

(19) (12) (KR) (B1)

(51) 。 Int. Cl. ⁶ (45) 2001 11 30
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(22) 1995 05 30 (43) 1996 01 25

(30) P4420501.5 1994 06 13 (DE)
(73) . . .

00144 47

(72) , 20060, 7
, 20133, 4
, 21100, 가 57
, 20147, 99
, 20091, 1

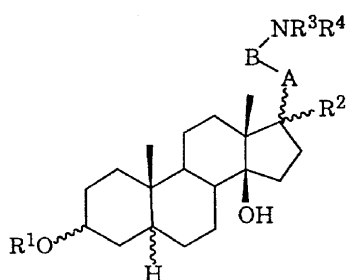
(74)
:

(54) - 14 -

(l) 17 -
-, 17 - -, 17 - -, 17 -
-, 17 - -, 17 - -, 17 -
-, 17 - -, 17 - -, 17 -
- 14 -

17 - -5 - -3 ,14 - 17 - -5 -
 -3 ,14 - Na⁺, K⁺ - ATPase , (intropic agents)
 [Gelbart A. and Thomas R., J. Med. Chem., 1978, 21, 283; Schonfeld W. and Repke K., Qu
 ant. Struct. - Act. Relat., 1988, 7, 160]. 17 - -5 ,14 -
 (4,227,605), -5 ,14 - (4,227,626) , 17
 - 17 - -14 - -5 - (4,344,236) Na⁺, K⁺ - ATPase
 -5 - (Templeton J.F. et al., J. Med. Chem., 1993, 36, 42; Templeton J.F. et al., J. C
 hem. Soc. Perkin Trans., 1992, 2503; Beard N.A. et al., Br. J. Pharmacol., 1975, 54, 65; Boutagy J. and T
 homas R., Aust. J. Pharm. Sci., 1973, [NS]2, 9; US 5,144,017 - A] N - 17 - -14 -
 -5 - [Schonfeld W. et al., Biochem. Pharmacol. 1986, 35, 3221; DD 235, 649 - A1)가

(I)



(I)

A $\text{-(CH}_2\text{)}_m$, -(CH=CH)_n , $\text{-(CH=CCH}_3\text{)}_n$, m 0 4, n 0 2 ;
 B CHR⁵, n=0 B NHC(=NH)NH₂, m 0 R² ;
 R⁵ ; R¹, NR⁶R⁷, C₂~C₄ ; R⁶ R⁷ C₂~C₄ ;
 NR⁶R⁷, C₂~C₄ R⁶ R⁷ ;
 ; R³ 5 6 ; R⁴ NHC(=NR⁸)NR⁹R¹⁰ OR¹ ; R⁸ ;
 , NR⁶R⁷ C₂~C₄ ; R⁹ R¹⁰ ; R⁸, R⁹ R¹⁰ ;
 5 , 6 7 .

(I)

(tautomer), 가

(I)

(I)

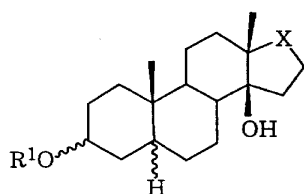
Z , E , ,

17 - [N - N - (4 -)] - 5 - - 3 , 14 - ,
 17 - [2 - ()] - 5 - - 3 , 14 - ,
 17 - [2 - (N -) - 5 - - 3 , 14 - ,
 17 - [2 - (N, N -) - 5 - - 3 , 14 - ,
 17 - [2 - (2 - - 2 -) - 5 - - 3 , 14 - ,
 17 - [2 - (1 - - 2 - - 2 -) - 5 - - 3 , 14 - ,
 17 - [2 - (1, 4, 5, 6 - - 2 -) - - 5 - - 3 , 14 - ,
 17 - [2 - (N - (2 -))] - 5 - - 3 , 14 - ,
 17 - [2 - (N -)] - 5 - - 3 , 14 - ,
 17 - - 5 - - 3 , 14 - ,
 17 - - 5 - - 3 , 14 - ,
 17 - (2 -) - 5 - - 3 , 14 - ,
 17 - (3 -) - 5 - - 3 , 14 - ,
 17 - (4 -) - 5 - - 3 , 14 - ,
 17 - (2 -) - 5 - - 3 , 14 - ,
 17 - (3 -) - 5 - - 3 , 14 - ,
 17 - (4 -) - 5 - - 3 , 14 - ,
 17 - [N - N - (2 -)]] - 5 - - 3 , 14 - ,
 17 - [N - N - (3 -)]] - 5 - - 3 , 14 - ,
 17 - [N - N - (4 -)]] - 5 - - 3 , 14 - ,
 17 - (2 -) - 5 - - 3 , 14 - ,
 17 - (3 -) - 5 - - 3 , 14 - ,
 17 - (4 -) - 5 - - 3 , 14 - ,
 20 - (2 -) - 5 - - 3 , 14 - ,
 20 - [2 - (2 - - 2 -)] - 5 - - 3 , 14 - ,

20 - [2 - (1 - - 2 - - 2 -)] - 5 - - 3 ,14 - ,
 20 - [2 - (1,4,5,6 - - 2 -)] - 5 - - 3 ,14 - ,
 20 - - 5 - - 3 ,14 - ,
 20 - (2 -) - 5 - - 3 ,14 - ,
 20 - (3 -) - 5 - - 3 ,14 - ,
 20 - (4 -) - 5 - - 3 ,14 - ,
 20 - (2 -) - 5 - - 3 ,14 - ,
 20 - (3 -) - 5 - - 3 ,14 - ,
 20 - (4 -) - 5 - - 3 ,14 - ,
 20 - [N - - N - (2 -)] - 5 - - 3 ,14 - ,
 20 - [N - - N - (3 -)] - 5 - - 3 ,14 - ,
 20 - [N - - N - (4 -)] - 5 - - 3 ,14 - ,
 20 - (2 -) - 5 - - 3 ,14 - ,
 20 - (3 -) - 5 - - 3 ,14 - ,
 20 - (4 -) - 5 - - 3 ,14 - ,
 21 - (2 -) - 5 - - 3 ,14 - ,
 21 - [2 - (2 - - 2 -)] - 5 - - 3 ,14 - ,
 21 - [2 - (1 - - 2 - - 2 -)] - 5 - - 3 ,14 - ,
 21 - [2 - (1,4,5,6 - - 2 -)] - 5 - - 3 ,14 - ,
 21 - - 5 - - 3 ,14 - ,
 21 - (2 -) - 5 - - 3 ,14 - ,
 21 - (3 -) - 5 - - 3 ,14 - ,
 21 - (4 -) - 5 - - 3 ,14 - ,
 21 - (2 -) - 5 - - 3 ,14 - ,
 21 - (3 -) - 5 - - 3 ,14 - ,

21 - (4 -) - 5 - - 3 ,14 - ,
 21 - [N - - N - (2 -)] - 5 - - 3 ,14 - ,
 21 - [N - - N - (3 -)] - 5 - - 3 ,14 - ,
 21 - [N - - N - (4 -)] - 5 - - 3 ,14 - ,
 21 - (2 -) - 5 - - 3 ,14 - ,
 21 - (3 -) - 5 - - 3 ,14 - ,
 21 - (4 -) - 5 - - 3 ,14 - ,
 17 - [3 - (2 -)] - 5 - - 3 ,14 - ,
 17 - [3 - [2 - (2 - - 2 -)]] - 5 - - 3 ,14 - ,
 17 - [3 - [2 - (1 - - 2 - - 2 -)]] - 5 - - 3 ,14 - ,
 17 - [3 - [2 - (1,4,5,6 - - 2 -)]] - 5 - - 3 ,14 - ,
 17 - (3 -) - 5 - - 3 ,14 - ,
 17 - [3 - (2 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (3 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (4 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (2 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (3 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (4 -)] - 5 - - 3 ,14 - ,
 17 - [3 - [N - - N - (2 -)]] - 5 - - 3 ,14 - ,
 17 - [3 - [N - - N - (3 -)]] - 5 - - 3 ,14 - ,
 17 - [3 - [N - - N - (2 -)]] - 5 - - 3 ,14 - ,
 17 - [3 - (2 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (3 -)] - 5 - - 3 ,14 - ,
 17 - [3 - (4 -)] - 5 - - 3 ,14 - ,
 (E) - 17 - [3 - [2 - ()]] - 1 - - 5 - - 3 ,14 - ,

- (E) - 17 - [3 - [2 - (2 - - 2 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - (1 - - 2 - - 2 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - (1,4,5,6 - - 2 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - (3 - - 1 -) - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (3 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (4 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (3 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (4 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [N - - N - (2 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [N - - N - (3 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [N - - N - (4 -)] - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (3 -) - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - ()] - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - (2 - - 2 -)] - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - (1 - - 2 - - 2 -)] - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - [2 - (1,4,5,6 - - 2 -)] - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - (3 - - 2 - - 1 -) - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (2 -) - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (3 -) - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (4 -) - 2 - - 1 -] - 5 - - 3 , 14 - ,
- (E) - 17 - [3 - (2 -) - 2 - - 1 -] - 5 - - 3 , 14 - ,



(II)

 R^1
 X
 NR^4 ; A,
 R^2 R^4

(II)

(acid)

(II)

$Pd/C, PtO_2$
 $Pd/C, PtO_2$
 (hydrogen transfer condition)
 $NaBH_4, NaBH_3CN, BH_3$

, 0

(acid)

가 , pH ,
 (base)

, 가 .

(I)

(I)

(I)

, R^3 R^6 R^7

(I)

R^3 ,
 R^6 R^7
 (alkylation)

R^3, R^6 R^7
 (reductive alkylation)

 aBH_3CN

(transformation)

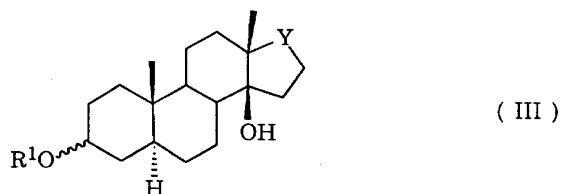
가

(J. March "Advanced Organic Chemistry", J. Wiley & Sons, 1985; D. Barton and W. D. Ollis "Comprehensive Organic Chemistry", Pergamon Press, 1979)

(transformation) , R^4

(II) C-5 가 -
[4,227,605 (92. 8. 20) ; 4,227,626 (92. 8. 20) ; 4,344,236 (93. 12. 23)].

, (II) C-5 가 - (III)
 $R^4 NH_2$



A, R^1 , R^2 ~~~~~

(4,227,605 (92. 8. 20) ; 4,227,626(92. 8. 20) ; 4,344,236 (93. 12. 23)].

(III) 3,14 - -5 - -17 - 3,14 -
5 - -20 - [Chambers V.E.M. et al., J. Chem. Soc., Perkin Trans. 1, 1975, 1, 55 ; Templeton J.F. et al., Steroids, 1993, 58, 518]. 3,14 - -5 - -17 -
(Uzarigenin) , (Boutagy)
(digitoxigenin) 3,14 - -5 - -17 -
(transformation) [Boutagy J.S. and Thomas R.E., Aust. J. Chem., 1971, 24, 2723]. 5 -
[4,227,605 ; 4,227,626 ; 4,344,236].

(I) 가

(I) 가
(ouabain), (digitoxin) 4,227,605 4,227,626
(therapeutic index)가

(I) Na^+ , K^+ - ATPase

Na⁺,K⁺ - ATPase

(a) (Jorghensen) (Erdmann) Na⁺,K⁺ - ATPase
³H - (³H - ouabain) (Jorghensen P., BBA, 1974, 356, 36; Erdmann E. et al., Arz
 neim. Forsh., 1984, 34, 1314),

(b) 가 가 Na⁺,K⁺ - ATPase ³²P - ATPase 가
 (%) (Doucet A. et al., Am. J. Physiol, 1986, 251, F851).

4 (MHS SHR) - (tail - cuff)
 (Systolic blood pressure, SBP) (heart rate, HR)
 7
 (Methocel) 0.5%(w/v) 5 ,

6 24 SBP HR , 9
 , 5 1

- (- blocker)
 (SHR) 5

[Takeda K. et al., Japan J. Pharmacol, 1979, 29, 171; Takeda K. et al., Japan J. Pharmacol, 19
 82, 32, 283; Richer C. et al., Eur. J. Pharmacol., 1978, 47, 393].

(I)

1

화합물	결합 (-log IC ₅₀) ³ H-와바인 지환	억제활성 (-log IC ₅₀)
I-aa	6.9	5.7
I-ab	6.6	5.5
I-ac	6.0	5.0
I-ad	6.5	5.4
I-ae	5.4	4.5
I-af	5.0	4.2
I-ag	6.5	5.2
I-ah	5.0	4.1
I-ai	5.1	4.1
I-aj	7.2	6.0
I-ak	6.9	5.6
I-al	6.2	4.8
I-am	6.1	4.3
I-an	5.8	4.2
I-ao	5.9	4.1
I-ap	5.0	4.0
I-aq	6.0	4.4
I-ar	5.7	4.2
I-as	6.0	4.5
I-at	6.7	5.0
I-au	5.9	4.4
I-av	5.7	4.2
I-ax	5.7	4.4
I-ay	5.8	4.4
I-ba	5.2	4.0
I-bb	6.3	4.5
I-bc	6.1	4.4
I-bd	6.2	4.5
I-be	6.0	4.3

(I)

2

고혈압증에 걸린 쥐 (MHS)에 대한 5주간 투약 후 고혈압의 진전도

화합물	쥐의 수 (마리)	투여량* (mg/Kg/os)	SBP (mmHg)	HR (박동수/분)
대조군	7	메토셀	170+/-5.5	378+/-12.0
I-aj	7	0.1	150+/-4.1	372+/-11.7
I-am	7	10	149+/-4.5	370+/-14.7
I-am	7	1	152+/-5.3	365+/-10.1
I-bb	7	10	150+/-4.2	375+/-12.1
I-bb	7	1	153+/-6.2	367+/-14.3

* 메토셀에 0.5% (w/v) 농도로 현탁시킴.

[1]

[17 - [2 - ()] - 5 - - 3 ,14 - (I - aa)]

(25ml) (E) - 17 - - 5 - - 3 ,14 - (0.50g, 4,2
27,626) PtO₂ (0.40g) 가 , 4.2atm 8
(I - aa, 0.30g)

¹H-NMR (300 MHz, DMSO-d₆) : δ 0.80 (s, 3H), 0.85 (s, 3H), 2.68 (t, 1H), 2.78 (dd, 1H), 3.85 (bs, 1H)

[2]

[17 - [2 - (2 - - 2 -)] - 5 - - 3 ,14 - (I - ab)]

(E) - 17 - (2 - - 2 -) - 5 - - 3 ,14 - (0.45g,
4,227,626) 1
(I - ab, 0.29g)

¹H-NMR (300 MHz, DMSO-d₆) : δ 0.70 (s, 3H), 0.86 (s, 3H), 2.68 (t, 1H), 2.78 (dd, 1H), 3.30 (s, 4H), 3.85 (bs, 1H)

[3]

[17 - [2 - (1 - 2 - 2 -)] - 5 - - 3 ,14 - (I - ac)]

(E) - 17 - (1 - 2 - 2 -) - 5 - - 3 ,14 - (0.55
g, 4,227,626) 1
(I - ac, 0.35g) .

¹H-NMR(300 MHz, DMSO-d₆) : δ 0.80(s, 3H), 0.85(s, 3H), 2.70(t,
1H), 2.80(dd, 1H), 3.10(s, 3H),
3.65(s, 4H), 3.90(bs, 1H)

[4]

[17 - [2 - (1,4,5,6 - 2 -)] - 5 - - 3 ,14 - (I - ad)]

(E) - 17 - (1,4,5,6 - 2 -) - 5 - - 3 ,14 -
(0.60g, 4,227,626) 1
(I - ad, 0.32g) .

¹H-NMR(300 MHz, DMSO-d₆) : δ 0.80(s, 3H), 0.85(s, 3H), 2.70(t,
1H), 2.80(dd, 1H), 3.25(m 4H),
3.85(bs, 1H)

[5]

[17 - [2 - [N - (2 -)] - 5 - - 3 ,14 - (I - ae)]

(E) - 17 - [3 - (2 -)] - 5 - - 3 ,14 - (0.5
5g, 4,227,626) 1
(I - ae, 0.38g) .

¹H-NMR(300 MHz, DMSO-d₆) : δ 0.81(s, 3H), 0.85(s, 3H), 2.65(t,
1H), 2.75(dd, 1H), 2.80(s, 6H),
3.20(m, 2H), 3.60(m, 2H), 3.87(bs,
1H)

[6]

[17 - [2 - (N -)] - 5 - - 3 ,14 - (I - af)]

(E) - 17 - (3) - 5 - - 3 ,14 - (0.55g, 4,227,626
) , 가 1
(I - af, 0.37g) .

¹H-NMR(300 MHz, DMSO-d₆) : δ 0.85(s, 3H), 0.87(s, 3H), 2.70(t, 1H), 2.80(dd, 1H), 3.85(bs, 1H), 7.00(m, 1H), 7.30(m, 2H), 7.60(m, 2H)

[7]

[20 - (2 -) - 5 - - 3 ,14 - (I - ag)]

(E) - 20 - - 5 - - 3 ,14 - (0.65g, 4,227,626)
6 (I - ag, 0.38g)

¹H-NMR(300 MHz, DMSO-d₆) : δ 0.80(s, 3H), 0.85(s, 3H), 1.50(bs, 3H), 2.70~2.80(m, 1H), 3.85(bs, 1H)

[8]

[17 - - 5 - - 3 ,14 - (I - ah)]

(6ml) (E) - 17 - - 5 - - 3 ,14 - (0.60g, 4,227,605
) 가 , 1N HCl pH 3 Na
BH₃ CN(0.30g) 가 , pH가 2.8~3.0 0.1N HCl 가 , 6
NaBH₃ CN(0.15g) 가 2.5N NaOH 가 pH 10
, , ,
(: / =20/
80) 가
(I - ah)

¹H-NMR(300 MHz, CD₃OD) : δ 0.97(s, 3H), 0.98(s, 3H), 3.25~3.35(m, 2H), 4.05(bs, 1H)

[9]

[17 - - 5 - - 3 ,14 - (I - ai)]

(E) - 17 - - 5 - - 3 ,14 - (0.60g, 4,227,605
) 8 (I - ai, 0.40g)

¹H-NMR(300 MHz, CD₃OD) : δ 0.97(s, 3H), 0.98(s, 3H), 3.25(dd, 1H), 3.33(dd, 1H), 3.80(s, 3H), 4.05(bs, 1H)

[10]

[17 - (2 -) - 5 - - 3 ,14 - (I - aj)]

(E) - 17 - (2 -) - 5 - - 3 ,14 - (0.40g, 4,227,605
/26%) 8 , /

=90/90/1 (造鹽)
(I - aj, 0.23g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 3.33(m, 2H),
3.40~3.55(m, 2H), 4.05(m, 1H),
4.42(t, 2H)

[11]

[17 - (3 -) - 5 - - 3 ,14 - (I - ak)]

(E) - 17 - (3 -) - 5 - - 3 ,14 - (0.45g, 4,227,605
0.29g) 10 (I - ak,

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 3.15(m, 2H),
3.40~3.55(m, 2H), 4.05(m, 1H),
4.20(t, 2H)

[12]

[17 - (4 -) - 5 - - 3 ,14 - (I - al)]

(E) - 17 - (4 -) - 5 - - 3 ,14 - (0.35g, 4,227,605
25g) 10 (I - al, 0.

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 3.05(m, 2H),
3.40~3.55(m, 2H), 4.05(m, 3H)

[13]

[17 - (2 -) - 5 - - 3 ,14 - (I - am)]

(E) - 17 - (2 -) - 5 - - 3 ,14 - (1.70g, 4,227,605
am, 1.37g) 10 (I -

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 0.99(s, 3H), 2.99(s, 6H),
3.40~3.55(m, 2H), 3.57(t, 2H),
4.05(m, 1H), 4.53(t, 2H)

[14]

[17 - (3 -) - 5 - - 3 ,14 - (I - an)]

(E) - 17 - (3 -) - 5 - - 3 ,14 - (0.50g, 4,227,60
5) 10 (I - an, 0.37g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 0.99(s, 3H), 2.97(s, 6H),
3.35(t, 2H), 3.40~3.55(m, 2H),
4.05(m, 1H), 4.20(t, 2H)

[15]

[17 - (4 -) - 5 - - 3 ,14 - (I - ao)]

(E) - 17 - (3 -) - 5 - - 3 ,14 - (0.48g, 4,227,60
5) 10 (I - ao, 0.27g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 2.97(s, 6H),
3.20(t, 2H), 3.40~3.55(m, 2H),
4.05(m, 1H), 4.10(t, 2H)

[16]

[17 - [N - - N - (2 -)] - 5 - - 3 ,14 - (I - ap)]

(10ml) 17 - (2 -) - 5 - - 3 ,14 - (I - am, 0.41g)
37% (1.0ml) 가 , NaBH₃CN(0.20g) 가 28
0.1N , 2.5N NaOH pH 9.5
- (: / /26% =90/9/1)
가 (I - ap, 0.33g)

¹H-NMR (300 MHz, CD₃OD) : δ 0.97(s, 3H), 0.99(s, 3H), 2.60(s, 3H),
2.70~2.90(m, 2H), 2.90(s, 6H),
3.32(t, 2H), 3.95~4.00(m, 2H),
4.05(m, 1H)

[17]

[17 - (2 -) - 5 - - 3 ,14 - (I - aq)]

(E) - 17 - (2 -) - 5 - - 3 ,14 - (0.40g, 4,227,605
) 10 (I - aq,
0.17g)

¹H-NMR (300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 3.30(m, 2H),
3.40~3.55(m, 2H), 4.05(m, 1H),
4.40(t, 2H)

[18]

[20 - (2 -) - 5 - - 3 ,14 - (I - ar)]

(E) - 20 - (2 -) - 5 - - 3 ,14 - (0.41g, 4,227,605
) 10 (I - ar, 0.23
g)

¹H-NMR (300 MHz, CD₃OD) : δ 0.98(s, 3H), 0.99(s, 3H), 1.55(s, 3H),
2.99(s, 6H), 3.35~3.55(m, 2H),
3.55(t, 2H), 4.05(m, 1H), 4.50(t, 2H)

[19]

[(E) - 17 - [3 - [2 - ()] - 1 -] - 5 - - 3 ,14 - (I - as)]

17 - [3 - [- 1 - (E) -]] - 5 - - 3 ,14 - (0.40g, 4,227,6
05) 10
(I - as, 0.18g)

¹H-NMR (300 MHz, CD₃OD) : δ 0.85(s, 3H), 0.95(s, 3H), 3.50(dd,
2H), 4.05(m, 1H), 5.40(m, 1H),
5.6(dd, 1H)

[20]

[(E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 ,14 - (I - at)]

17 - [3 - (2 -) - 1 - (E) -) - 5 - - 3 ,14 - (0.50g, 4,3
44,236) 10 , (造鹽)
(I - at, 0.30g) .

¹H-NMR(300 MHz, CDCl₃) : δ 0.83(s, 3H), 0.95(s, 3H), 2.65(t, 2H),
3.45(d, 2H), 3.66(t, 2H), 4.10(bs,
1H), 5.30(dt, 1H), 5.55(dd, 1H)

[21]

[(E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 ,14 - (I - au)]

(E) - 17 - [3 - (2 -) - 1 - (E) -) - 5 - - 3 ,14 - (0.65g,
4,344,236) 20
(I - au, 0.36g) .

¹H-NMR(300 MHz, CDCl₃) : δ 0.83(s, 3H), 0.95(s, 3H), 2.25(m, 6H),
2.49(t, 2H), 3.47(d, 2H), 3.77(t, 2H),
4.10(bs, 1H), 5.30(dt, 1H), 5.57(dd,
1H)

[22]

[(E) - 17 - [3 - (2 -) - 2 - - 1 -] - 5 - - 3 ,14 - (I - av)
]

17 - [3 - (2 -) - 2 - - 1 - (E) -] - 5 - - 3 ,14 - (0.37g,
4,344,236) 20
(I - av, 0.22g) .

¹H-NMR(300 MHz, CDCl₃) : δ 0.83(s, 3H), 0.95(s, 3H), 1.50(s, 3H),
2.25(m, 6H), 2.50(t, 2H), 3.45(m,
2H), 3.75(t, 2H), 4.10(bs, 1H),
5.30(m, 1H)

[23]

[(E),(E) - 17 - [5 - (2 -) - 1,3 -] - 5 - - 3 ,14 - (I - aw)
]

17 - [5 - (2 -) - (E,E) - 1,3 -] - 5 - - 3 ,14 - (0.42g,
4,344,236) 20
(I - aw, 0.28g) .

¹H-NMR(300 MHz, CDCl₃) : δ 0.83(s, 3H), 0.95(s, 3H), 2.25(m, 6H),
2.50(t, 2H), 3.50(d, 2H), 3.75(t, 2H),
4.10(bs, 1H), 5.20~5.70(m, 4H)

[24]

[17 - [2 - (2 -)] - 5 - - 3 ,14 - (I - ax)]

17 - [2 - (2 -)] - 5 - - 3 ,14 - (0.32g, 4,344,236
) 10 (I -
ax, 0.24g) .

¹H-NMR(300 MHz, CDCl₃) : δ 0.98(s, 3H), 1.00(s, 3H), 3.00(s, 6H),
3.35~3.50(m, 2H), 3.55(t, 2H),
4.05(m, 1H), 4.55(t, 2H)

[25]

[17 - [3 - (2 -)] - 5 - - 3 ,14 - (I - ay)]

17 - [2 - (2 -)] - 5 - - 3 ,14 - (0.47g, 4,344,23
6) 10 (I -
ay, 0.32g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.97(s, 3H), 1.00(s, 3H), 2.99(s, 6H),
3.35~3.50(m, 2H), 3.55(t, 2H),
4.05(m, 1H), 4.55(t, 2H)

[26]

[17 - (2 -) - 5 - - 3 ,14 - (I - az)]

17 - (2 -) - 5 - - 3 ,14 - (0.40g, 4,227,626
) 10 (I - az, 0.12g)
.

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.10(s, 3H), 3.00(s, 6H),
3.55(t, 2H), 3.60~3.75(m, 2H),
4.05(m, 1H), 4.50(t, 2H)

[27]

[17 - (2 -) - 5 - - 3 ,14 ,17 - (I - ba)]

(E) - 17 - (2 -) - 5 - - 3 ,14 ,17 - (0.38g, 4,2
27,605) 10
(I - ba, 0.17g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.98(s, 3H), 1.00(s, 3H), 3.00(s, 6H),
3.50~3.65(m, 2H), 3.60(t, 2H),
4.05(m, 1H), 4.55(t, 2H)

[28]

[3 - (3 -) - 17 - (2 -) - 5 - - 14 - (I - bb)]

3 - (3 -) - 17 - (2 -) - 5 - - 14 - (0.44g,
4,227,605) 20
(I - bb, 0.20g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.95(s, 3H), 0.97(s, 3H), 2.25(t, 2H),
2.30(s, 6H), 2.55(t, 2H), 2.90~3.10
(m, 4H), 3.70(m, 1H), 3.80(t, 2H)

[29]

[3 - (2 -) - 17 - (2 -) - 5 - - 14 - (I - bc)]

3 - 2 -) - 17 - (2 -) - 5 - - 14 - (0.43g,
4,227,605) 20
(I - bc, 0.18g) .

¹H-NMR(300 MHz, CD₃OD) : δ 0.95(s, 3H), 0.97(s, 3H), 2.30(s, 6H),
2.35(t, 2H), 2.55(t, 2H), 2.90(dd,
1H), 3.10(dd, 1H), 3.60(m, 1H),
3.80(t, 2H)

[30]

[3 - [2 - (1 -)] - 17 - (2 -) - 5 - - 3 ,14 - (I - bd)]

3 - [2 - (1 -)] - 17 - (2 -) - 5 - - 3 ,14 - (0.48g, 4,227,605) 20 (I - bd, 0.17g) .

¹H-NMR (300 MHz, CD₃OD) : δ 0.95(s, 3H), 0.97(s, 3H), 2.25(m, 4H),
2.30(s, 6H), 2.55(t, 2H),
2.85~3.10(m, 5H), 3.70(m, 1H),
3.80(t, 2H)

[31]

[3 - [3 - (1 -)] - 17 - (2 -) - 5 - - 3 ,14 - (I - be)]

3 - [3 - (1 -)] - 17 - (2 -) - 5 - - 3 ,14 - (0.42g, 4,227,605) 20 (I - be, 0.22g) .

¹H-NMR (300 MHz, CD₃OD) : δ 0.95(s, 3H), 0.97(s, 3H), 2.15(m, 6H),
2.25(t, 2H), 2.30(s, 6H), 2.55(t, 2H),
2.90(dd, 1H), 3.10(dd, 1H), 3.70(m, 1H), 3.80(t, 2H)

[32]

[(E,E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 ,14 - (I - bf)]

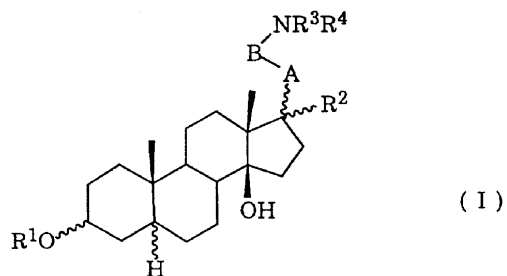
(E,E) - 17 - [3 - (2 -) - 1 -] - 5 - - 3 ,14 - (0.37g, 4,344,236 , 20 (I - bf, 0.16g) .

¹H-NMR (300 MHz, CDCl₃) : δ 0.83(s, 3H), 0.95(s, 3H), 2.25(m, 6H),
2.50(t, 2H), 3.47(d, 2H), 3.77(t, 2H),
3.70(s, 1H), 5.30(dt, 1H), 5.55(dd, 1H)

(57)

1.

(I)



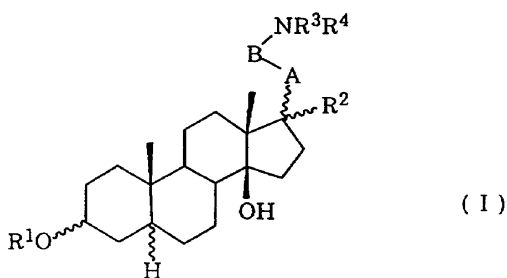
(I)

, $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; A $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; B $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^1 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^2 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^3 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^4 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^5 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^6 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^7 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^8 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^9 $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m
 $n=0, 1, 2, 3, 4$; R^{10} $\text{---CH}_2\text{---}$, ---CH=CH--- , $\text{---CH=C(CH}_3\text{)---}$, m

2.

(I)

가



(I)

, A, B, R¹, R², R³, R⁴

1

3.

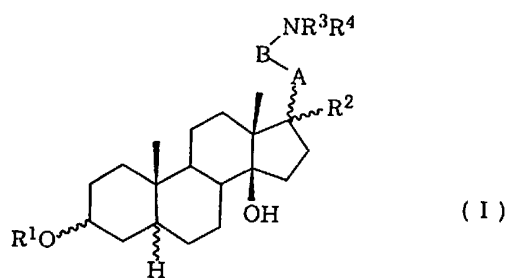
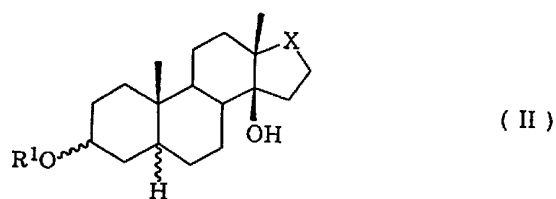
1 (I) 17 - (2 -) -5 - -3 ,14 -
 , 17 - [2 - (2 - -2 -) -5 - -3 ,14 - , 17 - -5
 - -3 ,14 - , 17 - (2 -) -5 - -3 ,14 - , 17 - (3 -
) -5 - -3 ,14 - , 17 - (4 -) -5 - -3 ,14
 - , 17 - (2 -) -5 - -3 ,14 - , 17 - (3 -
) -5 - -3 ,14 - , 17 - (4 -) -5 - -3 ,14 -
 , 17 - [N - -N - (2 -)] -5 - -3 ,14 - , 17 - [N - -N -
 (3 -)] -5 - -3 ,14 - , 17 - [N - -N - (4 -)]
] -5 - -3 ,14 - , 17 - [2 - ()] -5 - -3 ,14 -
 , 17 - [2 - (N -)] -5 - -3 ,14 - , 17 - [2 - (N,N -
)] -5 - -3 ,14 - , 17 - [2 - (2 - -2 -)] -5 -
 -3 ,14 - , 17 - [2 - (1 - -2 - -2 -)] -5 - -3 ,14 -
 , 17 - [2 - (1,4,5,6 - -2 -)] -5 - -3 ,14 - , 17
 - [2 - (N - (2 -))] -5 - -3 ,14 - , 17 - [2 - (N -
)] -5 - -3 ,14 - , 17 - -5 - -3 ,14
 - , 17 - -5 - -3 ,14 - , 17 - (2 -) -5 -
 -3 ,14 - , 17 - (3 -) -5 - -3 ,14 - , 17 - (4 -
) -5 - -3 ,14 - , 17 - (2 -) -5 -
 -3 ,14 - , 17 - (3 -) -5 - -3 ,14 - , 17 - (4 -
) -5 - -3 ,14 - , 17 - [N - -N - (2 -)]
] -5 - -3 ,14 - , 17 - [N - -N - (3 -)] -5 -
 -3 ,14 - , 17 - [N - -N - (4 -)] -5 - -3 ,14 -
 , 17 - (2 -) -5 - -3 ,14 - , 17 - (3 -
) -5 - -3 ,14 - , 17 - (4 -) -5 - -3 ,14
 - , 20 - (2 -) -5 - -3 ,14 - , 20 - [2 - (2 - -2 -)]
 -5 - -3 ,14 - , 20 - [2 - (1 - -2 - -2 -)] -5 - -3 ,14
 - , 20 - [2 - (1,4,5,6 - -2 -)] -5 - -3 ,14 - , 20 -
 -5 - -3 ,14 - , 20 - (2 -) -5 - -3 ,14 - , 20 - (3 -
) -5 - -3 ,14 - , 20 - (4 -) -5 - -3 ,14 -
 , 20 - (2 -) -5 - -3 ,14 - , 20 - (3 -) -
 5 - -3 ,14 - , 20 - (4 -) -5 - -3 ,14 - , 20 - [N -
 -N - (2 -)] -5 - -3 ,14 - , 20 - [N - -N - (3 -
)] -5 - -3 ,14 - , 20 - [N - -N - (4 -)] -5 -
 3 ,14 - , 20 - (2 -) -5 - -3 ,14 - , 20 - (3 -
) -5 - -3 ,14 - , 20 - (4 -) -5 - -3 ,14 - , 21 - (2
 -) -5 - -3 ,14 - , 21 - [2 - (2 - -2 -)] -5 -
 -3 ,14 - , 21 - [2 - (1 - -2 - -2 -)] -5 - -3 ,14 - , 21 - [2
 - (1,4,5,6 - -2 -)] -5 - -3 ,14 - , 21 - -5 -
 -3 ,14 - , 21 - (2 -) -5 - -3 ,14 - , 21 - (3 -
) -5 - -3 ,14 - , 21 - (4 -) -5 - -3 ,14 - , 21 - (2 -
) -5 - -3 ,14 - , 21 - (3 -) -5 -
 -3 ,14 - , 21 - (4 -) -5 - -3 ,14 - , 21 - [N - -N - (2 -
)] -5 - -3 ,14 - , 21 - [N - -N - (3 -)] -5
 - -3 ,14 - , 21 - [N - -N - (4 -)] -5 - -3 ,14 - ,
 21 - (2 -) -5 - -3 ,14 - , 21 - (3 -) -5 -
 -3 ,14 - , 21 - (4 -) -5 - -3 ,14 - , 17 - [3 - (2 -)]
] -5 - -3 ,14 - , 17 - [3 - [2 - (2 - -2 -)]] -
 5 - -3 ,14 - , 17 - [3 - [2 - (1 - -2 - -2 -)]] -5 -
 -3 ,14 - , 17 - [3 - [2 - (1,4,5,6 - -2 -)]] -5 -

-3 ,14 - , 17 - (3 -) -5 - -3 ,14 - , 17 - [3 - (2 -
)] -5 - -3 ,14 - , 17 - [3 - (3 -)] -5 -
 -3 ,14 - , 17 - [3 - (4 -)] -5 - -3 ,14 - , 17 - [3 - (2 -
)] -5 - -3 ,14 - , 17 - [3 - (3 -)] -5 - -3 ,14 - , 17 - [3 - (4 -)] -5 -
 ,14 - , 17 - [3 - [N - -N - (2 -)]] -5 - -3 ,14 - ,
 17 - [3 - [N - -N - (3 -)]] -5 - -3 ,14 - , 17 - [3 -
 [N - -N - (2 -)]] -5 - -3 ,14 - , 17 - [3 - (2 -
)] -5 - -3 ,14 - , 17 - [3 - (3 -)] -5 -
 - -3 ,14 - , 17 - [3 - (4 -)] -5 - -3 ,14 - ,
 (E) - 17 - [3 - [2 - ()]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [2 -
 (2 - -2 -)]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [2 - (1 -
 -2 - -2 -)]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [2 - (1,4,5,
 6 - -2 -)]] -1 -] -5 - -3 ,14 - , (E) - 17 - (3 -
 -1 -) -5 - -3 ,14 - , (E) - 17 - [3 - (2 -)] -1 -
] -5 - -3 ,14 - , (E) - 17 - [3 - (3 -)] -1 -] -5 -
 -3 ,14 - , (E) - 17 - [3 - (4 -)] -1 -] -5 - -3 ,14 - , (E)
 - 17 - [3 - (2 -)] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 -
 (3 -)] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - (4 -
)] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [N - -N - (2 -
)]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [N - -N - (3 -
)]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [N - -N - (4 -
)]] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - (2 -
)] -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - (3 -)] -1 -]
 -5 - -3 ,14 - , (E) - 17 - [3 - [2 - ()]] -2 - -1 -] -5 -
 -3 ,14 - , (E) - 17 - [3 - [2 - (2 - -2 -)]] -2 - -1 -] -5 -
 -3 ,14 - , (E) - 17 - [3 - [2 - (1 - -2 - -2 -)]] -2 - -1 -
] -5 - -3 ,14 - , (E) - 17 - [3 - [2 - (1,4,5,6 - -2 -)]] -2 -
 -1 -] -5 - -3 ,14 - , (E) - 17 - (3 - -2 - -1 -) -5 -
 - -3 ,14 - , (E) - 17 - [3 - (2 -)] -2 - -1 -] -5 -
 -3 ,14 - , (E) - 17 - [3 - (3 -)] -2 - -1 -] -5 - -3 ,14
 - , (E) - 17 - [3 - (4 -)] -2 - -1 -] -5 - -3 ,14 - , (E)
 - 17 - [3 - (2 -)] -2 - -1 -] -5 - -3 ,14 - , (E) - 17
 - [3 - (3 -)] -2 - -1 -] -5 - -3 ,14 - , (E) - 17 - [3
 - (4 -)] -2 - -1 -] -5 - -3 ,14 - , (E) - 17 - [3 - [N -
 -N - (2 -)]] -2 - -1 -] -5 - -3 ,14 - , (E) - 17 -
 [3 - [N - -N - (3 -)]] -2 - -1 -] -5 - -3 ,14 - , (E)
 - 17 - [3 - [N - -N - (4 -)]] -2 - -1 -] -5 - -3 ,14
 - , (E) - 17 - [3 - (2 -)] -2 - -1 -] -5 - -3 ,14 - , (E)
 - 17 - [3 - (3 -)] -2 - -1 -] -5 - -3 ,14 - , (E,E) -
 17 - [5 - [2 - ()]] -1,3 -] -5 - -3 ,14 - , (E,E) - 17 - [5 - [2
 - (2 - -2 -)]] -1,3 -] -5 - -3 ,14 - , (E,E) - 17 - [5 - [2 -
 (1,4,5,6 - -2 -)]] -1,3 -] -5 - -3 ,14 - , (E,E) -
 17 - (5 - -1,3 -) -5 - -3 ,14 - , (E,E) - 17 - [5 - (2 -
) -1,3 -] -5 - -3 ,14 - , (E,E) - 17 - [5 - (3 -)] -1,
 3 -] -5 - -3 ,14 - , (E,E) - 17 - [5 - (2 -)] -1,3 -] -
] -5 - -3 ,14 - , (E,E) - 17 - [5 - (3 -)] -1,3 -] -
 5 - -3 ,14 - , (E,E) - 17 - [5 - (2 -)] -1,3 -] -5 - -3 ,
 -3 ,14 - , (E,E) - 17 - [5 - (3 -)] -1,3 -] -5 - -3 ,
 14 - ; 3 - (2 -) , 3 - (2 -) , 3 - (2 -) ,

3 - [2 - (1 -)], 3 - (3 -), 3 - (3 -), 3 - (),
 3 - [3 - (1 -)], 3 - [2 - (2 -)], 3 - [3 - (2 -)],
], 3 - [2 - [2 - (1 -)]], 3 - [3 - [2 - (1 -)]]
 ; 3 - 3 - ; 17 - ;
 5 - 5 - .

4.

(II)
 0 , , , , , (I)



1 , X $\text{H}_3\text{C}-\text{C}(\text{NR}^4)=\text{C}(\text{R}^2)-$, $\text{CH}=\text{NR}^4$ $\text{C}(\text{NR}^4)=$; wavy, A, B, R¹, R², R³ R⁴

5.

4 , Pd/C, PtO₂
 (I)

6.

4 , Pd/C, PtO₂ , (I)

7.

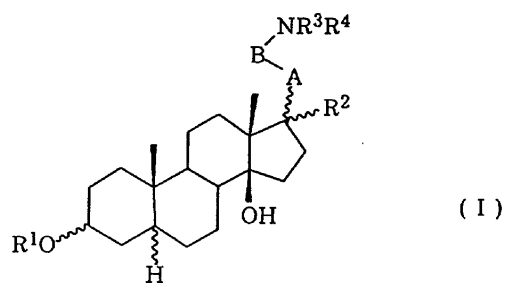
4 , NaBH₄, NaBH₃CN BH₃
 (I)

8.

4 , pH (base) 가 , (acid) (I)

9.

(I)



(I)

, A, B, R¹, R², R³, R⁴

1

10.

9 ,