

가 (mast cell)
 가 (emedastine difumarate) (levocabastine hydrochloride)
 (Ophthalmic Drug Facts 1999, Facts and Comparisons, St. Louis, MO, pp. 59 - 80).

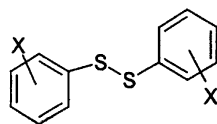
가 (olopatadine) (U. S. Paten
 t No. 5,641,805) (cromolyn sodium)

4,705,805

'705

가

(I)



(I)

X -NH-C(=O)-R -NH-C(=O)-OR ;

R H; () ; () ; OH, OR², NR³R⁴ C₁-C₈
 ; C₄-C₇ , () , () 5 7 ;
 C₁-C₆ ; ; OH; CN; CF₃; NO₂; CO₂R² ;

R² C₁-C₃ ;

R^3 R^4 H; ; $C_1 - C_8$; $C_4 - C_7$; () ; ()
 5 7 ; ; $C_1 - C_6$; ; OH; CN; CF_3 ; NO_2 ;
 CO_2R^2

가 (I)

(I) :

, X -NH-C(=O)-R ;

R -C(- R^5)-C=C(- R^6) R^7 -C(- R^5)-C(-OH) R^6 ;

R^5 H, $C_1 - C_3$;

R^6 H, $C_1 - C_3$;

R^7 H, $C_1 - C_4$.

(I)

Aldrich Chemical Company (Sigma Aldrich Library of Rare Chemicals, Milwaukee, Wisconsin and Maybridge Chemical Company Ltd. in the U. K)
 가 Domagala JM [Bioraanic and Medicinal Chemist volume 5 No. 3 pages 569 - 79 (1997), and US patent No. 4,705,805 (Yamotsu K. et al., 1987)]

(I)

X , ,

X -NH-C(=O)-R ;

$R = OH, OR^2, NR^3R^4$; $C_1 - C_8$; $C_4 - C_7$; ()
 , () 5 7 ; ; $C_1 - C_6$;
 ; OH; CN; CF_3 ; NO_2 ; CO_2R^2

$R = OH, OR^2, NR^3R^4$; $C_1 - C_5$; $C_4 - C_7$; ()
 , () 5 7 ; ; $C_1 - C_6$;
 ; OH; CN; CF_3 ; NO_2 ; CO_2R^2

(I)

(mist); ; ; (, , -)

가 (I) (I) 0.00001 5 % 가

() 0.5

0.65

0.01

NaOH/HCl pH 6 - 8

100

2:

(wt. %)

(I) 0.0001 0.2

974 P 0.8

0.01

80 0.05

0.01

NaOH/HCl pH 6 - 8

100

3: - (2 -) - (II)

(2,7ml, 34.85mmol)

(1.97ml, 23.23mmol)

2

(80)

10ml

2 -

(

, 1.44g, 5.8mmol)

가

10

(7ml, 50mmol)

가

10

1

70

, 1N HCl(20ml),

NaHCO₃ (20ml),

(20ml)

NaCl(20ml)

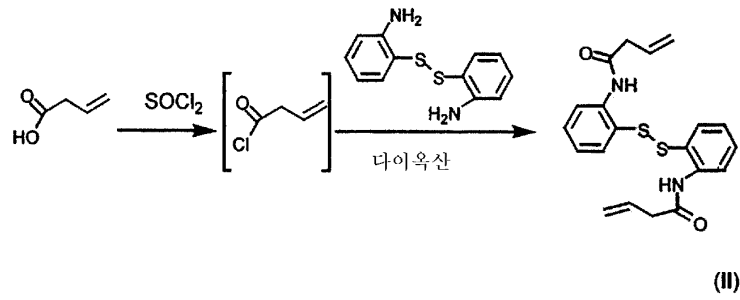
, MgSO₄

CH₂Cl₂

0.71g

(II)

¹H NMR (CDCl₃) δ 9.73 (s, 2H), 7.63-7.18 (m, 8H), 6.21-5.90 (m, 2H), 5.27-5.13 (m, 4H), 3.16-3.13 (d, 4H, J = 6.0). ¹³C NMR (CDCl₃) δ 169.74 (C=O), 136.43 (C), 132.57 (CH), 131.94 (C), 129.52 (CH), 128.59 (CH), 126.92 (CH), 126.36 (CH), 118.38 (CH₂), 40.95 (CH₂).
 C₂₀H₂₀O₂N₂S₂ 계산 분석치: C, 62.47; H, 5.24; N, 7.28%. 측정치, C, 62.40; H, 5.28; N, 7.20%.



4: - (2 - (3 - -))] -

2 - (1.5g, 6mmol) THF(8ml) 3 - (2.5g, 24mmol)
 0 가 . (4.95g, 24mol) 가 . 5 1
 (50ml) 가 , (3 × 20ml) NaCl(20ml) MgSO₄
 0.31g . 50%

¹H

NMR (CDCl₃) δ 7.80-7.76 (m, 2H), 7.48-7.43 (m, 2H), 7.37-7.29 (m, 2H), 7.14-7.07 (m, 2H), 4.22-4.13 (m, 2H), 2.46-2.42 (m, 4H), 1.27-1.24 (d, 6H, J = 6.0). ¹³C NMR (CDCl₃) δ 172.88 (C=O), 139.42 (C), 134.60 (CH), 131.08 (CH), 130.11 (C), 126.96 (CH), 125.49 (CH), 65.77 (CH), 46.68 (CH₂), 23.56 (CH₃). ESI LC/MS [M+H]⁺: 421.

5:

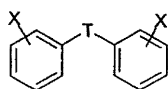
HCTMC (US Patent No. 5,360,720 and Miller et al, Ocular Immunology and Inflammation, 4 (1) : 39 - 49 (1996)).
 8 Dexsol^R
 0.1% Tyrode (Tyrode (mM): 137 NaCl, 2.7 KCl, 0.35 NaH₂PO₄, 1.8 CaCl₂, 0.98 MgCl₂, 11.9 NaHCO₃, 5.5)
 (2 X 200 U / , 2 - 4 X 2000 U /) (30 , 37)
 Nitex^R (100µm , Tetko, Briarcliff Manor)
 825 x g(7) 1.058
 g/ Percoll^R RPMI 1640
 37

(viability) (trypan blue exclusion)
 (O) Tyrode's (15 ; 37) (5000/
 ; 1Ml) 15 - - - IgE (10µg/Ml)
 0.1% Triton X - 100 IgG (10 pg/Ml) (500xg, 4 , 10)
 . RIA(Beckman Coulter, Chicago, IL) - 20


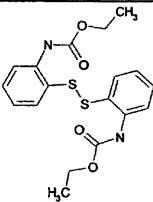

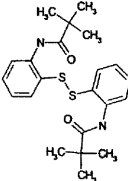
0.1 % Tyrode's 가 10mM DMSO ,

Dunnett's t - (Dunnett," A multiple comparison procedure for comparing treatm
 ents with a control" , J. Amer. Stat. Assoc. (1955), 50: 1096 - 1121) - IgE
 . IC₅₀ (50%
) 4 - 1

1



| 화합물번호 | T | X | 물구조 | IC50(nM) |
|-------|-----|---|-----|---------------------|
| 1 | S-S | | | 85 27 [56] |
| 2 | S-S | | | 656 306 [481] |
| 3 | S-S | | | 690 292 [491] |
| 4 | S-S | | | 3180 <1000 |

| 화합물번호 | T | X | 분구조 | IC50(nM) |
|-------|-----|---|---|-----------------------|
| 5 | S-S |  |  | 174 2200 [1187] |
| 6 | S-S |  |  | 1700 |

1 (I)

5:

(wt. %)

(I) 0.0001 0.2

0.001 0.1

() 0.5

0.65

0.01

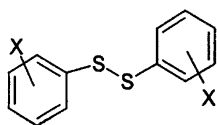
NaOH/HCl pH 6 - 8

100

(57)

1.

(I)



(I)

X -NH-C(=O)-R -NH-C(=O)-OR ;

R R¹ H; () ; () ; OH, OR², NR³R⁴
 C₁-C₈ ; C₄-C₇ , () , () 5 7
 ; C₁-C₆ ; ; OH; CN; CF₃; NO₂; CO₂R²

R² C₁-C₃ ;

R³ R⁴ H; ; C₁-C₈ ; C₄-C₇ ; () ; ()
 5 7 ; C₁-C₆ ; ; OH; CN; CF₃; NO₂;
 CO₂R²

2.

1 , X ,

X -NH-C(=O)-R ;

R OH, OR², NR³R⁴ C₁-C₈ ; C₄-C₇ , ()
 , () 5 7 ; C₁-C₆ ;
 ; OH; CN; CF₃; NO₂; CO₂R²

3.

2 ,

R OH, OR², NR³R⁴ C₁-C₅ ; C₄-C₇ , ()
 , () 5 7 ; C₁-C₆ ;
 ; OH; CN; CF₃; NO₂; CO₂R²

4.

3 , X -NH-C(=O)-CH₂CH=CH₂; -NH-C(=O)-CH₃; -NH-C(=O)-C(=CH₂)-CH₃; -NH-C(=O)-CH₂-CH(-OH)-CH₃; -NH-C(=O)-O-CH₂-CH₃; -NH-C(=O)-C(CH₃)₃

5.

1, 0.00001 5 % 가

6.

5, 가 0.0001 0.2 % .

7.

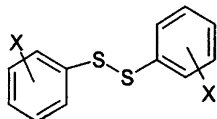
6, 가 0.0001 0.01 % .

8.

1, 10 1000mg 가

9.

150 450 mOsm (I) , , , , - , 가 가



(I)

X -NH-C(=O)-R -NH-C(=O)-OR ;

R R¹ H; () ; () ; OH, OR², NR³R⁴
 C₁-C₈ ; C₄-C₇ , () , () 5 7
 ; C₁-C₆ ; ; OH; CN; CF₃; NO₂; CO₂R²

R² C₁-C₃ ;

R³ R⁴ H; ; C₁-C₈ ; C₄-C₇ ; () ; ()
 5 7 ; C₁-C₆ ; ; OH; CN; CF₃; NO₂;
 CO₂R²

10.

9, X ,

X -NH-C(=O)-R ;

R OH, OR², NR³R⁴ ; C₁-C₈ ; C₄-C₇ , ()
 , () 5 7 ; C₁-C₆ ;
 ; OH; CN; CF₃; NO₂; CO₂R² .

11.

10 ,

R OH, OR², NR³R⁴ ; C₁-C₅ ; C₄-C₇ , ()
 , () 5 7 ; C₁-C₆ ;
 ; OH; CN; CF₃; NO₂; CO₂R² .

12.

11 , X -NH-C(=O)-CH₂CH=CH₂; -NH-C(=O)-CH₃; -NH-C(=O)-C(=CH₂)-CH₃; -NH-C(=O)-CH₂-CH(-OH)-CH₃; -NH-C(=O)-O-CH₂-CH₃; -NH-C(=O)-C(CH₃)₃

13.

9 , 가 0.00001 5 % .

14.

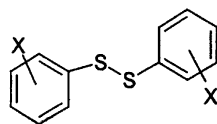
13 , 가 0.0001 0.2 % .

15.

14 , 가 0.0001 0.01 % .

16.

(I) :



(I)

, X -NH-C(=O)-R ;

R -C(-R⁵)-C=C(-R⁶)R⁷ -C(-R⁵)-C(-OH)R⁶ ;

R⁵ H, C₁-C₃ ;

R^6 H, $C_1 - C_3$;

R^7 H, $C_1 - C_4$.

17.

16 , R -C(- R^5)-C=C(- R^6) R^7 , R^5, R^6 R^7 H .

18.

16 , R -C(- R^5)-C(-OH) R^6 , R^5 H , R^6 CH_3 .