

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl.⁷
C07D 257/02

(11)
(43)

10-2004-0030826
2004 04 09

(21)	10-2004-7000906		
(22)	2004 01 19		
	2004 01 19		
(86)	PCT/EP2002/007999	(87)	WO 2003/009874
(86)	2002 07 18	(87)	2003 02 06

(30) 10135356.1 2001 07 20 (DE)

(71) 178 (: -13353)

(72)

12621		55	
-			
12161	20		
,			
15562	-	-	14
,			
12247	-	-	41
,			
10589	4		
,			
12279	-	-	24
,			
13465		132	
,			
14129		23	
,			
13403		11	

(74)

:

(54)

NMR

NMR

NMR

NMR

[P. Caravan et al., Chem. Rev. 1999, 99, 2293-2352]

가 (III)

NMR

가
Gd³⁺, Fe³⁺, Mn²⁺

, NMR

T_{1c}

T₁

T

R

가

가

(Tumbling Motion Time).

NMR

가
가

Gd-DTPA(adiol. 1987, 22, 665-671]

[U.Schmiedl et al., Radiology 1987, 162, 205-210]

[M.D.Organ et al., Invest. R

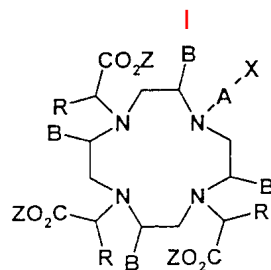
WO 95/31444
 2
 , WO 01/08712
 가 WO 97/02051 (cascade)

가 EP-A-0 565 930

,가 ,가 가 NMR
 NMR , NMR 가 ,가

가 1,4,7,10-

가



Z , 2 Z 가 ,
 B C₁₋₄ - ,
 R , , -SO₃H , -PO₃H₂ C₁₋₁₀ - C₁₋₁₀ -
 () 1 2 , B R
 A 1 5 , 1 5 () -NR' (, R' R
 ,) 1 5 C₁₋₃₀ -
 , 1 3 , -SO₃H 1 3 , -PO₃H₂ 1 3 ()
 , X가 3 A가

X

4 가 -CH(CO₂H)CH₂CH₂-CO₂H
 [P. Caravan et al., Chem. Rev. 1999, 99, 2293-2352]

가 WO 97/02051

EP-A-0-565 930

A가 -CH(R⁴)-CO-NR²-U⁶
 A가 -CH(R³)-C(O)-NH-(CH₂)₁₋₆-NH-D-
 가

1

가

가

5 6 ()

(), () ()가

4 3

Z 가

3

R 가

B R

B 가

()

가 가

가

B

C₁₋₄-

C₁₋₄-

B가

I

,R

()

C₁

-10-
3 H₂

(C₅₋₁₀-)

,

, -SO₃H

-PO

, C₁₋₁₀-

() 1 2

C₁₋₁₀-

C₁₋₄-

, n-

, n-

tert-

. R C₁₋₁₀-

C₅₋₁₀-

, -SO₃H

-PO₃H₂

-CH₂-COOH

-C(CH₃)₂-COOH가

, C₁₋₁₀-

() 1 2

)_p-Y

2

R

-(CH₂)_m-(O)_n-(

(, m 1 5 , n 0 1 , p 0 1 , Y

R

, -SO₃H

-PO₃H₂

B가

, R

, tert-

C₅₋₁₀-

, -CH₂-COOH, -C(CH₃)₂-COOH,

-(CH₂)_m-(O)_n-()_p-Y

(, m 1 5 , n 1 0 , p 0 1 , Y

, -SO₃H -PO₃H₂)

, R

I

(spacer) A

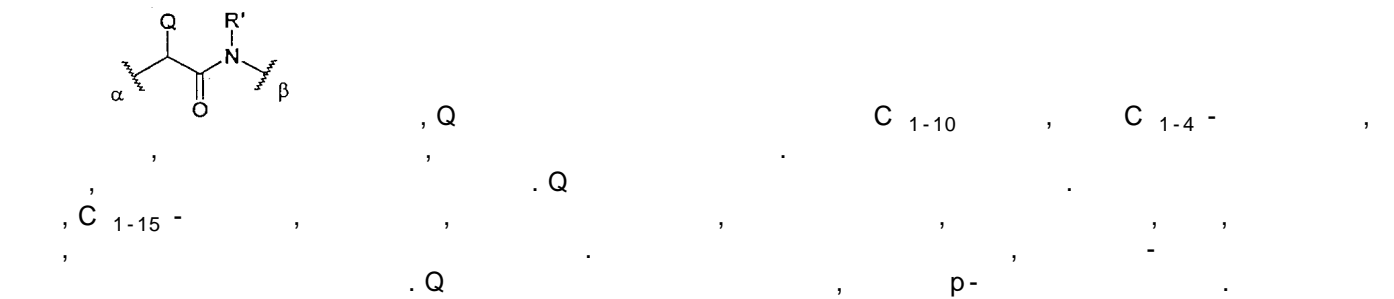
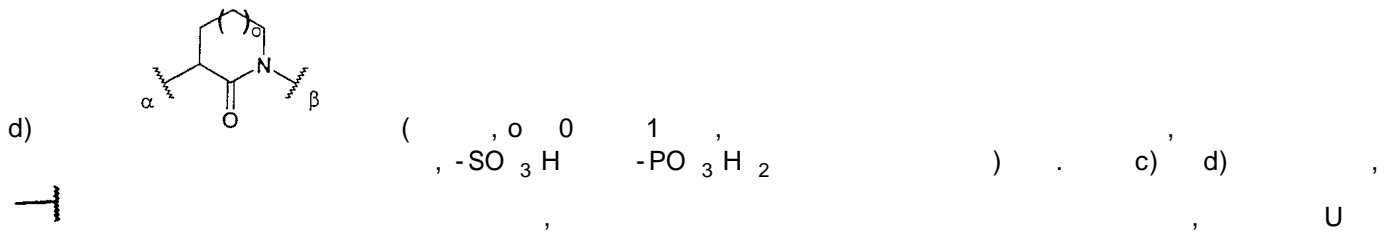
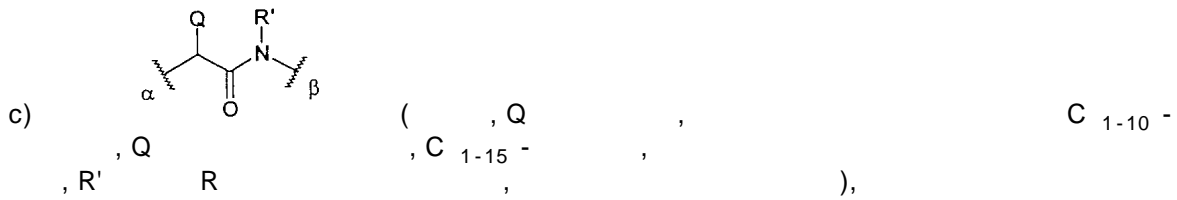
X
 A 1 5 () -NR' (, R
 C₁₋₃₀ 1 3 , 1 3 , -SO₃H 1 3 , -PO₃H₂ 1
 , X가 3 A가

가 X 3 X 4 가 4 가

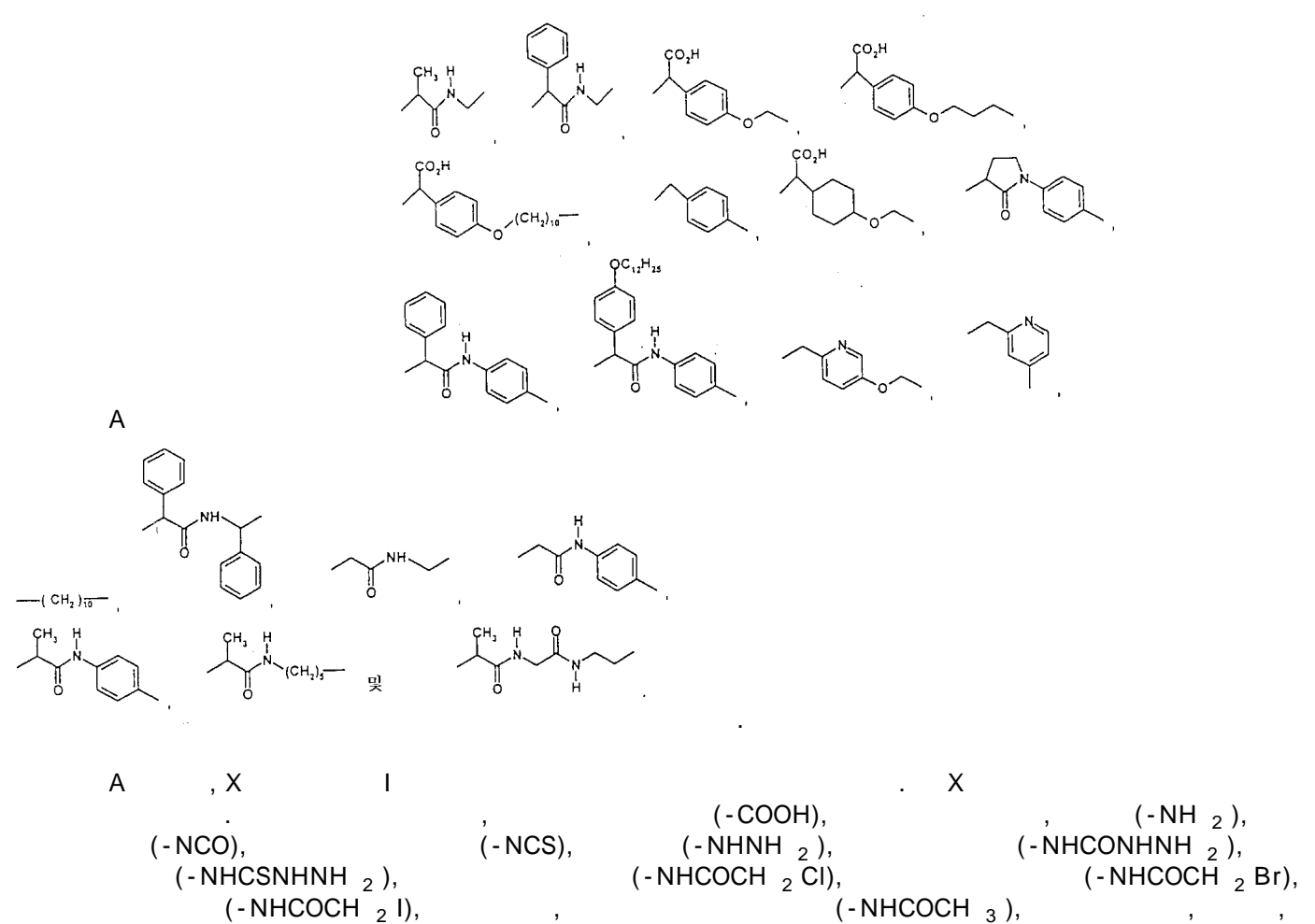
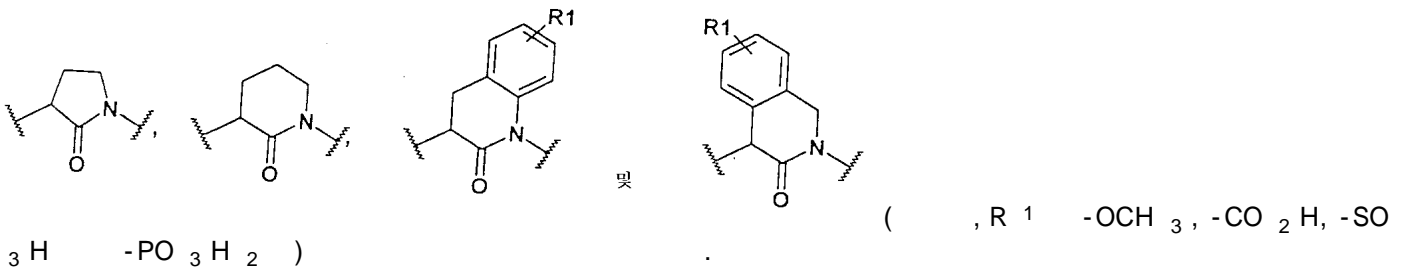
-A-X -CH(R)-CO₂Z

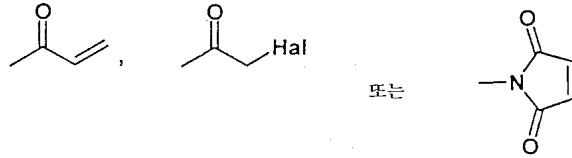
U X A'-U , A'

- a) ,
- b) -CH(CO₂H)-,



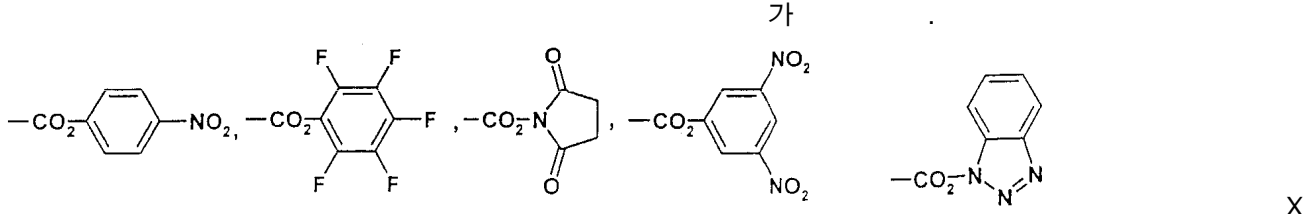
R' R , R . R'
 A' , -CH(CO₂H)-, -C(CH₃)H-CO-NH-, -C()H-CO-NH-, -C(p-)H-CO-NH-,





Hal,)가

[M. and A. Bodanszky, 'The Practice of Peptide Synthesis', Springer
 verlag 1984]



I, Z

가

NMR

NMR

NMR

EP 71564, EP 130934

DE-OS 34 01 052

가
 iotracers for Medical Applications,' Vol. I, CRC Press, Boca Raton, Florida]

['Rad

1. 가 21-29, 42, 44 58-70 NMR
 (III), (II), (II), (II), (II), (III), (III), (III), (III)
 (III) . 가 (III), (III), (III), (III), (III), (III), (II) (III)
 NMR

2. 가 26, 27, 29, 31, 32, 37-39, 43, 46, 47, 49, 61, 62, 64, 67, 70, 71, 75, 77, 82 83

가

가

가

가

NMR

NMR

100

1000

가

가

NMR

['Radiotracers for Medical Applications,' CRC Press, Boca Raton, Florida 1983] [E
 ur. J. Nucl. Med. 17 (1990) 346-364] [Chem. Rev. 93 (1993) 1137-1156]

SPECT ¹¹¹In ^{99m}Tc

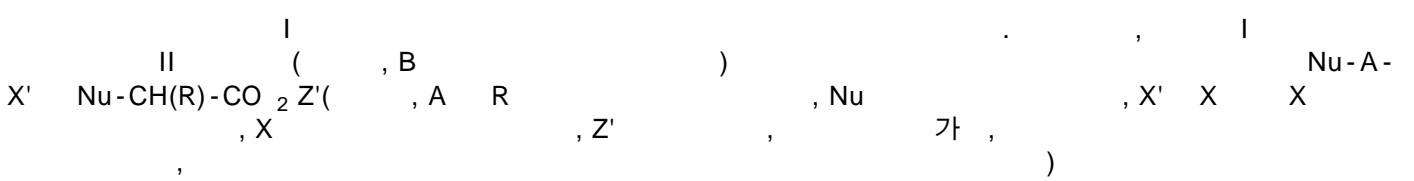
⁴³Sc, ⁴⁴Sc, ⁵²Fe, ⁵⁵Co, ⁶⁸Ga, ⁶⁴Cu, ⁸⁶Y ^{94m}Tc
 ([Heiss, W. D.; Phelps, M. E.; Pos
 itron Emission Tomography of Brain, Springer Verlag Berlin, Heidelberg, New York 1983]).

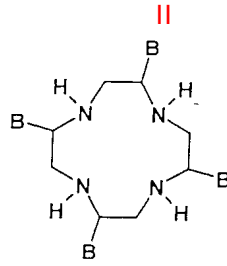
(
)
 가
 (X)
 가
 (Moessbauer)

⁴⁶Sc, ⁴⁷Sc, ⁴⁸Sc, ⁷²Ga, ⁷³Ga, ⁹⁰Y, ¹⁷⁷Lu, ⁷²Ga, ¹⁸⁸Re, ⁹⁰Y, ¹⁷⁷Lu, ⁷²Ga, ¹⁸⁸Re, ²¹¹At, ²¹¹Bi, ²¹²Bi, ²¹³Bi
⁵³Sm, ⁶⁷Cu, ²¹⁴Bi, ²¹²Bi가, ¹⁵⁸Gd, ¹⁵⁷Gd

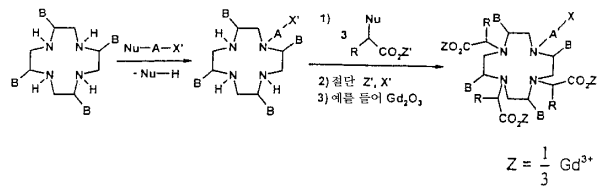
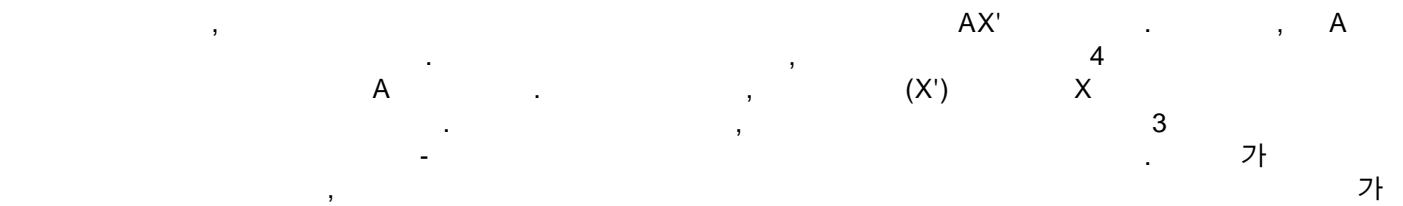
R. L. (Mills) ([Nature Vol. 336 (1988), p. 787])
⁵⁷Fe ¹⁵¹Eu

N,N-
 가
 ()
 가
 ()
 가
 ()
 가

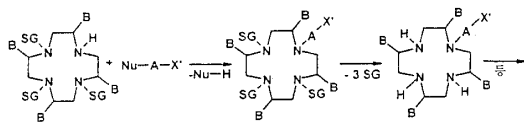
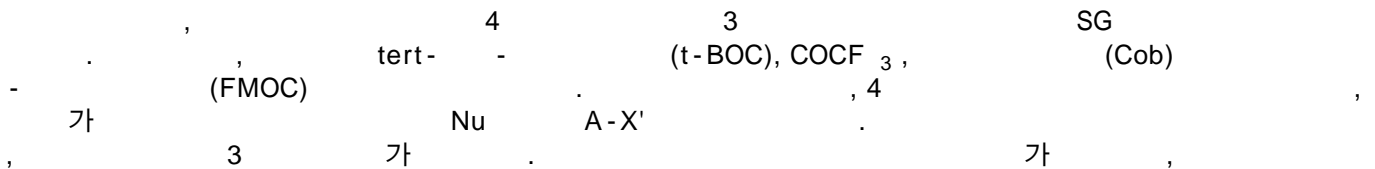




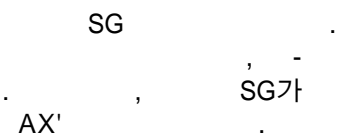
3가

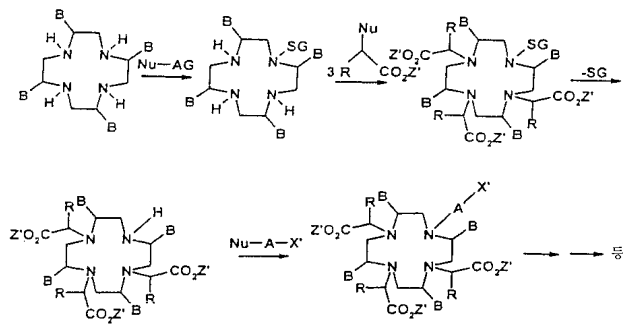


Nu = 핵배적이탈기 (예를 들어, Br, I, O-트리플레이트, 메실레이트, 토실레이트 등)
 Z' = 카르복실산의 보호기



SG = 보호기 (예를 들어, BOC, Cbo, COCF₃, Fmoc, 등)





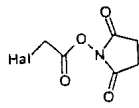
: Cl, Br, I, O-

-10 100 , 0 30

C₁-C₆ , C₆-C₁₀ , C₆-C₁₀-Ar(C₁-C₄)-
 , n- i- tert- 가

0 50

NH , N-
 ([H. Newman, J. Org. Chem., 30: 287 (1965)], [M. A. Schwartz et al., J. Am. Chem. Soc., 95 G12 (1973)]), ([M. Imazama and F. Eckstein, J. Org. Chem., 44: 2039 (1979)]) . tert- ([B. F. Lundt et al., J. Org. Chem., 43: 2285 (1978)]) . 가
 NH . N- /Pd-C([W. H. Hartung and R. Rimonoﬀ, Org. Reactions VII, 262 (1953)]) ([L. Zervas et al., J. Am. Chem. Soc., 78: 1359 (1956)]) ([M. Bergmann L. Zervas Ber. 65: 1192 (1932)])



(Hal =) N-

가

Nu-A-X

가

(BOP) O-(
 DCC 가

(EDC), -1- (NHS) N-

(DCC), 1- -3-(3-)-

(HBTU) O- 가

X가

가

, , I
 N- , X가 ,
 , 가 .
 , X ,
) , X (NH₂, SH) , (,
 , I
 , 가 ,
 , 가 .
 , 가 ,
 , 가 ,
 가 ,
 (, , ,))
) (, , ,) (building block)(, , , ,
 , II X
 , 가 .

TU-Graz ['Chemie der Biomolekuele(Cheistry of Biomolecules)'
]([H. Berthold , Institut fuer Organische Chemie(Institute for Organic Chemistry), Tu-Graz, 2001])
www.orgc.tu-graz.ac.at

, 가 .
 , HSA, BSA , (, ,)
 (,) , , ,
 (,), (,) , , ,
 , , , , (,)
), , (, CAA) , (, X - X
 A DNA(DNA RNA(SELEX) DNA RNA , RN
 가), PNA((Hoechst)) , - ((Seebach)),
 , , , ()

500 mL 3
 (: / : 20/1)
 : 32.0 g(73%)
 :

계산치: C 68.39 H 7.23 N 7.98

실측치: C 67.95 H 7.41 N 8.22

b) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

1a 26.3 g(30 mmol) 400 mL , 40 mL
 (10% Pd/C) 3 g 가 . 50 8
 : 15.7 g()
 :

계산치: C 51.05 H 7.60 N 13.53

실측치: C 50.71 H 7.83 N 13.25

c) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-
 Gd

1b 10.4 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가
 pH 7.4 (: / / : 20/20/1)
 IR-120(R) (H +) 가
 : 10.1 g(69%)

(- (Karl-Fischer)): 8.3%

():

계산치: C 39.33 H 5.40 Gd 23.41 N 10.42

실측치: C 39.21 H 5.88 Gd 22.93 N 10.11

2

a) 10-[4-()-1- -2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 1a 1-[4-(-)-1- -2- -3-]-1,4,7,10- 19.6 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()- ([Walker et al., Tetrah
 edron (1997), 53(43), 14591]) 68.1 g(0.2 mol) 가 6
 500 mL 3 : / : 20/1

: 33.7 g(70%)

:

계산치: C 69.90 H 7.86 N 7.28

실측치: C 69.77 H 7.51 N 7.22

b) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

2a 28.9 g(30 mmol) 400 mL , 40 mL ,
(10% Pd/C) 3 g 가 . 50 8

: 18.0 g()

:

계산치: C 55.89 H 8.54 N 11.64

실측치: C 55.63 H 8.83 N 11.31

c) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

2b 12.0 g(20 mmol) 200 mL 80 mL , 5 mL
가 가 3.6 g(10 mmol) 가 , 3 가 ,
pH 7.4 , (: 20/20/1)
IR-120(R) (H +) 가

: 12.0 g(72%)

(-): 9.1%

():

계산치: C 44.49 H 6.40 Gd 20.80 N 9.26

실측치: C 44.21 H 6.72 Gd 20.23 N 9.11

3

a) 10-[4-()-1- -2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 1a 1-[4-()-1- -2- -3-]-1,4,7,10- 19.6 g(50 mmol) N- 60 mL(0.35 mol)
400 mL 2-()-2- ([Qabar et al., T
etrahedron Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 가 6
500 mL 3 , / : 20/1)

: 41.1 g(76%)

:

계산치: C 72.13 H 8.10 N 6.47

실측치: C 71.88 H 8.21 N 6.25

b) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

3a 32.5 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8
 : 22.0 g()

계산치: C 61.56 H 8.80 N 9.70

실측치: C 61.17 H 8.98 N 9.41

c) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

3b 14.4 g(20 mmol) 150 mL 150 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 8 가 ,
 pH 7.4 (: / / : 20/20/1)
 가

: 12.4 g(65%)
 (-): 8.0%
 ():

계산치: C 50.72 H 6.90 Gd 17.95 N 7.99

실측치: C 51.03 H 7.08 Gd 17.42 N 8.11

4

a) 10-[4-(t-)-1- -2- -3-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

N-[2- -2-]- -t- (WO 98/24775 6a) 26.6 g(81.1 mmol) 1,4,7,
 10- 27.9 g(162.2 mmol) 가 , 300 mL ,
 . 250 mL 가 , 200 mL 2
 25% = 10/5/1) (: / /
)-1- -2- -3-]-1,4,7,10- (21.0 g; 50 mmol; 1-[4-(t- 62%) N-
 60 mL(0.35 mol) 400 mL 2-()
 ([Kitazaki et al., Chem. Pharm. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 ,
 6 500 mL 3
 (: / : 20/1)

: 34.0 g(75%)
 :

계산치: C 68.93 H 7.45 N 7.73

실측치: C 69.12 H 7.57 N 7.60

b) 10-(4-t- -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

4a 27.2 g(30 mmol) 400 mL , 40 mL ,
(10% Pd/C) 3 g 가 . 50 8

: 17.5 g()

:

계산치: C 55.95 H 7.13 N 12.08

실측치: C 56.21 H 6.99 N 11.83

c) 10-(4- -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-
0- Gd

4b t- 11.6 g(20 mmol) ,
15 250 mL 가 , 2 ,
200 mL 80 mL ,

pH 7.4 5 mL 가 가 3.6 g(10 mmol) 가 , 3
가 pH 7.4 (: /
/ : 20/20/1) IR-120(R)
(H +) 가 .

: 11.6 g(72%)

(-): 9.0%

():

계산치: C 44.19 H 5.22 Gd 21.43 N 9.54

실측치: C 43.91 H 5.27 Gd 21.09 N 9.77

5

a) 4-()-

18.4 g(133 mmol) 가 ((Aldrich)) 10 g(60.2 mmol) 75 mL .
가 , 가 4 17.8 mL(123 mmol) 15
(/ 3:1) .

: 14.6 g(96%)

:

계산치: C 61.90 H 6.39

실측치: C 61.67 H 6.50

b) - -4-()-

5a 13.5 g(53.5 mmol) 75 mL . N- 9.52 g(53.5 mmol)
 48 mg 가 , 5
 2 1 ,
 (/ 3:1)
 : 15.4 g(87%)

계산치: C 47.15 H 4.57 Br 24.13

실측치: C 47.01 H 4.76 Br 23.70

c) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

5b 26.9 g(81.1 mmol) 1,4,7,10- 27.9 g(162.2 mmol)
) 가 , 300 mL , 250 mL 가 ,
 , 200 mL 2 ,
 (: / / = 10/5/0.1)
 . 1-[-(4-(-))-]-1,4,7,10-
 (21.1 g; 50 mmol; 62%) 200 mL N- 60 mL(0.35 mol)
 400 mL 2-() ([Kitazaki et al., Chem. Pharm.
 Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
 . 500 mL 3 ,
 (: / : 20/1)
 : 34.1 g(75%)

계산치: C 67.38 H 7.10 N 6.16

실측치: C 67.20 H 7.33 N 6.31

d) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

5c 27.3 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 ,
 : 19.3 g()

계산치: C 56.42 H 7.26 N 8.77

실측치: C 56.21 H 7.56 N 8.47

e) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10- Gd

5d 13.3 g(20 mmol) 2N 250 mL 250 mL
 , 40 5 (Amberlite) IR-120(R) (H +)
 pH 7 , 80 mL 가 , 5 mL 가 가 3.6 g(10 mmol) 가 , 3 가 , pH 7.4 ,

(IR-120(R) / (H +) : 20/20/1) 가 .

: 8.6 g(61%)

(-): 9.3%

():

계산치: C 43.19 H 4.97 Gd 20.94 N 7.46

실측치: C 43.22 H 5.29 Gd 20.42 N 7.11

6

a) 4-()-

.4 g(133 mmol) 가 . 4- () 10 g(60.2 mmol) 75 mL . 18
 가 , 가 4 17.8 mL(123 mmol) 15
 , (/ , 3:1) , ,

: 16.4 g(97%)

:

계산치: C 64.27 H 7.19

실측치: C 64.41 H 6.92

b) - [4-()-]-

6a 15.0 g(53.5 mmol) 75 mL . N- 9.52 g(53.5
 mmol) 48 mg 가 , 5 ,
 2 1 , (/ , 3:1) ,

: 15.9 g(83%)

:

계산치: C 50.16 H 5.33 Br 22.24

실측치: C 50.33 H 5.04 Br 21.94

c) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

6b 29.1 g(81.1 mmol) 1,4,7,10- 27.9 g(162.2 mmol)
) 가 , 300 mL , 250 mL 가 ,
 , 200 mL 2
 (: / / = 10/5/0.1)
 . 200 mL 1-[-(4-())-]-1,4,7,1
 0- (22.5 g; 50 mmol; 62%) N- 60 mL(0.35 mol)
 400 mL 2-() ([Kitazaki et al., Chem. Phar
 m. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
 . 500 mL 3 , ,

(: / : 20/1)

: 30.5 g(65%)

:

계산치: C 67.93 H 7.31 N 5.98

실측치: C 67.95 H 7.22 N 6.13

d) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- (

6c 28.1 g(30 mmol) 400 mL , 40 mL ,
(10% Pd/C) 3 g 가 . 50 8 . ,

: 20.0 g()

:

계산치: C 57.64 H 7.56 N 8.40

실측치: C 57.43 H 7.77 N 8.69

e) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,
4,7,10- Gd

6d 13.3 g(20 mmol) 2N 250 mL 250 mL
, 40 5 IR-120(R) (H +) pH 7
, 80 mL 가 , 5 mL 가 가 pH 7.4 3.6 g(10 mmol)
가 , 3 가 , (IR-
: / / : 20/20/1) .
120(R) (H +) 가 .

: 9.3 g(55%)

(-): 8.0%

():

계산치: C 44.72 H 5.31 Gd 20.19 N 7.19

실측치: C 44.31 H 5.88 Gd 19.93 N 7.11

7

a) 4-()-

.4 g(133 mmol) 가 , () 10 g(60.2 mmol) 75 mL . 18
50 mL - 36.1 g(123 mmol) 가 , 8
, ' (/ 3:1) . ,

: 20.3 g(89%)

:

계산치: C 69.81 H 9.05

실측치: C 69.50 H 8.91

b) - [4-()]-]-

7a 20.2 g(53.5 mmol) 75 mL . N- 9.52 g(53.5 mmol)
 48 mg 가 , 5
 2 1 ,
 (/ , 3:1)
 : 21.0 g(86%)

계산치: C 57.77 H 7.27 Br 17.47

실측치: C 57.95 H 7.41 Br 17.02

c) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

7b 37.1 g(81.1 mmol) 1,4,7,10- 27.9 g(162.2 mmol)
) 가 , 300 mL , 250 mL 가 ,
 , 200 mL 2 ,
 (: / / = 10/5/0.1)
 200 mL 1-[-(4-())-]-1,4,7,
 10- (27.4 g; 50 mmol; 62%) N- 60 mL(0.35 mol)
 400 mL 2-() 가 , 6 ([Kitazaki et al., Chem. Phar
 m. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
 500 mL 3 , ,
 (: / : 20/1)
 : 33.6 g(65%)

계산치: C 69.61 H 7.98 N 5.41

실측치: C 69.75 H 7.88 N 5.12

d) 10-[-(4-())-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

7c 31.1 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 ,

: 23.0 g()

계산치: C 61.24 H 8.43 N 7.32

실측치: C 60.96 H 8.61 N 7.22

e) 10-[-(4-)-]-1,4,7- , ' , '- -1,4,7- ()-1,4

,7,10-

Gd

7d 15.3 g(20 mmol) 2N 250 mL 250 mL
 , 40 5 80 mL 가 , 5 mL 가 IR-120(R) (H +) pH 7
 가 , 3 / / : 20/20/1 가 pH 7.4 3.6 g(10 mmol)
 : 120(R) (H +) 가 IR-
 : 11.5 g(60%)
 (-): 8.5%
 ():

계산치: C 49.30 H 6.32 Gd 17.93 N 6.39

실측치: C 49.56 H 6.10 Gd 17.52 N 6.63

8

a) 10-(p-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

150 mL 4- () 18.6 g(81.1 mmol) 1,4,7,10-
 27.9 g(162.2 mmol) 가 , 300 mL
 250 mL 가 , 200 mL 2 (: / 25% = 8/1)
 200 mL 1-(p-)-1,4,7,10-
 (21.6g; 67.3 mmol; 83%) N- 60 mL(0.35 mol) 400 m
 L 2-() 가 , 6 ([Kitazaki et al., Chem. Pharm. Bull. (1999), 4
 7(3), 360]) 62.45 g(0.2 mol) 가 ,
 500 mL 3 : / : 20/1
 : 41.8 g(77%)
 :

계산치: C 69.95 H 7.24 N 6.94

실측치: C 69.57 H 7.39 N 7.12

b) 10-(p-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

8a 24.2 g(30 mmol) 400 mL , 15N 100 mL
 , 6 , IR-120(R) (H+) 가 pH 7 200 mL
 : n- / / / ; 12/6/3/3
 : 16 g

c) 10-(p-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-
 Gd

8b 11 g(20 mmol) 200 mL 80 mL 5 mL
 가 가 3.6 g(10 mmol) 가 3
 pH 7.4 (: / / : 20/20/1)
 IR-120(R) (H +) 가

: 8.9 g(61%)

(-): 7.2%

():

계산치: C 44.37 H 5.21 Gd 23.23 N 8.28

실측치: C 44.12 H 5.46 Gd 22.93 N 8.51

9

a) 10-(p-)-1,4,7- , ' , '- ()-1,4,7- (-)-1,4,7,10-

200 mL 8a 1-(p-)-1,4,7,10-
 21.6 g(67.3 mmol) N- 60 mL(0.35 mol) 400 mL 2-(
)- 가 , 6 ([Walker et al., Tetrahedron (1997), 53(43), 14591]
) 85.1 g(0.25 mol) 가 , 500 mL
 3 : / : 20/1)
 .

: 48.5 g(81%)

:

계산치: C 71.43 H 7.92 N 6.29

실측치: C 71.12 H 7.79 N 6.55

b) 10-(p-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

9a 26.7 g(30 mmol) 400 mL , 15N 100 mL
 , 6 , IR-120(R) (H +) 가 pH 7 , 200 mL

: n- / / / ; 12/6/3/3

: 19 g

c) 10-(p-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-
 Gd

9b 12.6 g(20 mmol) 200 mL 80 mL 5 mL
 가 가 3.6 g(10 mmol) 가 3
 pH 7.4 (: / / : 20/20/1)
 IR-120(R) (H +) 가

: 10.9 g(65%)

(-): 9.0%

():

계산치: C 48.93 H 6.23 Gd 20.66 N 7.36

실측치: C 48.87 H 6.01 Gd 20.22 N 7.59

10

a) 10-(p-)-1,4,7- , ' , '- ()-1,4,7- (-)-1,4,7,10-

200 mL 8a 1-(p-)-1,4,7,10-
 21.6 g(67.3 mmol) N- 60 mL(0.35 mol) 400 mL 2-(
)-2- ([Qabar et al., Tetrahedron Letters (1998),
 39(33), 5895]) 95.1 g(0.25 mol) 가 , 6 , .
 500 mL 3 (: / : 20/1) , .
 (: / : 20/1) .
 : 48.3 g(71%)
 :

계산치: C 73.63 H 8.17 N 5.54

실측치: C 73.42 H 8.39 N 5.75

b) 10-(p-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

10a 30.3 g(30 mmol) 400 mL , 15N 100 mL
 , 6 , IR-120(R) , (H +) 가 pH 7 , 200 mL
 : n- / / / ; 12/6/3/3
 : 22.5 g

c) 10-(p- Gd)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

10b 15.0 g(20 mmol) 200 mL 80 mL 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 ,
 pH 7.4 , (: / / : 20/20/1) ,
 가
 : 11.9 g(63%)

(-): 7.0%

():

계산치: C 54.52 H 6.75 Gd 17.85 N 6.36

실측치: C 54.19 H 6.83 Gd 17.61 N 6.69

11

a) 10-(p-)-1,4,7- , ' , '- -1,4,7- (-)-1,4,7,10-

200 mL 8a
 21.6 g(67.3 mmol) N-
)-2- 1-(p-)-1,4,7,10-
 5895]) 93.6 g(0.25 mol) 가 , 6 (60 mL(0.35 mol) 400 mL 2-(
 mL 3 [Qabar et al., Tetrahedron Letters (1998), 39(33),
 (: / : 20/1) . 500
 : 50.8 g(76%)

계산치: C 74.98 H 6.49 N 5.64

실측치: C 75.22 H 6.61 N 5.47

b) 10-(p-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

11a 29.8 g(30 mmol) 400 mL , 15N 100 mL
 , 6 , IR-120(R) (H +) 가 pH 7 , 200 mL
 : n- / / ; 12/6/3/3
 : 22.0 g

c) 10-(p-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-
 Gd

11b 14.6 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 가
 pH 7.4 (: / / : 20/20/1)
 가
 : 13.1 g(70%)
 (-): 8.1%
 ():

계산치: C 55.67 H 4.79 Gd 18.22 N 6.49

실측치: C 55.33 H 4.97 Gd 17.92 N 6.54

12

a) 10-[4-(t-)-1- -2- -3-]-1,4,7- , ' , '- -1,4,7- -(

2- ([Teger- Nilsson et al., WO 93/11152, page 38]) 23.2 g(81.1 m
 mol) 1,4,7,10- 34.4 g(0.2 mol) 가 , 300 mL
 . 250 mL 가 , 200 mL 2
 / 25% = 10/5/1) . 200 mL 1-[4-(/
)-2- -3-]-1,4,7,10- (19.6 g; 50 mmol; 62%) N-
 60 mL(0.35 mol) 400 mL 2-()-
 ([Walker et al., Tetrahedron (1997), 53(43), 14591]) 68.1 g(0.2 mol) 가 ,
 500 mL 3
 (: / : 20/1)
 : 37.0 g(78%)

계산치: C 69.67 H 7.76 N 7.39

실측치: C 69.51 H 7.88 N 7.39

b) 10-(4- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,
 7,10-
 13a 28.4 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8
 : 17.7 g()

계산치: C 55.18 H 8.40 N 11.92

실측치: C 54.97 H 8.70 N 11.88

c) 10-(4- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7
 ,10- Gd
 13b 11.8 g(20 mmol) 200 mL 80 mL 5 mL
 가 가 3.6 g(10 mL) 가 , 3 가 ,
 pH 7.4 , (: / / : 20/20/1)
 IR-120(R) (H +) 가 .
 : 12.1 g(75%)

(-): 8.0%

():

계산치: C 43.71 H 6.25 Gd 21.19 N 9.44

실측치: C 43.90 H 6.40 Gd 20.80 N 9.33

14

a) 10-[4-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 13a 18.9 g(50 mmol) N- 1-[4-()-2- -3-]-1
 ,4,7,10- 400 mL 2-()-2- 60 mL(0.35 mol)
 n Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 가 , 6 ([Qabar et al., Tetrahedro
 500 mL 3 : / : 20/1)
 : 38.5 g(72%)

계산치: C 71.95 H 8.02 N 6.56

실측치: C 71.90 H 8.21 N 6.73

b) 10-(4- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,
 7,10-

14a 32.1 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8
 : 21.2 g()

계산치: C 61.08 H 8.69 N 9.89

실측치: C 61.27 H 8.55 N 9.41

c) 10-(4- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,
 ,10- Gd

14b 14.2 g(20 mmol) 150 mL 가 150 mL , 5 m
 L 가 가 3.6 g(10 mmol) 가 , 8 가 가
 pH 7.4 (: / / : 20/20/1)
 가
 : 13.5 g(71%)

(-): 9.0%

():

계산치: C 50.15 H 6.78 Gd 18.24 N 8.12

실측치: C 49.92 H 6.51 Gd 18.01 N 8.31

15

a) 10-[4-()-1- -2- -3-]-2,5,8,11- -1,4,7,10-
 -1,4,7- -t-

2- (WO 98/24774 1e) 0.50 g(1.67 mmol) 2,5,8,11-
 -1,4,7,10- (Petrov et al., DE 19608307 ; Ranganathan et al., WO 95/31444) 14
 .4 g(5 mmol) 가 , 10 mL , 250 mL 가 ,

200 mL 2
 (: / / 25% = 10/5/1)
 -tert- 822 mg(4.2 mmol) 5 mL 1-[
 4-()-1- -2- -3-]-2,5,8,11- -1,4,7,10- (0.7
 0 g; 1.27 mmol; 76%) 541 mg(5.1 mmol) 가 , 60 12
 0 / , = 20:1) (:

: 964 mg(85%)

계산치: C 56.49 H 8.01 N 7.84 Na 2.57 Br 8.95

실측치: C 56.37 H 7.88 N 7.61 Na 2.33 Br 8.59

b) 10-(4- -1- -2- -3-)-2,5,8,11- -1,4,7,10- -1,4,7
 - - -tert- ()

15a 893 mg(1.0 mmol) 10 mL , (10% Pd/C)
 가 가 , ,

: 562 mg(70%)

계산치: C 52.36 H 8.16 N 8.72 Na 2.86 Br 9.95

실측치: C 52.51 H 8.30 N 8.93 Na 2.71 Br 9.44

c) 10-(4- -1- -2- -3-)-2,5,8,11- -1,4,7,10- -1,4,7
 - 가 가

15b 803 mg(1.0 mmol) 5 mL 3
 5 PVP 가 , 300 mL , (Reillex;) 42
 (446 mg; 0.84 mmol) 4 mL 가 , 152 mg(0.42 mmol) 가 , 3
 90 가 . () , 90%
 . , 1 , ,

130 (24)
 : 469 mg(65%)

: 5%

():

계산치: C 40.28 H 5.58 N 10.21 Gd 22.93

실측치: C 40.06 H 5.75 N 10.43 Gd 22.40

16

10-[8-(N-)-1- -2,5- -3,6-]-1,4,7- , ' , '- ()-1,4,7-
 ()-1,4,7,10- Gd

2 Gd 2.27 g(3 mmol) DMF 15 mL , N-
 380 mg(3.3 mmol) 681 mg(3.3 mmol) ,
 1 , DMF 10 mL N-(2-) (

[Arano et al., J. Med. Chem., 1996, 39, 3458]) 839 mg(3.3 mmol) N,N- 0.7 mL(4 mmol) 가 (: / : 1/1)

: 997 mg(35%)

(-): 7.5 %

():

계산치: C 46.51 H 6.20 Gd 17.91 N 11.17

실측치: C 46.28 H 6.44 Gd 17.31 N 11.26

17

10-[8-(N-)-1- -2,5- -3,6-]-1,4,7- , ' ' - -()-1,4,7- ()-1,4,7,10- Gd

3 Gd 2.63 g(3 mmol) DMF 15 mL , N- 380 mg(3.3 mmol) 681 mg(3.3 mmol) ,

1 , DMF 10 mL N-(2-) ([Arano et al., J. Med. Chem., 1996, 39, 3458]) 839 mg(3.3 mmol) N,N- 0.7 mL(4 mmol) 가 (: / : 1/1)

1) (: / : 1/1)

: 1.24 g(39%)

(-): 6.0%

():

계산치: C 51.74 H 6.66 Gd 15.75 N 9.82

실측치: C 51.77 H 6.41 Gd 15.25 N 10.02

18

a) (3- -2- - -1-)

L , 0 45 67.7 g(0.2 mol) 61.2 mL(0.44 mol) 200 mL 2,4- (200 m [Grama in et al. Synth. Commun. (1997), (27), 1827]] 52.9 g(0.2 mol) 가 , 18 가 (15), 30 32% 400 mL 2 g 200 mL 3) (

: 29.3 g(47%)

:

계산치: C 50.02 H 4.52 N 4.49

실측치: C 50.34 H 4.44 N 4.41

b) 10-[1-()-2- -3-]-1,4,7- , ' , '- -1,4,7- -()-1,4,7,10-

(3- -2- - -1-) 20.7 g(66.3 mmol) 1,4,7,10-
 28.7 g(165.8 mmol) 가 , 300 mL , 250 mL
 가 , , 200 mL 2 , .
 , (: / / 25%
 = 10/5/1) 200 mL 1-[1-(/ 25%
)-2- - -3-]-1,4,7,10- (20.9 g; 51.8 mmol; 78%) N-
 60 mL(0.35 mol) 400 mL 2-()
 ([Kitazaki et al., Chem. Pharm. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
 , 500 mL 3 , / : 20/1)
 : 32.7 g(71%)

계산치 : C 68.82 H 7.13 N 7.87

실측치 : C 68.54 H 7.28 N 8.01

c) 10-[1-()-2- - -3-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-

18b 26.7 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 ,
 : 15.8 g()

계산치 : C 52.16 H 7.42 N 13.22

실측치 : C 52.32 H 7.35 N 13.11

d) 10-[1-()-2- - -3-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10- Gd

18c 10.6 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)
 : 9.7 g(67%)
 (-): 8.3%
 ():

계산치 : C 40.40 H 5.31 Gd 23.00 N 10.24

실측치 : C 39.99 H 5.55 Gd 22.93 N 10.45

a) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 18b 1-[1-()-2- -3-]-1,4,7,10- 20.2 g(50 mmol) N- 60 mL(0.35 mol) [Walker et al., Tetrahedron (1997), 53(43), 14591]] 68.1 g(0.2 mol) 가 , 6 ()-1,4,7,10- 2-()- ()-1,4,7,10- 400 mL 500 mL 3 (: / : 20/1) : 34.1 g(70%)

계산치 : C 70.27 H 7.76 N 7.19

실측치 : C 70.45 H 7.61 N 7.11

b) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

19a 29.2 g(30 mmol) 400 mL , 40 mL , (10% Pd/C) 3 g 가 . 50 8 : 18.4 g()

계산치 : C 56.75 H 8.38 N 11.41

실측치 : C 56.89 H 8.31 N 11.37

c) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

19b 12.3 g(20 mmol) 200 mL 가 가 3.6 g(10 mmol) 가 , 80 mL , 5 mL 가 , pH 7.4 , (: / / : 20/1) , IR-120(R) (H +) : 11.9 g(75%)

(-): 8.2%

():

계산치 : C 45.36 H 6.30 Gd 20.48 N 9.12

실측치 : C 45.89 H 6.22 Gd 20.23 N 9.01

19b 12.3 g(20 mmol), 가 3.73 g(10 mmol) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Dy : 11.4 g(71%)

(-): 8.0%

(): :

계산치 : C 45.05 H 6.26 Dy 21.02 N 9.06

실측치 : C 45.35 H 6.22 Dy 20.88 N 9.04

20

a) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 18b 1-[1-()-2- -3-]-1,4,7,10- 20.2 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()-2- ([Qabar et al., T
 etrahedron Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 가 , 6
 500 mL 3 ,
 (: / : 20/1)

: 37.2 g(68%)

:

계산치 : C 72.43 H 8.01 N 6.40

실측치 : C 72.55 H 7.98 N 6.35

b) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

20a 32.8 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 50 8 ,

: 22.0 g()

:

계산치 : C 62.19 H 8.65 N 9.54

실측치 : C 62.44 H 8.56 N 9.46

c) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

20b 14.6 g(20 mmol) 150 mL 150 mL , 5 mL
 가 가 가 3.6 g(10 mmol) 가 8 가
 pH 7.4 , (: / / : 20/
 20/1) , 가 ,

: 12.1 g(65%)

(-): 7.0%

():

계산치 : C 51.39 H 6.81 Gd 17.70 N 7.89

실측치 : C 51.64 H 6.77 Gd 17.44 N 7.77

21

a) (3- -2- - -1-)

4- 45.5 g(0.2 mol) 30.6 mL(0.22 mol) 200 mL
 , 0 45 200 mL 2,4- ([Gramain
 et al. Synth. Commun. (1997), (27), 1827)] 52.9 g(0.2 mol) 가 , 18
 . 0 32% 400 mL 2 g 가
 (15), 30 . , 200 mL 3
) . , , ()
 : 38.2 g(51%)

계산치 : C 57.77 H 4.31 N 3.74

실측치 : C 57.99 H 4.27 N 3.66

b) 10-[1-(4-)-2- - -3-]-1,4,7- , ' , '- -1,4,7- -(
)-1,4,7,10-

(3- -2- - -1-) 26.9 g(71.9 mmol) 1,4,7,10-
 31.2 g(180 mmol) 가 , 300 mL . 250 mL
 가 , , 200 mL 2 . ,
 (: / / 25%)
 = 10/5/1) 200 mL 1-[1-(4-)
 -2- - -3-]-1,4,7,10- (26.1 g; 56.1 mmol; 78%) N-
 60 mL(0.35 mol) 400 mL 2-()
 ([Kitazaki et al., Chem. Pharm. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
 , 500 mL 3 . ,
 (: / : 20/1)
 : 36.3 g(68%)

계산치 : C 70.64 H 6.88 N 7.36

실측치 : C 70.89 H 6.81 N 7.29

c) 10-[1-(4-)-2- - -3-]-1,4,7- , ' , '- -1,4,7- ()-1,
 4,7,10-

21b 28.6 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 . ,
 : 17.7 g()

:

계산치 : C 56.84 H 6.98 N 11.84

실측치 : C 57.04 H 6.91 N 11.79

d) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- -1,4,7- ()-1, 4,7,10- Gd

21c 11.8 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)

가 . . .
 : 11.1 g(71%)
 (-): 7.5%
 ():

계산치 : C 45.09 H 5.13 Gd 21.08 N 9.39

실측치 : C 45.45 H 5.11 Gd 20.78 N 9.40

22

a) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 21b 1-[1-(4-)-2- -3-]-1,4,7,10- 23.3 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()- ([Walker et al., Tetra
 hedron (1997), 53(43), 14591]) 68.1 g(0.2 mol) 가 , 6 ,
 500 mL 3 , ,
 (: / : 20/1)

: 35.3 g(68%)
 :

계산치 : C 71.86 H 7.49 N 6.76

실측치 : C 71.99 H 7.46 N 6.71

b) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

22a 31.1 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 50 8 , ,

: 20.2 g()
 :

계산치 : C 60.43 H 7.90 N 10.36

실측치 : C 60.59 H 7.82 N 10.31

c) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

22b 13.5 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)

가

: 12.4 g(72%)

(-): 7.8%

():

계산치 : C 49.20 H 6.07 Gd 18.94 N 8.44

실측치 : C 49.51 H 6.04 Gd 18.71 N 8.45

22b 13.5 g(20 mmol), 가 3.73 g(10 mmol)
 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Dy

: 13.0 g(75%)

(-): 7.5%

():

계산치 : C 48.89 H 6.03 Dy 19.45 N 8.38

실측치 : C 49.11 H 6.04 Dy 19.22 N 8.36

23

a) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 21b 1-[1-(4-)-2- -3-]-1,4,7,10- 23.3 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()-2- ([Qabar et al
 ., Tetrahedron Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 76.1 g(0.2 mol) 가 , 6
 , 500 mL 3 , / : 20/1)

: 41.1 g(71%)

:

계산치 : C 73.74 H 7.76 N 6.06

실측치 : C 73.91 H 7.69 N 6.01

b) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

23a 34.7 g(30 mmol) 400 mL , 40 mL ,
(10% Pd/C) 3 g 가 . 50 8 . ,

: 23.8 g()

:

계산치 : C 64.88 H 8.23 N 8.80

실측치 : C 65.04 H 8.19 N 8.70

c) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-
Gd

23b 15.9 g(20 mmol) 150 mL 150 mL , 5 mL
가 가 3.6 g(10 mmol) 가 , 8 가
pH 7.4 , (: / / : 20/
20/1) , 가 , .

: 12.9 g(65%)

(-): 7.0%

():

계산치 : C 54.35 H 6.58 Gd 16.55 N 7.37

실측치 : C 54.66 H 6.57 Gd 16.32 N 7.32

24

a) (3- -2- - -1-)

67.7 g(0.2 mol) 61.2 mL(0.44 mol) 200
mL , 0 45 200 mL 2,5- ([Okaw
ara et al. Chem. Pharm. Bull. (1982), (30), 1225]) 55.7 g(0.2 mol) 가 , 18
가 (15), 30 32% 400 mL 2 g
200 mL 3
) ()

: 33.2 g(51%)

:

계산치 : C 51.55 H 4.94 N 4.29

실측치 : C 51.86 H 4.91 N 4.18

b) 10-[1-()-2- -3-]-1,4,7- , ' , '- -1,4,7- -()-1,4,7,10-

(3- -2- - -1-) 18.9 g(58 mmol) 1,4,7,10-
 30.3 g(175 mmol) 가 , 300 mL , 250 mL
 가 , , 200 mL 2 , ,
 = 10/5/1) (: / / 25% ,
 - - -3-]-1,4,7,10- 200 mL 1-[1-()-2
 60 mL(0.35 mol) 400 mL 2-((20.3 g; 48.6 mmol; 84%) N- ()
 [Kitazaki et al., Chem. Pharm. Bull. (1999), 47(3), 360] 62.45 g(0.2 mol) 가 , 6 ()
 , , 500 mL 3 , ,
 , (: / : 20/1)
 : 32.5 g(74%)

계산치 : C 69.08 H 7.25 N 7.75

실측치 : C 69.34 H 7.19 N 7.66

c) 10-[1-()-2- - -3-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7
 ,10-
 24b 27.1 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 ,
 : 16.3 g()

계산치 : C 53.03 H 7.60 N 12.88

실측치 : C 53.34 H 7.54 N 12.79

d) 10-[1-()-2- - -3-]-1,4,7- , ' , '- -1,4,7- ()-1,4,7
 ,10- Gd
 24c 10.9 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 가 , IR-120(R) (H +)
 : 9.6 g(65%)
 (-): 7.2%
 ():

계산치 : C 41.31 H 5.49 Gd 22.53 N 10.04

실측치 : C 41.67 H 5.48 Gd 22.21 N 9.97

25

a) 10-[1-()-2- - -3-]-1,4,7- , ' , '- ()-1,4,7- ()
)-1,4,7,10-

200 mL 24b 1-[1-()-2- -
 -3-]-1,4,7,10- 20.9 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()- ([Walker et al., Tetrahed
 ron (1997), 53(43), 14591]) 68.1 g(0.2 mol) 가 , 6 ,
 500 mL 3 , ,
 (: / : 20/1)

: 36.2 g(73%)

:

계산치 : C 70.49 H 7.85 N 7.09

실측치 : C 70.61 H 7.83 N 7.01

b) 10-[1-()-2- - -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10-

25a 29.6 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 . 50 8 , ,

: 18.8 g()

:

계산치 : C 57.40 H 8.51 N 11.16

실측치 : C 57.64 H 8.45 N 11.09

c) 10-[1-()-2- - -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10-
 Gd

25b 12.6 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)

: 11.7 g(71%)

(-): 8.1%

(): :

계산치 : C 46.08 H 6.44 Gd 20.11 N 8.96

실측치 : C 46.34 H 6.41 Gd 19.99 N 8.91

25b 12.6 g(20 mmol), 가 3.73 g(10 mmol)
 10-[1-()-2- - -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10-
 Dy .

: 10.8 g(66%)

(-): 7.6%

():

계산치 : C 45.77 H 6.40 Dy 20.64 N 8.90

실측치 : C 46.01 H 6.46 Dy 20.34 N 8.91

26

a) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 24b 1-[1-()-2- -3-]-1,4,7,10- 20.9 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()-2- ([Qabar et al., T
 etrahedron Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 가 , 6
 500 mL 3 ,
 (: / : 20/1)

: 39.8 g(72%)

:

계산치 : C 72.60 H 8.09 N 6.32

실측치 : C 72.89 H 7.98 N 6.27

b) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

26a 33.3 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 50 8 ,

: 22.4 g()

:

계산치 : C 62.63 H 8.76 N 9.36

실측치 : C 62.77 H 8.71 N 9.29

c) 10-[1-()-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- Gd

26b 14.9 g(20 mmol) 150 mL 150 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 8 가
 pH 7.4 , (: / / : 20/
 20/1) , 가 ,

: 12.9 g(68%)

(-): 7.6%

():

계산치 : C 51.92 H 6.93 Gd 17.43 N 7.76

실측치 : C 52.09 H 6.88 Gd 17.21 N 7.77

27

a) (3- -2- - -1-)

4- 45.5 g(0.2 mol) 30.6 mL(0.22 mol) 200 mL 2,5- (18 [Okawara
et al. Chem. Pharm. Bull. (1982), (30), 1225]) 55.3 g(0.2 mol) 가 , 2 g
가 (15), 30 32% 400 mL 200 mL 3
)
: 38.8 g(50%)

계산치 : C 58.78 H 4.67 N 3.61

실측치 : C 59.01 H 4.50 N 3.59

b) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- -1,4,7- -(
)-1,4,7,10-

(3- -2- - -1-) 26.6 g(68.5 mmol) 1,4,7,10-
31.2 g(180 mmol) 가 , 300 mL , 250 mL
가 , 200 mL 2
(: / / 25%
= 10/5/1) 200 mL 1-[1-(4-)
-2- - -3-]-1,4,7,10- (27.6 g; 57.5 mmol; 84%) N-
60 mL(0.35 mol) 400 mL 2-()
([Kitazaki et al., Chem. Pharm. Bull. (1999), 47(3), 360]) 62.45 g(0.2 mol) 가 , 6
500 mL 3
(: / : 20/1)
: 39.4 g(71%)

계산치 : C 70.86 H 6.99 N 7.25

실측치 : C 71.11 H 6.81 N 7.17

c) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- -1,4,7- ()-1,
4,7,10-

27b 29.0 g(30 mmol) 400 mL , 40 mL ,
(10% Pd/C) 3 g 가 50 8
: 18.1 g()

계산치 : C 57.51 H 7.16 N 11.56

실측치 : C 57.72 H 7.11 N 11.50

d) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- -1,4,7- ()-1, 4,7,10- Gd

가 27c 12.1 g(20 mmol) 200 mL 가 80 mL , 5 mL
 가 3.6 g(10 mmol) 가 3 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)
 : 11.4 g(72%)

(-): 7.1%

():

계산치 : C 45.84 H 5.31 Gd 20.69 N 9.22

실측치 : C 45.99 H 5.26 Gd 20.55 N 9.21

28

a) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

200 mL 27b 1-[1-(4-)-2- -3-]-1,4,7,10- 24.0 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()-2- ([Walker et al., Te
 tragedron (1997), 53(43), 14591]) 68.1 g(0.2 mol) 가 , 6 ,
 500 mL 3 , ,
 (: / : 20/1)
 : 37.8 g(72%)

:

계산치 : C 72.04 H 7.58 N 6.67

실측치 : C 72.32 H 7.46 N 6.59

b) 10-[1-(4-)-2- -3-]-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-

28a 31.5 g(30 mmol) 400 mL , 40 mL ,
 (10% Pd/C) 3 g 가 50 8 , ,
 : 20.7 g()

:

계산치 : C 60.94 H 8.04 N 10.15

실측치 : C 60.87 H 8.05 N 10.11

c) 10-[1-(4-)-2- -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10- Gd

28b 13.8 g(20 mmol) 200 mL 80 mL , 5 mL
 가 가 3.6 g(10 mmol) 가 , 3 가 가
 , pH 7.4 , (: / / : 20/20/1)
 , IR-120(R) (H +)
 가 .
 : 12.0 g(68%)
 (-): 7.5%
 ():

계산치 : C 49.80 H 6.21 Gd 18.63 N 8.30
 실측치 : C 49.99 H 6.17 Gd 18.51 N 8.21

28b 13.8 g(20 mmol), 가 3.73 g(10 mmol)
 10-[1-(4-)-2- -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10- Dy .
 : 12.4 g(70%)
 (-): 7.5%
 ():

계산치 : C 49.50 H 6.17 Dy 19.13 N 8.25
 실측치 : C 49.77 H 6.18 Dy 18.89 N 8.27

29

a) 10-[1-(4-)-2- -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10-

200 mL 27b 1-[1-(4-)-2- -3-]-1,4,7,10- N- 60 mL(0.35 mol)
 -3-]-1,4,7,10- 24.0 g(50 mmol) N- 60 mL(0.35 mol)
 400 mL 2-()-2- ([Qabar et al
 ,, Tetrahedron Letters (1998), 39(33), 5895]) 76.1 g(0.2 mol) 가 , 6 ,
 500 mL 3 , / : 20/1)
 (: / : 20/1)
 : 40.9 g(70%)
 :

계산치 : C 73.88 H 7.84 N 5.98
 실측치 : C 74.12 H 7.69 N 5.89

b) 10-[1-(4-)-2- -3-]-1,4,7- , ', '- ()-1,4,7- ()-1,4,7,10-

29a 35.1 g(30 mmol) 400 mL , 40 mL ,

(10% Pd/C) 3 g 가 . 50 8 ,

: 24.3 g()

:

계산치: C 65.24 H 8.34 N 8.65

실측치: C 65.48 H 8.22 N 8.60

c) 10-[1-(4-)-2- -3-]-1,4,7- , ' '- ()-1,4,7- ()

29b 16.2 g(20 mmol) 150 mL 150 mL 5 mL
 가 가 가 3.6 g(10 mmol) 가 , 8 가 가
 , pH 7.4 , (: / / : 20/
 20/1) , 가 ,

: 13.6 g(68%)

(-): 7.5%

():

계산치: C 54.81 H 6.69 Gd 16.31 N 7.26

실측치: C 55.11 H 6.57 Gd 16.09 N 7.24

30-90

30-90 가 1a 1d , 'AAV'
 I-IV , 'ACTH' , 'RP-18' ,
 ICP()

(AAV) I: -

Gd 3 mmol DMF 15 mL , N- 380 mg(3.3 mmol)
 681 mg , ,
 30 (pH 7.4) 150 mL 1 (BSA) 16.75 g(0.25 mmol) 가 ,
 2 (batch) (AMICON)(R) YM30(- 30,000 Da)
 , (Sephadex)(R) G50-

(AAV) II: -

DMF 1 mL Gd 0.0438 mmol (BSA) 0.84 g(0.0125 mmol) 가 ,
 (pH 7.4) 15 mL , 1 (R) , (R)
 YM30(- 30,000 Da) , (R) G50-

(AAV) III:

Gd 3 mmol DMF 15 mL , N- 380 mg(3.3 mmol)
 681 mg , , 1

DMF 15-150 mL

2.5 mmol

가

(AAV) IV:

-SH

DMF 15 mL

Gd

3 mmol

DMF 15-150 mL

SH

2.5 mmol

가

1

[1a]

실시에	Gd-착물 유번호 (실시에 번호)	분주개이션	(기원)	AAV	생체분자량 좌분의 수 (ICP)	비고	수용 (%)
30	1	BSA	시그마	I	3.7	-	정량적임
31	2	BSA	시그마	I	6.1	-	정량적임
32	3	BSA	시그마	I	2.9	-	정량적임
33	4	BSA	시그마	I	3.5	-	정량적임
34	5	BSA	시그마	I	4.2	-	정량적임
35	6	BSA	시그마	I	6.5	-	정량적임
36	7	BSA	시그마	I	5.0	-	정량적임
37	16	BSA	시그마	II	0.71	-	정량적임
38	17	BSA	시그마	II	0.55	-	정량적임
39	8	BSA	시그마	I	3.0	-	정량적임
40	9	BSA	시그마	I	4.7	-	정량적임
41	10	BSA	시그마	I	5.1	-	정량적임
42	11	BSA	시그마	I	2.7	-	정량적임
43	12	BSA	시그마	I	4.0	-	정량적임
44	13	BSA	시그마	I	3.3	-	정량적임
45	14	BSA	시그마	I	5.8	-	정량적임
46	15	BSA	시그마	I	4.6	-	정량적임

[1b]

47	18	BSA	시그마	I	3.7	-	정량적임
48	19	BSA	시그마	I	4.1	-	정량적임
49	20	BSA	시그마	I	2.8	-	정량적임
50	21	BSA	시그마	I	3.5	-	정량적임
51	22	BSA	시그마	I	3.3	-	정량적임
52	23	BSA	시그마	I	2.9	-	정량적임
53	24	BSA	시그마	I	4.0	-	정량적임
54	25	BSA	시그마	I	3.5	-	정량적임
55	26	BSA	시그마	I	3.0	-	정량적임
56	27	BSA	시그마	I	3.9	-	정량적임
57	28	BSA	시그마	I	3.1	-	정량적임
58	29	BSA	시그마	I	3.4	-	정량적임
59	11	(D-Lys16)-ACTH (1-24 인자)	파켈	I	2.0	-	정량적임
60	12	ACTH (1-17)	파켈	I	1.7	-	정량적임
61	14	H-β-Ala-Phe	파켈	III	1.0	RP-18 상에서 정제됨	95
62	8	항염증 펩티드 2	파켈	I	1.0	-	정량적임
63	9	L-카르노신	파켈	III	1.0	RP-18 상에서 정제됨	97
64	16	호모글루타민산	파켈	IV	1.0	RP-18 상에서 정제됨	94

[1c]

65	17	구아닐 -Cys-OH	바깥	IV	1.0	RP-18 상에서 정제됨	93
66	8	H-DL-d-히드록시 -DL-Lys-OH	바깥	III	1.0	RP-18 상에서 정제됨	85
67	7	H-β-Ala-Lys-OH	바깥	III	1.0	RP-18 상에서 정제됨	87
68	16	H-Arg-Gly-Asp-Cys-OH	바깥	III	1.0	RP-18 상에서 정제됨	91
69	9	H-Asp-Leu-Trp-Gln-Lys-OH	바깥	III	1.0	RP-18 상에서 정제됨	94
70	12	H-Ala-His-Lys-OH	바깥	III	2.0	RP-18 상에서 정제됨	91
71	13	Endothelin-2 (인간)	바깥	I	0.87	-	정량적인
72	14	인간 혈청 알부민	바깥	I	5.1	-	정량적인
73	7	인간 혈청 알부민	바깥	I	3.1	-	정량적인
74	8	인간 혈청 알부민	바깥	I	2.3	-	정량적인
75	17	티오구아노신	안드리아	IV	1.0	RP-18 상에서 정제됨	96
76	5	6-아미노노페니실린	안드리아	III	1.0	RP-18 상에서 정제됨	92
77	11	4-아미노노페노티올론	안드리아	III	1.0	RP-18 상에서 정제됨	65
78	4	2-아미노-푸린티올	안드리아	IV	1.0	RP-18 상에서 정제됨	94

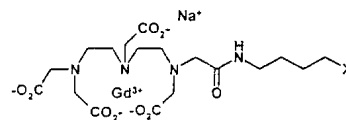
[1d]

79	12	5-아자시타딘	알드리히	III	1.0	RP-18 상에서 정제됨	96
80	17	4,5-다이메틸-2,6-디아카토펜리미딘	알드리히	IV	1.0	RP-18 상에서 정제됨	71
81	13	미토마이신 C	알드리히	III	1.0	RP-18 상에서 정제됨	81
82	12	유람산	알드리히	III	1.0	RP-18 상에서 정제됨	92
83	6	푸로마이신	시그마	III	1.0	RP-18 상에서 정제됨	90
84	11	독소루비신	시그마	III	1.0	RP-18 상에서 정제됨	89
85	12	스펙티노마이신	시그마	III	1.0	RP-18 상에서 정제됨	88
86	4	스트렙토마이신	시그마	III	1.0	RP-18 상에서 정제됨	62
87	14	네오마이신 B	시그마	III	1.0	RP-18 상에서 정제됨	52
88	8	니스타틴	시그마	III	1.0	RP-18 상에서 정제됨	72
89	3	히그로마이신	시그마	III	1.0	RP-18 상에서 정제됨	71
90	2	암페실린	시그마	III	1.0	RP-18 상에서 정제됨	42

91

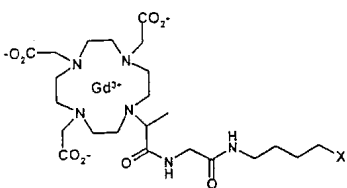
30-38

가



Gd-DTPA(1)

(BSA)



Gd-GlyMeDOTA(2)

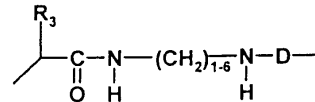
, +37

20 MHz

2

, 가

b) B가 NR^2U^6- (R^4 , R^2 , A , $-\text{CH}(\text{R}^4)-\text{CO}-$)
 $\text{C}_{1-30}-$ ()
 U^6
 $\text{C}_{1-20}-$



c) B가 (R_3 , R , $\text{C}_{1-4}-$, A , D , X)
 $\text{C}_{1-4}-$

2.

$\text{H}_3)_2-\text{COOH}$, $\text{C}_{1-10}-$, $-\text{CH}_2-\text{COOH}$, $-\text{C}(\text{C})$
 $\text{C}_{1-4}-$, $-\text{SO}_3\text{H}$, $-\text{PO}_3\text{H}$

3.

$\text{C}_{5-10}-$, B가, R , $-\text{CH}_2-\text{COOH}$, $-\text{C}(\text{CH}_3)_2-\text{COOH}$, tert-
 $\text{C}_{1-4}-$, $-\text{SO}_3\text{H}$, $-\text{PO}_3\text{H}_2$, $-\text{CH}_2-\text{COOH}$, $-\text{C}(\text{CH}_3)_2-\text{COOH}$, $-\text{C}(\text{C})$

4.

3, B가, R

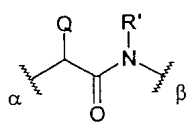
5.

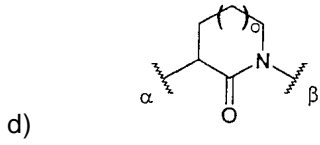
1, 4, A가, A'-U, A', U X

A'

a)

b) $-\text{CH}(\text{CO}_2\text{H})-$,

c)  (Q , R' , $\text{C}_{1-15}-$, R')
 R , $\text{C}_{1-15}-$

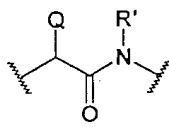


($\text{-SO}_3\text{H}$, $\text{-PO}_3\text{H}_2$)



U가 1 3, 1 3 ($\text{-NR}'$) (R') R
 C_{1-30}
 A' U, X가 3 A'가

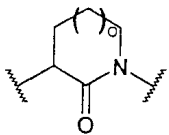
6.



5, A')H-CO-NH-

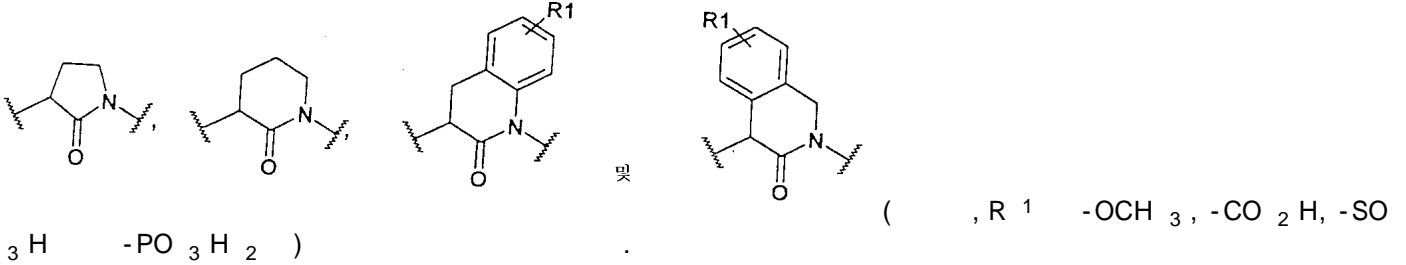
가 -C(CH₃)H-CO-NH-, -C()H-CO-NH- -C(p-

7.



5, A'

가

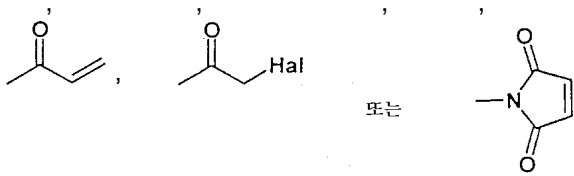


8.

5 7, U가 -CH₂-, -(CH₂)₅-, -(CH₂)₁₀-, -O-CH₂-, -O-(CH₂)₃-, -O-(CH₂)₁₀-, -CH₂-, -O-CH₂-, -CH₂-, -CH₂-CO-NH-CH₂-CH₂-

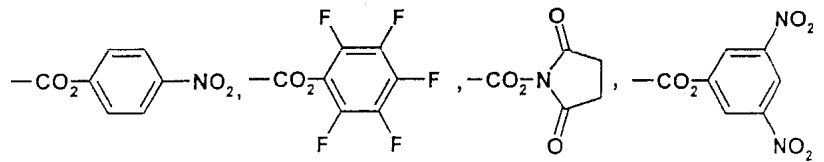
9.

1 8, X가



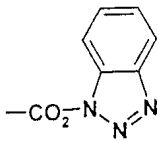
(Hal)

10.



9

가



11.

10-(4- -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10
 - , 10-(4- -1- -2- -3-)-1,4,7- , ' , '- ()-1,
 4,7- ()-1,4,7,10- , 10-(4- -1- -2- -3-)-1,
 4,7- , ' , '- ()-1,4,7- ()-1,4,7,10- , 10-(4-(t-
 -1- -2- -3-)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10-
 , 10-[-(4-())]-1,4,7- , ' , '-
 -1,4,7- ()-1,4,7,10- , 10-[-(4-())]-
]-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10- , 10
 -[-(4-())]-1,4,7- , ' , '- -1,4,7- ()
)-1,4,7,10- , 10-(p-)-1,4,7- , ' , '- -1,4,7- ()
)-1,4,7,10- , 10-(p-)-1,4,7- , ' , '- ()-1,4,7-
 ()-1,4,7,10- , 10-(p-)-1,4,7- , ' , '- ()-
 1,4,7- ()-1,4,7,10- , 10-(p-)-1,4,7- , ' , '- -
 1,4,7- ()-1,4,7,10- , 10-(4-(t- -1- -2- -3-
)-1,4,7- , ' , '- -1,4,7- ()-1,4,7,10- , 10-(4-
 -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()-1,4,7,10-
 , 10-(4- -2- -3-)-1,4,7- , ' , '- ()-1,4,7- ()
)-1,4,7,10- , 10-(4- -1- -2- -3-)-2,5,8,11- -
 1,4,7,10- -1,4,7- - -tert- , 10-[8-(N-)-1-
 -2,5- -3,6-]-1,4,7- , ' , '- -()-1,4,7- ()-1,4,7,10-
)-1,4,7- 10-[8-(N-)-1- -2,5- -3,6-]-1,4,7- , ' , '- ()

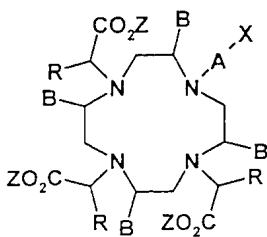
12.

1 11 , 2 Z가 21 29, 31, 32, 37 39, 42
 44, 46, 47, 49, 58 71, 75, 77, 82 83 가

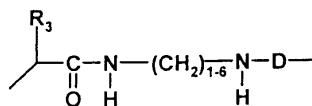
13.

|

< |>



Z, B, R, A X 1 , B R , B가

R C₁₋₄-C₁₋₄-C₁₋₄-

, A

, D

, D X

).

(, R₃

,