

(19) (KR)
(12) (A)

(51) Int. Cl.⁷
C07D 487/04

(11)
(43)

10-2004-0041166
2004 05 14

(21)	10-2004-7003997		
(22)	2004 03 18		
	2004 03 18		
(86)	PCT/EP2002/009935	(87)	WO 2003/031447
(86)	2002 09 05	(87)	2003 04 17

(30) 10148883.1 2001 10 04 (DE)

(71) 64293 250

(72) - 49

가
64297 53

64367 17

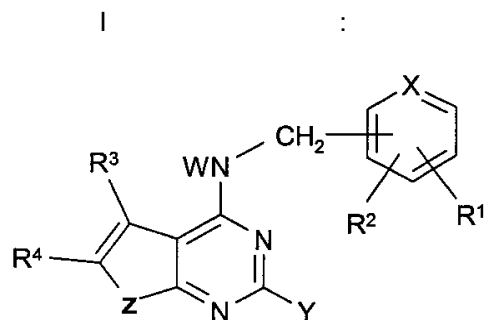
64354 - - 11

63322 10

(74)

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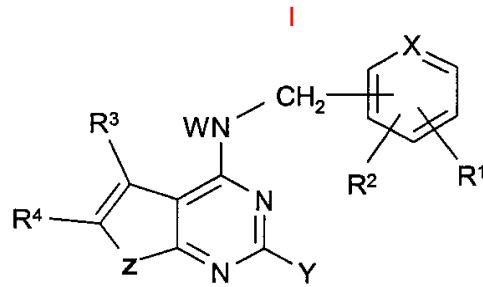
(54)



(, R¹, R², R³, R⁴, W, X, Y Z 1)

가 V

I :



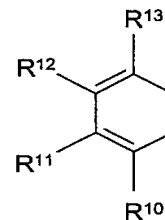
(,

R¹ R² H, A, OH, OA Hal ,

R¹ R² 3 5 , -O-CH₂-CH₂-, -CH₂-O-CH₂-, -O-CH₂-O-
-O-CH₂-CH₂-O- ,

R³ R⁴ , , H, A Hal ,

R³ R⁴ 3 5 ,



W H 1, 2, 3 4 ,

X CH N ,

Y (CH₂)_nR²⁰ , (CH₂)_q-R⁷ R⁵, R⁶ R⁹ ,

Z O, NH NA' ,

A' 1 6 , -CHAr -CHAr-A' ,

A' 1 6 ,

R⁵ CH₂ 가 -CH=CH- , -C C- , -O-, CO, -S-, -SO-, -SO₂-, -NH- -NA-
1 10 ,

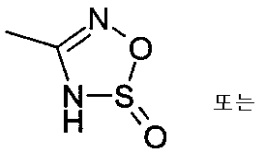
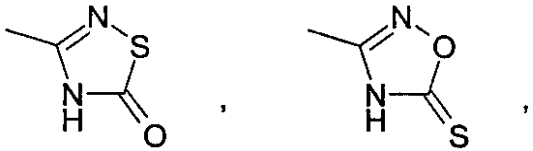
R⁶ 5 12 ,

R⁷, S, R²⁰, A, Hal, CF₃, 1, 4, N, O

R⁹ Ar, (CH₂)_k-Ar,

R¹⁰, R¹¹, R¹², R¹³ H, A, Hal, OA, OH, NH₂, NHA, NA₂, R²⁰,

R²⁰ -COOH, -COOA, -CONH₂, -CONHA, -CONA₂, -CN, -5-, -S(O)_mA, -S(O)_mNH₂, -S(O)_mOH,



또는

A₁₋₇ H 가 F 1-6,

Ar Hal, A, OA, OH, SO₂NH₂, SO₂NHA, SO₂NA₂, CN,

Hal F, Cl, Br, I,

k, q, 0, 1, 2, 3, 4,

m 1, 2,

n 0, 1, 2, 3)

()

, EP 0920431, EP 0934321, WO 99/28325, WO 99/55708, WO 00/78767 WO 01/21620

가

I

/

가

cGMP

(PDE V)

가

가

cGMP

d. 37, 2106 (1994))

(J. Med. Chem. 36, 3765 (1993) ibi

P I cAMP , WO 93/06104 IC₅₀ (50% . cGM)

(, W.J. Thompson et al., Biochem, 1971, 10 , 311) (W.J. Thompson and M.M. Appleman (Biochem. 1979, 18 , 5228)) (b atch method)

US 6,043,252 cGMP- PDE(PDE V) () /

(cor pulmonale), (COPD), (ulcus pecticum)(percutaneous transluminal coronary angioplasty), ()

, WO 94/28902 {F. Holmquist et al. in J. Urol., 150 , 1310-1315 (1993)}

2 V(PDE V) WO 00/15639 WO 00/15228

WO 00/15639 WO 00/15228 V(PDE V)

V WO 99/21558 ()

(R.T. Schermuly et al. in the *American Journal of Respiratory and Critical Care Medicine* , 160 , 1500-6 (1999)) PDE PDE / I₂ (PGI₂)

{Pneumologie (54, Sppl. 1, S42, 2000), R. Schermuly et al.} PDE-V 가 (vasorelaxation)

(=) V(PDE V) WO 00/15639

PDE V , WO 99/64004

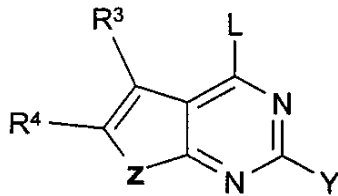
/10542 PDE V V(PDE V) WO 00/15228 WO 00 (antianginal agent) V

가

I , 가

, I

a) :

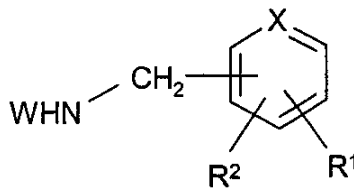


(,

Y, Z, R¹ R² 1 ,

L Cl, Br, OH, SCH₃ OH)

:



(, X, W, R¹ R² 1)

b) , COOH 가 COOH , I
X X

/ I , 1

(), ,

가 , -

{Int. J. Pharm. 115 , 61-67 (1995)}

:5, 1:10, 1:100 1:1000 I , 가 1:1, 1:2, 1:3, 1:4, 1

R¹, R², R³, R⁴, W, X, Y, Z L

A 1 6

1, 2, 3, 4, 5 6 가

A 2 6

A

A' 1, 2, 3, 4, 5 6 , Ar -CHAr -CHAr-A'

A' 1, 2, 3, 4, 5 6

Hal F, Cl Br, I

X CH, N

R¹ R² 3- 4- H, OH, , F, Cl, Br I

R¹ , 3-H, 3-Cl 3-

R² , 4-H, 4- 4-

R¹ R² , -OCH₂O-

R⁷ 2- 3- , 2- 3- , 1-, 2- 3- , 1-, 2-,
 4- 5- , 2- -1- -1-, 1-, 3-, 4- 5- , 2-, 4- 5- , 3-, 4-
 5- , 2-, 4- -1-, -4- 5- , 2-, 3- 4- , 2-, 4-, 5-
 6- , 1,2,3- -1-, -4- -5- , 1,2,4- -1-, -3- -5- , 1-
 5- , 1,2,3- -4- -5- , 1,2,4- -3- -5- , 1,3,4- -2-
 -5- , 1,2,4- -3- -5- , 1,2,3- -4- -5- , 3- 4-

R³ R⁴ -(CH₂)₃-, -(CH₂)₄- -CH=CH-CH=CH-

R⁵ , , , , , , , 2- , 1-,
 2- 3- , 1,1-, 1,2- 2,2- , 1- , 1-, 2-, 3- 4- , 1,1-, 1
 , 2-, 1,3-, 2,2-, 2,3- 3,3- , 1- 2- , 1- -1- , 1- -2- , 1,
 1,2- 1,2,2- , 1 10

R⁵ , -2- -3-

CH₂ 가 O

R⁶ 5 12

Ic

Y $\text{COOH, COOA} \quad \text{-S(O)}_m \text{A}$, , 1- ,
;

Id

R³ R⁴ , , H, A, OA Hal ,
R¹ R² -O-CH₂-CH₂-, -O-CH₂-O- -O-CH₂-CH₂-O- ,

Y $\text{COOH, COOA} \quad \text{-S(O)}_m \text{A}$, , 1- ,
;

Ie

R³ R⁴ -(CH₂)₃-, -(CH₂)₄- -CH=CH-CH=CH- ,

R¹ R² , , H, OA Hal ,

R¹ R² -CH₂-O-CH₂- ,

Y $\text{COOH, COOA} \quad \text{-S(O)}_m \text{A}$, , 1- ,
;

If

Y $\text{COOH} \quad \text{COOA}$, , , ,
;

Ig

Y $\text{COOH, COOA, CONH}_2, \text{CONA}_2, \text{CONHA} \quad \text{-S(O)}_m \text{A}$, R⁵ R⁶ ;

Ih

Y $\text{-(CH}_2)_n \text{-R}^{20}$, R⁵, R⁶ R⁹ ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ $\text{COOH, COOA, CONH}_2, \text{CONA}_2, \text{CONHA} \quad \text{-S(O)}_m \text{A}$;

Ii

X CH ,

Y $\text{-(CH}_2)_n \text{-R}^{20}$, R⁵, R⁶ R⁹ ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA ;

lj ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

Z NH NHA' ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA ;

lk ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

Z O ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA ;

ll ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

Z NH NHA' ,

R³ R⁴ 3 4 ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA ;

lm ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

Z O ,

R³ R⁴ 3 4 ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA ;

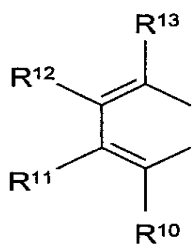
In ,

R¹ R² , , H, A, OH, OA Hal ,

R¹ R² 3 5 , -O-CH₂-CH₂-, -CH₂-O-CH₂-, -O-CH₂-O-
-O-CH₂-CH₂-O-

R³ R⁴ , , H, A Hal ,

R³ R⁴ 3 5 ,



W H ,

X CH N ,

Y (CH₂)_nR²⁰ , (CH₂)_q-R⁷, R⁵, R⁶ R⁹ ,

Z O, NH, NA' ,

A' 1 6 , -CHAr -CHAr-A' ,

A' 1 6 ,

R⁵ 1 10 ,

R⁶ 5 12 ,

R⁷ R²⁰, A, Hal CF₃ 1 2 N
, 5 7 ,

R⁹ Ar (CH₂)_k-Ar ,

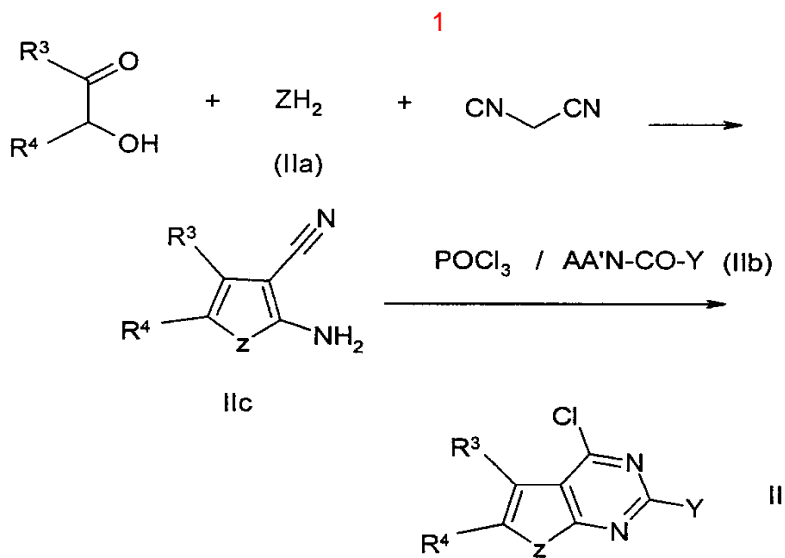
R¹⁰, R¹¹, R¹² R¹³ H ,

R²⁰ -COOH, -COOA -S(O)_mA ,

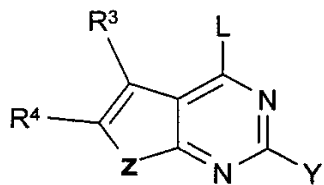
A 1 7 H 가 F 1 6 ,

Ar ,
 Hal F, Cl, Br I ,
 k q , , 0, 1, 2, 3 4 ,
 m 1 2 ,
 n 0, 1, 2 3 I 가 / .
 I
 en Chemie[], Georg-Tieme-Verlag, Stuttgart (, Houben-Weyl, Methoden der organisch)

L) 6 OH 10 , (1 - 6 p- (, 2-)) .
 I



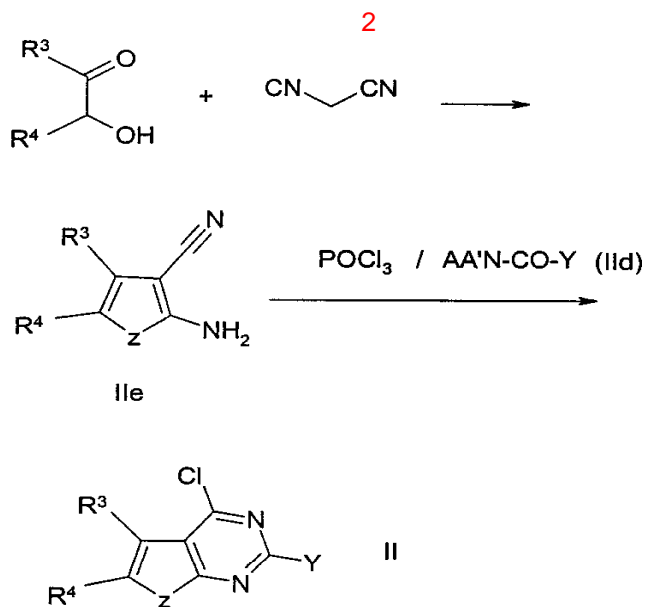
[]



(
 Z NH NHA' ,
 L Cl ,
 Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,
 R³ R⁴ , , H, A Hal ,
 R³ R⁴ 3 5 ,
 n, R²⁰, R⁵, R⁶ R⁹ 1)

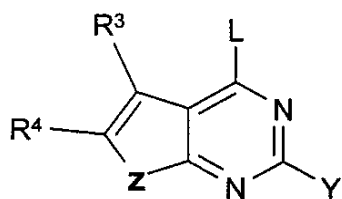
1 ,
 R³ R⁴ , , H, A Hal ,
 R³ R⁴ 3 5 .
 a , Z A' 1 NH NA' .
 b ,

A A' , , H 1, 2, 3 4 ,
 Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,
 n, R²⁰, R⁵, R⁶ R⁹ 1 .
 c , Z NH NA' , A' 1 .
 , 2:



:

[]



(,

Z O ,

L Cl ,

Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,

R³ R⁴ , , H, A Hal ,

R³ R⁴ 3 5 ,

n, R²⁰, R⁵, R⁶ R⁹ 1)

2 ,

R³ R⁴ , , H, A Hal ,

R³ R⁴ 3 5 .

d ,

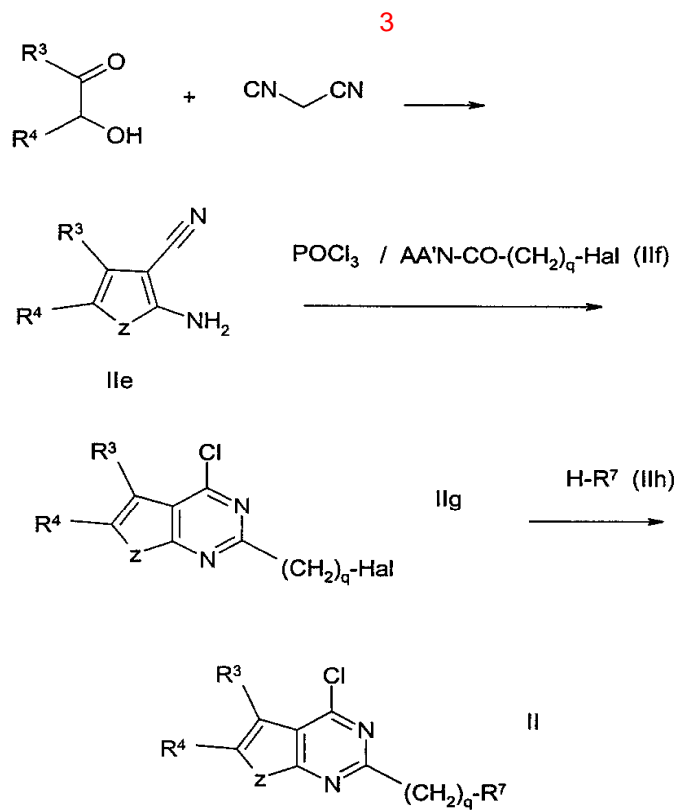
A A' , , H 1, 2, 3 4 ,

Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,

n, R²⁰, R⁵, R⁶ R⁹ 1 .

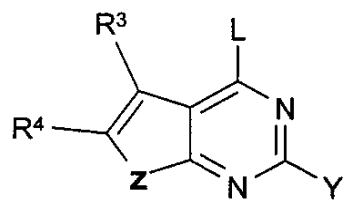
e, Z O() .

, 3:



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(,

Z O ,

L Cl ,

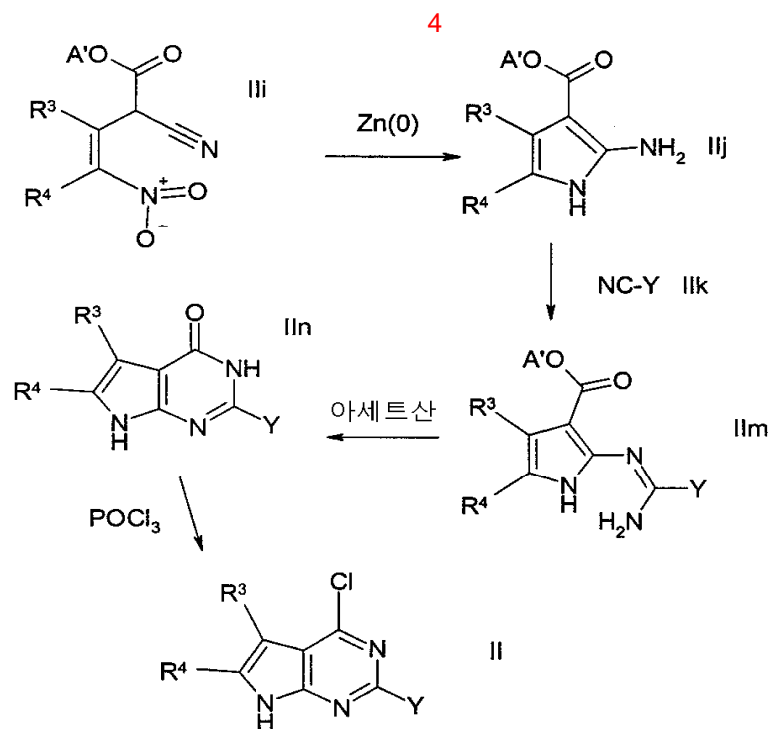
Y (CH₂)_q-R⁷ ,

R³ R⁴ , , H, A Hal ,

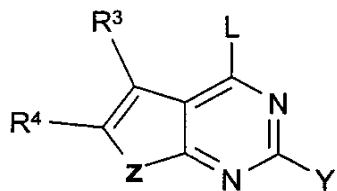
R³ R⁴ 3 5 ,

q R⁷ 1 ,

R⁷ N)
 3 ,
 R³ R⁴ , , H, A Hal ,
 R³ R⁴ 3 5 .
 f ,
 A A' , , H 1, 2, 3 4 ,
 Hal Cl Br .
 g ,
 Z O ,
 q 0, 1, 2, 3 4 ,
 Hal Br Cl .
 h 가 , R⁷ 1 ,
 , 4



[]

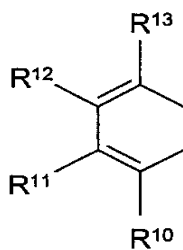


(,

Z NH ,

L Cl ,

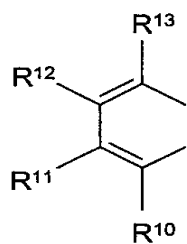
Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,



R³ R⁴

n, R²⁰, R⁵, R⁶ R⁹ 1)

4 , R³ R⁴



(, R¹⁰, R¹¹, R¹² R¹³ 1)

{I.T. Fordes, C.N. Johnson, M. Thompson, J. Chem. Soc. Perkin Trans. 1, 2, 275-282 (1992)}

i , A' 1, 2, 3 4 .

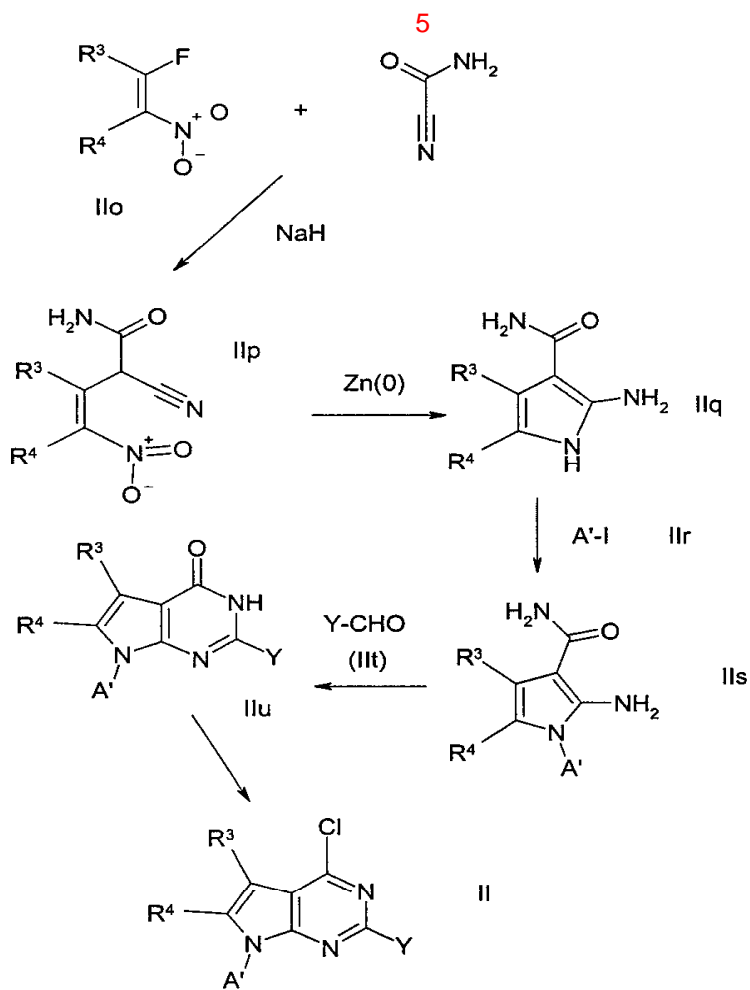
j , A' 1, 2, 3 4 .

k , Y (CH₂)_nR²⁰ R⁵, R⁶ R⁹ ,
n, R²⁰, R⁵, R⁶ R⁹ 1 .

m , A' 1, 2, 3 4 , Y (CH₂)_nR²⁰
, R⁵, R⁶ R⁹ , n, R²⁰, R⁵, R⁶ R⁹ 1 .

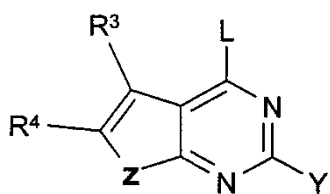
n , Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ , n, R²⁰,
R⁵, R⁶ R⁹ 1 .

5



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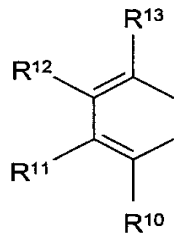


(,

Z NA' ,

L Cl ,

Y (CH₂)_nR²⁰ , R⁵, R⁶ R⁹ ,

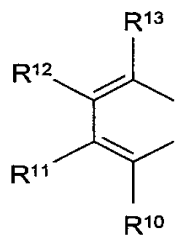


R³ R⁴

A', n, R²⁰, R⁵, R⁶ R⁹ 1)

5

R³ R⁴



(, R¹⁰, R¹¹, R¹² R¹³ 1)

1 (CH₂)_n R²⁰ , A' R⁵, R⁶ R⁹ , n, R²⁰, R⁵, R⁶ R⁹ , Y

-20 150 °, 20 100 °

가가

가,

, n-
(THF)
()

, n-

3 -

(DMF)

가 COOH

I

X

, 0 100 °

NaOH

KOH

, /THF /

I , - 가

가

가 /
1 kg 0.02 1 500 mg, 5 100 mg
가

() / 가

(a) / (

(b) 가 ()

/ 가 (

(COPD), () () ()
가 /

ACE() , NEP(EI)

PGE₀, PGA₁, PGB₁, PGF₁, PGA₂, PGB₂, 19-
A₁, 19- (PGE₁), -PGB₁, 19- (PGF₂), -PGA₂, 19- (PGE₂), -PGB₂, PGE₃, PGF₃,
(PGI₂); -PG

(PGE₁), (PGF₂), (PGE₂), (PGI₂);
가

PGE₁

l

가

가

가

l

(Xa a)

K

K

(b/ a)

, EP 0 623 615 B1(2) EP 0 741 133 A2(2 2 4 56)

Xa a WO 99/16751, WO 99/31092. WO 99/57096, WO 00/12479, WO 00/20416, WO 00/40583 WO 00/51989

Xa

a) WO 97/30971, 4 , 5 13 19 ;

b) EP 0 921 116 A1, 2 , 1 51 ;

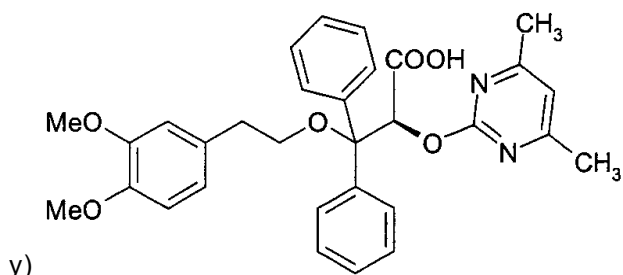
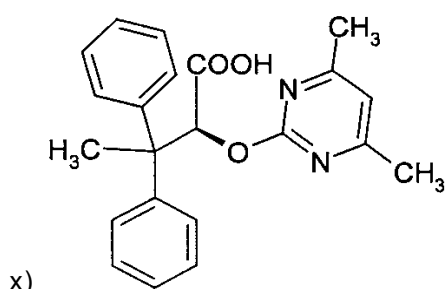
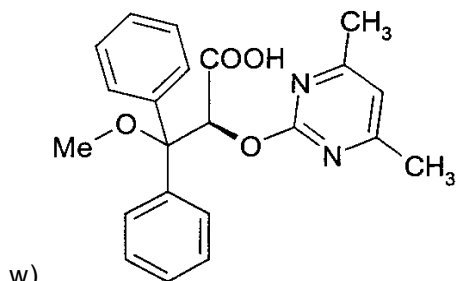
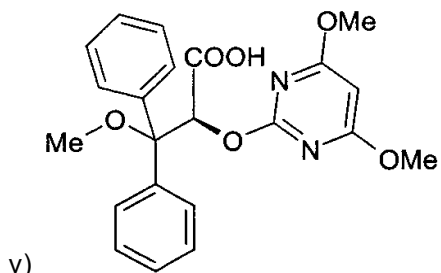
c) EP 0 540 051 B1, 2 , 41 3 14 ;

d) EP 0 798 295 A1, 69 , 10 71 , 53

I

1997). (TBC- 11251; J.Med.Chem., 40, No.11, 1690-97,

- a) BMS-193884(EP 558258),
- b) BMS-207940(Pharmaprojects (13.06.97)),
- c) BQ-123 (Exp. Opin. Invest. Drugs, 1997, 6, No.5, 475-487),
- d) SB-209670 (Exp. Opin. Invest. Drugs, 1997, 6, No.5, 475-487),
- e) SB-217242 (Exp. Opin. Invest. Drugs, 1997, 6, No.5, 475-487),
- f) SB-209598 (Trends in Pharmacol. Sci., 17, 177-81, 1996),
- g) TAK-044 (Exp. Opin. Invest. Drugs, 1997, 6, No.5, 475-487),
- h) (Trends in Pharmacol. Sci., 18, 408-12, 1997),
- i) PD-156707 (J. Med. Chem., 40, No.7, 1063-74, 1997),
- j) L-749329 (Bioorg. Med. Chem. Lett., 7, No.3, 275-280, 1997),
- k) L-754142 (Exp. Opin. Invest. Drugs, 1997, 6, No.5, 475-487),
- l) ABT-627 (J. Med. Chem., 40, No.20, 3217-27, 1997),
- m) A-127772 (J. Med. Chem., 39, No.5, 1039-1048, 1996),
- n) A-206377 (213th American Chemical Society National Meeting, San Francisco, California, USA, 13 - 17 April 1997, Poster, MEDI 193),
- o) A-182086 (J. Med. Chem., 40, No.20, 3217-27, 1997),
- p) EMD-93246 (211th American Chemical Society National Meeting, New Orleans, USA, 1996, Poster, MED I 143),
- q) EMD-122801 (Bioorg. Med. Chem. Lett., 8, No.1, 17-22, 1998),
- r) ZD-1611 (Trends in Pharmacol. Sci., 18, 408-12, 1997),
- s) AC-610612 (Ramp;D Focus Drug News (18.05.98)),
- t) T-0201 (70th Annual Meeting of the Japanese Pharmacological Society, Chiba, Japan, 22-15 March 1997, Lecture, O-133),
- u) J-104132 (Ramp;D Focus Drugs News (15.12.97)),



, EP 0733626, EP 0755934, EP 0757039, EP 0796250, WO 97/19077, WO 97/30982, WO 97/30996, DE 19609597, DE 19612101, WO 98/27091, WO 98/27077, WO 98/41515, WO 98/41521, WO 98/42702, WO 98/42709 WO 99/05132

, (a) , N-[3-
]-L- , (b) ,
 , (c) , (d) , (e) , S- -N- -D,L-
 S- , (f) , (g) , 1,2,5- 2- N-
 , (h) , (i) ,
 , (j) , NO

가

(CHF), (COPD), /
 가 PDE V
 ()
 (CHF), (COPD), /
 (CHF), (COPD), /
 (CHF), (COPD), /
 (CHF), (COPD), /

pH 2 10

가 ,
/

(MS): EI() M +

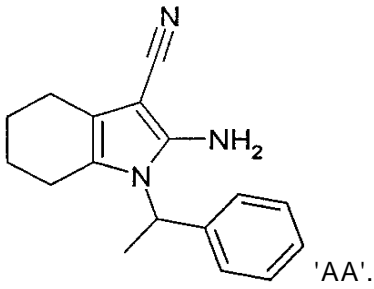
FAB() (M+H) +

1

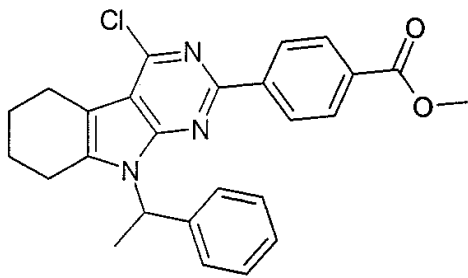
4-[4-(3- -4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -

1.1 400 Mℓ 2- 56.6 g, 60.6 g p-
 10 Mℓ 10 50 ° 가 ,

('AA') 45 g, m.p. 129 ° , 2- -1-(1-)-4,5,6,7- -1H- -3-



1.2 30 4-N,N- 'AA' 2 g 가 , 1.8 g POCl₃ 1 Mℓ 가 ,
 , 4-[4- -9-(1-)-6,7,8,9- 80 3 ,
 ('AB') 1.6 g : -5 H -1,3,9- -2-]



'AB'.

1.3 1- -2- 30 Mℓ 'AB' 1.6 g 3- -4- 가 , 1
 00° 4 . 4-[4-(3- -4-)-9-(1-
)-6,7,8,9- -5 H -1,3,9- -2-] ('AC') 1.4 g .

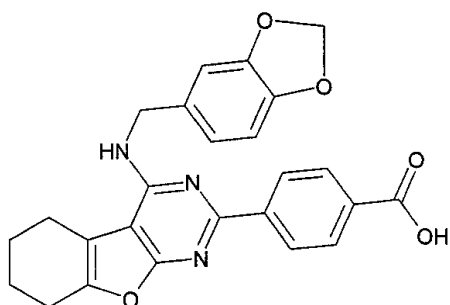
1.4 가 20 Mℓ 'AC' 0.5 g NaOH 20 Mℓ 가 , 3
 가 .
 KOH 가 . 가 , , 4-[4-(3-
 - -4-)-9-(1-)-6,7,8,9- 가 , -5 H -1,3,9- -2-]
 0.11 g, , m.p. 179° .

PDE V : IC₅₀ [mol/] 3.0E-07

4-[4- -6,7,8,9- -5 H -1,3,9- -2-]

- 3,4- ,
- 3,4- ,
- 3,4- , 가
- 4-[4- -9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ;
- 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]
 ;
- 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]
 ;
- 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]

4-[4- -6,7,8,9- -5 H -1,3,9- -2-]
 3- -4- ,
 ,
 3,4- ,
 3,4- ,
 3,4- , 가
 4-[4-(3- -4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -
 2-] , ;
 4-[4- -9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ;
 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]
 ;
 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]
 ;
 4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-]
]
 _____ 2
 4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-]



2.1 25 Mℓ 2- 11.0 g 9.6 g 4.8 Mℓ
 가 , 4 , 2- -
 4,5,6,7- -3- ('BA') 12.8 g, m.p. 179 °
 2.2 THF 200 Mℓ 40% 30 Mℓ 4- 20 g
 THF 300 Mℓ 가 , 2) ('BB') 19.2 g, m.p. 107 °
 , 4-(N,N-)
 2.3 'BB' 5.0 g POCl₃ 3.3 Mℓ 가 , 30
 'BA' 5.9 g 가 , 80° 30
 , 4-(4- -5,6,7,8- [4,5] [2,3- d] -2
 -) ('BC') 5.2 g
 2.4 1- -2- 30 Mℓ 'BC' 2.5 g 3,4- 2.4 g 가 ,
 100° 4 , 4-[4-(3,4-)-

5,6,7,8- [4,5] [2,3- d] -2-] ('BD') 2.2 g .

2.5 가 10 Mℓ 'BD' 1.0 g NaOH 10 Mℓ 가 , 3

가 . ,

[4,5] [2,3- d] -2-] 0.5 g, , m.p. 205 °)-5,6,7,8-

4-(4- -5,6,7,8- [4,5] [2,3- d] -2-)

3- -4- ,

,

3,4- ,

3,4- ,

C - -3- , 가

4-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

, m.p. 205 ° ;

4-(4- -5,6,7,8- [4,5] [2,3- d] -2-) , ;

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

;

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

;

4-{4-[(-3-)]-5,6,7,8- [4,5] [2,3- d] -2- } ,

, m.p. >250 ° .

3

4-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-]

3.1 4-(N,N-) 5.5 g POCl₃ 3.3 Mℓ 가 ,

30 , 'BA' 5.9 g 가 , 80 ° 3 .

) ('CA') 5.2 g 4-(4- -5,6,7,8- [4,5] [2,3- d] -2-

3.2 1- -2- 20 Mℓ 'CA' 2.0 g 3- -4- 2.3 g 가 ,

80 ° 3 , 4-[4-(3- -4-

)-5,6,7,8- [4,5] [2,3- d] -2-] ('CB') 2.2 g .

3.3 10 Mℓ 'CB' 0.8 g 2N NaOH 10 Mℓ 가 , 50 ° 2 .

. HCl 가 .

2,3- d] -2-] , 4-[4-(3- -4-)-5,6,7,8- [4,5] [

0.25 g, , m.p. 205 ° .

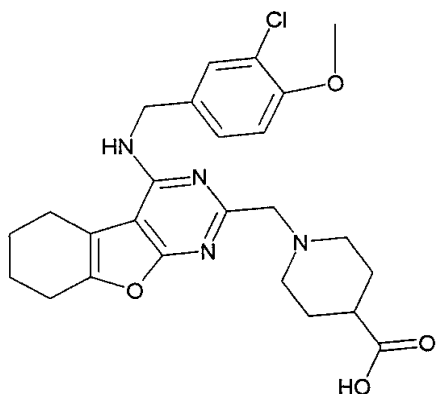
4-(4- -5,6,7,8- [4,5] [2,3- d] -2-) 3,4-

가 4-[4-(3,4-)-5,6,7,8-

[4,5] [2,3- d] -2-] , .

4

1-[4-(3-
-4-)-5,6,7,8- [4,5] [2,3- d] -2-]



4.1 10 2- 'BA' 10.0 g 가 , 6.2 Mℓ POCl₃ 6.7 Mℓ 가 , 80 ° 30 [4,5] -[2,3- d] ('DA') 8.3 g

4.2 THP 100 Mℓ 'DA' 8.3 g -4- 10 Mℓ 가 , 가 , 3 - (MTB) . MTB ('X') HCl . NaOH -5,6,7,8- HCl [4,5] [2,3- d] , MTB -2-) -4- , 1-(4- ('DB') 2.9 g

'X' 1-(2- -5,6,7,8- [4,5] [2,3- d] -4-) -4 - 4.3 1- -2- 50 Mℓ 'DB' 2.9 g 3- -4- 3.0 g 가 , 1-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] -4- ('DC') 2.9 g, m.p. 152 °

4.4 1 30 Mℓ 'DC' 2.8 g NaOH(3%) 3 Mℓ 가 , 60 ° pH 4 [4,5] -[2,3- d]] -2-] , 1-[4-(3- -4-)-5,6,7,8- 1.5 g, m.p. 233-235 °

5

1-[4-(3-
-4-)-5,6,7,8- [4,5] [2,3- d] -2-]-4-

5.1 2.85 g 가 , 'DA' 4.7 g (f) 1.8 g -N- , 1-(4- -5,6,7,8- [4,5] [2,3- d] -2-)-4- ('E A')

5.2 1,4- 80 Mℓ 'EA' 3.4 g 3- -4- 3.49 g 가 , 11 5 ° 16 115 ° 1.5 . 1- -2- 10 Mℓ 가 , , 1-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-]-4- ('E')

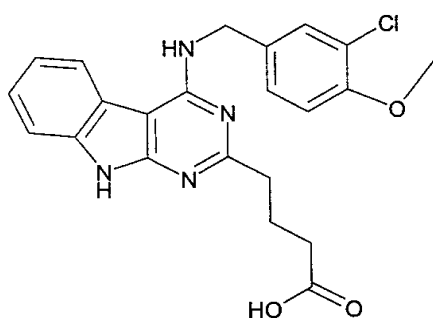
B') 3.25 g

5.3 20 Mℓ 'EB' 3.25 g 32% NaOH 3.5 Mℓ 가 ,
 110 ° 5 1-[4-(3- -4-)-5,6,
 7,8- [4,5] [2,3- d] -2-] ('EC') 1.99 g

5.4 50 Mℓ 'EC' 2.0 g 360 mg 520 mg 가 ,
 3 1-[4-(3- -4-)-
 5,6,7,8- [4,5] [2,3- d] -2-]-4- 1.0 g,

6

4-[4-(3- -4-)-9 H -1,3,9- -2-]



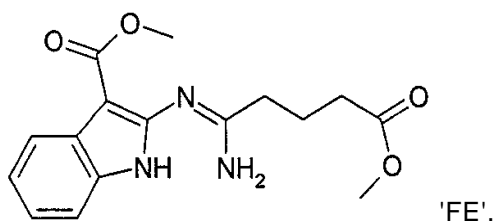
6.1 가 THF 350 Mℓ 30
 4- 30 g 가 , 4-
 ('FA') 23.4 g, m.p. 80 °

6.2 -2 0 ° 300 Mℓ DMF 15 Mℓ 가 , 15 Mℓ 가 ,
 30 0 ° 'FA' 23.25 g 가 , 15 4- ('
 29 Mℓ 가 가 ,
 FB') 20 g

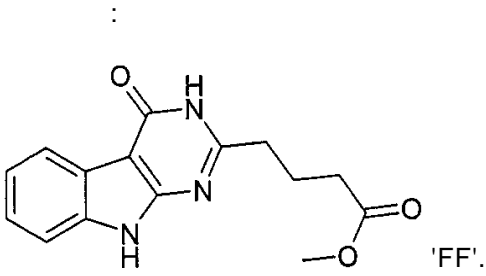
6.3 0 5 ° DMF 2 NaH 88 g DMF 300 Mℓ
 180 Mℓ 가 30
 100 Mℓ o- 106 Mℓ 가 , 14 DMF
 0% HCl (2-) .1
) 165 g, m.p. 58-60 ° ('FC'

6.4 180 Mℓ 550 Mℓ 'FC' 74 g 80 ° 가 ,
 (80-85 °) 130 g 가 , 14
 , 2- -3- ('FD') 30 g, m.p. 136 °

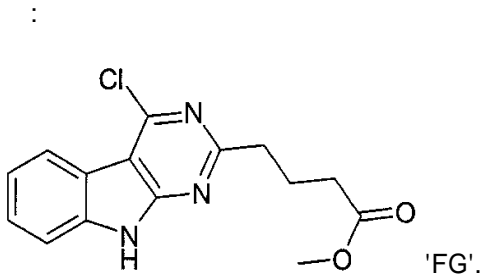
6.5 30 ° 1,4- 60 Mℓ 'FD' 4.0 g 'FB' 2.8 g HCl 2
 48 2-[(4-
)]-1H- -3- ('FE') 1.4 g, m.p. 95 ° :



6.6 50 Mℓ 'FE' 1.4 g 가 , 1
 , 4-(4- -4,9- -3 H -1,3,9- -2-) ('FF') 1.0 g, m.p. 258 °



6.7 'FF' 1.0 g POCl₃ 40 Mℓ 3 . POCl₃ 2
 , 4-(4- -9 H -1,3,9- -2-) ('FG') 1.0 g, m.p. 258 °



6.8 1- -2- 30 Mℓ 'FG' 1.0 g 3- -4- 1.0 g 180 ° 가
 . H -1,3,9- -2-] n- ('FH') 0.45 g , 4-[4-(3- -4-)-9

6.9 20 Mℓ 'FH' 0.35 g 2N NaOH 10 Mℓ 1 가 .
 , 가 , HCl , 4-[4-(3- -4-)-9 H -1,3,9- -2-] 300 mg, m.p. 258 ° .

4-[4-(3- -4-)-9 H -1,3,9- -2-] 가 , 가 ,
 .p. 143 ° 280 mg, , m

'FB' 4- 4-[4-(3- -4-)-9 H -1,3,9- -2-] , m.p. >250 ° .

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-(4- -9 H -1,3,9- -2-) ,

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-{4-[(-3-)]-9 H -1,3,9- -2- } ,

4-[4-(3- -4-)-9 H -1,3,9- -2-] ,

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-(4- -9 H -1,3,9- -2-) ,

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-[4-(3,4-)-9 H -1,3,9- -2-] ,

4-[4-[(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3- -4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-(4- -9 H -1,3,9- -2-) ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-[(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3- -4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-(4- -9 H -1,3,9- -2-) ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-(3,4-)]-9 H -1,3,9- -2-] ,
 4-[4-[(3,4-)]-9 H -1,3,9- -2-] .

7

4-[4-(3,4-)]-9- -9 H -1,3,9- -2-]
 7.1 NaH 448 g DMF 9 2 8° 1
 967 g 가 . 30 , 1- -2- 6
 00 Mℓ 가 , 2 . 50 HCl
 가 , 2- -2-(2-) ('GA') 956 g, m.p. 172-174
 .
 7.2 6.4 , 'GA' 956 g 2- -3- ('GB') 352 g .
 7.3 NaH 13 g DMF 500 Mℓ . 0° DMF 200 Mℓ 'GB' 52.6 g
 가 . DMF 100 Mℓ 26 Mℓ 가 , 1 .
 , 2- -3- -1- ('GC') 67.9 g .
 7.4 N,N- 100 Mℓ 'GC' 10.0 g, 4- 8.0 g 9.4
 g 160° 7 . 4-(9- -4- -4,9- -3 H
 -1,3,9- -2-) ('GD') 4.8 g .
 7.5 100 Mℓ 'GD' 4.8 g DMF 5 Mℓ 가 . (batch) 60
 , 4-(4- -9- -9 H -1,3,9- -2-)
 ('GE') 3.9 g .
 7.6 1- -2- 5 Mℓ 'GE' 2.4 g 2 Mℓ 110° (bath) 2
 -2-] ('GF') 2.7 g 4-[4-(3,4-)]-9- -9 H -1,3,9-
 .
 7.7 10 Mℓ NaOH(32%) 5 Mℓ 'GF' 2.6 g 4-[4-(3,4-
)]-9- -9 H -1,3,9- -2-] 2.4 g, , m.p. > 250° .

'GE' 3- -4- 가 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] , , m.p. > 250 ° .

8

4-[4-(3- -4-)-9- -9 H -1,3,9- -2-]

8.1 N,N- 200 Mℓ 'GB' 38 g, -4- 36.1 g 41.8 g
 140 ° 3 ('HA') 30 g, m.p. > 250 ° 4-(4- -4,9- -3 H
 -1,3,9- -2-) .

8.2 100 Mℓ 'HA' 10 g DMF 30 Mℓ 가 . 16 ('HB') 8.5 g
 4-(4- -9 H -1,3,9- -2-)

8.3 DMF 50 Mℓ 'HB' 3.2 g NaH() 400 mg 가 , 1 4-(4-
 2 Mℓ 가 , 1 ('HC') 3.0 g
 -9- -9 H -1,3,9- -2-)

8.4 7.6 , 'HC' 1.5 g 3- -4- 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] ('HD') 1.0 g, m.p. 205-206 ° .

8.5 7.7 'HD' 가 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] , , m.p. > 250 ° .

'HC' 3,4- 가 4-[4-(3,4-)-9- -9 H -1,3,9- -2-] , , m.p. > 250 ° .

'GB' 5- , , 3- -4- 5-[4-(3- -4-)-9- -9 H -1,3,9- -2-] , .

'HB' , 3- -4- 가 , m.p.
 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] , , m.p.
 > 250 ° .

'HB' 2- , 3- -4- 가 ,
 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] , , m.p. > 250 ° .

:

A:

2N 3 l 100 g 2 5 g pH 6.5
 , 5 mg , , .

B:

l 20 g 100 g 1400 g , .
 20 mg .

C:

g 940 Mℓ l 1 g, NaH₂PO₄ · 2H₂O 9.38 g, Na₂HPO₄ · 12H₂O 28.48 g
 0.1 g . pH 6.8 1 가 .

D:

I 500 mg 99.5 g .

E:

I 가 1 kg, 4 kg, 1.2 kg, 0.2 kg 0.1 kg
10 mg .

F:

E , , , 가 .

G:

I 2 kg 20 mg .

H:

60 I 1 kg , ,
10 mg .

I:

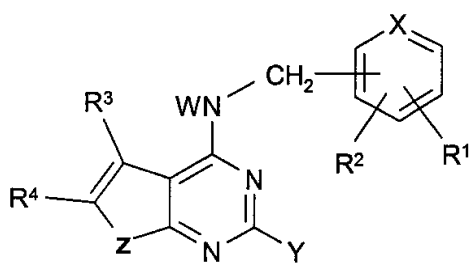
I 14 g NaCl 10 ,
. 1 (0.1 Mℓ) 0.14 mg .

(57)

1.

I :

[I]

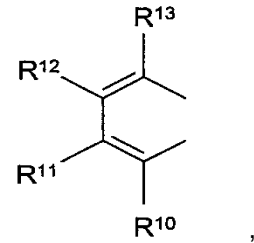


(,

R¹ R² H, A, OH, OA Hal ,

R¹ R² 3 5 , -O-CH₂-CH₂-, -CH₂-O-CH₂-, -O-CH₂-O-
-O-CH₂-CH₂-O- ,

R³ R⁴ H, A Hal ,



R³, R⁴, 3, 5, ,

W, H, 1, 2, 3, 4, ,

X, CH, N, ,

Y, (CH₂)_n-R²⁰, (CH₂)_q-R⁷, R⁵, R⁶, R⁹, ,

Z, O, NH, NA', ,

A', 1, 6, , -CHAr, -CHAr-A', ,

A', 1, 6, ,

R⁵, CH₂가, -CH=CH-, -C=C-, -O-, CO, -S-, -SO-, SO₂, -NH-, -NA-,
1, 10, ,

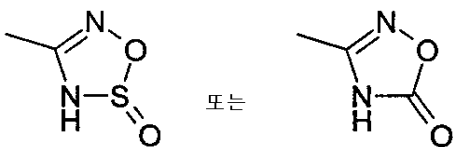
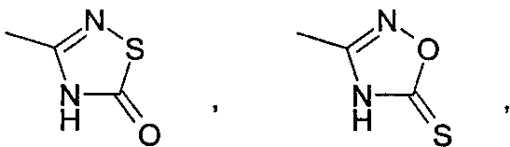
R⁶, 5, 12, ,

R⁷, R²⁰, A, Hal, CF₃, , 1, 4, N, O,
S, 5, 7, ,

R⁹, Ar, (CH₂)_k-Ar, ,

R¹⁰, R¹¹, R¹², R¹³, , H, A, Hal, OA, OH, NH₂, NHA, NA₂, R²⁰, ,

R²⁰, -COOH, -COOA, -CONH₂, -CONHA, -CONA₂, -CN, -5-, -S(O)_mA, -S(O)_mNH₂,
-S(O)_mOH,



A, 1, 7, H, 가F, 1, 6, ,

Ar, Hal, A, OA, OH, SO₂NH₂, SO₂NHA, SO₂NA₂, CN, ,

Hal, F, Cl, Br, I, ,

k, q, , 0, 1, 2, 3, 4, ,

m, 1, 2, ,

n 0, 1, 2 3)

, ().

2.

1 ,

X가 CH

I , ().

3.

1 2 ,

R⁹ COOH, COOA, CONH₂, CONA₂, CONHA, CN, NHSO₂A, N(SO₂A)₂ SO₂
A , ().

4.

1 2 ,

Y COOH, COOA -S(O)_mA , 1- ,
().

5.

1 2 ,

R³ R⁴ H, A, OA Hal ,

R¹ R² -O-CH₂-CH₂-, -O-CH₂-O- -O-CH₂-CH₂-O- ,

Y COOH, COOA -S(O)_mA , 1- ,
().

6.

1 2 ,

R³ R⁴ -(CH₂)₃-, -(CH₂)₄- -CH=CH-CH=CH- ,

R¹ R² , H, OA Hal ,

R¹ R² -CH₂-O-CH₂- ,

Y COOH, COOA -S(O)_mA , 1- ,
().

7.

1 2 ,

Y COOH COOA , , ,
().

8.

1 2 ,

Y COOH COOA, CONH₂, CONA₂, CONHA₂ -S(O)_mA , R⁵ R⁶
 I
).

9.

1 2 ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH, COOA, CONH₂, CONA₂, CONHA₂ -S(O)_mA I
 ().

10.

1 ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA I
 ().

11.

1 ,

X CH ,

Y -(CH₂)_n-R²⁰ , R⁵, R⁶ R⁹ ,

Z NH NHA' ,

R⁵ , , ,

R⁹ ,

n 0 1 ,

R²⁰ COOH COOA I
 ().

12.

1 ,

X CH ,

Y $-(CH_2)_n-R^{20}$, R^5, R^6 R^9 ,

Z O ,

R^5 , , ,

R^9 ,

n 0 1 ,

R^{20} COOH COOA I ,
().

13.

1 ,

X CH ,

Y $-(CH_2)_n-R^{20}$, R^5, R^6 R^9 ,

Z NH NHA' ,

R^3 R^4 3 4 ,

R^5 , , ,

R^9 ,

n 0 1 ,

R^{20} COOH COOA I ,
().

14.

1 ,

X CH ,

Y $-(CH_2)_n-R^{20}$, R^5, R^6 R^9 ,

Z O ,

R^3 R^4 3 4 ,

R^5 , , ,

R^9 ,

n 0 1 ,

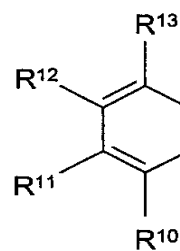
R^{20} COOH, COOA I ,
().

15.

R^1 R^2 H, A, OH, OA Hal ,

R^1 R^2 3 5 , -O-CH₂-CH₂-, -CH₂-O-CH₂-, -O-CH₂-O

-O-CH₂-CH₂-O- ,
 R³ R⁴ H, A Hal ,



R³ R⁴ 3 5 ,

W H ,

X CH N ,

Y (CH₂)_nR²⁰ , (CH₂)_q-R⁷ R⁵, R⁶ R⁹ ,

Z O, NH NA' ,

A' 1 6 , -CHAr -CHAr-A' ,

A' 1 6 ,

R⁵ 1 10 ,

R⁶ 5 12 ,

R⁷ R²⁰, A, Hal CF₃ 1 2 N
 5 7 ,

R⁹ Ar (CH₂)_k-Ar ,

R¹⁰, R¹¹, R¹² R¹³ H ,

R²⁰ -COOH, -COOA -S(O)_mA ,

A 1 7 H 가 F 1 6 ,

Ar ,

Hal F, Cl, Br I ,

k q 0, 1, 2, 3 4 ,

m 1 2 ,

n 0, 1, 2 3)

, ()).

16.

1 ,

4-[4-(3- -4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -
 2-] ,

4-[4- -9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H - 1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3- -4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -] ,

4-[4- -9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-9-(1-)-6,7,8,9- -5 H -1,3,9- -2-] ,

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

4-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

4-(-5,6,7,8- [4,5] [2,3- d] -2-) ,

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

4-{4-[(-3-)]-5,6,7,8- [4,5] [2,3- d] -2- } ,

4-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

4-[4-(3,4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

1-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

1-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-] ,

1-[4-(3- -4-)-5,6,7,8- [4,5] [2,3- d] -2-]-4- ,

4-[4-(3- -4-)-9 H -1,3,9- -2-] ,

4-[4-(3- -4-)-9 H -1,3,9- -2-] ,

4-[4-(3,4-)-9- -9 H -1,3,9- -2-] ,

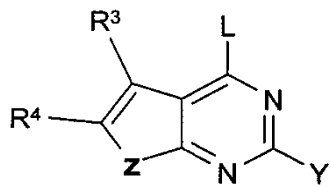
4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] ,

4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] ,
 4-[4-(3,4-)-9- -9 H -1,3,9- -2-] ,
 5-[4-(3- -4-)-9- -9 H -1,3,9- -2-] ,
 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] ,
 4-[4-(3- -4-)-9- -9 H -1,3,9- -2-] |

17.

a) :

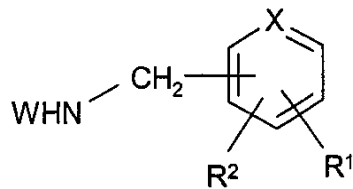
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(,
 Y, Z, R¹ R² 1 ,
 L Cl, Br, OH, SCH₃ OH)

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(, X, W, R¹ R² 1)

b) , COOH 가 COOH , |
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- h) ACE ,
- i) NEP ,
- j) , - ,
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24.

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(b) 가

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25.

