# **NAGASE's Library of Unnatural Amino Acids**

Jan. 2017 Ver.23

NAGASE provides unique  $\alpha$ -mono- and  $\alpha,\alpha$ -disubstituted unnatural amino acids (UNAA) that can open new avenues for drug development and accelerate the development of drug candidates in your pipeline NAGASE UNAAs can be supplied in gram to multi-kg and larger quantities manufactured via stereoselective alkylation of glycine or alanine NAGASE UNAAs are manufactured without the use of metal catalysts by a safe and environmentally friendly process

### **NEW PRODUCTS RELEASED**



# Reactive Amino Acids ( $\alpha$ -Alkenyl or $\alpha$ -Alkynyl Glycines and Alanines )

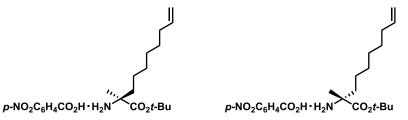
# α-AlkenylAla

$\alpha$ -Alken	<u>/IAIa</u>		
335438	( <i>S</i> )-α-Allylalanine-H <sub>2</sub> O (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 300
	[CAS No.96886-55-4] $C_6H_{11}NO_2 \cdot H_2O = 147.17$		
335437	( <i>R</i> )-α-Allylalanine-H <sub>2</sub> O (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 300
	[CAS No.96886-56-5] $C_6H_{11}NO_2 \cdot H_2O = 147.17$		
	H-N COoH		
358028	(S)-N-Fmoc-α-Allylalanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	(NET) 1 g	\$ 900(*)
	[CAS No.288617-71-0] $C_{21}H_{21}NO_4 = 351.40$		
	Containing 20-50% Methyl tert-butyl ether		
358027	( <i>R</i> )-N-Fmoc-α-Allylalanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	(NET) 1 g	\$ 900(*)
	[CAS No.288617-76-5] $C_{21}H_{21}NO_4 = 351.40$		
	Containing 20-50% Methyl tert-butyl ether		
	FmocHN CO <sub>2</sub> H FmocHN CO <sub>2</sub> H		
	2		
354283	( <i>R</i> )-N-Boc-α-Allylalanine ethyl ester (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 600
	[CAS No.1263046-12-3] $C_{13}H_{23}NO_4 = 257.33$		
	BocHN CO₂H		
365023	(S)-N-Fmoc-α-(4-Pentenyl)alanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	(NET) 1 g	\$ 800(*)
	[CAS No.288617-73-2] $C_{23}H_{25}NO_4 = 379.46$	(NET) 5 g	\$ 1,800(*)
	Containing 20-50% Methyl tert-butyl ether		
364440	( <i>R</i> )-N-Fmoc-α-(4-Pentenyl)alanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	(NET) 1 g	\$ 800(*)
	[CAS No.288617-77-6] $C_{23}H_{25}NO_4 = 379.46$	(NET) 5 g	\$ 1,800(*)
	Containing 20-50% Methyl tert-butyl ether		
	FmocHN CO <sub>2</sub> H FmocHN CO <sub>2</sub> H		
411751	(S)-α-(4-Pentenyl)alanine <i>tert</i> -butyl ester <i>p</i> -Nitrobenzoate (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 350
	[CAS No.1323987-70-7] $C_{12}H_{23}NO_2 \cdot C_7H_5NO_4 = 380.44$	5 g	\$ 1,400
411752	(R)-α-(4-Pentenyl)alanine <i>tert</i> -butyl ester p-Nitrobenzoate (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 350
	[CAS No.1323987-68-3] $C_{12}H_{23}NO_2 \cdot C_7H_5NO_4 = 380.44$	5 g	\$ 1,400
	$p-NO_2C_6H_4CO_2H\cdot H_2N$ $CO_2t-Bu$ $p-NO_2C_6H_4CO_2H\cdot H_2N$ $CO_2t-Bu$		

364441	(S)-N-Fmoc-α-(7-Octenyl)alanine (≥	≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	(NET) 1 g	\$ 1,000(*)
	[CAS No.288617-75-4]	$C_{26}H_{31}NO_4 = 421.54$	(NET) 5 g	\$ 1,900(*)
	Containing 10-40% of Methyl tert-butyl ether			
363955	955 ( <i>R</i> )-N-Fmoc- $\alpha$ -(7-Octenyl)alanine ( $\geq$ 98.0%, $\geq$ 98.0%ee) (refrigerated transport)			\$ 1,000(*)
	[CAS No.945212-26-0]	$C_{26}H_{31}NO_4 = 421.54$	(NET) 5 g	\$ 1,900(*)
Containing 10-40% of Methyl tert-butyl ether				



411915 (S)-α-(7-Octenyl)alanine tert-butyl ester p-Nitrobenzoate (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 700 [CAS No.1375908-92-1]  $C_{15}H_{29}NO_2 \cdot C_7H_5NO_4 = 422.52$  5 g \$ 1,500 388630 (R)-α-(7-Octenyl)alanine tert-butyl ester p-Nitrobenzoate (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 700 [CAS No.1375904-22-5]  $C_{15}H_{29}NO_2 \cdot C_7H_5NO_4 = 422.52$  5 g \$ 1,500



Hydrocarbon-stapling of natural peptides enhances helicity, protease resistance, and cell-permeability as well as improves pharmacologic properties.

C. E. Schafmeister, et. al. J. Am. Chem. Soc. 2000, 122, 5891-5892.

L. D. Walensky, et. al. Science 2004, 305, 1466-1470.

Young-Woo Kim et. al. Org. Lett. 2010, 12, 3046-3049.

[CAS No.403519-98-2]

### <u>α-AlkynylAla</u>

339271 (S)-α-Propargylalanine ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) 1 g \$ 300 [CAS No.1231709-27-5]  $C_6H_9NO_2 = 127.14$  339270 (R)-α-Propargylalanine ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) 1 g \$ 300

 $C_6H_9NO_2 = 127.14$ 





358026 (S)-N-Fmoc-α-Propargylalanine ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) (refrigerated transport) (NET) 1 g \$ 800(\*) [CAS No.1198791-58-0] C<sub>21</sub>H<sub>19</sub>NO<sub>4</sub> = 349.39 Containing 20-50% Methyl *tert*-butyl ether

358029 (*R*)-N-Fmoc-α-Propargylalanine ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) (refrigerated transport) (NET) 1 g \$ 800(\*) [CAS No.1198791-65-9] C<sub>21</sub>H<sub>19</sub>NO<sub>4</sub> = 349.39 Containing 20-50% Methyl *tert*-butyl ether



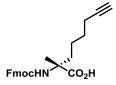
385412 (S)-N-Fmoc-α-(4-Pentynyl)alanine ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport) (NET) 1 g \$ 800(\*) [CAS No.1050501-65-9] C<sub>23</sub>H<sub>23</sub>NO<sub>4</sub> = 377.44 (NET) 5 g \$ 2,400(\*) Containing 20-50% Methyl *tert*-butyl ether

385411 (*R*)-N-Fmoc-α-(4-Pentynyl)alanine ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport) (NET) 1 g \$ 800(\*) [CAS No.1198791-56-8] C<sub>23</sub>H<sub>23</sub>NO<sub>4</sub> = 377.44 (NET) 5 g \$ 2,400(\*) Containing 20-50% Methyl *tert*-butyl ether



468736 (*R*)-N-Fmoc-α-(5-Hexynyl)alanine ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport) (NET) 1 g \$ 850(\*) [CAS No.1198791-69-3] C<sub>24</sub>H<sub>25</sub>NO<sub>4</sub> = 391.47 (NET) 5 g \$ 2,750(\*) Containing 5-40% of Methyl *tert*-butyl ether





# α-AlkenylGly

345277 (S)-α-Allylglycine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) 5 g \$ 500 [CAS No.16338-48-0] C<sub>5</sub>H<sub>9</sub>NO<sub>2</sub> = 115.13

345276 (R)-α-Allylglycine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) 5 g \$ 500 [CAS No.54594-06-8] C<sub>5</sub>H<sub>9</sub>NO<sub>2</sub> = 115.13



lg \$ 500

[CAS No.121786-40-1]

 $C_7H_{11}NO_3 = 157.17$ 

358025 (S)-N-Boc- $\alpha$ -Allylglycine Dicyclohexylamine salt (≥ 98.0%, ≥ 98.0%ee)

25 g \$ 800

[CAS No.143979-15-1]

 $C_{10}H_{17}NO_4 \cdot C_{12}H_{23}N = 396.57$ 

100 g \$ 2,500

363068 (S)- $\alpha$ -Allylglycine ethyl ester  $\rho$ -Toluenesulfonate ( $\geq 97.0\%$ ,  $\geq 98.0\%$ ee)

5 g \$ 200

[CAS No.1231709-21-9]

 $C_7H_{13}NO_2 \cdot C_7H_8O_3S = 315.39$ 

25 g \$ 800 100 g \$ 2,500

413726 (R)- $\alpha$ -Allylglycine ethyl ester p-Toluenesulfonate ( $\geq 97.0\%$ ,  $\geq 98.0\%$ ee)

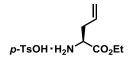
5 g \$ 200

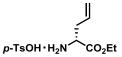
[CAS No.1432914-51-6]

 $C_7H_{13}NO_2 \cdot C_7H_8O_3S = 315.39$ 

25 g \$ 800

100 g \$ 2,500





Applycation of Allylglycine as the building block for intermediate of pharmaceutical compounds. Rutjes, F. P. J. T. *et al. Org. Biomol. Chem.* **2005**, 3, 3435.

Rutjes, F. P. J. T. et al. J. Chem. Soc. Perkin Trans. 1, 2000, 4197.

# α-AlkynylGly

345279 (S)- $\alpha$ -Propargylglycine (≥ 98.0%, ≥ 98.0%ee)

1 g \$ 250

[CAS No.23235-01-0]

 $C_5H_7NO_2 = 113.12$ 

345278 (*R*)- $\alpha$ -Propargylglycine (≥ 98.0%, ≥ 98.0%ee)

1 g \$ 250

[CAS No.23235-03-2]

 $C_5H_7NO_2 = 113.12$ 



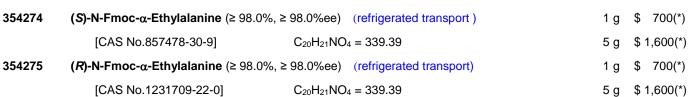


 $\alpha$ -Propargyl Amino Acids – Derived Optically Active Novel Substituted Polyacetylenes: Synthesis, Second Structures, and Responsiveness to lons.

Sogawa, H. et al. J. Poly. Sci., Part A: Polym. Chem. 2012, 50, 2008.



<u>α,α-Diall</u>	kenvlGlv			
462304	N-Fmoc-α,α-Bis(4-pentenyl)glyc	ine (≥ 98.0%)	1 g	\$ 600
	[CAS No.1068435-19-7]	$C_{27}H_{31}NO_4 = 433.55$	5 g	\$ 2,400
N	FmocHN CO₂H			
α-Sub	stituted Alanine derivatives			
<u>Alanine</u>	(Ala)			
328959	(S)-α-Ethylalanine-H <sub>2</sub> O (≥ 98.0%	, ≥ 98.0%ee)	1 g	\$ 250
	[CAS No.595-40-4]	$C_5H_{11}NO_2 \cdot H_2O = 135.16$	5 g	\$ 800
328962	(R)-α-Ethylalanine-H <sub>2</sub> O (≥ 98.0%	, ≥ 98.0%ee)	1 g	\$ 250
	[CAS No.3059-97-0]	$C_5H_{11}NO_2 \cdot H_2O = 135.16$	5 g	\$ 800
	″., Н <sub>2</sub> N СО <sub>2</sub> Н	H₂N CO₂H		
358835	(S)-N-Boc-α-Ethylalanine (≥ 98.0	%, ≥ 98.0%ee)	1 g	\$ 300
	[CAS No.151171-11-8]	$C_{10}H_{19}NO_4 = 217.27$	5 g	\$ 900
395454	( <i>R</i> )-N-Boc-α-Ethylalanine (≥ 98.0	)%, ≥ 98.0%ee)	1 g	\$ 300
	[CAS No.123254-58-0]	$C_{10}H_{19}NO_4 = 217.27$	5 g	\$ 900
	BocHN CO₂H	BocHN CO₂H		





472923 (S)-N-Fmoc-α-Methylnorleucine ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport) 1 g \$ 700(\*)

 $C_{22}H_{25}NO_4 = 367.45$ 



467664 (S)-N-Fmoc-α-Methyl-β-tert-butylalanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport) 1 g \$1,800(\*)

[CAS No.1934266-56-4]

 $C_{23}H_{27}NO_4 = 381.47$ 



470629 (S)-N-Fmoc-α-Methylcyclohexylalanine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) (refrigerated transport) 1 g \$ 700(\*)

[CAS No.1934266-55-3]

 $C_{25}H_{29}NO_4 = 407.51$ 





## $\alpha$ -Methyl or $\alpha$ -Ethyl derivatives of natural Amino Acids

### Aspartic acid (Asp)

**346838** (*S*)- $\alpha$ -Methylaspartic acid (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 400

[CAS No.3227-17-6]  $C_5H_9NO_4 = 147.13$ 

**346839** (*R*)-α-Methylaspartic acid ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) 1 g \$ 400

[CAS No.14603-76-0]  $C_5H_9NO_4 = 147.13$ 

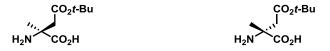


357392 (S)-α-Methylaspartic acid 4-tert-butyl ester ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee) 1 g \$ 300

[CAS No.1217977-71-3]  $C_9H_{17}NO_4 = 203.24$  5 g \$ 650

359455 (*R*)-α-Methylaspartic acid 4-*tert*-butyl ester ( $\geq$  98.0%,  $\geq$  98.0%ee) 1 g \$ 300

[CAS No.1231709-25-3]  $C_9H_{17}NO_4 = 203.24$  5 g \$ 650



357393 (S)-N-Fmoc- $\alpha$ -Methylaspartic acid 4-tert-butyl ester ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport)

[CAS No.1072845-47-6]  $C_{24}H_{27}NO_6 = 425.48$  (NET) 1 g \$ 800(\*)

Containing ≤10% Methyl *tert*-butyl ether (NET) 5 g \$ 1,400(\*)

359457 (*R*)-N-Fmoc-α-Methylaspartic acid 4-*tert*-butyl ester ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport)

[CAS No.1231709-26-4]  $C_{24}H_{27}NO_6 = 425.48$  (NET) 1 g \$ 800(\*)

Containing ≤10% Methyl *tert*-butyl ether (NET) 5 g \$ 1,400(\*)



### Asparagine (Asn)

412813	(S)-N-Fmoc-α-Methylasparagine (≥ 98.0%, ≥ 98.0%ee)		1 g \$ 600
	[CAS No.1403590-49-7]	$C_{20}H_{20}N_2O_5 = 368.39$	5 g \$1,800
412814	(R)-N-Fmoc-α-Methylasparagine	(≥ 98.0%, ≥ 98.0%ee)	1 g \$ 600
	[CAS No.1403590-50-0]	$C_{20}H_{20}N_2O_5 = 368.39$	5 g \$ 1,800

### Cysteine (Cys)

369043 (*R*)-L-α-Methylcysteine-HCI (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 400 [CAS No.148766-37-4] 
$$C_4H_9NO_2S$$
·HCI = 171.65 5 g \$ 1,600 388254 (*S*)-D-α-Methylcysteine-HCI (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 1,500

[CAS No.151062-55-4]  $C_4H_9NO_2S\cdot HCI = 171.65$ 

[CAS No.1198791-74-0]  $C_{39}H_{35}NO_5S = 629.77$  5 g \$2,400(\*)



## Glutamine (Glu)

**462535** (S)-N-Fmoc-α-Methylglutamic acid 5-*tert*-butyl ester ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport)

[CAS No.1072845-48-7]  $C_{25}H_{30}NO_6 = 440.51$  1 g \$ 900(\*)



[CAS No.29589-03-5]

### Leucine (Leu)

**328961** (S)-α-Methylleucine (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 250

[CAS No.105743-53-1]  $C_7H_{15}NO_2 = 145.20$ 

**328960** (*R*)- $\alpha$ -Methylleucine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) 1 g \$ 250

 $C_7H_{15}NO_2 = 145.20$ 

5 g \$3,600(\*)

357394	(S)-N-Fmoc-α-Methylleucine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.312624-65-0] $C_{22}H_{25}NO_4 = 367.45$	3 +()
357395	( <i>R</i> )-N-Fmoc-α-Methylleucine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1231709-23-1] $C_{22}H_{25}NO_4 = 367.45$	
	$\checkmark$	
	FmocHN CO <sub>2</sub> H FmocHN CO <sub>2</sub> H	
465357	(S)-N-Fmoc-α-Ethylleucine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1934266-50-8] $C_{23}H_{27}NO_4 = 381.47$	5 g \$ 2,400(*)
465358	( <i>R</i> )-N-Fmoc-α-Ethylleucine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1934266-51-9] $C_{23}H_{27}NO_4 = 381.47$	5 g \$ 2,400(*)
	FmocHN CO <sub>2</sub> H FmocHN CO <sub>2</sub> H	
Lysine (		
369412	(S)-N <sub>α</sub> -Fmoc-N <sub>α</sub> -Boc-α-Methyllysine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1202003-49-3] $C_{27}H_{34}N_2O_6 = 482.58$	5 g \$ 2,400(*)
369414	( <i>R</i> )-N <sub>α</sub> -Fmoc-N <sub>ω</sub> -Boc-α-Methyllysine ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1315449-94-5] $C_{27}H_{34}N_2O_6 = 482.58$	5 g \$ 2,400(*)
	NHBoc	
	FmocHN CO <sub>2</sub> H FmocHN CO <sub>2</sub> H	
454268	(C) N. Eman N. Allen & Mathyllygina (2.09.09/ 2.09.09/ co). (refrigorated transport)	1 a \$ 1 200/*\
454200	( <i>S</i> )-N <sub>α</sub> -Fmoc-N <sub><math>\alpha</math></sub> -Alloc-α-Methyllysine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport) [CAS No.1934266-47-3] $C_{26}H_{30}N_{2}O_{6} = 466.53$	1 g \$ 1,200(*) 5 g \$ 4,800(*)
	$[CA3 \text{ NO.1934200-47-3}] \qquad C_{2611301} \text{N}_2\text{C}_6 = 400.33$	5 g \$4,000( )
	NHAlloc	
	lew	
	FmocHN CO <sub>2</sub> H	
	<del>-</del>	
468644	(S)-N <sub>α</sub> -Fmoc-N <sub>ω</sub> -Mtt-α-Methyllysine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)	1 g \$ 800(*)
	[CAS No.1934266-54-2] $C_{42}H_{42}N_2O_4 = 638.81$	5 g \$ 2,400(*)
		<b>5</b>
	NHMtt	
( N	lew	
	FmocHN CO <sub>2</sub> H	

### Ornithine (Orn)

369026	$(S)$ - $N_{\alpha}$ -Fmoc- $N_{\omega}$ -Boc- $\alpha$ -Methylorn	(refrigerated transport)	1 g	\$ 800(*)	
	[CAS No.1315449-95-6]	$C_{26}H_{32}N_2O_6 = 468.55$		5 g	\$ 2,000(*)

[CAS No.171860-40-5] 
$$C_{26}H_{32}N_2O_6 = 468.55$$
 5 g \$2,000(\*)

**467089** (S)-N<sub>α</sub>-Fmoc-N<sub>ω</sub>-Mtt-α-Methylornithine (
$$\geq 98.0\%$$
,  $\geq 98.0\%$ ee) (refrigerated transport) 1 g \$ 800(\*)

[CAS No.1934266-52-0] 
$$C_{41}H_{40}N_2O_4 = 624.78$$
 5 g \$2,000(\*)



#### Phenylalanine (Phe) Substituted benzene ring derivatives are shown in pp. 13-15

[CAS No.23239-35-2] 
$$C_{10}H_{13}NO_2 \cdot H_2O = 197.23$$
 5 g \$ 900

**322898** (*R*)-α-Methylphenylalanine-
$$H_2O$$
 (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 300

[CAS No.17350-84-4] 
$$C_{10}H_{13}NO_2 \cdot H_2O = 197.23$$
 5 g \$ 900

**366011** (S)-N-Fmoc-α-Methylphenylalanine-3/2H<sub>2</sub>O (
$$\geq$$
 98.0%,  $\geq$  98.0%ee) 1 g \$ 300

[CAS No.135944-05-7] 
$$C_{25}H_{23}NO_4 \cdot 3/2H_2O = 428.48$$
 5 g \$ 900

**366012** (*R*)-N-Fmoc-α-Methylphenylalanine-3/2H<sub>2</sub>O (
$$\ge$$
 98.0%,  $\ge$  98.0%ee) 1 g \$ 300

[CAS No.152436-04-9] 
$$C_{25}H_{23}NO_4 \cdot 3/2H_2O = 428.48$$
 5 g \$ 900

### **Proline (Pro)**

**363402** (S)-N-Boc-α-Methylproline (
$$\ge 98.0\%$$
,  $\ge 98.0\%$ ee) 1 g \$ 400

[CAS No. 103336-06-7]  $C_{11}H_{19}NO_4 = 229.28$ \$1,200

363401 (*R*)-N-Boc- $\alpha$ -Methylproline (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 400

> [CAS No. 166170-15-6]  $C_{11}H_{19}NO_4 = 229.28$ \$1,200

386844	<b>(S)-N-Fmoc-α-Methylproline</b> (≥ 98.0%, ≥ 98.0%ee)		
	[CAS No.167275-47-0]	$C_{21}H_{21}NO_4 = 351.40$	5 g \$ 1,500
386843	( <i>R</i> )-N-Fmoc-α-Methylproline (≥ 98	3.0%, ≥ 98.0%ee)	1 g \$ 500
	[CAS No.1286768-33-9]	$C_{21}H_{21}NO_4 = 351.40$	5 g \$ 1,500
	N CO <sub>2</sub> H	N CO₂H Fmoc	

### Serine (Ser)

**471548** (S)-N-Fmoc-O-tert-Butyl-α-Methylserine ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport) 1 g \$ 850(\*)

[CAS No.914399-98-7]  $C_{23}H_{27}NO_5 = 397.47$  5 g \$ 2,550(\*)



### Tryptophan (Trp)

**350920** (S)- $\alpha$ -Methyltryptophan-1/2H<sub>2</sub>O (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 700

[CAS No.16709-25-4]  $C_{12}H_{14}N_2O_2 \cdot 1/2H_2O = 227.26$ 

**350921** (*R*)-α-Methyltryptophan-1/2H<sub>2</sub>O (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 700

[CAS No.56452-52-9]  $C_{12}H_{14}N_2O_2 \cdot 1/2H_2O = 227.26$ 



359456 (S)-N-Fmoc-N'-Boc- $\alpha$ -Methyltryptophan (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)

[CAS No.1315449-98-9]  $C_{32}H_{32}N_2O_6 = 540.62$  (NET) 200 mg \$ 800(\*)

Containing 5% n-Heptane (NET) 1 g \$ 1,200(\*)

**365299** (*R*)-N-Fmoc-N'-Boc- $\alpha$ -Methyltryptophan (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)

[CAS No.220155-72-6]  $C_{32}H_{32}N_2O_6 = 540.62$  (NET) 200 mg \$ 800(\*)

Containing 5% n-Heptane (NET) 1 g \$1,200(\*)



Boyle, S. et al. Bioorganic & Medicinal Chemistry 1994, 2, 357. van Megen, H. J. et al. Psychophormacology (Berlin) 1997, 129, 243. Dethlof, L. A. et al. Food Chem. Toxicol. 1998, 36, 61. Valerie, A. et al. J. Med. Chem. 2001, 44, 2276.



### Tyrosine (Tyr)

339269 (S)- $\alpha$ -Methyl-4-hydroxyphenylalanine ( $\geq$  98.0%,  $\geq$  98.0%ee)

1 g \$ 250

(S)-α-Methyltyrosine

[CAS No.672-87-7]

 $C_{10}H_{13}NO_3 = 195.22$ 

339268 (*R*)- $\alpha$ -Methyl-4-hydroxyphenylalanine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee)

g \$ 250

(R)- $\alpha$ -Methyltyrosine

[CAS No.672-86-6]

 $C_{10}H_{13}NO_3 = 195.22$ 



468643

(S)-N-Fmoc-α-Methyl-4-benzyloxyphenylalanine (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)

(S)-N-Fmoc-O-Benzyl- $\alpha$ -Methyltyrosine

1 g \$ 500(\*)

[CAS No.1283766-46-0]

 $C_{32}H_{29}NO_5 = 507.59$ 







**468642** (S)-N-Fmoc-α-Methyl-4-hydroxyphenylalanine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) (refrigerated transport)

(S)-N-Fmoc-α-Methyltyrosine

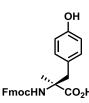
1 g \$ 500(\*)

[CAS No.246539-83-3]

 $C_{25}H_{23}NO_5 = 417.46$ 

5 g \$ 2,000(\*)





467091

**(S)-N-Fmoc-α-Methyl-4-triphenylmethoxyphenylalanine** (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)

(S)-N-Fmoc-O-Trityl- $\alpha$ -Methyltyrosine

1 g \$ 800(\*)

[CAS No.1934266-53-1]

 $C_{44}H_{37}NO_5 = 659.78$ 

5 g \$ 3,200(\*)





**387902** (*R*)-3-Hydroxyphenylalanine (≥ 98.0%, ≥ 98.0%ee)

lg \$ 500

(R)-m-Tyrosine

[CAS No.32140-49-1]

 $C_9H_{11}NO_3 = 181.19$ 

**387901** (*R*)-3-Methoxyphenylalanine- $H_2O$  ( $\ge 98.0\%$ ,  $\ge 98.0\%$ ee)

1g \$ 700

(R)-O-Methyl-m-tyrosine

[CAS No.145306-65-6]

 $C_{10}H_{13}NO_3 \cdot H_2O = 213.23$ 

### Valine (Val)

333444 (S)- $\alpha$ -Methylvaline (≥ 98.0%, ≥ 98.0%ee)

1 g \$ 300

[CAS No.53940-83-3]

 $C_6H_{13}NO_2 = 131.18$ 

333443 (*R*)- $\alpha$ -Methylvaline ( $\geq$  98.0%,  $\geq$  98.0%ee)

1g \$ 300

[CAS No.53940-82-2]

 $C_6H_{13}NO_2 = 131.18$ 

**358030** (S)-N-Fmoc-α-Methylvaline (≥ 98.0%, ≥ 98.0%ee) (refrigerated transport)

(NET) 1 g \$ 800(\*)

[CAS No.169566-81-8]

 $C_{21}H_{23}NO_4 = 353.42$ 

Containing ≤10% Methyl tert-butyl ether

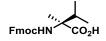
358031 (*R*)-N-Fmoc- $\alpha$ -Methylvaline ( $\geq$  98.0%,  $\geq$  98.0%ee) (refrigerated transport)

(NET) 1 g \$ 800(\*)

[CAS No.616867-28-8]

 $C_{21}H_{23}NO_4 = 353.42$ 

Containing ≤10% Methyl tert-butyl ether





# α-Methyl substituted Phenylalanines

### F-Phe

410325	(S)-α-Methyl-3-fluorophenylalanine (≥ 98.0%, ≥ 98.0%ee)		1 g \$ 400
	[CAS No.130855-56-0]	$C_{10}H_{12}FNO_2 = 197.21$	5 g \$ 1,200
411825	( <i>R</i> )- $\alpha$ -Methyl-3-fluorophenylalanin	<b>ne</b> (≥ 98.0%, ≥ 98.0%ee)	1 g \$ 400
	[CAS No.1270184-80-9]	$C_{10}H_{12}FNO_2 = 197.21$	5 g \$ 1,200
410133	(S)- $\alpha$ -Methyl-4-fluorophenylalanin	<b>le</b> (≥ 98.0%, ≥ 98.0%ee)	1 g \$ 300
	[CAS No.130855-57-1]	$C_{10}H_{12}FNO_2 = 197.21$	5 g \$ 900
410132	( <i>R</i> )- $\alpha$ -Methyl-4-fluorophenylalanin	<b>ne</b> (≥ 98.0%, ≥ 98.0%ee)	1 g \$ 300
	[CAS No. 422568-68-1]	$C_{10}H_{12}FNO_2 = 197.21$	5 g \$ 900
	F H <sub>2</sub> N CO <sub>2</sub> H	F H <sub>2</sub> N CO <sub>2</sub> H	

365442 (S)-N-Fmoc-α-Methyl-2-fluorophenylalanine (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 300 [CAS No.1172127-44-4]  $C_{25}H_{22}FNO_4 = 419.45$ 

364680 (*R*)-N-Fmoc-α-Methyl-2-fluorophenylalanine (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 300

 $C_{25}H_{22}FNO_4 = 419.45$ 

FmocHN CO<sub>2</sub>H FmocHN CO<sub>2</sub>

**468735** (S)-N-Fmoc-α-Methyl-3-fluorophenylalanine ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) (refrigerated transport)

[CAS No.1410792-22-1]  $C_{25}H_{22}FNO_4 = 419.45$  1 g \$ 500(\*)



[CAS No.1315449-93-4]

**386761** (S)-N-Fmoc-α-Methyl-2,6-difluorophenylalanine (≥ 98.0%, ≥ 98.0%ee) 1 g \$ 400

[CAS No.1223105-51-8]  $C_{25}H_{21}F_2NO_4 = 437.44$ 

FmocHN CO<sub>2</sub>H

Mapelli C. et. al. J. Med. Chem. 2009, 52, 7788-7799.

387097	(R)-α-Methyl-4-trifluoromethylphenylalanine ethyl ester-HCl-H <sub>2</sub> O (≥ 98.0%, ≥ 98.0%ee)

[CAS No.1315449-99-0]  $C_{13}H_{16}F_3NO_2 \cdot HCI \cdot H_2O = 329.75$  1 g \$ 600

411843	(S)-α-Methyl-4-trifluoromethoxyphenylalanine (≥ 98.0%, ≥ 98.0%ee)			\$ 800
	[CAS No. 1269926-90-0]	$C_{11}H_{12}F_3NO_3 = 263.22$	5 g	\$ 3,200
410538	(R)-α-Methyl-4-trifluoromethoxyp	henylalanine (≥ 98.0%, ≥ 98.0%ee)	1 g	\$ 800
	[CAS No.1269835-58-6]	$C_{11}H_{12}F_3NO_3 = 263.22$	5 a	\$ 3.200

# **Br-Phe**

322899	(S)- $\alpha$ -Methyl-2-bromophenylalanine-H <sub>2</sub> O ( $\geq$ 98.0%, $\geq$ 98.0%ee)			l g	\$ 450
	[CAS No.1212180-27-2]	$C_{10}H_{12}BrNO_2 \cdot H_2O = 276.13$			
322894	( <i>R</i> )-α-Methyl-2-bromophenylalanin	<b>e-H<sub>2</sub>O</b> (≥ 98.0%, ≥ 98.0%ee)	1	l g	\$ 450
	[CAS No.1212307-90-8]	$C_{10}H_{12}BrNO_2 \cdot H_2O = 276.13$			
328956	(S)-α-Methyl-3-bromophenylalanin	<b>e-H<sub>2</sub>O</b> (≥ 98.0%, ≥ 98.0%ee)	1	l g	\$ 300
	[CAS No.1212117-73-1]	$C_{10}H_{12}BrNO_2 \cdot H_2O = 276.13$			
328957	( <i>R</i> )-α-Methyl-3-bromophenylalanin	<b>e-H<sub>2</sub>O</b> (≥ 98.0%, ≥ 98.0%ee)	1	l g	\$ 300
	[CAS No.1212321-90-8]	$C_{10}H_{12}BrNO_2 \cdot H_2O = 276.13$			
322900	(S)-α-Methyl-4-bromophenylalanin	<b>e</b> (≥ 98.0%, ≥ 98.0%ee)	1	l g	\$ 400
	[CAS No.747397-27-9]	$C_{10}H_{12}BrNO_2 = 258.11$			
322897	( <i>R</i> )-α-Methyl-4-bromophenylalanine (≥ 98.0%, ≥ 98.0%ee)		1	l g	\$ 400
	[CAS No.752971-41-8]	$C_{10}H_{12}BrNO_2 = 258.11$			





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329205	(S)- $\alpha$ -Methyl-3-iodophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee)		•	1 g	\$ 350
	[CAS No.457653-01-9]	$C_{10}H_{12}INO_{2} \cdot H_{2}O = 323.13$			
329207	(R)-α-Methyl-3-iodophenylalanine-	<b>H</b> <sub>2</sub> <b>O</b> (≥ 98.0%, ≥ 98.0%ee)	•	1 g	\$ 350
	[CAS No.457652-83-4]	$C_{10}H_{12}INO_{2} \cdot H_{2}O = 323.13$			
329206	(S)- $\alpha$ -Methyl-4-iodophenylalanine ( $\geq$ 98.0%, $\geq$ 98.0%ee)		•	1 g	\$ 300
	[CAS No.1215092-16-2]	$C_{10}H_{12}INO_2 = 305.11$			
329204	( <i>R</i> )-α-Methyl-4-iodophenylalanine (≥ 98.0%, ≥ 98.0%ee)		•	1 g	\$ 300
	[CAS No.213203-06-6]	$C_{10}H_{12}INO_2 = 305.11$			



# NO<sub>2</sub>-Phe

(S)-α-Methyl-2-nitrophenylalanine·H₂O (≥ 98.0%, ≥ 98.0%ee)		1 9	g \$	200
[CAS No.1241680-71-6]	$C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$			
( <i>R</i> )- $\alpha$ -Methyl-2-nitrophenylalanine-H	l <sub>2</sub> <b>O</b> (≥ 98.0%, ≥ 98.0%ee)	1 (	<b>;</b> \$	200
[CAS No.1241680-73-8]	$C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$			
(S)-α-Methyl-3-nitrophenylalanine-H <sub>2</sub> O (≥ 98.0%, ≥ 98.0%ee)		1 (	<b>;</b> \$	200
[CAS No.1215092-14-0]	$C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$			
( <i>R</i> )-α-Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee)		1 (	<b>;</b> \$	200
[CAS No. 1215092-13-9]	$C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$			
	[CAS No.1241680-71-6]  (R)-α-Methyl-2-nitrophenylalanine-H  [CAS No.1241680-73-8]  (S)-α-Methyl-3-nitrophenylalanine-H  [CAS No.1215092-14-0]  (R)-α-Methyl-3-nitrophenylalanine-H	[CAS No.1241680-71-6] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (R)- $\alpha$ -Methyl-2-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) [CAS No.1241680-73-8] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (S)- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) [CAS No.1215092-14-0] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (R)- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee)	[CAS No.1241680-71-6] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (R)- $\alpha$ -Methyl-2-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 (CAS No.1241680-73-8] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (S)- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 (CAS No.1215092-14-0] $C_{10}H_{12}N_2O_4\cdot H_2O = 242.23$ (R)- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 (CAS No.1215092-14-0) 1 (C	[CAS No.1241680-71-6] $C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$ ( <i>R</i> )- $\alpha$ -Methyl-2-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 g \$  [CAS No.1241680-73-8] $C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$ ( <i>S</i> )- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 g \$  [CAS No.1215092-14-0] $C_{10}H_{12}N_2O_4 \cdot H_2O = 242.23$ ( <i>R</i> )- $\alpha$ -Methyl-3-nitrophenylalanine- $H_2O$ ( $\geq 98.0\%$ , $\geq 98.0\%$ ee) 1 g \$



# 4-Ph-Phe

335436 (S)- $\alpha$ -Methyl- $\beta$ -(4-biphenyl)alanine- $H_2O$  ( $\geq 98.0\%$ ,  $\geq 98.0\%$ ee) 1 g \$ 500 [CAS No.1231709-24-2]  $C_{16}H_{17}NO_2 \cdot H_2O = 273.33$ 







# D-Amino acids



Arg

**477449** (*R*)-Arginine (≥ 98.0%, ≥ 98.0%ee)

[CAS No.157-06-2]

 $C_6H_{14}N_4O_2 = 174.20$ 

$$HN \rightarrow NH_2$$
 $NH$ 
 $H_2N \rightarrow CO_2H$ 

Asn

**477452** (*R*)-Asparagine-H<sub>2</sub>O (≥ 98.0%, ≥ 98.0%ee)

[CAS No.5794-24-1]

 $C_4H_8N_2O_3 \cdot H_2O = 150.13$ 

<u>Asp</u>

**477473** (*R*)-Aspartic acid (≥ 98.0%, ≥ 98.0%ee)

[CAS No.1783-96-6]

 $C_4H_7NO_4 = 133.10$ 

Cys

**477470** (S)-D-Cysteine-HCI-H<sub>2</sub>O ( $\geq$  98.0%,  $\geq$  98.0%ee)

25 g \$ 170

25 g \$ 150

25 g \$ 130

25 g \$ 120

[CAS No.32443-99-5]

 $C_3H_7NO_2S \cdot HCI \cdot H_2O = 175.63$ 

Glu

**477465** (*R*)-Glutamic acid (≥ 98.0%, ≥ 98.0%ee)

25 g \$ 130

[CAS No.6893-26-1]

 $C_5H_9NO_4 = 147.13$ 

<u>GIn</u>

**477466** (*R*)-Glutamine (≥ 98.0%, ≥ 98.0%ee)

25 g \$ 150

[CAS No.5959-95-5]

 $C_5H_{10}N_2O_3 = 146.15$ 

<u>His</u>

**477467** (*R*)-Histidine (≥ 98.0%, ≥ 98.0%ee)

[CAS No.351-50-8]  $C_6H_9N_3O_2 = 155.16$ 

 $H_2N \longrightarrow CO_2H$ 

25 g \$ 150

Lys

**477469** (*R*)-Lysine·HCl (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 145

[CAS No.7274-88-6]  $C_6H_{14}N_2O_2 \cdot HCI = 182.65$ 

HCI·H<sub>2</sub>N CO<sub>2</sub>H

Met

**477464** (*R*)-Methionine (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 130

[CAS No.348-67-4]  $C_5H_{11}NO_2S = 149.21$ 

Phe

**477442** (*R*)-Phenylalanine (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 135

[CAS No.673-06-3]  $C_9H_{11}NO_2 = 165.19$ 

**Pro** 

**477476** (*R*)-Proline (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 125

[CAS No.344-25-2]  $C_5H_9NO_2 = 115.13$ 

N CO<sub>2</sub>H

Ser

**477443** (*R*)-Serine (≥ 98.0%, ≥ 98.0%ee)

[CAS No.312-84-5]  $C_3H_7NO_3 = 105.09$ 

H<sub>2</sub>N CO<sub>2</sub>H

25 g \$ 135

**Thr** 

**477468** (*R*)-Threonine (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 145

[CAS No.632-20-2]  $C_4H_9NO_2 = 119-12$ 

H³N, CO³H

**Trp** 

**477446** (*R*)-Tryptophan (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 150

[CAS No.153-94-6]  $C_{11}H_{12}N_2O_2 = 204.23$ 

NH H<sub>2</sub>N CO<sub>2</sub>H

Val

**477479** (*R*)-Valine (≥ 98.0%, ≥ 98.0%ee) 25 g \$ 120

[CAS No.640-68-6]  $C_5H_{11}NO_2 = 117.15$ 

H₂N CO₂H



# **Chemical Abbreviation Definitions**

We listed the abbreviations used in this catalog.

Abbreviation	Chemical Name	Chemical Structure
Ac	Acetyl	٨
Alloc	Allyloxycarbonyl	<b>&gt;</b> ~o <sup>□</sup>
Bn	Benzyl	
Вос	<i>tert</i> -Butoxycarbonyl	×.ji.
Fmoc	9-Fluorenylmethoxycarbonyl	j.
Mmt	4-Methoxytrityl	MeO—
Mtt	4-Methyltrityl	
Trt	Triphenylmethyl Trityl	

## Di-Peptides synthesized from our Unnatural Amino Acids

NAGASE is developing a range di-peptides which are composed of a natural amino acid connected to N-terminal of our unnatural,  $\alpha, \alpha$ -dialkylated amino acids.

Usually  $\alpha$ , $\alpha$ -dialkylated amino acids are not so reactive with other natural amino acids at the N-terminal position because of their steric hindrance around the chiral carbon center.

That is the reason why you may have obtained a peptide in low yield as a result of incomplete conjugation of the amino acid adjacent to the dialkylated amino acid.

As a result NAGASE commissioned certain peptide custom synthesis companies in Japan and China to provide N-Fmoc-protected di-peptide which is composed of a natural amino acid and  $\alpha$ , $\alpha$ -dialkylated amino acid and can be used in solid phase peptide synthesis

### **Examples**

Fmoc-Gly-(S)-Ala(4-Pte)-OH

Fmoc-Arg(Pbf)-(S)-Ala(4-Pte)-OH

## Application of Unnatural Amino Acids for Pharmaceuticals

Replacement of the  $\alpha$ -hydrogen atom of L- $\alpha$ -amino acids with an alkyl substituent results in  $\alpha$ , $\alpha$ -disubstituted amino acids has been reported in numerous scientific publications and is seen in APIs and developmental drug candidates. The modification changes the properties of amino acids as follows: 1) increased chemical stability, 2) increased hydrophobicity, 3) restriction of conformational freedom of side chains in amino acids. Incorporation of  $\alpha$ , $\alpha$ -disubstituted amino acids into peptides results in the restriction of conformational freedom and increased metabolic stability of the resultant peptides.

### Reference:

Tanaka, M. Chem. Pharm. Bull. 2007, 55, 349-358.

Walensky, L. D.; Kung, A. L.; Escher, I.; Malia, T. J.; Barbuto, S.; Wright, R. D.; Wagner, G.; Verdine, G. L. Science, 2004, 305, 1466.

Walensky, L. D.; Bird, G. H. J. Med. Chem. 2014, 57, 6275.

### Examples of investigational APIs including $\alpha,\alpha$ -disubstituted amino acids.

H<sub>3</sub>C N N CI

Chiral Analogue of Single S1P Receptor

Högenauer, K. et al. Bioorg. Med. Chem. Lett. 2010, 20, 1485-1487.

Integrin ab-2 (LFA-1) Antagonist LFA-1/ICAM-1 Interaction Inhibitors

Kelly, T.A. et al. J. Immunol, 1999, 163, 5173-5177.

Glucagon -like Peptide-1 Receptor Agonist with Antidiabetic Activity

Mapelli, C. et. al. J. Med. Chem. 2009, 52, 7788-7799.

**NK1** Receptor Antagonist

Boyle, S.et al. Bioorganic & Medicinal Chemistry 1994, 2, 357-370.

### α-Chymotrypsin Type:VII From Bovine Pancreas

$$R = H \text{ or } Me$$

$$Q_{2}N$$

$$H_{2}N$$

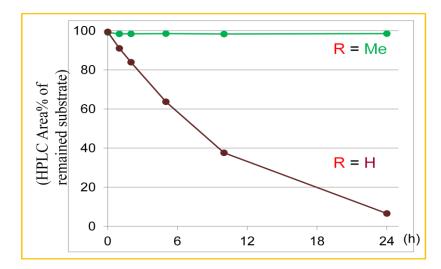
$$NHMe$$

$$Q_{2}N$$

$$NHMe$$

$$Q_{2}N$$

$$R = H \text{ or } Me$$



Incubated at 30 °C in 10% DMSO / 0.1 M Pi buffer (pH=8.0) solution

A tryptic digestion assay of an  $\alpha$ -methylphenylalanine-containing peptide was carried out to investigate the effect of the replacement of an  $\alpha$ , $\alpha$ -dialkylamino acid residue on resistance to protease degradation. The introduction of an  $\alpha$ , $\alpha$ -dialkylamino acid residue ( $\alpha$ -Methylphenylalanine) to the peptide backbone resulted in greater resistance to protease degradation over 24 hours than the peptide with  $\alpha$ -monoalkyl amino acid (phenylalanine). The peptide containing the  $\alpha$ , $\alpha$ -dialkylamino acid residue exhibited complete resistance to degradation under the experimental conditions.

### Reference:

Matsuyama, K.; Yamamoto, K.; Murakami, S.; Anzai, K. Construction of an unnatural amino acids library through asymmetric alkylation of glycine or alanine ester Shiff-base utilizing Maruoka Catalyst<sup>®</sup>.

Presented at the 5th International Peptide Symposium, Kyoto, Japan, December 4-9, 2010; P2-204.

# Asymmetric Phase-Transfer Reaction with Maruoka Catalyst<sup>®</sup> to Synthesize $\alpha$ -Monosubstituted and $\alpha$ , $\alpha$ -Disubstituted Amino Acids.

Ar = 
$$R^2$$
 $R^3$ 
 $R^4$ 
 $R^4$ 
 $R^5$ 
 $R^5$ 

Ikunaka, M. and Maruoka, K. 'Asymmetric Phase-Transfer Catalysts for the Production of Non-Proteinogenic alpha-Amino Acids' in *Asymmetric Catalysis on Industrial Scale* 2<sup>nd</sup> edition, Blaser, H-U. and Federsel, H.-J. eds. Wiley-VCH Verlag GmbH & Co. KGaA (2010)

According to the Makosza interfacial mechanism, protected  $\alpha$ -amino acid is converted into the potassium *E*-enolate. Due to the lipophilic nature of the quaternary ammonium salt it can move easily into the interface layer where cation exchange takes place with the potassium *E*-enolate. As the *si* face of the *E*-enolate is shielded by the molecular cavity of the catalyst, an alkyl halide can only approach the *re* face of the enolate. This results in the Maruoka Catalyst<sup>®</sup> exhibiting high reactivity and selectivity of the alkylation process.

### Reference:

Ooi, T., Kameda, M., and Maruoka, K. *J. Am. Chem. Soc.*, **2003**, *125*, 5139-5151.

Ooi, T., Kameda, M., Tannai, H., and Maruoka, K. Tetrahedron Lett., 2000, 41, 8339-8342.

Ooi, T., Takeuchi., M., and Maruoka, K. Synthesis 2001, 1716-1718.

Maruoka, K. Org. Process Research & Development 2008, 12, 679-687.

### Patents:

USP 6,340,753; 6,441,231; 7,928,224; 8,110,680; 8,252,952; 8,263,798; 8,614,316; 8,697,910; 8,716,524; 8,722,919

JP 4,217,085; 4,502,293; 4,605,606; 4,802,191; 4,879,896; 5,008,553; 5,108,777; 5,244,149; 5,344,523

CA 2,549,431; 2.610,776

SG 139,249; 149,879

IN 252,017; 260,006

CN ZL200580003716.6; ZL200680027800.6

### Trade mark

Maruoka Catalyst is the registered trade mark in Japan, US, UK, Germany and France.

### Sales Information for Unnatural Amino Acids:

### Pricing:

All prices are in U.S. dollars. All catalog products are available from inventory in Japan and can be delivered CIP to the designated airport (port of entry) by air within two weeks of confirmed Purchase Order. Prices are subject to change without notice.

Products marked with an asterisk (\*) mark may require an additional fee for refrigerated transport.

#### Ordering:

Orders can be placed by e-mail, phone or fax with the contact person in your region (see Contacts below).

#### Inquiries:

NAGASE offers a wide range of custom products not listed in this catalog. If you do not find a product you need in this catalog, please inquire about its availability by e-mail, phone or fax. NAGASE will promptly evaluate your request and a NAGASE representative will promptly contact you.

### **Bulk Quantities & Custom Manufacturing under cGMP:**

**NAGASE** has the technology, experience and capacity to supply bulk and commercial quantities of products as well as custom manufacturing to meet your specific needs. For further information, please contact NAGASE and a technical representative will contact you to discuss your specific project needs.

### General Information:

Company Profile: 'a technology and intelligence oriented company that turns wisdom into business.'

### Mission: 'Maintain Good and Fair Business Practice'

NAGASE & CO., LTD., the nucleus of our group, was established as a dyestuffs wholesaler in Kyoto, Japan in 1832. Since then, NAGASE has opened up new markets worldwide together with its customers and accumulated considerable know-how in its role as 'a technology and intelligence oriented trading company.' At the same time, it has enhanced its product offer with new R&D, manufacturing and processing technology. Today, The NAGASE Group is a 740 billion JPY (FY 2015) company and offers customers trading, marketing, R&D and manufacturing functions in its four strategic areas of Chemicals, Plastics, Electronics and Life Sciences.

### R&D Sites and Nagase Pharmaceutical Group:

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Nagase Medicals Co.,Ltd.

4-323, Senzo, Itami, Hyogo, 664-0898 JAPAN www.nagase-medicals.co.jp

HAYASHIBARA CO., LTD.

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