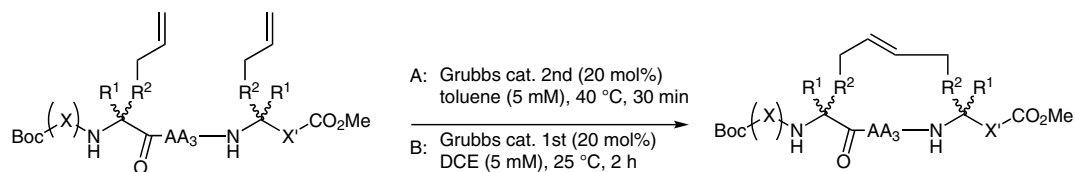


A. UEDA*, Y. MAKURA, S. KAKAZU, T. KATO, T. UMENO, K. HIRAYAMA, M. DOI, M. OBA, M. TANAKA* (NAGASAKI UNIVERSITY, JAPAN)

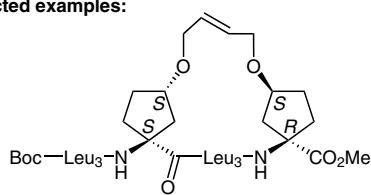
E-Selective Ring-Closing Metathesis in α -Helical Stapled Peptides Using Carbocyclic α,α -Disubstituted α -Amino Acids

Org. Lett. **2022**, *24*, 1049–1054, DOI: 10.1021/acs.orglett.1c04256.

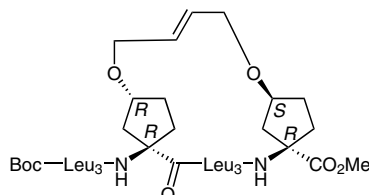
Cyclopeptide Synthesis by Ring-Closing Metathesis



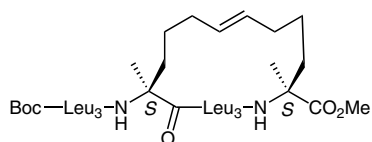
Selected examples:



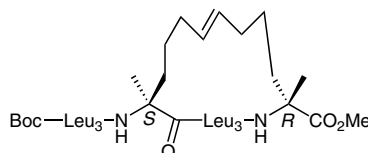
conditions A: 96% yield, *E/Z* = 24:1



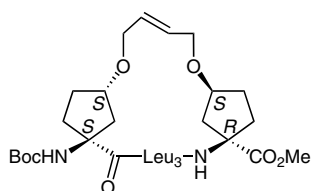
conditions A: 76% yield, *E/Z* = 6:1



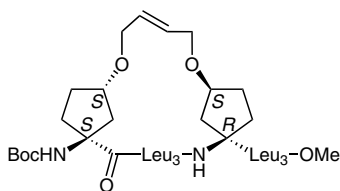
conditions A: 53% yield, *E/Z* = 1:2.2
conditions B: 73% yield, *E/Z* = 1:1.1



conditions A: 94% yield, *E/Z* = 1:1
conditions B: 99% yield, *E/Z* = 1.3:1

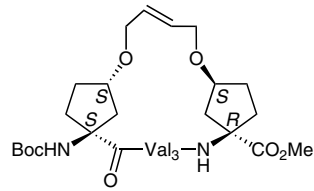


conditions A: 75% yield, *E/Z* = 26:1



conditions A: 98% yield, *E/Z* = 40:1

^aCH₂Cl₂ was used as solvent.



conditions B^a: 95% yield, *E/Z* = 16:1

Significance: Cyclopeptides are key moieties widely present in a number of bioactive products, including some with clinical applications. The authors developed ring-closing metathesis in α -helical stapled peptides.

Comment: The ring-closing metatheses of α -helical stapled peptides containing leucine or valine residues proceeded in moderate to high yields, generally in an *E*-selective manner.

SYNFACTS Contributors: Hisashi Yamamoto, Tomohiro Hattori

Synfacts 2022, 18(05), 0565 Published online: 20.04.2022

DOI: 10.1055/s-0041-1737572; Reg-No.: H02622SF

Category

Peptide Chemistry

Key words

cyclic peptides

ring-closing
metathesis

stereoselectivity

peptide stapling

Synfact
of the
Month