

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl. ⁷
C07D 498/06

(11)
(43)

2002 - 0049051
2002 06 24

(21)	10 - 2002 - 7006131
(22)	2002 05 13
	2002 05 13
(86)	PCT/EP2000/10765
(86)	2000 10 31

(87) WO 2001/36425
(87) 2001 05 25

(81)

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- 가

가

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가

가

가

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AP ARIPO : 가

EA :

EP :

OA OAPI : , 가 ,

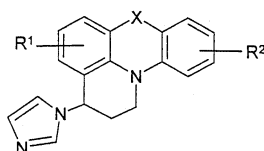
(30) 19954707.6 1999 11 13 (DE)

(71)

64293

250

(72)



[]

$$R^1 \quad R^2 \quad , \quad A^1, OA^1, SA^1 \quad Hal \quad ,$$
$$A^1 \quad H, A, \quad ,$$

A 1 - 10

Hal F, Cl, Br I

X	O, S, SO	SO ₂	1
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, M. Trkovnik, Org. Prep. Proced. Int. (1987), 19(6), 450 - 5 V.L.

Savel'ev , Khim - Farm. Zh. (1983), 17(6), 697 - 700

, V.L. Savel'ev, Khim. Geterotsikl. Soedin. (1980), (4), 479 - 83

가 , 가 .

가 ,
" (Rolipram) " cAMP (PDE)
, M. A. Giembycz , Br. J. Pharmacol. (1996), 118, 1945 - 1958
. cAMP (PDE) IC₅₀

(50%)
 , SK - N - SH 가 T - , PDE CI - 930
 . PDE (J.A. Bristol , J. Med. Chem. 1984, 27(9), 1099 - 1101).
 , HUT - 78 SK - N - SH , CI - 930 (D. Ruppert ,
 Life Sci. 31:2037, 1982).

38 - 447 (1971) . , T. Olsson, Acta allergologica 26, 4 .

cAMP (S. Kasugai, M 681, K. Miyamoto, M 682, Abstracts of the American Society for Bone and Mineral Research, 18 Annual Meeting, 1996),

Figure 1. Effect of TNF α on the expression of IL-1 β and IL-6 in the placenta. The placenta was incubated with TNF α (10 ng/ml) for 24 h. The expression of IL-1 β and IL-6 was measured by RT-PCR. The results are expressed as the mean $\pm$ SD of three independent experiments. *p < 0.05 compared with the control group.

[N. Sommer, Nature Medicine1, 244 - 248 (1995), L. Sekut, Clin. Exp. Immunol.100, 126 - 132 (1995)]

telli, J. Clin. Invest.95, 2367 ff. (1995); J.M. Argiles, Med. Res. Rev.17, 477 ff. (1997).) TNF - (P. Cos

, PDE , (PDE , ,
D. Marko , Cell Biochem. Biophys.28, 75 ff. (1998)).

가, , , AIDS , 가 T -
(L. Li , Science, 1999, 283, 848 - 851).

PDE

가

(,) ,

AIDS

A 1 - 10 1, 2, 3, 4, 5, 6, 7, 8, 9 10 가 , , , sec - , tert - n - , , 1 - 7 H 가 F / Cl . A , .

3 - 9 가

2 - 10 가

4 - 10 가

$$R^1 \quad R^2 \qquad , H, \qquad , \qquad , \qquad , \qquad , \qquad , \qquad ,$$

가

- a g ,

가 , 가

a X S ;

b X S ,

$$R^1 \quad H \quad ;$$

C X S ,

$$\text{R}^1 \quad \text{F} \quad \text{Cl} \quad ;$$

d X S ,

R^2 H ;

e X S ,

R^2 F Cl ;

f X S ,

R^1 H ,

R^2 F Cl ;

g X S ,

R^1 F Cl ,

R^2 H ;

h X S ,

A^1 H A ,

A 1, 2, 3 4 ;

i X S ,

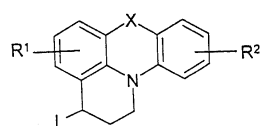
R^1 R^2 , A^1 Hal ,

A^1 H A ,

A 1, 2, 3 4 ,

Hal F Cl .

, , , 1 / .



[,

R^1, R^2 X ,

L Cl, Br, OH, SCH₃ OH].

(Houben - Weyl, Methoden der organischen chemie[], Georg - Thieme - Verlag, Stuttgart)

, R¹, R² X 가 , 가 .

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

- 20 150 , 20 100

가,

가가

, 1,2 - , n - , n - tert - (THF) (diglyme)); , N - (DMSO); (DMF);

- 가 가

가- 가

, 2 - , p- 가 가 가

/

가

가

AIDS

가

0.02 10 mg/kg 1 500 mg 5 100 mg

가

가

(,),

가

가

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PDE

가

가

AIDS

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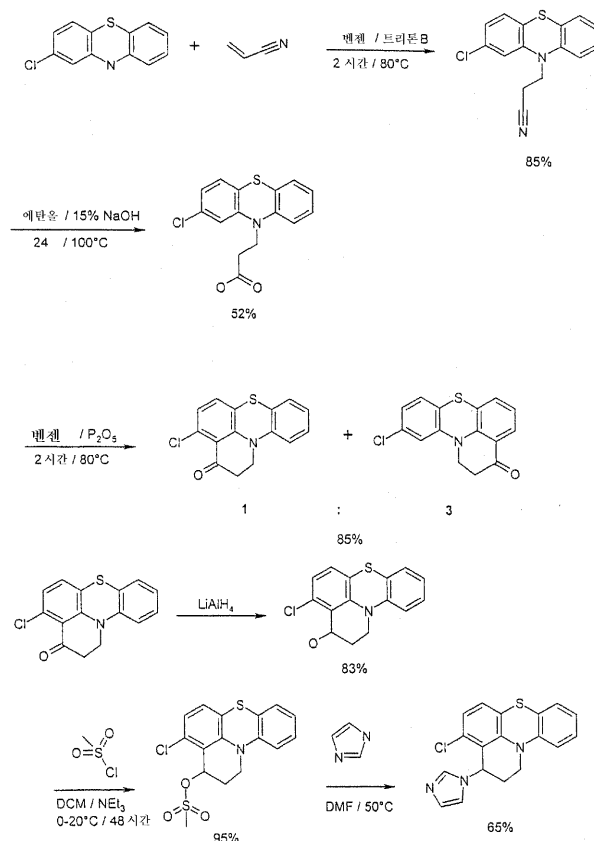
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
4 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
4,10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,
10 -	- 3 -	- 1 -	- 2,3 -	- 1H -	[3,2,1 - kl]	,

4 - - 3 - - 1 - - 2,3 - - 1H - [3,2,1 - kl] ,

10 - - 3 - - 1 - - 2,3 - - 1H - 7 - - 11b - [de] - ,

10 - - 3 - - 1 - - 2,3 - - 1H - [3,2,1 - kl] 7,7 - .

:



A :

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

B :

20g 100g 1400g ,
20 mg .

C :

940 ml 1 g, $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ 9.38 g, N
 $\text{a}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ 28.48 g 0.1 g . pH 6.8 , 1l
 , .

D :

500 mg 99.5 g .

E :

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

F :

E 가 , , , 가 ,
 .

G :

2 kg , 20 m
 g .

H :

60 l 1 kg , ,
 , 10 mg .

I :

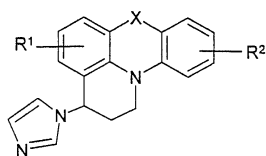
14 g NaCl 10 l , (0.1 ml)
 가 .
 0.14 mg .

(57)

1.

가 / :

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[
R¹ R² , , A¹, OA¹, SA¹ Hal ,
A¹ H, A, , ,
A 1 - 10 ,
Hal F, Cl, Br I ,
X O, S, SO SO₂].

2.

1. , 가 .

3.

2, .

4.

3. 가

5.

$$\frac{3}{4} \div \frac{1}{2} = \frac{3}{4} \times \frac{2}{1} = \frac{3 \times 2}{4 \times 1} = \frac{6}{4} = \frac{3}{2}$$

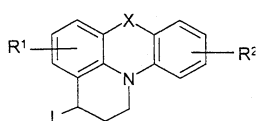
6.

가

AIDS

1

7.

$$[\quad]$$


[
 R^1, R^2 X
L Cl, Br, OH, SCH₃ OH].