Bachem's portfolio of α-methyl amino acids has been extended by a set of new innovative products, produced by our partner DOTTIKON Exclusive Synthesis AG.

α-Methyl amino acids can be obtained by various methods such as Cα-methylation of N,N-disubstituted amino acid derivatives in the presence of a chiral catalyst. The proprietary approach of Maruoka et al. starting from N-p-chlorobenzylidene amino acid esters is especially suited for the modification of aromatic amino acids. A biphenoxy-derived chiral phase-transfer catalyst promotes enantioselective alkylation.

For our complete range of amino acid derivatives, peptides, and biochemicals please visit shop.bachem.com.

Scalable synthetic methods, that allow Cα-alkylation of the complete range of amino acids, applicable ubiquitously with consistently good yield and high enantiomeric excess, have not been developed yet.

A proprietary process for α-methyl amino acids derivatives that are difficult to obtain by other synthetic methods has been developed by DOTTIKON. We offer a selection of such compounds, produced by Dottikon, as building blocks, in addition to our existing selection of α-methyl amino acids.

### Advanced technology
- Various different chiral amino nitriles synthesized in our laboratory (up to kg-scale).
- Technology principle successfully transferred to pilot scale.

### Selective
- Access to various compound classes in enantiopure form.
- Both enantiomers available with high enantiomeric excess in each case.

### Cost-effective
- Direct synthesis of enantiopure active target compounds avoiding racemate resolution with 50% less expensive waste.
- Readily available and low-cost raw materials.
The synthetic variant recently developed at DOTTIKON enabled chemists to prepare Cα-alkylated aliphatic and aliphatic amino acids, diamines, serine lactone derivatives and other valuable enantiopure building blocks via chiral α-aminonitriles. DOTTIKON’s approach uses a metal-free catalyst, a prerequisite for using the derivatives in the production of APIs. α-Methyl amino acids are constituents of natural compounds. Peptaibols, helical peptides produced by fungi contain Aib and Iva. L-α-Methylserine is a constituent of the piperazimycins, cytotoxic hexadepsipeptides from bacteria.

α-Methyl amino acids are valuable chiral reactants for use in organic synthesis as well as for incorporation into peptides. When coupling α-methyl amino acids during peptide synthesis, their low propensity for racemization compensates for increased steric hindrance. The coupling of the subsequent amino acid derivative requires most efficient activation reagents under conditions minimizing racemization. α-Methylation has a strong impact on peptide conformation, as it reduces the flexibility of the peptide backbone. Especially when incorporating, aliphatic α-methyl amino acids such as Aib or Iva, the resulting backbone modification induces or stabilizes α-helices. Hence, for obtaining “stapled” α-helical peptides by ring-closing metathesis, α-(ω-Alkenyl)-alanines are incorporated at defined positions. If an α-helical sequence is essential for the activity of a peptide, replacement of an amino acid by its α-methylated analog could increase it. Such phenomena make α-methyl amino acids valuable tools for SAR studies and drug development. Additionally, the substitution renders the peptide more stable to enzymatic cleavage.

Our technical brochures, Bachem’s “white papers”, provide more detailed information and literature on selected research areas.

References
A.M. Brunissen, M. Ayoub, S. Lavielle
C.E. Schafmeister, J. Po, G.L. Verdine
S. Sagan, P. Karoyan, O. Lequin, G. Chassaing, S. Lavielle
Z. Han, Y. Yamaguchi, M. Kitamura, K. Maruoka
N.D. Smith, A.M. Wohlrab, M. Goodman
E.D. Miller, C.A. Kauffman, P.R. Jensen, W. Fenical
Y.-G. Wang, M. Ueda, X. Wang, Z. Han, K. Maruoka
A. Fernandez-Tejada, F. Corzana, J.H. Busto, A. Avenoza, J.M. Peregrina
L. Gentilucci, R. De Marco, L. Cerisoli
Our custom synthesis team would be pleased to offer peptides containing the amino acids listed above.
Custom Synthesis at Bachem

✓ Quality
  • GMP and non-GMP quality
  • Broad range of impurities and related products
  • State-of-the-art analytical capabilities
  • ISO 13485 certified manufacturing site in St. Helens, UK

✓ Chemistry
  • Fmoc-, Boc-, Z- and other synthetic strategies
  • Native chemical ligation
  • Synthesis of complex peptides

✓ Capacity
  • Production sites in the USA and Europe
  • Largest production facilities in the market
  • Up-to-date technology

✓ Modifications
  • Acylation, acetylation, amidation, PEGylation etc.
  • Cyclizations
  • Stabilizing modifications

✓ Support
  • Highly qualified technical support team
  • Documentation
  • Confidentiality
  • Partnering to achieve client objectives

Marketing & Sales Contact

Americas
Bachem Americas, Inc.
Tel. +1 888 422 2436 (toll free in USA & Canada)
+1 310 539 4171
sales.us@bachem.com

Asia Pacific
Bachem Japan K.K.
Tel. +81 3 6661 0774
sales.jp@bachem.com

Europe, Africa, Middle East and India
Bachem AG
Tel. +41 58 595 2020
sales.ch@bachem.com

Visit our website
www.bachem.com
or shop online
shop.bachem.com

All information is compiled to the best of our knowledge. We cannot be made liable for any possible errors or misprints. Some products may be restricted in certain countries.