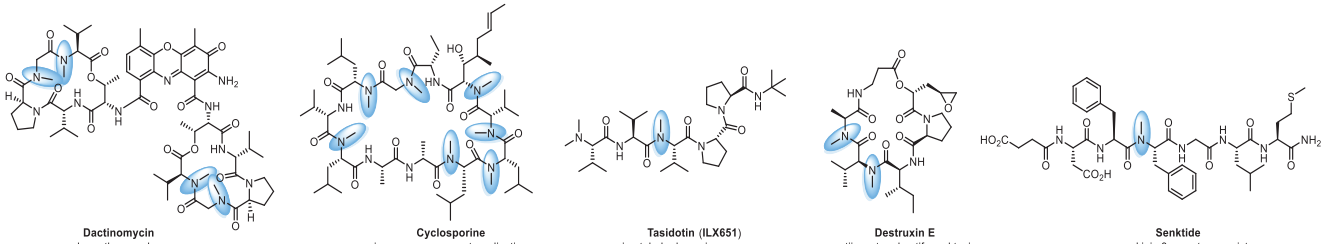
N-Methyl Amino Acids

Introduction

N-Methylation of peptides is a strategy for enhancement of their peptidase resistance. Methylated residues are widely present in natural products such as dactinomycin and cyclosporine, which are used as chemotherapy agents.[1] In recent years, numerous projects have included methylation of peptide backbone in the process of optimization of peptide therapeutics.[2] The use of *N*-methyl amino acids in peptide synthesis has been recently optimized in several works enabling the routine use of Fmoc-/Boc-building blocks in parallel synthesis of cyclic peptides.[3,4]



Dactinomycin
chemotherapy drug
FDA approved 1964
from *Streptomyces*

Cyclosporine
immunosuppressant medication
FDA approval 1983
Sandoz

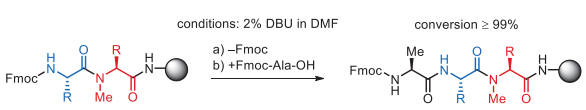
Tasidotin (ILX651)
microtubule dynamics suppressor
Phase 2 trials against cancers
BASF Bioresearch

Destruxin E
antiinsect and antifungal toxin
from *Metarhizium anisopliae*

Senktide
neurokinin 3 receptor agonist
therapy of reproductive dysfunctions in domestic animals

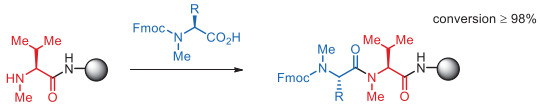
Optimization

A Fmoc-removal optimization
suppression of diketopiperazine excision

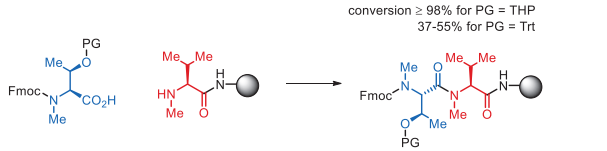


B Elongation reactivity optimization

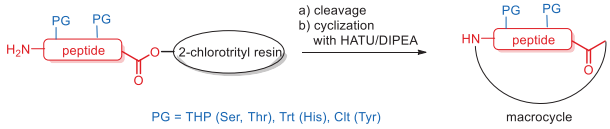
conditions: 3.6 equiv. Fmoc-AA-OH, 5.2 equiv. DIC, 2.3 equiv. HOAt, NMP/DMF, 40 °C, 2.5-6 h



C Ser/Thr protection optimization



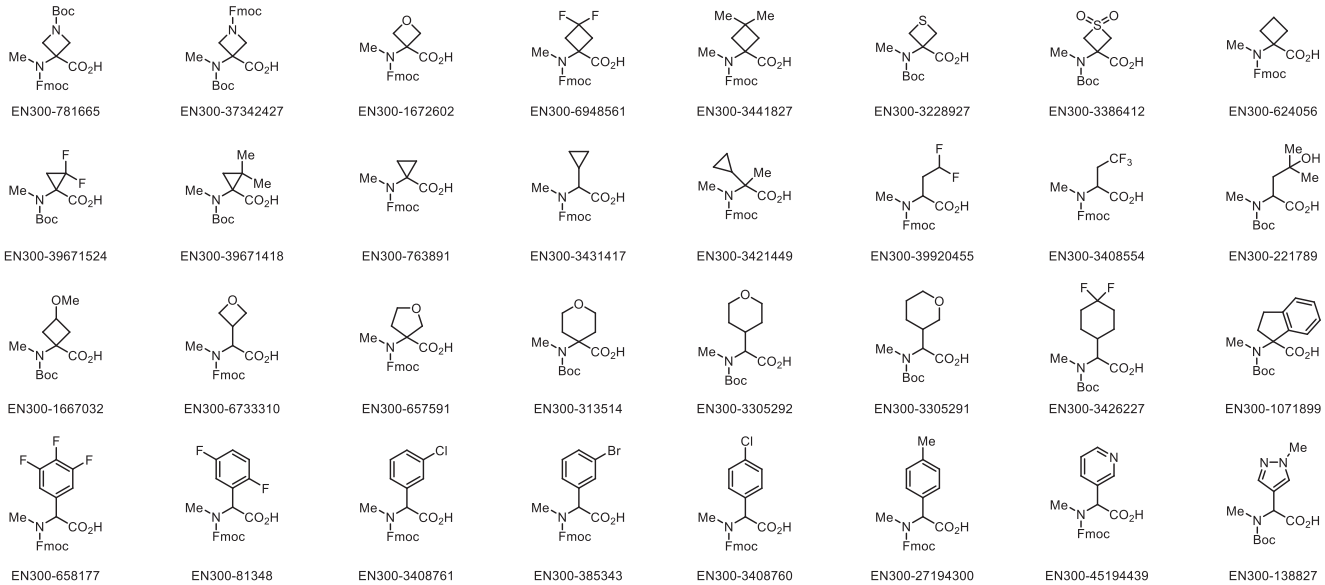
D Optimization of cleavage
to keep side-chain protection



PG = THP (Ser, Thr), Trt (His), Clt (Tyr)

Reference: K. Nomura et al., *J. Med. Chem.* **2022**, *65*, 13401

We offer: over 50 *N*-methyl amino acids from stock on 5-10 gram scale.



EN300-781665	EN300-37342427	EN300-1672602	EN300-6948561	EN300-3441827	EN300-3228927	EN300-3386412	EN300-624056
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EN300-1667032	EN300-6733310	EN300-657591	EN300-313514	EN300-3305292	EN300-3305291	EN300-3426227	EN300-1071899
EN300-658177	EN300-81348	EN300-3408761	EN300-385343	EN300-3408760	EN300-27194300	EN300-45194439	EN300-138827

References

1. J. Hyslop et al. *J. Biotechnol.* **2019**, *293*, 56.
2. T. Takeuchi et al. *J. Med. Chem.* **2022**, *65*, 8493.
3. Y. Otake et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 12925.
4. K. Nomura et al. *J. Med. Chem.* **2022**, *65*, 13401.