α-METHYL AMINO ACIDS BACHEM

LEADING PARTNER IN TIDES

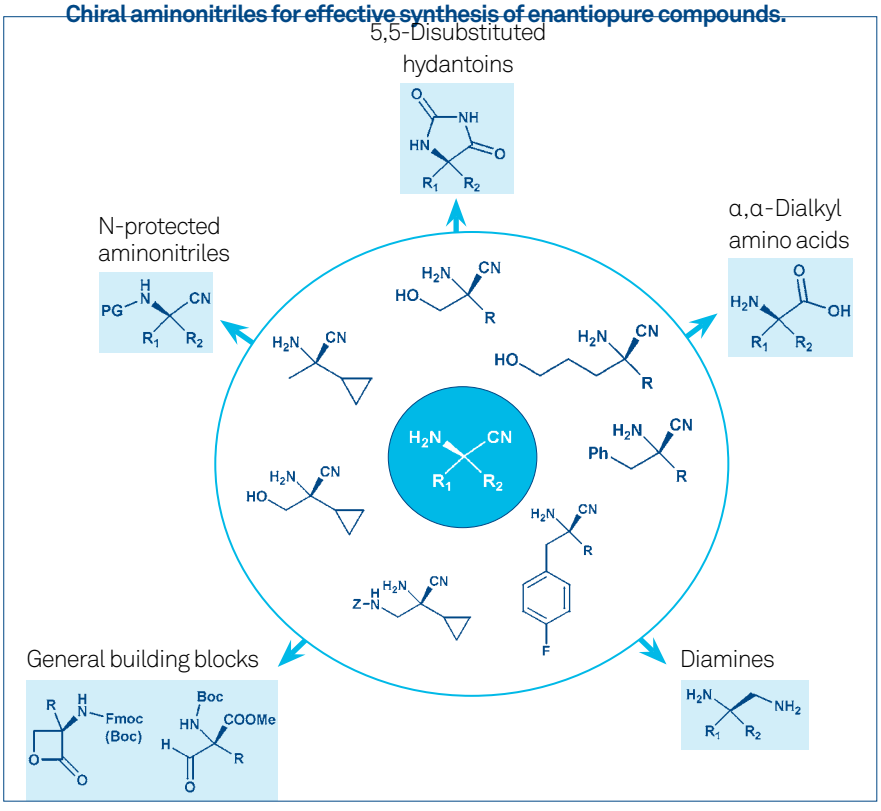
Bachem's portfolio of α-methyl amino acids has been extended by a set of new innovative products, produced by our partner DOTTIKON Exclusive Synthesis AG.
α-Methyl amino acids can be obtained by various methods such as Cα-methylation of N,N-disubstituted amino acid derivatives in the presence of a chiral 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 biphenyl-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.

dottikon
EXCLUSIVE SYNTHESIS

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.

Chiral aminonitriles for effective synthesis of enantiopure compounds.



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.

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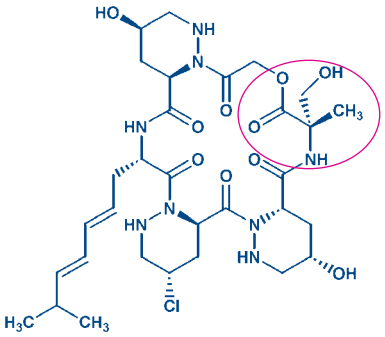
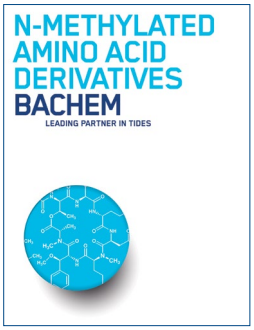
The synthetic variant recently developed at DOTTIKON enabled chemists to prepare Cα-alkylated aliphatic and aliphatic amino acids, diamines, serine lactone derivatives and other valuable enantiopure building blocks via chiral α-aminonitriles. DOTTIKON's approach uses a metal-free catalyst, a prerequisite 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.



Structure of piperazimycin A

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.
Cα-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.



You can download a copy at **www.bachem.com** or send an email to marketing@bachem.com

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α-METHYL AMINO ACIDS BACHEM

Aib (αMeAla)	
H-Aib-OtBu · HCl	4019068
H-Aib-OBzl · HCl	4066546
H-Aib-OMe · HCl	4047619
Boc-Aib-OH	4010082
Boc-Aib-OSu	4026057
Fmoc-Aib-OH	4013932
N-Me-Aib-OH	4003409
Z-Aib-OH	4018563

αMeLeu	
Fmoc-α-Me-Leu-OH	4040839
Fmoc-α-Me-D-Leu-OH	4066676
H-α-Me-Leu-OH	4040838
H-α-Me-D-Leu-OH	4047055
H-α-Me-DL-Leu-OH	4004270

αMePhe	
Fmoc-α-Me-Phe-OH	4084334
Fmoc-α-Me-D-Phe-OH	4028974
H-α-Me-Phe-OH	4017880
H-α-Me-D-Phe-OH	4025136
H-α-Me-DL-Phe-OH	4010083
H-α-Me-DL-Phe-OMe · HCl	4017873

αMePro	
H-α-Me-Pro-OH	4026653

αMeTrp	
H-α-Me-DL-Trp-OH	4008387
H-α-Me-DL-Trp-OMe	4008386

αMeVal	
Fmoc-α-Me-Val-OH	4052280
Boc-α-Me-DL-Val-OH	4026565
H-α-Me-Val-OH	4026440
H-α-Me-D-Val-OH	4026441
H-α-Me-DL-Val-OH	4026294

dottikon
EXCLUSIVE SYNTHESIS

NEW α-Methyl amino Acids produced by DOTTIKON	
H-4-fluoro-α-Me-Phe-OH	4101674
H-4-fluoro-α-Me-D-Phe-OH	4101675
Fmoc-4-fluoro-α-Me-Phe-OH · DCHA	4101676
Fmoc-4-fluoro-α-Me-D-Phe-OH · DCHA	4101677
H-α-cyclopropyl-Ala-OH · HCl	4101678
H-α-cyclopropyl-D-Ala-OH · HCl	4101679
Fmoc-α-cyclopropyl-Ala-OH	4101686
Fmoc-α-cyclopropyl-D-Ala-OH	4101687
H-α-Me-Ser-OH	4101680
H-α-Me-D-Ser-OH	4101681
Fmoc-α-Me-Ser-lactone	4101682
Fmoc-α-Me-D-Ser-lactone	4101683
Derivatives for click chemistry	
Fmoc-β-azido-α-Me-Ala-OH · BHA (Fmoc-β-azido-Aib-OH · BHA)	4101684
Fmoc-β-azido-α-Me-D-Ala-OH · BHA (Fmoc-β-azido-D-Aib-OH · BHA)	4101685

Our custom synthesis team would be pleased to offer peptides containing the amino acids listed above.

BACHEM

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

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