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(12) (A)

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(43)

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2004 04 13

(21)	10-2004-7001404		
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(86)	2002 07 25	(87)	2003 02 13

(30) 01830510.2 2001 07 30 EP(EP)

(71) () 5
-21040

(72) -20147 8

-20131 12

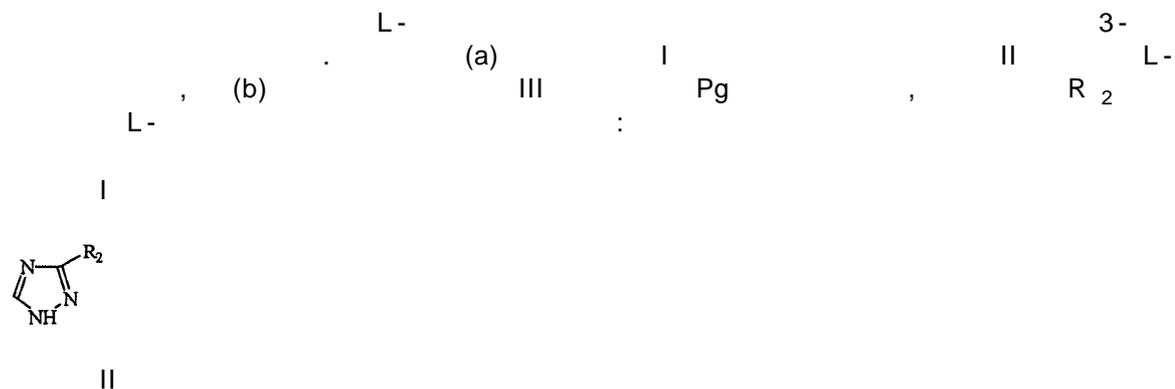
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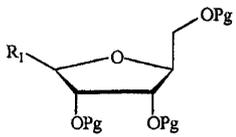
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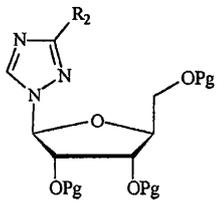
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(54) L -





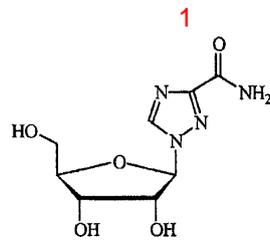
III



, .

, L- .

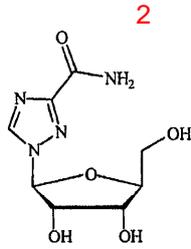
ex) 11) 1 C , 1- -D- -1H-1,2,4- -3- ((Merck Ind
-2b



, T- , .

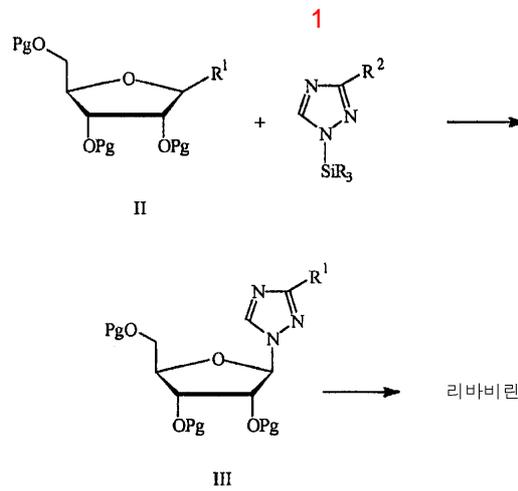
2 L- (1- -L- -1H-1,2,4- -3- ; ICN17261, L
; [J. Med. Chem., 43, 1019-1028 (2000)])
2

:



6,130,326

1



R¹ O- ;
 Pg , ;
 R² ;
 R , .
 (III)

[*J. Med. Chem.* (1972), 15 , 1150-1154]
 L-

D- (II)

(III)

2

1:1

1

(III)

가

([*Rev. Roum. Chim.* (1987), 32, 329-333]),
 (Friedel-Craft) (Lewis)

[*Chem. Ber.* (1981), 114, 1256-1268]),

([*Chem. Ber.* (1981),

(Vorbruggen) [*Chem. Ber.* (1981), 114, 1234-1255]
 (: SnCl₄)

HgBr₂
 260]

가 [*Nucl. Acid. Chem* (1978), 1, 255-

(CF₃CF₂OCF₂CF₂SO₃SiMe₃)
 ([*Nucleosides Nucleotides* (1991), 10, 619-20])

1972
 가

1991

가

가

[*J. Med. Chem.* (1972), 15, 1150-1154] (p-

3-

1:1

160

165

가

6,130,326

가

L-

III

a) (IV)
 ;

I

II

L-

b) 2 L-

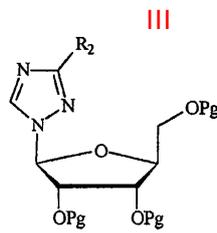
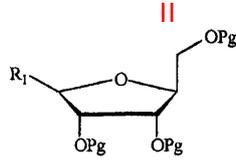
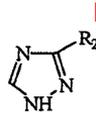
III

Pg

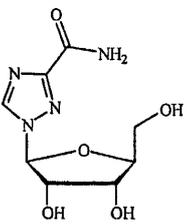
R₂

, L-

:



2



Pg

R₁ C₁-C₄

R₂ C₁-C₄

I

II

I

L-

, Pg

R₂가 C₁-C₄

3,798,209

R₂가

L-

가 (T. Green) (P. Wuts) ['Prot
ecting Groups in Organic Synthesis', chapter 2, page 17, 3rd Ed. (1999)]

II

R₁ C₁-C₄

C₁-C₄

(IV) (J. March)
 ['Advanced Organic Chemistry', page 227, 3rd Ed. (1985)]
 $AlCl_3$, $SbCl_5$, BF_4 , $SnCl_4$, $FeCl_3$, $SnCl_4$ 가

가
 2 (I), L- (II) (IV) (II) 1 (I) 1
 (IV) 1 1.5 (IV) 1 1.1 (II) 1
 (I) 1 1.2

-10
 가 5 20 가

III

R₂ L- III Pg

Pg
 ['Protecting Groups in Organic Synthesis', chapter 2, page 17, 3rd Ed. (1999)]

가
 , Pg가 가

R₂ , R₂ 가 CONH₂ 가 , L- III

R₂
 3rd Ed. (1985) ['Advanced Organic Chemistry', page 1152,

, R₂ 가 가 1 4 , (III) 1.9 2.5

III R₂ L-

, L- [J. Med. Chem. 1972, Vol.15, No.11, 1150-1154]
 (III)(Pg , R₂)

20 (IV) II L- 가
 가 가 가 20

(III) - 가 ,

가 , 가 (ammonolysis)
 L- , L- 50 1 2 5
 가 ,
 L- 가 ,

1-(2,3,5- -O- - -L-)-1H-1,2,4- -3-

(-L- , 3- , L-TARC, III, Pg=CH₃CO, R₂=COOCH₃)
 가 250Mℓ 4 42Mℓ, L-
 ((Fluka)) 10.0g 3- 4.6g
 5 , 9.0g 가 .
 2 가 가 15 20 , 가 ,
 15 20
 , 30% (4.4Mℓ) (38.0Mℓ) 20 가 45 , 15
 38.0Mℓ) , 30% (4.4Mℓ) ()
 45 , 15 ,
 30% (4.4Mℓ) (38.0Mℓ) .
 45 , 15 , (45)
 가 , 75Mℓ 가 , 200mbar
 (Buchner) . 2 5 10 , (2x5.0Mℓ)
 12.5g , 9.8g .

1- -L- -1H-1,2,4- -3-

(L- , L-RIBEST, III, Pg=H, R₂=COOCH₃)
 10 , 50.0Mℓ 가 , 0.2% 가 .
 30% 0.9g 30 가 .
 가 , 10 3 , 0.3g
 30 35 (50 300mbar) .

L-
 25.0Mℓ 1.6g 가 20 4
 (200mmHg, 40) 5.0Mℓ 가 60 70 가
 10.0Mℓ 가 .

L- 4 7.5g 0 5 , ,

_____ L- 7.5g(5.2g) 12.5Mℓ 가 , pH 7 8 5.0Mℓ 60 가 40 45
 . 2 5 , 5Mℓ .
 L- 5.4g 60 4.9g .

_____ :

:

[]_D (10mg/Mℓ; H₂O): +37.0 °

HPLC : 99.5%

NMR((Brucker) 300MHz, d₆-DMSO): ¹H 가 L- , ¹³C NMR 가 L- 1 .
 NOESY - 가 , 가 1

(57)

1.

(a) (IV) I II L-

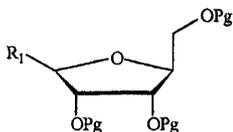
(b) III Pg , R₂ L-

, L- :

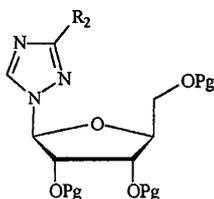
I



II



III



- Pg ;
- R₁ C₁-C₄ ;
- R₂ C₁-C₄ , , , .
- 2.**
1 ,
- R₂가 C₁-C₄ , .
- 3.**
1 ,
- Pg가 , , .
- 4.**
1 ,
- R₁ , C₁-C₄ , .
- 5.**
1 ,
- (IV) AlCl₃ , SbCl₅ , BF₄ , SnCl₄ FeCl₃ , SnCl₄ .
- 6.**
1 ,
- (a) 가 , .
- 7.**
1 ,
- (a) (I) 1 1.2 (II) 1 (IV) 1 (I) 1 2 (IV) 1 1.5 , (II) 1 (IV) 1 1.1 .
- 8.**
1 ,
- (a) 가 -10 .
- 9.**
1 ,
- L- .
- 10.**
9 ,
- 50 1 2 5 .