

(19)
(12)

(KR)
(A)

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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

(30) 19913699.8 1999 03 26 (DE)

(71)

- 67056 - - - 38

(72)

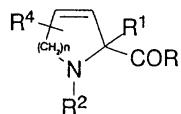
,	- 76889		22
,	- 69115	가	21
,	- 69168		52
,	- 69124	가	16
,	- 79539		48
,	- 5036		41

(74)

(54) 3.4 -

3.4 -

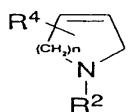
\wedge | \vee



$\text{R}_1 - \text{C}_6 - \text{A}1 - \text{A}3 - \text{C}_1 - \text{C}_6 - \text{Me}_3\text{Si}$, $\text{R}_2 - \text{S} - \text{R}^4$, $\text{Boc}, \text{C}_1 - \text{C}_6 - \text{n}$, H , $\text{C}_1 - \text{C}_6 - 1$, R^4 , R^1 , $\text{C}_1 - \text{C}_6 - \text{N}(\text{C}_1 - \text{C}_6 - \text{R}^1)_2, \text{OH}, \text{NH}_2$

$$\text{R} \quad \text{OH} \quad \text{CO}_2 \quad \text{,} \quad \text{II} \quad \text{,} \quad \text{III} \quad \text{,} \quad \text{IV} \quad \text{,} \quad \text{II} \quad \text{,} \quad \text{III} \quad \text{,} \quad \text{가}$$

||>



Λ ΙΙΙ ν



< IV >

R3³ - X

, R² Boc, C₁ - C₆ -, , , , A1 - A3 - , R⁴
H C₁ - C₆ -, , n 1 2 , R , C₁ - C₆ -, - NHC₁ - C₆ -, - N(C₁ - C₆ -)₂,
OH NH₂ , III R OH가 , Y Cl, C₁ - C₆ -, - NHC₁ - C₆ -, - N(C₁ - C₆ -)
2 N(C₁ - C₆ -)OC₁ - C₆ , X Cl, Br, I, MesO, TosO , R³ , C₁ - C₆ -
, Me₃Si, C₁ - C₆ - - S NH₄ , R³ - X (C₁ - C₆ - - S)₂ .

3,4 - , 3,4 -

3,4 - 3,4 - . ,

$$\text{R}^4 \text{---} \text{C}=\text{C}(\text{R}^1) \text{---} \text{C}(\text{COR})\text{---} \text{N}(\text{R}^2)\text{---} (\text{CH}_2)_n \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4$$

$$R - C_1 - C_6 - \dots - NHC_1 - C_6 - \dots - N(C_1 - C_6 - \dots)_2 - OH \quad NH_2 - \dots$$

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

R^2 Boc. C₁ - C₆ - A1 - A3 -

n 1 2

$$\mathbb{P}^4 \quad H \quad S \quad S$$

3.4 1

(1980) 761]

가 (Tschugaeff [P. Grogg, Angew. Chem. 92 (64%) , , . 180 190 12 Torr

R. Dormoy, Synthesis (1982) 752].

J.

[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 -

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

I 3,4 - 3,4 -

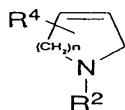
3 - [Grubbs, J. Org. Chem. 62 (1997) 7310; Pandit, Te
 trahedron Lett. 37 (1996) 547; Grubbs, J. Am. Chem. Soc. 115 (1993) 9856 ; Moreno - Manas, Tetrahed
 ron 54 (1998) 14869]

, 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 -
 , N - - 3 - - 2 -
 1 - (3 -) 65%



II



III**IV**R³ - X

,

R² Boc, C₁ - C₆ - , , , , , A1 - A3 - ,R⁴ H C₁ - C₆ - ,

n 1 2 ,

R , C₁ - C₆ - , - NHC₁ - C₆ - , - N(C₁ - C₆ -)₂, OH NH₂ , III R OH가Y Cl, C₁ - C₆ - , - NHC₁ - C₆ - , - N(C₁ - C₆ -)₂ N(C₁ - C₆ -)OC₁ - C₆ ,

X Cl, Br, I, MesO, TosO ,

R³ , C₁ - C₆ - , Me₃Si, C₁ - C₆ - - S NH₄ ,R³ - X (C₁ - C₆ - - S)₂ .**V****V**MNR⁵ R⁶⁶

,

M Na Li ,

R⁵ H C₁ - C₆ - ,R⁶ H C₁ - C₆ - .

III

- C₁ - C₆ - ,

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

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

3,4 -

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

가

I 3,4 - 3,4 -
94/29336 , 95/35309 ,
96/17860 , 96/24609 , 96/25426
98/06741 , ,

1

$$N - t^t = 3^3 =$$

4.1 Mℓ (48.7 mmol) N-t³ 8.2 g (48.5 mmol) THF 40 Mℓ
 , -5 . , LDA (, THF 2) 54 Mℓ
 가 4 가 20 , 가 .
 0 10 n- 150 Mℓ , 1N HCl 200 Mℓ
 , n- 50 Mℓ 3 , , 0.01 N HCl, Na
 HCO₃ NaCl 2 MgSO₄

120 150 /0.4 Torr . (seed) 가
 n - . 9.06 g; 82%;

2

N-t^t - 2 - - 3³ -
 N-t - - 3 - 1 (1.60 mmol =
 N-t - - 3 - 271 mg). 0 5
 . , 1 가 , 0 10
 . 3 - 24% . 가
 . 3 - 75% 320 mg (83%)
 .

3

N - - 3³ - - 2 -
 THF 3 Mℓ N - - 3 - 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 , ,
 NaCl MgSO₄ ,
 8:2) . : 201 mg (64%). 0.01 N HCl, NaHCO₃

4

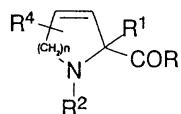
N-t - - (R) - - (R,S) -
 LDA (2M, 2.6 mmol - (Fluka)) 0 THF 5 Mℓ N-t - - (R) -
 - 524 mg (1.70 mmol) 0.3 Mℓ (357 mmol) 가
 0 15 1N HCl/n - , NaHCO₃ MgSO₄
 . 0.59 g PE:EA 7:3
 . : 307 mg (49%).

(57)

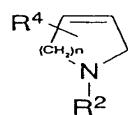
1.

II III , | 3,4 - , | 3,4 -
 R OH

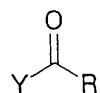
< | >



< || >



< III >



,

R , C₁ - C₆ - , - NHC₁ - C₆ - , - N(C₁ - C₆ -)₂, OH NH₂ , III R OH 가

,

R¹ , C₁ - C₆ - , Me₃Si C₁ - C₆ - - S ,R² Boc, C₁ - C₆ - , , , , A1 - A3 - ,

n 1 2 ,

R⁴ H, C₁ - C₆ - ,Y Cl, C₁ - C₆ - , - NHC₁ - C₆ - , - N(C₁ - C₆ -)₂, N(C₁ - C₆ -)OC₁ - C₆ .

2.

1 , II III 가 IV

< IV >

R³ - X

,

X Cl, Br, I, MesO, TosO ,

R³ , C₁ - C₆ - , Me₃Si, C₁ - C₆ - - S NH₄ ,R³ - X (C₁ - C₆ - - S)₂ .

3.

1 2 , III - C₁ - C₆ - .

4.

1 3 , A1 - A3 - 가

5.

1 4 , \mathbb{R}^2 , 가 가

6.

1 5 , 1 200 bar - 100 +100