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(A)

(51) 。 Int. Cl.⁷
C07D 209/30

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2004 11 30

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WO 2003/101961

(86) 2003 05 27

(87)

2003 12 11

(30) 0201635-0

2002 05 30

(SE)

(71) 151 85

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(54)

EPA 1 170 594

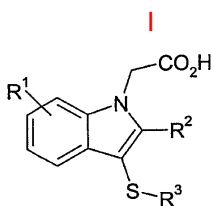
(orphan receptor) CRTh2

D2

. GB 1356834

, CRTh2

COPD



R¹ , , CN, , SO₂R⁴, OH, OR⁴, S(O)_xR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶
 , (, C₂-C₆) , C₂-C₆ C₁₋₆ , C₂-C₆
 , C₂-C₆ C₁₋₆ , OR⁸, NR⁵R⁶ S(O)_xR⁷(, x 0, 1 2) ;

R² , , CN, SO₂R⁴, CONR⁵R⁶, CH₂OH, CH₂OR⁴ C₁₋₇ , C₁₋₇
 , OR⁸, NR⁵R⁶ S(O)_xR⁷(, x 0, 1 2) 1 ;

R³ , , CN, , OH, SO₂R⁴, OR⁴, SR⁴, SOR⁴, SO₂
 NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NHCOR⁴, NHSO₂R⁴, NHCO₂R⁴, NR⁷SO₂R⁴, NR⁷CO₂R⁴,
 C₂-C₆ , C₂-C₆ , C₁₋₆
 C₂-C₆ , C₂-C₆ C₁₋₆ , OR⁸, NR⁵R⁶ S(O)_xR⁷(, x
 0, 1 2) 1 ;

R⁴ , , C₁₋₆ , , OR¹⁰, OH, NR¹¹R¹², S(O)_xR¹³(, x 0, 1 2) , CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴S
 O₂R¹⁵, CN, 1 ;

R⁵ R⁶ , , C₁₋₆ , (C₁₋₆ ,
 , OR⁸, NR¹⁴R¹⁵, CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴S
 O₂R¹⁵, CN, 1 , R⁵ R⁶
 O, S(O)_x(x 0, 1 2), NR¹⁶ 1 ;

- 가 4- 가 .
R 3 , () .
- 3-[(4-)]-2,5- -1H- -1- ;
 - 3-[(2- -4-)]-2,5- -1H- -1- ;
 - 3-[(3- -4-)]-2,5- -1H- -1- ;
 - 3-[(2-)]-2,5- -1H- -1- ;
 - 3-[(3-)]-2,5- -1H- -1- ;
 - 3-[(4-)]-2,5- -1H- -1- ;
 - 3-[(2-)]-2,5- -1H- -1- ;
 - 3-[(2,5-)]-2,5- -1H- -1- ;
 - 3-[(4-)]-2,5- -1H- -1- ;
 - 3-[(4- -2-)]-2,5- -1H- -1- ;
 - 3-[(4-)]-4- -2,5 -1H- -1- ;
 - 5- -3-[(4-)]-6- -2- -1H- -1- ;
 - 3-[(4-)]-4-()-7- -2- -1H- -1- ;
 - 3-[(4-)]-4-[()]-7- -2- -1H- -1- ;
 - 4- -3-[(4-)]-2- -1H- -1- ;
 - 5- -3-[(4-)]-2- -1H- -1- ;
 - 6- -3-[(4-)]-2- -1H- -1- ;
 - 7- -3-[(4-)]-2- -1H- -1- ;
 - 3-[(4-)]-2- -5-()-1H- -1- ;
 - 2- -3-[(4-)]-6-()-1H- -1- ;
 - 4- -3-[(4-)]-2- -1H- -1- ;
 - 3-[(4-)]-4-[4-[(1,1-)]-1-]-2- -1H- -1- ;
 - 3-[(4-)]-2- -4-(1-)-1H- -1- ;
 - 5- -3-[(4-)]-2- -1H- -1- ;
 - 3-[(4-)]-2- -5- -1H- -1- ;
 - 3-[(4-)]-5- -2- -1H- -1- ;

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

3-[(4-)]-4-()-2- -1H- -1- ;

3-[(4-)]-4- -2- -1H- -1- ;

3-[(4-)]-2- -4- -1H- -1- ;

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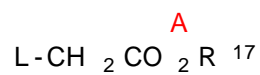
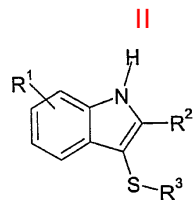
I

II

A

R¹⁷

가



R¹, R², R³

I

, R¹⁷

, L

17 C₁₋₆

A

tert-

THF

tert-

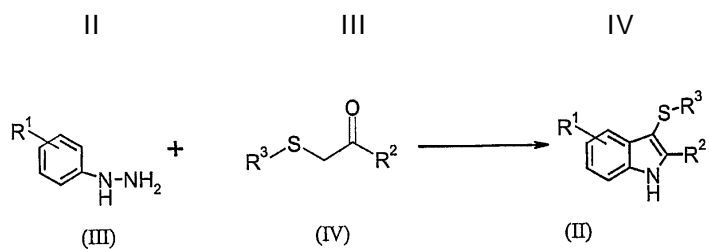
L

R

R¹⁷ 가

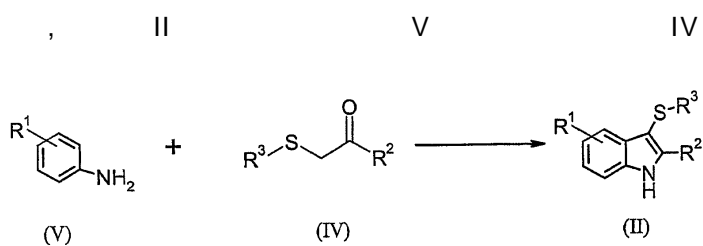
가

['Protective Groups in Organic Chemistry', edited by J. W. F. McOmie, Plenum Press (1973), 'Protective Groups in Organic Synthesis', 3rd edition, T. W. Greene and P. G. M. Wuts, Wiley-Interscience (1999)]



, R¹, R², R³ I

가

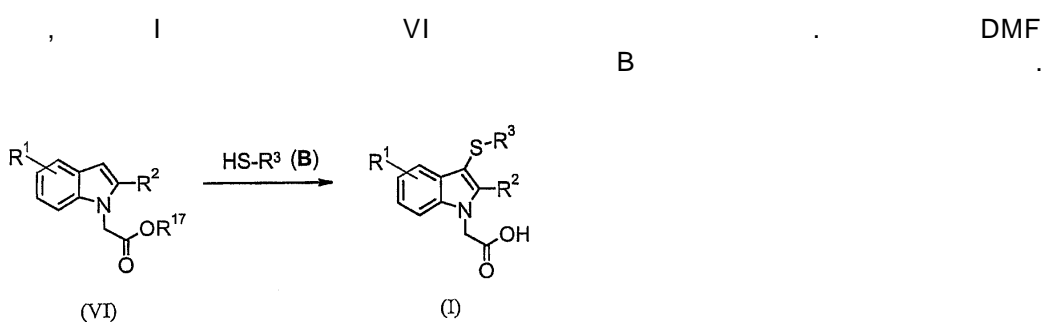


, R¹, R², R³ I

THF

tert-

III, IV, V



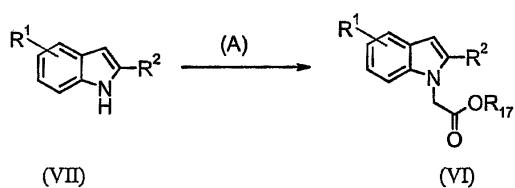
, R¹, R², R³, R¹⁷ I, A

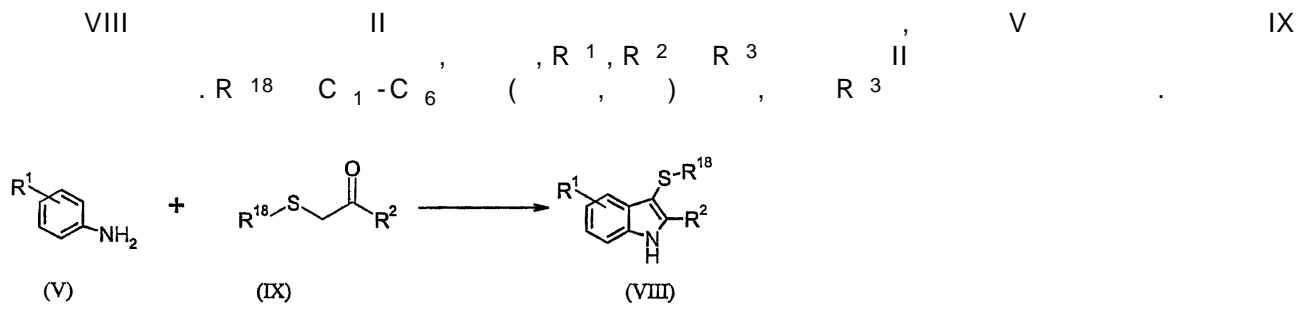
가

VI

A

VII

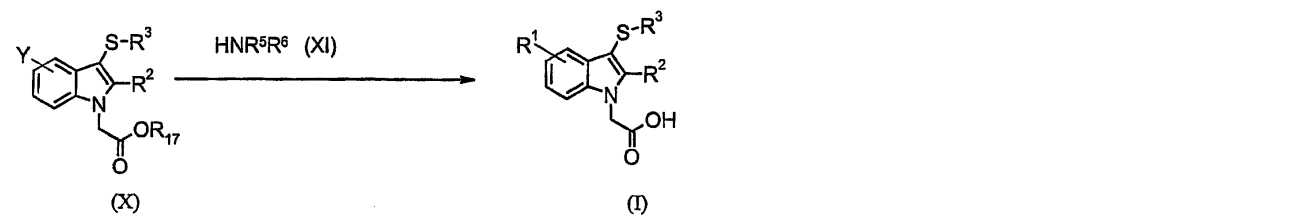




DMF, VII, B, I, A, 가



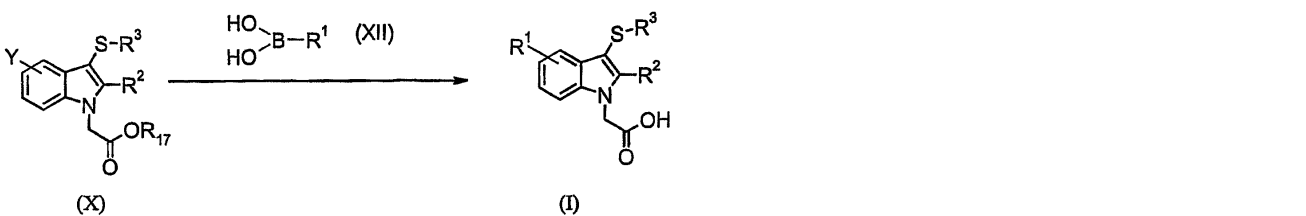
I, XI, X



R¹, R², R³, R⁵, R⁶, Y, R¹⁷, A

(Buchwald) Pd₂(dba)₃, BINAP, 110, tert-가

I, XII, X



(5) () - (, HIV (AIDS) , , ,) , CNS (- , / ,) , () , CNS , .

(6) () ; ; , I , , , 가 (AIDS), IgE , (, ,) , .

(7) () ; ; , , , , , , , ;

(8) PGD₂ . I , .

가 CRTh2 .

PGD₂ .

가 , I , .

가 , (, 2-

가 , CRTh2 I , .

가 I 가 , (CRTh2) ,

PGD₂ .

I , , , .

I / / () , , 0.05 99 %w (%),

0.05 80 %w, 0.10 70 %w, 0.10 50 %w

I , .

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

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

N,N- (15 ml) 3-[(4-)]-2,5- -1H- (300 mg) (116 μℓ)
 (60% 42 mg) . 10 , (200 ml) (3×100 ml)
 24 (MgSO₄), , - 10% (130 mg).

¹H NMR CDCl₃ : δ(1H, m), 7.17-7.03(4H, m), 6.94(2H, m), 4.85(2H, s), 4.22(2H, q), 2.46(3H, s), 2.40(3H, s), 1.26(3H, t).

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

(5 ml) (i) (120 mg) (5 ml) 2.5 N (1 ml)
 . 1 70 , . 2 N (102 mg).

¹H NMR d₆-DMSO : δ13.12(1H, br s), 7.41(1H, d), 7.27(1H, m), 7.24(1H, m), 7.15(1H, m), 7.01-6.94(3H, m), 5.08(2H, s), 2.39(3H, s), 2.34(3H, s).
 M.pt. 219-221°C

2 10 l .
 (15 ml) (1 g) (1) 가 1- (MgSO₄),
 (1) 가 2 (15 ml) 가
 5 70 가 HPLC ((25% MeCN/NH_{3(aq)}) (0.1%)
 1%) 95% MeCN//NH_{3(aq)} (0.1%)) 1

[1]

		MS: ES(-ve)(M-H)
(i)	3-[(2- -4-)]-2,5- -1H-	304
(ii)	3-[(3- -4-)]-2,5- -1H-	304
(iii)	3-[(2-)]-2,5- -1H-	282
(iv)	3-[(3-)]-2,5- -1H-	270
(v)	3-[(4-)]-2,5- -1H-	280
(vi)	3-[(2-)]-2,5- -1H-	286
(vii)	3-[(2,5-)]-2,5- -1H-	320
(viii)	3-[(4-)]-2,5- -1H-	270
(ix)	3-[(4- -2-)]-2,5- -1H-	300

, 10 1 N- 가 2

[2]

		MS: ES(-ve)(M-H)
2	3-[(2- -4-)]-2,5- -1H- -1-	362
3	3-[(3- -4-)]-2,5- -1H- -1-	362
4	3-[(2-)]-2,5- -1H- -1-	340
5	3-[(3-)]-2,5- -1H- -1-	328
6	3-[(4-)]-2,5- -1H- -1-	338
7	3-[(2-)]-2,5- -1H- -1-	344
8	3-[(2,5-)]-2,5- -1H- -1-	378
9	3-[(4-)]-2,5- -1H- -1-	328
10	3-[(4- -2-)]-2,5- -1H- -1-	358

11

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

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

-78 (150 ml) 1-[(4-)]- (6.14 g)
 (2.25 ml) .30 (80 ml) N,N,N',N'- -1,8-
 (6.01 g) 5- -2- - (3.89 g) 30 가 . 2
 (200 ml) , (4.26 ml) 가 , (MgSO₄) ,
 , 1 N HCl (1:1) (1)

¹H NMR CDCl₃: δ 12.52 (s, 1H), 7.74 (d, 1H), 7.38 (dd, 1H), 7.29 (m, 2H), 6.97 (m, 2H), 3.29 (s, 3H).

5- -3-[(4-)]-2- -1H- -6- (600 mg)

¹H NMR CDCl₃: δ 8.68 (1H, s), 7.69 (1H, s), 7.61 (1H, s), 7.15 (2H, dt), 6.91 (2H, dt), 2.57 (3H, s).

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

(5 ml) (15 ml) (60% 96.1 mg)
 3-[(4-)]-2,5- -1H- -4- (400 mg) 가 .30
 (177 μℓ) 4 (MgSO₄) ,
 (360 mg) (1:1)

¹H NMR CDCl₃: δ 7.37 (1H, d), 7.30 (1H, d), 7.18 - 7.13 (2H, m), 7.00 - 6.96 (2H, m), 4.92 (2H, s), 3.80 (3H, s), 2.55 (3H, s).

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

ii) 0.1 g THF (5 ml) NaOH (200 μ l, 1.25 M) . 3 , NaOH (200 μ l, 1.25 M)
 25 M) 가 , HCl (86 mg)

$^1\text{H NMR DMSO}$: δ 7.99 (1H, d), 7.47 (1H, d), 7.38 (2H, dt), 7.3 (2H, dt), 6.98 (2H, dt), 5.25 (2H, s), 2.49 (3H, s).

MS: APCI+ [M+H] 390

M.pt. 237-238°C

12

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

i) 5- -3-[(4-)]-6- -2- -1H- -1-

11 ii) 11 i)

ii) 5- -3-[(4-)]-6- -2- -1H- -1-

11 iii) i)

$^1\text{H NMR DMSO}$: δ 8.42 (1H, s), 7.59 (1H, s), 7.3 (2H, dt), 6.99 (2H, dt), 5.24 (2H, s), 2.46 (3H, s).

13

3-[(4-)]-4-()-7- -2- -1H- -1-

i) 3-[(4-)]-4-()-7- -2- -1H-

11 i) 3- -4-

$^1\text{H NMR CDCl}_3$: δ 9.00 (1H, s), 7.91 (1H, d), 7.12 (2H, dd), 6.86 (2H, m), 6.73 (1H, d), 4.05 (3H, s), 4.05 (3H, s), 3.46 (2H, q), 2.46 (3H, s) 및 1.16 (3H, t).

ii) 3-[(4-)]-4-()-7- -2- -1H- -1-

11 ii) i)

$^1\text{H NMR CDCl}_3$: δ 7.92 (1H, d), 7.13 (2H, dt), 6.85 (2H, dt), 6.73 (1H, d), 5.27 (2H, s), 3.98 (3H, s), 3.79 (3H, s), 3.48 (2H, q), 2.38 (3H, s) 및 1.18 (3H, t).

iii) 3-[(4-)]-4-()-7- -2- -1H- -1-

11 iii) ii)

$^1\text{H NMR DMSO}$: δ 7.72 (1H, d), 7.24 (2H, m), 6.96 (1H, d), 6.86 (2H, dt), 5.29 (2H, s), 5.27 (2H, s), 3.97 (3H, s), 3.41 (2H, q), 2.34 (3H, s) 및 1.01 (3H, t).

14

3-[(4-)]-4-[()]-7- -2- -1H- -1-

i) 3-[(4-)]-N,N- -7- -2- -1H- -4-

11 i) 3- -N,N- -4- -

¹H NMR CDCl₃: δ 7.80 (1H, d), 7.88 (1H, s), 7.08(2H, d), 6.85 (2H, d), 6.66 (1H, d), 4.04 (3H, s), 3.25 (4H, q), 3.79 (3H, s), 2.43 (3H, s) 및 0.98 (6H, t).

ii) 3- [(4-)]-4- [()]-7- -2- -1H- -1-

11 ii) i) , 가

iii) 3- [(4-)]-4- [()]-7- -2- -1H- -1-

11 iii) ii)

¹H NMR DMSO: δ 7.56 (1H, d), 7.18 (2H, dt), 6.85-6.79 (3H, m), 5.13 (2H, s), 3.94 (3H, s), 3.14 (4H, q), 2.29 (3H, s) 및 0.88 (6H, t).

15

4- -3- [(4-)]-2- -1H- -1-

i) 4- -3- [(4-)]-2- -1H-

(30 ml) (3-)- (2 g) 1- [(4-)]-
 (2.24 g), (20 ml) (10 ml) 가 (MgSO₄
) , NaOH (20 ml) 80 가 (MgSO₄
) (10% EtOAc/ EtOAc)
 0.816 g

¹H NMR CDCl₃: δ 8.38 (s, 1H), 7.27-7.23 (m, 1H), 7.14 - 7.07 (m, 4H), 6.96 (dt, 2H), 2.52 (s, 3H)

ii) 4- -3- [(4-)]-2- -1H- -1-

THF (5 ml) (i) (0.2 g) THF (0.65 ml) 1.0 M ()
 가 (30 (62 μl) 가 ,
 . THF 1.0 M () 0.3 ml, 30 μl
 가 3 (14% EtOAc/
) (0.21 g)

¹H NMR CDCl₃: δ 7.17-7.11 (m, 5H), 6.95 (dt, 2H), 4.89 (s, 2H), 3.78 (s, 3H), 2.49 (s, 3H)

iii) 4- -3- [(4-)]-2- -1H- -1-

THF (5 ml) (ii) (0.11 g) 1.25 M NaOH(aq) (0.25 ml) 가
 2 , EtOAc , MgSO₄ , pH HCl(aq)
 / NH₂ , 10%
 (0.06 g)

$^1\text{H NMR CDCl}_3$: δ 7.54 (dd, 1H), 7.27 (dt, 2H), 7.14 (d, 1H), 7.08 (dd, 1H), 6.95 (dt, 2H), 5.16 (s, 2H), 2.43 (s, 3H)
 MS: APCI- [M-H] 364
 M.pt. 184-187°C

16

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

i) 5- -3-[4(-)]-2- -1H-

15 (i) (4-)-
 (20% EtOAc/)

$^1\text{H NMR CDCl}_3$: δ 8.31 (s, 1H), 7.48 (d, 1H), 7.26 (m, 2H), 7.13 (m, 3H), 6.93 (m, 2H), 2.51 (s, 3H).

ii) 5- -3-[(4-)]-2- -1H- -1-

15 (ii) (i)

$^1\text{H NMR CDCl}_3$: δ 7.52 (d, 1H), 7.27 (d, 1H), 7.20-7.10(m, 3H), 6.97-6.89 (m, 2H), 4.80 (d, 2H), 3.79 (d, 3H), 2.47(d, 3H).

iii) 5- -3-[(4-)]-2- -1H- -1-

THF (5 ml)	(ii)	(0.11 g)	1.25 M NaOH(aq)	(0.25 ml)	가	
				/	pH	HCl(aq)
2	,		40			

$^1\text{H NMR CDCl}_3$: δ 7.60 (d, 1H), 7.32 – 7.26 (m, 3H), 7.19 (dd, 1H), 6.98 (dt, 2H), 5.15 (s, 2H), 2.42 (s, 3H).

MS: APCI- [M-H] 364
 M.pt. 분해 >211°C

17

6- -3-[(4-)]-2- -1H- -1-

i) 6- -3-[4(-)]-2- -1H-

15 (i)

$^1\text{H NMR CDCl}_3$: δ 8.27 (s, 2H), 7.39 (d, 1H), 7.34 (d, 1H), 7.10 (m, 3H), 6.92 (m, 2H), 2.50 (s, 3H).

ii) 6- -3-[(4-)]-2- -1H- -1-

15 (ii) (i)

$^1\text{H NMR CDCl}_3$: δ 7.43 (d, 1H), 7.27 - 7.25 (m, 1H), 7.14 - 7.09 (m, 3H), 6.92 (dd, 2H), 4.85 (s, 2H), 3.80 (d, 3H), 2.46 (d, 3H).

iii) 6- -3-[(4-)]-2- -1H- -1-

16 (iii) (ii)

¹H NMR CDCl₃: δ 7.71 (d, 1H), 7.33 (d, 1H), 7.26 (dt, 2H), 7.09 (dd, 1H), 6.96 (dt, 2H), 5.08 (s, 2H), 2.40 (s, 3H).

MS: APCI- [M-H] 364

M.pt. 분해 >189 °C

18

7- -3-[(4-)]-2- -1H- -1-

i) 7- -3-[4(-)]-2- -1H-

(2-)- () 15 (i)
() () 14% EtOAc/ ()

¹H NMR CDCl₃: δ 8.48 (s 1H) 7.40 (d, 1H), 7.19 (m, 1H) 7.13-7.11 (m, 2H), 7.06 (t, 1H), 6.96-6.92 (m, 2H), 2.55 (s, 3H).

ii) 7- -3-[(4-)]-2- -1H- -1-

(i) 15 (ii)

¹H NMR CDCl₃: δ 7.44 (d, 1H), 7.18 - 7.09 (m, 3H), 7.03 (td, 1H), 6.92 (dd, 2H), 5.37 (2H, d), 3.81 (3H, d), 2.46 (3H, d).

iii) 7- -3-[(4-)]-2- -1H- -1-

(ii) 16 (iii)

¹H NMR DMSO δ 7.35 (dd, 1H), 7.28 (dt, 2H), 7.20 (dd, 1H), 7.07 (t, 1H). 6.98 (dt, 2H), 5.36 (s, 2H), 2.45 (s, 3H).

MS: APCI- [M-H] 364

M.pt. 분해 > 207°C

19

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

i) 3-[(4-)]-2- -5-()-1H-

4- - 11 i)

¹H NMR CDCl₃: δ 8.78 (1H, s), 8.16 (1H,d), 7.74 (1H, dd), 7.47 (1H, d), 7.13 (2H, dt), 6.92 (2H, dt), 3.06 (3H, s), 2.55 (3H, s).

ii) 3-[(4-)]-2- -5-()-1H- -1-

i) 11 ii)

¹H NMR CDCl₃: δ 8.20 (1H, d), 7.79 (1H, dd), 7.38 (1H, d), 7.14 (1H, dd), 6.92 (2H, dd), 4.96 (2H,s), 3.79 (3H, d), 2.52 (3H, s).

iii) 3-[(4-)]-2- -5-()-1H- -1-

ii) (190 mg) (10 ml), LiOH (18.9 mg) (2 ml) , HCl 44 mg

¹H NMR CDCl₃: δ 8.19 (1H, d), 7.79 (1H, dd), 7.39 (1H, d), 7.13 (1H, dd), 6.91 (2H, dd), 4.98 (2H,s), 3.04 (3H, s), 2.53 (3H, s).

M.pt. 185-187

20

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

i) 3-[(4-)]-2- -4-()-1H- 3-[(4-)]-2- -6-()-1H-

3-())]-2- -6-()-1H- 3-[(4-)]-2- -4-()-1H- 19 i) 3-[(4-)]-2- -4-()-1H- 50% EtOAc/

¹H NMR DMSO : δ 7.77 (2H, ddd), 7.33 (2H, t), 7.24 (2H, dt), 6.87 (2H, dt), 3.32 (3H, s), 2.40 (3H, s).

3-[(4-)]-2- -6-()-1H- 2 i

¹H NMR DMSO: δ 12.30(1H, s), 7.93(1H, d), 7.50-7.59(2H, m), 7.27(2H, dd), 6.95-7. (2H,m), 3.19(3H, s), 2.52(3H, s).

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

THF (5 ml) 21 i (0.28 g) NaH (63 mg, 60%) 가 , 10 (0.13 ml) 가 , 3 Et OH (2 ml) NaOH (2 ml, 10%) 가 , 30 . EtOH , HCl (1M) 가 , (0 .351 g).

¹H NMR DMSO : δ 13.33 (1H, s), 8.02 (1H, dd), 7.81 (1H, dd), 7.40 (1H, t), 7.24 (2H, dt), 6.89 (2H, dt), 5.29 (2H, s), 3.32 (3H, s), 2.39 (3H, s)

MS: APCI+ [M+DMSO] 488

21

2- -3-[(4-)]-6-()-1H- -1-

i) 2- -3-[(4-)]-6-()-1H- -1-

]-2- -6-((10 ml) (60% 45 mg) 3-[(4-))-1H- (160 mg) (20 i) 가 . 30 , (78 μℓ) , 1 , (MgSO₄) , 30% , (180 mg).

MS: ES+[M+H] 438.

ii) 2- -3-[(4-)]-6-()-1H- -1-

ii) (180 mg) (5 ml) , NaOH (10% 1 ml) 가 . 1 ,
 , HCl (1M) ,
 , (MgSO₄), NH₂ (0.5 g)
 , MeCN , 5% /MeCN 30 mg .

¹H NMR DMSO : δ 8.11 (1H, s), 7.50-7.62 (2H, m), 7.24-7.29 (2H, m), 6.98 (2H, dd),
 4.96 (2H, s), 3.21 (3H, s), 2.48 (3H, s)
 MS: APCI+ [M+DMSO] 488.

22

4- -3-[(4-)]-2- -1H- -1-

i) 4- -3-[4(-)]-2- -1H-

(3-)- 15 (i)
 (10% EtOAc/) .

¹H NMR CDCl₃ δ 7.31 (1H, s), 7.30 (2H, d), 7.13 (2H, dt), 7.02 (1H, t), 6.94 (2H, dt), 2.52
 (3H, s).

ii) 4- -3-[(4-)]-2- -1H- -1- , 1,1-

(i) t- 11 (ii)
 (10% EtOAc/) .

¹H NMR CDCl₃: δ 7.31 (dd, 1H), 7.21 (dd, 1H), 7.14 – 7.10 (m, 2H), 7.05 (t, 1H), 6.94–
 6.91 (m, 2H), 4.77 (s, 2H), 2.49 (s, 3H), 1.43 (s, 9H).

iii) 4- -3-[(4-)]-2- -1H- -1-

(2 ml) (ii) (0.09 g) (0.1 ml) 가 .
 (0.025 g) , , 40

¹H NMR (DMSO) δ 7.59 (dd, 1H), 7.29–7.25 (m, 3H), 7.08 (t, 1H), 6.94 (dt, 2H), 5.16 (s,
 2H), 2.43 (s, 3H).
 MS: APCI+[M+H] 411
 M.pt. 분해 >213°C

23

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

22 (ii) (1 g), N-tert- (0.48 g), Pd₂(dba)₃ (3
 mg), 2,2'- ()-1,1'- (Binap) (10 mg) (5 ml) 11
 0 1 가 , EtOAc , MgSO₄
 , (25% EtOAc/ , 50% EtOAc/ /1%
) HPLC (MeCN/NH₃ ())
 (0.021 g) .

¹H NMR (DMSO) δ 7.22 (dt, 2H), 7.12 (d, 1H), 7.02 (t, 1H), 6.93 (dt, 2H), 6.66 (d, 1H),
 4.57 (s, 2H), 3.33 (s, 4H), 2.79 (s, 4H), 2.36 (s, 3H), 1.39 (s, 9H).
 MS: APCI+ [M+H] 516
 M.pt. 173°C

24

3-[(4-)]-2- -4-(1-)-1H- -1-

i) 3-[(4-)]-4-[4-[(1,1-)]-1-]-2- -1H- -1-
1,1-

23

(25% EtOAc/)

¹H NMR (DMSO) 90°C δ 7.21-7.15 (m, 3H), 7.08 (t, 1H), 6.92 (d, 2H), 6.72 (d, 1H), 4.99 (s, 2H), 3.26 (s, 4H), 2.81 (t, 4H), 2.40 (s, 3H), 1.40 (s, 18H).

ii) 3-[(4-)]-2- -4-(1-)-1H- -1-

(5 ml) (i) (0.34 g) (1.3 ml) 4M HCl 가 ,
 (6 ml) 가 , 18 (20 ml) ,
 40 (0.2 g) .

¹H NMR (DMSO) 90°C δ 7.28-7.20 (m, 3H), 7.12 (t, 1H), 6.95 (d, 2H), 6.77 (d, 1H), 5.02 (s, 2H), 3.08 (d, 4H), 3.00 (d, 4H), 2.42 (s, 3H).

MS: APCI-[M-H] 414
 M.pt. 분해 >249 °C

25

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

i) 5- -3-[4(-)]-2- -1H-

(4-)- 15 (i)
 (10% EtOAc/) .

¹H NMR (CDCl₃) δ 8.31 (s, 1H), 7.64 (d, 1H), 7.28 (dd, 2H), 7.22 (d, 2H), 7.13 (m, 2H), 6.93 (dt, 2H), 2.51 (s, 3H).
 MS: APCI+ [M+H] 352

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

(i) t- 11 (ii)
 (10% EtOAc/) .

¹H NMR (DMSO) δ 7.54 (d, 1H), 7.45 (d, 1H), 7.34 - 7.25 (m, 3H), 6.97 (m, 2H), 5.15 (s, 2H), 2.41 (s, 3H), 1.41 (s, 9H).

-2- -1H- -1- 가 , 5- -3-[(4-)]-1

¹H NMR (DMSO) δ 7.56 (d, 1H), 7.46 (d, 1H), 7.34 - 7.27 (m, 3H), 6.97 (dd, 2H), 5.27 (s, 2H), 4.17 (q, 2H), 2.41 (s, 3H), 1.21 (t, 3H).

iii) 5- -3-[(4-)]-2- -1H- -1-

(10 ml) (ii) (0.2 g) NaOH 1M (0.5 ml) 가 .
 , 40 (0.13 g) .

¹H NMR (DMSO) δ 7.39 (d, 1H), 7.37 (d, 1H), 7.26 (d, 2H), 7.21 (dd, 1H), 6.97 (dt, 2H), 4.47 (s, 2H), 2.38 (s, 3H).

26

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

i) 3-[(4-)]-2- -5- -1H- -1-

(0.8 ml) (3 ml) 25 (ii) (0.5 g) (1.4 ml) 2M
 , (0.131 g) () (0) (1.2 g) 가 . 2
 가 , , .
 (0.4 g) . (ii) .

ii) 3-[(4-)]-2- -5- -1H- -1-

26 (iii) . HPLC .

¹H NMR (DMSO) δ 7.61-7.53 (4H, m), 7.46-.38 (3H, m), 7.31 – 7.22 (3H, m), 7.01 (2H, dd), 4.91 (2H, s), 2.42 (3H, s).

MS: APCI- [M-H] 406

27

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

i) 3-[4-)]-5- -2- -1H-

-70 (150 ml) 4- (5 g) t- (4.6 g)
) 5 가 . 10 , 1-[(4-)]-2- (8.49 g)
 (20 ml) 가 . 1 , (5.9 ml) 가 ,
 가 . , HCl () , MgSO₄ (7.5 g) .

¹H NMR (CDCl₃) δ 8.61 (s, 1H), 7.84 (s, 1H), 7.44 (dd, 1H), 7.41 (d, 1H), 7.19 – 7.08 (m, 2H), 6.93 (dd, 2H), 2.56 (s, 3H).

ii) 3-[(4-)]-5- -2- -1H- -

(iii) (i) 11 (ii) .

iii) 3-[(4-)]-5- -2- -1H- -1-

(ii) 16 (iii) .

¹H NMR (DMSO) δ 13.34 (s, 1H), 7.82–7.77 (m, 2H), 7.57 (dd, 1H), 7.29 (dt, 2H), 7.02–6.98 (m, 2H), 5.23 (s, 2H), 2.46 (s, 3H).

MS: APCI-[M-H] 355

28

3-[(4-)]-2.5- -1H- -1- -

i) (2.5- -1H- -1-)

60% / (0.64 g) DMF (15 ml) 2,5- -1H- (2.0 g) 가 . 15 ,
 (2.7 ml) 가 , 20 1%
 (100 ml) , (2 x 100 ml) , (2 x 50 ml) (20 ml)
 (MgSO₄), , EtOH (20
 ml) , (1M, 10 ml) 가 . 1 , (1M, 10 ml)

pH 6 , (1
 -10%) . (1.3 g).

MS (APCI+) 204 [M+H]⁺

¹H NMR DMSO-d₆: δ 7.22 - 7.17 (2H, m), 6.85 (1H, d), 6.11 (1H, s), 4.87 (2H, s), 2.34 (3H, s), 2.30 (3H, s)

ii) {3-[(4-)]-2,5- -1H- -1- }

DMF (5 ml) 4- (0.27 g) 28 i) (0.2 g) (0.51 g)
 가 . 1 , HPLC . , (0.25 g).

MS: APCI- [(M-NH₄)-H]⁺ 334

¹H NMR DMSO-d₆: δ 7.62 (2H, d), 7.35 (1H, d), 7.10 (1H, s), 7.08 (2H, d), 6.97 (1H, d), 4.80 (2H, s), 2.36 (3H, s), 2.32 (3H, s)

29

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

DMF (5 ml) 3- (0.25 g) 28 i) (0.2 g) (0.51 g)
 가 . 1 , HPLC . , (0.22 g).

MS: APCI- [(M-H)]⁺ 340

¹H NMR DMSO-d₆: δ 7.40 (1H, d), 7.16 (1H, s), 7.11 (1H, t), 6.98 (1H, d), 6.63 (1H, d), 6.55 (1H, d), 6.45 (1H, s), 5.08 (2H, s), 3.61 (3H, s), 2.39 (3H, s), 2.34 (3H, s)

30

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

DMF (5 ml) 4- (0.25 g) 28 i) (0.2 g) (0.51 g)
 가 . 1 , HPLC . , (0.27 g).

MS: APCI- [(M-H)]⁺ 340

¹H NMR DMSO-d₆: δ 7.24 (1H, d), 7.15 (1H, s), 6.95 (2H, d), 6.90 (1H, d), 6.78 (2H, d), 4.60 (2H, s), 3.66 (3H, s), 2.38 (3H, s) 및 2.33 (3H, s).

31

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

DMF (5 ml) 2- (0.32 g) 28 i) (0.2 g) (0.44 g) 가
 . 1 , HPLC . , (0.18 g).

MS APCI [(M-NH₄)-H]⁺ 338

¹H NMR DMSO-d₆: δ 7.26 (1H, d), 7.16 (1H, d), 7.08 (1H, s), 7.01 - 6.85 (3H, m), 6.48 (1H, d), 4.57 (2H, s), 2.83 (2H, q), 2.34 (3H, s), 2.31 (3H, s), 1.31 (3H, t)

32

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

DMF (5 ml) 2- (0.16 g) 28 i) (0.2 g) (0.29 g) 가
 . 1 , HPLC , (0.16 g).

MS: APCI- [(M-H)]⁺ 324

¹H NMR DMSO-d₆: δ 7.24 (1H, d), 7.15 (1H, d), 7.07 (1H, s), 6.97 - 6.86 (3H, m), 6.47 (1H, d), 4.49 (2H, s), 2.42 (3H, s), 2.33 (3H, s), 2.31 (3H, s)

33

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

EtOH (5 ml) 3- (0.175 g) 28 i) (0.2 g) (0.29 g)
 가 . 1 , HPLC ,
 (10 ml) , (1M, 0.52 ml) ,
 (0.19 g).

MS APCI- [(M-Na)-H]⁺ 344

¹H NMR DMSO-d₆: δ 7.28 - 7.15 (2H, m), 7.13 - 7.06 (2H, m), 6.97 - 6.88 (3H, m), 4.42 (2H, s), 2.36 (3H, s), 2.33 (3H, s)

34

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

(0.51 g) DMF (5 ml) 2- (0.26 g) 28 i) (0.2 g)
 가 . 1 , HPLC ,
 MeOH (10 ml) , (1 M, 0.52 ml) ,
 (0.08 g)

MS APCI- [(M-Na)-H]⁺ 328

¹H NMR DMSO-d₆: δ 7.24 (1H, d), 7.18 (1H, m), 7.10 (1H, s), 7.09 (1H, m), 6.91 (1H, d), 6.56 (1H, m), 6.56 (1H, m), 4.42 (2H, s), 2.35 (3H, s), 2.33 (3H, s)

35

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

(0.51 g) DMF (5 ml) 2,6- (0.36 g) 28 i) (0.2 g)
 가 . 1 , HPLC ,
 , (0.22 g)

MS APCI- [M-H]⁺ 378

¹H NMR DMSO-d₆: δ 7.49 (2H, d), 7.29 (1H, m), 7.24 (1H, d), 7.13 (1H, s), 6.88 (1H, d), 4.81 (2H, s), 2.44 (3H, s), 2.29 (3H, s)

36

3-(1H- -2-)-2,5- -1H- -1-

(0.51 g) DMF (5 ml) 1H- -2- (0.20 g) 28 i) (0.2 g)
 가 . 1 , HPLC ,
 , (0.23 g)

MS APCI- [M-H]⁺ 300

¹H NMR DMSO-d₆: δ 8.15 (1H, s), 7.21 (1H, d), 7.21 (2H, s), 6.90 (1H, d), 4.51 (2H, s), 2.40 (3H, s), 2.35 (3H, s)

37

2,5- -3-(1H-1,2,4- -3-)-1H- -1-

2 g) (0.51 g) DMF (5 ml) 1H-1,2,4- -3- (0.20 g) 28 i) (0.24 g)
 가 . 1 , HPLC , , ,

MS APCI- [M-H]⁺ 301

¹H NMR DMSO-d6: δ 8.15 (1H, s), 7.21 (1H, d), 7.20 (1H, s), 6.90 (1H, d), 4.49 (2H, s), 2.40 (3H, s), 2.35 (3H, s)

38

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

(0.51 g) DMF (5 ml) 4- -4H-1,2,4- -3- (0.20 g) 28 i)
 (0.2 g) 가 . 1 , HPLC , (0.21 g)

MS APCI- [M-H]⁺ 315

¹H NMR DMSO-d6: δ 8.44 (1H, s), 7.29 (1H, s), 7.19 (1H, d), 6.90 (1H, d), 4.46 (2H, s), 3.52 (3H, s), 2.46 (3H, s), 2.35 (3H, s)

39

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

(0.51 g) DMF (5 ml) 4- -2- (0.23 g) 28 i) (0.2 g)
 가 . 1 , HPLC , (0.23 g)

MS APCI- [M-H]⁺ 315

¹H NMR DMSO-d6: δ 7.69 (1H, s), 7.29 (1H, d), 7.22 (1H, s), 6.95 (1H, d), 4.78 (2H, s), 2.42 (3H, s), 2.36 (3H, s), 1.99 (3H, s)

40

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

0.2 g) (0.51 g) DMF (5 ml) 1- -1H- -2- (0.23 g) 28 i) (0.21 g)
 가 . 1 , HPLC , ,

MS APCI- [M-H]⁺ 314

¹H NMR DMSO-d6: δ 7.37 (1H, s), 7.29 (1H, d), 7.15 (1H, s), 6.93 (1H, d), 6.84 (1H, s), 4.97 (2H, s), 3.60 (3H, s), 2.49 (3H, s), 2.36 (3H, s)

41

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

i) 4-()-

1- -4-()- (1.74 g) (0.67 g) DMF (10 ml)
 , 24 , , 2 M (20 ml)
 (2 x 50 ml) , (2 x 25 ml) (20 ml)
 (MgSO₄), , (1.8 g)

MS: ESI +: [M+H] 188

¹H NMR CDCl₃: δ 7.99 (2H, d), 7.27 (2H, d), 3.05 (3H, s)

ii) 2,5- -3- [(4- ())] -1H- -1- _____

(0.51 g) DMF (5 ml) 41 i) (0.565 g) 28 i)
 (0.2 g) 가 . 1 , HPLC , (0.25 g)

MS: APCI- [M-H] 388

¹H NMR DMSO-d₆: δ 7.69 (2H, d), 7.31 (1H, d), 7.15 (2H, d), 7.11 (1H, s), 6.95 (1H, d), 4.62 (2H, s), 3.13 (3H, s), 2.36 (3H, s), 2.33 (3H, s)

42

2,5- -3-(8-)-1H- -1- _____

(0.25 g) DMF (5 ml) 8- (0.16 g) 28 i) (0.1 g)
 가 . 1 , HPLC , (0.08 g)

MS: APCI - [M-H] 361

¹H NMR DMSO-d₆: δ 8.97 (1H, s), 8.37 (1H, d), 7.62 (2H, m), 7.32 (1H, d), 7.27 (1H, t), 7.08 (1H, s), 6.94 (1H, d), 6.71 (1H, d), 4.69 (2H, s), 2.36 (3H, s), 2.30 (3H, s)

43

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

i) 7- -5- -2,4- -3- -1H- _____

(100 ml) 2- -4- -5- (1.65 g) -65
 (5 ml) t- (1.13 g) , -65 10 , -65
 (5 ml) (1.080 g) , -65 1 , -65
 (1.05 g) , (MgSO₄),
 25%
 (1.7 g)

MS: APCI - [M-H] 242

¹H NMR DMSO-d₆: δ 11.67 (1H, s), 7.07 (1H, d), 2.71 (3H, d), 2.48 (3H, s), 2.19 (3H, s).

ii) 7- -5- -2,4- -1H- _____

(50 ml) i) (1.13 g) (1.43g) 60 2
 , (MgSO₄), , 1 N ,
 (0.82 g) 10%

MS: ESI 197 [M+H]

¹H NMR DMSO-d₆: δ 11.25 (1H, s), 6.97 (1H, d), 6.28 (1H, q), 2.40 (3H, d), 2.30 (3H, d)

iii) 5- -2,4- -1H- _____

(50 ml) 10% (200 mg) (2 ml) (2.3 g)
 , 1 , (10 ml) ii) (721 mg) , 2
 , 10% (500 mg) , 40 2 , (MgSO₄),

MS: ESI + [M+H] 163

¹H NMR CDCl₃: δ 7.82 (1H, s), 7.04 - 7.01 (1H, m), 6.82 (1H, dd), 6.21 - 6.21 (1H, m), 2.45 (3H, s), 2.40 - 2.40 (3H, m).iv) [5- -2,4- -1H- -1-]

(100 ml) iii) (2 g) (4.8 g)
 (4.22 g) , 가 , (2.4 g) (1.3 ml)
 , 2 가 , . (3 x)
 (MgSO₄), . 20%
 (2.57 g) .

MS: APCI-[M-H] 253

BP 176°C.

¹H NMR DMSO-d₆: δ 6.92 - 6.83 (2H, m), 6.30 (1H, s), 4.76 (2H, s), 3.74 (3H, s), 2.40 - 2.39 (6H, m).v) [5- -2,4- -1H- -1-]

THF (50 ml) iv) (2.51 g) (10 ml) (894 mg)
 , , THF 1 N ,
 (MgSO₄) (2.33 g) .

¹H NMR DMSO-d₆: δ 12.98 (1H, s), 7.16 (1H, dd), 6.83 (1H, dd), 6.27 (1H, s), 4.92 (2H, s), 2.32 - 2.32 (6H, m)

MS: APCI-[M-H] 220

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

DMF (2 ml) v) (221 mg) (508 mg) 4- (288 mg)
) , . HPLC (50 mg)

MS: APCI-[M-H] 362

¹H NMR DMSO-d₆: δ 7.30-7.25 (3H, m), 6.97 - 6.89 (3H, m), 4.74 (2H, s), 2.44 (3H, d), 2.36 (3H, s)443- [(4-)]-5- -2,4- -1H- -1-

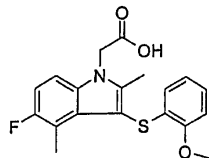
4- 49) vi) , 49 v) (221 mg), (508 mg)
 (270 mg) .

MS: APCI-[M-H] 353

¹H NMR DMSO-d₆: δ 7.68 - 7.63 (2H, m), 7.33 - 7.29 (1H, m), 7.12 - 7.08 (2H, m), 6.98 - 6.92 (1H, m), 4.78 (2H, s), 2.40 (3H, d), 2.35 (3H, s)453- [(2-)]-5- -2,4- -1H- -1-

2- 49) vi) , 49 v) (221 mg), (508 mg)
 (289 mg) .

MS: APCI-[M-H] 362

¹H NMR DMSO-d₆: δ 7.45 - 7.42 (1H, m), 7.25 - 7.21 (1H, m), 7.13 - 7.06 (2H, m), 6.94 - 6.87 (1H, m), 6.53 - 6.50 (1H, m), 4.53 (2H, s), 2.39 (3H, d), 2.33 (3H, s)465- -3-[(2-)]-2,4- -1H- -1-

2- 49) vi) , 49 v) (221 mg), (508 mg)
 (280 mg)

MS: APCI-[M-H] 358

¹H NMR DMSO-d₆: δ 7.39-7.34 (1H, m), 7.08-6.93 (3H, m), 6.74-6.69 (1H, m), 6.33 (1H, dd), 5.09 (2H, s), 3.89 (3H, s), 2.40 (3H, d), 2.34 (3H, s)475- -3-[(2-)]-2,4- -1H- -1-

2- 49) vi) , 49 v) (221 mg), (508 mg)
 (276 mg)

MS: APCI-[M-H] 356

¹H NMR DMSO-d₆: δ 7.28-7.23 (1H, m), 7.18 (1H, dd), 7.03-6.87 (3H, m), 6.47 (1H, dd), 4.71 (2H, s), 2.80 (2H, q), 2.40 (3H, d), 2.35 (3H, s), 1.29 (3H, t)485- -2,4- -3-[[2-(1-)]]-1H- -1-

2- 49) vi) , 49 v) (221 mg), (508 mg)
 (304 mg)

MS: APCI-[M-H] 370

¹H NMR DMSO-d₆: δ 7.29 - 7.25 (2H, m), 7.03 (1H, td), 6.95 - 6.88 (2H, m), 6.47 (1H, dd), 4.78 (2H, s), 3.44 (1H, 5중항), 2.40 (3H, d), 2.35 (3H, s), 1.30 (6H, d).495- -2,4- -3-[[2-()]]-1H- -1-

2- 49) vi) , 49 v) (221 mg), (508 mg)
 (356 mg)

MS: APCI-[M-H] 396

¹H NMR DMSO-d₆: δ 7.70 (1H, d), 7.38 (1H, t), 7.27 - 7.23 (2H, m), 6.91 (1H, t), 6.76 (1H, d), 4.57 (2H, s), 2.38 (3H, d) 및 2.35 (3H, s).502,5- -4-()-3-[(4- -2-)]-1H- -1-

i) 2,5- -4-()-3-()-1H-

4- -3-()- 43 i)

¹H NMR DMSO-d6: δ 11.94 (1H, s), 7.49 (1H, d), 7.01 (1H, d), 3.51 (3H, s), 2.69 (3H, s), 2.55 (3H, s), 2.19 (3H, d)

b) 2,5- -4-()-1H-

(20 ml) a) (1.00 g) (1.15 g) 60 2
, (MgSO₄), (0.47 g) , 1 N ,

¹H NMR DMSO-d6: δ 11.36 (1H, s), 7.46 (1H, d), 6.99 (1H, d), 6.64 (1H, d), 3.33 (3H, s), 3.10 (3H, s), 2.66 (3H, s)

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

DMF (2 ml) b) (200 mg) (210 mg) 2- , 4- (300 mg)
, 1 , 60% (4.0)
(0.20 g) 가 (0.30 g) 가 , 30 , (2 ml), (2 ml)
3 x 10 ml) 가 . 30 , (3 x 10 ml) , (2 M HCl, 5 ml), (MgSO₄),
HPLC (172 mg) .

MS: APCI-[M-H] 471
¹H NMR DMSO-d6: δ 7.94-.69 (4H, m), 7.49-7.24 (3H, m), 7.19 (1H, d), 5.05 (2H, s), 3.57 (3H, s), 3.34 (3H, s), 2.80 (3H, s).

51

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

ii) (200 mg) 3- HPLC (0.3 g) (40 mg) 50 iii)

MS: APCI-[M-H] 422
¹H NMR DMSO-d6: δ 7.83 - 7.69 (1H, m), 7.26 - 6.97 (3H, m), 6.88 - 6.73 (2H, m), 5.01 (2H, d), 3.57 (3H, s), 3.32 (3H, s), 2.69 (3H, s)

52

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

ii) (200 mg) 2- (0.3 g) , 57 iii)
(55 mg)

MS: APCI-[M-H] 422
¹H NMR DMSO-d6: δ 7.76 (1H, d), 7.39 (1H, m), 7.21 - 6.95 (3H, m), 6.34 (1H, m), 4.93 (2H, s), 3.64 (3H, s), 3.29 (3H, s), 2.69 (3H, s)

53

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

(i) 3-[(4-)]-2- -1H- -5-

(20 ml) 4 27 가 (i) (2 g) 12.5 M HCl () (5 ml) 가 pH 2 (2 g)

¹H NMR DMSO-d6: δ 12.51 (1H, s), 12.05 (1H, s), 7.96 (1H, d), 7.75 (1H, dd), 7.46 (1H, dd), 7.27 (2H, dd), 6.97 (2H, dd), 2.47 (3H, s)

(ii) 3-[(4-)]-2- -1H- -5-

(50 ml) (i) (1 g) / (12.6 ml) 가

¹H NMR DMSO-d6: δ 12.12 (1H, s), 7.97 (1H, d), 7.77 (1H, dd), 7.49 (1H, dd), 7.27 (2H, dt), 6.97 (2H, dt), 3.80 (3H, s), 2.47 (3H, s)

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

(ii) t- , 11 (ii) (: 14% EtOAc/)

¹H NMR DMSO-d6: δ 8.01 (1H, d), 7.82 (1H, dd), 7.67 (1H, d), 7.28 (2H, m), 6.97 (2H, dt), 5.20 (2H, s), 3.81 (3H, s), 2.44 (3H, s), 1.42 (9H, s)

(iv) 3-[(4-)]-5-()-2- -1H- -1-

(iii) , 22 (iii)

¹H NMR DMSO-d6: δ 13.28 (1H, s), 8.01 (1H, d), 7.81 (1H, dd), 7.68 (1H, d), 7.28 (2H, d), 6.98 (2H, d), 5.20 (2H, s), 3.82 (3H, s), 2.45 (3H, s).

MS: APCI- [M-H] 388

M.pt 221-223 °C

54

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

(i) 5- -3-[(4-)]-2- -1H- -1-

1 M () (3 ml) 53 (0.5 g) , pH 2
100 10 가 , 2 M HCl () (0.1 g)

55

3-[(4-)]-2- -4- -1H- -1-

i) 3-[(4-)]-2- -4- -1H-

-78 가 THF (700 ml) 3- (8 g) t- (6.3 g) 5
20 가 , 1-[(4-)]-2- (11.6 g)
(20 ml) 가 .2 , (8.1 ml) 가 ,
가 . 2M HCl () 가 , (5.8 g)

¹H NMR DMSO-d₆: δ 12.55 (s, 1H), 7.76 (dd, 1H), 7.63 (dd, 1H), 7.31-7.22 (m, 3H), 6.91 (dd, 2H), 2.47 (s, 3H)

ii) 3-[(4-)]-2- -4- -1H- -

THF (100 ml) (60%)(0.85 g) , (i) (5.6 g)
 THF (50 ml) 가 30 , (2.3 ml) 1
 0 가 2 , ,
 (MgSO₄) , (5 g)

¹H NMR DMSO-d₆: δ 7.97 (dd, 1H), 7.65 (dd, 1H), 7.35 (t, 1H), 7.26 (dt, 2H), 6.92 (dt, 2H), 5.40 (s, 2H), 4.19 (q, 2H), 2.45 (s, 3H), 1.22 (t, 3H).

iii) 3-[(4-)]-2- -4- -1H- -

THF (5 ml) (ii) (0.1 g) 1 M NaOH () (0.25 ml) 가
 pH 2 , 50 HCl ()
 07 g) (0.

¹H NMR DMSO-d₆: δ 13.37 (s, 1H), 7.97 (d, 1H), 7.64 (d, 1H), 7.34 (t, 1H), 7.25 (dt, 2H), 6.92 (dt, 2H), 5.28 (s, 2H), 2.45 (s, 3H).

MS: APCI- [M-H] 375

M.pt. dec>198°C

56

4- -3-[(4-)]-2- -1H- -1-

i) 4- -3-[(4-)]-2- -1H- -1-

(170 ml) 55 (ii) (2.25 g) , 5% Pt/C (0.5 g) H₂
 2 bar (: 14% EtOAc/) , (1.4 g)

¹H NMR (DMSO) δ 7.30 (dd, 2H), 7.00 (dt, 2H), 6.85 (t, 1H), 6.68 (dd, 1H), 6.23 (dd, 1H), 5.33 (s, 2H), 5.09 (s, 2H), 4.16 (q, 2H), 2.33 (s, 3H), 1.21 (t, 3H).

, 3-[(4-)]-4-()-2- -1H- -1- ,
 (0.33 g).

¹H NMR DMSO-d₆: δ 7.32 (dd, 2H), 7.01 (dd, 2H), 6.95 (t, 1H), 6.73 (d, 1H), 6.16 (d, 1H), 5.70 (t, 1H), 5.11 (s, 2H), 4.16 (q, 2H), 3.05 (dt, 2H), 2.34 (s, 3H), 1.21 (t, 3H), 1.02 (t, 3H).

ii) 4- -3-[(4-)]-2- -1H- -1-

1 (iii) (0.03 g).

¹H NMR (DMSO) δ 7.29 (dt, 2H), 7.01 (dt, 2H), 6.88 (t, 1H), 6.76 (d, 1H), 6.30 (d, 1H), 4.99 (s, 2H), 2.33 (s, 3H).

MS: APCI- [M-H] 345

M.pt. dec > 235 °C

57

3-[(4-)]-4-()-2- -1H- -1-

2 (i) , 55 (ii)
HPLC

¹H NMR DMSO-d6: δ 7.29 (dt, 2H), 7.02 (m, 2H), 6.88 (t, 1H) 6.64 (d, 1H), 6.11 (d, 1H), 5.66 (t, 1H), 4.51 (s, 2H), 3.04 (dt, 2H), 2.31 (s, 3H), 1.01 (t, 3H).
MS: APCI+ [M+H] 375.

58

3-[(4-)]-4- -2- -1H- -1-

(i) 3-[(4-)]-4- -2- -1H-

3- , 27 (i)
(: 14% EtOAc/)

¹H NMR DMSO-d6: δ 11.99 (1H, s), 7.50 (1H, dd), 7.44 (1H, dd), 7.26 (2H, m), 6.92 - 6.84 (3H, m), 2.43 (3H, s)

(ii) 3-[(4-)]-4- -2- -1H- -1-

(i) , 11 (ii) (iii)

¹H NMR DMSO-d6: δ 7.52 (2H, d), 7.25 (2H, dt), 6.93 - 6.86 (3H, m), 4.86 (2H, s), 2.40 (3H, s)
MS: APCI- [M-H] 456

59

3-[(4-)]-2- -4- -1H- -1-

i) 3-[(4-)]-2- -4- -1H- -1- , 1,1-

(0.8 ml) (3 ml) 22 (ii) (0.5 g) 2 M
(1.4 ml), (0.131 g) () (0) (1.2 g) 가 . 2
가 , 가 (ii)
(0.4 g) 가

ii) 3-[(4-)]-2- -4- -1H- -1-

(10 ml) (i) (0.4 g) (2 ml) 가 ,
pH 2 , 2 M HCl ()
3 () , 2 M HCl () HPLC (: MeCN/NH
g) , 40 pH 2 (0.15)

¹H NMR DMSO-d6: δ 7.55 (d, 1H), 7.26 – 7.07 (m, 8H), 6.87 (d, 1H), 6.56 (m, 2H), 5.18 (s, 2H), 2.40 (s, 3H).
MS: APCI+[M+H] 408

(比) 100-210 Ci/mmol [³ H]PGD₂ (Perkin Elmer Life Sciences)

rhCRTh2/G 16 HEK , 10% ((HyClone)), 1 mg/ml , 2 mM L
 - 1% DMEM , 2
 ((Fisher), : TKT-170-070E) HEK
 18 , 500 mM 가
 (PBS, 1 50 ml) 1 50 ml
 [20 mM HEPES (pH 7.4), 0.1 mM , 1 mM EDTA, 0.1 mM
 100 μg/ml (bacitracin)] 가 , 4 220xg 10
 (Polytron) 20 2 . 4 22
 0xg 10 , 4 90000xg 30
 1 4 ml ,
 -80

(Corning) 96- NBS () , CR
 Th2 HEK SPA PVT WGA ((Amersham)) , 1
 mg 가 25 μg (batch) , 4
 (800xg 7) (5 mM) (4
 7.4) 1 , 가 10 mg/ml 50 mM HEPES, pH

6.25 nM [³ H]PGD₂ 20 μℓ, SPA 20 μℓ,
 13,14- -15- D₂ (DK-PGD₂, -
 (Cayman chemical company)) 10 μℓ DK-PGD₂ DMSO ,
 100 가 DMSO 10%가
 (2) (Wallac Microbeta) (1
 1).

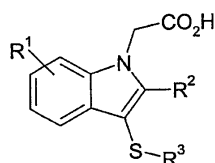
(I) IC₅₀ 10 μM .
 , 23 pIC₅₀ 6.05 , 50 pIC₅₀ 7.2 , 29
 pIC₅₀ 8.35 .

(57)

1.

I

< I >



R¹ , , CN, , SO₂R⁴, OH, OR⁴, S(O)_xR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶
 , () , C₂-C₆ , C₂-C₆ C₁₋₆ , C₂-C₆

, C₂-C₆ C₁₋₆, OR⁸, NR⁵R⁶ S(O)_xR⁷ (x = 0, 1, 2)

R², CN, SO₂R⁴, CONR⁵R⁶, CH₂OH, CH₂OR⁴ C₁₋₇, C₁₋₇, OR⁸, NR⁵R⁶ S(O)_xR⁷ (x = 0, 1, 2)

R³, CN, OH, SO₂R⁴, OR⁴, SR⁴, SOR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NHCOR⁴, NHSO₂R⁴, NHCO₂R⁴, NR⁷SO₂R⁴, NR⁷CO₂R⁴, C₂-C₆, C₂-C₆, C₁₋₆, OR⁸, NR⁵R⁶ S(O)_xR⁷ (x = 0, 1, 2)

R⁴, OR¹⁰, OH, NR¹¹R¹², S(O)_xR¹³ (x = 0, 1, 2), CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, CN,

R⁵R⁶, OR⁸, NR¹⁴R¹⁵, CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, NR¹⁴SO₂R¹⁵, CN, O, S(O)_x(x = 0, 1, 2), NR¹⁶, R⁵R⁶, C₁₋₃

R⁷R¹³, C₁-C₆

R⁸, C(O)R⁹, ()C₁-C₆, ()

R⁹, R¹⁰, R¹¹, R¹², R¹⁴R¹⁵, C₁-C₆, ()

R¹⁶, C₁₋₄, -COC₁-C₄, COYC₁-C₄ (Y = O, NR⁷), R¹, R²가, R³ 2-

2.

R¹, SO₂Me, SO₂Et, NR⁴R⁵, N-

3.

R²가 C₁₋₆

4.

R³ 1, SO₂Me,

5.

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

3-[(3-)]-2,5- -1H- -1- ;
 3-[(4-)]-2,5- -1H- -1- ;
 3-[(2-)]-2,5- -1H- -1- ;
 3-[(2,5-)]-2,5- -1H- -1- ;
 3-[(4-)]-2,5- -1H- -1- ;
 3-[(4- -2-)]-2,5- -1H- -1- ;
 3-[(4-)]-4- -2,5- -1H- -1- ;
 5- -3-[(4-)]-6- -2- -1H- -1- ;
 3-[(4-)]-4-()-7- -2- -1H- -1- ;
 3-[(4-)]-4-[()]-7- -2- -1H- -1- ;
 4- -3-[(4-)]-2- -1H- -1- ;
 5- -3-[(4-)]-2- -1H- -1- ;
 6- -3-[(4-)]-2- -1H- -1- ;
 7- -3-[(4-)]-2- -1H- -1- ;
 3-[(4-)]-2- -5-()-1H- -1- ;
 2- -3-[(4-)]-6-()-1H- -1- ;
 4- -3-[(4-)]-2- -1H- -1- ;
 3-[(4-)]-4-[4-[(1,1-)]-1-]-2- -1H- -1- ;
 3-[(4-)]-2- -4-(1-)-1H- -1- ;
 5- -3-[(4-)]-2- -1H- -1- ;
 3-[(4-)]-2- -5- -1H- -1- ;
 3-[(4-)]-5- -2- -1H- -1- ;
 3-[(4-)]-2,5- -1H- -1- ;
 3-[(3-)]-2,5- -1H- -1- ;
 3-[(4-)]-2,5- -1H- -1- ;
 3-[(3-)]-2,5- -1H- -1- ;
 2,5- -3-[(2-)]-1H- -1- ;
 3-[(3-)]-2,5- -1H- -1- ;
 3-[(2-)]-2,5- -1H- -1- ;

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

6.

1 5 , | .

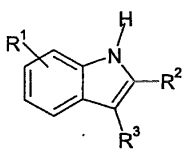
7.

1 6 , | D2 .

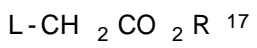
7 8. , .

9. II A ,
 . ,
 . R¹⁷ 가 ,
 .
 , I .

< II >



< A >



R¹, R², R³ I , R¹⁷ , L

9 10. II .

11. D2 I .