

(19)  
(12)

(KR)  
(A)

(51) 。 Int. Cl. <sup>7</sup>  
C07D 211/72

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(43)

2001 - 0104730  
2001 11 26

(21)	10 - 2001 - 7012187
(22)	2001 09 25
	2001 09 25
(86)	PCT/EP2000/02377
(86)	2000 03 17

(87) WO 2000/58284  
(87) 2000 10 05

[illegible]

(30) 19913699.8 1999 03 26 (DE)

(71)

- 67056 - - 38

(72)	,		
	- 76889		22
	,		
	- 69115	가	21
	,		
	- 69168		52
	,		
	- 69124	가	16
	,		
	- 79539		48
	,		
	- 5036		41

(74)

:

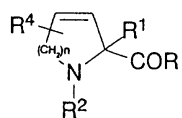
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(54) 3,4 - 3,4 -

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I .

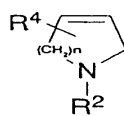
&lt; I &gt;



$C_1 - C_6 -$ , R,  $C_1 - C_6 -$ , - NHC $_1 - C_6 -$ , N(C $_1 - C_6 -$ ) $_2$ , OH, NH $_2$ , R $^1$ , C  
 $C_1 - C_6 -$ , Me $_3$ Si,  $C_1 - C_6 -$ , - S, R $^2$ , Boc,  $C_1 - C_6 -$ , ,  
 A1 - A3 - , n 1 2 , R $^4$  H  $C_1 - C_6 -$  .

R OH, CO $_2$  II III ,  
 IV 가

&lt; II &gt;



&lt; III &gt;



&lt; IV &gt;

 $R^3 - X$ 

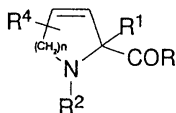
,  $R^2$  Boc,  $C_1 - C_6 -$ , , , ,  $A1 - A3 -$ ,  $R^4$   
 $H$   $C_1 - C_6 -$ ,  $n$  1 2,  $R$ ,  $C_1 - C_6 -$ ,  $-NHC_1 - C_6 -$ ,  $-N(C_1 - C_6 -)_2$ ,  
 $OH$   $NH_2$ , III  $R$   $OH$ 가,  $Y$   $Cl$ ,  $C_1 - C_6 -$ ,  $-NHC_1 - C_6 -$ ,  $-N(C_1 - C_6 -)$   
 $2$   $N(C_1 - C_6 -)OC_1 - C_6$ ,  $X$   $Cl$ ,  $Br$ ,  $I$ ,  $MesO$ ,  $TosO$ ,  $R^3$ ,  $C_1 - C_6 -$   
 $, Me_3Si, C_1 - C_6 - -S$   $NH_4$ ,  $R^3 - X$   $(C_1 - C_6 - -S)_2$ .

3,4 - , 3,4 - ,

3,4 - 3,4 - .

I

I



,

 $R$ ,  $C_1 - C_6 -$ ,  $-NHC_1 - C_6 -$ ,  $N(C_1 - C_6 -)_2$ ,  $OH$   $NH_2$ ,

 $R^1$ ,  $C_1 - C_6 -$ ,  $Me_3Si$   $C_1 - C_6 - -S$ ,

 $R^2$  Boc,  $C_1 - C_6 -$ , , , ,  $A1 - A3 -$ ,
 $n$  1 2 , $R^4$   $H$   $C_1 - C_6 -$  .
 3,4 - 4 - 가 (Tschugaeff [P. Grogg, Angew. Chem. 92  
 (1980) 761] (64%)

. 180 190 12 Torr

 , , , [J.  
 R. Dormoy, Synthesis (1982) 752]. , .

[J.W. Scott, Synth. Commun. 10 (1980) 529].  
 Bio. Chem. 251 (1976) 503; 4066658 ] [S. S. Kerwar, J.  
 [A. Corbella, Chem. Ind. ( 1969 ) 583  
 50%

98/04523

(Birch) [J. Org. Chem. 61 (1996) 7664]  
 (T.J. Donohoe) - 2 -

98/55456

- 2 -

- 2 -

3,4 - - 2 - (D'Ambra, Bell) [J. Org. Chem. 54 (1  
 989) 5632] 가 - (Krogs gaard - Larsen) [J. Labeled Compd. 19 (1982) 689]  
 가 ( )

I 3,4 -

3,4 -

3 - [Grubbs, J. Org. Chem. 62 (1997) 7310; Pandit, Te  
 trahedron Lett. 37 (1996) 547; Grubbs, J. Am. Chem. Soc. 115 (1993) 9856 ; Moreno - Manas, Tetrahed  
 ron 54 (1998) 14869]

, 2 3 - [Meyers, J. Am. Chem. Soc. 107 (1985) 7974; Macdonald, J. Org. C  
 hem. 45 (1980) 193; Francke, Liebigs Ann. (1995) 193] [I  
 zawa, Bull. Chem. Soc. Jpn. 64 (1991) 620]

[Beak, J. Am. Chem. Soc. 116 (1994) 3231]

(Colegate)

[Austral. J. Chem. 37 (1984) 1503]

- 3 -

1 - (3 -

) 65%

N -

- 3 -

- 2 -

,

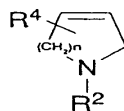
II  
 I R OH  
 가

3,4 -  
 CO<sub>2</sub>

IV

III

II



III



IV

R<sup>3</sup> - X

,

R<sup>2</sup> Boc, C<sub>1</sub> - C<sub>6</sub> - , , , A1 - A3 - ,R<sup>4</sup> H C<sub>1</sub> - C<sub>6</sub> - ,

n 1 2 ,

R , C<sub>1</sub> - C<sub>6</sub> - , - NHC<sub>1</sub> - C<sub>6</sub> - , - N(C<sub>1</sub> - C<sub>6</sub> - )<sub>2</sub>, OH NH<sub>2</sub> , III R OH가

,

Y Cl, C<sub>1</sub> - C<sub>6</sub> - , - NHC<sub>1</sub> - C<sub>6</sub> - , - N(C<sub>1</sub> - C<sub>6</sub> - )<sub>2</sub> N(C<sub>1</sub> - C<sub>6</sub> - )OC<sub>1</sub> - C<sub>6</sub> ,

X Cl, Br, I, MesO, TosO ,

R<sup>3</sup> , C<sub>1</sub> - C<sub>6</sub> - , Me<sub>3</sub> Si, C<sub>1</sub> - C<sub>6</sub> - - S NH<sub>4</sub> ,R<sup>3</sup> - X (C<sub>1</sub> - C<sub>6</sub> - - S)<sub>2</sub> .

V

.

V

MNR<sup>5</sup> R<sup>6</sup>

,

M Na Li ,

R<sup>5</sup> H C<sub>1</sub> - C<sub>6</sub> - ,R<sup>6</sup> H C<sub>1</sub> - C<sub>6</sub> - .III - C<sub>1</sub> - C<sub>6</sub> - ,

.

A1 - A3 - 3 , ( (proteinogenic)) ( ) . A1 - A3 . A1 - A

3 - .

A1, A2 A3 t - , t - , , , D -

$C_6$  - ,  $C_1$  -  $C_6$  - /DMPU ,  $C_2$  -  $C_8$  , THF  $C_1$  -  
 0 - 100 +100 1 200 bar - 20 +2  
 ) , ( , GC, HPLC TLC

가

3,4 -

3,4 -

94/29336 , 95/35309 ,

96/17860 , 96/24609 , 96/25426

98/06741 , ,

1

N - t<sup>t</sup> - 3<sup>3</sup> -

4.1 Mℓ (48.7 mmol) N - t<sup>t</sup> 3 - 8.2 g (48.5 mmol) THF 40 Mℓ

가 4 , - 5 , LDA ( , THF 2 ) 54 Mℓ

가 20 , 가 .

0 10 n - 150 Mℓ , 1N HCl 200 Mℓ .

HCO<sub>3</sub> , n - 50 Mℓ 3 , , 0.01 N HCl, Na

NaCl 2 , , MgSO<sub>4</sub> ,

120 150 /0.4 Torr . (seed) 가

n - . 9.06 g; 82%;

2

N - t<sup>t</sup> - 2 - - 3<sup>3</sup> -

N - t<sup>t</sup> - 3<sup>3</sup> - 1 ( 1.60 mmol =  
 N - t<sup>t</sup> - 3<sup>3</sup> - 271 mg). 가 0 5  
 . , 0.1 Mℓ (1.61 mmol) 가 . , 0 10  
 1 . 가 N - t<sup>t</sup>  
 - 3<sup>3</sup> - 24% 75% 320 mg ( 83%)  
 .

3

N - - 3<sup>3</sup> - - 2 -

THF 3 Mℓ N - - 3<sup>3</sup> - 228 mg (1.47 mmol) 0.14 Mℓ (1.66 m  
 mol) 0 LDA ( , THF 2 ) 1.5 Mℓ 가 .  
 0 10 1 N HCl 5 Mℓ tert - 10 Mℓ .  
 n - 10 Mℓ 3 , 0.01 N HCl, NaHCO<sub>3</sub>  
 NaCl . , MgSO<sub>4</sub> ,  
 8:2) . : 201 mg ( 64%). ( :  
 .

4

N - t - - (R) - - (R,S) -

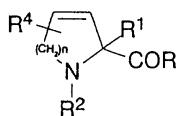
LDA (2M, 2.6 mmol - (Fluka)) 0 THF 5 Mℓ N - t - - (R) -  
 - 524 mg (1.70 mmol) 0.3 Mℓ (357 mmol) 가 .  
 0 15 1N HCl/n - , NaHCO<sub>3</sub> MgSO<sub>4</sub>  
 . 0.59 g . PE:EA 7:3  
 . : 307 mg ( 49%).

(57)

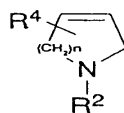
1.

II , III , I  
 R OH , I 3,4 - 3,4 -  
 .

&lt; I &gt;



&lt; II &gt;



< III >



,  
R, C<sub>1</sub> - C<sub>6</sub> -, -NHC<sub>1</sub> - C<sub>6</sub> -, -N(C<sub>1</sub> - C<sub>6</sub> - )<sub>2</sub>, OH, NH<sub>2</sub>, III R OH가

R<sup>1</sup>, C<sub>1</sub> - C<sub>6</sub> -, Me<sub>3</sub>Si, C<sub>1</sub> - C<sub>6</sub> - -S,

R<sup>2</sup> Boc, C<sub>1</sub> - C<sub>6</sub> -, A1 - A3 - ,

n 1 2 ,

R<sup>4</sup> H, C<sub>1</sub> - C<sub>6</sub> - ,

Y Cl, C<sub>1</sub> - C<sub>6</sub> -, -NHC<sub>1</sub> - C<sub>6</sub> -, -N(C<sub>1</sub> - C<sub>6</sub> - )<sub>2</sub>, N(C<sub>1</sub> - C<sub>6</sub> - )OC<sub>1</sub> - C<sub>6</sub> .

2.

1, II III 가 IV

< IV >

R<sup>3</sup> - X

X Cl, Br, I, MesO, TosO ,

R<sup>3</sup>, C<sub>1</sub> - C<sub>6</sub> -, Me<sub>3</sub>Si, C<sub>1</sub> - C<sub>6</sub> - -S NH<sub>4</sub> ,

R<sup>3</sup> - X (C<sub>1</sub> - C<sub>6</sub> - -S)<sub>2</sub> .

3.

1 2, III -C<sub>1</sub> - C<sub>6</sub> - .

4.



1 3 , A1 - A3 - 가

.

5.

1 4 ,  $R^2$  , 가 가

.

6.

1 5 , 1 200 bar - 100 +100

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