

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl. ⁷
C07D 487/16

$$\begin{pmatrix} 11 \\ 43 \end{pmatrix}$$

2001 - 0080402
2001 08 22

(21)	10 - 2001 - 7005818
(22)	2001 05 08
	2001 05 08
(86)	PCT/US1999/26984
(86)	1999 11 12

(87)	WO 2000/27850
(87)	2000 05 18

(81)

가

가

가

가

가

AP ARIPO : 가

EA : 가

EP : 가

OA OAPI : 가

(30)	09/190,958	1998	11	12	(US)
	09/400,744	1999	09	21	(US)

(71)

92121

10555

(72)	,		
	92104	,	3545
	,		
	92126	,	11036
	,		
	46077	,	4037

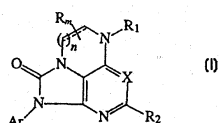
(74)

:

(54) C R F

CRF

() : , n, m, R, R₁, R₂, X Ar
가



CRF , , ,

CRF

CRF(cortisone - releasing factor)

41

(Vale et al.,Science213:1394 - 1397, 1981).

CRF

, CRF 41 7 가

(River et al.,Proc.

Natl. Acad. Sci. USA 80:4851, 1983; Shibahara et al.,EMBO J. 2:775, 1983).

CRF가

. CRF

ACTH(a

drenocorticotropic hormone), - , POMC(pro - opiomelanocortin) -

(Vale et al.,Science 213:1394 - 1397, 1981).

, C

RF (DeSouza et al.,Science 224:1449 - 1451, 1984), (DeSouza et al.,Methods Enzymol.124:56

0, 1986; Wyne et al.,Biochem. Biophys. Res. Comm.110:602 - 608, 1983), (Udelsman et al.,Nature 319

:147 - 150, 1986) (Webster, E. L., and E.B. DeSouza,Endocrinology122:609 - 617, 1988)

CRF cAMP(Bilezikjian, L. M., and W.W. Vale,Endocrinology 113:657 - 662, 1983)

CRF - 가 GTP - (Perrin et al.,Endocrinology 118:1171 - 1179, 1986)

CRF (Perrin et al.,Endo 133(6):3058 - 3061, 1993), (Chen et al.,PNA

S 90(19):8967 - 8971, 1993; Vita et al.,FEBS 335(1):1 - 5, 1993)

7

415

(97%)

CRF ACTH POMC

가, CRF
(Crofford et al., J. Clin. Invest. 90:2555 - 2564, 1992; Spolsky et al., Science 238:522 - 524, 1987; Tilders et al., Regul. peptides 5:77 - 84, 1982).

CRF

CRF (Sutton et al., Nature 297:331, 1982), (electroencephalogram) (Ehlers et al., Brain Res. 278:332, 1983), (Brown et al., Endocrinology 110:928, 1982), 가 (Fisher et al., Endocrinology 110:222, 1982), 가 (Brown et al., Life Sciences 20:207, 1982), (Williams et al., Am. J. Physiol. 253:G582, 1987), (Levine et al., Neuropharmacology 22:232, 1983), (Sirinathsinghji et al., Nature 305:232, 1983), (Irwin et al., Am. J. Physiol. 255:R744, 1988) CRF가 (DeSouza, Ann. Reports in Med. Chem. 25:215 - 223, 1990). CRF 가 CRF 가 /

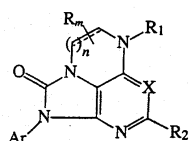
CRF (Rivier et al., U.S. Patent No. 4,605,642; Rivier et al., Science 224:889, 1984) CRF 가 CRF 가 CRF 가 4 - - 5 - - 3 - (Abreu et al., U.S. Patent No. 5,063,245) 2 - (Courtemanche et al., Australian Patent No. AU - A - 41399/93) 가 CRF RF가 1 - 10 μ M 0.1 - 10 μ M

CRF

: WO94/13643, WO94/13644, WO94/13661, WO94/13676, WO94/13677, WO95/10506, WO95/33750, WO96/35689, WO97/00868, WO97/35539, WO97/35580, WO97/35846, WO97/44038, WO98/03510, WO98/0561, WO98/08846, WO98/08847, WO98/11075, WO98/15543, WO98/21200 WO98/29413.

CRF CRF 가 CRF 가

CRF CRF 가 CRF 가 CRF 가 CRF 가



, m, n, X, R, R₁, R₂ Ar

CRF

가

CRF

가

/

CRF

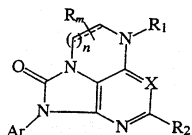
가

가

(CRF)

CRF

가



, n 1 2; m 0, 1, 2 3; X N CR'; R

C₁₋₆ Ar ; R' , C₁₋₆ ; R₁ - C(H)_{0.1} (R₃)(R₄); R₂
C₁₋₆ ; R₃ , C₁₋₆ (C₃₋₆) , C₃₋₆ , C₃₋₆
C₁₋₆ , C₁₋₆ C₁₋₆ , C₁₋₆ C₁₋₆ ,

R₄ , AR₁, C₁₋₆ Ar¹, OAr¹, C₁₋₈ , C₁₋₆ , C₃₋₆ , - (C₃₋₆
) , C₃₋₆ , C₃₋₆ , C₁₋₆ C₁₋₆ , C₁₋₆ Ar¹, C₁₋₆ , C₁₋
6 , C₁₋₆ , C₁₋₆ C₁₋₆ , - (C₁₋₆) , (C₁₋₆)(A
r¹) , (C₁₋₆) , (C₁₋₆ Ar¹) , (C₁₋₆)(Ar¹) , C₁₋₆ C₁₋₆ ,
C₁₋₆ C₁₋₆ , (C₁₋₈) , C(=O)C₁₋₆ , C₁₋₈ , Ar¹, O
Ar¹, NHAr¹, C(=O)Ar¹, C(=O)NHAr¹ - C(=O)NH₂, - (C₁₋₆) - Y - (CO)_{0.1} - Ar¹
(, Y O, NH,),

R₃ R₄ C₅₋₈ , C₅₋₈ , C₃₋₁₂ , ,
, Ar¹ C₅₋₈ , C₁₋₆

Ar , C₃₋₁₂ , , C₁₋₆ , , O(
) , , C₁₋₆ , , - (C₁
-6) , (C₁₋₆)(C₁₋₆) , 1, 2 3
가 ,
/ C₁₋₆ C₁₋₆ ;

Ar¹ , C₃₋₁₂ , , C₁₋₆ , C₁₋₆ , (C₁₋₆)
, (C₁₋₆) C₁₋₆ , (C₁₋₆), C₁₋₆
1, 2 3 .

, .

" " = "O " .

" C₁₋₆ " " C₁₋₈ " , , n - , , n - , - , n -
1 6 1 8 가 .

" C₁₋₆ " , - O(C₁₋₆) .

" C₁₋₆ " - SCH₃, - SCH₂CH₃ - S(C₁₋₆) .

" C₃₋₆ " , , , 3 6 .

" C₅₋₈ " , 5 8 .

" C₅₋₈ " 5 8 .

" C₃₋₆ " 3 6 가 , , 1 - , 2 - , 2 - .

" C₃₋₆ " 3 6 가 , , 1 - , 2 - , 2 - .

" C₁₋₆ " - CH₂OH, - CH(OH)CH₃ C₁₋₆ .

" - (C₃₋₆) " , C₃₋₆ .

" C₁₋₆ C₁₋₆ " - COC₁₋₆ C₁₋₆ .

" C₁₋₆ C₁₋₆ " - COOC₁₋₆ C₁₋₆ .

" C₁₋₆ C₁₋₆ " - OC₁₋₆ C₁₋₆ .

" C₁₋₆ C₁₋₆ " - SC₁₋₆ C₁₋₆ .

" (C₁₋₆)" - SO₂ - SO₂ (C₁₋₆) .

" - (C₁₋₆) " C₁₋₆ C₁₋₆ .

" (C₁₋₆)(C₁₋₆) " C₁₋₆ C₁₋₆ (, C(="O)" (C₁₋₆)) .


" - (C₁₋₆) C₁₋₆ " - - (C₁₋₆) C₁₋₆ .

" C₁₋₆ ' (- CH₂ -), (- CH₂CH₂ -) 2가 C₁₋₆ .

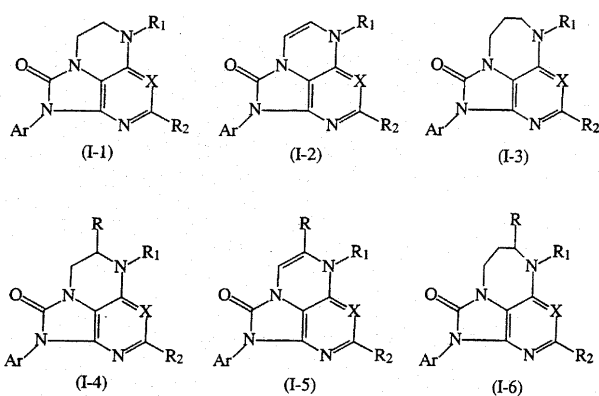
" , , / , , C 1-6
" -OCH₂O-, -OCH₂CH₂O- (" CH₂") ,

"C₃₋₁₂"

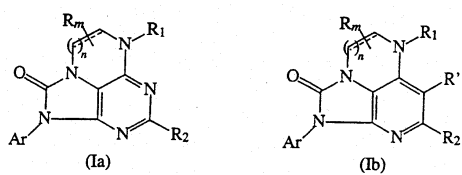
" " , , .



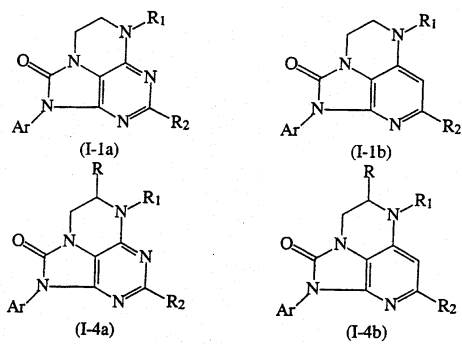
-CH₂CH₂- - CH="CH-" 1 2 R (, n="1" m="0," 1 2)
1, 2 3 R (, n="2" m="0," 1, 2, 3)
-CH₂CH₂CH₂- . , ()
(-1), (-2), (-3), (-4), (-5) (-6) ;



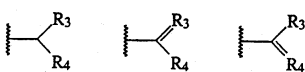
\dots , X , \dots , CRF (a) (b)



CRF, CRF (a).
 CRF (b) (R').
 b), (- 4a) (- 4b) : (- 1a), (- 1)



, R_1 - $CH(R_3)(R_4)$ - $C(R_3)(R_4)$ - $C(H)_{0.1}(R_3)(R_4)$.
 R_1 :

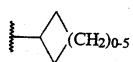


, R_3 가 , R_1 :

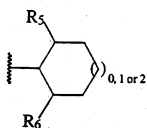


$(=O)N(C_{1-6})^{R_1}(C_{1-6})$ - $C(=O)R_4$, - $C(=O)OR_4$, - $C(=O)NH_2$, - $C(=O)NH(C_{1-6})$ - C .

R_1 R_3 R_4 가 C_{3-8} , R_1 가 :

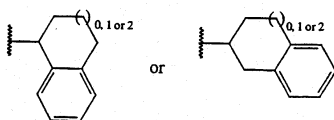


C_{3-8} C_{1-6} C_{5-7} , R_1 가 :



, R_5 R_6 C_{1-6} .

, R_1 R_3 R_4 Ar C_{5-8} , R_1 :



Ar 2,4,6- , 2- -4- ,
 2- -4- , 2- -4- , 2- -4- , 2- -4- ,
 , 2- -4- , 2- -4- , 2,4- , 2,6-
 - -4- , 4- , 2,4- , 2,4- , 2- , 3- , 2-
 -4- , 3,4- , 3,5- , 4- , 4- , 2,4,6-
 , 2- -4-N()₂ , 2- -4-(OCF₃) , 4- -2- -3- , 4-
 -6- -2- , 4- -3- , 4-N(CH₃)(COCH₃) - , 3,4-
 3,4- .

R , , n- , - , - , = "CH₂ " = "CHCH₃ .

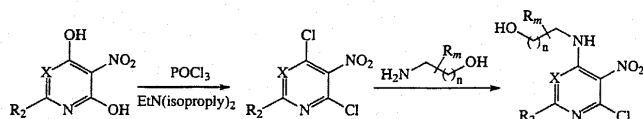
R' , , , , , .

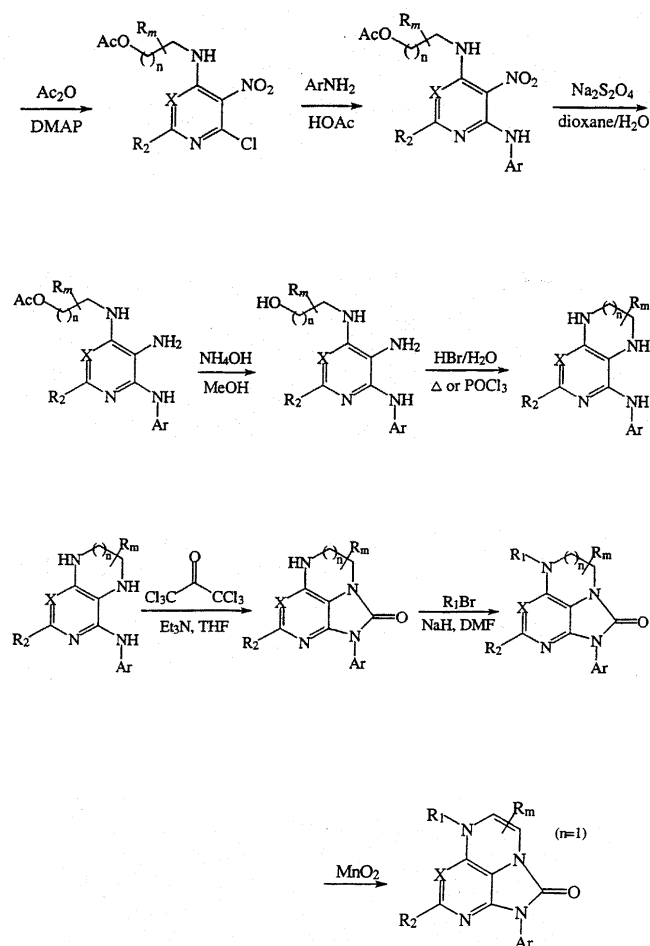
R₁ , , n- , - , n- , - , - , n- , - , -
 , -CH()₂ , -CH(n-)₂ , -CH(n-)₂ , -CH₂CH₂OCH₃ , -CH() (CH₂OCH₃) , -CH() (CH₂OCH₃)₂ , -CH(n-) (CH₂OCH₃) , -CH(n-) (CH₂OCH₃) , -CH() (CH₂OCH₃) , -CH(CH₂OCH₃)₂ , -CH() (CH₂OCH₃) , -CH(4-) (CH₂OCH₃) , -CH(CH₂OCH₃)(CH₂CH₂SCH₃) , -CH() (CH₂O) , -C CH₃ , -CH() () , -CH() (n-) , -CH() (n-) , -CH() (n-) , -CH() (CH₂CH₂CH₂CH(CH₃)₂) , -CH() (n-) , -CH() (n-) , -CH() (n-) , -CH(n-) (n-) , -CH(n-) (n-) ,
 3- , 1,2,3,4- (1 2) , 2- , -CH() () , -CH() () , -CH(n-) () , -CH(n-) () , -CH₂() , -CH₂() , -CH₂CH() C H₂CH₃ , -CH₂CH()CH₂CH₃ , -CH₂C()₃ , -CH₂CC CH₃ , -CH₂C(="O) , " -C(="O) , " -C(="O)NH , " -C(="O) , " -C(="O) , " -C(="O) , " -C(="O)CH₂C(="O)O , " -C(="O)CH() , " C(="O) , " -C(="O)(4-N,N'-) , " -C(="O)CH₂O , -C(="O)CH()₂ , -C(="O)n- , " -C(="O)CH₂CH₂()₂ , -C(="O)n- , " -C(="O)CH₂CH₂ , -CH₂CH₂NH , -CH₂CH₂C(="O)O , " -CH₂CH₂CH₂ , -CH₂CH₂-N- , -CH₂CH₂C(="O)O , -CH₂CH₂O , -CH₂CH()₂ , -CH₂C(="O)O , " -CH₂C(="O) , " -C H₂CH₂O , -CH₂CH₂CH₂CH₂-N- , -CH₂C(="O)Ot- , " -CH₂CH₂CH()₂ , -CH₂C(="O) NH₂ , -CH₂-4-(SO₂CH₃) , -CH₂CH₂ .

R₂ , , , .

가

가





CRF

CRF

CRF (DeSouza et al., J. Neuroscience 7:88, 1987)

al., Synapse 1:572, 1987)

가

CRF

CRF (CRF, [¹²⁵ I] - CRF)가

(DeSouza et al., supra, 1987)

CRF

50%

IC₅₀

" Ki"

$$K_i = \frac{IC_{50}}{1 + L/K_D}$$

, L = " " K_D = " " (Cheng and Prusoff, Biochem. Phar macol. 22:2099, 1973)

CRF , CRF CRF

. , CRF 가
 . , cAMP CRF -
 CRF 가
 (Battaglia et al., supra, 1987) CRF -
 CRF , CRF (((supra, 1987)) cAMP
 supra, 1987)) (

CRF , CRF , CRF 10 μ M Ki 가 .
 , CRF 1 μ M , 0.25 μ M (, 250nM) Ki .
 Ki , (- 1) (- 25) (- 29) (- 33) . 1 μ M

CRF CRF , , , CRF
 CRF . CRF CRF
 , CRF 가 CRF
 ; , ,
 - ; , ,
 . CRF 가 -
 CRF (, , ,
 G.I.), , ,
 ()) .

, CRF . CRF (,
 ()) 가 / . CRF
 - , CRF , CRF 0.1 mg 25
 0 mg, 1 mg 60 mg .

가 가 / , , , ,
 가 / , CRF , , ,
 , , , , (Remington's P
 harmaceutical Sciences, Gennaro, Ed., Mack publishing Co., Easton, PA 1990)
 CRF .

(4)

- 30 mmol) EtOH(30mL) 4,6 - EtOH 1 - - 2 - (870mg, 10mmol) - 5 - (3; J. Chem. Soc. 1954, 3836)(2.23g, 11 - 30 1 EtOAc (4) .

(5)

(15mL) (4)(2.07g, 8 mmol) 2,4,6 - (1.35g, 10 mmol) , (1.52g, 15mmol) 2 () , EtOAc (5) .

(6)

(5)(2.14g, 6mmol) 1:1 / (20mL) , (5mL) (3.12g, 18mmol) EtOAc 가 8 () , (6) .

(7)

THF(10mL) (6)(654mg, 2 mmol) (500mg) (217mg, 0.73m mol) EtOAc 1 () , (7) .

(8)

DMF(3 mL) (7)(353mg, 1 mmol) NaH(120mg, 3 mmol, 60% in oil) . EtO 1,2 - (654mg, 3 mmol) 가 10 () Ac (8) . LC - MS 380(MH+).

(9)

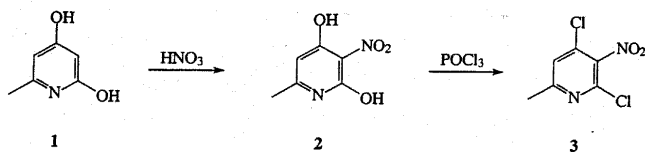
(2ml) (8)(38mg, 0.1 mmol) (100mg) 16 (1:1) TLC() (9) .

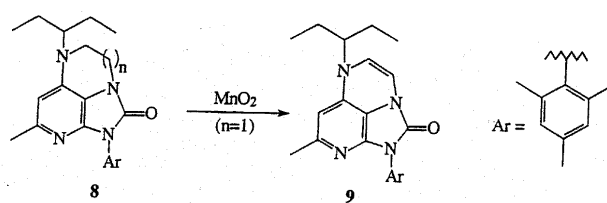
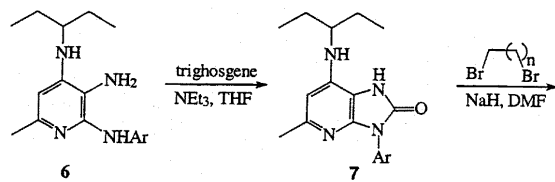
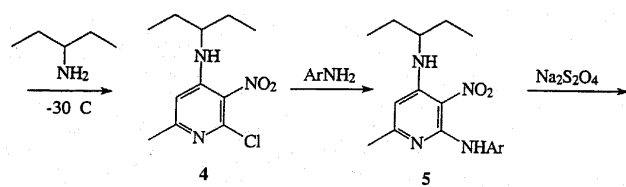
2

B

B

1 , (1)





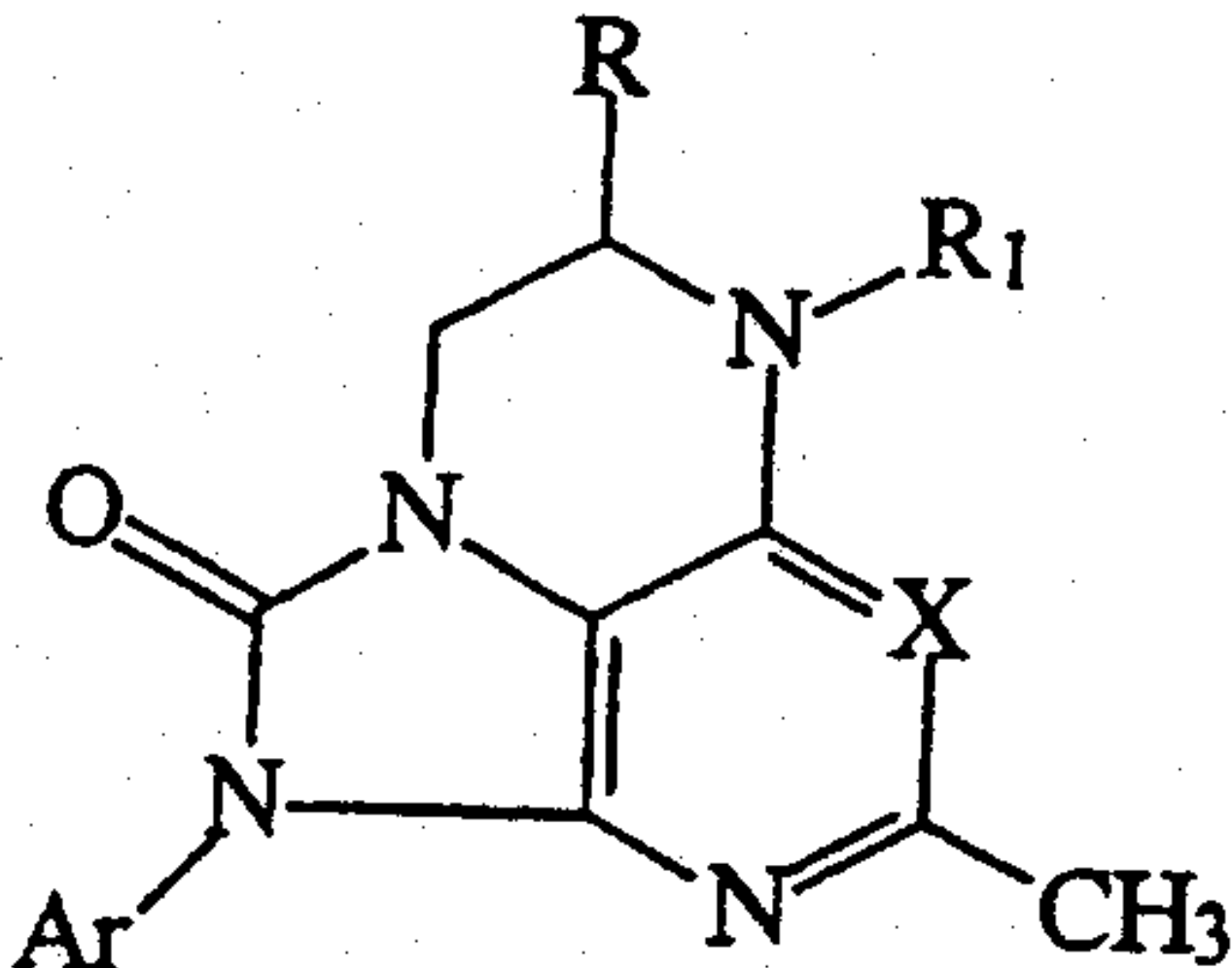
3

/

1

2

[1]



	R	X	R ₁	Ar
(- 1)	H	N	- CH(CH ₂ CH ₂ CH ₃) ₂	2,4,6 -
(- 2)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 -
(- 3)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 -
(- 4)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2,4 -
(- 5)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2,6 - - 4 -
(- 6)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 -
(- 7)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 -
(- 8)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 -

	R	X	R ₁	Ar
(- 9)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2,4 -
(- 10)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 -
(- 11)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	3,4 -
(- 12)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 -
(- 13)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 -
(- 14)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2,4,6 -
(- 15)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 - ()
(- 16)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	
(- 17)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2 - - 4 - (OCF ₃)
(- 18)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	3 -
(- 19)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	2,4 -
(- 20)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	
(- 21)	H	CH	- CH(CH ₂ CH ₃)((CH ₂) ₃ CH ₃)	2 - - 4 -
(- 22)	H	CH	- CH(CH ₂ CH ₃) ₂	2 - - 4 -
(- 23)	H	CH	- CH(CH ₂ CH ₃)((CH ₂) ₂ CH ₃)	2 - - 4 -
(- 24)	H	CH	- CH(CH ₂ CH ₃)((CH ₂) ₄ CH ₃)	2 - - 4 -
(- 25)	H	CH	- CH((CH ₂) ₂ CH ₃)((CH ₂) ₃ CH ₃)	2 - - 4 -
(- 26)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	3,5 -
(- 27)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	3 - (5 -)
(- 28)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 -
(- 29)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - - 3 -
(- 30)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - - 3 -
(- 31)	(S)	CH	- CH ₂ CH ₂ OCH ₃	4 -
(- 32)	(S)	CH	- CH ₂ CH ₂ OH	4 -
(- 33)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - (N - - N -)
(- 34)	(S)	CH	- CH ₂ CH ₂ N(CH ₂ CH ₃) ₂	4 -
(- 35)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - (COOMe)
(- 36)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - - 3 -
(- 37)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - (COMe)
(- 38)	H	CH	- CH(CH ₂ CH ₂ CH ₃) ₂	4 - (CH(OH)(CH ₃) ₂)
(- 39)	(S)	CH	C(O)CH ₃	4 -
(- 40)	(S)	CH	C(O)CH ₂ Ph	4 -
(- 41)	(S)	CH	C(O)Ph	4 -
(- 42)	(S)	CH	C(O)CH ₂ CH ₃	4 -
(- 43)	(S)	CH	C(O)CH ₂ CO ₂ CH ₂ CH ₃	4 -

	R	X	R ₁	Ar
(- 44)	(S)	CH	C(O)	4 -
(- 45)	(S)	CH	C(O)CH(Ph)CH ₂ CH ₃	4 -
(- 46)	(S)	CH	C(O)4 -	4 -
(- 47)	(S)	CH	C(O)4 - (N,N -)	4 -
(- 48)	(S)	CH	C(O)CH ₂ OCH ₃	4 -
(- 49)	(S)	CH	C(O)3 -	4 -
(- 50)	(S)	CH	C(O)CH(CH ₂ CH ₃)CH ₂ CH ₃	4 -
(- 51)	(S)	CH	C(O)CH ₂ CH ₂ CH ₂ CH ₃	4 -
(- 52)	(S)	CH	C(O)CH ₂ CH(CH ₃) ₂	4 -
(- 53)	(S)	CH	C(O)CH ₂ CH ₂ CH ₃	4 -
(- 54)	(S)	CH	C(O)CH ₂ CH ₂ Ph	4 -
(- 55)	(S)	CH	CH ₂ - 3 -	4 -
(- 56)	(S)	CH	CH ₂ CH ₂ NHPh	4 -
(- 57)	(S)	CH	CH ₂ CH ₂ CO ₂ CH ₂ CH ₃	4 -
(- 58)	(S)	CH	CH ₂ CH ₂ CH ₂ Ph	4 -
(- 59)	(S)	CH	CH ₂ CH ₂ - N -	4 -
(- 60)	(S)	CH	CH ₂ CH ₂ CH ₂ CO ₂ CH ₂ CH ₃	4 -
(- 61)	(S)	CH	CH ₂ CH ₂ OCH ₂ CH ₃	4 -
(- 62)	(S)	CH	CH ₂ CH(CH ₃) ₂	4 -
(- 63)	(S)	CH	CH ₂ CO ₂ CH ₂ CH ₃	4 -
(- 64)	(S)	CH	CH ₂ C(O)(4 -)	4 -
(- 65)	(S)	CH	CH ₂ CH ₂ OPh	4 -
(- 66)	(S)	CH	CH ₂ CH ₂ CH ₂ CH ₂ - N -	4 -
(- 67)	(S)	CH	CH ₂ CO ₂ tBu	4 -
(- 68)	(S)	CH	CH ₂ CH ₂ CH((CH ₃) ₂)	4 -
(- 69)	(S)	CH	CH ₂ C(O)NH ₂	4 -
(- 70)	(S)	CH	CH ₂ - 4 - (SO ₂ CH ₃)Ph	4 -
(- 71)	(S)	CH	CH ₂ CH ₂ -	4 -
(- 72)	(S)	CH	CH ₂ Ph	4 -

	(MS/ ¹ H NMR)
(- 1)	
(- 2)	
(- 3)	
(- 4)	
(- 5)	LC?MS 471 (M + H)
(- 6)	
(- 7)	
(- 8)	
(- 9)	LC/MS 425 (M + H)
(- 10)	LC/MS 395 (M + H)
(- 11)	LC/MS 425 (M + H)
(- 12)	LC/MS 433 (M + H)
(- 13)	LC/MS 395 (M + H)
(- 14)	
(- 15)	
(- 16)	
(- 17)	
(- 18)	
(- 19)	
(- 20)	

	(MS/ ¹ H NMR)
(- 21)	
(- 22)	
(- 23)	
(- 24)	
(- 25)	
(- 26)	
(- 27)	
(- 28)	
(- 29)	
(- 30)	
(- 31)	
(- 32)	
(- 33)	
(- 34)	
(- 35)	
(- 36)	

	(MS/ ¹ H NMR)
(- 37)	
(- 38)	

(DeSouza et al., J. Neurosci. 7:88 - 100, 1987)

CRF 가 , CRF
CRF 가 , CRF
CRF

10⁶ CRF 1.5m (sauvagine),
(urotensin) CRF(, 1 μM)
10 mM , 20 μM) 0.1 ml, [¹²⁵ I] - CRF(, 200pM
K_D) 0.1ml CRF 0.1ml 22 2

80%
(Munson and Rodbard, Anal. Biochem. 107:220, 1990) LIGAND

5

CRF -

가 가 , CRF -
(battaglia et al., Synapse 1:572, 1987)

MEM , 0.5ml : 2mM L - , 20mM HEPES, D
1 mM IMBX. , CRF 가 24 -
37 1 - CRF -
cAMP 95% , 20mM 300 μl 가
- 20 16 18 . 1.5ml 가
/ 200 μl 500 μl
cAMP (Biomedical technologies Inc., Sto
ughton, MA) 가 , CRF cAM
P 80% (10⁻¹² 10⁻⁶ M)

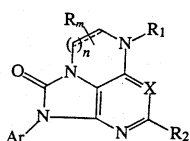
가

가 , 가

(57)

1.

가 .



,
n 1 2;

m 0, 1, 2 3;

X N CR';

R , C₁₋₆ , C₃₋₆ C₁₋₆ C₁₋₆ Ar ;

R' , C₁₋₆ ;

R₁ - C(H)_{0.1} (R₃)(R₄);

R₂ C₁₋₆ ;

R₃ , , C₁₋₆ , (C₃₋₆) , C₃₋₆ , C₃₋₆ , C₁₋₆
, C₁₋₆ C₁₋₆ , C₁₋₆ C₁₋₆ ,

R₄ , AR₁, C₁₋₆ Ar¹, OAr¹, C₁₋₈ , C₁₋₆ , C₃₋₆ , - (C₃₋₆
) , C₃₋₆ , C₃₋₆ , C₁₋₆ C₁₋₆ , C₁₋₆ Ar¹, C₁₋₆ , C₁₋
6 , C₁₋₆ , C₁₋₆ C₁₋₆ , - (C₁₋₆) , (C₁₋₆)(A
r¹) , (C₁₋₆) , (C₁₋₆ Ar¹) , (C₁₋₆)(Ar¹) , C₁₋₆ C₁₋₆ ,
C₁₋₆ C₁₋₆ , (C₁₋₈) , C(=O)C₁₋₆ , C₁₋₈ , Ar¹, O
Ar¹, NHar¹, C(=O)Ar¹, C(=O)NHar¹ - C(=O)NH₂, - (C₁₋₆) - Y - (CO)_{0.1} - Ar¹
(, Y O, NH,),

R₃ R₄ C₅₋₈ , C₅₋₈ , C₃₋₁₂ , ,
, Ar¹ C₅₋₈ , C₁₋₆ ;

Ar , C₃₋₁₂ , , ,1-6 , , O(
) , , C₁₋₆ , , C₁₋₆ , , - (C₁₋₆
) , (C₁₋₆)(C₁₋₆) , , 1, 2 3
, 가 ,
/ C₁₋₆ C₁₋₆ ;

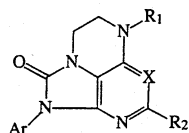
Ar¹ , C₃₋₁₂ , , C₁₋₆ , C₁₋₆ , (C₁₋₆)
, (C₁₋₆) C₁₋₆ , (C₁₋₆), C₁₋₆
1, 2 3 .

2.

1 , n 1 .

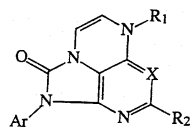
3.

2 , .



4.

2, , .

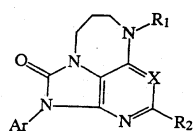


5.

1, n 2, .

6.

5, , .

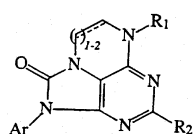


7.

1, m 0, .

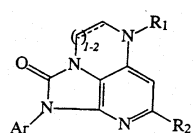
8.

7, , .



9.

7, , .

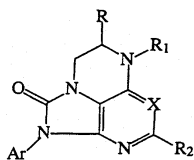


10.

1, m 1.

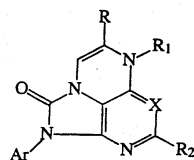
11.

10, .



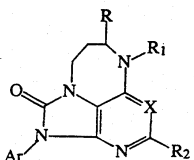
12.

10, .



13.

10, .



14.

1, X가 CR' R'.

15.

1, X N.

16.

1, R C₁₋₆.

17.

1, R.

