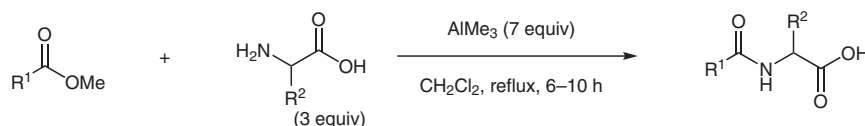


Trimethylaluminum-Mediated Peptide Synthesis



Substrate scope				
Entry	Ester	H-Xaa-OH	R-CO-Xaa-OH	Yield (%)
1	PhCO ₂ Me	Phe	PhCO-Phe-OH	77
2	PrCO ₂ Me	Phe	PrCO-Phe-OH	69
3	γ-butyrolactone	Pro	HO(CH ₂) ₃ CO-Pro-OH	64
4	γ-butyrolactone	Phe	HO(CH ₂) ₃ CO-Phe-OH	67
5	γ-butyrolactone	Phe-Leu	HO(CH ₂) ₃ CO-Phe-Leu-OH	59
6	MeCO ₂ -Phe-OMe	Phe	MeCO ₂ -Phe-Phe-OH	60
7	Boc-Phe-OMe	Val	Boc-Phe-Val-OH	50
8	Boc-Phe-OMe	Phe	Boc-Phe-Phe-OH	45 (<1) ^a
9	Boc-Val-OMe	Val	Boc-Val-Val-OH	37
10	Boc-Val-OMe	Phe	Boc-Val-Phe-OH	31
11	Boc-Phe-OMe	Phe-Leu	Boc-Phe-Phe-Leu-OH	42 (<3%) ^b

^a <1% of the epimer detected by reversephase HPLC analysis. ^b <3% of the epimer detected by ¹H NMR analysis.

Significance: The amide bond is ubiquitous; in particular, it is present in the backbones of peptides and in many natural products. Consequently, it has gained considerable importance in organic synthesis. Chemists are therefore continually searching for new methods for amide and/or peptide bond-forming reactions. In 1998, Martin and co-workers invented an AlMe₃-mediated peptide synthesis from unprotected amino acids in the solution phase.

Comment: This inexpensive AlMe₃-mediated solution-phase amide bond forming reaction proceeds smoothly to afford the desired products in moderate to good yields. The method can also be applied in syntheses of tripeptides in moderate yields.

Category

Peptide Chemistry

Key words

trimethylaluminum

solution-phase synthesis

peptide coupling

unprotected amino acids

Synfact
Classic