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Synthesis of Peptides Employing Fmoc-Amino Acid Chlorides and Commercial Zinc Dust
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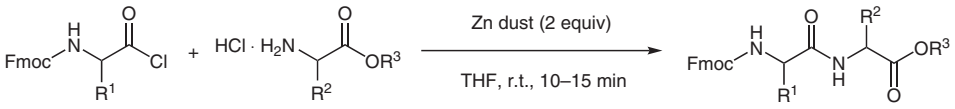
Zinc Dust Mediated Peptide Synthesis from Fmoc-Amino Acid Chlorides and Amino Acid Hydrochlorides



Substrate scope

Entry	Product	Yield (%)	Mp (°C)	$[\alpha]^{25}_D$ (*c*1, $CHCl_3$)
1	Fmoc-Phg-Phe-OMe	89	194–96	+24.0
2	Fmoc-D-Phg-Phe-OMe	90	193–95	–24.0
3	Fmoc-Phe-Leu-OMe	90	163–65	–21.6
4	Fmoc-Phe-Phg-OMe	88	158–60	+22.6
5	Fmoc-Phe-Ala-OMe	89	183–85	–18.0
6	Fmoc-Phe-Phe-OEt	87	169–71	–22.3
7	Fmoc-Ile-Gly-OEt	89	110–12	–30.4
8	Fmoc-Ala-Leu-OMe	90	125–27	–28.6
9	Fmoc-Gly-Val-OMe	89	97–99	+18.6
10	Fmoc-Pro-Pro-OMe	88	118–20	+40.1
11	Fmoc-Ile-Pro-OMe	86	65–67	+19.6
12	Fmoc-Tyr(Bzl)-Phe-OMe	87	171–73	+16.2

Significance: The construction of peptide bonds is one of the most essential and widely encountered chemical transformations in organic synthesis. In general, coupling of Fmoc-amino acid chlorides with amino acid esters requires the use of an aqueous inorganic base or an organic base. The use of these bases can cause severe issues of epimerization or cleavage of the Fmoc group. In 1998, Gopi and Suresh Babu developed a method for peptide synthesis from Fmoc-amino acid chlorides and amino acid hydrochloride salts mediated by commercially available zinc dust.

Comment: The zinc-mediated peptide coupling of Fmoc-amino acid chlorides with amino acid hydrochloride salts proceeds quickly and affords the desired peptides in high yields. This protocol is straightforward in practice, racemization free, and avoids side reactions.

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Category
Peptide Chemistry

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