

(19)  
(12)

(KR)  
(A)

(51) 。 Int. Cl.<sup>7</sup>  
A61K 31/55

(11)  
(43)

2003-0087069  
2003 11 12

(21) 10-2003-7013214

(22) 2003 10 09

2003 10 09

(86) PCT/US2002/11285

(87)

WO 2002/83125

(86) 2002 04 10

(87)

2002 10 24

(30) 60/282,693

2001 04 10

(US)

(71)

19103

(72)

19406

709

(74)

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(54)

(superfamily)

v 3 ( )

v 3

[Ross, et al., J. Biol. Chem., 1987, 262, 7703].

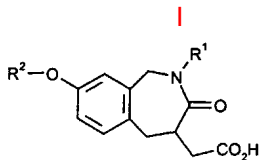
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v 3  
( [Brow

n, et al., Cardiovascular Res., 1994, 28, 1815]). 가 , [Okada, et al., Am. J. Pathol., 1996, 149 (1), 37] v 3 (vascular integrity)

, 가 ,

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192 ) PCT 가 PCT/US97/18001 (1997 10 1 , 1998 4 9 WO 98/14



R<sup>1</sup> R<sup>7</sup> , R<sup>10</sup> R<sup>7</sup> 가 A-C<sub>2-4</sub> , A-C<sub>2-4</sub> , A-C<sub>3-4</sub> , A-C<sub>3-4</sub> , A-C<sub>1-4</sub> A-C<sub>0-4</sub> , A-C<sub>3-4</sub>

A H, C<sub>3-6</sub> , Het Ar ;

R<sup>7</sup> -COR<sup>8</sup> , -COCR'<sub>2</sub>R<sup>9</sup> , -C(S)R<sup>8</sup> , -S(O)<sub>m</sub>OR', -S(O)<sub>m</sub>NR'R', -PO(OR') , -PO(OR')<sub>2</sub> , -NO<sub>2</sub> , ;

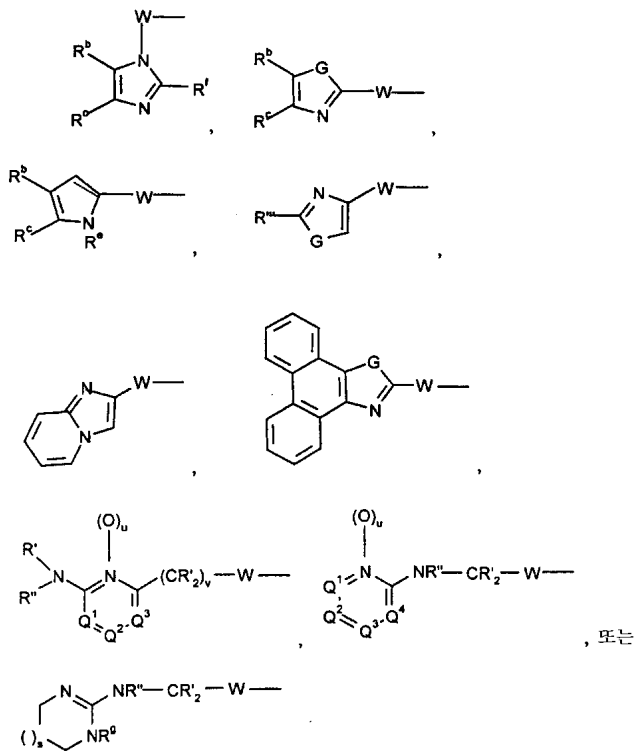
R<sup>8</sup> -OR', -NR'R', -NR'SO<sub>2</sub>R', -NR'OR', -OCR'<sub>2</sub>CO(O)R' ;

R<sup>9</sup> -OR', -CN, -S(O)<sub>r</sub>R', -S(O)<sub>m</sub>NR'<sub>2</sub> , -C(O)R', C(O)NR'<sub>2</sub> , -CO<sub>2</sub>R' ;

R<sup>10</sup> H, , -OR<sup>11</sup> , -CN, -NR'R<sup>11</sup> , -NO<sub>2</sub> , -CF<sub>3</sub> , CF<sub>3</sub>S(O)<sub>r</sub> , -CO<sub>2</sub>R', -CONR'<sub>2</sub> , A-C<sub>0-6</sub> , A-C<sub>1-6</sub> , A-C<sub>2-6</sub> , A-C<sub>2-6</sub> , A-C<sub>0-6</sub> , A-C<sub>0-6</sub> A -C<sub>0-6</sub> -S(O)<sub>r</sub> ;

R<sup>11</sup> R', -C(O)R', -C(O)NR'<sub>2</sub> , -C(O)OR', -S(O)<sub>m</sub>R', -S(O)<sub>m</sub>NR'<sub>2</sub> ;

R<sup>2</sup>



W  $-(CHR^g)_a-U-(CHR^g)_b-$  ;

U  $CO, CR^g_2, C(=CR^g_2), S(O)_k, O, NR^g, CR^gOR^g, CR^g(OR^k)CR^g_2, CR^g_2$   
 $CR^g(OR^k), C(O)CR^g_2, CR^g_2C(O), CONR^i, NR^iCO, OC(O), C(O)O, C(S)O, OC(S), C(S)NR^g, NR^g$   
 $C(S), S(O)_2NR^g, NR^gS(O)_2, N=N, NR^gNR^g, NR^gCR^g_2, CR^g_2NR^g, CR^g_2O, OCR^g_2, C$   
 $CR^g=CR^g$  ;

G  $NR^e, S, O$  ;

R<sup>g</sup>  $H, C_{1-6}, Het-C_{0-6}, C_{3-7}, -C_{0-6}, Ar-C_{0-6}$  ;

R<sup>k</sup>  $R^g, -C(O)R^g, -C(O)OR^f$  ;

R<sup>i</sup>  $H, C_{1-6}, Het-C_{0-6}, C_{3-7}, -C_{0-6}, Ar-C_{0-6}, C_{1-6}, CN, NR^g_2, OR^g, SR^g, CO_2R^g, CON(R^g)_2$  ;

R<sup>f</sup>  $H, C_{1-6}, Ar-C_{0-6}$  ;

R<sup>e</sup>  $H, C_{1-6}, Ar-C_{0-6}, Het-C_{0-6}, C_{3-7}, -C_{0-6}, (CH_2)_kCO_2R^g$  ;

R<sup>b</sup>  $R^c, H, C_{1-6}, Ar-C_{0-6}, HetC_{0-6}, C_{3-6}, -C_{0-6}, CF_3, OR^f, S(O)_kR^f, COR^f, NO_2, N(R^f)_2, CO(NR^f)_2, CH_2N(R^f)_2, (R^b)(R^c), CF_3, C_{1-4}, OR^f, S(O)_kR^f, COR^f, CO_2R^f, OH, NO_2, N$   
 $(R^f)_2, CO(NR^f)_2, CH_2N(R^f)_2$  ;

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup> Q<sup>4</sup> N C-R<sup>y</sup> , Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup> Q<sup>4</sup> N ;

R<sup>l</sup>  $H, C_{1-6}, Ar-C_{0-6}, C_{3-6}, -C_{0-6}$  ;

R<sup>l</sup>  $R^l, -C(O)R^l, -C(O)OR^l$  ;

R<sup>h</sup>  $H, C_{1-6}, Ar-C_{0-6}, Het-C_{0-6}, C_{3-6}, -C_{0-6}, CF_3, OR^f, S$

(O) k R f , COR f , NO 2 , N(R f ) 2 , CO(NR f ) 2 , CH 2 N(R f ) 2 ;

R y H, , -OR g , -SR g , -CN, -NR g R k , -NO 2 , -CF 3 , CF 3 S(O) r -, -CO 2 R g , -COR g  
-CONR g 2 , , -OR g , -SR g , -CN, -NR g R', -NO 2 , -CF 3 , R'S(O) r -, -CO 2 R g , -CO  
R g -CONR g 2 C 1-6 ;

a 0, 1 2 ;

b 0, 1 2 ;

k 0, 1 2 ;

m 1 2 ;

r 0, 1 2 ;

s 0, 1 2 ;

u 0 1 ;

v 0 1 .

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

가 : PCT  
PCT/US95/08306 (1995 6 29 , 1996 1 11 WO 96/00730 ); PCT  
PCT/US95/08146 (1995 6 29 , 1996 1 11 WO 96/00574 ); PCT PCT  
/US96/11108 (1996 6 28 , 1997 1 16 WO 97/01540 ); PCT PCT/US9  
6/20748 (1996 12 20 , 1997 7 10 WO 97/24119 ); PCT PCT/US96/2  
0744 (1996 12 20 , 1997 7 10 WO 97/24122 ); PCT PCT/US96/2032  
7 (1996 12 20 , 1997 7 10 WO 97/24124 ); PCT PCT/US98/00490  
(1998 1 8 , 1998 7 16 WO 98/30542 ); PCT PCT/US98/19466 (1998  
9 18 , 1999 4 1 WO 99/15508 ); PCT PCT/US99/28662 (1999  
12 3 , 2000 6 15 WO 00/33838 ). PCT WO 00/33838  
(S)-10,11- -3-[2-(5,6,7,8- -1,8- -2- )-1- ]-5H- [a,d]  
-10-

(surgical intervention)

(adhesion)

가

5 %

가

가

20 mg/kg    1 g    ;    가    20

가    0.1    50 mg/kg    가    가    0.5

0.4    400 mg/kg/    0.01    100 mg/kg;    0.1    20 mg/kg

1    1    4

[Rogers, et al., J. Invest. Surg., 9: 388-391 (1996)]    [Rodgers, et al., Fertility and Surgery, 69 (3): 403-408 (1998)]  
 (rabbit sidewall model);    [Harris, et al., Surgery, 117: 663-669 (1995)]

\_\_\_\_\_ :

\_\_\_\_\_ :    (2.4 - 2.7 kg)    2    가

12:12    (    )    8    10

\_\_\_\_\_ :    1 (S)-3-    -8-[3-(    -2-    )-1-    (Vicryl)    (    )    ]-2-(2,2,2-    )-2,3,4,5

-    -1H-2-    -4-    .

\_\_\_\_\_ :    (    )    1    . 55 mg/kg    5 m

g/kg    2    (Rompum)

가

7    14    ,    가    가    :

0 =

1 = 가 가

2 = ; 가 , 가

3 = : 가 , 가

0

0.5+ , 1 2

1.0+ , 0.5

1.5+ 1 가

2.0+ , 가 ,

2.5+ 가 가 , 2

3.0+ 2 , 가 , ,

3.5+ 3 , 가

4.0+ , ,

가 2 가 .

\_\_\_\_\_ : t- (Student's t-test)

\_\_\_\_\_ : 2 1 60 mg/kg , 1 2  
 1 (1 mg/ml 0.1 mg/ml) , 12 ml (10 % CMC)

\_\_\_\_\_ : : 0.1 1.0 mM (7 10 µl/hr). 1  
 (Alzet miniosmotic pump)  
 (Clay Adams polyethylene tubing) PE-60 ID 0.76 mm (0.030") OD 1.22  
 mm (0.048")) 5-0 . 0.1 1 mM 1 (7 10 µl/  
 ) 8 % 8 %  
 가 0.8 % 7 .

\_\_\_\_\_ : 24 48 1 2 (60 mg/kg, 0.1 N  
 NaOH 5 mg/ml) , 가 60 mg/kg ,  
 14 60 mg/kg 1 .

\_\_\_\_\_ + \_\_\_\_\_ :  
 , 1 2 (60 mg/kg, ) , SB  
 267268 (10 % CMC) 1 0.1 mg/ml) 12 ml ,  
 2 , 12 ml (10 % CMC)  
 7 14

:  
+

[ 1 ]

대조군 동물로부터의 데이터, 2주 부검 시간

관련된 자궁각 %

우측각				좌측각				전체
장	방광	자궁	좌측	장	방광	자궁	우측	
40(2)	10(1)	30(2)	30(2)	40(2)	10(1)	50(3)	30(2)	3.5
-	50(2)	40(2)	50(2)	-	50(2)	30(2)	50(2)	3.0
-	40(3)	50(2)	50(2)	-	40(3)	50(2)	50(2)	3.5
30(1)	70(1)	30(1)	30(1)	30(1)	70(1)	30(1)	30(1)	3.0
40(1)	-	50(2)	20(1)	40(1)	-	50(2)	20(1)	2.5
40(2)	-	30(1)	20(1)	40(2)	-	40(1)	20(1)	2.5
30(1)	40(1)	30(1)	30(2)	30(1)	40(1)	30(1)	30(2)	3.0
10(1)	30(1)	30(1)	40(2)	10(1)	30(1)	50(1)	40(2)	2.5
40(2)	30(1)	40(1)	50(1)	40(2)	30(1)	40(1)	50(1)	3.0
20(1)	30(1)	40(2)	50(2)	20(1)	30(1)	60(1)	50(2)	3.0
25.0±5.2	30.0±7.0	37.0±2.6	37.0±4.0	25.0±5.2	30.0±7.0	43.0±3.4	37.0±4.0	66.5±2.8

[ 2 ]

플라시보 대조군 동물로부터의 데이터, 2주 부검 시간

관련된 자궁각 %

우측각				좌측각				전체
장	방광	자궁	좌측	장	방광	자궁	우측	
30(2)	50(1)	40(2)	40(2)	30(2)	50(1)	40(3)	40(2)	3.5
30(1)	10(1)	40(2)	30(1)	30(1)	10(1)	20(1)	30(1)	2.0
-	30(1)	10(1)	30(1)	-	30(1)	-	30(1)	1.5
-	20(1)	-	10(1)	-	20(1)	20(1)	10(1)	1.5
40(1)	40(1)	-	40(2)	40(1)	40(1)	40(2)	40(2)	3.0
-	50(1)	10(1)	30(1)	-	50(1)	30(1)	30(1)	2.0
30(1)	20(1)	30(1)	40(2)	30(1)	20(1)	10(1)	40(2)	2.5
40(1)	10(1)	-	30(1)	40(1)	10(1)	10(1)	30(1)	2.0
-	-	30(1)	30(1)	-	-	40(1)	30(1)	1.5
-	40(1)	40(1)	40(1)	-	40(1)	-	40(1)	2.0
17.0±5.8	27.0±5.6	20.0±5.6	32.0±2.9	17.0±5.8	27.0±5.6	21.0±5.0	32.0±2.9	45.2±5.9

[ 3 ]

처리된 동물로부터의 데이터, 1mg/ml 화합물 1, 2주 부검

관련된 자궁각 %

우측각				좌측각				우측	전체
장	방광	자궁	좌측	장	방광	자궁			
10(1)	10(1)	-	-	-	-	-	-	0.5	
30(1)	-	40(1)	-	30(1)	-	40(1)	-	2.0	
-	-	30(1)	-	-	-	30(1)	-	1.0	
10(1)	-	20(1)	-	-	-	20(1)	-	1.0	
30(2)	-	30(2)	30(2)	30(2)	-	30(2)	30(2)	2.5	
-	-	-	-	30(1)	-	10(1)	-	1.0	
10(1)	10(1)	10(1)	-	10(1)	-	-	-	1.0	
-	-	-	-	40(2)	20(2)	10(2)	-	1.5	
10(1)	20(1)	-	-	-	20(1)	20(1)	-	1.0	
30(1)	-	-	20(1)	30(1)	-	20(1)	20(1)	1.5	
13.0±4.0	4.0±2.2	13.0±5.0	5.0±3.4	17.0±5.2	4.0±2.7	18.0±4.2	5.0±3.4	21.2±5.5	

[ 4 ]

처리된 동물로부터의 데이터, 0.1mg/ml 화합물 1, 2주 부검

관련된 자궁각 %

우측각				좌측각				우측	전체
장	방광	자궁	좌측	장	방광	자궁			
20(1)	50(1)	30(2)	10(1)	20(1)	50(1)	30(2)	10(1)	2.5	
-	-	-	40(1)	-	-	20(1)	40(1)	1.5	
10(1)	-	30(1)	30(2)	10(1)	-	30(1)	30(2)	2.5	
-	-	40(1)	30(1)	-	-	40(1)	30(1)	1.5	
-	10(1)	30(2)	30(2)	10(1)	10(1)	30(2)	30(2)	2.0	
10(1)	10(1)	10(1)	40(1)	-	10(1)	-	40(1)	2.0	
20(1)	-	-	-	20(1)	-	20(1)	-	1.0	
-	10(1)	-	-	-	-	10(1)	-	0.5	
40(1)	-	-	20(1)	40(1)	-	20(1)	20(1)	1.5	
-	10(1)	20(1)	10(1)	-	-	20(1)	10(1)	1.0	
10.0±4.2	9.0±4.8	16.0±5.0	21.0±4.8	10.0±4.2	7.0±5.0	22.0±3.6	21.0±4.8	30.2±6.2	

[ 5 ]

대조군 동물로부터의 데이터, 1주 부검 시간

관련된 자궁각 %

우측각				좌측각				우측	전체
장	방광	자궁	좌측	장	방광	자궁			
50(1)	30(1)	30(1)	40(1)	50(1)	30(1)	30(1)	40(1)	3.0	
50(1)	30(2)	60(1)	50(1)	50(1)	30(2)	60(1)	50(1)	3.5	
40(1)	20(1)	40(1)	50(1)	40(1)	20(1)	40(1)	50(1)	3.0	
50(2)	10(1)	40(1)	30(2)	50(2)	10(1)	30(2)	30(2)	3.5	
20(1)	30(1)	30(1)	40(1)	20(1)	30(1)	40(2)	40(1)	3.0	
30(1)	40(2)	40(1)	40(1)	30(1)	40(2)	40(1)	40(1)	3.0	
30(1)	40(1)	40(1)	40(1)	30(1)	40(1)	30(1)	40(1)	2.5	
50(2)	-	30(1)	40(2)	50(2)	-	50(1)	40(2)	3.0	
-	40(1)	50(1)	40(2)	-	40(1)	50(1)	40(2)	3.0	
30(2)	30(1)	50(2)	40(2)	30(2)	30(1)	50(2)	40(2)	3.0	
35.0±5.2	27.0±4.2	41.0±3.1	41.0±1.8	35.0±5.2	27.0±4.2	42.0±3.3	41.0±1.8	69.1±2.1	

[ 6 ]

플라시보 대조군 동물로부터의 데이터, 1주 부검 시간

관련된 자궁각 %

우측각				좌측각				전체
장	방광	자궁	좌측	장	방광	자궁	우측	
-	30(1)	40(1)	20(1)	-	30(1)	40(1)	20(1)	2.0
20(1)	30(1)	40(1)	30(1)	20(1)	30(1)	40(1)	30(1)	2.5
20(1)	30(1)	30(1)	40(1)	20(1)	30(1)	20(1)	40(1)	2.0
60(1)	-	30(1)	30(1)	60(1)	-	30(1)	30(1)	3.0
-	40(2)	30(1)	10(1)	-	40(2)	50(1)	10(1)	2.5
20(1)	10(1)	10(1)	20(1)	20(1)	10(1)	30(1)	20(1)	2.0
-	-	30(1)	30(1)	-	-	30(1)	30(1)	1.5
-	20(1)	40(2)	50(1)	-	20(1)	40(2)	50(1)	2.5
40(1)	20(1)	40(2)	30(2)	40(1)	20(1)	-	30(2)	2.5
30(1)	10(1)	30(1)	20(1)	30(1)	10(1)	30(1)	20(1)	2.0
19.0±6.4	19.0±4.3	32.0±2.9	28.0±3.6	19.0±6.4	19.0±4.3	31.0±4.3	28.0±3.6	48.7±3.9

[ 7 ]

처리된 동물로부터의 데이터, 1mg/ml 화합물 1, 2주 부검

관련된 자궁각 %

우측각				좌측각				전체
장	방광	자궁	좌측	장	방광	자궁	우측	
30(1)	-	40(1)	-	30(1)	-	40(1)	-	2.0
-	10(1)	10(1)	30(1)	20(1)	-	-	30(1)	1.5
30(1)	-	-	30(1)	30(1)	-	30(1)	30(1)	1.5
30(1)	-	-	-	30(1)	-	20(1)	-	1.0
-	-	20(1)	20(1)	-	-	20(1)	20(1)	1.0
10(1)	-	-	-	-	-	30(1)	-	0.5
20(1)	10(1)	-	10(1)	-	-	30(1)	10(1)	1.5
30(1)	-	20(1)	30(1)	30(1)	-	-	30(1)	1.5
20(1)	10(1)	-	20(2)	20(1)	-	10(1)	20(2)	1.5
20(1)	-	10(1)	10(1)	20(1)	-	-	10(1)	1.0
19.0±3.8	3.0±1.5	10.0±4.2	15.0±4.0	18.0±4.2	0.0±0.0	18.0±4.7	15.0±4.0	21.3±3.9

[ 8 ]

처리된 동물로부터의 데이터, 0.1mg/ml 화합물 1, 2주 부검

관련된 자궁각 %

우측각				좌측각				전체
장	방광	자궁	좌측	장	방광	자궁	우측	
-	-	10(1)	-	30(1)	-	40(1)	-	1.5
-	20(1)	-	20(1)	-	20(1)	30(1)	20(1)	1.5
10(1)	-	10(1)	30(1)	-	-	-	30(1)	1.0
40(1)	30(1)	30(1)	-	40(1)	30(1)	30(1)	-	2.0
30(1)	10(1)	-	10(1)	30(1)	10(1)	30(1)	10(1)	1.5
10(1)	10(1)	10(1)	40(1)	10(1)	10(1)	-	40(1)	1.5
30(1)	-	10(1)	30(1)	30(1)	-	50(1)	30(1)	2.0
-	-	30(1)	-	-	-	20(1)	-	1.0
-	-	10(1)	20(1)	-	-	-	20(1)	0.5
10(1)	-	-	-	10(1)	-	30(1)	-	0.5
13.0±4.7	7.0±3.4	11.0±3.5	15.0±4.8	15.0±5.0	7.0±3.4	23.0±5.6	15.0±4.8	22.0±4.8

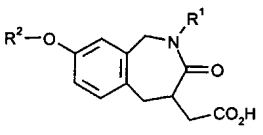
[ 9 ]

	( )	(%)
, 2	8	10.0
, 2	17	21.25
1 mg/ml 1	45	56.25
0.1 mg/ml 1	31	38.75
, 1	4	5.0
, 1	3	16.25
1 mg/ml 1	36	45.0
0.1 mg/ml 1	34	42.5

(57)

1.

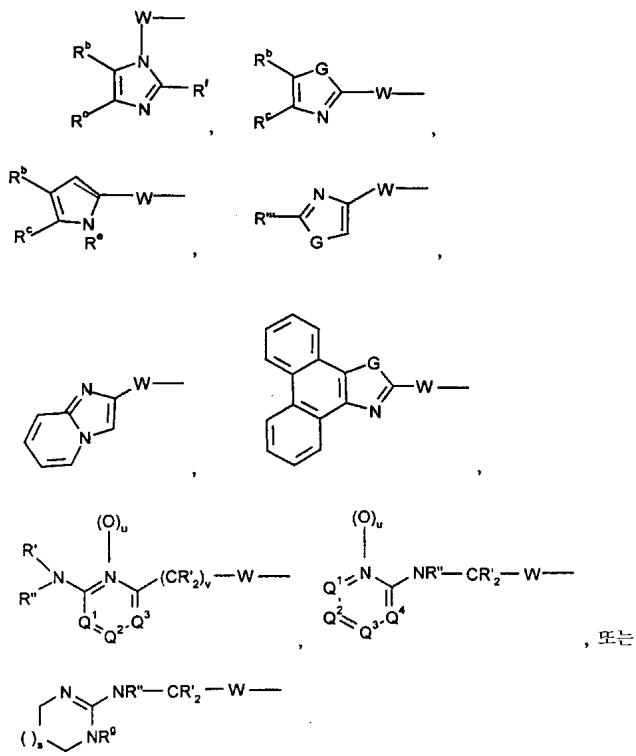
< | >



$R^1$ , A-C<sub>2-4</sub>,  $R^7$ , A-C<sub>2-4</sub>,  $R^{10}$ , A-C<sub>3-4</sub>,  $R^7$ , A-C<sub>3-4</sub>, 가, A-C<sub>3-4</sub>, A-C<sub>1-4</sub>, A-C<sub>0-4</sub>, A-C<sub>3-4</sub> ;  
 $A$  H, C<sub>3-6</sub>, Het, Ar ;  
 $R^7$  -COR<sup>8</sup>, -COCR'<sub>2</sub>R<sup>9</sup>, -C(S)R<sup>8</sup>, -S(O)<sub>m</sub>OR', -S(O)<sub>m</sub>NR'R', -PO(OR'), -PO(OR')<sub>2</sub>, -NO<sub>2</sub>, ;  
 $R^8$  -OR', -NR'R', -NR'SO<sub>2</sub>R', -NR'OR', -OCR'<sub>2</sub>CO(O)R' ;  
 $R^9$  -OR', -CN, -S(O)<sub>r</sub>R', -S(O)<sub>m</sub>NR'<sub>2</sub>, -C(O)R', C(O)NR'<sub>2</sub>, -CO<sub>2</sub>R' ;  
 $R^{10}$  H, -OR<sup>11</sup>, -CN, -NR'R<sup>11</sup>, -NO<sub>2</sub>, -CF<sub>3</sub>, CF<sub>3</sub>S(O)<sub>r</sub>-, -CO<sub>2</sub>R', -CONR'<sub>2</sub>, A-C<sub>0-6</sub>, A-C<sub>1-6</sub>, A-C<sub>2-6</sub>, A-C<sub>2-6</sub>, A-C<sub>0-6</sub>, A-C<sub>0-6</sub>, A-C<sub>0-6</sub>, -S(O)<sub>r</sub>- ;

R<sup>11</sup> R<sup>1</sup>, -C(O)R<sup>1</sup>, -C(O)NR<sup>1</sup><sub>2</sub>, -C(O)OR<sup>1</sup>, -S(O)<sub>m</sub>R<sup>1</sup>, -S(O)<sub>m</sub>NR<sup>1</sup><sub>2</sub> ;

R<sup>2</sup>



W -(CHR<sup>g</sup>)<sub>a</sub>-U-(CHR<sup>g</sup>)<sub>b</sub>- ;

U CO, CR<sup>g</sup><sub>2</sub>, C(=CR<sup>g</sup><sub>2</sub>), S(O)<sub>k</sub>, O, NR<sup>g</sup>, CR<sup>g</sup>OR<sup>g</sup>, CR<sup>g</sup>(OR<sup>k</sup>)CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>CR<sup>g</sup>(OR<sup>k</sup>), C(O)CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>C(O), CONR<sup>i</sup>, NR<sup>i</sup>CO, OC(O), C(O)O, C(S)O, OC(S), C(S)NR<sup>g</sup>, NR<sup>g</sup>C(S), S(O)<sub>2</sub>NR<sup>g</sup>, NR<sup>g</sup>S(O)<sub>2</sub>N=N, NR<sup>g</sup>NR<sup>g</sup>, NR<sup>g</sup>CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>NR<sup>g</sup>, CR<sup>g</sup><sub>2</sub>O, OCR<sup>g</sup><sub>2</sub>, C<sub>1-6</sub>CR<sup>g</sup>=CR<sup>g</sup> ;

G NR<sup>e</sup>, S O ;

R<sup>g</sup> H, C<sub>1-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub> Ar-C<sub>0-6</sub> ;

R<sup>k</sup> R<sup>g</sup>, -C(O)R<sup>g</sup>, -C(O)OR<sup>f</sup> ;

R<sup>i</sup> H, C<sub>1-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub>, Ar-C<sub>0-6</sub>, C<sub>1-6</sub>, CN, NR<sup>g</sup><sub>2</sub>, OR<sup>g</sup>, SR<sup>g</sup>, CO<sub>2</sub>R<sup>g</sup>, CON(R<sup>g</sup>)<sub>2</sub> ;

R<sup>f</sup> H, C<sub>1-6</sub> Ar-C<sub>0-6</sub> ;

R<sup>e</sup> H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub>, (CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>R<sup>g</sup> ;

R<sup>b</sup> R<sup>c</sup> H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, HetC<sub>0-6</sub>, C<sub>3-6</sub> -C<sub>0-6</sub>, CF<sub>3</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub>, R<sup>b</sup> R<sup>c</sup>, CF<sub>3</sub>, C<sub>1-4</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, CO<sub>2</sub>R<sup>f</sup>, OH, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub> ;

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup> Q<sup>4</sup> N C-R<sup>y</sup>, Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup> Q<sup>4</sup> N ;

R<sup>1</sup> H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub> C<sub>3-6</sub> -C<sub>0-6</sub> ;

R' R', -C(O)R' -C(O)OR' ;

R'' H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-6</sub>, -C<sub>0-6</sub>, CF<sub>3</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub> ;

R<sup>y</sup> H, -OR<sup>g</sup>, -SR<sup>g</sup>, -CN, -NR<sup>g</sup>R<sup>k</sup>, -NO<sub>2</sub>, -CF<sub>3</sub>, CF<sub>3</sub>S(O)<sub>r</sub>-, -CO<sub>2</sub>R<sup>g</sup>, -COR<sup>g</sup>, -CONR<sup>g</sup><sub>2</sub>, -OR<sup>g</sup>, -SR<sup>g</sup>, -CN, -NR<sup>g</sup>R', -NO<sub>2</sub>, -CF<sub>3</sub>, R'S(O)<sub>r</sub>-, -CO<sub>2</sub>R<sup>g</sup>, -CO  
R<sup>g</sup> -CONR<sup>g</sup><sub>2</sub> C<sub>1-6</sub> ;

a 0, 1 2 ;

b 0, 1 2 ;

k 0, 1 2 ;

m 1 2 ;

r 0, 1 2 ;

s 0, 1 2 ;

u 0 1 ;

v 0 1 .

**2.**

1 (S)-3- -8-[3-( -2- )-1- ]-2-(2,2,2- )-2,3,4,5- -1H-2- -4- .

**3.**

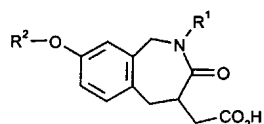
1 (S)-8-[2-[6-( ) -2- ]-1- ]-3- -2-(2,2,2- )-2,3,4,5- -1H-2- -4- .

**4.**

-2- )-1- ]-5H- [a,d] (S)-10,11- -3-[2-(5,6,7,8- -1,8- -10- )-1- ]-5H- [a,d] .

**5.**

I , .  
< I >



R<sup>1</sup> R<sup>7</sup> , A-C<sub>2-4</sub> , A-C<sub>2-4</sub> , A-C<sub>3-4</sub> R<sup>10</sup> R<sup>7</sup> 가 A-C<sub>3-4</sub> , A-C<sub>3-4</sub> , A-C<sub>1-4</sub> A-C<sub>0-4</sub> , A-C<sub>3-4</sub> ;

A H, C<sub>3-6</sub> , Het Ar ;

R<sup>7</sup> -COR<sup>8</sup>, -COCR'<sub>2</sub>R<sup>9</sup>, -C(S)R<sup>8</sup>, -S(O)<sub>m</sub>OR', -S(O)<sub>m</sub>NR'R', -PO(OR'), -PO(OR')<sub>2</sub>, -NO<sub>2</sub>,  
;

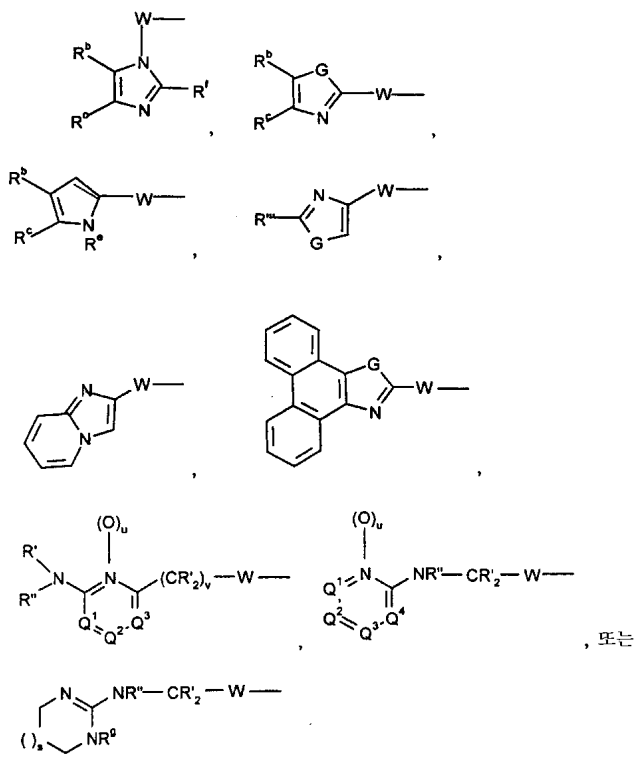
R<sup>8</sup> -OR', -NR'R', -NR'SO<sub>2</sub>R', -NR'OR', -OCR'<sub>2</sub>CO(O)R' ;

R<sup>9</sup> -OR', -CN, -S(O)<sub>r</sub>R', -S(O)<sub>m</sub>NR'<sub>2</sub>, -C(O)R', C(O)NR'<sub>2</sub>, -CO<sub>2</sub>R' ;

R<sup>10</sup> H, -OR<sup>11</sup>, -CN, -NR'R<sup>11</sup>, -NO<sub>2</sub>, -CF<sub>3</sub>, CF<sub>3</sub>S(O)<sub>r</sub>-, -CO<sub>2</sub>R', -CONR'<sub>2</sub>, A-C<sub>0-6</sub>  
-, A-C<sub>1-6</sub>-, A-C<sub>2-6</sub>-, A-C<sub>2-6</sub>-, A-C<sub>0-6</sub>-, A-C<sub>0-6</sub>- A  
-C<sub>0-6</sub>-S(O)<sub>r</sub>- ;

R<sup>11</sup> R', -C(O)R', -C(O)NR'<sub>2</sub>, -C(O)OR', -S(O)<sub>m</sub>R', -S(O)<sub>m</sub>NR'<sub>2</sub> ;

R<sup>2</sup>



W -(CHR<sup>g</sup>)<sub>a</sub>-U-(CHR<sup>g</sup>)<sub>b</sub>- ;

U CO, CR<sup>g</sup><sub>2</sub>, C(=CR<sup>g</sup><sub>2</sub>), S(O)<sub>k</sub>, O, NR<sup>g</sup>, CR<sup>g</sup>OR<sup>g</sup>, CR<sup>g</sup>(OR<sup>k</sup>)CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>  
CR<sup>g</sup>(OR<sup>k</sup>), C(O)CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>C(O), CONR<sup>i</sup>, NR<sup>i</sup>CO, OC(O), C(O)O, C(S)O, OC(S), C(S)NR<sup>g</sup>, NR<sup>g</sup>  
C(S), S(O)<sub>2</sub>NR<sup>g</sup>, NR<sup>g</sup>S(O)<sub>2</sub>N=N, NR<sup>g</sup>NR<sup>g</sup>, NR<sup>g</sup>CR<sup>g</sup><sub>2</sub>, CR<sup>g</sup><sub>2</sub>NR<sup>g</sup>, CR<sup>g</sup><sub>2</sub>O, OCR<sup>g</sup><sub>2</sub>, C  
CR<sup>g</sup>=CR<sup>g</sup> ;

G NR<sup>e</sup>, S O ;

R<sup>g</sup> H, C<sub>1-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub> Ar-C<sub>0-6</sub> ;

R<sup>k</sup> R<sup>g</sup>, -C(O)R<sup>g</sup>, -C(O)OR<sup>f</sup> ;

R<sup>i</sup> H, C<sub>1-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub>, Ar-C<sub>0-6</sub>, CN, NR<sup>g</sup>  
R<sup>g</sup><sub>2</sub>, OR<sup>g</sup>, SR<sup>g</sup>, CO<sub>2</sub>R<sup>g</sup>, CON(R<sup>g</sup>)<sub>2</sub> 1 3 C<sub>1-6</sub> ;

R<sup>f</sup> H, C<sub>1-6</sub> Ar-C<sub>0-6</sub> ;

R<sup>e</sup> H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-7</sub> -C<sub>0-6</sub>, (CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>R<sup>g</sup>

;

$R^b$ ,  $R^c$ , H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, HetC<sub>0-6</sub>, C<sub>3-6</sub>, -C<sub>0-6</sub>, CF<sub>3</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub>, (R<sup>b</sup>), (R<sup>c</sup>), CF<sub>3</sub>, C<sub>1-4</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, CO<sub>2</sub>R<sup>f</sup>, OH, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub>, 3, 5, 6;

Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, Q<sup>4</sup>, N, C-R<sup>γ</sup>, Q<sup>1</sup>, Q<sup>2</sup>, Q<sup>3</sup>, Q<sup>4</sup>, N;

R' H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, C<sub>3-6</sub>, -C<sub>0-6</sub>;

R' R', -C(O)R' -C(O)OR' ;

R'' H, C<sub>1-6</sub>, Ar-C<sub>0-6</sub>, Het-C<sub>0-6</sub>, C<sub>3-6</sub>, -C<sub>0-6</sub>, CF<sub>3</sub>, OR<sup>f</sup>, S(O)<sub>k</sub>R<sup>f</sup>, COR<sup>f</sup>, NO<sub>2</sub>, N(R<sup>f</sup>)<sub>2</sub>, CO(NR<sup>f</sup>)<sub>2</sub>, CH<sub>2</sub>N(R<sup>f</sup>)<sub>2</sub> ;

R<sup>γ</sup> H, -OR<sup>g</sup>, -SR<sup>g</sup>, -CN, -NR<sup>g</sup>R<sup>k</sup>, -NO<sub>2</sub>, -CF<sub>3</sub>, CF<sub>3</sub>S(O)<sub>r</sub>-, -CO<sub>2</sub>R<sup>g</sup>, -COR<sup>g</sup>, -CONR<sup>g</sup><sub>2</sub>, -OR<sup>g</sup>, -SR<sup>g</sup>, -CN, -NR<sup>g</sup>R', -NO<sub>2</sub>, -CF<sub>3</sub>, R'S(O)<sub>r</sub>-, -CO<sub>2</sub>R<sup>g</sup>, -COR<sup>g</sup>, -CONR<sup>g</sup><sub>2</sub>, C<sub>1-6</sub> ;

a 0, 1, 2 ;

b 0, 1, 2 ;

k 0, 1, 2 ;

m 1, 2 ;

r 0, 1, 2 ;

s 0, 1, 2 ;

u 0, 1 ;

v 0, 1 .

### 6.

5, (S)-3-8-[3-(2-)-1-]-2-(2,2,2-)-2,3,4,5-1H-2-4-

### 7.

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

### 8.

(S)-10,11-3-[2-(5,6,7,8-1,8-2-)-1-]-5H-[a,d]-10-