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C07D 487/04

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(24)

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2003 07 02

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(30)	10/136960	1998 05 19	(JP)						
(73)	가 가			115					
(72)	,								
	772-0017			188				-10	
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	772-0003		가	183-9					
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	772-0052			146					
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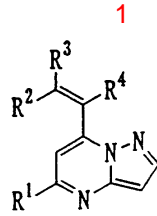
(74) :

(54) [1,5- a]

1

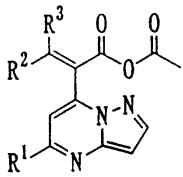
[1,5-a]

가

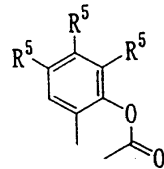


1

R¹ ;
 R² R³ ; ; ; ;
 ; , N,N- 가 ; 1 3 ;
 R⁴ ; ; ; ; ; ;
 ; 1 3 ;
 ; N-() ; N- ; N-() ;
 ; N-(1-2-) ; N-(1-2-)



(, R¹, R² R³)



(, R⁵)

, R²가 , R³ R⁴)

1 6

, , , ,

, tert- ,
 2- , 3- 가
 1- 2- 가
 2- 3- 가
 2- , 3- 4- 가
 1 6

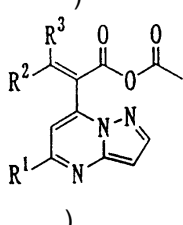
, 1- , 2- , 3- , 4- , 5- 1 6 , 6-

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

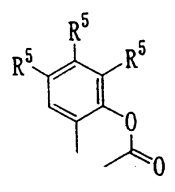
) , N-(5-) , N-(6-)
 N-() , N-(-C₁₋₆-) , N-()
) , N-(2-) , N-(3-) , N-(4-)
 , N-(5-) , N-(6-)
 N- N
 - , N-(2-) , N-(3-) , N-(4-) , N-(4-)
 , N-(2-) , N-(3-) , N-(3-) , N-(4-) , N-(2-)
) , N-(3-) , N-(4-) , N-(2-) , N-(2-)
 N-(3-) , N-(4-) , N-(2-)
 N-(1- -2-) , N-[1-(C₁₋₆-) -2-]
 , N-(1- -2-) , N-(1- -2-)
 N-(1- -2-) , N-(1- -2-) , N-(1- -2-)
 -2-) , N-(1- -2-) , N-(1- -2-)
 , 2- , 3- , 4- , 2- , 3- , 4- , 3- , 2- , 4-
 , 3- , 4-
 [1,5-a]
 가 (endotoxin shock),

(i) 1 , R¹
 (ii) 1 , R¹ , R² R³ 가 , 가
 1 3 , R⁴가 ,

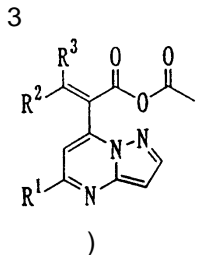
(i) (1a), (1b) (1c)
 (1a) R¹ , R⁴가
 (1b) R¹ , R² R³ 가 , 가 1
 3 , R⁴가 ; ; ; 1
 3 ; N- ; N- ; N-() ; N-(
 ; N- ; N-(1- -2-) ;



(, R¹, R² R³ 1 , (1b)



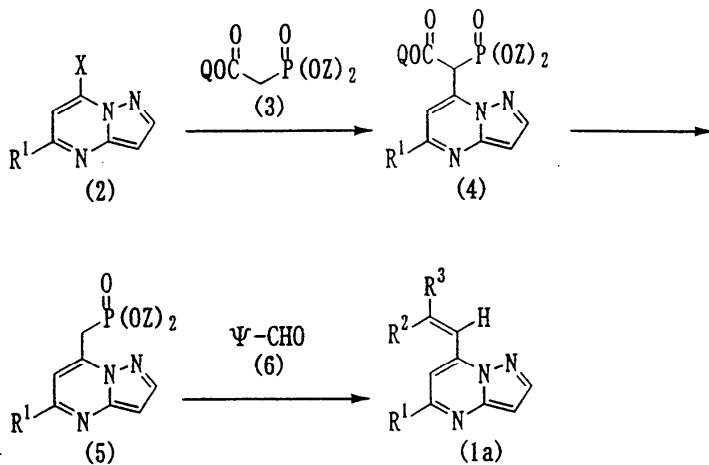
(1c) R¹ , R²가 , R³ R⁴가 (, R⁵
 (1a) (1c) , R¹ , n-
 , (ii) R¹ , R² R³ 가 ,
 가 1 3 , R⁴가 ,
 , (a) R¹ n- , R²가 , R³
 , R⁴가 , (b) R¹ n- n- , R²가
 1 3
 가 , N,N- , R³ , R⁴가 , 1



2- , R⁴ 가 R¹ n- , R² 가 , R³ , R² 가
 3 , R³ , R⁴ 가 2
 3,4,5-

1 10

1



, R¹, R² R³

, X

, Q Z

N-

, N,

X 가

가

(4) 1

(2)

(3)

(4)

(5)

(2)

(3)

(6)

(3)

(1a)

(DMA),

(THF),

(DME),

(DMF), N,N-

(2)

-t-
5

(3)

2

100

(4)

30

5

(5)

100

(5)

(6)

(1a)

-10
(6)

10
(5)

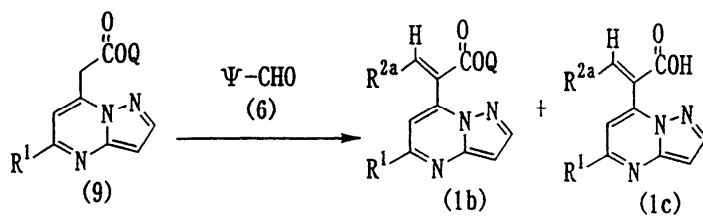
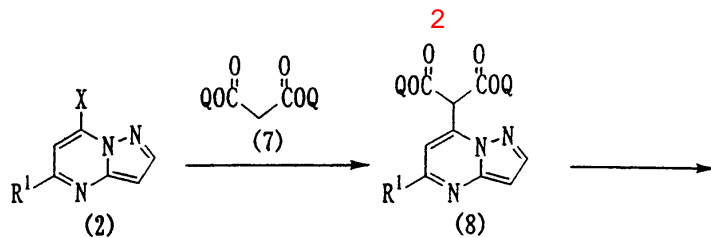
3

1

(4)

(5)

(1a)



R¹, Q, X

R^{2a}

N,N-

2

(2)

(7)

DMF, DMA, THF, DME,

1 3

(7)

(2)

5

1 50

(8)

-DMF

2

3

50

(2)

가

(8)

(9)

(9)

(9)

(6)

, THF, 1,4-

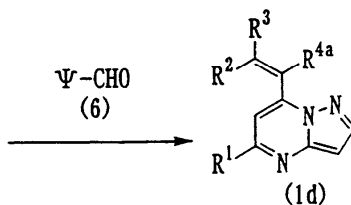
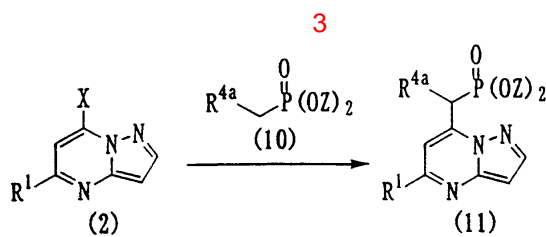
-100

5

100

(6)

(5)



R¹, R², R³, X, Z

R^{4a}

3

(2)

(10)

THF, 1,4-

, DMF

n-

, n-

(10)

-100

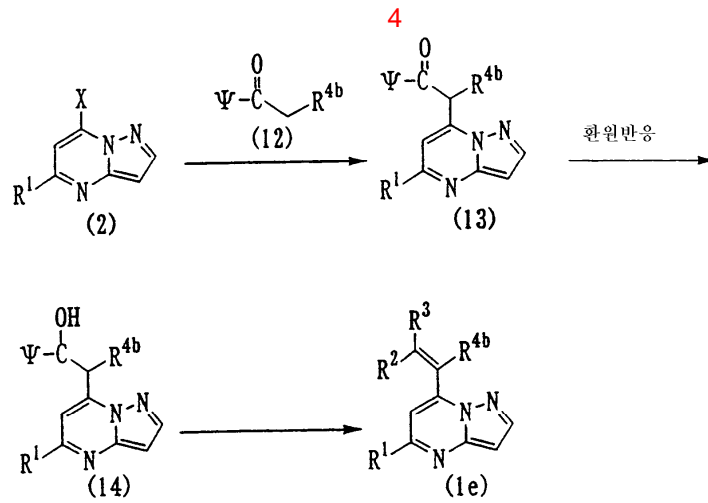
(2)

5

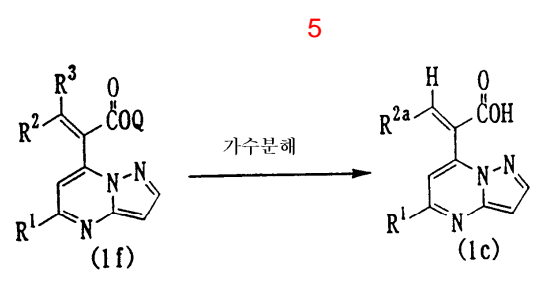
10

3

(11) (6) (1d)
 , t- , THF
 1 150 (6) (



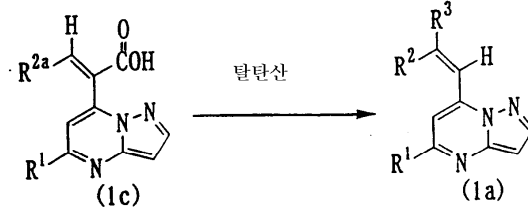
, R¹, R², R³ (2) , R^{4b}
 , THF, 1,4- (12) -100 5 100
 (2) (13) 5 가
 , THF
 1 6 O 10
 (14) (1e) 가
 (14) p-
 1 10 가
 (14) , 1,2- 가 가
 0 5 2
 1,8- [5,4-0]-7- (DBU), , N,N- , 4-(N,N-)
 0 10 2 3



R¹, R², R^{2a}, R³ Q
5 (1f) 가

(1f)
0.5 10

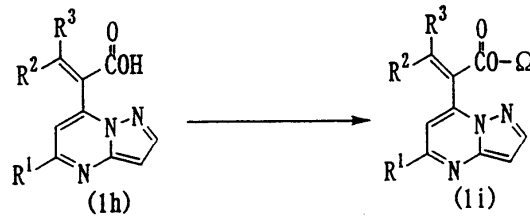
6



R¹, R², R^{2a}, R³ Q
6 (1c) N,N-30 4-(N,N-5) 가

DBU,

7



R¹, R² R³

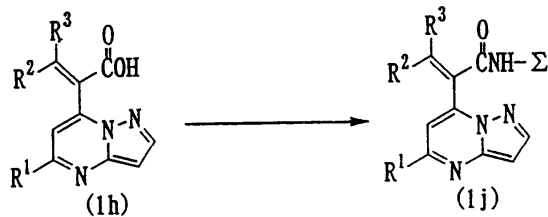
1 3

3- 2- 3- 4- 3- 3- 1 3
3- 3- 2- 3- 4- 4- 4- 4-
3,5- 2- 3- 4- 2,3- 2,4- 3,4- 2,4-
3,5- 2,3- 2,4- 2,3,5- 3,4- 2,3,6- 3,5- 2,4,5-
2,4,6- 3,4,5- 2,4,6- 2,4,6-
4- 4- 2- 3- 4- 4- 4-
7 (1h) (1i) 가

(1) (1h) DMF, DMA, THF, N,N- 4-(N,N)
() -X (X (1h)) 3

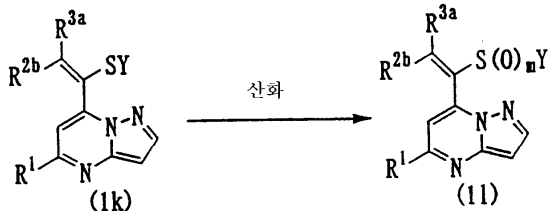
(2) (1h) 1,2- (DEPC) -OH ((1h)) (DCC),
0 5 100

8

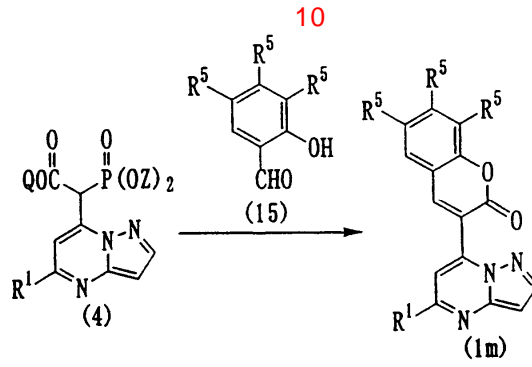


R^1, R^2, R^3
 1-
 -2-
 (C₁₋₆-) (C₁₋₆-)
 1-
 -2-
 1-(C₁₋₆-) -2-
 8 (1h) (1j) (1h) THF
) , 1,4- 3 , N,N- , 4-(N,N-
) , 3 -NH₂ ()
 (1h)
 10 1 , 0 30 10 0
 , 8 (1h) (1j) -NH₂ () (2)
 , (1h) -NH₂ () 7 (2)
 , 7 (2)

9



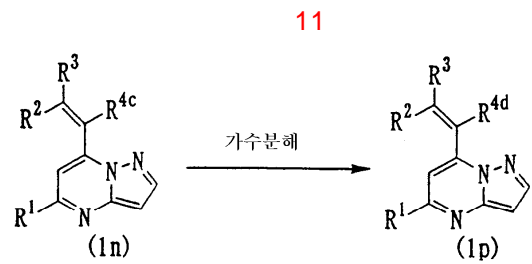
R^1 , R^{2b} R^{3a}
 N,N- 1 3
 9 (1k) 가 , ,
 , m- , ,
 (n=1) , 0 15 10
 가 , 2 ,
 , n=2 , 0 15 10
 () n=1 ()



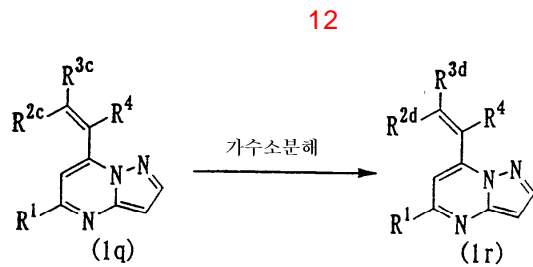
10, R¹, R⁵, Q, Z (4) (15) 3 (11)
(6)

18- -6

가



N-(1- (R¹, R², R³ -2-) (1n) 가
N-(1- (R^{4c} N-()) (1n) 가
(1p) (R^{4d} N-()) (1p) 가
11 (1p) 8 가 (1n) 가 (1f) 가



3, R¹, R⁴ 가, R^{2c}, R^{3c} 가, R^{2d}, R^{3d} 가
3d R^{2c} R^{3c} 가, R^{2c} R^{3c} 가, R^{2d} R^{3d} 가
3 가, 1 2 가, (, R^{2d} R^{3d})
12 가, (1q) 가
0 (1r)
5 1
R^{2c} R^{3c} 가 가 가

가 , 가

, p-

가

R S

가

()

가

4

가 (tragacanth)

(laminaran),

가

(macrogol),

가

1

[1,5-a]

, R 4 가
()

pH가 6

(1:1)

(

:

(Eudragit L10

0, (Rohm Pharm. Co., Ltd.)

)가

1

()

1 70 %

1

2

4

1

1 kg

0.5

20 mg

()

< 1 >

60 % 12.0 g DMF 100 ml 가 O 70.
 6 g 가 0 1 , 4 . 0 , 5-n- -7-
 [1,5-a] 30 g DMF 20 ml 0 30 , 65
 . 2 n- 600 ml 2 , 5 % 100 ml
 . 300 ml 42 g 가 30 ,
 (... :n- =1:1) (5-n- [1,5-a] -7-)
 41 g .

- . (5- [1,5-a] -7-)
- . (5- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . [5-(2-) [1,5-a] -7-]
- . [5-(3-) [1,5-a] -7-]
- . (5- [1,5-a] -7-)

< 2>
 1 (5-n- [1,5-a] -7-) 5 g 2 %
 50 ml 가 , 60 1.5 가 , 1.75 g
 가 (... :n- =1:2 2:1) (5-n-
 [1,5-a] -7-) 2.6 g .

- . (5- [1,5-a] -7-)
- . (5- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . (5-n- [1,5-a] -7-)
- . [5-(2-) [1,5-a] -7-]
- . [5-(3-) [1,5-a] -7-]
- . (5- [1,5-a] -7-)

< 1>
 (E)-5-n- -7-[2-(3,4,5-)] [1,5-a]
 2 (5-n- [1,5-a] -7-) 1.0 g 3,4,5-
 가 , 0 0.66 g 5.0 ml 0 5 % 3.8 ml
 . 10 % 0.72 g 1 .

< 2 7>
 1 , 1 .
 < 8 9>
 (E) (Z)-5-n- -7-[2-(4-)] [1,5-a]
 2 (5-n- [1,5-a] -7-) 4-
 1 E () .
 (... :n- =1:4) , Z (,) .

< 10 11>
 8 9 , 1 .
 < 3>
 n- (1.63 M, n-) 30.7 ml THF 35 ml -78
 , 5-n- -7- [1,5-a] 10.4 g THF 10 ml 가 -78 1
 . 5 g THF 5 ml -78 1
 (... :n- =1:3 1:1) , (5-n-
 [1,5-a] -7-) 5.9 g .

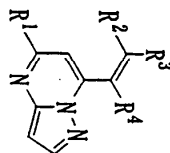
- . (5- [1,5-a] -7-)
- . (5- [1,5-a] -7-)

· (5-n- [1,5-a] -7-)
· (5-n- [1,5-a] -7-)
· (5-n- [1,5-a] -7-)
· [5-(2-) [1,5-a] -7-]
· [5-(3-) [1,5-a] -7-]
· (5- [1,5-a] -7-)
· (5-n- [1,5-a] -7-)
· (5-n- [1,5-a] -7-)-n-
· (5-n- [1,5-a] -7-)-n-
· (5-n- [1,5-a] -7-)-n-
· (5-n- [1,5-a] -7-)-n-
< 12>
(Z)-5-n- -7-[1- -2-(3,4,5-)] [1,5-a]
3 (5-n- [1,5-a] -7-) 5.5 g
25 ml 0 -t- 2.0 g 가 0 15 ,
3,4,5- 3.2 g 가 15 ,60 3 .
, (... :n- =1:2) , -n-
1.7 g . 1 .
< 13 26>
1 , 12 1
.
< 4>
5-n- -7- [1,5-a] , 3
1-(5-n- [1,5-a] -7-)
· 1-(5- [1,5-a] -7-)
· 1-(5- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-[5-(2-) [1,5-a] -7-]
· 1-[5-(3-) [1,5-a] -7-]
· 1-(5- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
· 1-(5-n- [1,5-a] -7-)
< 27>
(E)-5-n- -7-[1-(3,4,5-) -2-] [1,5-a]
4 1-(5-n- [1,5-a] -7-) ,
12 1 .
< 28 29>
(E) (Z)- 2-(5-n- [1,5-a] -7-)-3-(4-) 4-
1 (5-n- [1,5-a] -7-)
, 12 , (...
:n- =1:10 1:3) , Z , E .
1 .
< 30 39>
28 29 , 1 .
< 40>
(E)-2-(5-n- [1,5-a] -7-)-3-(3,4,5-)
31 18.0 g 180 ml , 5 % 36 ml 가 4
, 6.38 g 가 ,
, 117 120 , 13.65 g , -n-
, 가 n- 가 .
153 , .

1
 가
 30
 < 41 59>
 40
 < 60>
 (E)-5-n- -7-[2-(4-)] [1,5-a]
 44 0.50 g 10 ml 0.1 ml DBU 0.1 ml 가 1
 n- 0.28 g 1
 < 61 69>
 60
 < 70>
 (E)- -2-(5-n- [1,5-a] -7-)-3-(3,4,5-)
 40 2.0 g DMF 10 ml 1.0 ml 0.78 ml 가
 60 2
 (... :n- =1:4 1:1)
 (31) 1.55 g -n-
 < 71 75>
 70
 < 76>
 (E)-2-(5-n- [1,5-a] -7-)-4- -3-(3,4,5-)-
 40 0.50 g 4- 0.16 g 4 ml 0
 DCC 0.25 g 1 ml 가 0 1 , 60
 (... :n- =1:4 1:2)
 -n- 0.48 g
 1
 < 77 79>
 76
 < 80>
 (E)-2-(5-n- [1,5-a] -7-)-N- -3-(3,4,5-)
 40 0.70 g THF 5 ml 0 , 2 M THF 0.28 ml
 THF 0.24 ml 가 0 30 , 2 M THF 0.94 ml 2 ml
 가 , 0 1 , 2
 -n-
 0.62 g 1
 < 81 87>
 80
 < 88>
 (Z)-5-n- -7-[1- -2-(3,4,5-)] [1,5-a]
 12 0.50 g 5 ml , 30 % 0.14 ml 가
 4 (... :n- =1:1
 =10:1) , -n-
 0.38 g 1
 < 89>
 (E)-5-n- -7-[1- -2-(3,4,5-)] [1,5-a]
 12 0.50 g 3 ml , 30 % 0.34 ml 가 60
 4 (... :n- =2:3)
 -n- 0.24 g
 1
 < 90>
 5-n- -7-(6,7,8- -3-) [1,5-a]
 3,4,5- 0.21 g THF 3 ml , -t- 0.12 g 가 1
 0 1 (5-n- [1,5-a] -7-)

0.35 g THF 2 ml 가 , 10 , 18- -6 0.28 g 가
 120
 (... :n- =1:2)
 -n- 0.14 g 1
 > 91
 90 , 1


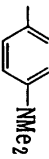
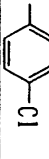
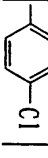
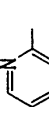
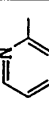
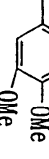
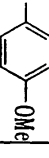
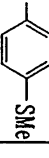
[1a]



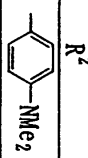
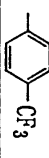
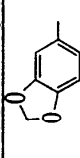
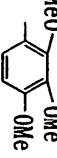
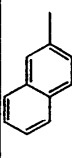
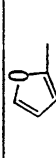
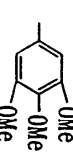

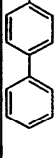
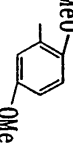
Me=메틸기, Et=에틸기, i-Pr=이소프로필기, n-Bu=n-부틸기, Ph=페닐기

실시 예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
1	n-Bu	H		H	83~85 (에탄올-n-헥산)
2	n-Bu	H	Ph	H	74~76 (에탄올-물)
3	n-Bu	H		H	69~71 (에탄올-물)
4	n-Bu	H		H	116~118 (에탄올-물)
5	n-Bu	H		H	67~69 (아세트산-에탄-n-헥산)

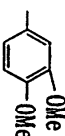
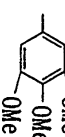
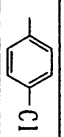
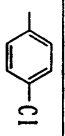
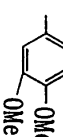
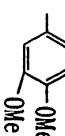
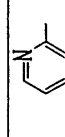
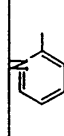

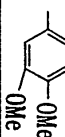
[1b]

실시예No.	R ¹	R ²	R ³	R ⁴	융점 (°C) / 재결정 용매
6	n-Bu	H		H	55~57 (에탄올-물)
7	n-Bu	H		H	131~133 (아세트산 에틸-n-헥산)
8	n-Bu	H		H	92~94 (에탄올-물)
9	n-Bu		H	H	유상물 (NMR 1)
10	n-Bu	H		H	67~69 (에탄올-물)
11	n-Bu		H	H	62~64 (에탄올-물)
12	n-Bu	H		-SMe	71~73 (n-헥산)
13	n-Bu	Ph	H	-COOEt	유상물 (NMR 2)
14	n-Bu		H	-COOEt	유상물 (NMR 3)
15	n-Bu		H	-COOEt	유상물 (NMR 4)


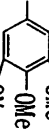
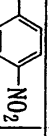
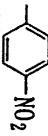
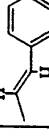
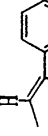
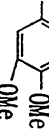
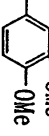
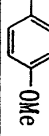
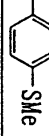
[1c]

질서 예No.	R ¹	R ²	R ³	R ⁴	융점 (°C) / 재결정 용매
16	n-Bu		H	-COOEt	유상물 (NMR 5)
17	n-Bu		H	-COOEt	유상물 (NMR 6)
18	n-Bu		H	-COOEt	유상물 (NMR 7)
19	n-Bu		H	-COOEt	유상물 (NMR 8)
20	n-Bu		H	-COOEt	유상물 (NMR 9)
21	n-Bu		H	-COOEt	유상물 (NMR 10)
22	Ph		H	-COOEt	유상물 (NMR 11)
23	n-Bu		H	-COOEt	78~80 (에탄올-물)
24	n-Bu		H	-COOEt	106~108 (에탄올-물)
25	n-Bu		H	-COOEt	유상물 (NMR 12)

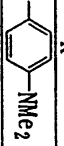


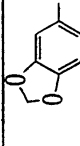
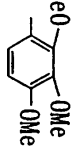
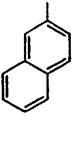
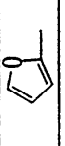
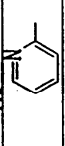
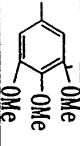
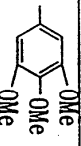
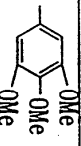
[1d]

실시예No.	R ¹	R ²	R ³	R ⁴	응점 (°C) / 재결정 용매
26	n-Bu		H	-COOEt	유상물 (NMR 1 3)
27	n-Bu	H		-Me	1 2 2 ~ 1 2 4 (염산염) (아세트산 에틸)
28	n-Bu	H		-COOEt	유상물 (NMR 1 4)
29	n-Bu		H	-COOEt	유상물 (NMR 1 5)
30	n-Bu	H		-COOEt	유상물 (NMR 1 6)
31	n-Bu		H	-COOEt	5 0 ~ 5 2 (n-헥산)
32	n-Bu	H		-COOEt	7 2 ~ 7 5 (n-헥산)
33	n-Bu		H	-COOEt	유상물 (NMR 1 7)
34		H		-COOEt	1 6 6 ~ 1 6 8 (아세트산 에틸-n-헥산)

[1e]

실시예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
35			H	-COOEt	유상물 (NMR 18)
36	n-Bu	H		-COOEt	96~98 (아세트산 에틸-n-헥산)
37	n-Bu		H	-COOEt	116~118 (아세트산 에틸-n-헥산)
38	n-Bu	H		-COOEt	118~120 (n-헥산)
39	n-Bu		H	-COOEt	103~105 (아세트산 에틸-n-헥산)
40	n-Bu		H	-COOH	117~120 (분해) (아세트산 에틸-n-헥산)
41	n-Bu		H	-COOH	149~150 (분해) (아세트산 에틸-n-헥산)
42	n-Bu	Ph	H	-COOH	유상물 (NMR 19)
43	n-Bu		H	-COOH	157~158 (분해) (아세트산 에틸-n-헥산)
44	n-Bu		H	-COOH	133~135 (분해) (아세트산 에틸-n-헥산)




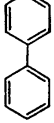
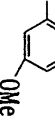
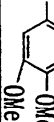
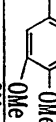
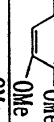
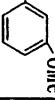
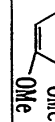

[1f]

질서 예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
45	n-Bu		H	-COOH	165~166 (분해) (아세트산 에틸-n-헥산)
46	n-Bu		H	-COOH	140~142 (분해) (아세트산 에틸-n-헥산)
47	n-Bu		H	-COOH	130~132 (분해) (아세트산 에틸-n-헥산)
48	n-Bu		H	-COOH	166~168 (분해) (아세트산 에틸-n-헥산)
49	n-Bu		H	-COOH	유상물 (NMR 2.0)
50	n-Bu		H	-COOH	110~113 (분해) (아세트산 에틸-n-헥산)
51	n-Bu		H	-COOH	155~156 (분해) (아세트산 에틸-n-헥산)
52	n-Bu		H	-COOH	열산염 130~132 (분해) (아세트산 에틸)
53	Ph		H	-COOH	206~208 (분해) (클로로포름-아세트산 에틸)
54			H	-COOH	212~214 (분해) (클로로포름-아세트산 에틸)

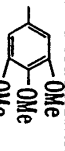
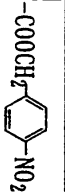
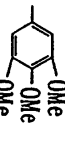
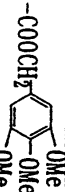

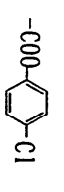
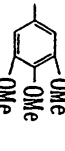

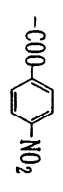
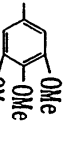
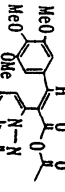
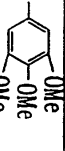
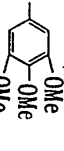

[19]

실시예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
55	n-Bu		H	-COOH	168~169 (분해) (아세트산 에틸-n-헥산)
56	n-Bu		H	-COOH	158~159 (분해) (아세트산 에틸-n-헥산)
57	n-Bu		H	-COOH	160~161 (분해) (아세트산 에틸-n-헥산)
58	n-Bu	H	H	-COOH	유상물 (NMR 2.1)
59	n-Bu		H	-COOH	195~196 (분해) (클로로포름-아세트산 에틸)
60	n-Bu	H		H	89~91 (n-헥산)
61	n-Bu	H		H	66~68 (n-헥산)
62	n-Bu	H		H	134~136 (분해) (아세트산 에틸-n-헥산)
63	Ph	H		H	119~121 (아세트산 에틸-n-헥산)
64		H		H	133~135 (아세트산 에틸-n-헥산)


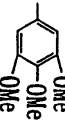
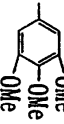
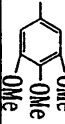

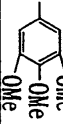

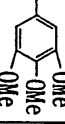
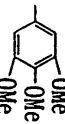
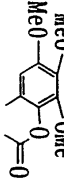
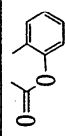
[1h]

질서 예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
65	n-Bu	H		H	125~127 (아세트산 에틸- <i>n</i> -헥산)
66	n-Bu	H		H	89~91 (아세트산 에틸- <i>n</i> -헥산)
67	n-Bu	H		H	71~73 (에탄올-물)
68	n-Bu	H		H	117~119 (물투엔)
69	n-Bu	H		H	64~66 (에탄올- <i>n</i> -헥산)
70 (=31)	n-Bu		H	-COOEt	50~52 (<i>n</i> -헥산)
71	n-Bu		H	-COOCH ₂ SPh	유상물 (NMR 2.2)
72	n-Bu		H	-COOCH ₂ - 	유상물 (NMR 2.3)
73	n-Bu		H	-COOCH ₂ - 	99~101 (아세트산 에틸- <i>n</i> -헥산)

[1i]

실시예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
74	n-Bu		H		89~91 (아세트산 에틸-n-헥산)
75	n-Bu		H		유상물 (NMR 24)
76	n-Bu		H		78~80 (디에틸에테르-n-헥산)
77	n-Bu		H	-COOPh	유상물 (NMR 25)
78	n-Bu		H		110~111 (디에틸에테르-n-헥산)
79	n-Bu		H		123~125 (디에틸에테르-n-헥산)
80	n-Bu		H	-CONHEt	150~152 (아세트산 에틸-n-헥산)
81	n-Bu		H	-CONH ₂	134~136 (아세트산 에틸-n-헥산)
82	n-Bu		H	-CONHMe	128~130 (아세트산 에틸-n-헥산)

[1]

실시 예No.	R ¹	R ²	R ³	R ⁴	용점 (°C) / 재결정 용매
83	n-Bu		H	-CONH-i-Pr	126~128 (아세트산 에틸-n-헥산)
84	n-Bu		H	-CONHCH ₂ Ph	154~155 (디에틸에테르)
85	n-Bu		H	-CONHCH ₂ CO ₂ Et	135~136 (아세트산 에틸-n-헥산)
86	n-Bu		H	-CONH 	101~103 (아세트산 에틸-n-헥산)
87	n-Bu		H	-CONH 	161~163 (아세트산 에틸-n-헥산)
88	n-Bu	H		-SOMe	100~102 (아세트산 에틸-n-헥산)
89	n-Bu		H	-SO ₂ Me	97~100 (아세트산 에틸-n-헥산)
90	n-Bu	H			127~129 (아세트산 에틸-n-헥산)
91	n-Bu	H			116~118 (아세트산 에틸-n-헥산)

^

^NMR

NMR 1 (CDCl₃, δ ppm) :

0. 8 9 (3 H, t, J = 7. 2), 1. 2 - 1. 4
(2 H, m), 1. 5 - 1. 6 (2 H, m), 2. 6 5
(2 H, t, J = 7. 4), 6. 4 9 (1 H, s),
6. 6 4 (1 H, d, J = 2. 5), 7. 0 8 (1 H,
d d, J = 1 2. 6, 0. 5), 7. 1 4 (1 H, d,
J = 1 2. 6), 8. 1 0 (1 H, d, J = 2. 5)。

NMR 2 (CDCl₃, δ ppm) :

0. 8 8 (3 H, t, J = 7. 2), 1. 1 8 (3 H,
t, J = 7. 2), 1. 2 - 1. 4 (2 H, m),
1. 6 - 1. 7 (2 H, m), 2. 7 6 (2 H, t, J
= 7. 4), 4. 2 4 (2 H, q, J = 7. 2),
6. 5 1 (1 H, s), 6. 6 5 (1 H, d, J =
2. 5), 7. 1 - 7. 3 (3 H, m), 8. 0 7 (1
H, d, J = 2. 5), 8. 1 7 (1 H, s)。

NMR 3 (CDCl₃, δ ppm) :

0. 9 1 (3 H, t, J = 7. 2), 1. 1 7 (3 H,
t, J = 6. 9), 1. 2 - 1. 4 (2 H, m),
1. 6 - 1. 8 (2 H, m), 2. 8 0 (2 H, t, J
= 7. 4), 3. 7 5 (3 H, s), 4. 2 2 (2 H,
q, J = 6. 9), 6. 5 8 (1 H, s), 6. 6 5
(1 H, d, J = 2. 2), 6. 6 8 (2 H, d, J =

8. 7), 6. 9 6 (2 H, d, J = 8. 7),
8. 0 6 (1 H, d, J = 2. 2), 8. 1 1 (1 H,
s).

NMR 4 (CDCl₃, δ ppm) :

0. 9 1 (3 H, t, J = 7. 4), 1. 1 8 (3 H,
t, J = 6. 9), 1. 3 - 1. 4 (2 H, m),
1. 6 - 1. 8 (2 H, m), 2. 4 1 (3 H, s),
2. 7 9 (2 H, t, J = 7. 7), 4. 2 3 (2 H,
q, J = 6. 9), 6. 5 5 (1 H, s), 6. 6 5
(1 H, d, J = 2. 2), 6. 9 1 (2 H, d, J =
8. 7), 6. 9 9 (2 H, d, J = 8. 7),
8. 0 6 (1 H, d, J = 2. 2), 8. 1 0 (1 H,
s).

NMR 5 (CDCl₃, δ ppm) :

0. 9 2 (3 H, t, J = 7. 4), 1. 1 7 (3 H,
t, J = 7. 2), 1. 3 - 1. 4 (2 H, m),
1. 7 - 1. 8 (2 H, m), 2. 8 1 (2 H, t, J
= 7. 7), 2. 9 4 (6 H, s), 4. 2 1 (2 H,
q, J = 7. 2), 6. 4 2 (2 H, d, J = 9. 2),
6. 6 4 (1 H, d, J = 2. 5), 6. 6 5 (1 H,
s), 6. 8 8 (2 H, d, J = 9. 2), 8. 0 4
(1 H, d, J = 2. 5), 8. 0 7 (1 H, s).

NMR 6 (CDCl₃, δ ppm) :

0.87 (3H, t, $J=7.4$), 1.19 (3H, t, $J=6.9$), 1.2-1.4 (2H, m), 1.6-1.7 (2H, m), 2.76 (2H, t, $J=7.4$), 4.26 (2H, q, $J=6.9$), 6.45 (1H, s), 6.67 (1H, d, $J=2.5$), 7.12 (2H, d, $J=7.9$), 7.44 (2H, d, $J=7.9$), 8.08 (1H, d, $J=2.5$), 8.18 (1H, s).

NMR 7 (CDCl₃, δ ppm) :

0.91 (3H, t, $J=7.2$), 1.17 (3H, t, $J=6.9$), 1.3-1.4 (2H, m), 1.7-1.8 (2H, m), 2.81 (2H, t, $J=7.7$), 4.22 (2H, q, $J=6.9$), 5.91 (2H, s), 6.36 (1H, d, $J=1.5$), 6.58 (1H, s), 6.6-6.7 (3H, m), 8.06 (1H, s), 8.06 (1H, d, $J=1.5$).

NMR 8 (CDCl₃, δ ppm) :

0.88 (3H, t, $J=7.4$), 1.18 (3H, t, $J=7.2$), 1.2-1.4 (2H, m), 1.6-1.7 (2H, m), 2.75 (2H, t, J

= 7. 7), 3. 7 7 (3 H, s), 3. 8 1 (3 H, s), 3. 8 9 (3 H, s), 4. 2 4 (2 H, q, J = 7. 2), 6. 3 0 (2 H, d, J = 1. 0), 6. 4 7 (1 H, s), 6. 6 3 (1 H, d, J = 2. 2), 8. 0 7 (1 H, d, J = 2. 2), 8. 3 2 (1 H, s).

NMR 9 (CDCl₃, δ ppm) :

0. 8 0 (3 H, t, J = 7. 4), 1. 2 1 (3 H, t, J = 7. 2), 1. 2 - 1. 3 (2 H, m), 1. 6 - 1. 7 (2 H, m), 2. 7 4 (2 H, t, J = 7. 7), 4. 2 7 (2 H, q, J = 7. 2), 6. 5 4 (1 H, s), 6. 6 8 (1 H, d, J = 2. 2), 6. 9 0 (1 H, dd, J = 1. 7, 8. 7), 7. 4 - 7. 6 (3 H, m), 7. 6 - 7. 8 (3 H, m), 8. 0 9 (1 H, d, J = 2. 2), 8. 3 3 (1 H, s).

NMR 10 (CDCl₃, δ ppm) :

0. 9 6 (3 H, t, J = 7. 4), 1. 1 9 (3 H, t, J = 7. 2), 1. 4 - 1. 5 (2 H, m), 1. 7 - 1. 9 (2 H, m), 2. 8 7 (2 H, t, J = 7. 7), 4. 2 3 (2 H, q, J = 7. 2), 6. 3 6 (1 H, dd, J = 2. 0, 3. 5), 6. 4 9

(1 H, d, $J = 3.5$), 6.62 (1 H, d, $J = 2.2$), 6.71 (1 H, s), 7.20 (1 H, d, $J = 2.0$), 7.91 (1 H, s), 8.00 (1 H, d, $J = 2.2$).

NMR 11 (CDCl₃, δ ppm) :

1.23 (3 H, t, $J = 7.2$), 3.44 (6 H, s), 3.77 (3 H, s), 4.28 (2 H, q, $J = 7.2$), 6.26 (2 H, s), 6.79 (1 H, d, $J = 2.2$), 7.21 (1 H, s), 7.4 - 7.6 (3 H, m), 8.0 - 8.1 (2 H, m), 8.15 (2 H, br s).

NMR 12 (CDCl₃, δ ppm) :

0.86 (3 H, t, $J = 7.4$), 1.20 (3 H, t, $J = 7.2$), 1.2 - 1.3 (2 H, m), 1.6 - 1.7 (2 H, m), 2.72 (2 H, t, $J = 7.4$), 3.22 (3 H, s), 3.61 (3 H, s), 4.25 (2 H, q, $J = 7.2$), 6.15 (1 H, d, $J = 2.7$), 6.43 (1 H, s), 6.62 (1 H, d, $J = 2.2$), 6.7 - 6.9 (2 H, m), 8.09 (1 H, d, $J = 2.2$), 8.35 (1 H, s).

NMR 13 (CDCl₃, δ ppm) :

0. 9 1 (3 H, t, J = 7. 2), 1. 2 1 (3 H, t, J = 7. 2), 1. 3 - 1. 4 (2 H, m), 1. 6 - 1. 8 (2 H, m), 2. 8 0 (2 H, t, J = 7. 4), 3. 3 0 (3 H, s), 3. 8 3 (3 H, s), 4. 2 5 (2 H, q, J = 7. 2), 6. 2 2 (1 H, d, J = 2. 0), 6. 6 0 (1 H, s), 6. 6 5 (1 H, d, J = 2. 2), 6. 7 0 (1 H, d, J = 8. 2), 6. 7 9 (1 H, d d, J = 2. 0, 8. 2), 8. 0 6 (1 H, d, J = 2. 2), 8. 1 2 (1 H, s).

NMR 1 4 (C D C l 3, δ ppm) :

0. 9 8 (3 H, t, J = 7. 2), 1. 1 4 (3 H, t, J = 7. 2), 1. 4 - 1. 5 (2 H, m), 1. 7 - 1. 8 (2 H, m), 2. 8 7 (2 H, t, J = 7. 7), 4. 2 5 (2 H, q, J = 7. 2), 6. 6 2 (1 H, d, J = 2. 2), 6. 7 8 (1 H, s), 7. 3 7 (2 H, d, J = 8. 7), 7. 4 5 (2 H, d, J = 8. 7), 7. 6 9 (1 H, s), 8. 0 4 (1 H, d, J = 2. 2).

NMR 1 5 (C D C l 3, δ ppm) :

0. 9 0 (3 H, t, J = 7. 2), 1. 1 8 (3 H, t, J = 7. 2), 1. 2 - 1. 4 (2 H, m),

1. 6 - 1. 7 (2 H, m), 2. 7 8 (2 H, t, J = 7. 7), 4. 2 4 (2 H, q, J = 7. 2), 6. 5 0 (1 H, s), 6. 6 6 (1 H, d, J = 2. 4), 6. 9 4 (2 H, d, J = 6. 7), 7. 1 4 (2 H, d, J = 6. 7), 8. 0 7 (1 H, d, J = 2. 4), 8. 1 1 (1 H, s).

NMR 1 6 (C D C l₃, δ ppm) :

0. 9 5 (3 H, t, J = 7. 4), 1. 1 5 (3 H, t, J = 6. 9), 1. 4 - 1. 5 (2 H, m), 1. 8 - 1. 9 (2 H, m), 2. 8 7 (2 H, t, J = 7. 7), 3. 8 8 (6 H, s), 3. 9 1 (3 H, s), 4. 2 5 (2 H, q, J = 6. 9), 6. 6 2 (1 H, d, J = 2. 5), 6. 7 8 (1 H, s), 6. 8 2 (2 H, s), 7. 7 2 (1 H, s), 8. 0 5 (1 H, d, J = 2. 5).

NMR 1 7 (C D C l₃, δ ppm) :

0. 9 0 (3 H, t, J = 7. 4), 1. 2 2 (3 H, t, J = 7. 2), 1. 3 - 1. 4 (2 H, m), 1. 6 - 1. 8 (2 H, m), 2. 7 9 (2 H, t, J = 7. 7), 4. 2 7 (2 H, q, J = 7. 2), 6. 5 5 (1 H, s), 6. 6 1 (1 H, d, J = 2. 5), 7. 1 0 (1 H, d d, J = 4. 2, 7. 9),

7. 11 (1H, d, $J = 7.9$), 7. 53 (1H, dt, $J = 1.7, 7.9$), 7. 99 (1H, d, $J = 2.5$), 8. 16 (1H, s), 8. 27 (1H, dd, $J = 1.7, 4.2$).

NMR 18 (CDCl₃, δ ppm) :

1. 22 (3H, t, $J = 7.2$), 3. 45 (6H, s), 3. 77 (3H, s), 4. 27 (2H, q, $J = 7.2$), 6. 28 (2H, s), 6. 72 (1H, d, $J = 2.5$), 7. 08 (1H, s), 7. 12 (1H, dd, $J = 3.7, 4.9$), 7. 51 (1H, dd, $J = 1.0, 4.9$), 7. 60 (1H, dd, $J = 1.0, 3.7$), 8. 11 (1H, d, $J = 2.5$), 8. 14 (1H, s).

NMR 19 (CDCl₃, δ ppm) :

0. 87 (3H, t, $J = 7.4$), 1. 2 - 1. 4 (2H, m), 1. 6 - 1. 7 (2H, m), 2. 76 (2H, t, $J = 7.4$), 6. 54 (1H, s), 6. 68 (1H, d, $J = 2.5$), 6. 9 - 7. 0 (2H, m), 7. 1 - 7. 3 (3H, m), 8. 10 (1H, d, $J = 2.5$), 8. 22 (1H, s).

NMR 20 (CDCl₃, δ ppm) :

0. 87 (3H, t, $J = 7.2$), 1. 2 - 1. 4

(2 H, m), 1.6 - 1.8 (2 H, m), 2.76
(2 H, t, J = 7.4), 3.77 (3 H, s),
3.81 (3 H, s), 3.88 (3 H, s),
6.30 (2 H, s), 6.52 (1 H, s),
6.66 (1 H, d, J = 2.0), 8.08 (1 H,
d, J = 2.0), 8.42 (1 H, s).

NMR 21 (CDCl₃, δ ppm) :

0.85 (3 H, t, J = 7.2), 1.2 - 1.3
(2 H, m), 1.5 - 1.7 (2 H, m), 2.72
(2 H, t, J = 7.7), 3.20 (3 H, s),
3.61 (3 H, s), 6.13 (1 H, d, J =
3.0), 6.48 (1 H, s), 6.65 (1 H, d,
J = 2.5), 6.73 (1 H, d, J = 9.2),
6.80 (1 H, dd, J = 3.0, 9.2),
8.12 (1 H, d, J = 2.5), 8.45 (1 H,
s).

NMR 22 (CDCl₃, δ ppm) :

0.90 (3 H, t, J = 7.2), 1.2 - 1.4
(2 H, m), 1.6 - 1.7 (2 H, m), 2.77
(2 H, t, J = 7.7), 3.44 (6 H, s),
3.79 (3 H, s), 5.48 (2 H, s),
6.19 (2 H, s), 6.57 (1 H, s),

6. 6 5 (1 H, d, J = 2. 5), 7. 1 - 7. 2
 (5 H, m), 8. 0 6 (1 H, d, J = 2. 5),
 8. 1 4 (1 H, s)。

NMR 2 3 (C D C 1 3, δ ppm) :

0. 9 0 (3 H, t, J = 7. 4), 1. 3 - 1. 4
 (2 H, m), 1. 6 - 1. 8 (2 H, m), 2. 7 8
 (2 H, t, J = 7. 7), 3. 4 4 (6 H, s),
 3. 7 5 (3 H, s), 3. 7 8 (3 H, s),
 5. 2 1 (2 H, s), 6. 1 8 (2 H, s),
 6. 5 8 (1 H, s), 6. 6 4 (1 H, d, J =
 2. 2), 6. 7 - 6. 9 (3 H, m), 7. 2 2 (1
 H, t, J = 7. 9), 8. 0 9 (1 H, d, J =
 2. 2), 8. 1 4 (1 H, s)。

NMR 2 4 (C D C 1 3, δ ppm) :

0. 8 9 (3 H, t, J = 7. 2), 1. 2 - 1. 4
 (2 H, m), 1. 6 - 1. 7 (2 H, m), 2. 7 8
 (2 H, t, J = 7. 7), 3. 4 4 (6 H, s),
 3. 7 7 (6 H, s), 3. 7 8 (3 H, s),
 3. 8 2 (3 H, s), 5. 1 6 (2 H, s),
 6. 1 8 (2 H, s), 6. 3 8 (2 H, s),
 6. 5 9 (1 H, s), 6. 6 4 (1 H, d, J =
 2. 5), 8. 0 8 (1 H, d, J = 2. 5),
 8. 1 4 (1 H, s)。

NMR 2 5 (C D C 1 3, δ ppm) :

0. 9 1 (3 H, t, J = 7. 4), 1. 3 - 1. 5
 (2 H, m), 1. 7 - 1. 8 (2 H, m), 2. 8 2
 (2 H, t, J = 7. 7), 3. 4 7 (6 H, s),
 3. 8 1 (3 H, s), 6. 2 6 (2 H, s), 6. 6
 6 (1 H, d, J = 2. 2), 6. 7 0 (1 H, s),
 7. 1 - 7. 4 (5 H, m), 8. 1 4 (1 H, d, J
 = 2. 2), 8. 2 8 (1 H, s)。

< 92>

1

60

2

< 93 94>

8 9

2

< 95 98>

3

. 1-(5-n- [1,5-a] -7-)
 . 1-(5-n- [1,5-a] -7-)-(4-)

1
12 (5-n- [1,5-a] -7-)
2

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85 86 40 가 , 2

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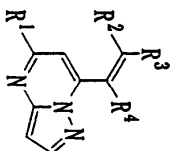
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· (E)- -2-(5- [1,5-a] -7-)-3-(3,4,5-)
· (E)- -2-(5-n- [1,5-a] -7-)-3-(3,4,5-)
97 98 40 가

2
< 106 108>
101 103 60 , 2

< 109>
(E)-2-(5-n- [1,5-a] -7-)-3-(4- -3,5-)
105 2 g 20 ml , 5 % - 0.2 g 가
, 30 (: 94 ml). , 5 % -
5:1) , -n- (... 1.5 g : =2
2

< 110>
1 (5-n- [1,5-a] -7-) 3-
-4,5- 12 (E)- -2-(5-n- [1,5-a]
-7-)-3-(3- -4,5-) 가 2
, 109 가 2

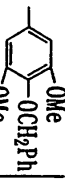
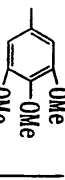


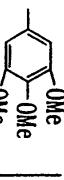
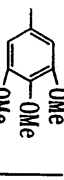
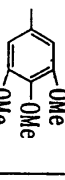
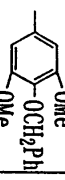
[2a]



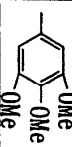
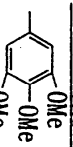
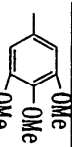
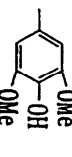
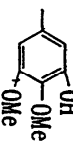
Me=메틸기, Et=에틸기, i-Pr=이소프로필기, n-Pr=n-프로필기, n-Bu=n-부틸기
Ph=페닐기

실시예No.	R ¹	R ²	R ³	R ⁴	융점 (°C) / 재결정 용매
92	n-Bu	H		H	64~66 (n-헥산)
93	n-Bu	H	-C≡C-Ph	H	79~83 (에탄올-물)
94	n-Bu	-C≡C-Ph	H	H	49~50 (에탄올-물) :
95	n-Bu		H	Ph	103~105 (다이소프로필에테르)
96	n-Bu		H		89~92 (다이에틸에테르-n-헥산)

[2b]

실시 예No.	R ¹	R ²	R ³	R ⁴	융점 (°C) / 재결정 용매
97	n-Bu	-C≡C-Ph	H	-COOMe	100~103 (디이소프로필에테르)
98	n-Bu		H	-COOMe	134~137 (메탄올)
99	n-Bu		H	-CONHCH ₂ CO ₂ H	113 이상 (분해) (아세트산 에틸-n-헥산)
100	n-Bu		H	-CONH- 	127~130 (디에틸에테르-n-헥산)
101	Me		H	-COOH	172 이상 (분해) (아세트산 에틸-n-헥산)
102	Et		H	-COOH	165 이상 (분해) (아세트산 에틸-n-헥산)
103	n-Pr		H	-COOH	175 이상 (분해) (아세트산 에틸-n-헥산)
104	n-Bu	-C≡C-Ph	H	-COOH	155 이상 (분해) (아세트산 에틸-n-헥산)
105	n-Bu		H	-COOH	155 이상 (분해) (아세트산 에틸-n-헥산)

[2c]

실시예No.	R ¹	R ²	R ³	R ⁴	응점 (°C) / 재결정 용매
106	Me	H		H	157~160 (에탄올)
107	Et	H		H	164~166 (아세트산에틸-n-헥산)
108	n-Pr	H		H	96~99 (아세트산에틸-n-헥산)
109	n-Bu		H	-COOH	152이상 (분해) (아세트산에틸-n-헥산)
110	n-Bu		H	-COOH	185이상 (분해) (에탄올-n-헥산)

< 1> 10 , 1 250 mg (1000)

	(g)
10	250
()	33.5
()	16.5
()	12.5
()	6.0
()	1.5
	320.0

, 10 , , 24

< 2> 40 , 1 250 mg (1000)

	(g)
40	250
()	30
()	17
()	2
()	1
	300

< 1>
 6 S.D. 1 7
 () [Randall, L. O. and Sellitto. J.J., Arch. Int. Pharmacodyn.,
 111, 409(1957)]
 " " 5 % 5 %
 10 ml/kg
 (substance) P 25 ng/0.1 ml
 P
 " "
 () (%)
 (%) = { [() - ()] / [() - ()] } × 100
 () 3

[3]

실시예 No.	회복률	측정시 (분후)
1	4 7 . 8	6 0
8	3 6 . 2	3 0
1 0	5 8 . 7	6 0
1 2	4 1 . 5	6 0
4 0	4 7 . 2	6 0
4 3	4 6 . 3	3 0
4 5	4 0 . 4	6 0
4 6	4 8 . 9	6 0
4 7	5 7 . 1	3 0
6 2	5 0 . 0	3 0
6 5	3 0 . 1	3 0
6 6	3 2 . 2	6 0
7 4	5 0 . 3	1 5
7 8	6 0 . 1	1 5
7 9	4 1 . 2	6 0
9 8	4 4 . 7	6 0
9 9	3 2 . 2	6 0
1 0 3	5 4 . 8	6 0
1 0 5	5 0 . 4	6 0
1 0 9	5 2 . 1	6 0
1 1 0	5 8 . 0	6 0

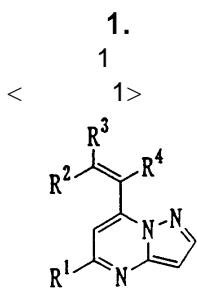
3

가

[1,5-a]

가

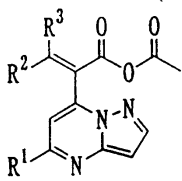
(57)



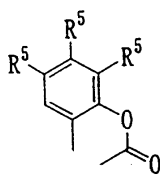
[1,5-a]

R¹ ,
 R² R³ , ; ; ; ; ;
 , N,N- , 1 3
 , 가 ,

R⁴ ; ; ; ; ;
 ; ; 1 3
 ; N- ; N- ; N-()
 ; N-() ; N- ; N-(1- -2-)
 ; N-(1- -2-) ; ; -2-)



(, R¹, R² R³) ,



(, R⁵

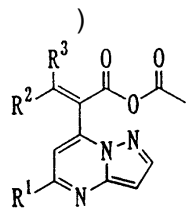
, R² 가 , R³ R⁴)

2.

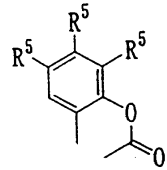
(i) R¹ , (ii) R¹ , R² R³ 가 ,
 가 1 3 , R⁴ 가 ,
 [1,5-a] .

3.

(1a) R¹ , R⁴ 가 , (i) ,
 (1b) R¹ , R² R³ 가 , 가 1
 3 , R⁴ 가 ; ; ; 1
 ; N- ; N- ; N-() ; N-(
) ; N-(1- -2-) ;



(, R¹, R² R³) (i)



(, R⁵

(1c) R¹ , R² 가 , R³ R⁴ 가
 [1,5-a])

(i)

4.

3 , R¹ n- [1,5-a] .

5.

2 , R¹ , R² R³ 가 , 가
 1 3 , R⁴ 가 , (ii)
 [1,5-a] .

6.

(i) R¹ n- , R² 가 , R³ ; ;
 3 ; , R⁴ 가 1

(ii) R¹ n- , R² 가 1, 3 , R³ , N,N- , R⁴ 가 ,



[1,5-a]
7.

6
(i) R³ , R⁴ 가 (i)
(ii) R¹ n- , R² 가

3

[1,5-a]

8.

7
(i) R³ 2- (i)
(ii) R² 가 3,4,5- , R⁴ 가 (ii)

[1,5-a]

9.

1 [1,5-a]

10.

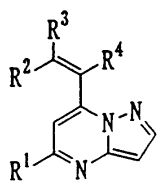
11.

12.

13.

1 [1,5-a]
가

< 1 >



, R¹ , R² R³
, R⁴ ,

[1,5-a]