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(12)

(KR)  
(A)

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C07D 239/42

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(86) 2000 11 18

(87) WO 2001/42226  
(87) 2001 06 14

(30) 19959291.8 1999 12 09 (DE)

(71) - 65929 50

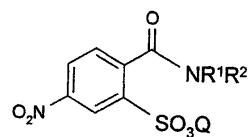
(72) 65812 가 19  
65510 33

(74)

(54)

I : :

I



,

R<sup>1</sup> 1 10 , 1 6 ;R<sup>2</sup> 1 10 , 1 6 ,NR<sup>1</sup>R<sup>2</sup> NR<sup>1</sup>R<sup>2</sup> N, O S

1 2 가 , 3 8

;

Q H

( : )

,

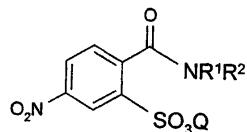
3,055,928 5,550,237 가 ,

, ( : )

( : )

- 4 - - 2 -

1



,

$$R^1 \quad 1 \quad 10 \quad , \quad 1 \quad 6$$

$$R^2 \quad 1 \quad 10 \quad , \quad 1 \quad 6 \quad , \quad 1 \quad 4$$

$R^2 \nmid C_1 - C_6 - \dots, C_2 - C_6 - \dots, C_2 - C_6 - \dots, C_5 - C_6 - \dots ( \dots 4 \dots, C_1 - C_4 - \dots, C_1 - C_4 - \dots, C_1 - C_4 - \dots, \dots, \dots, \dots, C_1 - C_4 - \dots, (C_1 - C_4 - \dots) - \dots, (C_1 - C_4 - \dots) - \dots, C_1 - C_4 - \dots, C_1 - C_4 - \dots, \dots ) \dots, \dots$

NR<sup>1</sup>R<sup>2</sup> 가 N O 가  
C<sub>1</sub> - C<sub>4</sub> - , 4, 5 6 ;

Q가 H, K, Li, Na

$$R^1 \quad C_1 - C_4 - \quad , \quad , \quad R^2 \nmid C_1 - C_4 - \quad , \quad , \quad Q \nmid H, Na \quad K$$

1

N,N - 4 - - 2 - ,

N,N - 4 - - 2 - ,

$$N, N - \quad 4 - \quad - 2 - \quad ,$$

N,N - 4 - - 2 - ,

N,N - 4 - - 2 -

N,N - 4 - - 2 - .

,  $\text{CF}_3$ ,  $\text{CHF}_2$ ,  $\text{CH}_2\text{F}$ ,  $\text{CF}_3\text{CF}_2$ ,  $\text{CH}_2\text{FCHCl}$ ,  $\text{CCl}_3$ ,  $\text{CHCl}_2$ ,  $\text{CH}_2\text{CH}_2\text{Cl}$ ,  $\text{OCF}_3$ ,  $\text{OCHF}_2$ ,  $\text{OCH}_2\text{F}$ ,  $\text{CF}_3\text{CF}_2\text{O}$ ,  $\text{OCH}_2\text{CF}_3$ ,  $\text{OCH}_2\text{CH}_2\text{Cl}$ , ,

, , , N, O S  
, , 5 6 1, 2 3

( )

N S

, 3 ,

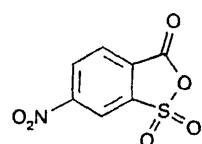
( : ,  
(Aliquat 336; )),

3 , , , N - , N - , N -  
, 2-, 3- 4- , 2,3-, 2,4-, 2,5-, 2,6-, 3,4- 3,5-  
N,N- ( : N,N- )가 , .

C<sub>1</sub> - C<sub>8</sub> -

, (acidic acid),  
N -

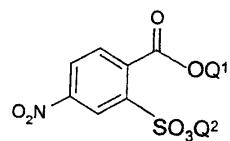
11



1 10 , 1 4 , 1 2 (NHR<sup>1</sup>R<sup>2</sup>) II  
 3 . - 50 300 , - 20 180 , | 가 ( :

II , [Helv. Chim. Acta, 1949, 32, 172] , a) Q<sup>1</sup> Q<sup>2</sup> 가 K  
 III 4 - - 2 - , b) Q<sup>1</sup> H Q<sup>2</sup> 가 K  
 III 4 - - 2 - , c) Q<sup>1</sup> Q<sup>2</sup> 가 K  
 H III 4 - - 2 - , 184

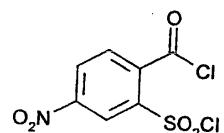
111



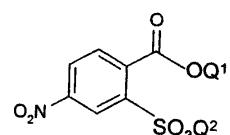
# IV

# III

IV

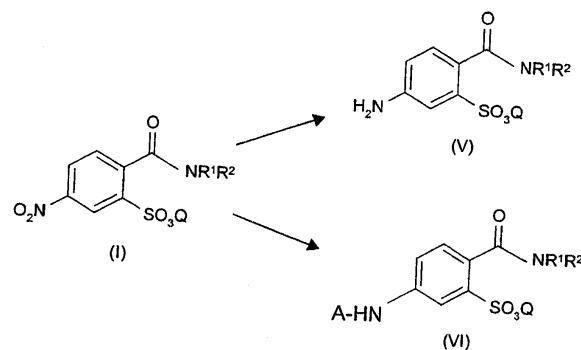


111



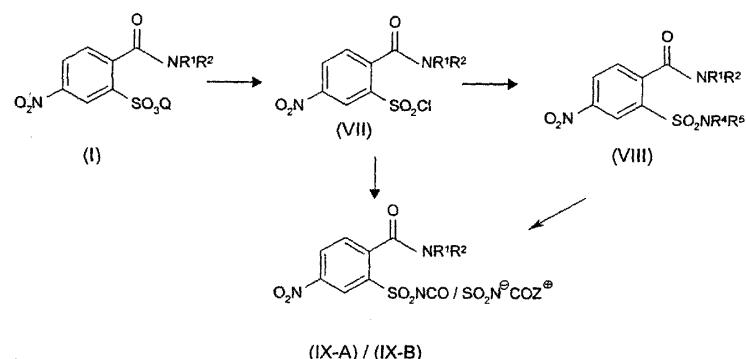
R<sup>1</sup> R<sup>2</sup> 1 | , , | V( , Q,  
 - Ni | ( ) ) , 偈 . Pd/C, Pt/C, Ru/C  
 , ( , , , , , ( , , )  
 , | , -30 300 , -10 150 , )

1



2

2

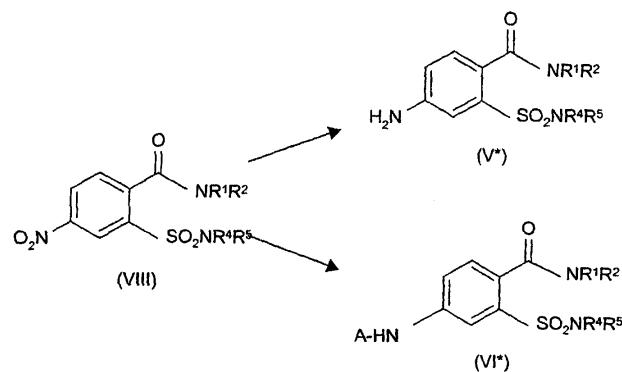


VIII

가

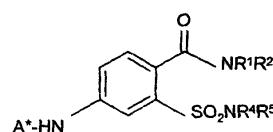
VIII

3



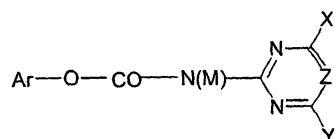
VIII , IX - A IX - B

A



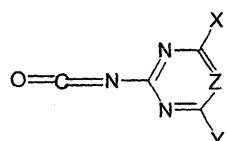
[ ,  
 R<sup>1</sup> R<sup>2</sup> | ;  
 R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - ;  
 A<sup>\*</sup> ]

X



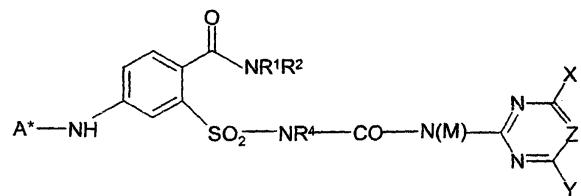
[ ,  
 Ar ;  
 M H, C<sub>1</sub> - C<sub>4</sub> - ;  
 X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> , C<sub>1</sub> - C<sub>6</sub> - ( , ,  
 , C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - , C<sub>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
 C<sub>3</sub> - C<sub>6</sub> - ;  
 Z CH N ]

XI



[ ,  
 X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> , C<sub>1</sub> - C<sub>6</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>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
 C<sub>3</sub> - C<sub>6</sub> - ;  
 Z CH N ]

XIV



[  
,

$R^1, R^2, R^4$  VIII

M, X, Y Z X ;

$$A^* \quad ]$$

VIII

WO 97/16419

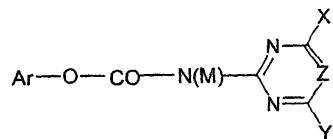
X

WO 95/29899 (

EP - A - 757679

) WO 00/05220  
- 50 150 , IX - A/IX - B ,  
) ( : ) ,  
, ( XII -

X



[  
,

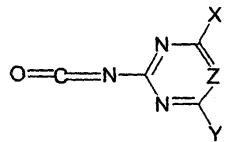
Ar

M H, C<sub>1</sub> - C<sub>4</sub> -

X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> , C<sub>1</sub> - C<sub>6</sub> - ( ,  
 , C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - ) , C<sub>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
 C<sub>3</sub> - C<sub>6</sub> - ;

Z CH N ]

XI

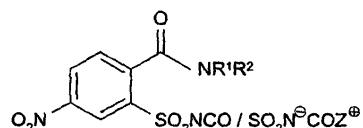


[ ,

X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> , C<sub>1</sub> - C<sub>6</sub> - ( ,  
 , C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - ) , C<sub>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
 C<sub>3</sub> - C<sub>6</sub> - ;

Z CH N ]

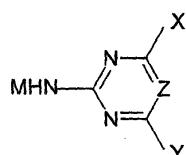
IX - A/IX - B



[ ,

R<sup>1</sup> R<sup>2</sup> 1 3 | ]

XI\*

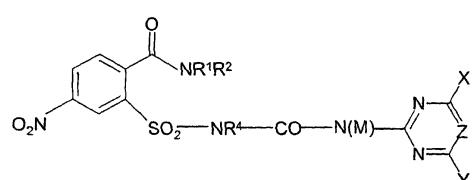


[ ,

M H, C<sub>1</sub> - C<sub>4</sub> - ;

X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> , C<sub>1</sub> - C<sub>6</sub> - ( ,  
, C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - ) , C<sub>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
C<sub>3</sub> - C<sub>6</sub> - ;

xii



1

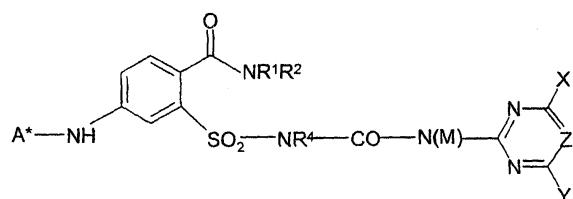
$\mathbb{R}^1, \mathbb{R}^2, \mathbb{R}^4$       VII

M, X, Y Z X

WO 97/16419

XIV

xiv



$$\mathbb{R}^1, \mathbb{R}^2, \mathbb{R}^4 \quad \text{VIII}$$

M, X, Y Z X

$A^*$     $H$

A H .

, Pd/C, Pt/C, Ru/C - Ni ( ) , 가 , , , ( ) , , , ( : )

) , , , , ( : ) ( ( ) , - 30 300 , - 10 150 ,

I VIII

WO 97/16419

III XII , M, X, Y Z X C<sub>1</sub> - C<sub>8</sub> - C<sub>1</sub> - C<sub>8</sub> - XIV( , A \* , R<sup>1</sup>, R<sup>2</sup> R<sup>4</sup> V  
- 가 . )

, a) 가

(

1

- Ni

1: N,N - 4 - - 2 - (1)

A) (240ml) 4 - - 2 - (III) 31.9g 가 , 0.6  
 0.8ml . , 85 90 , (0.23ml) (0.16  
 ml) 가 , 4 (10.1g) 가 . 85 90 가 2 가 ,  
 . , 98 103  
 ×20ml) (4.78g) 가 . 1 , 20 (2  
 75 /50 : 35.1g (=90%), 80.1% w/w;  
 320 ( ).

B) (120ml) 4 - - 2 - (50g), (14.2g)  
 (1.0g) 100 가 , 45 (15ml) 가  
 2 , 20 , (2 x 50ml) . : 61.72g (=91.3%), 70.0% w/w.

2: N,N - 2 - - 4 - (VIII)

A) (570ml) 4 - - 2 - (I) 79.9g 88 92 가  
 (1ml) 가 , (58g) 3 가 . 가 1 ,  
 , 4 - - 2 - (75.7g) (0.6ml) 가

1 138 가 95 100 , 2 (23.5g) 가  
 30 가 . , 70 75 2 (10ml)  
 (0.38ml) (77.1g) 가 . 1 ,  
 0 5 . , (19.5g) 가 5  
 , 20 가 (420ml) (7.4g) ( pH=4) 가 5  
 . (5 x 100ml) 75 /50  
 111.4g (=81%), 93.4% w/w.

B) 4 - - 2 - (III) 31.9g (240ml) 가 , 0.6 0.  
 8ml . , 82 87 (0.91g)  
 가 2 (9.2ml) 가 . 가 1 ,  
 (25ml) , 95 100 (7.5g) 가 .  
 1 , 70 75 , 2 (2ml)  
 I) (15.8g) 가 . 1 , 40 가 , ,  
 (4g) 가 . (85ml) (2.5ml)  
 . , 75 /50 . : 23.6g (=82%), 95.6% w/w, : 1  
 61 - 162 .

3: N,N - 2 - - 4 - (VI\*<sup>\*</sup>)

(200ml) N,N - 2 - - 4 - (VIII) 40g, (0.08g) Pd  
 /C(3g, 5%, 50% ) 50 40 7 (20m)  
 I) . . (200ml) 가 . 20 2 (20ml) 50  
 , , . : 35.3g (=84.3%), 94.1% w/w, : 192 - 193 .  
 /50

4: N,N - 2 - (N - (N - (4,6 - - 2 - ) - ) - ) - 4 -  
 (XII)

0 2.5 (70ml) (VIII) 20g (20g) (200ml) N,N - 2 -  
 - 4 - . (39ml) 가 . 30 ,  
 11.9g) . . . . (80ml) 2 - - 4,6 - (5N, 45ml) 가 ,  
 . . . . (2 x 50ml) , (3N, 35ml) pH 2 ,  
 . . . . 40 /50 . 22.3g (=58%), 87.1% w/w.

5: N,N - 2 - (N - (N - (4,6 - - 2 - ) - ) - ) - 4 -  
 (XIV)

A) (225ml) N,N - 2 - (N - (N - (4,6 - - 2 - ) - ) - ) - 4 -  
 - (XII) 75g, (0.05g) Pd/C(3g, 5%, 50% ) 30 35

3 (20ml) (35 )  
 (240ml) 가 45 1 , 0 5 가 2  
 (2 x 25ml) (200ml)  
 50 55 2 가 20 , (2 x 25ml)  
 45 /50 60.6g (=83.6%), 95.5% w/w.

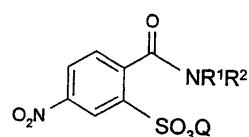
B) (250ml) N,N - 2 - - 4 - (VI \*) 30g N - (4,6 -  
 - 2 - ) 3.3g 20 (30g) . 3 , N - (4,6 -  
 - 2 - ) (2g) 가 가 . 1 , (400ml) 가  
 (45 ) . , (1N, 400ml) 가 , (2 x 2  
 00ml), (2 x 200ml) . 42g (=66.1%), 78.7% w/w.

(57)

1.

1

1



R<sup>1</sup> 1 10

•  
,

R<sup>2</sup> 1 10

NR<sup>1</sup> R<sup>2</sup>

NR<sup>1</sup> R<sup>2</sup>

3 8

■

Q H

2.

1

$R^2$   $C_1 - C_6 -$ ,  $C_2 - C_6 -$ ,  $C_2 - C_6 -$ ,  $C_5 - C_6 -$ , ( , 4  
 $, C_1 - C_4 -$ ,  $C_1 - C_4 -$ ,  $C_1 - C_4 -$ ,  $C_1 - C_4 -$ ,  $- (C_1 - C_4 -$  ) - ,  
 $, (C_1 - C_4 -$  ) - ,  $(C_1 - C_4 -$  ) - ,  $C_1 - C_4 -$ ,  $C_1 - C_4 -$   
 $)$  ,

NR<sup>1</sup>R<sup>2</sup>가 N-O 가  
C<sub>1</sub>-C<sub>4</sub>- , 4, 5 6 ;

3.

1 2 ..

$$R^1 - C_1 - C_4 - \dots ,$$

$\mathbb{R}^2$  가  $C_1 - C_4 - \dots$ ,

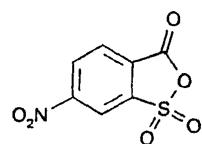
Q가 H, Na K I .

4.

NHR<sup>1</sup> R<sup>2</sup> ( , R<sup>1</sup> R<sup>2</sup>  
||

1

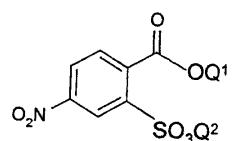
11



5.

$$\text{NHR}^1\text{R}^2 \left( \text{R}^1, \text{R}^2 \right) \text{III} \quad \begin{matrix} 1 \\ 3 \end{matrix} \quad \left| \quad \begin{matrix} 1 \\ 3 \end{matrix} \right. \quad \begin{matrix} 1 \\ 3 \end{matrix}$$

1



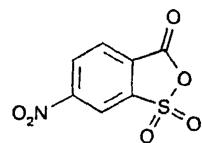
Q<sup>1</sup> Q<sup>2</sup> , H .

6.

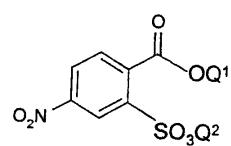
III

II

II



III



Q<sup>1</sup> Q<sup>2</sup> , H .

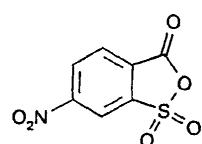
7.

IV

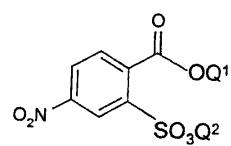
III

II

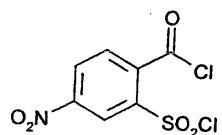
II



III



IV

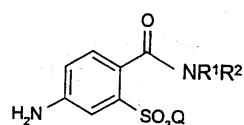


$$Q^1 \quad Q^2 \quad , \quad H$$

8.

1 3  
V

V



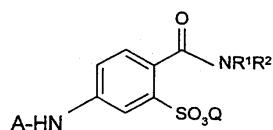
Q, R<sup>1</sup> R<sup>2</sup> 1 3

9.

1 3

VI

vi



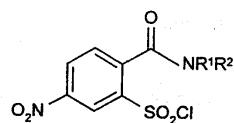
Q, R<sup>1</sup> R<sup>2</sup> 1 3

A

10.

1            3            |  
,            VII            :

VII

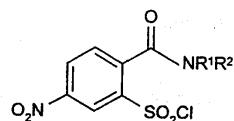


R<sup>1</sup>    R<sup>2</sup>    1            3            |

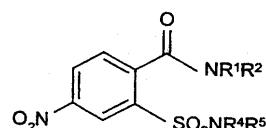
11.

VII            NHR<sup>4</sup>R<sup>5</sup> (            , R<sup>4</sup>    R<sup>5</sup>    C<sub>1</sub> - C<sub>12</sub> - )  
,            VIII            :

VII



VIII



R<sup>1</sup>    R<sup>2</sup>    1            3            |

R<sup>4</sup>    R<sup>5</sup>    C<sub>1</sub> - C<sub>12</sub> - ;

12.

6    ,    4    ,    10    ,    11    ;    7    ,    4    ,    10    ,    11  
;    ,    4    ,    10    ,    11    ;    6    ,    5    ,    10    ,    11  
;    ,    7    ,    5    ,    10    ;    5    ,    10    ,    11  
;    ,    10    ,    11    ,    11    ,    11    VIII

13.

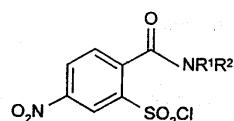
6 , 4 10 ; 7 4 10 ; ; 4  
10 ; 6 , 5 10 ; 7 , 5 10  
; 5 10 , , VII

14.

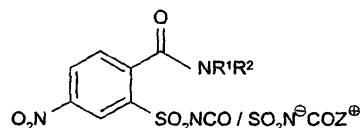
VII

IX - A/IX - B

vii



IX - A/IX - B



R<sup>1</sup> R<sup>2</sup> 1 3 |

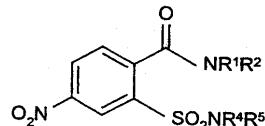
IX - B Z 3

15.

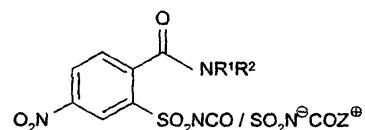
VIII

IX - A/IX - B

VIII



IX - A/IX - B



R<sup>1</sup> R<sup>2</sup> 1 3 | ;

IX - B Z 3 ;

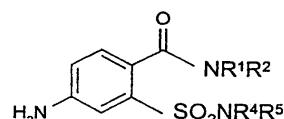
R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - .

16.

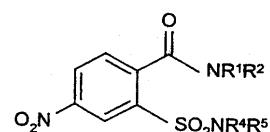
VIII , V\*

:

V\*



VIII



R<sup>1</sup> R<sup>2</sup> 1 3 | ;

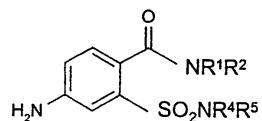
R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - .

17.

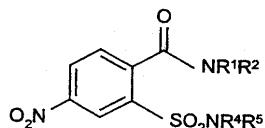
VIII ,

VI\* :

VI\*



VIII



R<sup>1</sup> R<sup>2</sup> 1 3 | ;

R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - ;

A .

18.

a) NHR<sup>1</sup>R<sup>2</sup> ( , R<sup>1</sup> R<sup>2</sup> 1 3 | | | , )

| ;

b) a) | , , VII

;

c) b) VII NHR<sup>4</sup>R<sup>5</sup> ( , R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - ) , ,

VIII ;

d) c) VIII ,

) , A i) X , A\* , , A , ii) )

XI ,

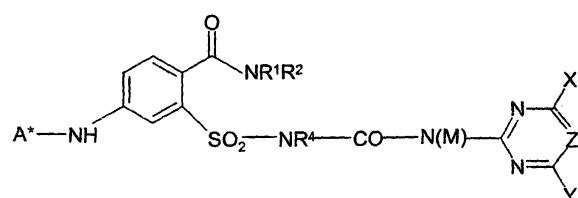
) X , XII -

,

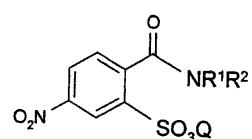
) XI , XII -

,

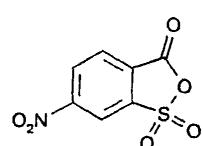
)
 , IX - A/IX - B
 , IX - A/IX - B  
 XI\*, XII
 ;  
 e) ) d) ), ) XII
 , A\* A\* H
 , XIV
 ,  
 XIV
 ,  
 XIV
 ,  
 XIV
 ,



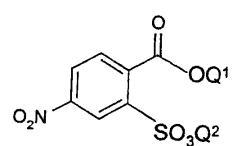
I



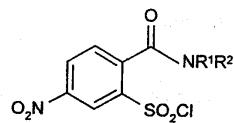
II



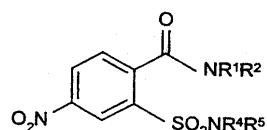
III



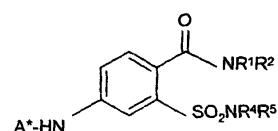
VII



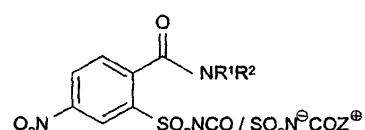
VIII



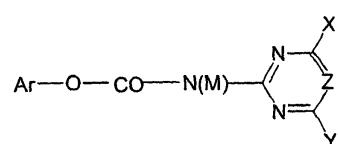
A



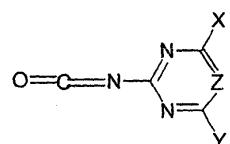
IX - A/IX - B



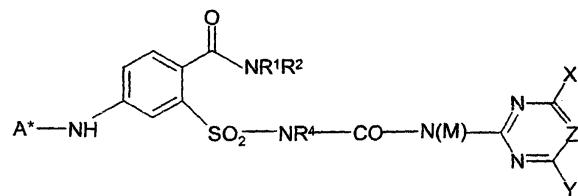
X



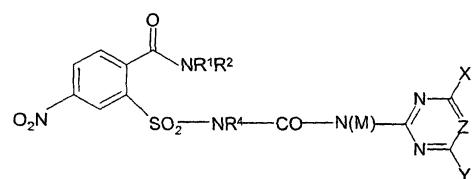
XI



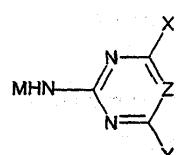
XIV



XII



XI\*

R<sup>1</sup> 1 10 ;R<sup>2</sup> 1 10 ,NR<sup>1</sup> R<sup>2</sup> NR<sup>1</sup> R<sup>2</sup> , 3 8 ;

Q H ;

R<sup>4</sup> R<sup>5</sup> C<sub>1</sub> - C<sub>12</sub> - ;

A\* ;

M H, C<sub>1</sub> - C<sub>4</sub> - ;

X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</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>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
C<sub>3</sub> - C<sub>6</sub> - ;

Z CH N ;

IX - B Z 3 ;

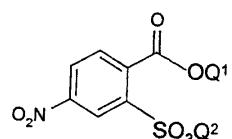
Ar .

19.

4 18 ,

III , a) ) II :

III



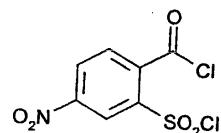
Q<sup>1</sup> Q<sub>2</sub> , H .

20.

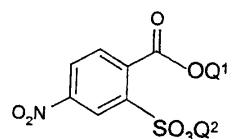
4 18 ,

IV III , a) ) II :

IV

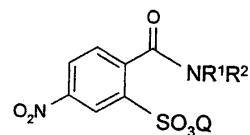
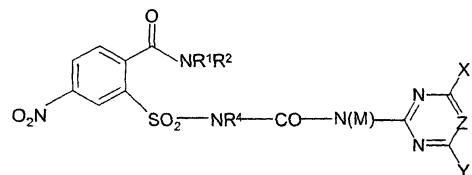


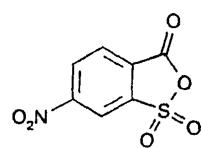
III



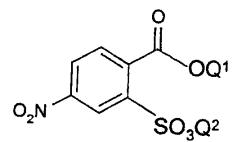
$$Q^1 \quad Q^2 \quad \quad \quad , \quad H$$

21.

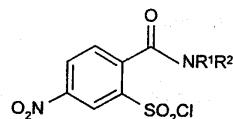




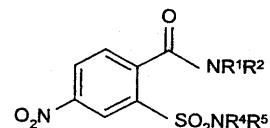
III



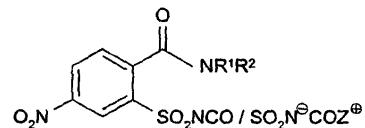
VII



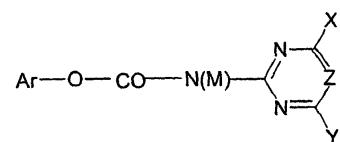
VIII



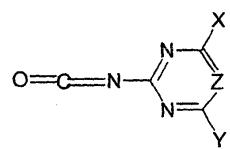
IX - A/IX - B



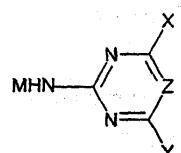
X



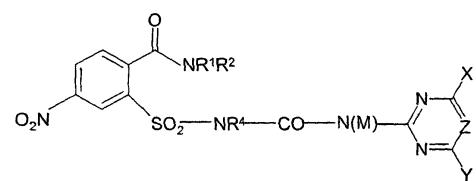
XI



XI\*



XII



R <sup>1</sup>	1	10			;
R <sup>2</sup>	1	10			,
NR <sup>1</sup> R <sup>2</sup>			NR <sup>1</sup> R <sup>2</sup>		N, O S
	1	2	가	, 3	8
;					
Q H				;	
R <sup>4</sup> R <sup>5</sup>		C <sub>1</sub> - C <sub>12</sub>	-	;	
Ar				;	
M H, C <sub>1</sub> - C <sub>4</sub>				;	

X Y , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> - , C<sub>1</sub> - C<sub>6</sub> - ( , , ,  
 , C<sub>1</sub> - C<sub>4</sub> - C<sub>1</sub> - C<sub>4</sub> - C<sub>3</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>2</sub> - C<sub>6</sub> - , C<sub>3</sub> - C<sub>6</sub> -  
 C<sub>3</sub> - C<sub>6</sub> - ;

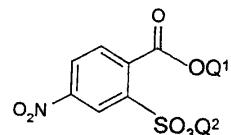
Z CH N ;

IX - B Z 3 .

22.

21 ,

III a) ) II :  
 III

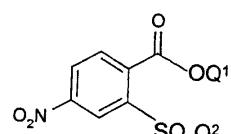


Q<sup>1</sup> Q<sup>2</sup> , H .

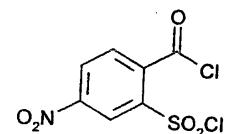
23.

21 ,

IV III a) ) II :  
 III



IV



Q<sup>1</sup>    Q<sup>2</sup>

, H

24.

18

XIV

, 1

3

,

21

|

XII