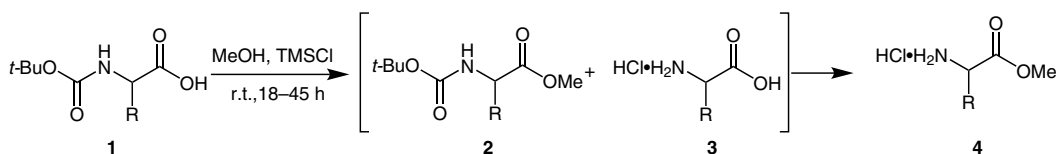


B.-C. CHEN*, A. P. SKOUMBOURDIS, P. GUO, M. S. BEDNARZ, O. R. KOCY, J. E. SUNDEEN, G. D. VITE (BRISTOL-MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE, PRINCETON, USA)

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

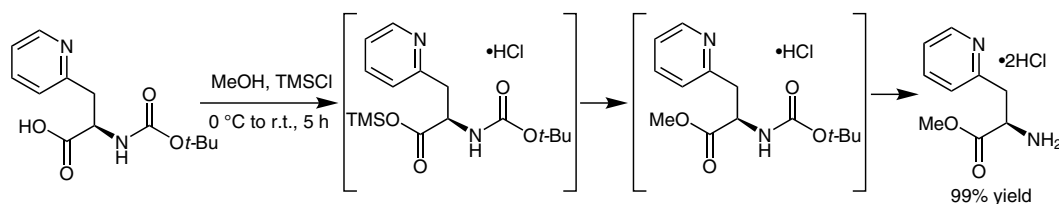


Substrate scope

Entry	Substrate	R	time (h)	Product	% ee ^b	yield (%) ^a
1	(<i>S</i>)- 1a	PhCH ₂	19	(<i>S</i>)- 4a	>99.9	94
2	(<i>R</i>)- 1a	PhCH ₂	19	(<i>R</i>)- 4a	>99.9	96
3	(<i>S</i>)- 1b	4-MeOC ₆ H ₄ CH ₂	18	(<i>S</i>)- 4b	98.2	95
4	(<i>R</i>)- 1b	4-MeOC ₆ H ₄ CH ₂	22	(<i>R</i>)- 4b	99.7	90
5	(<i>S</i>)- 1c	4-HOC ₆ H ₄ CH ₂	21	(<i>S</i>)- 4c	>99.9	93
6	(<i>R</i>)- 1d	4-FC ₆ H ₄ CH ₂	24	(<i>R</i>)- 4d	>99.9	97
7	(<i>S</i>)- 1e	Me	18	(<i>S</i>)- 4e	>99.9 ^c	91
8	(<i>R</i>)- 1f	Ph	45	(<i>R</i>)- 4f	97.4	91

^aIsolated yield after crystallization. ^bee was determined by using chiral HPLC. ^c*N*-Cbz derivative.

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



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.

SYNFACTS Contributors: Hisashi Yamamoto, Isai Ramakrishna
 Synfacts 2021, 17(07), 0833 Published online: 17.06.2021
 DOI: 10.1055/s-0040-1706223; Reg-No.: H04821SF

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Category

Peptide Chemistry

Key words

amino acid methyl esters

esterification

amino acids

Synfact
 Classic

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