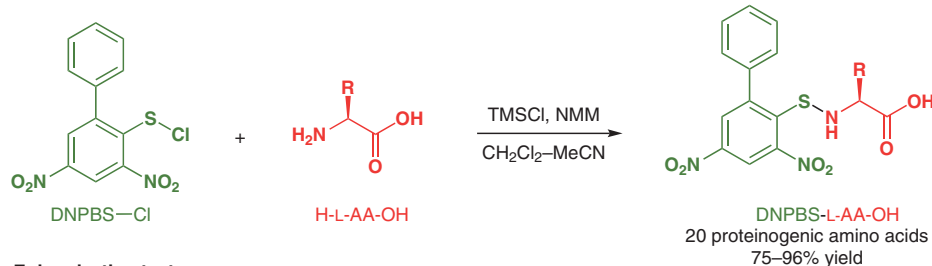
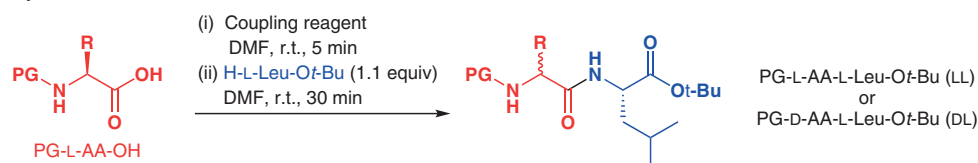


Thiol-Labile Amino Protecting Group that Suppresses the Epimerization in Peptide Synthesis

Synthesis of α -amino acids:



Epimerization test:



Coupling reagent	PG-L-Cys(Try)-OH		PG-L-His(Try)-OH		PG-L-Ser(Ot-Bu)-OH	
	Fmoc (LL/DL)	DNPBS (LL/DL)	Fmoc (LL/DL)	DNPBS (LL/DL)	Fmoc (LL/DL)	DNPBS (LL/DL)
DIC (1.1 equiv) Oxyma (1.1 equiv)	100:0	100:0	98.2:1.8	100:0	100:0	100:0
DIC (1.1 equiv) Oxyma (1.1 equiv) 55 °C	100:0	100:0	69.0:1.8	31:0	100:0	100:0
EDCI (1.1 equiv) HOBT (0.2 equiv)	98.3:1.7	100:0	51.8:48.2	100:0	100:0	100:0
PyBop (1.1 equiv) DIPEA (2 equiv)	96.7:3.3	100:0	98.0:2.0	100:0	100:0	100:0
HBTU (1.1 equiv) DIPEA (2 equiv)	96.2:3.8	100:0	96.9:3.1	100:0	100:0	100:0
HATU (1.1 equiv) NMM (2 equiv)	81.0:19.0	100:0	86.8:13.2	100:0	97.3:2.7	100:0

Significance: In peptide synthesis, epimerization is a long-standing problem, which is why various researchers have conducted investigations to suppress it. The authors have developed a thiol-labile amino protecting group that effectively suppresses the epimerization.

Comment: DNPBS-protected amino acids were easily prepared in good yields for all proteinogenic amino acids. In the peptide coupling reaction, the use of DNPBS-protected amino acids suppressed epimerization more effectively than the use of carbamate-protected amino acids. This method was also applied to solid-phase peptide synthesis.