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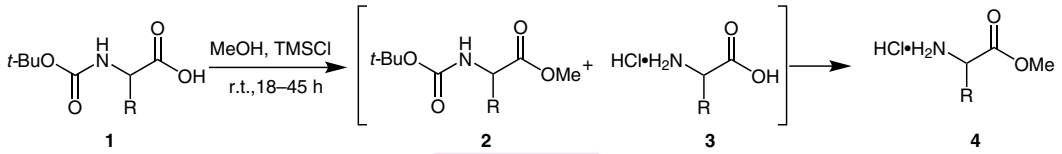
A Facile Method for the Transformation of *N*-(*tert*-Butoxycarbonyl) α-Amino Acids to *N*-Unprotected α-Amino Methyl Esters
J. Org. Chem. **1999**, *64*, 9294–9296, DOI: 10.1021/jo990311w.

Synthesis of N-Unprotected α-Amino Acid Methyl Esters



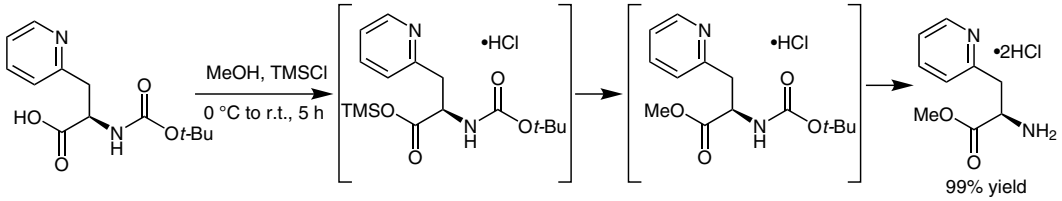
1 2 3 4

Substrate scope

Entry	Substrate	R	time (h)	Product	% ee[b]	yield (%)[a]
1	(*S*)-**1a**	$PhCH_2$	19	(*S*)-**4a**	>99.9	94
2	(*R*)-**1a**	$PhCH_2$	19	(*R*)-**4a**	>99.9	96
3	(*S*)-**1b**	4-$MeOC_6H_4CH_2$	18	(*S*)-**4b**	98.2	95
4	(*R*)-**1b**	4-$MeOC_6H_4CH_2$	22	(*R*)-**4b**	99.7	90
5	(*S*)-**1c**	4-$HOC_6H_4CH_2$	21	(*S*)-**4c**	>99.9	93
6	(*R*)-**1d**	4-$FC_6H_4CH_2$	24	(*R*)-**4d**	>99.9	97
7	(*S*)-**1e**	Me	18	(*S*)-**4e**	>99.9[c]	91
8	(*R*)-**1f**	Ph	45	(*R*)-**4f**	97.4	91

[a]Isolated yield after crystallization. [b]ee was determined by using chiral HPLC. [c]*N*-Cbz derivative.

Synthesis of (*R*)-3-(3-pyridyl)alanine methyl ester dihydrochloride



99% yield

Significance: N-Unprotected α-amino acid methyl esters play a crucial role in synthetic organic chemistry, particularly in peptide drug discovery. In 1999, Chen and co-workers developed a simple and straightforward one-pot method for the synthesis of N-unprotected α-amino acid methyl esters from *N*-(Boc)-protected α-amino acids.

Comment: The transformation of *N*-Boc protected α-amino acids into N-unprotected α-amino acid methyl esters mediated by TMSCl and MeOH proceeded smoothly and delivered the desired products in high yields and with excellent enantioselectivities. This method does not require column chromatography for the purification of the products.

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Peptide Chemistry

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esterification
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