

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

(51) 。 Int. Cl.<sup>7</sup>  
A61K 31/397  
A61P 9/00

(11)  
(43)

10-2004-0025890  
2004 03 26

(21) 10-2003-7009794

(22) 2003 07 24

2003 07 24

(86) PCT/US2002/002013

(87)

WO 2002/58734

(86) 2002 01 25

(87)

2002 08 01

(30)	60/264,396	2001 01 26	(US)
	60/264,600	2001 01 26	(US)
	60/264,275	2001 01 26	(US)
	60/324,123	2001 09 21	(US)

(71) 07033 2000

(72) 18929-1178 2457

08822-5910 16

08833 14

08540 6

(74)

:

(54)

; (b)

, (a)

2001 9 21  
60/264,396 , 2001 1 26  
가 60/264,275 (

가 60/324,124 , 2001 1 26  
가 60/264,600 2001 1 26  
)

가

(blood modifier)

가  
(large vessel)

(underlying)

가 , 가 ( ) .225 250mg/dl

가  
가

가

(homeostasis)

(liver)

(VLDL)

VLDL

가

(LDL)

LDL

(VLDL)

LD

L

(clearance)

가

5,767,115 , 5,624,920 , 5,668,990 , 5,656,624 5,688,787

5,846,966 5,661,145  
HMG CoA

PCT

WO 00/38725

(microsomal)

(ileal)

5,698,527

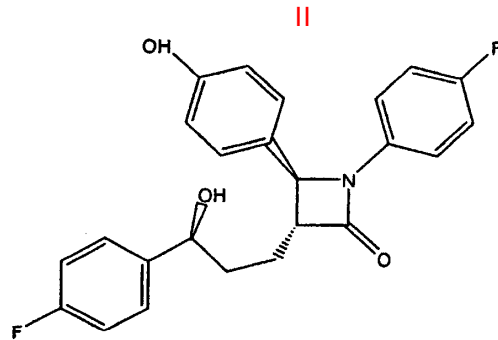
가

(thrombus)[ : (blood colt)

me) (zymogen), (cascade)' (proenzy  
) 'a' 가 ( : fVIIa). 가 , ,  
X(fXa) X 2가 가 .  
fVIIa IXa TF VIIIa X Xa  
TF VIIa mostasis) Ca<sup>2+</sup> IX X f (he  
TF 2가 , fVIIa  
fVII - Xa, XIIa, IXa, fVIIa - fVIIa  
Xa fVII 가  
, fVII K , fVII -  
fVII Arg 152-Ile 153  
TF, , - fVIIa가 X  
IX Xa , fVII  
(SMCs) . SMC , 6  
MC (bypass grafts) 30% , / S  
(restenosis)  
fVIIa (procoagulant)  
( 5,639,739 ).  
( , WO 01/21/21259  
)  
\_\_\_\_\_  
(a) , ; (b) (a)  
(a) - , -  
; (b) (a) ,

(a) II , ;

(b) (a) , :



가

가

가

( )

CoA VIIa Xa

HMG

가 (2- , 1-[(2S)-5-[(  
 ) ]-1- -2-[[1,2,3,4- -3- -8- ) ] ]-4- -, CAS  
 RN 74863-84-6); (L- , D- -L- -L- -L- -L- -L- )  
 -L- -L- -L- -L- -L- -L- -L- -L- -L- )  
 , Pharmacia amp; Upjohn 가 FRAGMIN ); ( (Hirudo medicinalis  
 HV1), 63- CAS RN 120993-53-5); (2H-1- -2- , 3,3'- [4-  
 - CAS RN 66-76-2, , Sanofi-Synthelabo 가 MEBARAL );  
 ( , CAS RN 25053-27-4); ( , 4-[(  
 ) ]-, 6-( )-2- CAS RN 82956-11-4);  
 (2H-1- -2- , 4- -8- -3-(1- )- CAS RN 132605-68-6);  
 ( , CAS RN 9041-08-1, , DuPont 가 INNOHEP );  
 (3-(( )- )-4- , CAS RN 129-06-6, , DuPont  
 가 )

(6,7- -1,5- [2,1-b] -2(3H)-  
 , Shire US 가 AGRYLIN );  
 ; (6-[4-(1- -1H- -5- ) ]-3,4- -2(1H)- , CAS RN 7  
 3963-72-1, , PLETAL (Pharmacia amp; Upjohn)); ( );  
 ( , Organon 가 ORGARAN ); ( )  
 (GP) IIb/IIIa(( ) IIb ( ) 3)  
 7E3 Fab  
 (( ) v ( ) 3 ) , Lily 가 Abciximab, REOPRO ); ( )  
 , 2-[[1(1S,2R,3S,4R)-3-[4-[( ) ]-2- ]-7- [2.2.1] -2  
 - ] - CAS RN 143443-90-7); ( ) );  
 가 (L- , N- -D- -N-[[1(1S)-4-[( ) ]-1- ]-  
 , (1:1) CAS RN 126721-07-1); ( , 4-[2-(1H- -1- ) ]-  
 ]-, CAS RN 74226-22-5); ( )  
 ( 84%), ( 12%) ( 4%) (hog)  
 )-2,3,4,5- -4- -3- -, (2S)- CAS RN 179599-  
 82-7); ( , 2-[[1(1S,2R,3S,4R)3-[4-[( ) ]-2- ]-7-  
 [2.2.1] -2- ] ]-, CAS RN 156715-37-6); ( , [[1-[(2S)-2-  
 [[4-( ) ] ]-3-(4- )-1- ]-4- ] ]-, CAS RN 1  
 44412-49-7); (1,1'- , 4'- -2- - CAS RN 56917-29-4); ( )  
 , CAS RN 9041-08-1); ( - , N-[[[(3S)-1-[4-(  
 ) ]-2- -3- ] ] ]-, (4:4:1), C  
 AS RN 165800-05-5); 가 ( , N-[[[(3S)-1-( )-3- ] ] ]-N2-(2-  
 )-L- -N- , CAS RN 154397-77-0); (L- , 3-[[  
 [(5R)-3-[4-( ) ]-4,5- -5- ] ] ]-N-( )- ,  
 , CAS RN 176022-59-6); ( , [[1-[(2S)-2-[[4-[(Z)- ( )  
 ) ] ] ]-1- ]-4- ] ]-, CAS RN 172927-65-0);  
 ( G1, -( CD5( ) ))( H65-RTA 1- ),  
 H65-RTA , ( A- ) , CAS RN 141483-7  
 2-9); ( , 2-[2-(4,5- -1H- -2- ) ]-N,N- -, CAS RN 84203-09  
 -8)

( ); ( );  
 ( ); 7E3( (GP) IIb/IIIa(( ) IIb ( ) 3)  
 7E3 Fab ); ( )  
 , N-[[[(3S)-1-[4-( ) ]-2- -3- ] ] ]-, CAS  
 RN 163250-90-6); (4- , 3-[[4-[[4-( ) ] ]-1,4- ] ]  
 ]-, (3S)-, CAS RN 149820-74- 6); (3- , 5-[[[4'-(  
 ) ] ] ]-

) [1,1'- ]-4- ] ] ]-2- -, (3S,5S)-, CAS RN 148396-36-5); (L- , N-(  
)-O-[4-(4- ) ]-, CAS RN 144494-65-5, , Merck 가 AGGRASTATt  
( )  
( , )  
( : (PDGF)  
( [3,2-c] -5(4H)- ,  
- (2- )-6,7- -, ( S)-, (1:1), , Sanofi-Synthelabo  
가 PLAVIX ); ( , Merck 가 INDOCIN I.V.(  
)); ( , First Horizon 가 Ponstel Kapsea  
ls ( ) 2- {(2,3- ) -N-2,3- ); ( [3,2  
-c] , 5- [(2- ) ]-4,5,6,7- -, , Roche Laboratori  
es 가 TICLID ); ( -5,13- -1- , 6,9- -11,15-  
-, , (5Z,9 11 , 13E,15S)- CAS RN 61849-14-7, , Glaxo Wellcome  
가 FLOLAN ); ( , 2-( )- CAS RN 50-78-2); ( )  
-5,13- -1- , 6,9- -11,15- -, (5Z,9 ,11 ,13E,15S)-, CAS RN 35121-  
78-9); (2- , 6- - - -, ( S)- CAS RN 22204-53-1, , Roche  
Laboratories 가 EC-NAPROSYN - ); ( , - -4-(2-  
)-, CAS RN 15687-27-1); (2H,5H-1,3- [5,6-c][1,2] -2,4(3H)- , 5-  
-3-(2- )-, 6,6- , CAS RN 90101-16-9); ( , 2- [(2,6-  
) ]- CAS RN15307-86-5, , Searle 가 Arthrotec ); (3,5-  
, 1,2- -4-[2-( ) ]- CAS 57-96-5, , Wyeth-Ayerst  
가 Sectral ); (2H-1,2- -3- , 4- -2- -N-2- -,  
1,1- , CAS 36322-90-4, , Pfizer 가 FELDENEC );  
( , 2,2',2',2''- [(4,8- -1- [5,4-d] -2,6- ) ] - CAS  
58-32-2, , Boehringer Ingelheim 가 Aggrenox ); (L-  
, N- -N- [[4- [(2- -1H- [4,5-c] -1- ) ] ] ]-, , CAS  
139133-26-9); (4- [3- [4-(2- )-9- -6H- [3,2- f][1,2,4]  
[4,3-a][1,4] -2- ]-1- ]-, CAS 105219-56-5)

(1H- [b] -5- , 2,3,3a,8b-  
-2- -1-(3- -4- -1- -6- )-, CAS RN 88430-50-6); (1H- -  
4- , 5- -1- -D- -, CAS RN 2627-69-2); (1H-  
[b] -5- , 2,3,3a,8b- -2- -1-(3- -4- -1- -6-  
)-, , CAS RN 88475-69-8); ( , 5- [(3aS,5R,6R,6aR)- -5-  
-6- [(1E,3S)-3- -1- ]-3a- -2-(1H)- ]-, (2:1), (5Z)- CAS  
81703-55-1); ( , 4,5- (4- )-2-( )- CAS 70529-  
35-0); ( , 1-( )-4- [[5- -2-(4- )-1H- -4- ] ]-, CAS  
119514-66-8); (6- , 3,4- -1-( )-5,7- -4-  
-, , CAS 56611-65-5)

(1H- -2,6- , 3,7- -3,7- -1-(5- )- ( )- ( )  
9CI)(CA INDEX NAME) , 1-(5- )-, CAS 6493-05-6, , Aventis  
가 TRENTALI )

( )

가 (deformability) 가 ,

가

(LACI) 38,000Kd  
 ( )  
 5,110,730 5,106,833 가  
 VII Xa ) LACI 3 (Kunitz) 가 2 가  
 가 , LACI , LACI 가  
 가 ( 6,063,74 ).

VIIa VIIa VIIa가 4H-3,1- -4- , 4H-3,  
 1- -4- ; -4- ; 6,180,625 6,180,625 TFPI- 5,639,739 가  
 가 VIIa -2- {1-[3-( )- ]-2- - -3-(  
 S)- } -2- {1-[3-( )- ]-5- - -3-  
 }- , -4- {1-[3-( )- ]-2- - -3-(S)- }-  
 , 3,4- -1H- -2- {1-[3-( )- ]-2- - -3-(S)-  
 }- .

Xa X가 6,191,159  
 Xa ; (LACI)( );  
 ; 6,207,697  
 2가( ) ; [J. Med. Chem. 37:1200-1207 (1994)]  
 ; 6,057,342 5,612,378  
 ; 6,043,257  
 ) ] Xa ; 6,080,767 n-[(  
 ) ] ;

(leech)- 119- (soft tick)- TAP(  
 ) Xa 가  
 [ : Mellott et al., Circulation Research 70:1152-1160 (1992); Sitko et al., Circulation  
 n 85:805-815 (1992)]. 5,385,885 (1995. 1. 31 )  
 a 가 [ : Seymour et al., Biochemistry 33:3949  
 -3959 (1994); PCT WO 94/20535, 1994. 9. 14]. (Ixodidae), 가  
 s and Hemostasis 72:477-479 (1994)]. Xa [ : Markwardt, Thrombosi

Xa - 가 CAS  
 , CAS 110119-38-5; , (  
 , TAP) CAS 129737-17-3; , ( ) CAS 87  
 928-05; 가 , CAS 53092-89-0; , CAS 11011-09-9; (Markwa  
 rdt, 1994 )가 .

가 2000 10000

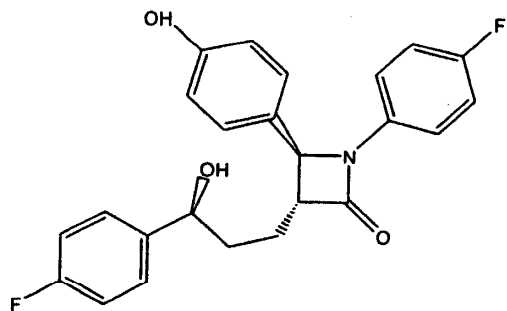
CAS 308068-55-5( , Orga  
 ran Injection Organon)





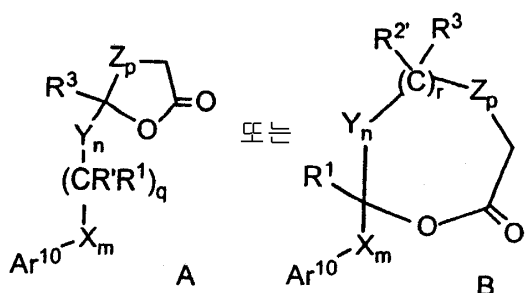


II



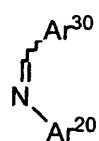
46,966 , 6,207,822 , 가 60/279,288 (2001. 3. 28 5,631,365 , 5,767,115 , 5,8 ) PCT WO 93/ 02048( ),

(a)



[ , R' R 2' R R 2 , ; Ar 10 Ar 1 , ; B , n r 0 , p 1 4 ]

(b) (a)



[ , Ar 20 Ar 2 , ; Ar 30 Ar 3 , ]

(c) ;

(d) , R', R 2', Ar 10, Ar 20 Ar 30 ;

(e) , R, R 2, Ar 1, Ar 2 Ar 3

, IA IB :



COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>- , S(O)<sub>0-2</sub>- , -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, o- , m- , o- , m- , -( )-COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup>

R<sup>3</sup> R<sup>4</sup> , R<sup>5</sup>, , p- , , -NO<sub>2</sub>, -CF<sub>3</sub> p-

R<sup>6</sup>, R<sup>7</sup> R<sup>8</sup> , , - ;

R<sup>9</sup> , - .

III Ar<sup>1</sup> R<sup>3</sup>- , (4-R<sup>3</sup>)- . Ar<sup>2</sup> R<sup>4</sup>- , (4-R<sup>4</sup>)- . Ar<sup>3</sup> R<sup>5</sup>- , (4-R<sup>5</sup>)- . Ar<sup>1</sup>, Ar<sup>2</sup> Ar<sup>3</sup> . Ar

Y Z , -CH<sub>2</sub>- . R<sup>2</sup>가 ( , R<sup>1</sup> -OR<sup>6</sup> , R<sup>6</sup> O)NR<sup>6</sup>R<sup>7</sup> . , R<sup>1</sup> R<sup>2</sup>가 =O ( , -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup> -O(C

q p , Y가 -CH<sub>2</sub>- R<sup>1</sup> R<sup>2</sup>, R<sup>6</sup> . p가 0 q가 1 . p가 0

Ar<sup>1</sup> R<sup>3</sup>- , Ar<sup>2</sup>가 R<sup>4</sup>- , Ar<sup>3</sup> R<sup>5</sup>-

Ar<sup>1</sup> R<sup>3</sup>- , Ar<sup>2</sup>가 R<sup>4</sup>- , Ar<sup>3</sup> R<sup>5</sup>- , p q R<sup>1</sup> R<sup>2</sup>, R<sup>6</sup> . p가 0 q가 1 . p가 0 , Ar<sup>1</sup> R<sup>3</sup>- , Ar<sup>2</sup>가 R<sup>4</sup>- , Ar<sup>3</sup> R

A -O- .

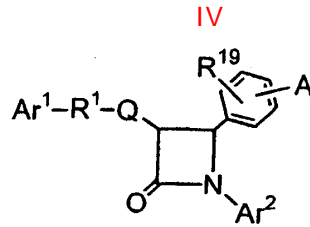
R<sup>3</sup> -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>- , S(O)<sub>0-2</sub>- , NO<sub>2</sub> . R<sup>3</sup> , .

R<sup>4</sup>가 , R<sup>6</sup> R<sup>7</sup> , -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, COR<sup>6</sup> , R<sup>9</sup>가 . R<sup>4</sup> , .

R<sup>5</sup>가 -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -( )-COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> , R<sup>6</sup> R<sup>7</sup> , R<sup>9</sup>가 . R<sup>5</sup> -OR<sup>6</sup>, -( )-COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> , R<sup>6</sup> .

III 가 5,68 8,990 ( ) .

IV , IV , IV IV , IV , IV



A, R<sup>2</sup> - , R<sup>2</sup> - , R<sup>2</sup> - , R

Ar<sup>1</sup> R<sup>3</sup> - ;

Ar<sup>2</sup> R<sup>4</sup> - ;

Q , 3- , ;

R<sup>1</sup>

-(CH<sub>2</sub>)<sub>q</sub>-[ , q 2 6 , Q가 , q 0 1 ];

-(CH<sub>2</sub>)<sub>e</sub>-G-(CH<sub>2</sub>)<sub>r</sub>-[ , G -O-, -C(O)-, , -NR<sup>8</sup>- -S(O)<sub>0-2</sub>- , e 0 5  
r 0 5 , e r 1 6 ];

-(C<sub>2</sub>-C<sub>6</sub> )-;

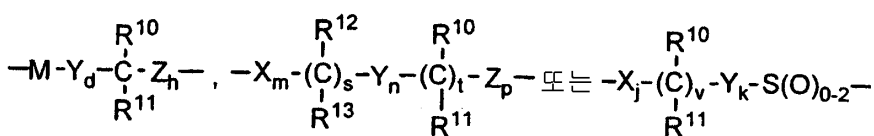
-(CH<sub>2</sub>)<sub>f</sub>-V-(CH<sub>2</sub>)<sub>g</sub>-[ , V C<sub>3</sub>-C<sub>6</sub> , f 1 5 g 0 5 , f  
g 1 6 ] ;

R<sup>5</sup>는  $\begin{matrix} | \\ -CH- \\ | \end{matrix}$ ,  $\begin{matrix} | \\ -C(C_1-C_6 \text{ 알킬})- \\ | \end{matrix}$ ,  $\begin{matrix} | \\ -CF- \\ | \end{matrix}$ ,  $\begin{matrix} | \\ -C(OH)- \\ | \end{matrix}$ ,  $\begin{matrix} | \\ -C(C_6H_4-R^9)- \\ | \end{matrix}$ ,  $\begin{matrix} | \\ -N- \\ | \end{matrix}$ , 또는  $\begin{matrix} | \\ -NO^+ \\ | \end{matrix}$  ;

R<sup>6</sup> R<sup>7</sup> -CH<sub>2</sub>-, -CH(C<sub>1</sub>-C<sub>6</sub> )-, -C( -(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>5</sup></sub> ), -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub><sub>R<sup>7</sup></sub>)=CH-  
-, -CH=CH- -CH=C(C<sub>1</sub>-C<sub>6</sub> )- ;

a b 0, 1, 2 3 , 가 0 ; R<sup>6</sup> -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub>)=CH-  
, a 1 ; R<sup>7</sup> -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub>)=CH- , b 1 ; a가 2 3 , R<sup>6</sup>  
; b가 2 3 , R<sup>7</sup> ;

Q가 , R<sup>1</sup>



M -O-, -S-, -S(O)- -S(O)<sub>2</sub>- ;

X, Y Z -CH<sub>2</sub>-, -CH(C<sub>1</sub>-C<sub>6</sub> )- -C( -(C<sub>1</sub>-C<sub>6</sub>) )

R<sup>10</sup> R<sup>12</sup> -OR<sup>14</sup>, -O(CO)R<sup>14</sup>, -O(CO)OR<sup>16</sup> -O(CO)NR<sup>14</sup>R<sup>15</sup>  
;

R<sup>11</sup> R<sup>13</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>12</sup> R<sup>13</sup></sub>, =O ; R<sup>10</sup> R<sup>11</sup>

d 1, 2 3 ;

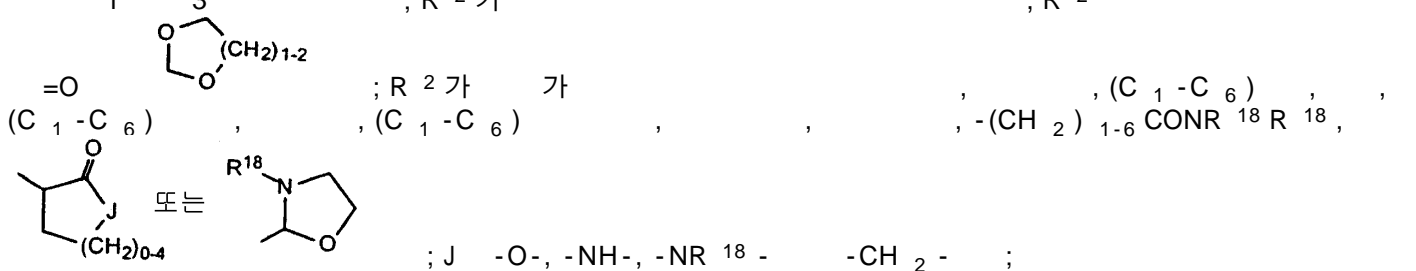
h 0, 1, 2, 3 4 ;

s 0 1 ; t 0 1 ; m, n p 0 4 , s t 1 , m, n  
, p, s t 1 6 ; p가 0 t가 1 , m, s n 1 5 ; p가 0 s가 1 , m, t  
n 1 5 ;

v 0 1 ;

j k 1 5 , j, k v 1 5 ;

R<sup>2</sup>, (C<sub>1</sub>-C<sub>10</sub>)<sub>R<sup>17</sup>-</sub>, (C<sub>2</sub>-C<sub>10</sub>)<sub>R<sup>17</sup>-</sub>, (C<sub>2</sub>-C<sub>10</sub>)<sub>R<sup>17</sup>-</sub>, (C<sub>3</sub>-C<sub>6</sub>)<sub>R<sup>17</sup>-</sub>, (C<sub>3</sub>-C<sub>6</sub>)<sub>R<sup>17</sup>-</sub>,  
-NR<sup>14</sup>R<sup>15</sup>, NR<sup>14</sup>R<sup>15</sup>(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>15</sup>-</sub>-, NR<sup>14</sup>R<sup>15</sup>C(O)(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>15</sup>-</sub>-, -NHC(O)R<sup>16</sup>, OH, C<sub>1</sub>-  
-C<sub>6</sub>, -OC(O)R<sup>16</sup>, -COR<sup>14</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>, NO<sub>2</sub>, -  
S(O)<sub>0-2</sub>R<sup>16</sup>, -SO<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>-(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>15</sup>-</sub>COOR<sup>14</sup> ; R<sup>2</sup>가 , R<sup>2</sup>



R<sup>3</sup> R<sup>4</sup> (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>3</sup>-</sub>, -OR<sup>14</sup>, -O(CO)R<sup>14</sup>, -O(CO)OR<sup>16</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>14</sup>, -O(CO)NR<sup>14</sup>R<sup>15</sup>, -NR<sup>14</sup>R<sup>15</sup>, -NR<sup>14</sup>(CO)R<sup>15</sup>, -NR<sup>14</sup>(CO)OR<sup>16</sup>, -NR<sup>14</sup>(CO)NR<sup>15</sup>R<sup>19</sup>, -NR<sup>14</sup>SO<sub>2</sub>R<sup>16</sup>, -C  
OOR<sup>14</sup>, -CONR<sup>14</sup>R<sup>15</sup>, -COR<sup>14</sup>, -SO<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, S(O)<sub>0-2</sub>R<sup>16</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>14</sup>, -O(CH  
2)<sub>1-10</sub>CONR<sup>14</sup>R<sup>15</sup>, -(C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>-COOR<sup>14</sup>, -CH=CH-COOR<sup>14</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub>  
1 3 ;

R<sup>8</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>8</sup>-</sub>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>8</sup>-</sub>, -C(O)R<sup>14</sup> -COOR<sup>14</sup> ;

R<sup>9</sup> R<sup>17</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>9</sup>-</sub>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>9</sup>-</sub>, -COOH, NO<sub>2</sub>, -NR<sup>14</sup>R<sup>15</sup>, OH ;

R<sup>14</sup> R<sup>15</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>, - (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>14</sup>-</sub>

R<sup>16</sup> (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>16</sup>-</sub>, R<sup>17</sup>- ;

R<sup>18</sup> (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>18</sup>-</sub> ;

R<sup>19</sup>, (C<sub>1</sub>-C<sub>6</sub>)<sub>R<sup>19</sup>-</sub> .

IV, 'A', 1 2, R<sup>2</sup>- 6  
'A', R<sup>2</sup>, R<sup>19</sup>

Ar<sup>2</sup> , R<sup>4</sup> - , (4-R<sup>4</sup>)- . R<sup>4</sup>

Ar<sup>1</sup> R<sup>3</sup> - , (4-R<sup>3</sup>)- .

-R<sup>1</sup>-Q- 가 :

Q가 R<sup>1</sup> , ;

Q가 , R<sup>6</sup> R<sup>7</sup> R<sup>5</sup>가  
 $\overset{|}{-CH-}$  또는  $\overset{|}{-C(OH)-}$  ;

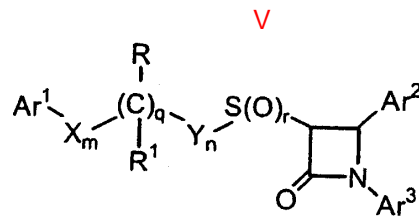
Q가 R<sup>1</sup>  $\overset{R^{10}}{\overset{|}{-M-Y_d-C-Z_n-}}$  [ , R<sup>1</sup> -O-CH<sub>2</sub>-CH(OH)- ] ;

Q가 R<sup>1</sup>  $\overset{R^{12}}{\overset{|}{-X_m-(C)_s-Y_n-}}$   $\overset{R^{10}}{\overset{|}{(C)_t-Z_p-}}$  [ , R<sup>1</sup> -CH(OH)-(CH<sub>2</sub>)<sub>2</sub>- ] ;

Q가 R<sup>1</sup>  $\overset{R^{10}}{\overset{|}{-X_j-(C)_v-Y_k-S(O)_{0-2}-}}$  [ , R<sup>1</sup> -CH(OH)-CH<sub>2</sub>-S(O)<sub>0-2</sub>- ] .

IV  
 6,624 ( ) . 가 5,65

, V , V V V , V



Ar<sup>1</sup> , R<sup>10</sup> - ;

Ar<sup>2</sup> R<sup>4</sup> - ;

Ar<sup>3</sup> R<sup>5</sup> - ;

X Y -CH<sub>2</sub> -, -CH( )- -C( - )- ;

R<sup>4</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -CO R<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -( )COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

q 0 1 ;

r 0, 1 2 ;

m n , 0, 1, 2, 3, 4 5 , m, n q 1, 2, 3, 4 5 ;

R<sup>4</sup> , -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -CO R<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -( )COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

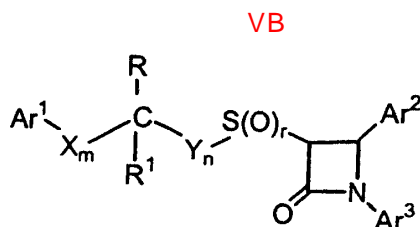
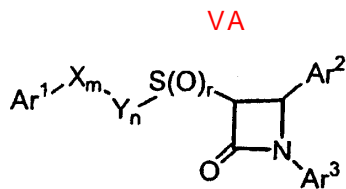
R<sup>5</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO) R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub>, , -( )COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

R<sup>6</sup>, R<sup>7</sup> R<sup>8</sup> , , - ;

R<sup>9</sup> , - ;

R<sup>10</sup> , -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -C OR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -CF<sub>3</sub>, -C N, -NO<sub>2</sub> .

V 2가 가 VA , q가 0 가 , VB , q가 1 가 :



R<sup>4</sup>, R<sup>5</sup> R<sup>10</sup> , , (4-R<sup>10</sup>)- 1 3 . Ar<sup>1</sup> , R<sup>10</sup> - , (4-R<sup>4</sup>)- V R<sup>5</sup> . Ar<sup>2</sup> , R<sup>4</sup> - , (4-R<sup>5</sup>)- . Ar<sup>1</sup> R<sup>10</sup> - . Ar<sup>3</sup> , R<sup>10</sup> ,



u가 2, 3, R<sub>3</sub> ;

R<sub>4</sub> B-(CH<sub>2</sub>)<sub>m</sub>C(O)-[ , m 0, 1, 2, 3, 4 5 ];

B-(CH<sub>2</sub>)<sub>q</sub>-[ , q 0, 1, 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>e</sub>-Z-(CH<sub>2</sub>)<sub>r</sub>-[ , Z -O-, -C(O)-, , -N(R<sub>8</sub>)- -S(O)<sub>0-2</sub> - , e 0, 1, 2, 3, 4 5 r 0, 1, 2, 3, 4 5 , e r 0, 1, 2, 3, 4, 5 6 ];

B-(C<sub>2</sub>-C<sub>6</sub> )-;

B-(C<sub>4</sub>-C<sub>6</sub> )-;

B-(CH<sub>2</sub>)<sub>t</sub>-Z-(C<sub>2</sub>-C<sub>6</sub> )-[ , Z , t 0, 1, 2 3 , 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>f</sub>-V-(CH<sub>2</sub>)<sub>g</sub>-[ , V C<sub>3</sub>-C<sub>6</sub> , f 1, 2, 3, 4 5 g 0, 1, 2, 3, 4 5 , f g 1, 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>t</sub>-V-(C<sub>2</sub>-C<sub>6</sub> )-

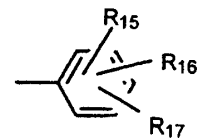
B-(C<sub>2</sub>-C<sub>6</sub> )-V-(CH<sub>2</sub>)<sub>t</sub>-[ , V t , 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>a</sub>-Z-(CH<sub>2</sub>)<sub>b</sub>-V-(CH<sub>2</sub>)<sub>d</sub>-[ , Z V , a, b d 0, 1, 2, 3, 4, 5 6 ];

T-(CH<sub>2</sub>)<sub>s</sub>-[ , T 3 6 , s 0, 1, 2, 3, 4, 5 6 ] ;

R<sub>1</sub> R<sub>4</sub> , **B-CH=C-** ;

B , , , , , W- , , , , ,



; , - , N-

W , , , , , ( , -CF<sub>3</sub>, -OCF<sub>3</sub>, , R<sub>7</sub> - , R<sub>7</sub> - , R<sub>7</sub> - , NO<sub>2</sub>, -N(R<sub>8</sub>)(R<sub>9</sub>), N(R<sub>8</sub>)(R<sub>9</sub>)- , N(R<sub>8</sub>)(R<sub>9</sub>)- , OH, , -CN, -N<sub>3</sub>, -NHC(O)OR<sub>10</sub>, -NHC(O)R<sub>10</sub>, R<sub>11</sub>O<sub>2</sub>SNH-, (R<sub>11</sub>O<sub>2</sub>S)<sub>2</sub>N-, -S(O)<sub>2</sub>NH<sub>2</sub>, -S(O)<sub>0-2</sub>R<sub>8,3</sub> - , -C(O)R<sub>12</sub>, -COOR<sub>19</sub>, -C ON(R<sub>8</sub>)(R<sub>9</sub>), -CH=CHC(O)R<sub>12</sub>, -C(O)R<sub>12</sub>, R<sub>10</sub>C(O)( )-, N(R<sub>8</sub>)(R<sub>9</sub>)C(

O)( )- **-CH<sub>2</sub>-N** ( ) ( ) , -C(O)OR<sub>10</sub>, -C(O)R<sub>10</sub>, OH, N(R<sub>8</sub>)(R<sub>9</sub>)- , N(R<sub>8</sub>)(R<sub>9</sub>)- , -S(O)<sub>2</sub>NH<sub>2</sub> 2-( )-

R<sub>7</sub> 1 3 , -COOH, NO<sub>2</sub>, -N(R<sub>8</sub>)(R<sub>9</sub>), OH ;

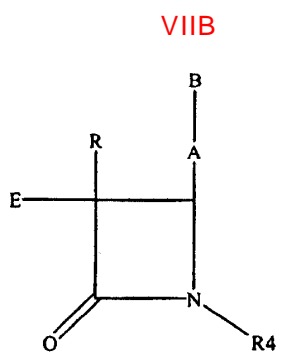
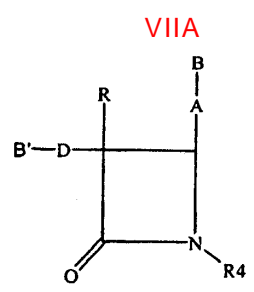
R<sub>8</sub> R<sub>9</sub> H ;



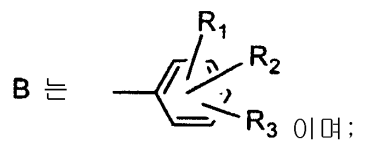
R<sub>21</sub> , F- .  
 2 , R<sub>4</sub> 가 B-(CH<sub>2</sub>)<sub>q</sub> - , R<sub>1</sub> , B가 , R<sub>2</sub> R<sub>3</sub> -CH<sub>2</sub>- , u=v=2 , q가 0 , R<sub>21</sub> ,  
 , R<sub>20</sub> , OH- , F-

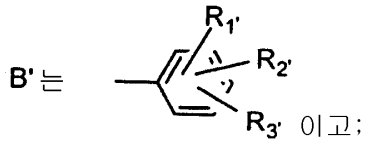
VI 8,548 ( ) 가 5,69

VIIA , VIIB , VIIA , VIIB , VIIA , VIIB :  
 IA , VIIB , VI



A -CH=CH-, -C C- -(CH<sub>2</sub>)<sub>p</sub> - [ , p 0, 1 2 ] ;





D -(CH<sub>2</sub>)<sub>m</sub>C(O)- (CH<sub>2</sub>)<sub>q</sub>- [ , m 1, 2, 3 4 , q 2, 3 4 ] ;

E C<sub>10</sub> C<sub>20</sub> -C(O)-(C<sub>9</sub> C<sub>19</sub>)- ,

R , C<sub>1</sub>-C<sub>15</sub> ( 1 ), B-(CH<sub>2</sub>)<sub>r</sub> - [ , r 0, 1, 2 3 ] ;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>1'</sub>, R<sub>2'</sub> R<sub>3'</sub> , , NO<sub>2</sub>, NH<sub>2</sub>, OH, , -NHC(O)OR<sub>5</sub>, R<sub>6</sub>O<sub>2</sub>SNH- -S(O)<sub>2</sub>NH<sub>2</sub> ;



R<sub>5</sub> ;

R<sub>6</sub> OH, , [ , , , NO<sub>2</sub>, NH<sub>2</sub> , OH, , - 1 3 ] .

R<sub>VIIA</sub> , - C<sub>1</sub>-C<sub>10</sub> VIIA D가 [ , -(CH<sub>2</sub>)<sub>q</sub>-( , q 3 )] .  
 VIIA R<sub>4</sub>가 p- 2,4,6-  
 VIIA A가 [ , -(CH<sub>2</sub>)<sub>p</sub>-( , p 0 )] .  
 , R<sub>1'</sub>, R<sub>2'</sub> R<sub>3'</sub> , R<sub>2</sub> R<sub>3</sub> , , t-

R<sub>1'</sub>, R<sub>2'</sub> R<sub>3'</sub> ; R<sub>1</sub> , , t-  
 R<sub>2</sub> R<sub>3</sub> ; R<sub>2</sub> , , ; R<sub>4</sub>가 p-  
 2,4,6- ; A가 VIIA .

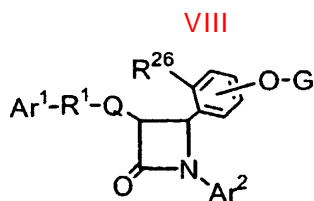
B'가 VIIA :

D	R	A	B	R4
-(CH2)3-	H	---	p-MeO- 페닐	p-MeO- 페닐
-(CH2)C(O)-	페닐	---	페닐	p-MeO- 페닐
-(CH2)3-	H	---	페닐	p-MeO- 페닐
-(CH2)3-	H	---	p-OH- 페닐	p-MeO- 페닐
-(CH2)3-	H	에틸렌	p-MeO- 페닐	p-MeO- 페닐
-(CH2)3-	H	---	3-MeO- 페닐	p-MeO- 페닐
-(CH2)3-	에틸	---	페닐	p-MeO- 페닐
-(CH2)3-	페닐	---	페닐	p-MeO- 페닐
-(CH2)3-	에틸	---	페닐	2,4,6-트리-MeO- 페닐
-(CH2)3-	메틸	---	페닐	p-MeO- 페닐
-(CH2)3-	H	---	p-NH2- 페닐	p-MeO- 페닐

(3R,4S)

1-

IB E가, VIIB R, R<sub>4</sub>가 p-A가, 7-Z-, 2,4,6-  
 ; R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, VIIB VI  
 2,4,6-R<sub>3</sub>, VIIB ; A가, R, ; E가, 7-Z-, ; R<sub>4</sub>가 p-  
 ; R<sub>1</sub>, R<sub>2</sub>  
 VIIB E가, R, B-A가, R<sub>4</sub>가 p-  
 VIII, VIII, VIII, VIII, VIII





R<sup>1</sup>

-(CH<sub>2</sub>)<sub>q</sub>-[ , q 2 6 , Q가 , q 0 1 ];

-(CH<sub>2</sub>)<sub>r</sub>-E-(CH<sub>2</sub>)<sub>r</sub>-[ , E -O-, -C(O)-, , -NR<sup>22</sup>- -S(O)<sub>0-2</sub>- , e 0 5 ];

-(C<sub>2</sub>-C<sub>6</sub>) -;

-(CH<sub>2</sub>)<sub>f</sub>-V-(CH<sub>2</sub>)<sub>g</sub>-[ , V C<sub>3</sub>-C<sub>6</sub> , f 1 5 g 0 5 , f ];

R<sup>12</sup>는  $\overset{|}{-CH-}$ ,  $\overset{|}{-C(C_1-C_6 \text{ 알킬})-}$ ,  $\overset{|}{-CF-}$ ,  $\overset{|}{-C(OH)-}$ ,  $\overset{|}{-C(C_6H_4-R^{23})-}$ ,  $\overset{|}{-N-}$ , 또는  $\overset{|}{-NO-}$  ;

R<sup>13</sup> R<sup>14</sup> -CH<sub>2</sub>-, -CH(C<sub>1</sub>-C<sub>6</sub>)-, -C( -C<sub>1</sub>-C<sub>6</sub> ), -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub>)=C  
H- , -CH=CH- -CH=C(C<sub>1</sub>-C<sub>6</sub>)- ; R<sup>12</sup> R<sup>13</sup> R<sup>14</sup>

a b 0, 1, 2 3 , 가 0 ;

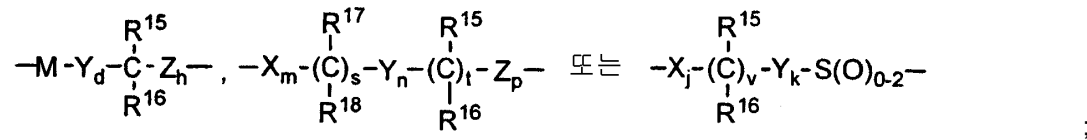
, R<sup>13</sup> -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub>)=CH- , a 1 ;

R<sup>14</sup> -CH=CH- -C(C<sub>1</sub>-C<sub>6</sub>)=CH- , b 1 ;

a가 2 3 , R<sup>13</sup> ;

b가 2 3 , R<sup>14</sup> ;

Q가 , R<sup>1</sup>



M -O-, -S-, -S(O)- -S(O)<sub>2</sub>- ;

X, Y Z -CH<sub>2</sub>-, -CH(C<sub>1</sub>-C<sub>6</sub>)- -C( -C<sub>1</sub>-C<sub>6</sub> )

R<sup>10</sup> R<sup>11</sup> (C<sub>1</sub>-C<sub>6</sub>), -OR<sup>19</sup>, -O(CO)R<sup>19</sup>, -O(CO)OR<sup>21</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub> OR<sup>19</sup>, -O(CO)NR<sup>19</sup>  
R<sup>20</sup>, -NR<sup>19</sup>R<sup>20</sup>, -NR<sup>19</sup>(CO)R<sup>20</sup>, -NR<sup>19</sup>(CO)OR<sup>21</sup>, -NR<sup>19</sup>(CO)NR<sup>20</sup>R<sup>25</sup>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>21</sup>, -  
COOR<sup>19</sup>, -CONR<sup>19</sup>R<sup>20</sup>, -COR<sup>19</sup>, -SO<sub>2</sub>NR<sup>19</sup>R<sup>20</sup>, S(O)<sub>0-2</sub>R<sup>21</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>19</sup>, -O(C  
H<sub>2</sub>)<sub>1-10</sub>CONR<sup>19</sup>R<sup>20</sup>, -(C<sub>1</sub>-C<sub>6</sub>)<sub>1 3</sub>-COOR<sup>19</sup>, -CH=CH-COOR<sup>19</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub> ;

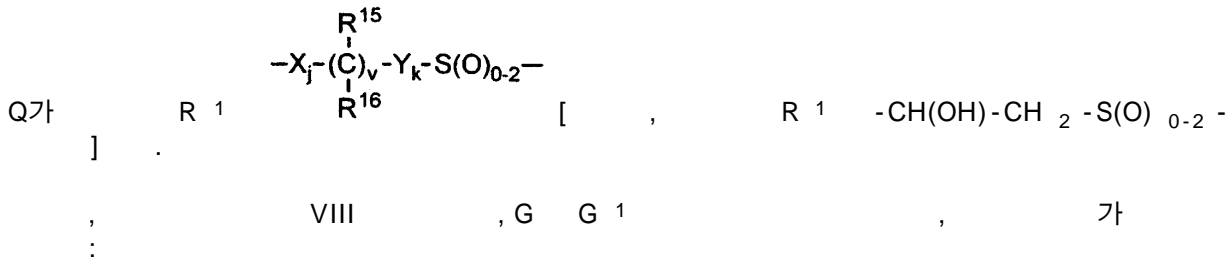
R<sup>15</sup> R<sup>17</sup> -OR<sup>19</sup>, -O(CO)R<sup>19</sup>, -O(CO)OR<sup>21</sup> -O(CO)NR<sup>19</sup>R<sup>20</sup> ;

R<sup>16</sup> R<sup>18</sup> H, (C<sub>1</sub>-C<sub>6</sub>) , R<sup>15</sup> R<sup>16</sup>  
, =O R<sup>17</sup> R<sup>18</sup> , =O ;

d 1, 2 3 ;

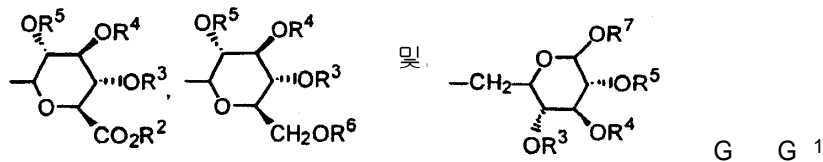
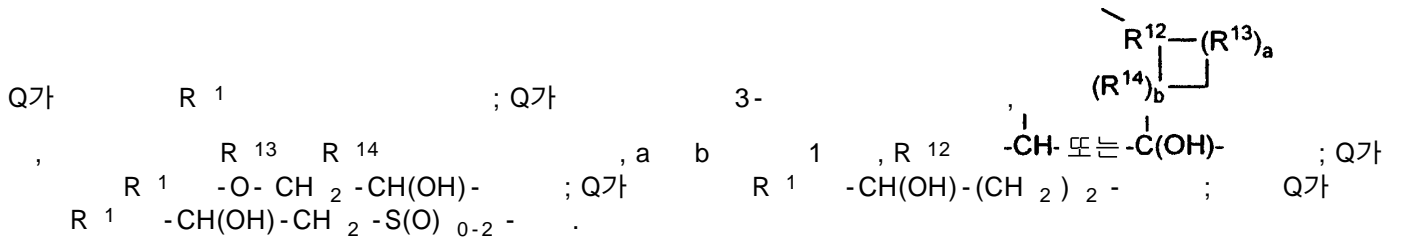
h 0, 1, 2, 3 4 ;



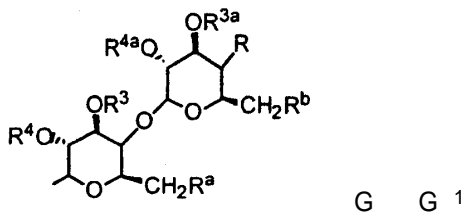


Ar<sup>1</sup> R<sup>10</sup> - , R<sup>10</sup> ;

Ar<sup>2</sup> 가  $R^{11} -$  , R<sup>11</sup> C<sub>1</sub>-C<sub>6</sub>  
 1 3 ;



R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> R<sup>7</sup> H, (C<sub>1</sub>-C<sub>6</sub>) ,



R<sup>3</sup>, R<sup>3a</sup>, R<sup>4</sup> R<sup>4a</sup> H, (C<sub>1</sub>-C<sub>6</sub>) ,

R, R<sup>a</sup> R<sup>b</sup> H, -OH, , -NH<sub>2</sub>, , (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>)- -W-R<sup>30</sup>

W -O-C(O)- -O-C(O)-N(R<sup>31</sup>)- , R<sup>31</sup> H , R<sup>30</sup> (C<sub>1</sub>-C<sub>6</sub>) , -C(O)-(C<sub>1</sub>-C<sub>4</sub>)  
 (C<sub>1</sub>-C<sub>6</sub>) , T, T-(C<sub>1</sub>-C<sub>6</sub>) , T T-(C<sub>1</sub>-C<sub>6</sub>) [ , T<sub>1</sub> T<sub>2</sub> ] .

R<sup>30</sup> 2- , 2,4- - , 2,6- , 2- , 2- , 2-  
 - , -2- - , 2- , 2- .

R, R<sup>a</sup> R<sup>b</sup> :

1) R, R<sup>a</sup> R<sup>b</sup> -OH -O-C(O)-NH-R<sup>30</sup> , R<sup>a</sup> -OH R R<sup>b</sup> -O-C(O)-  
 NH-R<sup>30</sup> , R<sup>30</sup> R R<sup>a</sup> -OH R<sup>b</sup> -OH , R<sup>b</sup> -

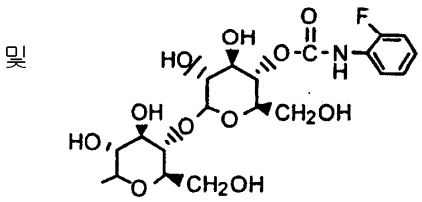
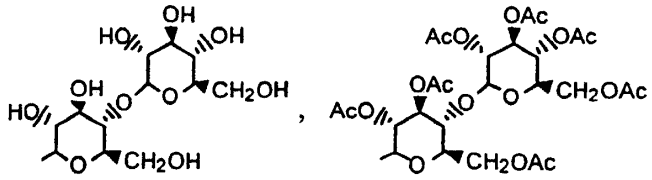
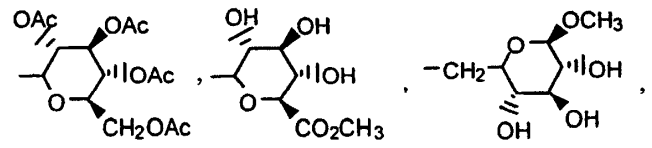
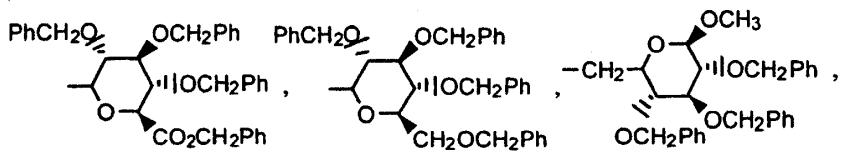
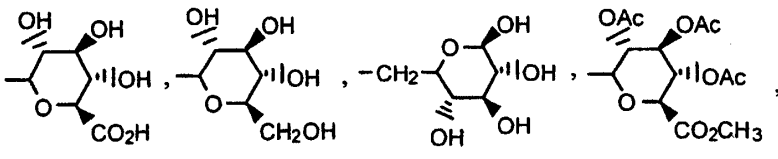
O-C(0)-NH-R<sup>30</sup>, R<sup>30</sup> 2-, , 2,4-, , 2,6- ;

2) R<sup>a</sup> -OH, (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>) , R<sup>b</sup> H, R<sup>a</sup>가 -OH, R<sup>b</sup>가 H, R<sup>30</sup> 2- ;

3) R, R<sup>a</sup> R<sup>b</sup> -OH -O-C(0)-R<sup>30</sup>, R<sup>30</sup> (C<sub>1</sub>-C<sub>6</sub>), T, R<sup>1</sup> R<sup>2</sup> R<sup>30</sup> 2- ;

4) R, R<sup>a</sup> R<sup>b</sup> -OH . 3가 가 C<sup>1'</sup> 가 , C<sup>2'</sup> 가 , R

G G<sup>1</sup> , :



Ac Ph , R<sup>26</sup> H OH, H . -O-G , 4-

IX

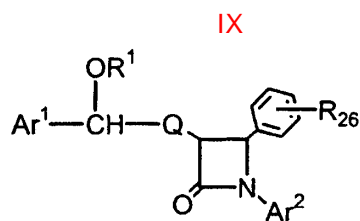
IX

IX

IX

IX

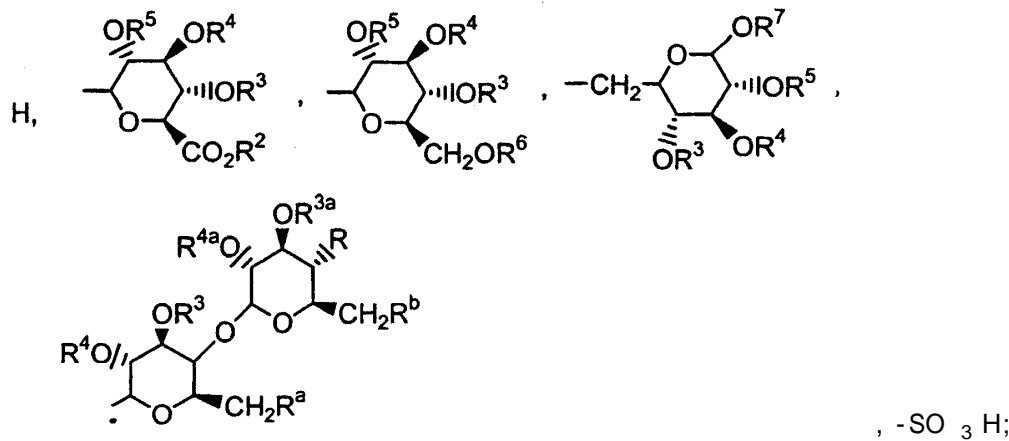
:



R<sup>26</sup>

- (a) OH;
- (b) OCH<sub>3</sub>;
- (c)
- (d)

R<sup>1</sup>



R, R<sup>a</sup>, R<sup>b</sup> H, -OH, , -NH<sub>2</sub>, , (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>)- -W-R<sup>30</sup>

W -NH-C(O)-, -O-C(O)-, -O-C(O)-N(R<sup>31</sup>)-, -NH-C(O)-N(R<sup>31</sup>)- -O-C(S)-N(R<sup>31</sup>)-

R<sup>2</sup>, R<sup>6</sup> H, (C<sub>1</sub>-C<sub>6</sub>) , (C<sub>1</sub>-C<sub>6</sub>) ;

R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>3a</sup>, R<sup>4a</sup> H, (C<sub>1</sub>-C<sub>6</sub>) , (C<sub>1</sub>-C<sub>6</sub>) , -C(O)(C<sub>1</sub>-C<sub>6</sub>) -C(O)

R<sup>30</sup>, R<sup>32</sup> - T, R<sup>32</sup> - -T-(C<sub>1</sub>-C<sub>6</sub>) , R<sup>32</sup> - -(C<sub>2</sub>-C<sub>4</sub>) , R<sup>32</sup> - -(C<sub>1</sub>-C<sub>6</sub>) -C<sub>1</sub>-C<sub>6</sub> , R<sup>32</sup> - -(C<sub>3</sub>-C<sub>7</sub>) R<sup>32</sup> - -(C<sub>3</sub>-C<sub>7</sub>) (C<sub>1</sub>-C<sub>6</sub>)

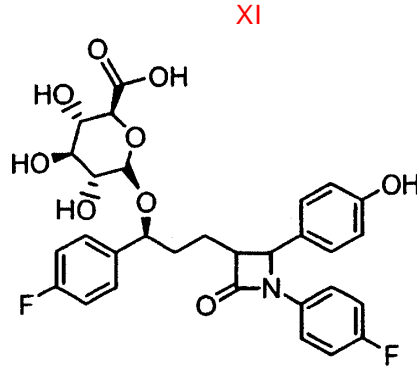






R<sup>1</sup>

XI, XI, XI



(a) 1 ; (b) 2

2 ( ), [ , 1 ],

I XI  
4,983,597 N- -2-  
[ : Ram et al., Indian J. Chem. Sect. B. 29B, 12(1990), p. 1134-7; ]  
4-(2- -4- ) - 가

I XI , WO 93/02048 -R<sup>1</sup>-Q-가 ;  
; WO 94/17038 Q가 ; WO 95/08532 -  
R<sup>1</sup>-Q-가 - ; PCT/US 95/03196 -R<sup>1</sup>-  
-Q-가, -O- S(O)<sub>0-2</sub> - Ar<sup>1</sup> -  
; 08/463,619 (1995. 6. 5 ) -R<sup>1</sup>-Q-가, -S(O)<sub>0-2</sub>-

10mg 1 0.1 1000mg, 2 4 0.25 50mg,

가 가 .  
/ 가 가 .  
가 가 .

HMG CoA  
HMG CoA

( : Merck amp; Co. 가 PRAVACHOL ), 가 MEVACOR ), (Bristol Meyers Squibb 가 ZOCOR ),  
 ( 7-(4- )-2,6- -5- )-3- )-3,5- -6- ), CI-981 ( : Negma Kowa of Japan NK-104);  
 HMG CoA , L-659,699((E,E)-11-[3'R-( - )-4'- -2'R- ]-3,  
 5,7R- -2,4- ); , NB-598((E)-N- -N-(6,6- -2- -4- )-3-[(3,3'- -5- ) ] HMG  
 CoA , , DMP-565가 . 가 HMG CoA

0mg/ , 1 2 3 0.1 160mg/ , 0.2 8  
 oA , , , , / , 가 HMG C  
 , , 가 ( ) / , 가

가 , , , , ,  
 -3- -2- (5- -2- 4- )가 . 가  
 VLDL Kos LDL 가 NIASPAN ( - ) 가  
 8000mg/ , 1 3000 500 10,000mg/ , 1000  
 6000mg/ ,

oA: O- 가 ('ACAT') , LDL VLDL C  
 , 가 . ACAT VLDL , B-100-

ACAT - ([2,4,6- (1- ) ] ) , 2,6- ( (1- ) ) ; CI-1011 ), HL-004, (DuP-128) CL-277082(N-(2,4- )-N-[[4-(2,2- ) ] ]-N- )가 [ : P. Chang et al., 'Current, New and Future Treatments in Dyslipidaemia and Atherosclerosis', Drugs 2000 Jul; 60(1); 55-93; ] .

: 6,121,319 6,147,250 가 LDL AGI-1067 ) , ( 가 .  
 1500mg/ , 1 10 2000mg/ , 500  
 2 4

(LDL) , 가  
 LDL- 가 LDL  
 HOE-402가 [ : M. Huettinger et al., 'Hypolipidemic activity of HOE-42 is Mediated by Stimulation of the LDL Receptor Pathway', Arterioscler. Thromb. 1993; 13:1005-12].

, LDL 1 1 1000mg/ ,

2 4 .

가 3 (3-PUFA) (fish oil) VLDL 가 3  
 1 1 30g/ 2 4

가 (psyllium) 가 1  
 0.1 10g/ 2 4

/ , , BENECOL 가 가  
 0.5 20g/ / 2 4 1

- , , 가 B<sub>6</sub> B<sub>12</sub> , , , ,  
 4 1 0.05 10g/ 가 2

) , , 가 (

(fecal) 가 (enterohepatic circulation)  
 가 (apo) B/E(LDL) LDL

- [ 4  
 STRAN LIGHT ], Bristol-Myers Squibb 가 QUESTRAN QUE  
 ia 가 COLESTID ], 1- -2,3- , Pharmac  
 WelChol ( 가 1- (6- )- 가  
 ( )], , 3,3- , N-( ) 가 P

CT WO 97/11345 WO 98/57652, 3,692,895 5,703,188 ( +  
 ) 가 .

, 2 4 1 1 50g, 1 2 16g ,  
 , - (PPAR) 가

. 3가 PPAR (PPAR ) - (PPAR ) (PPAR ) , PPAR 가 P  
 PAR NUC1 ,

PPAR . PPAR (fibrate) ,  
 . PPAR . PPAR . PPAR





- 17 - , 17 - , 17 -  
17 - , 9
- (b) (Estinyl) Schering Plough Corporation(Kenilworth, NJ) 가  
(19- -17 - -1,3,5(10)- -20- -3,17- ;
- (c) (Estratab) Solvay 가 (Menest) Monarch  
Pharmaceuticals(Bristol, TN) 가 , ,
- (d) (Ogen) Pharmacia amp; Upjohn(Peapack, NJ) 가 - (Ortho  
-Est) Women First Health Care, Inc.(San Diego, CA) 가 , ( )  
-1,3,5(10)- -17- , 3-( )- );
- (e) (Premarin) Wyeth -Ayerst Pharmaceuticals(Philadelphia, PA) 가  
(17 - , 17 - , 17 - ).  
0.1 1mg 0.05 2.0mg 0.001 2mg ,  
0.01 0.5mg ;
- (a) (Activella) Pharmacia amp; Upjohn(Peapack, NJ) 가 , ( )  
-1,3,5(10)- -3,17 - ) (17 - -19- -17 - )  
-4- -20- -3- ) ;
- (b) (Alesse) Wyeth -Ayerst 가 , (Levora) (Trivora)  
Watson Laboratories, Inc.(Corona, CA) 가 , (Nordette) Monar  
ch Pharmaceuticals 가 (Triphasil) Wyeth -Ayerst 가 ,  
(d(-)-13 - -17 - -17 - -4- -3- ) ;
- (c) (Demulen) G.D. Searle amp; Co.(Chicago, IL) 가 (Zovia)  
Watson 가 , (19- -17 - -4- -20- -3 ,17- )
- (d) (Desogen) (Mircette) Organon 가 - (Ortho-C  
ept) Ortho-McNeil Pharmaceutical(Raritan, NJ) 가 , (13- -11- )  
-18,19- -17 - -4- -20- -17- ) ;
- (e) (Estrostep) (femhrt) Parke -Davis(Morris Plains, NJ) 가  
(Micrgestin), (Necon) - (Tri -Norinyl) Watson  
가 (Modicon) - (Ortho -Novum) Ortho - McNeil 가  
(Ovcon) Warner Chilcott Laboratories(Rockaway, NJ) 가 , ;
- (f) (Ovral) / (Lo/Ovral) Wyeth -Ayerst 가 (Ogestrel)  
el) - (Low -Ogestrel) Watson 가 , ((±)-13- )  
-17- -18,19- -17 - -4- -20- -3- ) ;
- (g) (Brevicon) (Norinyl) Watson 가 , ,  
(3- -19- -17 - -1,3,5(10)- -20- -17- ) ;
- (h) - (Ortho -Prefest) Ortho -McNeil 가 , 17 - ( )  
-1,3,5(10)- -3,17 - ) (17 -17-( )-13- -18,19- )  
-4- -20- -3- -3- ) ;







## II

1): CH<sub>2</sub>Cl<sub>2</sub> (200ml) (S)-4- -2- (41g, 0.25mol) 4- (2.5g, 0.02mol) (84.7ml, 0.61mol) 가 , 0 -4-( ) (50g, 0.3mol) CH<sub>2</sub>Cl<sub>2</sub> (375ml) 1 가 , 22 가 . 17 , H<sub>2</sub>SO<sub>4</sub> (2N, 100ml) 가 , NaOH(10%), NaCl( ) MgSO<sub>4</sub> .

2): 0 CH<sub>2</sub>Cl<sub>2</sub> (600ml) TiCl<sub>4</sub> (18.2ml, 0.165mol) (16.5ml, 0.055mol) 가 . 15 , 1 (49.0g, 0.17mol) CH<sub>2</sub>Cl<sub>2</sub> (100ml) 가 . 5 , (DIPEA)(65.2ml, 0.37mol) 가 , 0 1 , -20 , 4- (4- ) (114.3g, 0.37mol) 가 , -20 4 , CH<sub>2</sub>Cl<sub>2</sub> 15 가 , 0 가 , H<sub>2</sub>SO<sub>4</sub> (2N) 가 . 1 /

3): 50 (100ml) 2 (8.9g, 14.9mmol) N,O- ( ) (BSA)(7.50ml, 30.3mmol) 가 . 0.5 , TBAF(0.39g, 1.5mmol) 가 , 50 3 . 22 , CH<sub>3</sub>OH(10ml) 가 . HCl(1N), NaHCO<sub>3</sub> (1N) NaCl( ) , MgSO<sub>4</sub> .

4): CH<sub>3</sub>OH(3ml) 3 (0.94g, 2.2mmol) (1ml) LiOH·H<sub>2</sub>O(102mg, 2.4mmol) 가 . 22 1 , 가 LiOH·H<sub>2</sub>O(54mg, 1.3mmol) 가 . 2 , HCl(1N) EtOAc 가 , , 22 CH<sub>2</sub>Cl<sub>2</sub> (0.91g, 2.2mmol) ClCOCOCl(0.29ml, 3.3mmol) 가 , 16 .

5): 4 4- (THF 1M, 4.4ml, 4.4mmol) ZnCl<sub>2</sub> (0.6g, 4.4mmol) (0.25g, 0.21mmol) 가 , THF(2ml) (4.4mmol) ( ) (0.94g, 2.2mmol) 가 , EtOAc . 22 0.5 . HCl(1N, 5ml) 가 , )-4(S)-(4- )-3(R)-(3- -3- )-2- : C<sub>24</sub>H<sub>19</sub>F<sub>2</sub>NO<sub>3</sub> HRMS : 408.1429, : 408.1411.

6): THF(3ml) 5 (0.95g, 1.91mmol) (R)- -1- -3,3- -1H,3H- -[1,2-c][1,3,2] (120mg, 0.43mmol) 가 , -20 . 5 , (THF 2M, 0.85ml, 1.7mmol) 0.5 가 . 1.5 , CH<sub>3</sub>OH 가 , HCl(1N) 가 , EtOAc 1-(4- )-3(R)-[3(S)-(4- )]-4(S)-[4-( )]-2- ( 6A-1) . 1 H(CDCl<sub>3</sub> d ) H<sub>3</sub>=4.68. J=2.3Hz. Cl(M+H) 500.

(S)- -1- -3,3- -1H,3H- -[1,2-c][1,3,2] 3(R)- ( 6B-1) . 1 H(CDCl<sub>3</sub> d ) H<sub>3</sub>=4.69. J=2.3Hz. Cl(M+H) 500.

(2ml) 6A-1(0.4g, 0.8mmol) 10% Pd/C(0.03g) 가 , H<sub>2</sub> (60psi) 16 , 6A : 1 64-166 ; Cl(M+H) 410.

[ ] D<sup>25</sup> = -28.1 ° (c 3, CH<sub>3</sub>OH). C<sub>24</sub>H<sub>21</sub>F<sub>2</sub>NO<sub>3</sub> : : C 70.41; H 5.17; N 3.42; : C 70.25; H 5.19; N 3.54.

6B-1 : 6B : 129.5-132.5 ; Cl(M+H) 410. C<sub>24</sub>H<sub>21</sub>F<sub>2</sub>NO<sub>3</sub> : C 70.41; H 5.17; N 3.42; : C 70.30; H 5.14; N 3.52.

6' ( ): (2ml) 5 (0.14g, 0.3mmol) 10% Pd/C(0.03g) 가 ,  
 H<sub>2</sub> (60psi) 16 , 6A 6B  
 1:1 . ,

가

(57)

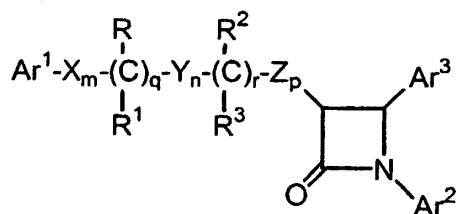
1.

(a) , ;

(b) (a) ,

2.

1 , 가 | , | ,  
 | , : | ,  
 |



Ar<sup>1</sup> Ar<sup>2</sup> R<sup>4</sup> - ;

Ar<sup>3</sup> R<sup>5</sup> - ;

X, Y Z -CH<sub>2</sub>-, -CH( )-, -C( - )- ;

R R<sup>2</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup> -O(CO)NR<sup>6</sup>R<sup>7</sup> ;

R<sup>1</sup> R<sup>3</sup> , ;

q 0 1 ;

r 0 1 ;

m, n p 0, 1, 2, 3 4 , q r 1 , m, n, p, q r  
 1, 2, 3, 4, 5 6 ; p가 0 r 1 , m, q n 1, 2, 3, 4 5 ;

R<sup>4</sup> , -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -  
 NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -CO  
 R<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -(

)COOR<sup>6</sup>, -CH=CH-COOR<sup>6</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub>  
5 ;

1

R<sup>5</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)  
R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>  
NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -( )COOR<sup>6</sup>  
-CH=CH-COOR<sup>6</sup> 1 5 ;

R<sup>6</sup>, R<sup>7</sup> R<sup>8</sup> , , - ;

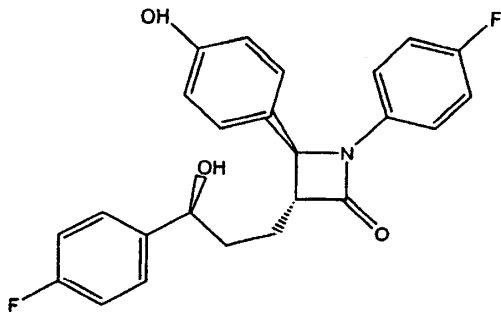
R<sup>9</sup> , - .

3.

2 II , 가 II , ,

:

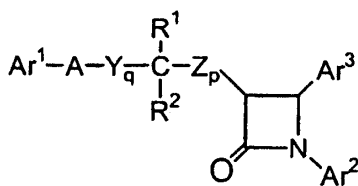
II



4.

1 III , 가 III , III , III , III

III



Ar<sup>1</sup> R<sup>3</sup> - ;

Ar<sup>2</sup> R<sup>4</sup> - ;

Ar<sup>3</sup> R<sup>5</sup> - ;

Y Z -CH<sub>2</sub>-, -CH( )-, -C( - )- ;

A -O-, -S-, -S(O)- -S(O)<sub>2</sub>- ;

R<sup>1</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup> -O(CO)NR<sup>6</sup>R<sup>7</sup> ; R<sup>2</sup> ,  
, R<sup>1</sup> R<sup>2</sup> , =O ;

q 1, 2 3 ;

p 0, 1, 2, 3 4 ;

R<sup>5</sup> -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>9</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>- , -NR<sup>6</sup>SO<sub>2</sub>- , -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>- , S(O)<sub>0-2</sub>- , -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, o- , m- , o- , m- , -( )-COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

R<sup>3</sup> R<sup>4</sup> , R<sup>5</sup>, , p- , , -NO<sub>2</sub>, -CF<sub>3</sub> p-

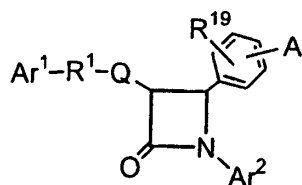
R<sup>6</sup>, R<sup>7</sup> R<sup>8</sup> , , - ;

R<sup>9</sup> , - .

5.

1 IV , 가 IV , IV , IV ;

IV



A R<sup>2</sup>- , R<sup>2</sup>- , R<sup>2</sup>- ;

Ar<sup>1</sup> R<sup>3</sup>- ;

Ar<sup>2</sup> R<sup>4</sup>- ;

Q , 3- , ;

R<sup>1</sup>

-(CH<sub>2</sub>)<sub>q</sub>-[ , q 2 6 , Q가 , q 0 1 ];

-(CH<sub>2</sub>)<sub>e</sub>-G-(CH<sub>2</sub>)<sub>r</sub>-[ , G -O-, -C(O)-, , -NR<sup>8</sup>- -S(O)<sub>0-2</sub>- , e 0 5 ;

-(C<sub>2</sub>-C<sub>6</sub> )-;

-(CH<sub>2</sub>)<sub>f</sub>-V-(CH<sub>2</sub>)<sub>g</sub>-[ , V C<sub>3</sub>-C<sub>6</sub> , f 1 5 g 0 5 , f



R<sup>3</sup>, R<sup>4</sup> (C<sub>1</sub>-C<sub>6</sub>), -OR<sup>14</sup>, -O(CO)R<sup>14</sup>, -O(CO)OR<sup>16</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>14</sup>, -O(CO)NR<sup>14</sup>  
R<sup>15</sup>, -NR<sup>14</sup>R<sup>15</sup>, -NR<sup>14</sup>(CO)R<sup>15</sup>, -NR<sup>14</sup>(CO)OR<sup>16</sup>, -NR<sup>14</sup>(CO)NR<sup>15</sup>R<sup>19</sup>, -NR<sup>14</sup>SO<sub>2</sub>R<sup>16</sup>, -  
COOR<sup>14</sup>, -CONR<sup>14</sup>R<sup>15</sup>, -COR<sup>14</sup>, -SO<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, S(O)<sub>0-2</sub>R<sup>16</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>14</sup>, -O(C  
H<sub>2</sub>)<sub>1-10</sub>CONR<sup>14</sup>R<sup>15</sup>, -(C<sub>1</sub>-C<sub>6</sub>)<sub>1</sub>-COOR<sup>14</sup>, -CH=CH-COOR<sup>14</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub> ;

R<sup>8</sup>, (C<sub>1</sub>-C<sub>6</sub>), (C<sub>1</sub>-C<sub>6</sub>), -C(O)R<sup>14</sup> -COOR<sup>14</sup> ;

R<sup>9</sup>, R<sup>17</sup>, (C<sub>1</sub>-C<sub>6</sub>), (C<sub>1</sub>-C<sub>6</sub>), -COOH, NO<sub>2</sub>, -NR<sup>14</sup>R<sup>15</sup>, OH ;

R<sup>14</sup>, R<sup>15</sup>, (C<sub>1</sub>-C<sub>6</sub>), - (C<sub>1</sub>-C<sub>6</sub>) ;

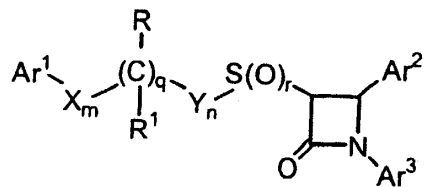
R<sup>16</sup> (C<sub>1</sub>-C<sub>6</sub>), R<sup>17</sup> - ;

R<sup>18</sup> (C<sub>1</sub>-C<sub>6</sub>) ;

R<sup>19</sup>, (C<sub>1</sub>-C<sub>6</sub>) .

6.

1, 가 V, V, V, V ;



Ar<sup>1</sup>, R<sup>10</sup> - ;

Ar<sup>2</sup>, R<sup>4</sup> - ;

Ar<sup>3</sup>, R<sup>5</sup> - ;

X, Y -CH<sub>2</sub>-, -CH( )-, -C( - )- ;

R<sup>6</sup>, -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup> ; R<sup>1</sup>, R<sup>1</sup>, =O ;

q 0, 1 ;

r 0, 1, 2 ;

m, n, 0, 1, 2, 3, 4, 5, m, n, q 1, 2, 3, 4, 5 ;

R<sup>4</sup>, -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -  
NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -CO  
R<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -(  
)COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

$R^5$  -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub>,  
 , -( )COOR<sup>6</sup> -CH=CH-COOR<sup>6</sup> ;

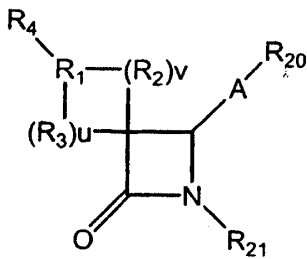
$R^6, R^7$  R<sup>8</sup> , , - R<sup>8</sup> ;

$R^9$  , - R<sup>9</sup> ;

$R^{10}$  , -OR<sup>6</sup>, -O(CO)R<sup>6</sup>, -O(CO)OR<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-5</sub>OR<sup>6</sup>, -O(CO)NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>R<sup>7</sup>, -NR<sup>6</sup>(CO)R<sup>7</sup>, -NR<sup>6</sup>(CO)OR<sup>9</sup>, -NR<sup>6</sup>(CO)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>6</sup>SO<sub>2</sub>R<sup>9</sup>, -COOR<sup>6</sup>, -CONR<sup>6</sup>R<sup>7</sup>, -COR<sup>6</sup>, -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>, S(O)<sub>0-2</sub>R<sup>9</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>-COOR<sup>6</sup>, -O(CH<sub>2</sub>)<sub>1-10</sub>CONR<sup>6</sup>R<sup>7</sup>, -CF<sub>3</sub>, -CN, -NO<sub>2</sub> .

7.

1 VI , 가 VI , VI , VI , VI : VI



$R_1$ 는  $\overset{|}{\text{C}}\text{H}$ -,  $\overset{|}{\text{C}}$ (저급 알킬)-,  $\overset{|}{\text{C}}\text{F}$ -,  $\overset{|}{\text{C}}(\text{OH})$ -,  $\overset{|}{\text{C}}(\text{C}_6\text{H}_5)$ -,  $\overset{|}{\text{C}}(\text{C}_6\text{H}_4\text{-R}_{15})$ -,  
 $\overset{|}{\text{N}}$ - 또는  $\overset{|}{\text{N}}\text{O}$ - 이고;

$R_2$   $R_3$  -CH<sub>2</sub>-, -CH( )-, -C( - ), -CH=CH- -C( )=CH-  
 CH=C( )- ; R<sub>1</sub> R<sub>2</sub> R<sub>1</sub> R<sub>3</sub> , -CH=CH- -

u v 0, 1, 2 3 , 가 0 ;

, R<sub>2</sub> -CH=CH- -C( )=CH- , v 1 ;

R<sub>3</sub> -CH=CH- -C( )=CH- , u 1 ;

v가 2 3 , R<sub>2</sub> ;

u가 2 3 , R<sub>3</sub> ;

R<sub>4</sub> B-(CH<sub>2</sub>)<sub>m</sub>C(O)-[ , m 0, 1, 2, 3, 4 5 ] ;

B-(CH<sub>2</sub>)<sub>q</sub>-[ , q 0, 1, 2, 3, 4, 5 6 ] ;

B-(CH<sub>2</sub>)<sub>e</sub>-Z-(CH<sub>2</sub>)<sub>r</sub>-[ , Z -O-, -C(O)-, , -N(R<sub>8</sub>)- -S(O)<sub>0-2</sub> - , e 0, 1, 2, 3, 4 5 r 0, 1, 2, 3, 4 5 , e r 0, 1, 2, 3, 4, 5 6 ];

B-(C<sub>2</sub>-C<sub>6</sub> )-;

B-(C<sub>4</sub>-C<sub>6</sub> )-;

B-(CH<sub>2</sub>)<sub>t</sub>-Z-(C<sub>2</sub>-C<sub>6</sub> )-[ , Z , t 0, 1, 2 3 , 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>f</sub>-V-(CH<sub>2</sub>)<sub>g</sub>-[ , V C<sub>3</sub>-C<sub>6</sub> , f 1, 2, 3, 4 5 g 0, 1, 2, 3 , 4 5 , f g 1, 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>t</sub>-V-(C<sub>2</sub>-C<sub>6</sub> )-

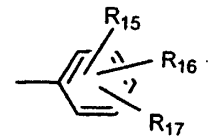
B-(C<sub>2</sub>-C<sub>6</sub> )-V-(CH<sub>2</sub>)<sub>t</sub>-[ , V t , 2, 3, 4, 5 6 ];

B-(CH<sub>2</sub>)<sub>a</sub>-Z-(CH<sub>2</sub>)<sub>b</sub>-V-(CH<sub>2</sub>)<sub>d</sub>-[ , Z V , a, b d 0, 1, 2, 3, 4, 5 6 ];

T-(CH<sub>2</sub>)<sub>s</sub>-[ , T 3 6 , s 0, 1, 2, 3, 4, 5 6 ] ;

R<sub>1</sub> R<sub>4</sub> , B-CH=C-<sup>I</sup> ;

B , , , , , W- , , , , ,



; , - , N-

W , , , , , ( , R<sub>7</sub>- , , R<sub>7</sub>- , NO<sub>2</sub>, -N(R<sub>8</sub>)(R<sub>9</sub>), N(R<sub>8</sub>)(R<sub>9</sub>)- , N(R<sub>8</sub>)(R<sub>9</sub>)- , OH, , -CN, -N<sub>3</sub>, -NHC(O)OR<sub>10</sub>, -NHC(O)R<sub>10</sub>, R<sub>11</sub>O<sub>2</sub>SNH-, (R<sub>11</sub>O<sub>2</sub>S)<sub>2</sub>N-, -S(O)<sub>2</sub>NH<sub>2</sub>, -S(O)<sub>0-2</sub>R<sub>8</sub>, 3 - , -C(O)R<sub>12</sub>, -COOR<sub>19</sub>, -CON(R<sub>8</sub>)(R<sub>9</sub>), -CH=CHC(O)R<sub>12</sub>, -C(O)R<sub>12</sub>, R<sub>10</sub>C(O)( )-, N(R<sub>8</sub>)(R<sub>9</sub>)C(O)(

-CH<sub>2</sub>-N<sub>6</sub>R<sub>13</sub> ( )-

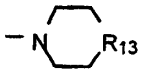
1 3 , -C(O)OR<sub>10</sub>, -C(O)R<sub>10</sub>, OH, N(R<sub>8</sub>)(R<sub>9</sub>)- , N(R<sub>8</sub>)(R<sub>9</sub>)- , -S(O)<sub>2</sub>NH<sub>2</sub>-2-( )-

R<sub>7</sub> 1 3 , -COOH, NO<sub>2</sub>, -N(R<sub>8</sub>)(R<sub>9</sub>), OH ;

R<sub>8</sub> R<sub>9</sub> H ;

R<sub>10</sub> , , R<sub>7</sub>- , R<sub>7</sub>- ;

R<sub>11</sub> OH, , , R<sub>7</sub>- R<sub>7</sub>- ;

$R_{12}$  H, OH, , , ,  ,  $-N(R_8)(R_9)$ , ,  $R_7 -$  ;

$R_{13}$   $-O-$ ,  $-CH_2-$ ,  $-NH-$ ,  $-N( )-$   $-NC(O)R_{19}$  ;

$R_{15}, R_{16}, R_{17}$  H; W  $R_{16}, R_{17}$  ,  $R_{15}$  ;

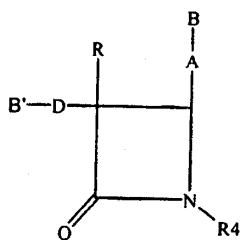
$R_{19}$  H, , ;

$R_{20}, R_{21}$  , W- , W- , W- , W- , ( , ) .

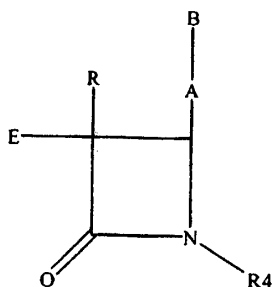
8.

1 , , 가 VIIA VIIB , VIIA VIIB , VIIA VIIB :  
 , VIIA VIIB VIIA VIIB ,

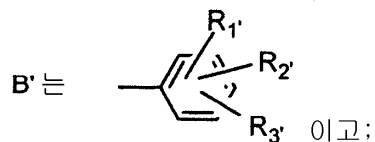
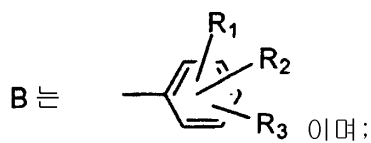
VIIA



VIIB



A  $-CH=CH-$ ,  $-C=C-$   $-(CH_2)_p-$  [ , p 0, 1 2 ] ;



D  $-(CH_2)_m C(O)-$   $-(CH_2)_q -[$  , m 1, 2, 3 4 , q 2, 3 4 ] ;

E  $C_{10}$   $C_{20}$   $-C(O)-(C_9$   $C_{19})-$  ,

R ,  $C_1-C_{15}$  ( 1 ) , B- $(CH_2)_r$  -[ , r 0, 1, 2 3 ] ;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>1'</sub>, R<sub>2'</sub> R<sub>3'</sub> , , NO<sub>2</sub>, NH<sub>2</sub>, OH, , -NHC(O)OR<sub>5</sub>, R<sub>6</sub>O<sub>2</sub>SNH- -S(O)<sub>2</sub>NH<sub>2</sub> ;

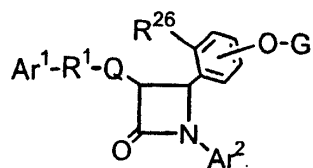


R<sub>5</sub> ;

R<sub>6</sub> OH, , , [ , , , , NO<sub>2</sub>, NH<sub>2</sub> , OH, ] .

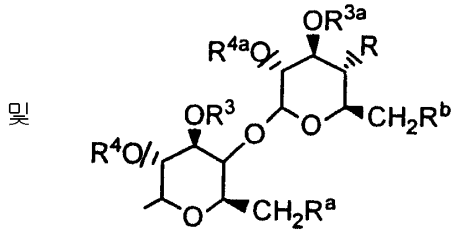
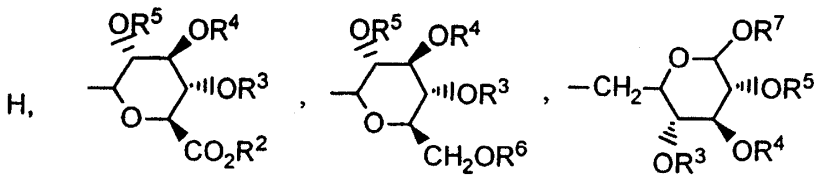
9.

1 VIII , 가 VIII , VIII VIII VIII VIII ;



R<sub>26</sub> H OG<sub>1</sub> ;

G G<sub>1</sub>



, R<sup>26</sup> H OH, G H가 ;

R, R<sup>a</sup> R<sup>b</sup> H, -OH, -NH<sub>2</sub>, (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>) -W-R<sup>30</sup> ;

W -NH-C(O)-, -O-C(O)-, -O-C(O)-N(R<sup>31</sup>)-, -NH-C(O)-N(R<sup>31</sup>)- -O-C(S)-N(R<sup>31</sup>)- ;

R<sup>2</sup> R<sup>6</sup> H, (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>) ;

R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>3a</sup> R<sup>4a</sup> H, (C<sub>1</sub>-C<sub>6</sub>) (C<sub>1</sub>-C<sub>6</sub>), -C(O)(C<sub>1</sub>-C<sub>6</sub>) -C(O) ;

R<sup>30</sup> R<sup>32</sup> - T, R<sup>32</sup> - -T-(C<sub>1</sub>-C<sub>6</sub>) , R<sup>32</sup> - -(C<sub>2</sub>-C<sub>4</sub>) , R<sup>32</sup> - -(C<sub>1</sub>-C<sub>6</sub>) , R<sup>32</sup> - -(C<sub>3</sub>-C<sub>7</sub>) R<sup>32</sup> - -(C<sub>3</sub>-C<sub>7</sub>) (C<sub>1</sub>-C<sub>6</sub>) ;

R<sup>31</sup> H (C<sub>1</sub>-C<sub>4</sub>) ;

T, ;

R<sup>32</sup> (C<sub>1</sub>-C<sub>4</sub>), -OH, -CF<sub>3</sub>, -NO<sub>2</sub>, (C<sub>1</sub>-C<sub>4</sub>), (C<sub>1</sub>-C<sub>4</sub>), (C<sub>1</sub>-C<sub>4</sub>), (C<sub>1</sub>-C<sub>4</sub>), -N(CH<sub>3</sub>)<sub>2</sub>, -C(O)-NH(C<sub>1</sub>-C<sub>4</sub>), (C<sub>1</sub>-C<sub>4</sub>), -C(O)-N((C<sub>1</sub>-C<sub>4</sub>))<sub>2</sub>, -C(O)-(C<sub>1</sub>-C<sub>4</sub>)<sub>1</sub>, -C(O)-(C<sub>1</sub>-C<sub>4</sub>)<sub>3</sub> ; R<sup>32</sup> ;

가 R<sup>31</sup> R<sup>32</sup> (C<sub>1</sub>-C<sub>4</sub>) - , N- , N- ;

Ar<sup>1</sup> R<sup>10</sup> - ;

Ar<sup>2</sup> R<sup>11</sup> - ;

Q, 3-  ;

R<sup>1</sup> -(CH<sub>2</sub>)<sub>q</sub> - [ , q 2 6 , Q가 , q 0 1 ] ;

-(CH<sub>2</sub>)<sub>e</sub> -E-(CH<sub>2</sub>)<sub>r</sub> - [ , E -O-, -C(O)-, -NR<sup>22</sup> - -S(O)<sub>0-2</sub> - , e 0 5 , r 0 5 , e r 1 6 ] ;

$-(C_2-C_6)$  -;

$-(CH_2)_f-V-(CH_2)_g-$  [ , V C<sub>3</sub>-C<sub>6</sub> , f 1 5 g 0 5 , f

R<sup>12</sup>는  $-\overset{|}{\text{C}}\text{H}-, -\overset{|}{\text{C}}(\text{C}_1-\text{C}_6 \text{ 알킬})-, -\overset{|}{\text{C}}\text{F}-, -\overset{|}{\text{C}}(\text{OH})-, -\overset{|}{\text{C}}(\text{C}_6\text{H}_4-\text{R}^{23})-, -\overset{|}{\text{N}}-,$  또는  $-\overset{|}{\text{N}}\text{O}^-$  ;

R<sup>13</sup> R<sup>14</sup>  $-\text{CH}_2-, -\text{CH}(\text{C}_1-\text{C}_6), -\text{C}(\text{C}_1-\text{C}_6), -\text{CH}=\text{CH}-, -\text{C}(\text{C}_1-\text{C}_6)=\text{C}$   
 $\text{H}-, -\text{CH}=\text{CH}-, -\text{CH}=\text{C}(\text{C}_1-\text{C}_6)-$  ; R<sup>12</sup> R<sup>13</sup> R<sup>14</sup>

a b 0, 1, 2 3 , 가 0 ;

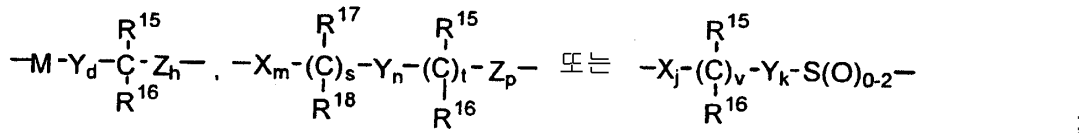
, R<sup>13</sup>  $-\text{CH}=\text{CH}-, -\text{C}(\text{C}_1-\text{C}_6)=\text{CH}-$  , a 1 ;

R<sup>14</sup>  $-\text{CH}=\text{CH}-, -\text{C}(\text{C}_1-\text{C}_6)=\text{CH}-$  , b 1 ;

a가 2 3 , R<sup>13</sup> ;

b가 2 3 , R<sup>14</sup> ;

Q가 , R<sup>1</sup>



M  $-\text{O}-, -\text{S}-, -\text{S}(\text{O})-, -\text{S}(\text{O})_2-$  ;

X, Y Z  $-\text{CH}_2-, -\text{CH}(\text{C}_1-\text{C}_6), -\text{C}(\text{C}_1-\text{C}_6)$  ;

R<sup>10</sup> R<sup>11</sup> (C<sub>1</sub>-C<sub>6</sub>) ,  $-\text{OR}^{19}, -\text{O}(\text{CO})\text{R}^{19}, -\text{O}(\text{CO})\text{OR}^{21}, -\text{O}(\text{CH}_2)_{1-5}\text{OR}^{19}, -\text{O}(\text{CO})\text{NR}^{19}$   
 $\text{R}^{20}, -\text{NR}^{19}\text{R}^{20}, -\text{NR}^{19}(\text{CO})\text{R}^{20}, -\text{NR}^{19}(\text{CO})\text{OR}^{21}, -\text{NR}^{19}(\text{CO})\text{NR}^{20}\text{R}^{25}, -\text{NR}^{19}\text{SO}_2\text{R}^{21}, -$   
 $\text{COOR}^{19}, -\text{CONR}^{19}\text{R}^{20}, -\text{COR}^{19}, -\text{SO}_2\text{NR}^{19}\text{R}^{20}, \text{S}(\text{O})_{0-2}\text{R}^{21}, -\text{O}(\text{CH}_2)_{1-10}-\text{COOR}^{19}, -\text{O}(\text{C}$   
 $\text{H}_2)_{1-10}\text{CONR}^{19}\text{R}^{20}, -(\text{C}_1-\text{C}_6)_1-\text{COOR}^{19}, -\text{CH}=\text{CH}-\text{COOR}^{19}, -\text{CF}_3, -\text{CN}, -\text{NO}_2$  ;

R<sup>15</sup> R<sup>17</sup>  $-\text{OR}^{19}, -\text{O}(\text{CO})\text{R}^{19}, -\text{O}(\text{CO})\text{OR}^{21}, -\text{O}(\text{CO})\text{NR}^{19}\text{R}^{20}$  ;

R<sup>16</sup> R<sup>18</sup> H, (C<sub>1</sub>-C<sub>6</sub>) , R<sup>17</sup> R<sup>18</sup> , =O ; R<sup>15</sup> R<sup>16</sup>

d 1, 2 3 ;

h 0, 1, 2, 3 4 ;

s 0 1 ; t 0 1 ; m, n p 0 4 ,

s t 1 , m, n, p, s t 1 6 ;

p가 0 t가 1 , m, s n 1 5 ;

p가 0 s가 1 , m, t n 1 5 ;









-4- , -4- , - - TFPI-

**34.**  
 32 (S)- } , VIIa 가 -2- {1-[3-( )- ]-2- - -3-  
 }- , -4- {1-[3-( )- ]-2- - -3-  
 )- }- , 3,4- -1H- -2- {1-[3-( )- ]-2- - -3-(S)- }-  
 )- }-

**35.**  
 1 , 가 .

**36.**  
 35 , 가 HMG CoA .

**37.**  
 36 , HMG CoA 가 .

**38.**  
 1 , 가 .

**39.**  
 1 , 가 .

**40.**  
 1 , 가 3 가 .

**41.**  
 1 , 가 .

**42.**  
 1 , 가 .

**43.**  
 1 , 가, 1 1 1000mg .

**44.**  
 1 , 가, 1 0.1 1000mg .

**45.**  
 1 , , , .

**46.**  
 가 , , , .

(a) , , ;

(b) , , , , .

**47.**

- (a) 1 , ; ,
- (b) 2 , ( , 1 2  
, , , ) .

**48.**

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