



(74)

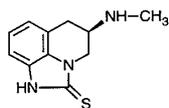
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(54) (5R) - ( ) - 5,6 - - 4H - [4,5,1 - i j] - 2(1H) -

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H) - (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) -  
 가 .



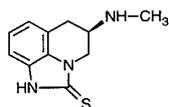
(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) -

5,273,975 (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) -

PCT/US00/00505 (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - ( )  
 6) (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - ( 7)

< >

(5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) -  
 가 .



5,273,975 (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] -  
 2(1H) -

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII)  
 (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - (2H) - (VII)  
 (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - (2H) - (VII)  
 1 1 - 6 ( A ).

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - (2H) - (VII) (5R) - ( ) - 5,6  
 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII)  
 가 가

가  
 가 , CH<sub>3</sub> - (CH<sub>2</sub>)  
 n<sub>1</sub> - COOH ( , n<sub>1</sub> 0 4 ), HOOC - (CH<sub>2</sub>)<sub>n<sub>1</sub></sub> - COOH ( , n<sub>1</sub> ), HOOC  
 - CH=CH - COOH - COOH 가 [Int. J. Pharm., 33, 201 - 217 (19  
 86)]

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - (2H) - (VII)  
 가 (5R) - 5 - ( ) - 5,6 - - 4H -  
 [4,5,1 - ij] - 2(1H) - (VIII) , (5R) - 5 - ( ) - 5,6 -  
 - 4H - [4,5,1 - ij] - 2(1H) - (VIII) 가  
 (IX)

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - (2H) - (VII) (5R) - 5 - ( ) -  
 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII) 11

(5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII)  
 가 (IX) 5,273,975

< >

< >

TLC

HPLC

( ) / , ( , )  
 ( )

IR .  
 CMR C-13 , TMS (ppm ( )) .  
 NMR ( ) , (ppm ( )) .

- (C<sub>6</sub>H<sub>5</sub>) .  
 [ ]<sub>D</sub><sup>25</sup> 25 D (589A) ( ) .

MS m/e, m/z / . [M+H]<sup>+</sup> +  
 . EI . CI . FAB .  
 가 / 가 ( ) .

, / (v/v) .  
 , / (w/v) .

가 , ( ) ;

< 1: (R) - >

R- ( [Can. J. Chem., 72(1), 142 - 5 (1994)] , (3.33 kg) DMF (8.2 ml)  
 가 (191.8 g) 가 가  
 , 5 10 , 20 25 가 . 가  
 , 가 , 0 , 가  
 , 20 25 .

1 , 가 , 2  
 , , 20 25 .

< 1: 1 - -4H - [4,5,1 - ij] -2(1H) - (II) >

DMF (10 ml) 4H - [4,5,1 - ij] -2(1H) - ( [I, J. Heterocyclic Chem., 19, 837 - 49 (198  
 2), 1.0 g, 5.8 mmol) 0 , 0 THF t- ( )  
 1.98 M, 3.2 ml, 6.3 mmol) . 0 10 ,  
 (0.73 ml, 6.1 mmol) 가 , t- (MTBE)  
 . MTBE 0 , 0 MTBE 2 .

50

CMR

(CDCl<sub>3</sub>, 100 MHz) 153.78, 136.44, 128.69, 127.67, 127.60, 126.73, 125.86, 122.90, 122.78, 121.28, 116.92, 116.17, 108.36, 44.95 및 42.37 δ.

< 2: (5R,6R) - 1 - - 5 - - 6 - - 5,6 - - 4H - [4,5,1 - ij] - 2 (1H) - (III) >

1 - - 4H - [4,5,1 - ij] - 2(1H) - (II, 1, 240 g), (1.086 kg), (227 ml)  
 l) (48.5%, 13.4 g) , 0 5 (163.5 g)  
 , 가 . 0 5 3 , ,  
 10 t - 45 가 . - 10 - 1  
 5 , 1 , . t - , 40

CMR (CDCl<sub>3</sub>) 156.0, 137.8,

130.5, 129.6, 129.3, 129.1, 126.6, 123.6, 122.5, 119.6, 110.4, 69.9, 49.6, 47.7, 46.9 및 43.8 δ.

< 3: (5S,6S) - 1 - - 5 - - 2 - - 1,2,5,6 - - 4H - [4,5,1 - ij] - 6 - (2R) - (6 - - 2 - ) (IVA) (5R,6R) - 1 - - 5 - - 2 - - 1,2,5,6 - - 4H - [4,5,1 - ij] - 6 - (2R) - (6 - - 2 - ) (IVB) >

(5R,6R) - 1 - - 5 - - 6 - - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (III, 2, 143 g), (3,136 g), N - (100.2 g) 4 - (497 mg)  
 가 , 0 5 . (694 ml) (R) -  
 ( 1, 118.5 g) 1 가 , 0 5 ,  
 . 가 가 .  
 가 . ,  
 , t - . - 10 ,  
 , 50 ,

(5S,6S) - 1 - - 5 - - 2 - - 1,2,5,6 - - 4H - [4,5,1 - ij] - 6 - (2R) - 2 - (6 - - 2 - ) (IVA)

CMR (CDCl<sub>3</sub>) δ 173.2, 157.8, 153.4,

136.1, 134.6, 133.7, 129.2, 128.8, 127.8, 127.8, 127.6, 127.2, 125.9, 125.9, 125.6, 121.5, 121.4, 119.1, 113.2, 109.0, 105, 105.6, 69.2, 55.3, 45.4, 45.2, 42.5, 41.7 및 18.3.

4,5,1 - ij] - 6 - (2R) - 2 - (6 - (5R,6R) - 1 - - 5 - - 2 - - 1,2,5,6 - - 4H - [ (IVB)

(5R,6R) - 1 - - 5 - - 6 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) -

CMR (CDCl<sub>3</sub>) δ 173.2, 157.9, 153.4, 136.1, 135.0, 133.8, 129.2, 128.9, 128.8, 127.8, 127.6, 127.4, 125.8, 125.8, 125.7, 121.6, 121.5, 119.3, 113.1, 109.1, 105.7, 68.7, 55.3, 45.3, 45.2, 42.2, 41.3 및 18.1.

< 4: (5R,6R) - 1 - - 5 - - 6 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2 (1H) - (V) >

(5S,6S) - 1 - - 5 - - 2 - - 1,2,5,6 - - 4H - [4,5,1 - ij] - 6 - (2R) - 2 - ( 6 - - 2 - ) (IVA, 3, 110 g) (1,297 g) . 가 , 30 12 가 가 (R - ) 가 , 가 , 가 , 50

CMR (CDCl<sub>3</sub>) δ 153.7, 136.3, 128.7, 127.8, 127.7, 125.7, 121.3, 119.9, 118.6, 107.5, 66.2, 60.1, 45.1, 42.6 및 34.0.

< 5: (7aS,8aR) - 4 - - 8 - - 7,7a,8,8a - [2,3 - c] [4,5,1 - ij] - 5(4H) - (VI) >

(5R,6R) - 1 - - 5 - - 6 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (V, 4, 70 g) THF (1,389 g) , n- 가 , n- 가 , 가 , 가 , 20 25 가 , 가 , , 40 50

CMR (CDCl<sub>3</sub>) δ 154.1, 136.3, 128.6, 127.9, 127.6, 124.3, 120.7, 119.7, 107.4, 46.7, 44.9, 40.7, 38.1 및 37.6.

< 6: (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VII) >

(7aS,8aR) - 4 - - 8 - - 7,7a,8,8a - [2,3 - c] [4,5,1 - ij] - 5(4H) - (V  
 l, 5, 40 g), t - (42.4 g) (1,200 g) - 33 30 60  
 가 , 가 . . . . .

< 7: (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2 - (1H) - (VIII) >



(300 mL) (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VII,  
 6, 15.0 g, 73.8 mmol) (36.1 g, 81.2 mmol) 125 가  
 5 20 25 ,  
 (2.2N, 200 mL) 가 , 가 (1N) 가  
 0 g) , ( , 225 g; / , 3.5 - 5.0/96.5 - 95) (4

IR ( 브리프 ) 2940, 2907, 2884, 1483, 1458,  
 1391, 1366, 1354, 1254, 1239, 1229, 895, 762, 734 및 630 cm<sup>-1</sup>; NMR (300 MHz,  
 CDCl<sub>3</sub>) δ 7.12, 7.03, 7.00, 4.30, 3.96, 3.30-3.50, 3.15, 2.88 및 2.57; MS (EI) m/z  
 219 (M<sup>+</sup>), 190, 189, 187, 186, 164, 163, 155, 145; HRMS (FAB) C<sub>11</sub>H<sub>13</sub>N<sub>3</sub>S (MH<sup>+</sup>)  
 에 대한 계산치 = 220.0908, 실측치 = 220.0904.

< 8: (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (IX) >



(~1 mL) (0.317 g, 2.36 mmol) (5R) - ( ) - 5,  
 6 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII, 7, 0.493 g, 2.25 mmol) 가

mp = 195-196°;  $[\alpha]^{25}_D = -60^\circ$  (c 0.93, 메탄올); IR (프리프트) 3140, 3112, 3060, 2969, 1627, 1619, 1568, 1481, 1455, 1398, 1389, 1361, 1220, 868 및 747  $\text{cm}^{-1}$ ; NMR (300 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  7.20-7.30, 7.10-7.20, 6.26, 4.49, 4.31, 4.05-4.20, 3.28 및 2.83; CMR (100 MHz,  $\text{DMSO-d}_6 + \text{CD}_3\text{OD}$ )  $\delta$  170.4, 169.4, 136.6, 131.1, 130.9, 125.1, 122.1, 116.2, 109.6, 53.9, 43.1, 31.9 및 27.2; MS (ESI)  $m/z = 220.1$  ( $\text{MH}^+$ ).

< 9: (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VII) >

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VII, 6, 28.0 g)  
 , 가 pH 10 . XAD - 16 가 ,

CMR ( $\text{DMSO-d}_6$ )  $\delta$  167.6, 153.9, 136.4, 127.1, 121.5, 119.6, 114.1, 107.5, 51.9, 31.3  
 및 26.5.

< 10: (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (VIII) >

(425 ml) (7.65 ) (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] -  
 2(1H) - (VII, 9, 850 g) 가 . 20 25 가 , 가

$[\alpha]^{25}_D = -35^\circ$   
 (물); UV 206 (59400), 227 (7020), 279 (5540), 282 (5570); NMR (400 MHz,  $\text{D}_2\text{O}$ )  
 $\delta$  7.05-7.09, 6.95-6.99, 4.73, 4.09-4.13, 3.96-4.01, 3.88-3.93, 2.94-3.25 및 2.76;  
 CMR (100 MHz,  $\text{D}_2\text{O}$ )  $\delta$  155.25, 126.26, 126.08, 123.08, 120.88, 114.27, 108.97,  
 52.60, 39.72, 31.49 및 26.34.

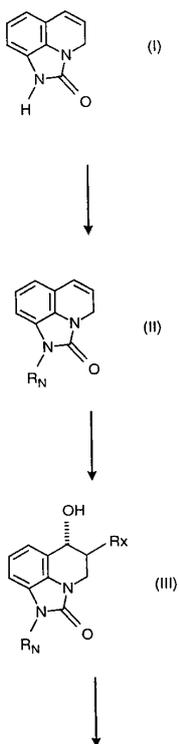
< 11: (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (IX) >

(5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - (V  
 III, 10, 11.0 kg) (20.4 kg)  
 , 가 pH 10.0 10.5  
 , 70 n - / (20/80)  
 가 (6.0 kg)  
 , 가

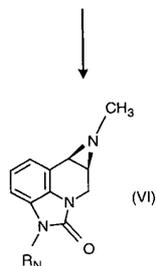
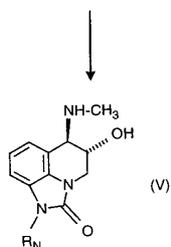
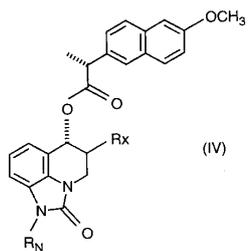
$[\alpha]^{25}_D = -56^\circ$  (물);

UV 215 (26800), 248 (18000), 299 (21800), 307 (29800); NMR (400 MHz, D<sub>2</sub>O)  $\delta$  7.33-7.37, 7.22-7.26, 6.34, 4.52-4.56, 4.35-4.40, 4.26-4.30, 3.50-3.55, 3.36-3.40 및 2.95; CMR (100 MHz, D<sub>2</sub>O)  $\delta$  171.02, 165.33, 134.80, 129.30, 124.93, 122.02, 115.58, 109.65, 52.92, 42.39, 31.48 및 26.22.

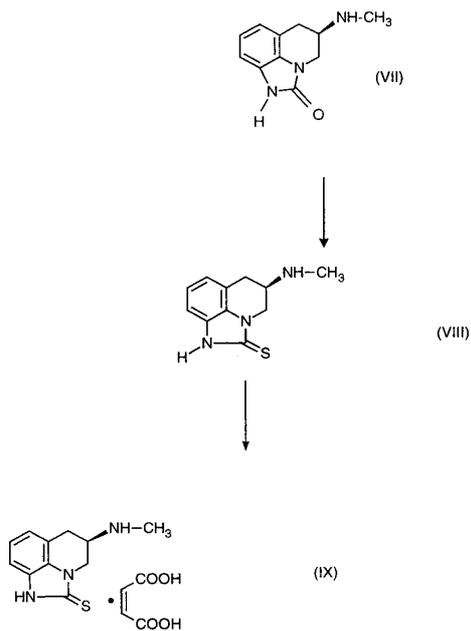
A



Aa



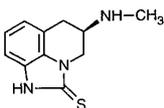
Ab



(57)

1.

가 .

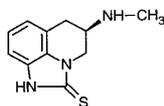


2.

1 , 가  
 $\text{CH}_3 - (\text{CH}_2)_{n1} - \text{COOH}$  ( ,  $n1$  0 4 ),  $\text{HOOC} - (\text{CH}_2)_{n1} - \text{COOH}$  ( ,  $n1$  ,  
 ) ,  $\text{HOOC} - \text{CH}=\text{CH} - \text{COOH}$  -  $\text{COOH}$  .

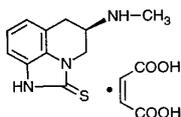
3.

1 , .



4.

3 , .



5.

(5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - 가

6.

5 , 가  
 , CH<sub>3</sub> - (CH<sub>2</sub>)<sub>n1</sub> - COOH ( , n1 0 4 ) , HOOC - (CH<sub>2</sub>)<sub>n1</sub> - COOH ( , n1 )  
 ) , HOOC - CH=CH - COOH - COOH .

7.

5 , (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - .

8.

7 , (5R) - 5 - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - .

9.

(1) (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - 가

(2) 100 가

(5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - .

10.

9 , 125 가 .

11.

9 , 가 .

12.

9 , (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - .

13.

9 , 가 , CH<sub>3</sub> - (CH<sub>2</sub>)<sub>n1</sub> - COOH ( , n1 0 4 ), HOOC - (CH<sub>2</sub>)<sub>n1</sub> - COOH ( , n1 ) , HOOC - CH=CH - COOH - COOH .

14.

9 , (5R) - ( ) - 5,6 - - 4H - [4,5,1 - ij] - 2(1H) - .