

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl. ⁷
C07D 413/14

(11)
(43)

2001 - 0070442
2001 07 25

(21) 10 - 2001 - 0000631
(22) 2001 01 05

(30) 61062000 2000 01 11 (JP)
3563032000 2000 11 22 (JP)

(71) 가 가
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(72) 가 1113
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가 1113
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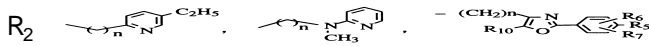
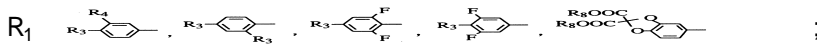
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

(54)

(I) ,
:

R₁ - A - R₂ (I)





((i)A가 -O- , n 2 3 , (ii) A가 $-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-$, n 1 2 . R₃ OH- , CH₃SO₂NH- , CF₃SO₂NH- , CH₃SO₂NHCH₂- , CF₃SO₂NHCH₂- , HOOC- , CH₃OOC- , $\text{R}_8-\text{OOC}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-$, HOOC-CH₂SO₂NH- , CF₃-CH₂SO₂NH- , HOOC--SO₂NH- , -NHSO₂- , R₈-NHSO₂-C₂H₂- , HOOC-C₂H₂-O- , HSO₃N="C₂H-," R₉-SO₂NHCO- ;

R₄ H, OH, O- O-CH₂OCH₃ ;

R₅ H, , -CH₂COOH OH ;

R₆ R₇ , t- ;

R₈ ;

R₉ ; R₁₀).

/

(Biguanide)
(hypoglycemia)

가

(acidosis)
가

-2,4- 가

(T. Yoshioka et al., J. Med. Chem. 1989, 32, 421),
ed. Chem. 1992,35,2617)
-2,4-

(H. Ikeda et al., J. M
(B.C.C.Cantello et al., J. Med. Chem. 1994, 37,3977)

-2,4-
etabolism Review 1998,14(3),207),

(R. Perfetti et al., Diabetes/M

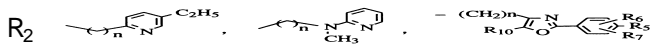
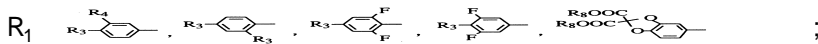
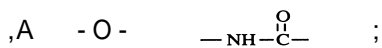
(AST), (ALT), (LDH) 가
(R.R.Henry, Endocrinol. Metab, Clin, North Am. 1997,26,553).




-2,4- , -2,4- (R.L.Dowet al., J. Med. Chem. 19
 91, 34,1538), 1- -2,4- -3,5- (S.W.Goldstein et al., J.Med.Chem. 1993,36,2238), -
 (R.A.DeFronzo, Diabetes, 1998,37,667) (H.Shinkai et al., J.Med.Chem.19
 98, 41,1927) - -2,4- .

(I)

(I)

R₁ - A - R₂ (I)



((i)A가 -O- , n 2 3 , (ii) A가 ---NH---C(=O)--- , n 1 2 . R₃ OH- , CH₃SO₂NH- , CF₃SO₂NH- , CH₃SO₂NHCH₂- , CF₃SO₂NHCH₂- , HOOC- , CH₃OOC- , $\text{R}_8\text{---OOC---C(=O)---NH---}$, HOOC-CH₂SO₂NH- , CF₃-CH₂SO₂NH- , HOOC--SO₂NH- , -SO₂NH- , -SO₂NH- , R₈-NHSO₂- , R₈-NHSO₂-CH₂- , HOOC-CH₂-O- , HSO₃N="CH-," R₉-SO₂NHCO- ;

R₄ H, OH, O- O-CH₂OCH₃ ;

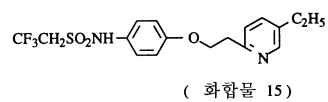
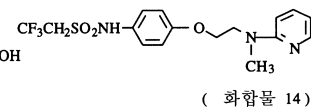
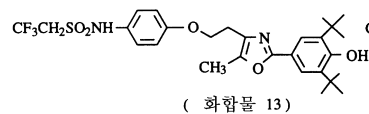
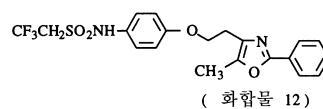
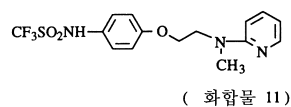
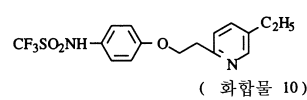
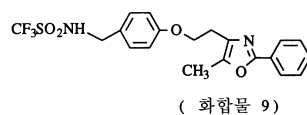
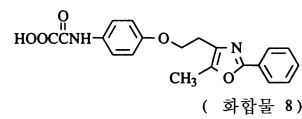
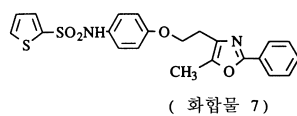
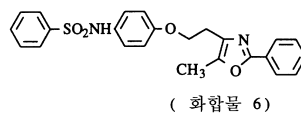
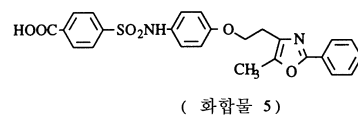
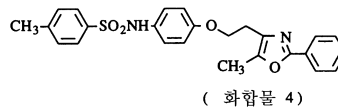
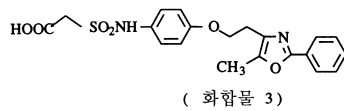
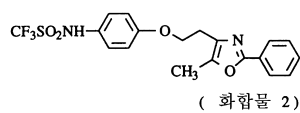
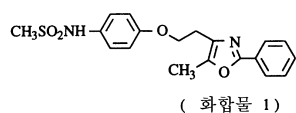
R₅ H, , -CH₂COOH OH ;

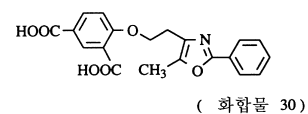
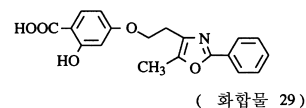
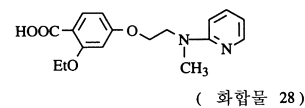
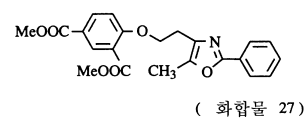
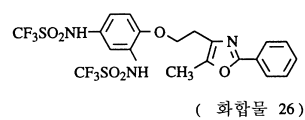
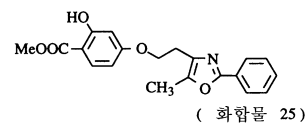
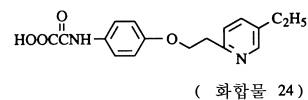
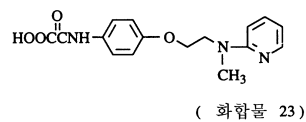
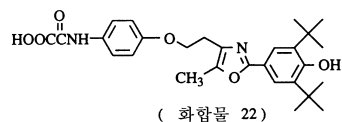
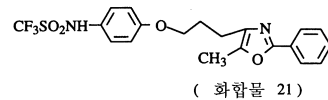
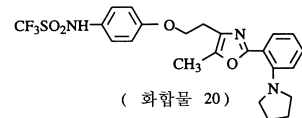
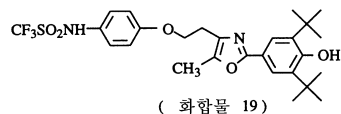
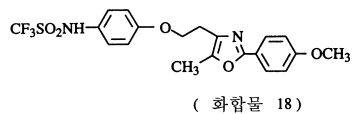
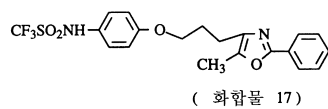
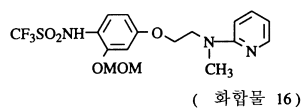
R₆ R₇ , t- ;

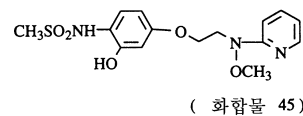
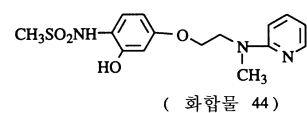
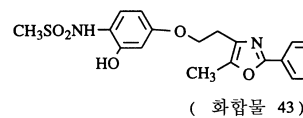
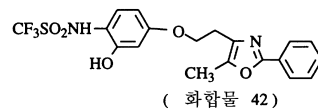
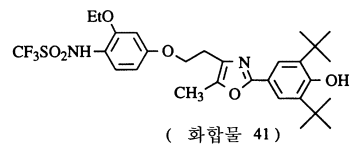
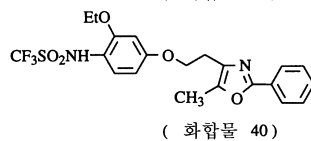
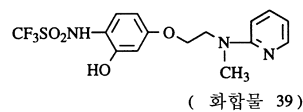
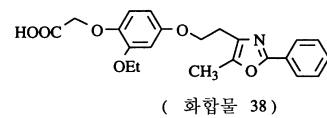
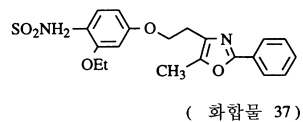
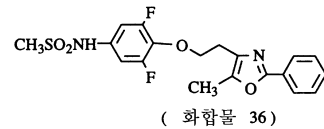
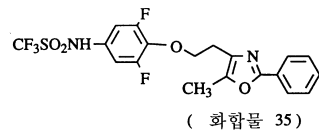
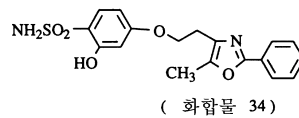
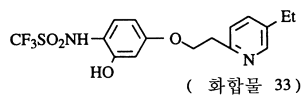
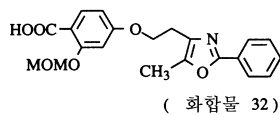
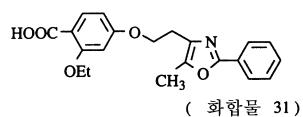
R₈ ;

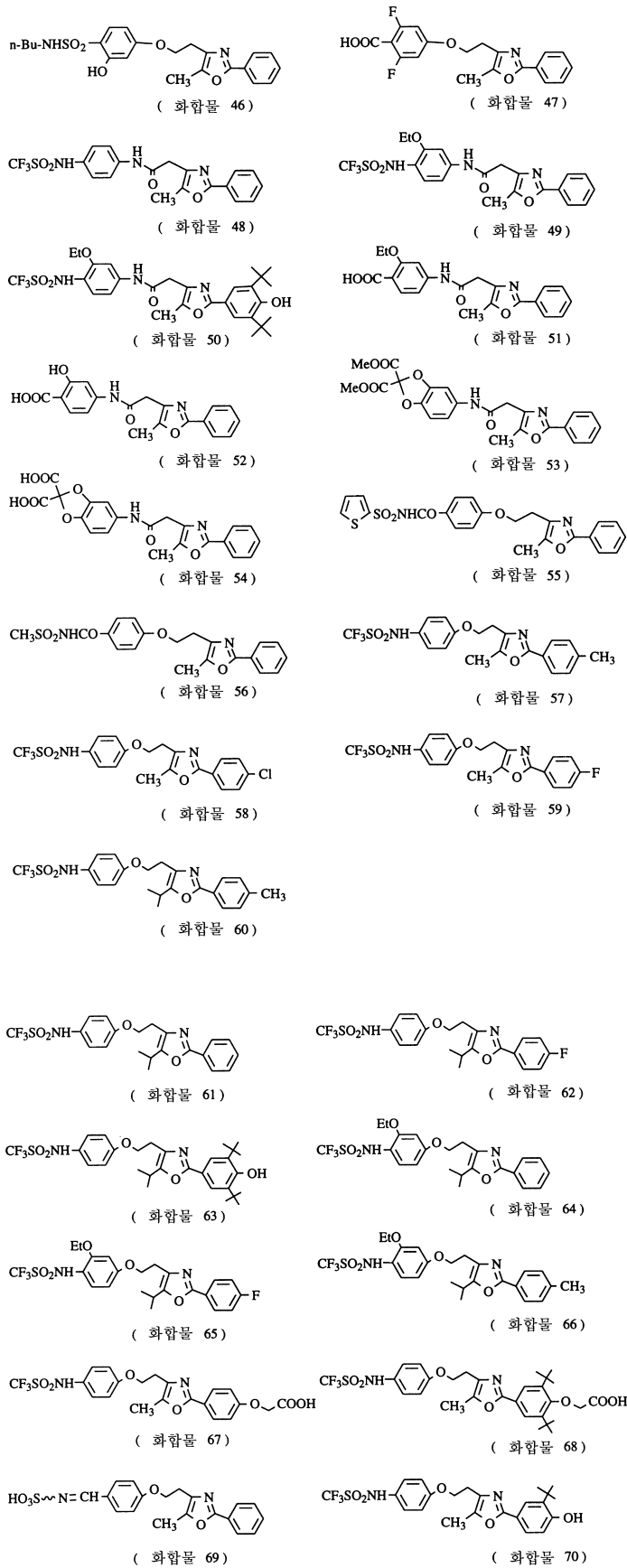
R₉ ;

R₁₀).

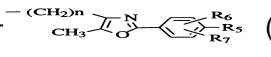


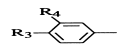


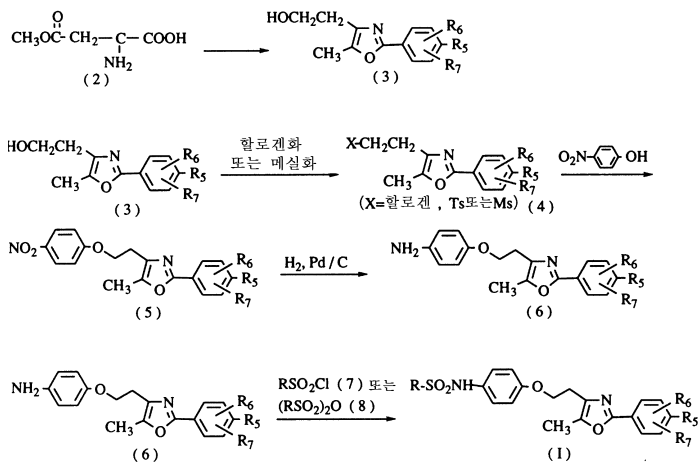


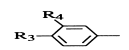


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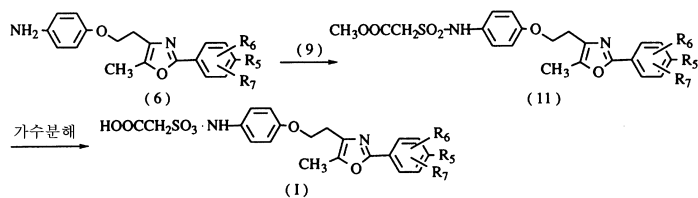
(I) A가 -O- ; R₂가  (, R₅, R₆, R₇ ; n 2)
 (I) :

(a) R₁  (, R₃ CH₃SO₂NH- CF₃SO₂NH- , R₄ H) ,
 : (2)(J. Arg. Chem.Soc.Japan, 1951 - 1952,25,129):C.A.47,6065i R.L.Prestige et al., J. Org.Chem. 1975,40,3287 (B.Helvin et al., J. Med.Chem. 1992,35,1853) (3) , (3)
 (4) (4) (5) , (5) H₂ - Pd/C
 (6) , (6) (7) (8) ,
 (I) :



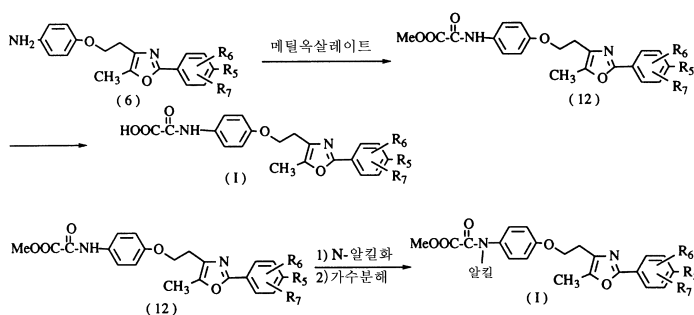
(b) R₁  (, R₃ HOOCCH₂SO₂NH- , R₄ H) ,
 : (6) EtOOC · CH₂SO₂Cl, CH₃OOCCH₂SO₂Cl(9)
 (11) , (11) 가 (I)

(9) (HOOCC₂SO₃H(10) SOCl₂ ,
 (R.L.Hinman et al. (J.Am. Chem. Soc. 1959,81,5655, (H.T.Lee et al., Bioorg. Med. Chem. Lett. 199 8,8,289)



(c) R₁  (, R₃ HOOC - CONH- , R₄ H) ,
 :

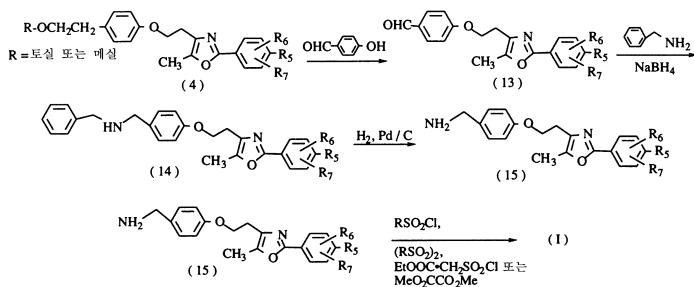
(6) (12) (12) , (12) 가 (1) (12) N - , 가 (1) :



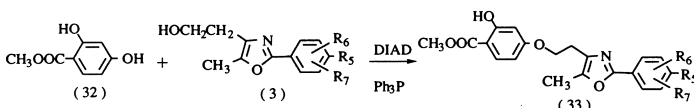
(d) R_1 (R_3 $CH_3 SO_2 NHCH_2 -$, $CF_3 SO_2 NHCH_2 -$ $HOOC - CONH -$, R_4 H)

(4) p - (13) , (13) (amination) (14) .

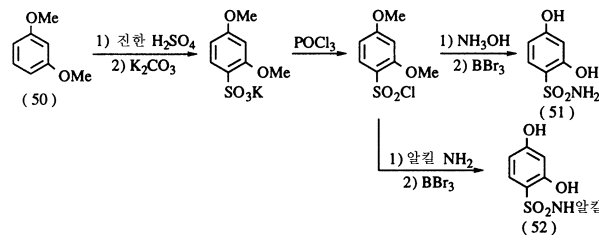
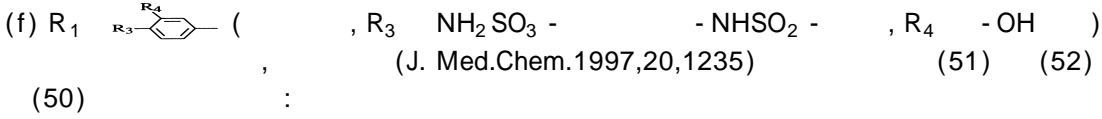
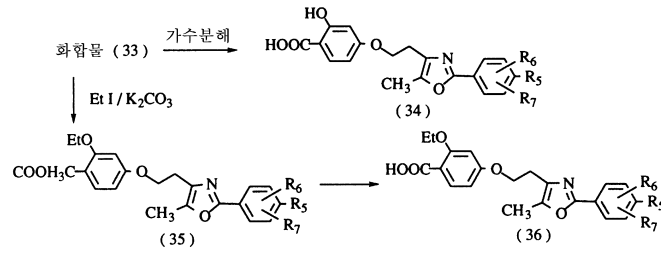
$H_2 - Pd/C$ (14) , (15) . (15) (6) (12) , $EtOOC \cdot CH_2 SO_2 Cl$, (1) :



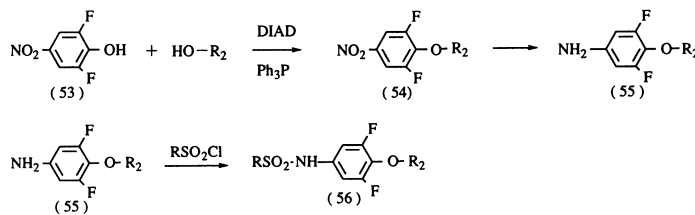
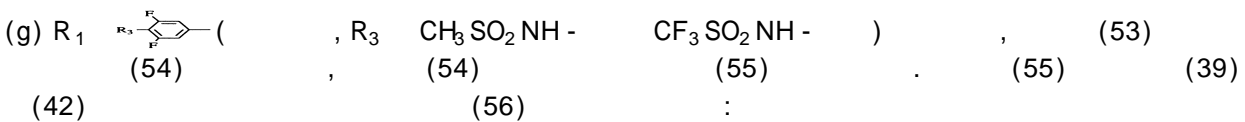
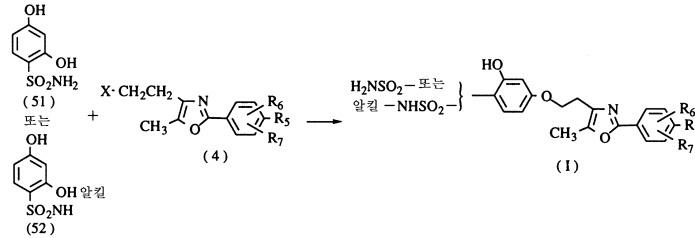
(e) R_1 (R_3 가 $HOOC -$ (32) $CH_3 OOC -$ (3) , R_4 - OH O - (MITSUNOBU)) (1) (33) .

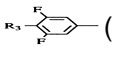


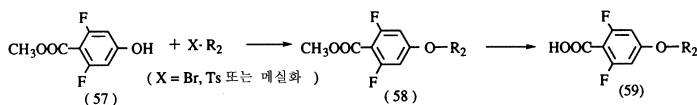
(33) (34) (36) :

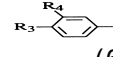


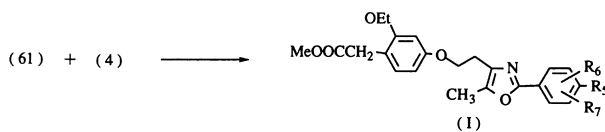
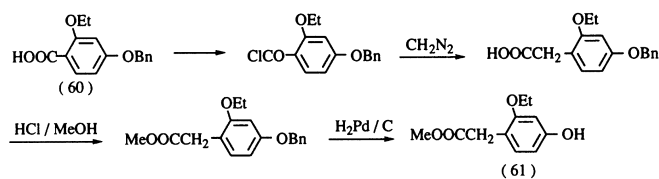
(51) (52) (4) (I) :

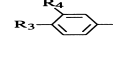


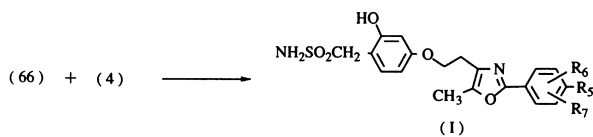
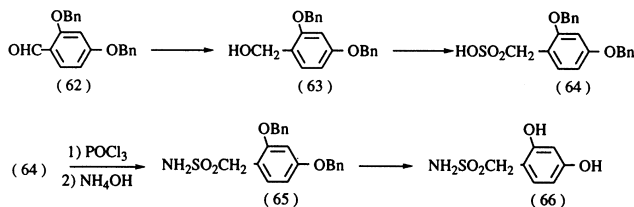
h) R₁  (4), R₃ -COOH (58), (58) 가 (I) (57) (5)



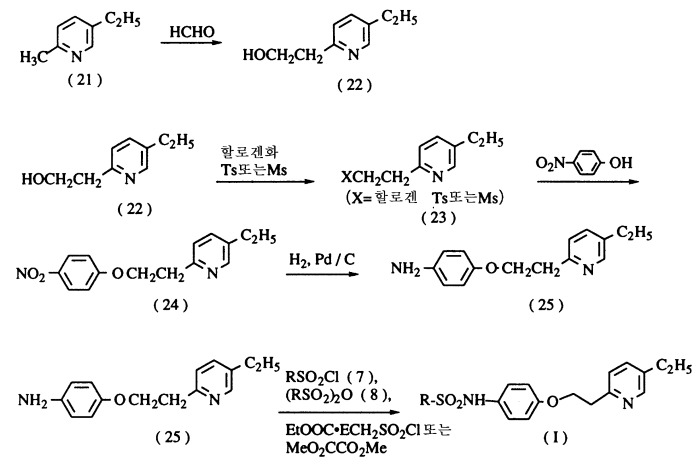
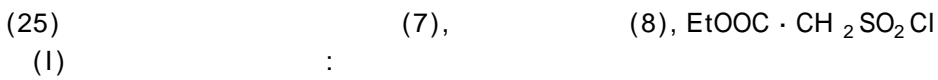
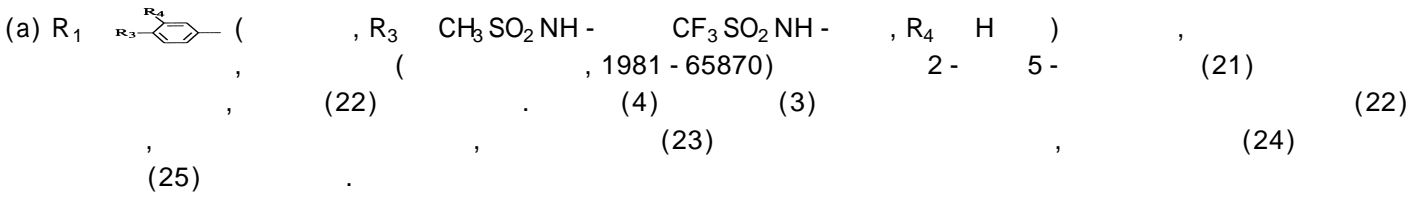
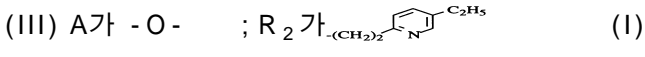
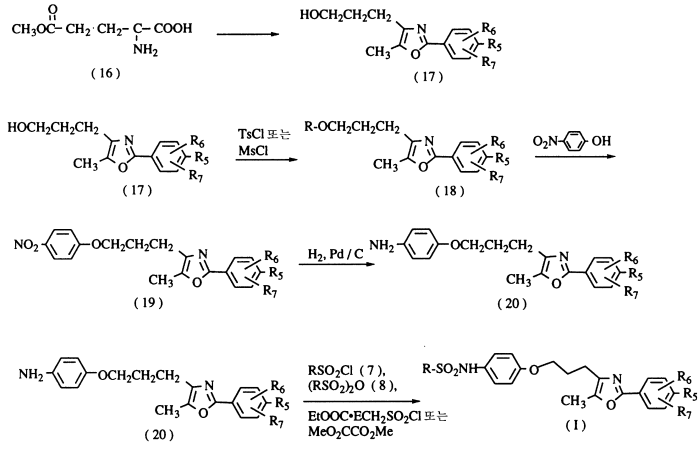
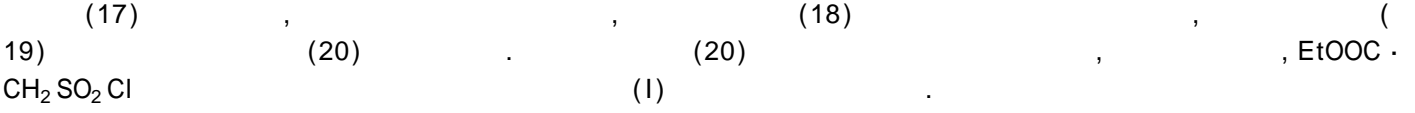
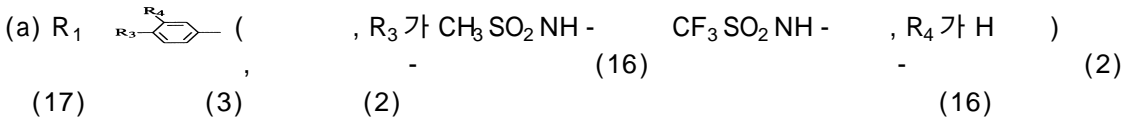
(i) R₁  (60), R₃ MeOOCCH₂- (61), R₄ -O- (4), (I) :

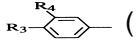


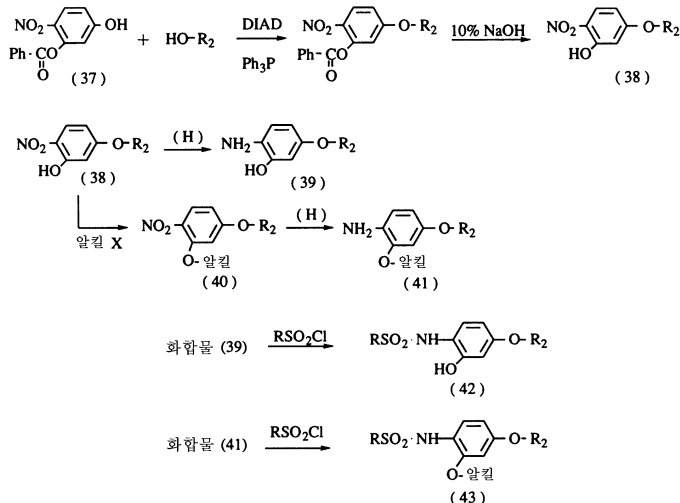
(j) R₁  (62), R₃ 가 NH₂SO₂CH₂- (63) Na₂SO₃ (64) POCl₃ (66) NH₃ (65) (I) (65) (66) (62) (64) (66) (J.C.S.Chem.Comm., 1989, 521)



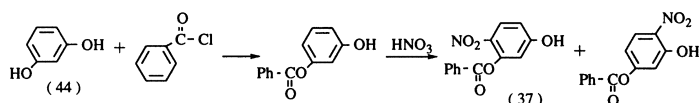
(II) A가 -O- ; R₂ 가  (CH₂)_n (I) ; R₅, R₆, R₇ ; n="3"



(b) R₁  (39), R₃ 가 CH₃ SO₂ NH - (37) CF₃ SO₂ NH - (38), R₄ - OH (38) - O - (38), (39), (38), (40), (40), (41), (39), (41) RSO₂ Cl (42), (43) :



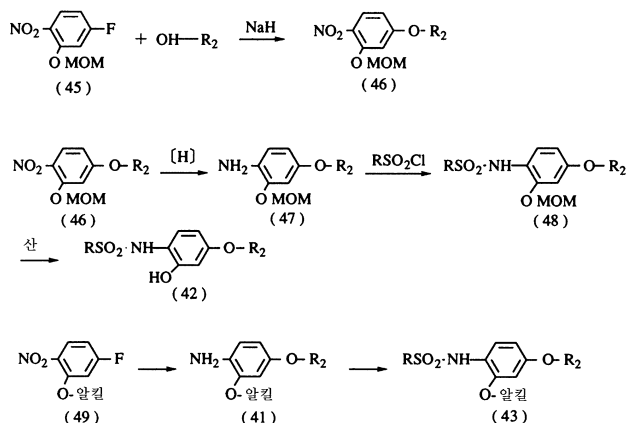
(37)

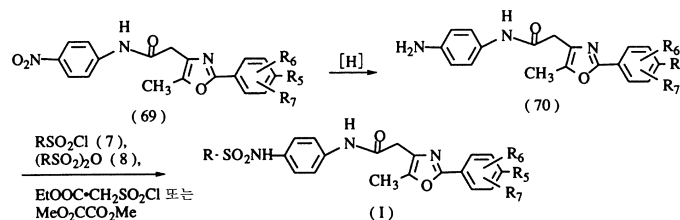
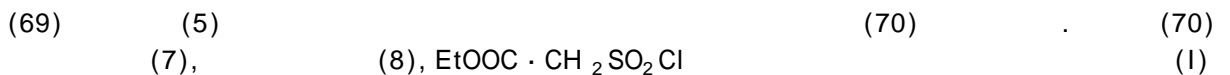
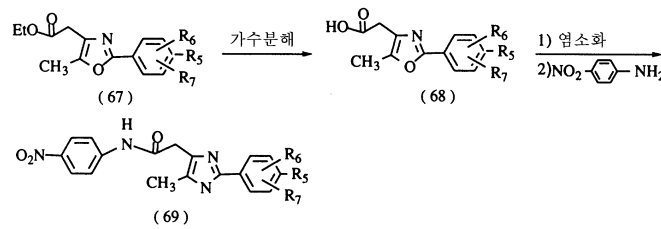
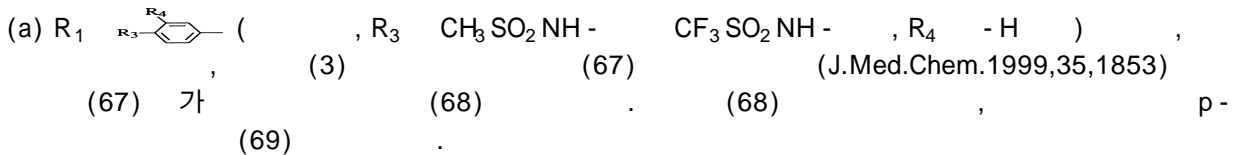
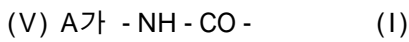
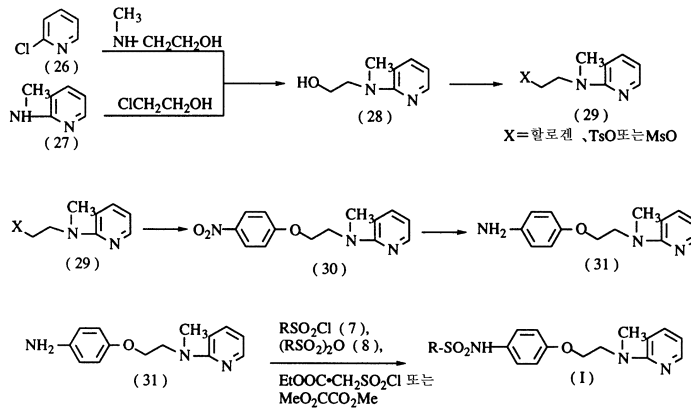
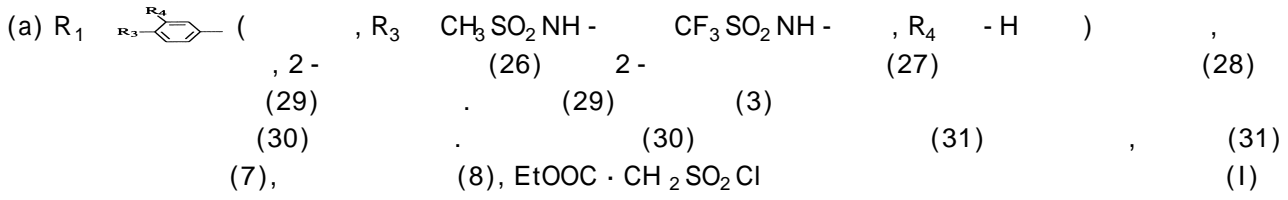
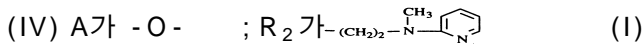


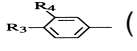
(42) (43) (Bioorg.Med.Chem.Lett., 199 4,4 (10),1181) , 2-OMOM() - 4 - (45) HO - R₂ (46) (46) (47)

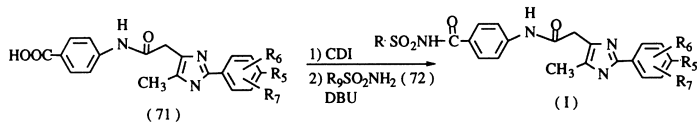
(47) RSO₂ Cl (48) , (48) MOM - (42)

(45) , (48) (46) (49) (41) , (43) (41)





(b) R₁  (, R₃ R₉ SO₂ NHCO - (R₉ = " ") , R₄ H) ,
 [5,4,0] - 7 -) (72) CDI() , DBU(1,8 -
 Med.Chem.Lett. 1955,1155). (I) (Bioorg.



(I) 가 , 가 .

R₁ , 가 .

(I) , ,

Nihon Clea 0.5%) (p.o.) . 4 1 3 - 30 mg/kg db/db (1 (300 mg/kg)

[1]

화합물 번호	투여량 (mg/kg)	혈당 저하 활성 (%)
1	30	24.6
2	10	49.0
8	10	26.0
9	10	24.0
10	10	32.4
11	10	15.4
18	10	34.7
19	10	12.8
21	10	34.6
24	10	25.7
26	30	15.1
30	30	22.1
31	30	19.0
35	30	28.8
40	30	53.4
42	10	29.6
47	10	25.6
48	30	65.4
50	30	21.9
52	30	10.5
57	3	44.0
58	3	43.4
59	3	18.4
63	3	18.4
67	3	33.1
68	3	21.2
70	30	51.0
트로글리타존	300	34.0

1

4 - [2 - (5 - 2 - 1,3 - 4 -)]

(a) 5 - 4 - 2 - -

22.2 g 5 - 4 - 2 - - (13 mL) (6 mL)

O₄ (50 mL) 가 CuSO₄ , H₂O NaCl Na₂S
 (: n - = "1:1")
 3.33 g(87.6%)

MASS(m/e):371(M+),216,186(BP),156,130,105,77,51

IR(cm⁻¹):1359,1173,966,927,834,813,753,666

¹HNMR(CDCl₃) δ : 2.01-2.08 (m, 2H, -CH₂-), 2.29 (s, 3H, -CH₃), 2.42 (s, 3H, -CH₃), 2.55 (t, 2H, -CH₂-, J=6.83,7.33Hz), 4.08 (t, 2H, -CH₂-, J=5.86,6.34Hz), 7.31 (d, 2H, 방향족, J=7.81Hz), 7.40-7.43 (m, 3H, 방향족), 7.78 (d, 2H, 방향족, J=8.3Hz), 7.93 (dd, 2H, 방향족, J=7.33, 7.81Hz)

(b) 5 - 4 - p - 2 - 1,3 -

0.21 g NaH 50 mL , n - 2 , 10 mL 가 . 0.6
 7 g p - 0 가 , 30 (5 mL)
 (a) (1.8 g) 가 , 80 ,
 (80 mL) . H₂O, NaCl , N
 a₂SO₄ 1.24 g(75.6%) ,
 (:n - = "1:3) " . m.p. = "100 - 103

MASS(m/e):338(M+),200,173(BP),130,104,77,51
 IR(cm⁻¹):1590,1500,1332,1263,1107,840
¹HNMR(CDCl₃) δ : 2.18-2.24 (m, 2H, -CH₂-), 2.29 (s, 3H, -CH₃), 2.71 (t, 2H, -CH₂-, J=7.33, 6.83Hz), 4.09 (t, 2H, -CH₂-, J=6.35, 5.86Hz), 6.95 (d, 2H, 방향족, J=9.28Hz), 7.41-7.44 (m, 3H, 방향족), 7.97 (dd, 2H, 방향족, J=7.32, 7.82Hz), 8.19 (d, 2H, 방향족, J=9.28Hz)

(c) 5 - - 4 - p - - 2 - - 1,3 -

(b) 1.23 g 25 mL - (1:1)
 0.25 g 5% Pd - C 가 . - 가 1
 1.02 g(91.1%) (:n - = "1:1) " . m.p. = "57 - 59

MASS(m/e):308(M+),200(BP),174,104,80,53
 IR(cm⁻¹):1512,1242,825,711,681
¹HNMR(CDCl₃) δ : 2.08-2.15 (m, 2H, -CH₂-), 2.28 (s, 3H, -CH₃), 2.68 (t, 2H, -CH₂-, J=7.33, 7.32Hz), 3.42 (bs, 2H, -NH₂), 3.90 (t, 2H, -CH₂-, J=6.35, 5.86Hz), 6.62-6.66 (m, 2H, 방향족), 6.73-6.76 (m, 2H, 방향족), 7.38-7.45 (m, 2H, 방향족), 7.96-7.99 (m, 2H, 방향족)

d) 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (1)

(c) 0.4 g (4 mL) 0.28 mL , 0.
 16 mL 0.16 mL 가 30 30 .
 NH₄Cl , NaCl , Na₂SO₄
 0.34 g(66.7%)
 (:n - = "1:1) " . m.p. = "121 - 123

MASS(m/e):372(M+),264,186(BP),149,104,79,55
 IR(cm⁻¹):3238,1506,1320,1281,1245,1212,1143,777
¹HNMR(CDCl₃) δ : 2.38 (s, 3H, -CH₃), 2.93 (s, 3H, -SO₂CH₃), 2.98 (t, 2H, -CH₂-, J=6.35, 6.84Hz), 4.23 (t, 2H, -CH₂-, J=6.83, 6.84Hz), 6.25 (s, 1H, -NH), 6.88 (d, 2H, 방향족, J=8.79Hz), 7.16 (d, 2H, 방향족, J=9.27Hz), 7.39-7.45 (m, 3H, 방향족), 7.97 (dd, 2H, 방향족, J=1.46, 1.95Hz)

2

4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (2)

4 mL 1 (c) (0.4 g) 0.27 mL
 (3.3 mL) 가 , 0 30 . 2 mL 1 m
 L 10% NaOH 가 , 10 , (20 mL) 가 ,
 NH₄Cl, NaCl , Na₂SO₄ . ,
 , 0.38 g(66.7%) . m.p. = "97 - 99 (:n - = "1:1) "

MASS(m/e):441(M+),200(BP),173,104,69
 IR(cm⁻¹):1455,1248,1215,1116,894,597
¹HNMR(CDCl₃) δ : 2.17-2.23 (m, 2H, -CH₂-), 2.29 (s, 3H, -CH₃), 2.70 (t, 2H, -CH₂-, J=6.83, 7.33Hz), 4.05 (t, 2H, -CH₂-, J=5.86, 6.34Hz), 6.97 (d, 2H, 방향족, J=8.79Hz), 7.40-7.44 (m, 3H, 방향족), 7.98 (dd, 2H, 방향족, J=7.32, 8.30Hz)

3

5 - 4 - [2 - (4 -)] - 2 - - 1,3 - (3)

(a) 5 - 4 - [2 - (4 -)] - 2 - -
 (8 mL) 1 (c) (0.36 g) (0.26 mL)
 (0.27 g) 0 가 , 2
 NH₄Cl, NaCl, Na₂SO₄
 0.32 g(59.1%)
 (n - = "1:1")

MASS(m/e):443(M+),186(BP),144,108,84,47
 IR(cm⁻¹):1734,1341,1299,1248,1158,753
¹HNMR(CDCl₃) δ : 1.32 (t, 3H, -COOEt, J=6.84, 7.32Hz), 2.38 (s, 3H, -CH₃), 2.98 (t, 2H, -CH₂-, J=6.83, 6.35Hz), 3.86 (s, 2H, -CH₂-), 4.23 (t, 2H, -CH₂-, J=6.83, 6.35Hz), 4.28 (q, 2H, -COOEt, J=7.32, 6.83Hz), 6.74 (s, 1H, -SO₂NH), 6.88 (d, 2H, 방향족, J=8.78Hz), 7.25 (d, 2H, 방향족, J=8.30Hz), 7.39-7.44 (m, 3H, 방향족), 7.97 (q, 2H, 방향족, J=1.46, 1.96Hz)

(b) 5 - 4 - [2 - (4 -)] - 2 - - 1,3 - (3)

(5 mL) (a) (0.3 g) 10% NaOH(2.5 mL) 가 ,
 1 . 10% HCl
 NaCl, Na₂SO₄
 . 0.2 g(71.4%)
 . m.p. = "164 - 167"

MASS(m/e):371(M+ -COOH),294,186(BP),144,104,77
 IR(cm⁻¹):3274,1713,1512,1338,1281,1245,1158,1107
¹HNMR (CDCl₃) δ :2.42 (s, 3H, -CH₃), 3.06 (t, 2H, -CH₂-, J=6.35Hz), 3.86 (s, 2H, -CH₂-), 4.24 (t, 2H, -CH₂-, J=6.83, 6.35Hz), 6.85 (d, 2H, 방향족, J=9.28Hz), 7.22 (d, 2H, 방향족, J=8.78Hz), 7.45-7.47 (m, 3H, 방향족), 7.95 (q, 2H, 방향족, J=2.44, 3.9Hz)

4 - 7

3 , 4 (), 5 (m.p. = "273 - 239"), 6 (m.p. = "143 - 145")
 7 (m.p. = "114 - 116") "

8

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

(a) 2 - [4 - (2 - (5 - - 2 - - 1,3 - - 4 -))] - 2 - -

1 (c) (0.5 g) (10 mL) (0.6 g)
 . 0.55 g (84.6%) . m.p. = "128 - 132

MASS(m/e):380(M+),321,186(BP),144,105,59

¹HNMR(CDCl₃) δ : 2.37 (s, 3H, -CH₃), 2.98 (t, 2H, -CH₂-, J=6.84, 6.35Hz), 3.96 (s, 3H, -COOMe), 4.24 (t, 2H, -CH₂-, J=6.35, 6.83Hz), 6.90 (d, 2H, 방향족, J=8.79Hz), 7.38-7.44 (m, 3H, 방향족), 7.53 (d, 2H, 방향족, J=8.79Hz), 7.97 (d, 2H, 방향족, J=5.86Hz), 8.76 (d, s, 1H, -NH)

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

8 (a) (0.53 g) (15 mL) 10% NaOH 1
 , (30 mL) 가 , 10% HCl (pH 4)
 (0.42 g, 82.3%) . m.p. = "196 - 198

MASS(m/e):366(M+),322,294,186(BP),144,104,77

¹HNMR(CDCl₃) δ : 2.36 (s, 3H, -CH₃), 2.92 (t, 2H, -CH₂-, J=6.35, 6.83Hz), 3.32 (bs, 1H, -NH), 4.19 (t, 2H, -CH₂-, J=6.34, 6.84Hz), 6.93 (d, 2H, 방향족, J=9.27Hz), 7.45-7.55 (m, 3H, 방향족), 7.67 (dd, 2H, 방향족, J=2.44Hz), 7.91 (dd, 2H, 방향족, J=1.47, 1.95Hz)

9

2 - [4 - (2 - (5 - - 2 - - 1,3 - - 4 -))] (9)

(a) 5 - - 4 - (2 - p -) - - 2 - - 1,3 -

(10 mL) 5 - - 4 - [2 - (p -)] - 2 - - 1,3 - (0.54 g) (0.21 m
 L) 10 , NaBH₃CN(0.11 g) 가 ,
 10% HCl 가 , NaHCO₃ 가 ,
 H₂O, NaCl , Na₂SO₄ ,
 0.43 g (61.4%)

MASS(m/e):398(M+),291,212,186(BP),146,104,77

IR(cm⁻¹):3022,2914,1608,1509,1452,1242,738,714

¹HNMR(CDCl₃) δ : 2.37 (s, 3H, -CH₃), 2.98 (t, 2H, -CH₂-, J=6.83, 6.84Hz), 3.73 (s, 2H, -CH₂-), 3.78 (s, 2H, -CH₂-), 4.24 (t, 2H, -CH₂-, J=6.84, 6.83Hz), 6.86 (d, 2H, 방향족, J=8.79Hz), 7.21-7.44 (m, 10H, 방향족), 7.97 (q, 2H, 방향족, J=1.46, 1.95Hz)

(b) 5 - - 4 - (2 - p -) - 2 - - 1,3 -

9 (a) (0.4 g) HOAc 5% Pd - C(80 mg)
 (10 mL) ,
 (CHCl₃:MeOH="10:1") " (0.21 g, 67.
 7%) . m.p. = "149 - 152

MASS(m/e):308(M+),291,186(BP),144,122,104,77

IR(cm⁻¹):3430,2962,1608,1248

¹HNMR(CDCl₃) δ : 3.88 (s, 2H, -CH₂-), 4.23 (t, 2H, -CH₂-, J=6.34, 6.84Hz), 6.90 (d, 2H, 방향족, J=8.79Hz), 7.27 (d, 2H, 방향족, J=8.78Hz), 7.41-7.46 (m, 3H, 방향족), 7.96 (d, 2H, 방향족, J=7.81Hz)

(c) 2 - [4 - (2 - (5 - - 2 - - 1,3 - - 4 -))] (9)

9 (b) (0.14 g) 2
(9) (0.55 g, 28%). m.p. = "113 - 115

MASS(m/e):440(M+),186,144,104(BP),77
IR(cm⁻¹):3310,1443,1368,1251,1227,1188,1146
¹HNMR(CDCl₃) δ : 2.38 (s, 3H, -CH₃), 2.98 (t, 2H, -CH₂-, J=6.83, 6.84Hz), 4.25 (t, 2H, -CH₂-, J=6.84, 6.34Hz), 4.37 (d, 2H, -CH₂-, J=4.89Hz), 5.05 (bs, 1H, -NHSO₂-), 6.90 (d, 2H, 방향족, J=8.79Hz), 7.22 (d, 2H, 방향족, J=8.79Hz), 7.41-7.45 (m, 3H, 방향족), 7.97 (q, 2H, 방향족, J=1.95, 1.96Hz)

10

4 - [2 - (5 - - 2 -)] (10)

(a) 2 - [2 - (4 -)] - 5 -

OH(3.4 g) 가 (100 mL) 2 - (5 -) (10 g) 4 - (9.3 g) Na (150 mL)
0 1
NaCl, Na₂SO₄
(EtoAc:n - = "1:2" 2:1) . EtoAc n -
(1:1) . 13.4 g(74.4%), m.p. = "45 - 47

MASS(m/e):272(M+),150,134(BP),119,93,77
IR(cm⁻¹):1593,1518,1491,1341,1260,1008,834
¹HNMR(CDCl₃) δ : 1.25 (t, 3H, -C₂H₅, J=7.81, 7.32Hz), 2.64 (q, 2H, -C₂H₅, J=7.33, 7.32Hz), 3.27 (t, 2H, -CH₂-, J=6.34, 6.84Hz), 4.46 (t, 2H, -CH₂-, J=6.34, 6.84Hz), 7.17 (d, 1H, 피리딘 J=8.31Hz), 7.47 (dd, 1H, 피리딘, J=2.44, 2.45Hz), 8.18 (dd, 2H, 방향족, J=6.83, 7.32Hz), 8.40 (d, 1H, 피리딘, J=1.95Hz)

(b) 2 - [2 - (4 -)] - 5 - -

10 (a) (1.85 g) 1 (c)
(1.62 g, 98.2%)

MASS(m/e):242(M+),134(BP),119,106,83,65
IR(cm⁻¹):2950,1509,1233,822
¹HNMR(CDCl₃) δ : 1.24 (t, 3H, -C₂H₅, J=7.81, 7.33Hz), 2.62 (q, 2H, -C₂H₅, J=7.33Hz), 3.19 (t, 2H, -CH₂-, J=6.35, 6.83Hz), 3.42 (bs, 2H, -NH₂), 4.26 (t, 2H, -CH₂-, J=6.35, 6.84Hz), 6.61-6.64 (m, 2H, 방향족), 6.72-6.76 (m, 2H, 방향족), 7.18 (d, 1H, 피리딘, J=7.81Hz), 7.44 (dd, 1H, 피리딘, J=1.95, 1.96Hz), 8.39 (d, 1H, 피리딘, J=2.46Hz)

(c) 4 - [2 - (5 - - 2 -)] (10)

10 (b) (1.2 g) 2
0.3 g (10) . m.p. = "76 - 78

MASS(m/e):373(M+ -1),134(BP),91,69
IR(cm⁻¹):1446,1263,1119,897,603
¹HNMR(CDCl₃) δ : 1.25(t, 3H, -C₂H₅, J=7.81, 7.33Hz), 2.63 (q, 2H, -C₂H₅, J=7.32, 7.82Hz), 3.25 (t, 2H, -CH₂-, J=6.83, 6.35Hz), 4.39 (t, 2H, -CH₂-, J=6.35Hz), 6.96 (dd, 2H, 방향족, J=6.84, 6.83Hz), 7.18 (d, 1H, 피리딘, J=7.81Hz), 7.28 (d, 2H, 방향족, J=9.28Hz), 7.46 (dd, 1H, 피리딘, J=7.81Hz), 8.40 (d, 1H, 피리딘, J=1.96Hz)

11

4 - [2 - (N - - N - 2 -)] (11)

(a) 4 - [2 - (N - - N - 2 -)] - 1 - - 2 - - 2 - (4.0 g)
 6 (a) 4 - (5.9 g, 82.2%)

MASS(m/e):273(M+),139,121(BP),94,78,51
 IR(cm⁻¹):2926,1590,1497,1425,1338,1260
¹HNMR(CDCl₃) δ : 3.14 (s, 3H, -CH₃), 4.03 (t, 2H, -CH₂, J=5.86, 5.37Hz), 4.30 (t, 2H, -CH₂, J=5.86Hz), 5.52 (d, 1H, 피리딘, J=8.79Hz), 6.59 (t, 1H, 피리딘, J=4.88, 6.35Hz), 6.97 (dd, 2H, 방향족, J=8.79Hz), 7.45-7.50 (m, 1H, 피리딘), 8.15-8.20 (m, 2H, 피리딘, 방향족)

b) 4 - [2 - (N - - N - 2 -)] - 1 -
 11 (a) (5.85 g) (c)
 (2.12 g, 40.7%)

MASS(m/e):243(M+),135(BP),121,108,94,78,65
 IR(cm⁻¹):3334,2914,1596,1557,1503,1425,1233,771

(c) 4 - [2 - (N - - N - 2 -)] (11)
 11 (b) (0.5 g) 2
 (0.67 g, 87.0%) . m.p. = "60 - 62"

MASS(m/e):375(M+),304,170,135,108,78(BP),52
 IR(cm⁻¹):1593,1503,1452,1218,1125,891,600
¹HNMR(CDCl₃) δ : 3.13 (s, 3H, -CH₃), 4.01 (t, 2H, -CH₂, J=5.86, 5.37Hz), 4.24 (t, 2H, -CH₂, J=5.86, 5.37Hz), 6.51 (d, 1H, 피리딘, J=8.30Hz), 6.57 (t, 1H, 피리딘, J=4.88, 6.84Hz), 6.97 (d, 2H, 방향족, J=9.27Hz), 7.27 (d, 2H, 방향족, J=9.77Hz), 7.44-7.49 (m, 1H, 피리딘), 8.15 (d, 1H, 피리딘, J=3.90Hz)

12 - 17

1 , 12(m.p. = "106 - 108)," 13(m.p. = "67 - 68)," 14(m.p. = "56 - 58),"
 15(m.p. = "128 - 130)," 16(126 - 127) 17(m.p. = "128 - 130) "

18 - 20

2 , 18(m.p. = "197 - 198)," 19(m.p. = "70 - 71)" 20(m.p. = "170 - 172) "

21

2 5 - - 4 - (3 -) - 2 - - 1,3 -
 21(m.p. = "113 - 114) "

22 - 24

4 , 22(m.p. = "128 - 130 ") 23(m.p. = "217 ()) "

25

2- - 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (25)

0.2 g 2,4 - 0.23 g (DIAD) 2 mL THF
 3 mL THF 0.29 g 5 - - 4 - - 3 - - 1,3 - 0.31 g
 Ph₃P 가 , (: = "1:5) "
 . 0.31 g (73.3%) . m.p. = "133 - 134

MASS(m/e):353(M+),217,185,136,104(BP),77,53

IR(cm⁻¹):1677,1617,1440,1320,1251,1188,1134

¹HNMR(CDCl₃) δ : 3.90 (s, 3H, -COOMe), 4.27 (t, 2H, -CH₂, J=6.34, 6.84Hz), 6.42 (dd, 1H, -
 방향족, J=8.79Hz), 6.46 (d, 1H, 방향족, J=2.44Hz), 7.39-7.44 (m, 3H, 방향족), 7.72 (d, 1H,
 방향족, J=9.28Hz), 7.97 (q, 2H, 방향족, J=7.33, 8.3Hz), 10.93 (s, 1H, -OH)

26 - 28

11 , 26(m.p. = "211 - 213)," 27(m.p. = "85 - 87 ") 28(m.
 p. = "130 - 132) "

29 - 30

2- - 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (29)

20 0.17 g 2 mL MeOH:THF(1:1) 2 mL 10% NaOH
 가 , 1 , , 10% HCl
 . (0.13 g, 81.3%) . m.
 p. = "192 - 194

MASS(m/e):339(M+), 295,217,186,104(BP)

IR(cm⁻¹):2920,1655,1260,1170

, 30 .(m.p. = "246 - 266)

31 - 32

2- - 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (31)

(a) 2- - 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)]

DMF(5 mL) 25(0.27 g) K₂CO₃ (0.16 g) EtI(0.07 mL) 가 ,
 Cl , Na₂SO₄ , (30 mL) . , Na
 . (:n - = "1:3) " 0.28 g(96.6%)

MASS(m/e):381(M+), 217,186,144,104(BP), 77, 51

IR(cm⁻¹):2926,1686,1605,1257, 1194

(b) 2- - 4 - [2 - (5 - - 2 - - 1,3 - - 4 -)] (31)

(0.22 g) 31 - 32 (a) 29 가 ,
 . m.p. = "128 - 130"

MASS(m/e):367(M+),217,186,144,104(BP),77,51
 IR(cm⁻¹):1686,1605,1572,1281,1263,1239,1191
¹HNMR(CDCl₃) δ : 2.99 (t, 2H, -CH₂-, J=6.84Hz), 4.25 (q, 2H, oEt, J=6.84Hz), 4.33 (t, 2H, -CH₂-, J=6.34, 6.84Hz), 6.50 (d, 1H, 방향족 , J=2.44Hz), 6.55 (dd, 1H, 방향족 , J=1.95Hz), 7.41-7.44 (m, 3H, 방향족), 7.96-7.99 (m, 2H, 방향족), 8.10 (d, 1H, 방향족 , J=8.79Hz)

, 25 32 . m.p. = "129 - 130"

33 - 38

3- - 4 - - 2,6 - - 4 - 5 - - 4 - - 2 - - 1,3 - 1 ()
 25 ,
 c) (d) 33(m.p. = "155 - 156) , " 35(m.p. = "143 - 144) "
 36(m.p. = "78 - 80) " 가 , 2,4 - - 5 - - 4 - - 3 -
 - 1,3 - 34(m.p. = "231 - 232) " 34
 37(m.p. = "171 - 173) " 4 - - 2 -
 , 가 38(m.p. = "154 - 156) "

39

4 - [2 - (N - - N - 2 -)] - 2 - (39)

(a) 4 - [2 - (N - - 2 - N -)] - 2 -

DMF(30 mL) 2 - (N - , N -) - (0.35 g) 4 - - 2 - -
 NaH(0.12 g) 가 ,
 NHCl , Na₂SO₄
 (0.44 g, 57.1%) (: n - = "1:2) "

MASS(m/e):333(M+),121(BP),78,52

IR(cm⁻¹): 2926, 1596, 1500, 1425, 1341, 1287, 1152

(b) 4 - [2 - (N - - N - 2 -)] - 2 - (33)

(a) 1 (c) ,
 (MOM,) (d) ,
 (33) n -

m.p. = "134 - 135

MASS(m/e):391(M+),135(BP),107,78
 IR(cm-1):1611,1509,1419,1404,1227,1176,1146
¹HNMR(CDCl₃) δ: 3.14 (s, 3H, Me), 3.93 (t, 2H, -CH₂, J=5.37Hz), 4.11 (2H, -CH₂, J=5.37Hz), 6.37-6.43, 6.53-6.59 (m, m, 4H, 방향족, 피리딘), 7.27 (d, 1H, 방향족, J=8.79Hz), 7.46-7.51 (m, 1H, 피리딘), 8.08 (d, 1H, 피리딘, J=4.88Hz)

40 - 41

40(m.p. = "133 - 135 ") 41(m.p. = "151 - 153 ") 39 (a)
 4 - - 2 - - .

42 - 45

39 (a) 2 - (N - , N -) , 5 - - 4 - - 2 - -
 1,3 - , 43(
 m.p. = "169 - 171 ") 39 (a)
 44(m.p. = "124 - 125 ") 가 , 39 (a) 2 - (N - , N -
) - 4 - - 2 - - (c)
 45 .

46 - 47

N - - 2,4 - - 5 - - 4 - - 2 - - 1,3 - 1 (b)
 46(m.p. = "137 - 139 ") . 2,6 - - 4 -
 - 5 - - 4 - - 2 - - 1,3 - , 47(m.p. = "163 -
 164 ") .

48 - 54

(68) , 4 - (6
 9) , 1 , 2
 53 가 54 .
 48(m.p. = "147 - 149 ") , 49(m.p. = "175 - 177 ") , 50(m.p. = "166 - 168 ") , 51(m.
 p. = "164 - 166 ") , 52(m.p. = "227 - 229 ") , 53() , 54(175 ,) .

55 - 56

(Bioorg.Med.Chem.Lett., 1995,1155) (71) ,
 DBU 55(m.p. = "150 - 152 ") 56(m.p. = "214 - 216 ") "

57 - 59

2 5- -4-p- -2- -1,3- , 5- -4-p- -2-p-
 - -1,3- , 5- -4-p- -2-p- -1,3- 5- -4-p-
 -2-p- -1,3- 2
 . 57(m.p.="173.5 - 175)," 58(m.p.="189 - 190)," 59(m.p.="161 - 163)

60 - 63

5- -4-p- -2- -1,3- , 5- -4-p- -2-p- -
 1,3- , 5- -4-p- -2- -1,3- , 5- -4-p- -2
 -p- -1,3- 5- -4-p- -2-(3,5- -t- -4-) -
 1,3- 2 60(m.p.="190
 -191)," 61(m.p.="155 - 156)," 62(m.p.="189 - 190)," 63(m.p.="142 - 144)."

64 - 66

5- -4- -2- -1,3- , 5- -4- -2-p- -1,3-
 5- -4- -2-p- -1,3- 39 4-
 -2 - 64(m.p.="142 - 144)," 65(m.
 p.="179 - 181)," 66(m.p.="122 - 124)."

67 - 68

5- -4- -2-(p-) -1,3- 5- -4- -2-(
 3,5- -t- -4-) -1,3- 39
 5- -4-p- -2-(p-) -1,3- 5- -4-p- -
 2-(3,5- -t- -4-) -1,3- 10% NaOH - MeO
 H 가 : 67(m.p.="167 - 168)," 68(m.p.="196 - 198).

69

5- -4-p- -2- -1,3- (1.0 g) (10 mL) ,
 o- (0.59 g) 가 . 30 , , MeOH
 . 1.03 g 69 . m.p.="165 - 167

MASS(m/e):403(M+1), 401(M - 1)

70

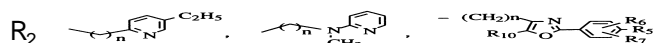
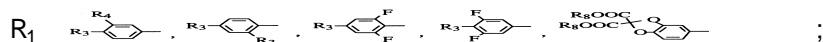
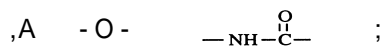
2 , 5- -4- -2-(3-t- -4-) -1,
 3- 70 . m.p.="58 - 60 "




(57)

1.

(I) :

R₁ - A - R₂ (I)



((i) A가 -O- , n 2 3 , (ii) A가 $\text{---NH---}\overset{\text{O}}{\parallel}{\text{C}}\text{---}$, n 1 2 . R₃ OH- , CH₃SO₂NH- , CF₃SO₂NH- , CH₃SO₂NHCH₂- , CF₃SO₂NHCH₂- , HOOC- , CH₃OOC- , $\text{---R}_8\text{---OOC---}\overset{\text{O}}{\parallel}{\text{C}}\text{---NH---}$, HOOC-CH₂SO₂NH- , CF₃-CH₂SO₂NH- , HOOC--SO₂NH- , -SO₂NH- , -SO₂NH- , R₈ - NHSO₂ - , R₈ - NHSO₂ - CH₂ - , HOOC - CH₂ - O - , HSO₃N="CH - , " R₉ - SO₂NHCO - ;

R₄ H, OH, O- O - CH₂OCH₃ ;

R₅ H, , -CH₂COOH OH ;

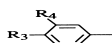
R₆ R₇ , t - ;

R₈ ;

R₉ ;

R₁₀).

2.

1 , R₁  (, R₃ R₄)

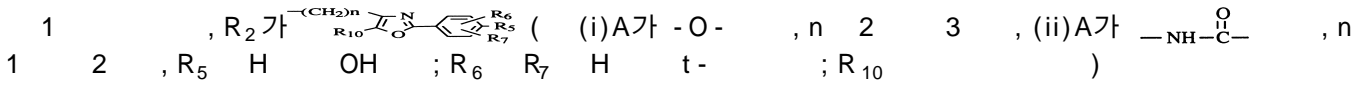
3.

1 , R₂가  .

4.



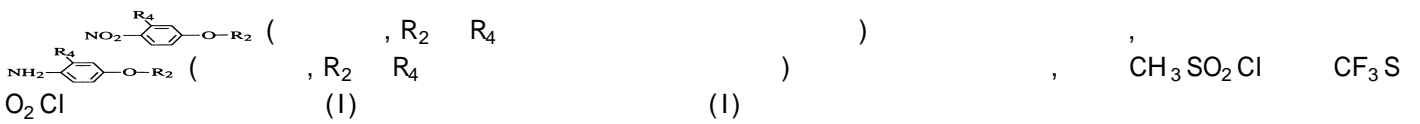
5.



6.



7.



((I) , A -O- ;



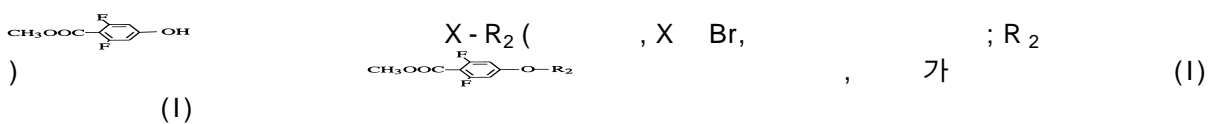
8.



((I) , A -O- ;

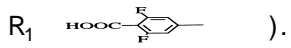


9.

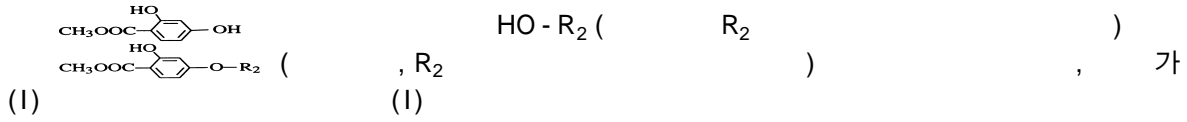


((I) , A -O- ;

R₂ 가 ,

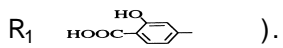


10.

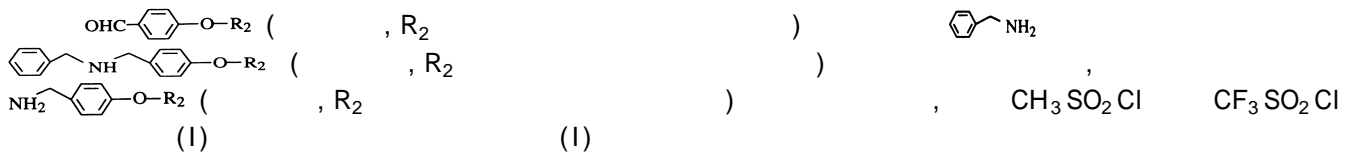


((I) , A -O- ;

R₂ 가 ;

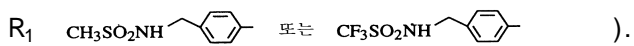


11.

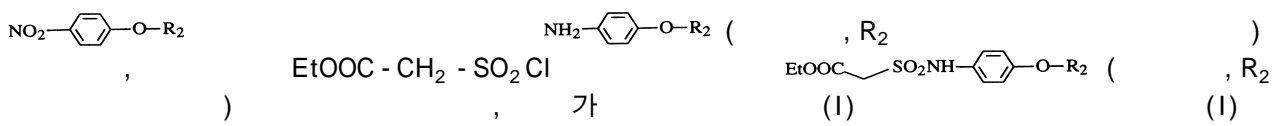


((I) , A -O- ;

R₂ 가 ;




12.



((I) A -O- ;

R₂ 가 ;



R₁ HOOC-CH₂-SO₂NH-).

13.



((I) , A -O- ;

R₂ 가 ;

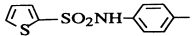
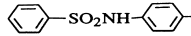
R₁ HOOC--SO₂NH-).

14.

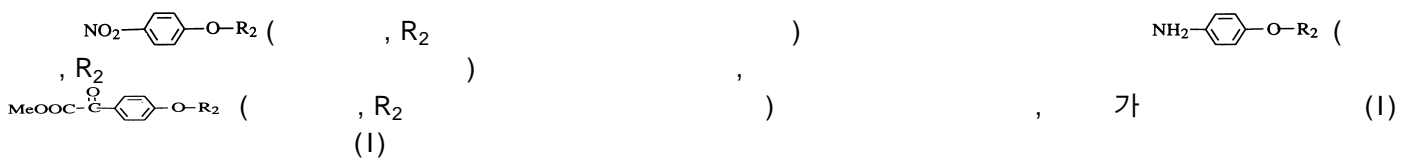


((I) , A -O- ;

R₂ 가 ;

R₁  또는 ).

15.



(I) A -O- ;

R₂ 가 ;

R₁ HOOC-C(=O)-c1ccc(cc1)-).

16.

NaH nBuNHSO2-c1ccc(O)cc1 HO - R₂ (, , R₂)
(I) (I)

(I) , A -O- ;

R₂ 가 ;

R₄ nBuNHSO2-c1ccc(cc1)-).

17.

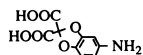
HOOC-c1ccc(O-R2)cc1 (, R₂) 1,8 - [5,4,0]
- 7 - (I) (I)

(I) A -O- ;

R₂ 가 ;

R₁ c1ccsc1-SO2NH-CO-c2ccc(cc2)- 또는 CH3SO2NH-CO-c1ccc(cc1)-).

18.

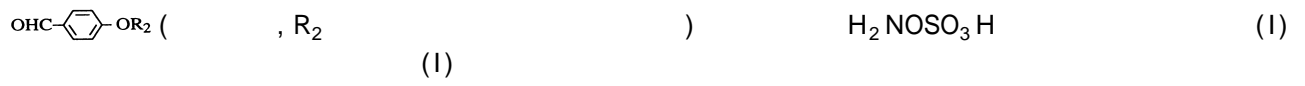


(I) , A -O- ;

R₂ 가 ;

R₁ NC1=CC=C(C=C1)OC(=O)C(=O)O).

19.



((I) , A -O- ;

R₂ 가 ;

R₁ HO₃S~N=CH-C₆H₄-OR₂).