

(72)

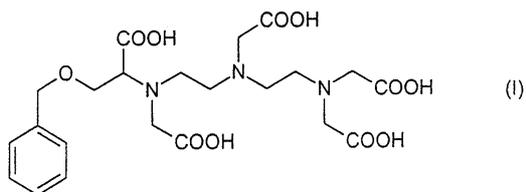
- 20134 . 50
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(74)

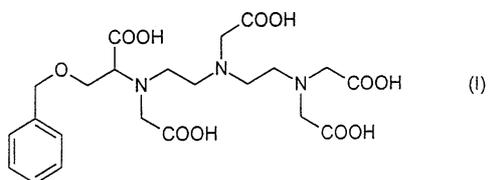
:

(54) 4 - - 5,8,11 - () - 1 - - 2 - - 5,8,11 - - 13 -

(I) - 13 - (BOPTA) 4 - - 5,8,11 - () - 1 - - 2 - - 5,8,11 -



(I) BOPTA 4 - - 5,8,11 - () - 1 - - 2 - - 5,8,11 - - 13 -



X - , (M.R.I)

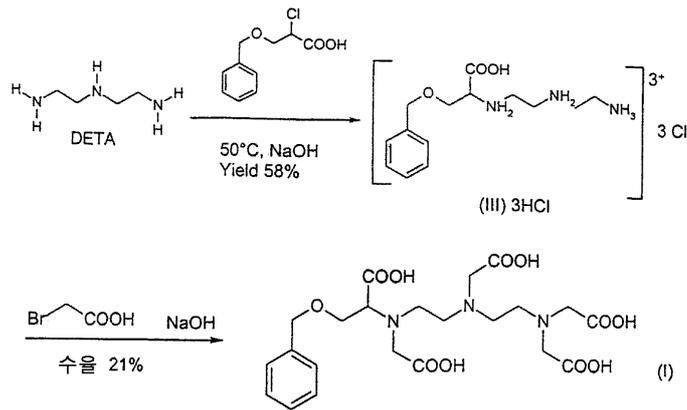
[Stark, D. D., Bradley, W.G., Jr., Eds. " Magnetic Resonance Imaging" The C.V. Mosby Company, St. Louis, Missouri (USA), 1988] , 2가 3가 /

M.R.I. (Gd - DTPA, N - , MAGNEVIST^(R) , Schering; GD - DOTA, 1,4,7,10 - - 1,4,7,10 - N - , DOTAREM^(R) , Guerbet)

, M.R.I. X

M.R.I. 가 가 가 가
Gd - BOPTA - Dimeg가
[Vittadini G., et al., Invest. Radiol., (1990), 25(Suppl. 1), S59 - S60] .

(I) EP230893 가 [Uggeri F., et al., Inorg. Chem., 1995, 34(3), 633 - 42]



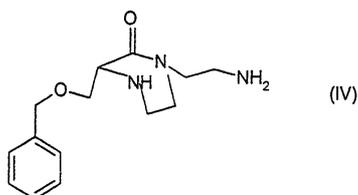
50 (DETA) (13)
1가 2- -3- () N
- [2 - [(2 -)]] - O - ()
2 , pH 10 ()
I)

:

- [Chem. Ber., Grassman et al., 1958, 91, 538]

2- -3 - () 가 (I)
, (HPLC : 90 - 92%) (I)

6 ()



A () (I) 2 , DET
(40) 10% 2
, ; 110mol
70% ()

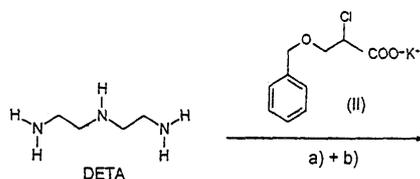
deral Register, Vol. 61, n ° 3, Jan. 4., 1996] [, Fe
ations test procedures and acceptance criteria for new drug substances and new drug procedures, Chem. S
ubst., July 16, 1996] :
(I) 99% 1% 1 0.1%

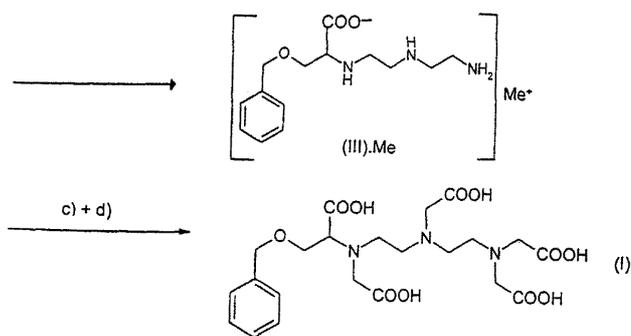
M.R.I.

(I)

(I)

1

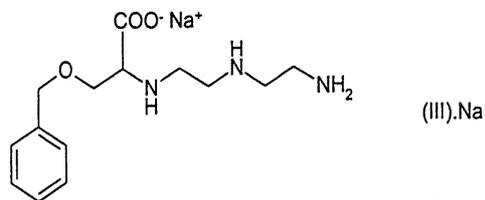




- a) 50 - 70 () 2 - 12 pH (Me) 가
 DETA () N - [2 - [(2 -
)] - O - () ;
 b) a) OH⁻ , NaCl/HCl 가
 () 가 c) 20 - 50% (w/w)가 ;
 c) pH 11 - 12 b) 가 (I)
 ;
 d) c) (I) (I)

-2- -3- [()] (HPLC 1)

- () ;



- pH

()

, 0.8 - 3%

, () , pH

pH

b) c)

a) () DETA (1:5 / 1:8) 80%

DETA 1g 0.1 0.3g

가 가 DETA가 가 50

가 50 가 가 60

, pH 가

pH가 12 () 2 , OH⁻ 가

30 %

() 1 0.9 OH⁻ 가

25 b)

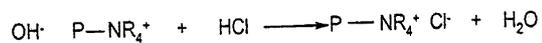
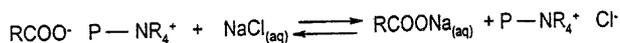
b) (percolation) 가 OH⁻

, DETA,

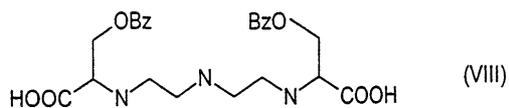
(,) 3 % ()

(0.5N) (0.3N) ()

OH⁻



pH 11.5
()



8 80% 가
(Bayer) OC 1062 (Diaion) HP 21

()

pH 12
40% (w/w)

, NaOH

pH 12.5 50 20 - 50%,

()

25

c) , b)

()

55 11 - 12 pH
() 1 6.7

4

80% w/w
H 가
pH

4

()

가 ; , 30% NaO
(Br⁻)

가

, pH
가

가

가

가

pH 11.5
pH

() 4

()

. pH가 OH⁻

55

5

. 34% (w/w) 가

pH 5

()

; ,

()

, 가 ;

, , ,

()

d) 가

:

d.1. b) () 가 ;

d.2. ;

d.3. () 가 .

() 가

d.1. , ()

Haas) XAD 1600 P 800 , 60% 가 (Rohm & (Diaion Relite SP 800) S
1600T, (Bayer) OC 1064,

d.2. , ,

40 - 60 ()

, 45 pH 2.0 ; , d.3., ()

가 , () pH
가 ,

pH 가 , pH

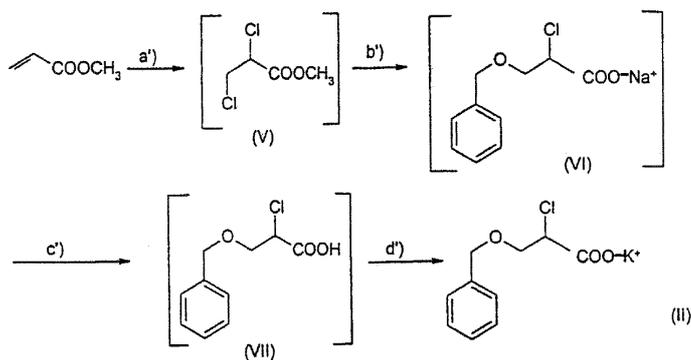
, pH

() 가 1:1.5

(27%)
 () 41 가 , 18
 , 5 25 가 24 17
 10% (w/w)

d.3. , 3

, 2 2- -3- ()



a') () 2,3-

;

b') 10 a')

가 ,

() 2- -3- () ;

c') b') () 2- -3- ()

;

d') c') , 2 가
 () 2- - ()

a') 3
 , DMF : 0.1

45

가

가

:

trope) / (30% NaOH , 20mbar 110 (heterogeneous azeo : Karl Fischer 0.4%(w/w)).

a') 120 - 140% 가 , 5 , 10 , 15 - 3 5 - 10 80 - 100% 3

0 , 15

0% NaOH 가 .

가 . ,

가 . 2 - -3 -

c') , 20 , 34% w/w HCl pH 2.5 ,

d') , 2 - -3 - 50% KOH 가 pH 7.2

30

() 20mbar 55 가 .

4 - 10% w/w

50 , 2 - 가 . 60 20mbar

60 - 70% .

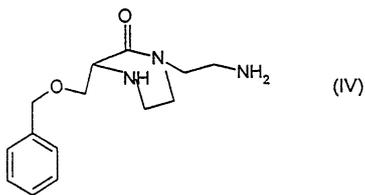
1

EP230893

[Uggeri F., et al., Inorg. Chem., 1995, 34(3), 633 - 42]

1 - () - 2 -

- 3 - [()] -



42.9g 2 - 3 - [()] (0.2mol) 50 400mL 268.2g DETA (2.
 58mol) , (Amberlite) (R) IRA 400 (1880mL) ,
 DETA 37% HC
 I (465mL) , 37% HCl (365mL) pH 2 . 8
 00g DETA
 (173.5g, 0.81mol) . 450g
 800mL , 0 - 5 2 DET
 A (313.4g, 1.47mol) .
 DETA
 80mL , XAD 2 700mL
 70mL TLC (R_f = "0.38").
 7.1g (0.021mol) .

: 10.5% m.p.: 163

HPLC : 95.8% (%)

C H Cl N

(%) 50.0 6.89 21.08 12.50

(%) 49.64 6.73 21.24 12.72

TLC: : 60F 254 (Merck)

: CHCl₃ / AcOH / H₂O = "5/5/1"

: 1N NaOH 1% KMnO₄, R_f = "0.38"

¹H - NMR, ¹³C - NMR, IR MS

2

1

()

149kg (1430mol) DETA , 23.7kg (110mol) 2 - 3 - () 250L
 L, OH⁻) , (Amberlite) (R) IRA 400 (1000m
 (2200L)가 , 1N HCl , 1mol/L

50

15

24kg

(71.5mol).

: 65%

-

1

3

: 66% ()

K.F.: 3.0% (w/w)

HPLC : 100.0% (ext. st..)HPLC : 0.15% (%)

: (LiChrospher) 100 RP8 (5mm, 25cm x 4mm)

: A) 1.2mL/L 85% H₃PO₄ (w/w)

B)

:

t ()%B(v/v)

040

1560

2560

2640

3640

: 1mL/

: 30

: UV, 215nm

- [Aime S., Inorg. Chem., 1992, 31, 1100]

4

DMF 1,2 -

가

34.83g

12.5g
5g

가

. 가 8

, 6g

가

40
. 40

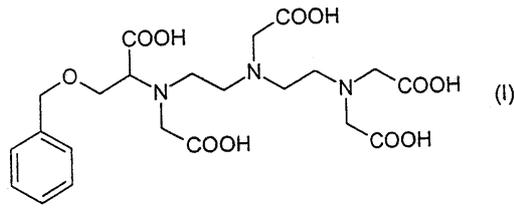
가
10

. 2
. 18.

18.

5

(I)



A) N - [2[(2 -)]] - O - ()

265kg () (1.05kmol) 129kg 758kg DETA (7.35kmol) ; 가
 50 가 50
 가 , 가 pH 12 60 , 10 30% (w/w)
 , DETA, 1200L , 25 , , OH⁻
 (,) , 210L
 pH 11.5
 ()
 , pH 12 , 40% (w/w)
 650kg (0.67kmol, () 63%).
 , 25 , ,

B) (I)

() 195.4kg (0.20kmol) 55 가 136.2kg 80%
 가 . 30% (w/w) pH 11.6 . 55
 11.2 pH 5 , 25 34% (w/w)
 pH 5.5 (I) (XAD 1600, 150L)
 ; ,
 가 (I)/ 1/6 , pH 2.0
 , 45 가 41 (I) 가 .
 18 ; , 25 5 , 가 24
 17 .
 , 10% (w/w) , 55
 가 , 47 .
 , 55 가 ,
 , 47 ,

127kg
(0.121kmol)

35 35mbar

68kg

: () 60.5%

K.F.: 8% (w/w)

가: 100.1% (ext. standard)

HPLC : 0.15%

(57)

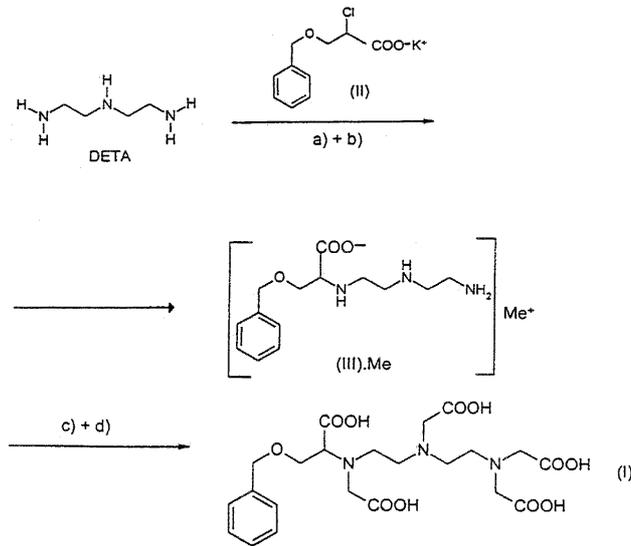
1.

1

(I)

:

1



a) 3 - ()

(Me) DETA

() 2 - -
() N - [2 - [(2 -

b) () ;

c) pH () ;

d) (I) .

2.

- 1 , a) .
- 3.
- 2 , DETA 1g 0.1 0.3g .
- 4.
- 1 , a) 50 - 70 .
- 5.
- 4 , 가 60 .
- 6.
- 1 , a) pH 12 .
- 7.
- 6 , () 1 0.9 OH⁻ 가 pH 12 .
- 8.
- 1 , a) , DETA () 6 - 7 .
- 9.
- 8 , () DETA 가 1:5 1:8 .
- 10.
- 1 , b) , OH⁻ a) , NaCl/HCl () .
- 11.
- 10 , 가 8 80%가 가 .
- 12.
- 1 , b) , () 가 () 가 20 - 50%가 .
- 13.

1 , c) pH 11 - 12 .

14.

13 , pH가 11.5 .

15.

13 14 , 가 pH .

16.

1 , c) 55 .

17.

1 , c) () 가 6.7:1 .

18.

1 , d)가 (I) 가 .

19.

18 , 가 60% 가 .

20.

18 , 40 - 60 .

21.

18 , 가 45 2.0 pH .

22.

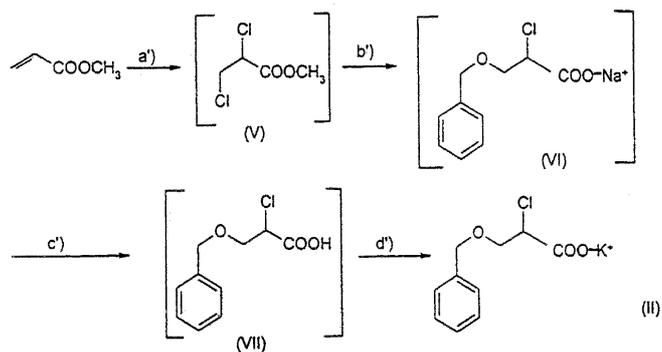
18 , (I) 가 1:15 .

23.

18 , 3 .

24.

: , 2 2- -3-()



- a) () 2,3- ;
- b) () () 2-
-3- () ;
- c) b) () 2- -3- () ;
- d) c) () .

25.

24 , a')가 .

26.

25 , 3 % .

27.

24 , a')가 0.1mbar .

28.

24 , a')가 45 .

29.

24 , b')가 10 .

30.

24 , b') .

31.

24 , b') 가 0.4% w/w

32.

24 , b') , 31
120 - 140% 가

33.

24 , b') , 30% 80 - 100%

34.

24 , c') 가 34% w/w HCl pH 2.5

35.

24 , d') 가 50% KOH 가 pH 7.2

36.

24 , d') () 가

37.

36 , 가 () 2 - 가

38.

37 , 가 20mbar 55

39.

38 , 가 4 10% w/w

40.

37 , 2 - 가가 50

41.

24 40 2 - - () ()

42.

1 23

, 24 40

()