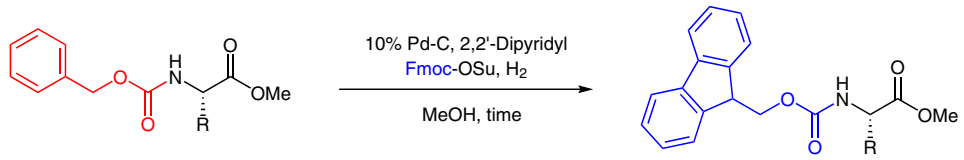
V. DZUBECK, J. P. SCHNEIDER* (UNIVERSITY OF DELAWARE, NEWARK, USA)

One-Pot Conversion of Benzyl Carbamates into Fluorenylmethyl Carbamates
Tetrahedron Lett. **2000**, *41*, 9953–9956, DOI: 10.1016/S0040-4039(00)01811-6.

Synthesis of N^a-Fmoc-Protected Amino Acid Esters and Peptides



Substrate scope

Entry	Substrate	Product	Time (h)	Yield (%)	% ee[a]
1	N^{α}-Cbz-Ala-OMe	N^{α}-Fmoc-Ala-OMe	3.5	90	≥99
2	N^{α}-Cbz-Phe-OMe	N^{α}-Fmoc-Phe-OMe	15.0	88	≥99
3	N^{α}-Cbz-Asp(*t*-Bu)-OMe	N^{α}-Fmoc-Asp(*t*-Bu)-OMe	4.5	89	–
4	N^{α}-Cbz-Leu-OMe	N^{α}-Fmoc-Leu-OMe	15.0	89	≥99
5	N^{α}-Cbz-Pro-OMe	N^{α}-Fmoc-Pro-OMe	3.5	79	≥99
6	N^{α}-Cbz-Lys(Boc)-OMe	N^{α}-Fmoc-Lys(Boc)-OMe	7.0	88	–
7	N^{α}-Cbz-Gly-Gly-OMe	N^{α}-Fmoc-Gly-Gly-OMe	4.0	84	–
8	N^{α}-Cbz-Thr(*t*-Bu)-Ala-OMe	N^{α}-Fmoc-Thr(*t*-Bu)-Ala-OMe	4.0	83	≥99[b]

[a]% ee values were determined by chiral HPLC using either Chiralcel OD or Chiralpak AS columns (0.46×25 cm) using hexane and isopropanol as eluent at 20 °C and 1 mL/min flow-rate, at 280 nm. Fmoc-D-products were synthesized and used as standards to demonstrate that resolution of possible enantiomers was achieved with the HPLC conditions employed.
[b]% ee value determined via RP-HPLC using a Vydac C4 peptide, protein column with water and 90% acetonitrile in water each containing 0.1% TFA as elution solvents.

Significance: Since the development of solid-phase peptide synthesis, the 9-fluorenylmethoxycarbonyl (Fmoc) group has been the protecting group of choice for obtaining peptides in high purities. Consequently, the peptide-chemistry industry has been searching for new methods to synthesize Fmoc-protected amino acids and peptides. In 2000, Schneider and Dzubeck developed a simple one-pot protocol for the conversion of *N*-benzyloxycarbonyl (CBz)-protected amino acid esters or peptides into the corresponding *N*-Fmoc-protected compounds.

Comment: Conversion of *N*-Cbz-protected amino acid esters or peptides into the corresponding *N*-Fmoc-protected derivatives proceeds smoothly through hydrogenation in the presence of Pd/C and 2,2′-bipyridine as a catalyst system in the presence of Fmoc-*O*-succinimide (Fmoc-OSu). The reaction gives the desired compounds in high yields with excellent stereoselectivities, and it tolerates various other functional groups.

SYNFACTS Contributors: Hisashi Yamamoto, Isai Ramakrishna
Synfacts 2022, 18(02), 0219 Published online: 18.01.2022
DOI: 10.1055/s-0041-1737513; **Reg-No.:** H13422SF

Category
Peptide Chemistry

Key words
benzyl carbamates
fluorenylmethyl carbamates
hydrogenation
protecting groups
solid-phase synthesis