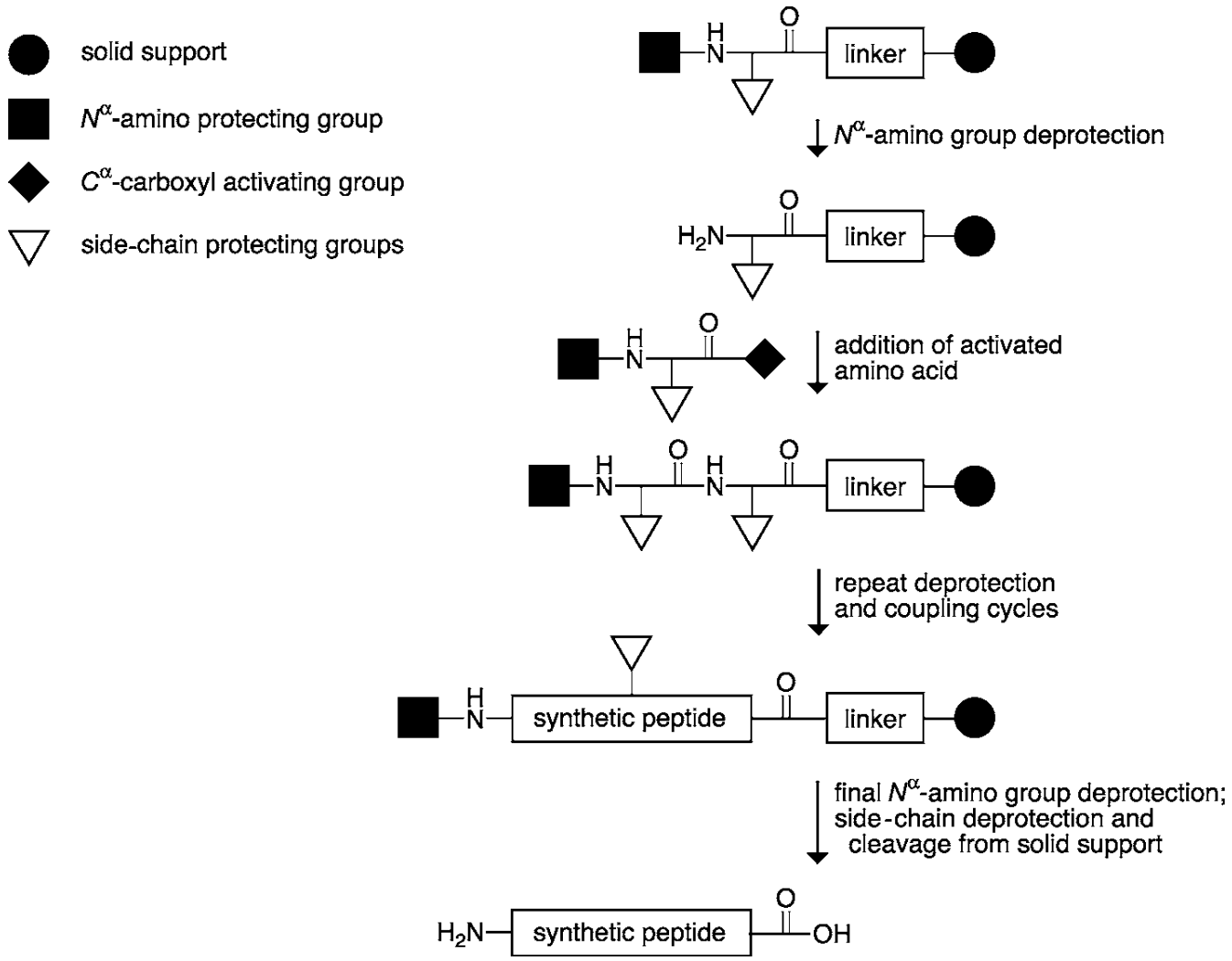
Chemical Synthesis of Protein

The chemical synthesis and semi-synthesis of proteins harbor the potential to overcome many of the disadvantages of current protein production methods (19, 29, 78). In particular, ***chemical synthesis using established solid-phase techniques*** *are rapid to effect, easily automated, and facilitate purification. Accordingly, the application of existing and emerging synthetic methods could facilitate research in all aspects of protein science.*

Chemical synthesis enables the facile incorporation of ***non-natura****l functionality into proteins. The genetic code limits the components of natural proteins to approximately 20 α-amino acids. Methods that overcome this limitation but still rely on the ribosome are similarly limited to a subset of α-amino acids and α-hydroxy acids (65, 91). In marked contrast, the non-natural functionality made available by chemical synthesis is limited only by* ***the constraints of the periodic table and the imagination of protein chemists****.*

Annu. Rev. Biophys. Biomol. Struct. 2005. 34:91–118

Chemical Synthesis of Protein



Annu. Rev. Biophys. Biomol. Struct. 2005. 34:91–118

Chemical Synthesis of Protein

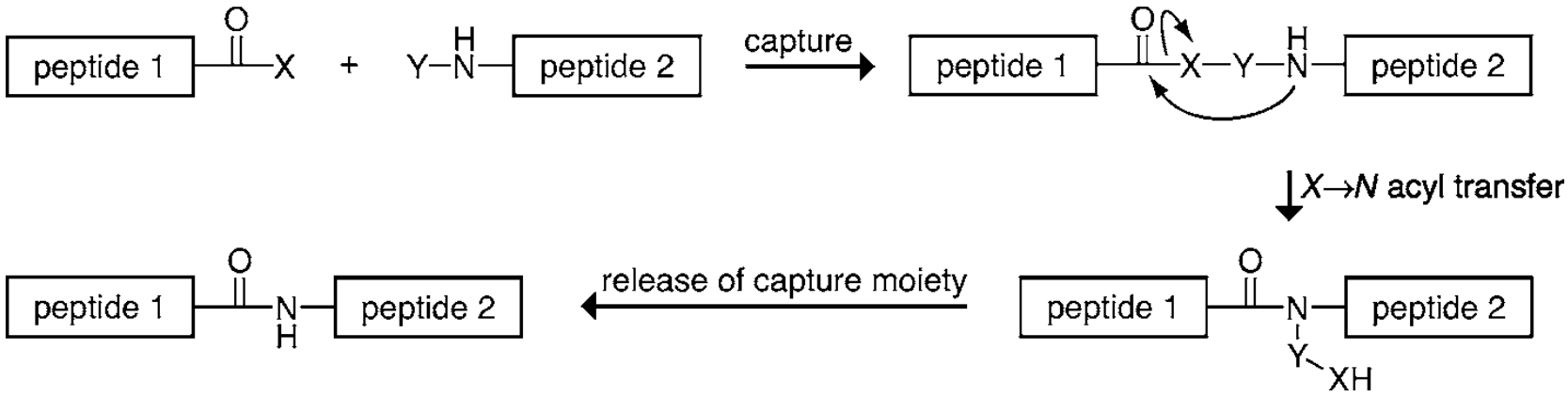
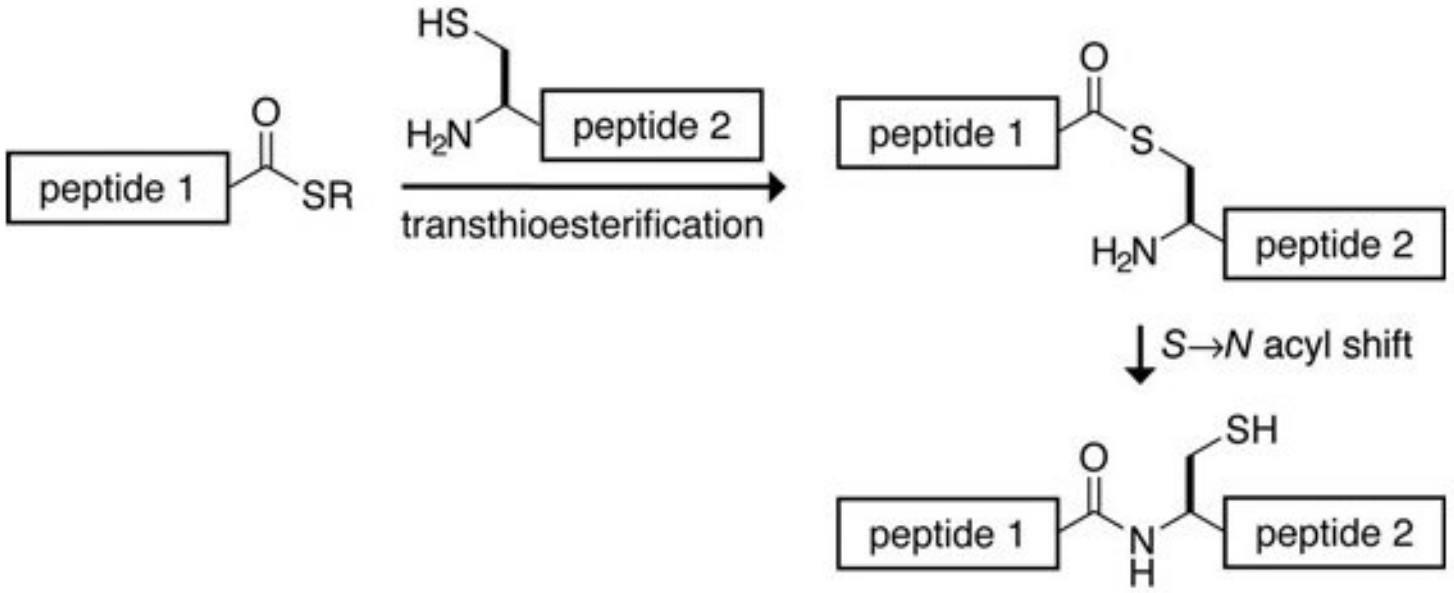


Figure 2 A general strategy for peptide ligation.

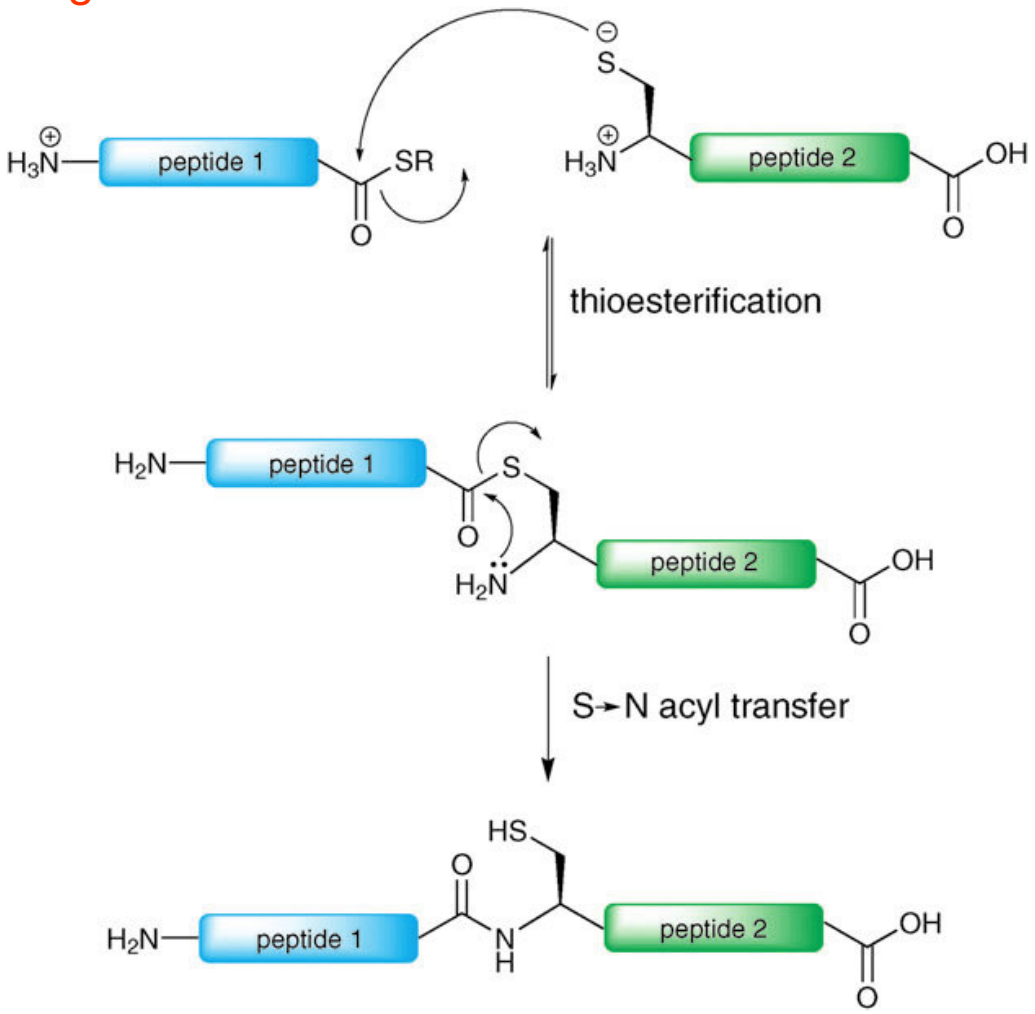
Chemical Synthesis of Protein

Native Chemical Ligation



Chemical Synthesis of Protein

Native Chemical Ligation



Scheme 1 Proposed mechanism of native chemical ligation (NCL).[21]

Chemical Synthesis of Protein

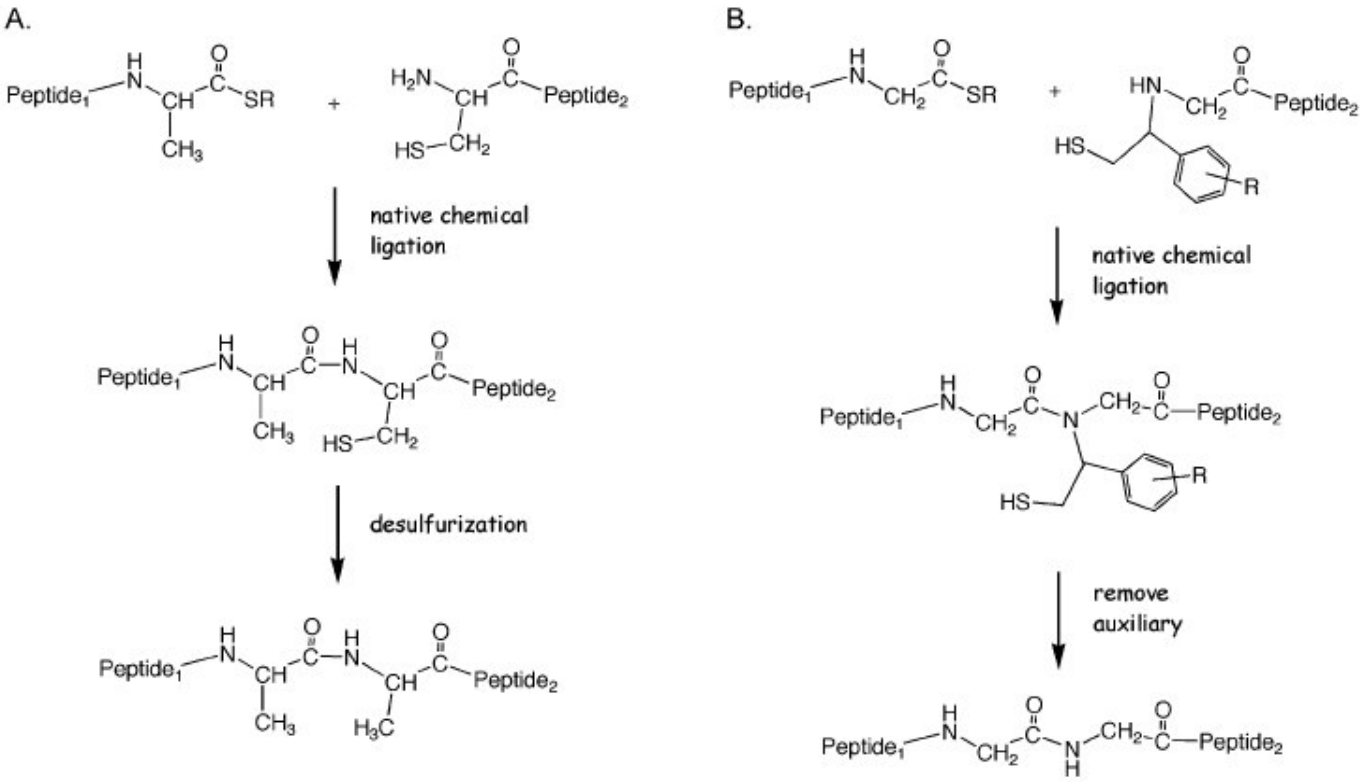
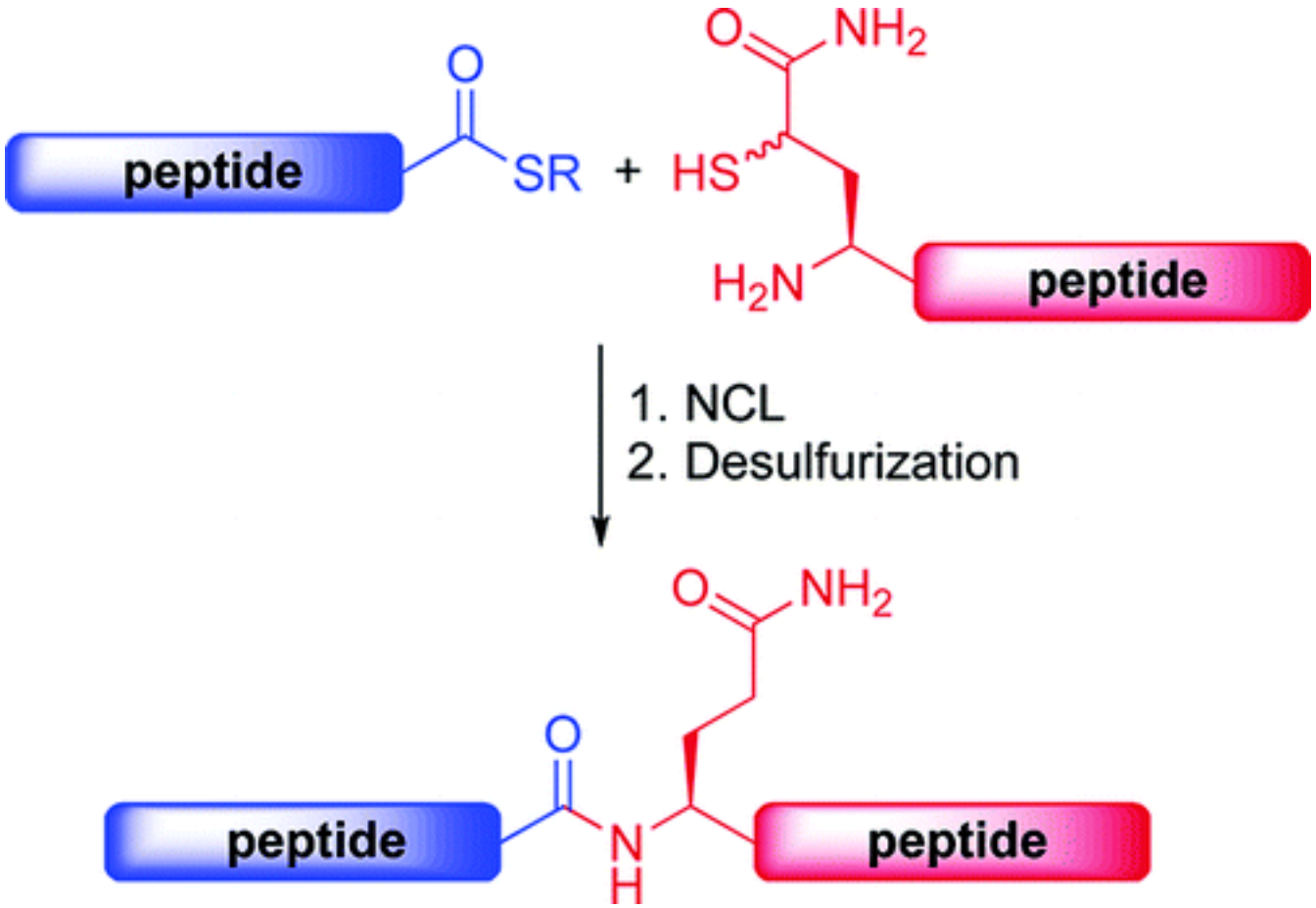


Fig. 7 Chemistries that can enable native chemical ligation at non-Cys sites. **A** After native chemical ligation, the Cys residue at the ligation site is desulfurized, forming an Xaa–Ala.[20] **B** A thiol-containing N(α) auxiliary moiety is used at the N-terminal of one peptide segment; after native chemical ligation, the auxiliary moiety is removed, *e.g.* by acidolysis (R = $(OMe)_2$).[22]

Chem. Soc. Rev., 2009, 38, 338–351

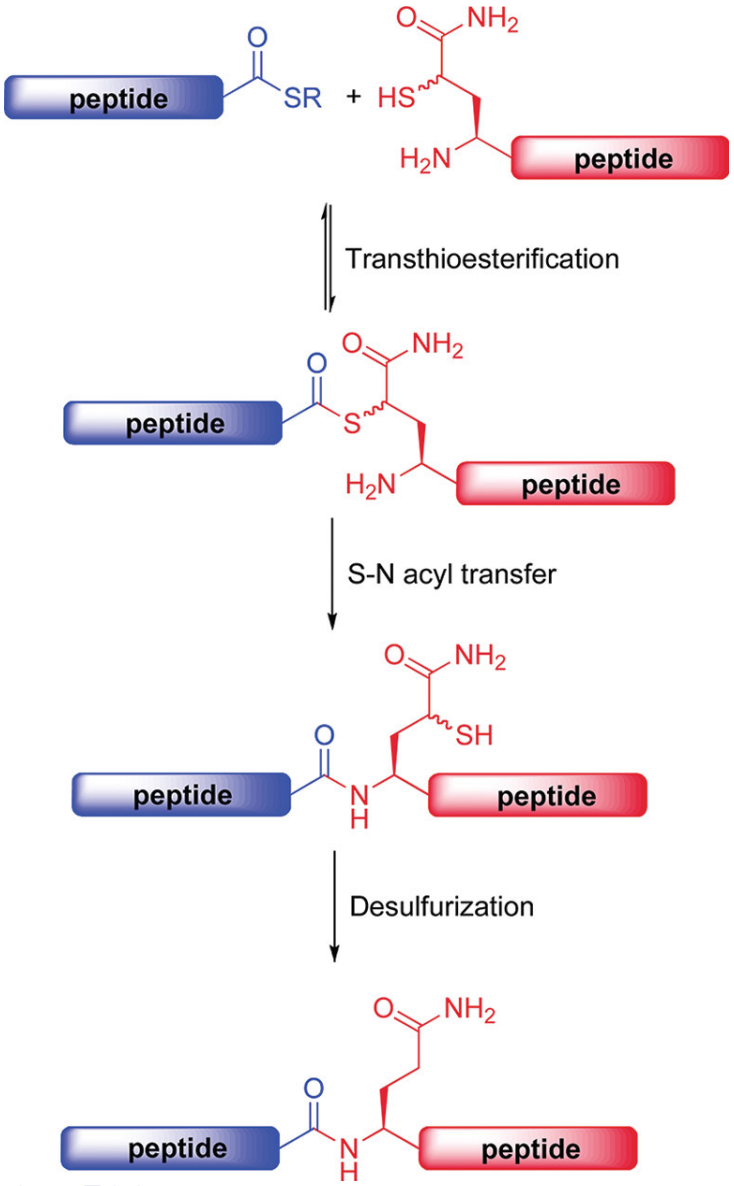
Chemical Synthesis of Protein

Native Chemical Ligation at Glutamine



Org. Lett., 2012, 14 (6), pp 1520–1523

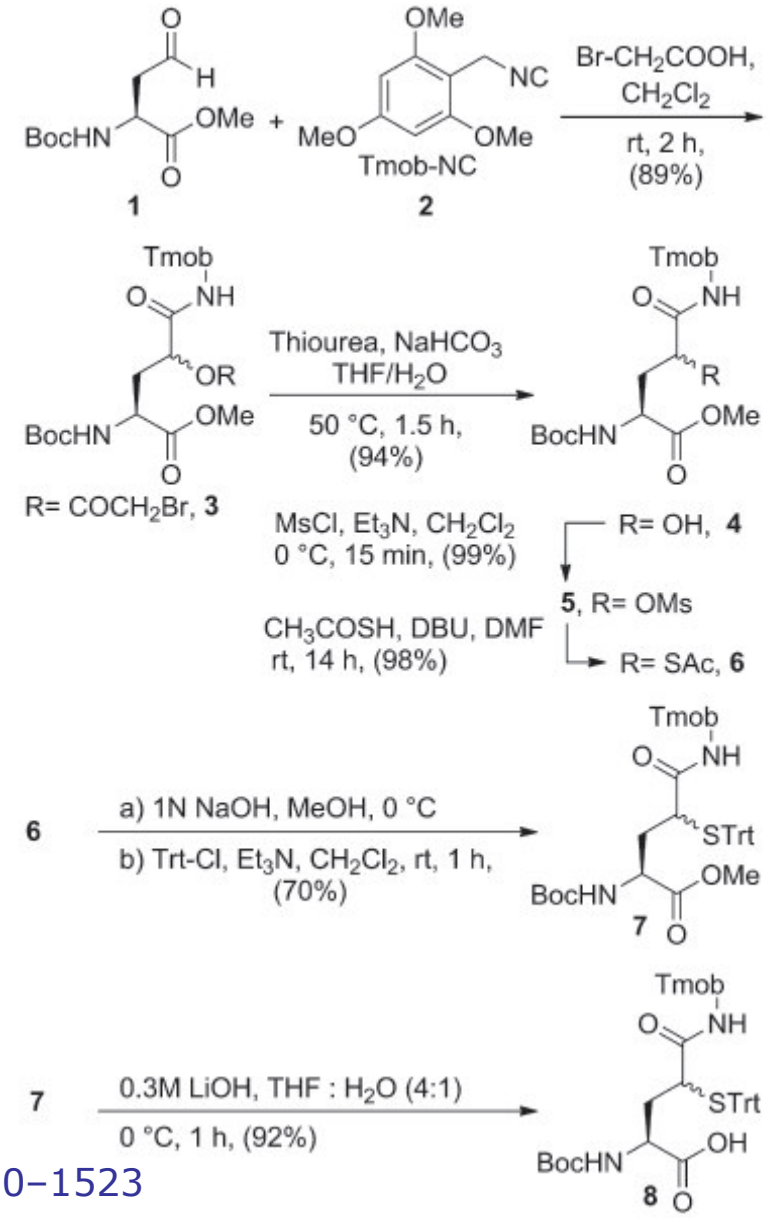
Chemical Synthesis of Protein



Org. Lett., 2012, 14 (6), pp 1520–1523

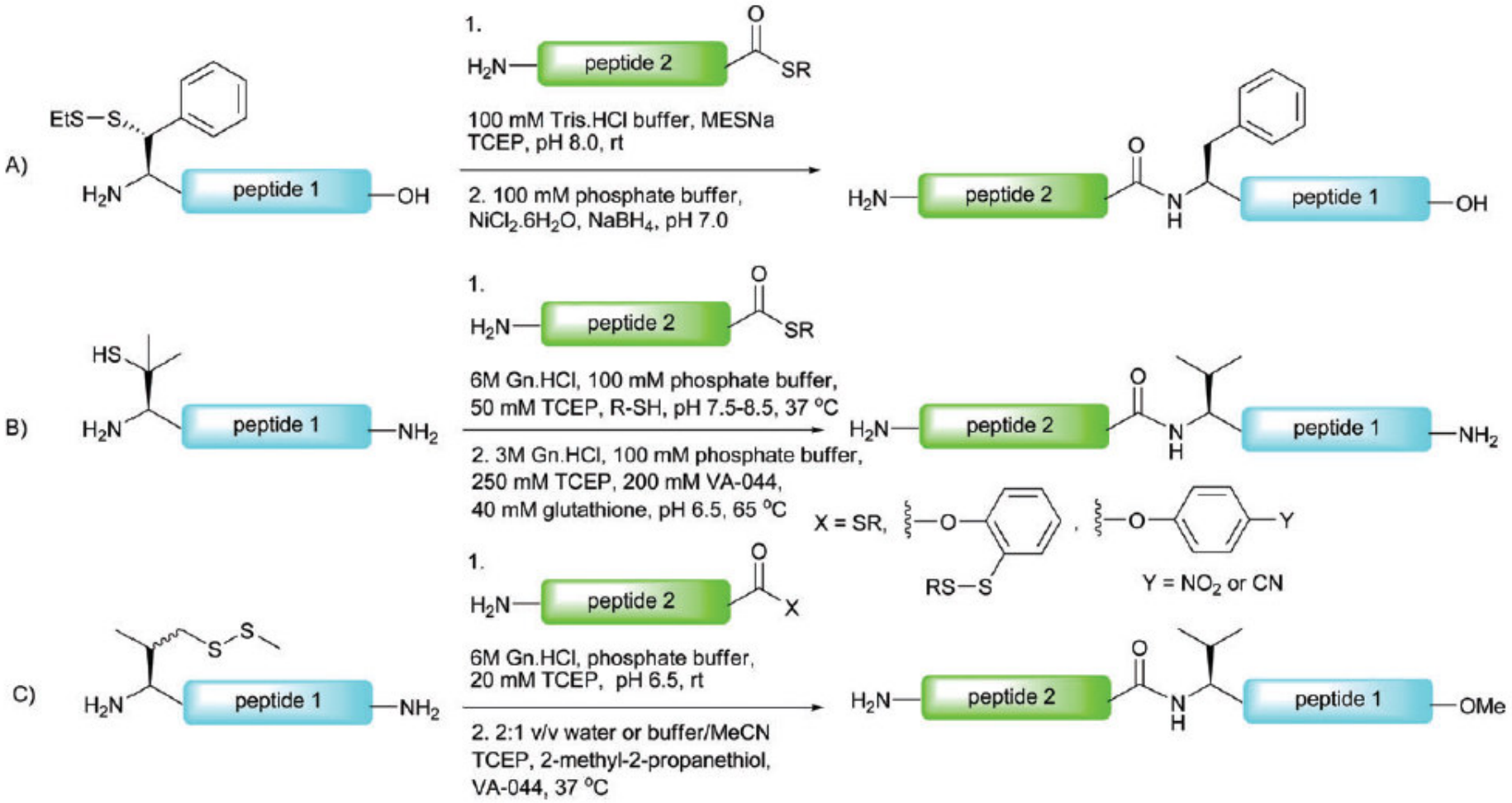
Chemical Synthesis of Protein

Scheme 2. Synthesis of γ -(*R*,*S*)-Mercapto-L-glutamine



Org. Lett., 2012, 14 (6), pp 1520–1523

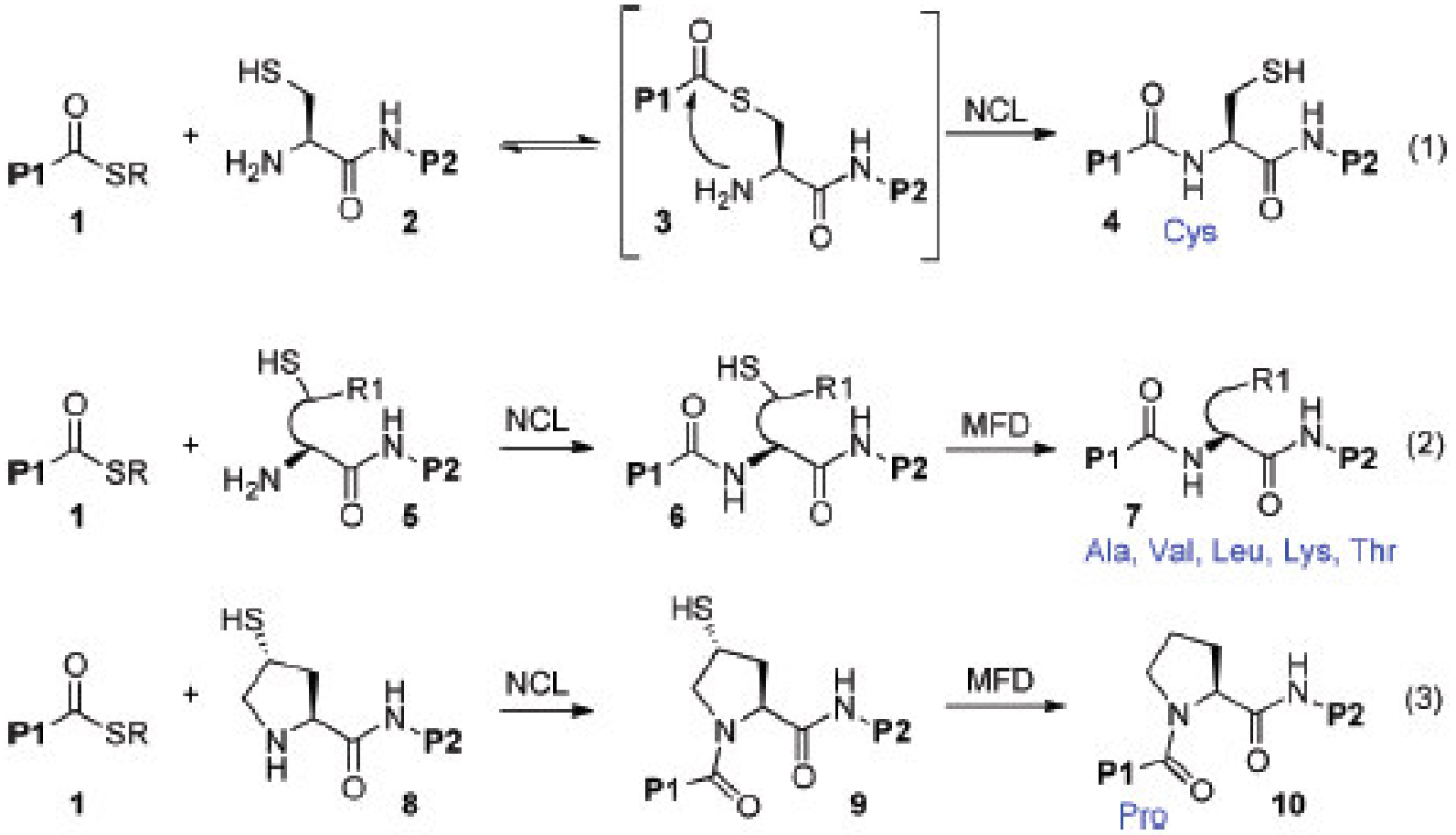
Chemical Synthesis of Protein



Scheme 19 NCL-desulfurisation at (A) phenylalanine[96] and (B) and (C) valine.[86,98]

Chemical Synthesis of Protein

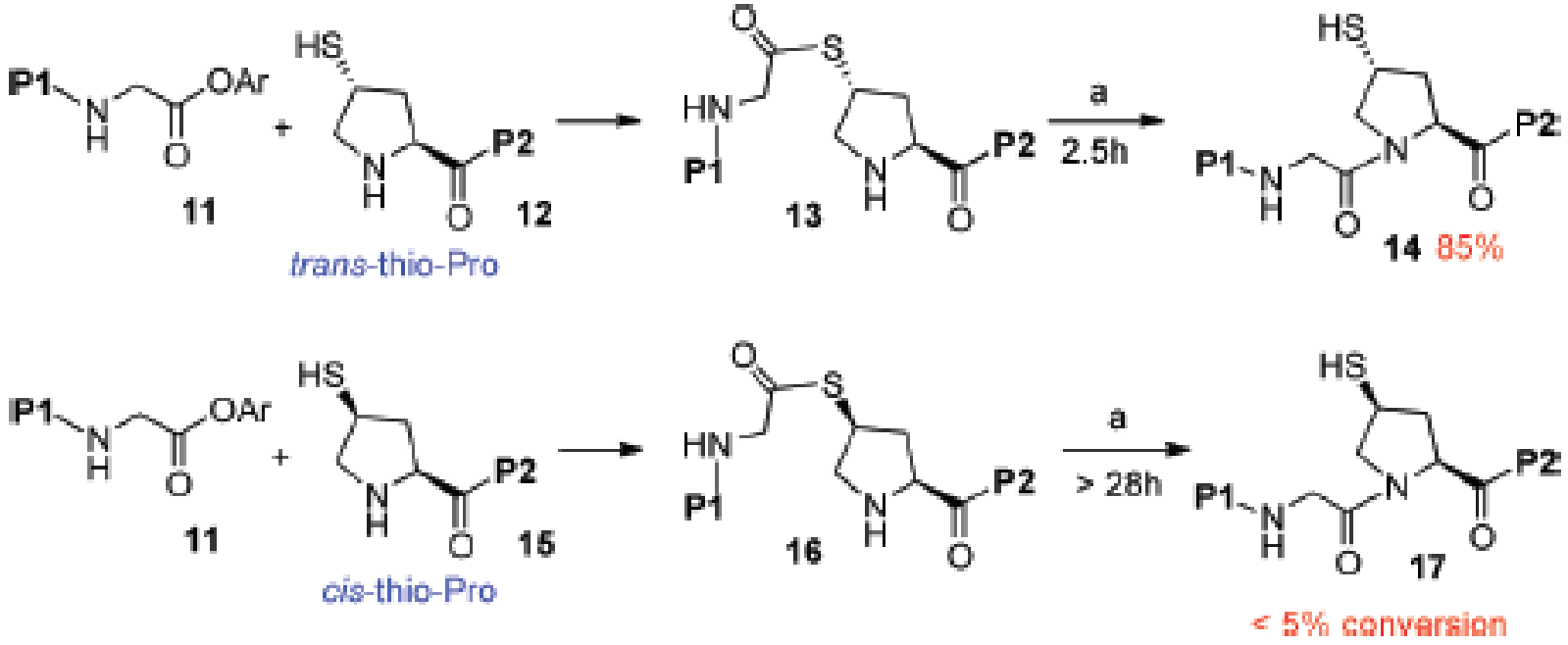
Scheme 1. Native Chemical Ligation (NCL)



J. Am. Chem. Soc. 2012, 134, 3912–3916

Chemical Synthesis of Protein

Scheme 2. Thio-Proline Ligation with Two Pro(SH) Diastereomers[a]

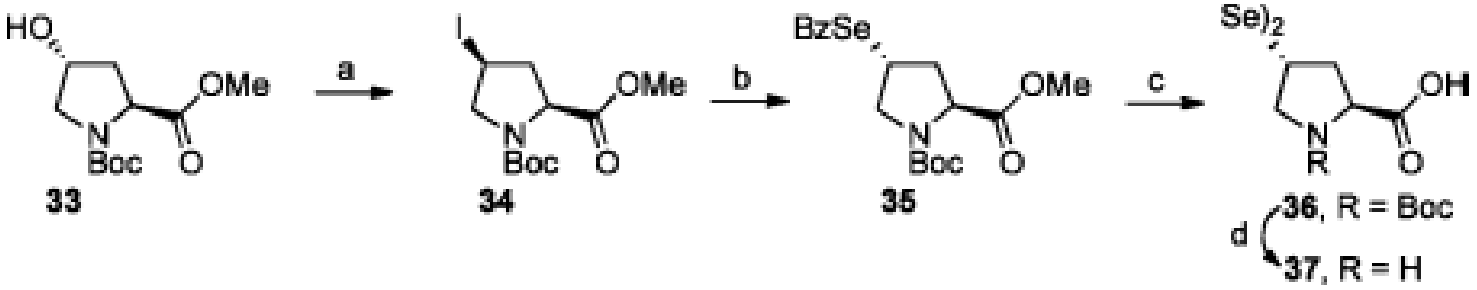


[a]Key: (a) 6 M Gn•HCl, 100 mM NaH_2PO_4, 50 mM TCEP, pH 7.5. P1: ALLVNSS–; P2: –WEPLN; Ar = 2-(ethyldithio)-phenyl; TCEP = tris(2-carboxyethyl)phosphine.

Chemical Synthesis of Protein

The first objective was to synthesize the previously unknown *trans*-selenoproline, 37.[20] Beginning with commercially available pyrrolidine 33, Mitsunobu inversion provided the *cis*-iodo proline derivative, 34, in high yield (Scheme 6).[21] Nucleophilic

Scheme 6. Synthesis of *trans*-Seleno-Pro, 37[a]

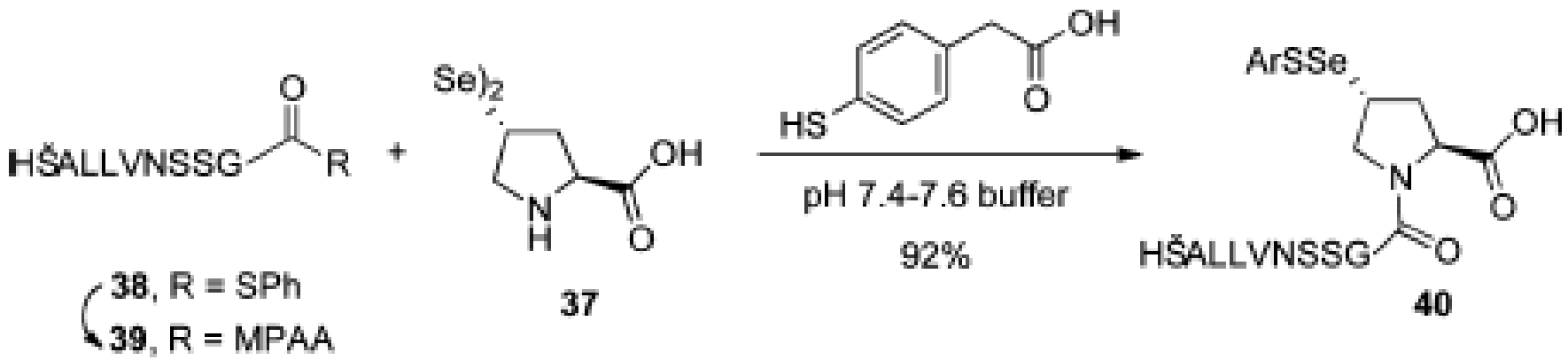


[a]Key: (a) PPh_3, DIAD, CH_3I, THF, 0 °C → 23 °C, 88–92% yield; (b) BzSeH, DIPEA, DMF, 60 °C, 84%; (c) K_2CO_3, aq. MeOH, 79%; (d) HCl/CH_2Cl_2, 95%.

J. Am. Chem. Soc. 2012, 134, 3912–3916

Chemical Synthesis of Protein

Scheme 7. Seleno-Proline Ligation between 38 and 37



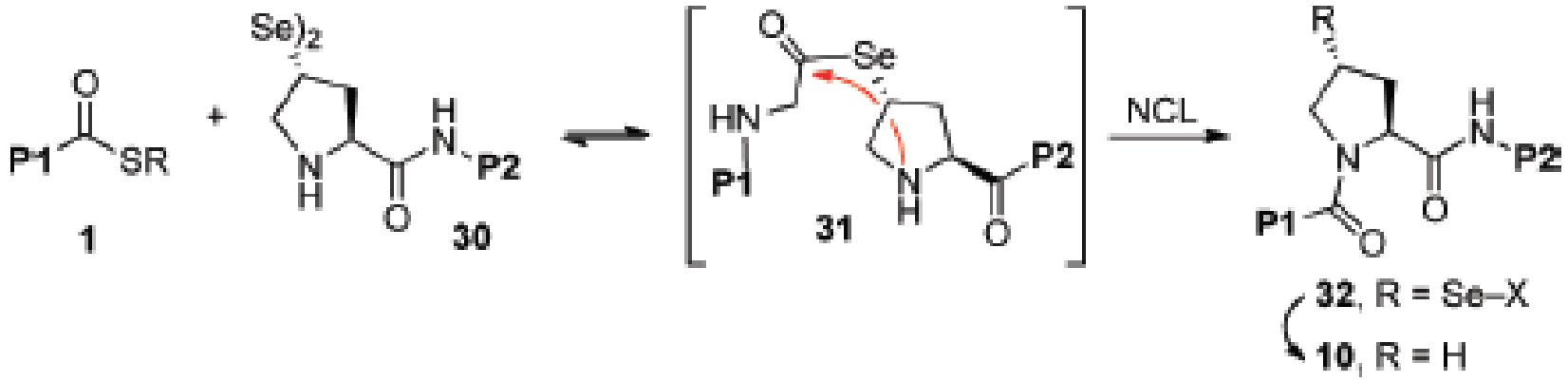
38, R = SPh
39, R = MPAA

37

40

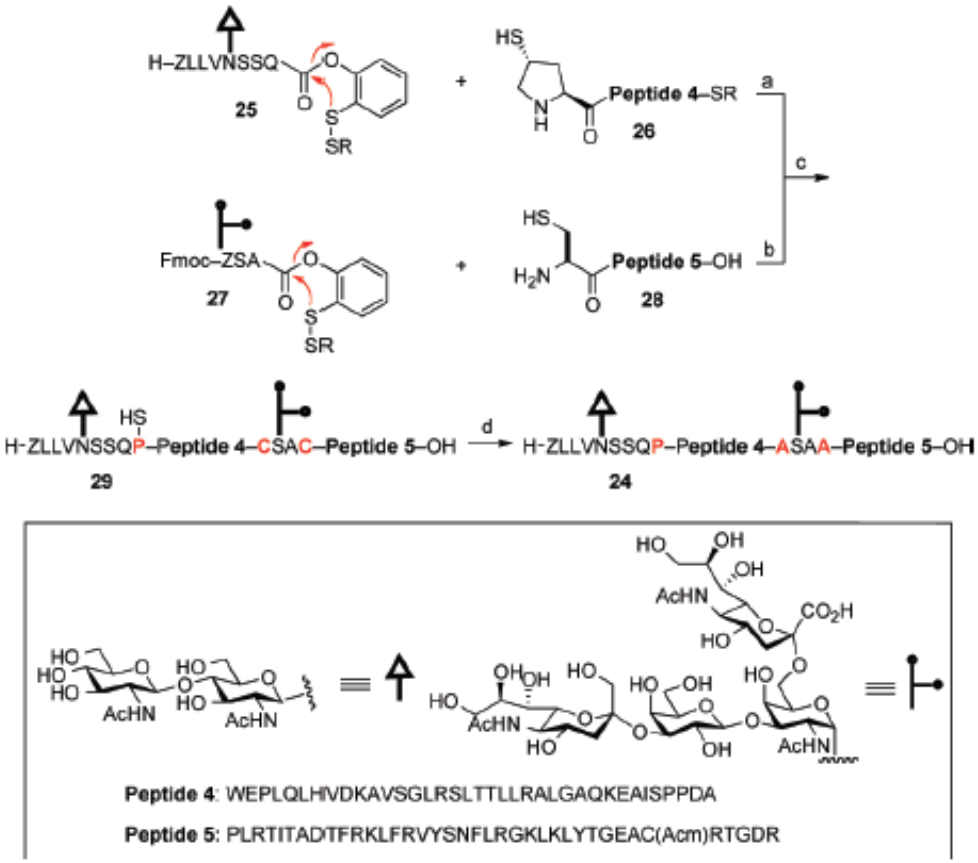
Chemical Synthesis of Protein

Scheme 5. Seleno-Proline Ligation between 1 and 30



Chemical Synthesis of Protein

Scheme 4. Synthesis of hEPO(79-166) Glycopeptide, 24[a]



[a]Key: (a) (1) 6 M Gn•HCl, 100 mM NaH_2PO_4, 50 mM TCEP, pH 7.5, 67%; (2) piperidine, DMSO, 61%; (3) 0.2 M $MeONH_2$, 60%; (b) 6 M Gn•HCl, 100 mM NaH_2PO_4, 50 mM TCEP, pH 7.5, 23%; (c) 6 M Gn•HCl, 100 mM NaH_2PO_4, 50 mM TCEP, 200 mM MPAA, pH 7.8, 40%; (d) TCEP, VA-044, *t*BuSH. Ar = 2-(ethyldithio)-phenyl; R = $CH_2CH_2CO_2Et$; VA-044 = 2,2′-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride.