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1-*tert*-Butoxy-2-*tert*-butoxycarbonyl-1,2-dihydroisoquinoline: A Novel and Chemoselective *tert*-Butoxycarbonylation Reagent
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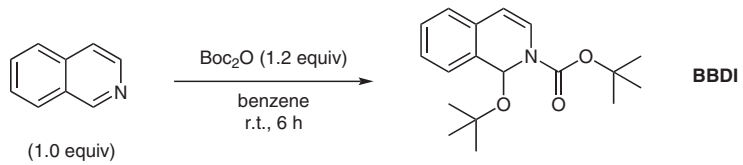
A Novel Reagent for *tert*-Butoxycarbonylation of Amino Acids

Category
Peptide Chemistry

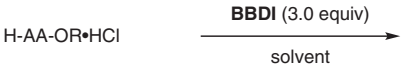
Key words
butoxycarbonylation
amino acids
chemoselectivity
isoquinolines

Sythesis of 1-*tert*-butoxy-2-*tert*-butoxycarbonyl-1,2-dihydroisoquinoline (BBDI):



(1.0 equiv) — **BBDI** — 92% yield

Examples:



Substrate	Method[a]	Product	Isolated yield (%)
H-Met-OMe•HCl	A	Boc-Met-OMe	93
H-Met-OMe•HCl	B	Boc-Met-OMe	95
H-Ala-OEt•HCl	B	Boc-Ala-OEt	87
H-Leu-OEt•HCl	B	Boc-Leu-OEt	91
H-Val-OMe•HCl	A	Boc-Val-OMe	86
H-Phe-OMe•HCl	A	Boc-Phe-OMe	97
H-Pro-OMe•HCl	A	Boc-Pro-OMe	98
H-Glu(OEt)-OEt•HCl	B	Boc-Glu(OEt)-OEt	98
H-Ser-OMe•HCl	A	Boc-Ser-OMe	92
H-Cys-OMe•HCl	A	Boc-Cys-OMe	87
H-Tyr-OMe•HCl	A	Boc-Tyr-OMe	76[b]

[a] Method A: 1,2-dimethoxyethane, r.t., overnight; method B: Et_2O, reflux, overnight. [b] Small amount of Boc-Tyr(Boc)-OMe was also obtained.

Significance: Boc-protected amino acids are important because of their good resistance in peptide synthesis. The authors developed (BBDI) as an alternative to the conventional *tert*-butoxycarbonylating reagent di-*tert*-butyl dicarbonate for the synthesis of Boc-protected α-amino acids.

Comment: With the *tert*-butoxycarbonylating reagent BBDI, various Boc-protected α-amino acids can be synthesized from amino acid ester hydrochlorides in excellent yields.

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