

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

(21) 10-1999-7010048 (65) 2001-0020423
(22) 1999 10 29 (43) 2001 03 15
1999 10 29
(86) PCT/EP1998/03929 (87) WO 1999/01458
(86) 1998 06 26 (87) 1999 01 14

AP ARIPO : , , , , , , , , ,

EA : , , , , , , ,

OA OAPI : , , , , , , , 가 ,

(30) 9713730.1 1997 06 30 (GB)

(73) -4056 35

(72) ,
- 79588 - 1/1

-1040 가 12/7

- 4055 40

- 1120 293/2/2

- 68730 35

- 4104

28

, - 79576

11

, - 79589

78

(74)

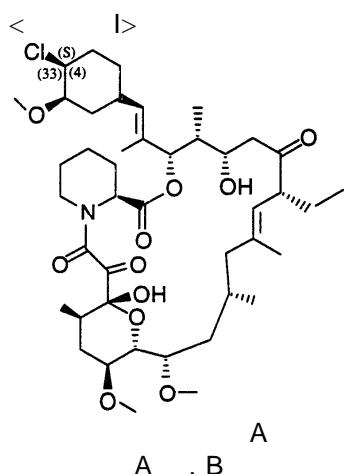
(54)

,

A B

(I) 33-

- 33 -



A , B

(I)

, B

(I)

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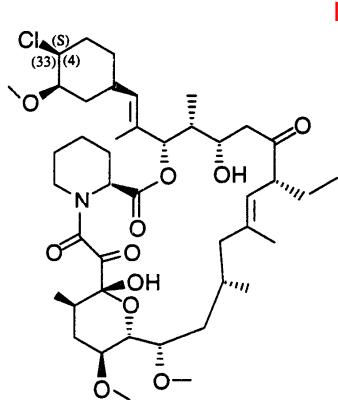
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, 33 -

- 33 -

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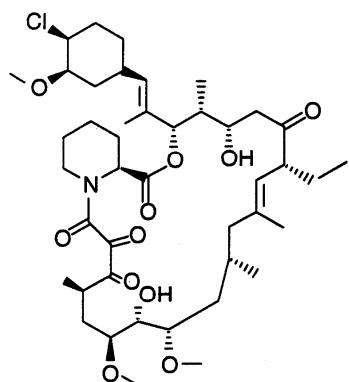


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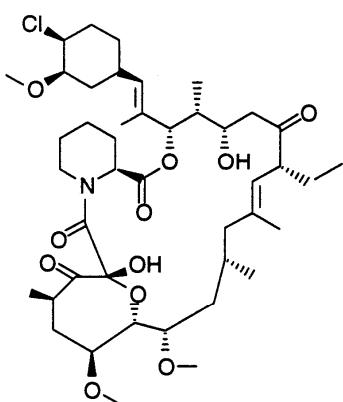
, "33- -33- -FR520" "33- -33- "
 {[1E-(1R,3R,4S)]1R,9S,12S,13R,14S,17R, 18E,21S,23S,24R,25S,27R} -12-[2-(4-
)-1-]-17- -1,14- -23,25- -13,19,21,27- -3-
 [22.3.1.0(4,9)] -18- -2,3,10,16- -11,28- -4-
 (I) (la) (lb)

(I)

la



la



Ib

(I) 4.56(m, H-33)] , EP 427 680 53(66a 가) (¹H-NMR=
 , (I) , 4 (가) I Ic 33 가
 , EP 427 680 NMR , ,

- 1) A

 - : , (/);
 - DSS(10° K/): 132 ;
 - (5): :
 - , , , : > 100 mg/ml
: <10 mg/ml;
 - (25): , , , , , , : > 50 mg/ml
: <1 mg/ml;
 - (/ 812 R 4:6): 2.49%;
 - : 98.5%;
 - : : 1.46% (Carl Fischer);
 - (SEM): (1 - 100 μ m);
 - ():
 - 1.49%(1 , 92%); 1.78%(1 , 25 , 75%);
 - DSC : 1 (Perkin Elmer DSC-7);
 - 42 200 , 가 10° K/);
 - FT-IR : 3 5 (PE FT-IR 1725X; KBr, ; 4000 - 400 cm^{-1});

- X : 6 (Scintag XDS 2000 ; Scintag, Santa Clara CA, USA);
 0.5 ° 1 ° / (2);
 2) B
- DSC(10 ° K/): 159 ;
 - (5): 0.3 mg/ml
 : 46.3 mg/ml
 : 18.1 mg/ml
 : > 50 mg/ml
 : 9.3 mg/ml
 : 1.9 mg/ml
 : 0.8 mg/ml;
 - (25): 0.4 mg/ml
 : >50 mg/ml
 : 24.4 mg/ml
 : > 50 mg/ml
 : 16.3 mg/ml
 : 3.1 mg/ml
 : 1.5 mg/ml;
- THF (/ 812 R 4:6): 0.37%;
 - : 99.9%;
 - : < 0.05%;
 - (SEM): ;
 - (): 1 , 92% 1 , 25 , 75% : ;
 - DSC : 2 (Perkin Elmer DSC-7);
 42 200 , 가 10 ° K/);
 - FT-IR : 4 5 (PE FT-IR 1725X; KBr, ; 4000-400 cm -1);
 - X : 6 (Scintag XDS 2000 ; 0.5 ° 1 ° / (2));
 3) , FT-IR 7 ;
 - : [] D 20 = -48.0 ° (± 0.2 °)(CDCl 3);
 - TLC: R f = 0.18 (; / 2:1)
 R f = 0.62 (; / 1:1)
 - ¹H-NMR (CDCl₃): 두 배좌 이성체 (Z:E = 1:2). 주 배좌이성체 d에 대한 특징적인 시그널 [ppm]: 5.35 (d,J = 1.7 Hz, H-26), 5.12 (d,J = 9.0 Hz, H-29), 5.05 (d,J = 9.4 Hz, H-20), 4.60 (d,J = 5.0 Hz, H-2), 4.56 (m,w_{1/2} = 10 Hz, H-33), 4.43 (d, J = 13.8 Hz, H-6e), 3.66 (dd, J = 9.6 Hz, J = 1.0 Hz, H-14), 3.92 (m,H-24), 2.80 (dd, J = 15.9 Hz, J = 2.7 Hz, H-23a);
 - ¹³C-NMR (CDCl₃): 두 배좌 이성체 (Z:E = 1:2). 주 배좌이성체에 대한 시그널 [ppm]: 213.7 (C-22), 196.3 (C-9), 169.1 (C-1), 164.8 (C-8), 138.8 (C-19), 132.5 (C-28), 129.2 (C-29), 122.0 (C-20), 97.0 (C-10), 79.2 (C-32), 76.7 (C-26), 75.2 (C-15), 73.7 (C-14), 72.9 (C-13), 70.2 (C-24), 59.3 (C-33), 56.7 (C-2), 54.7 (C-21), 48.6 (C-18), 39.2 (C-6), 42.7 (C-23), 39.4 (C-25), 34.7 (C-30), 34.6 (C-11), 32.8 (C-12), 32.1 (C-35), 31.7 (C-34), 27.7 (C-3), 26.4 (C-17), 25.5 (C-31), 24.5 (C-5), 24.2 (C-36), 21.1 (C-4), 20.6 (17-Me), 16.2 (11-Me), 15.9 (19-Me), 14.2 (28-Me), 11.7 (C-37), 9.3 (25-Me).
- NMR , (lc) :

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A B

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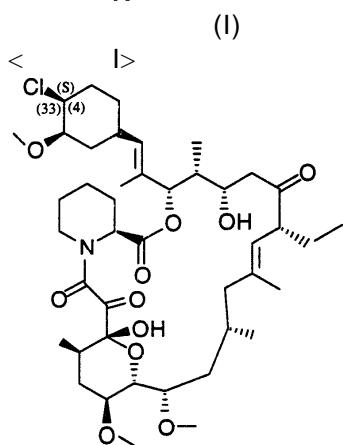
(I)

1:	33-	-33-	(A)
(180 ml	33-)
		-33-	가 (65 ml).
		10 ml	가 4 16 4 4
			1:1(v/v)
Hg) 20			(: 18 g; 135-136 ; (12 mm HPLC ;). 98%,
<u>2: 1%</u>	A	B	가
a)			1% 1%
			, 10 5 , 25 60-75 가
			, 3 25 40
			1% (1%)
			A 100% 가
b) B (I)		B 0%, 1%, 5% 10%	가 (1%)
			B A
			, 6 , 3 , 6 9
3: 33-	-33-	A	
(/ -33-)	
33-	/ 9:0.5:0.5 (v/v) (germ)	10g 70	1.5(w/w) A) 10 g /
% w/w)		A (0.06 g 10 , 0.5 μm)	가 (25 10
4	가 (9.3g	7.5),	2
가			B 2%
			A B 1:1
A		B 20%	
0			: , A B 1:1
	A 75%		
4: 33-	-33-	B	
(/ -33-)	
33-	/ 9:0.5:0.5 (v/v)	A (75g 70) (1:7(w/w) B ,) 25 g /	
30		0.1 g 24.6g	
4	가 (3.5)		
5: 33-	-33-	B	
(1500 ml	33-)
		-33-	
) 94.5 g (A)
B /			48-52 (400-50 mbar) /

. / 9.5:0.5 (v/v) 500 ml 48-52 (400-
 50 mbar) / 9.5:0.5 (v/v) 400 ml
 (70-75) 0.45 μm 30-40 20-25 , 200 ml
 가 A 20-25 1
 0-5 가 4 / 1:3 (v/
 v) 300 ml 45-50 (10-20 mbar, 16) (;) .
5: 33- -33- A
 (B)
 33- -33-) B 94.5g 1500 ml (B
 가) 5 (;)

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9.

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- 1 : , , (/);
- DSS(10 ° K/)

(5) : , , , : > 100 mg/ml

- (25%): , , , , , , : > 50 mg/ml
- <1 mg/ml;

- : 98.5%;
- : 1.46% (Carl Fischer);
- (SEM): (1 - 100 μm);
- ():
1.49%(1 , 92%); 1.78%(1 , 25 , 75%);
- DSC : 1 (Perkin Elmer DSC-7);
42 200 , 10 ° K/);
- FT-IR : 3 5 (PE FT-IR 1725X; KBr, ; 4000-400 cm $^{-1}$);
- X : 6 (Scintag XDS 2000 ; Scintag, Santa Clara CA, USA);
0.5 ° 1 ° / (2).

12.

1 , B .
- DSC(10 ° K/) : 159 ;
- (5): : 0.3 mg/ml
: 46.3 mg/ml
: 18.1 mg/ml
: > 50 mg/ml
: 9.3 mg/ml
: 1.9 mg/ml
: 0.8 mg/ml;
- (25): : 0.4 mg/ml
: >50 mg/ml
: 24.4 mg/ml
: > 50 mg/ml
: 16.3 mg/ml
: 3.1 mg/ml
: 1.5 mg/ml;
- THF (/ 812 R 4:6): 0.37%;
- : 99.9%;
- : < 0.05%;
- (SEM): ;
- (): 1 , 92% ; 1 , 25 , 75% : ;
- DSC : 2 (Perkin Elmer DSC-7);
42 200 , 10 ° K/);
- FT-IR : 4 5 (PE FT-IR 1725X; KBr, ; 4000-400 cm $^{-1}$);
- X : 6 (Scintag XDS 2000 ; 0.5 ° 1 ° / (2).

13.

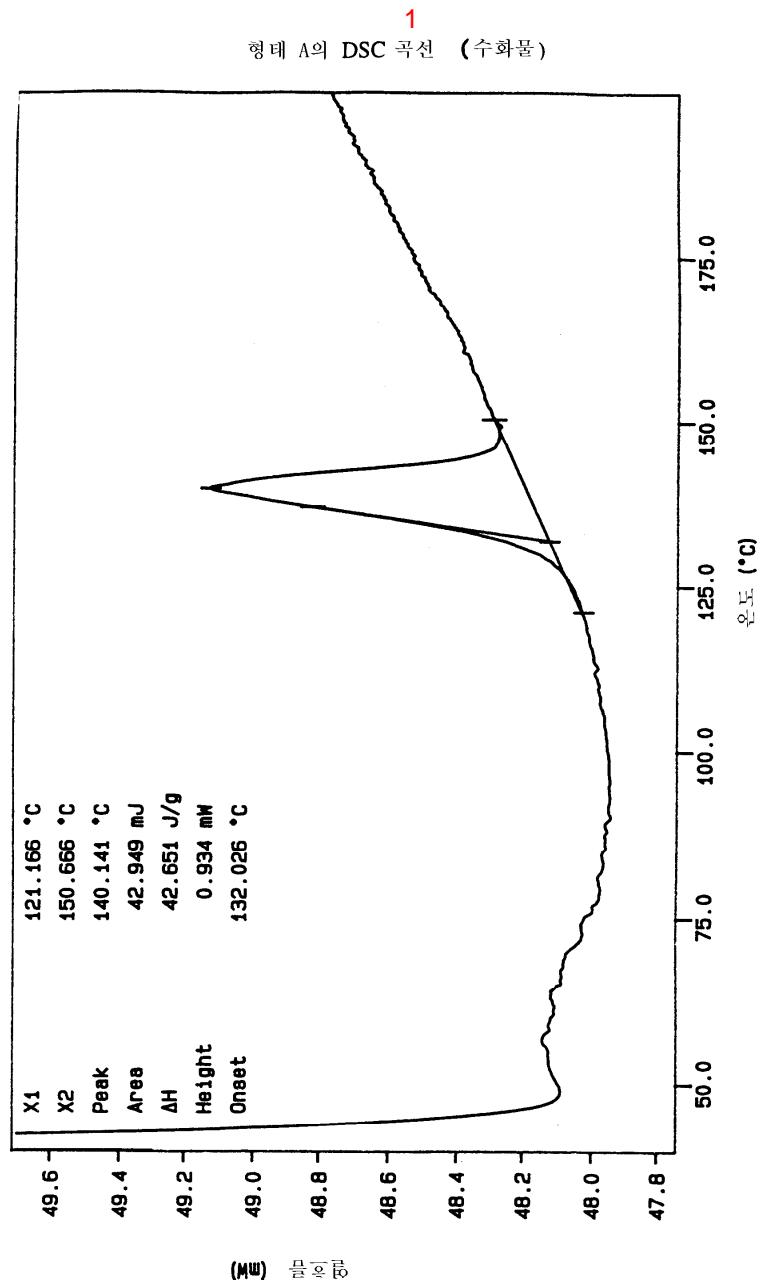
(I) ,
(I)

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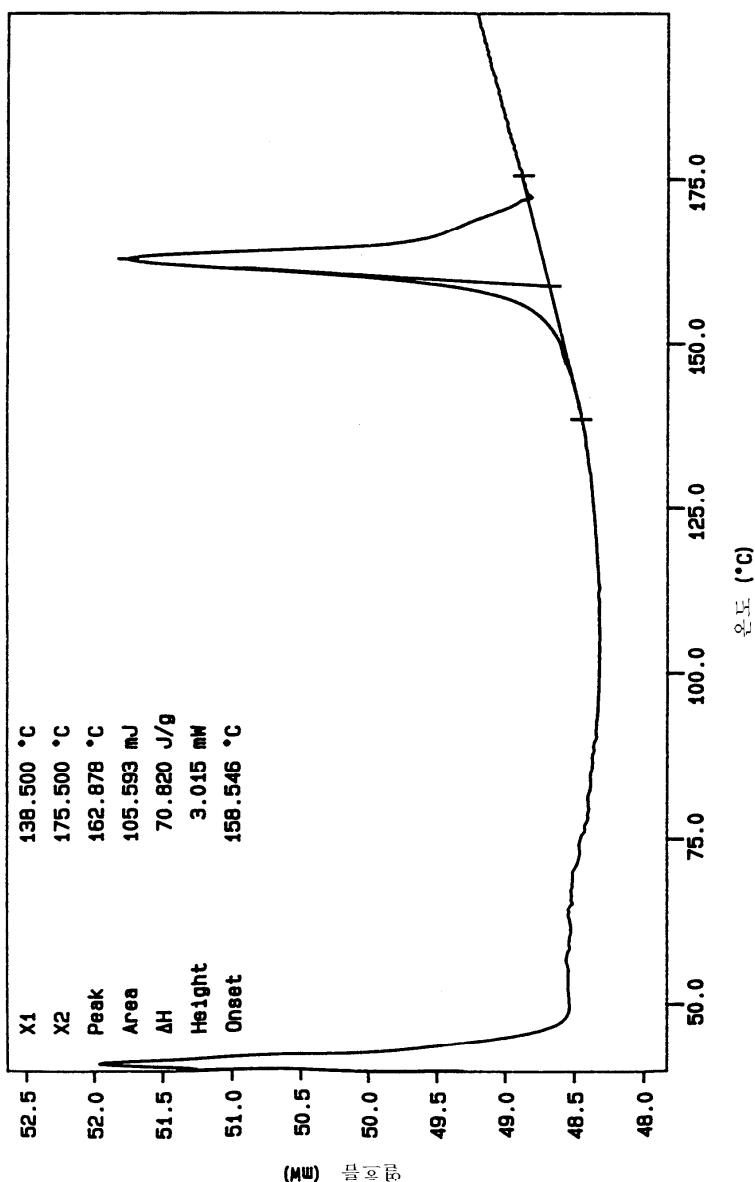
14.

(I) ,
(I)

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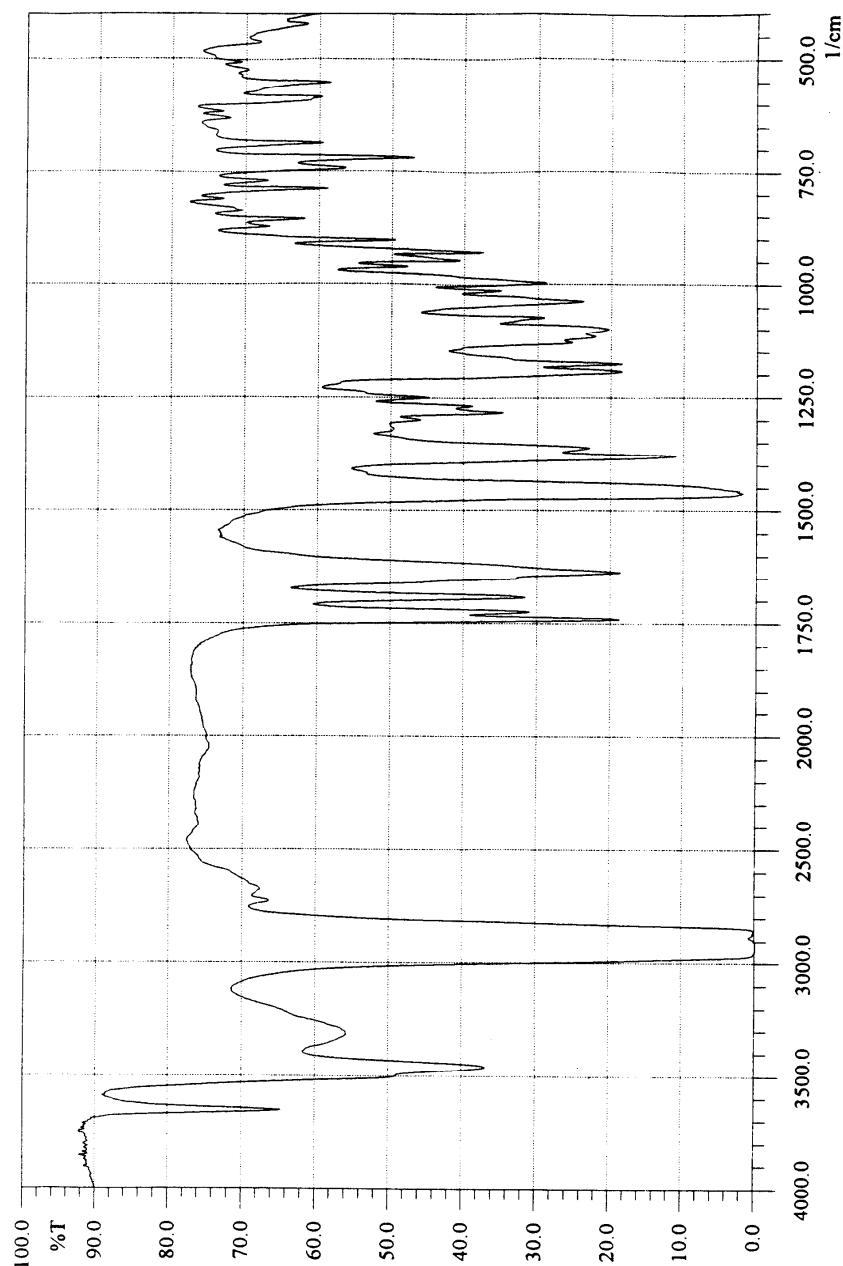


2
형태 B의 DSC 곡선



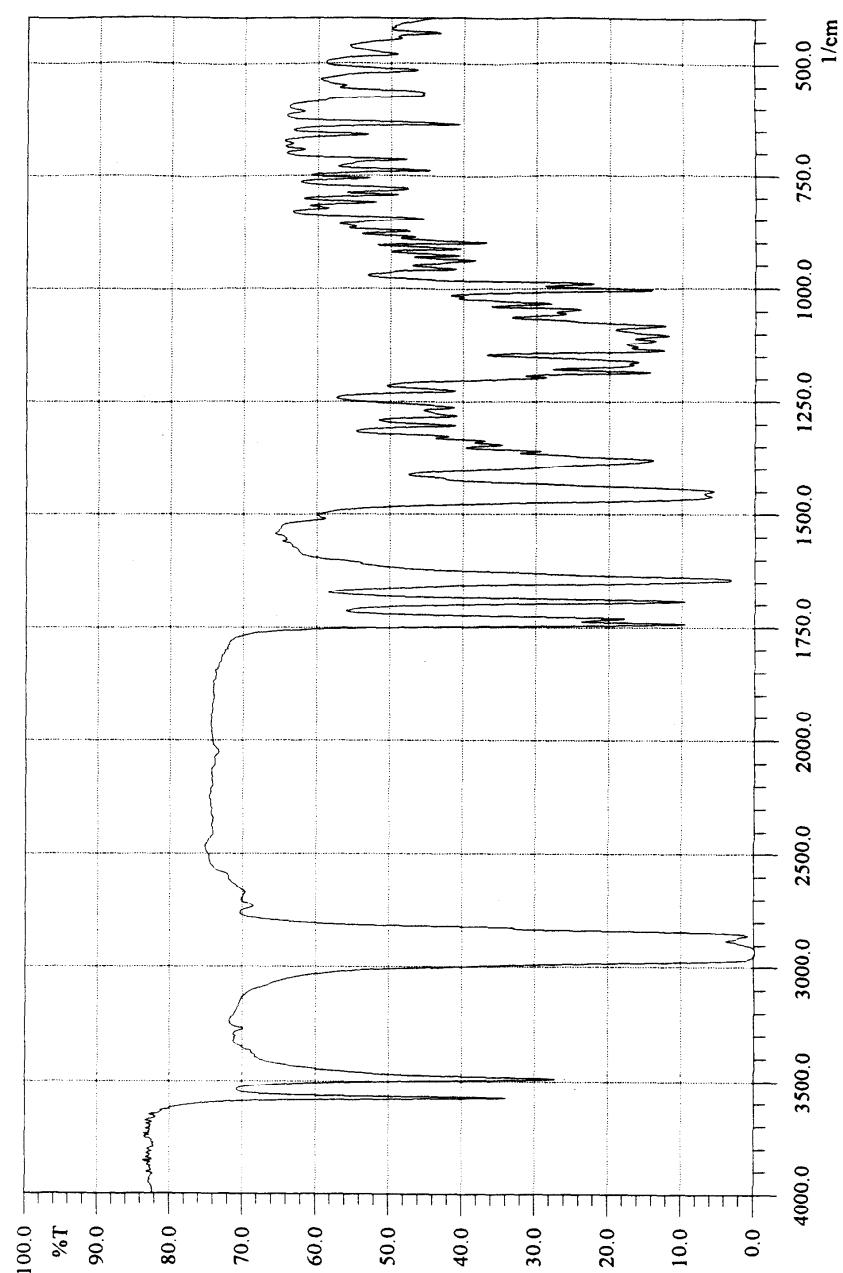
3

형태 A의 FT-IR스펙트럼 (수화물)



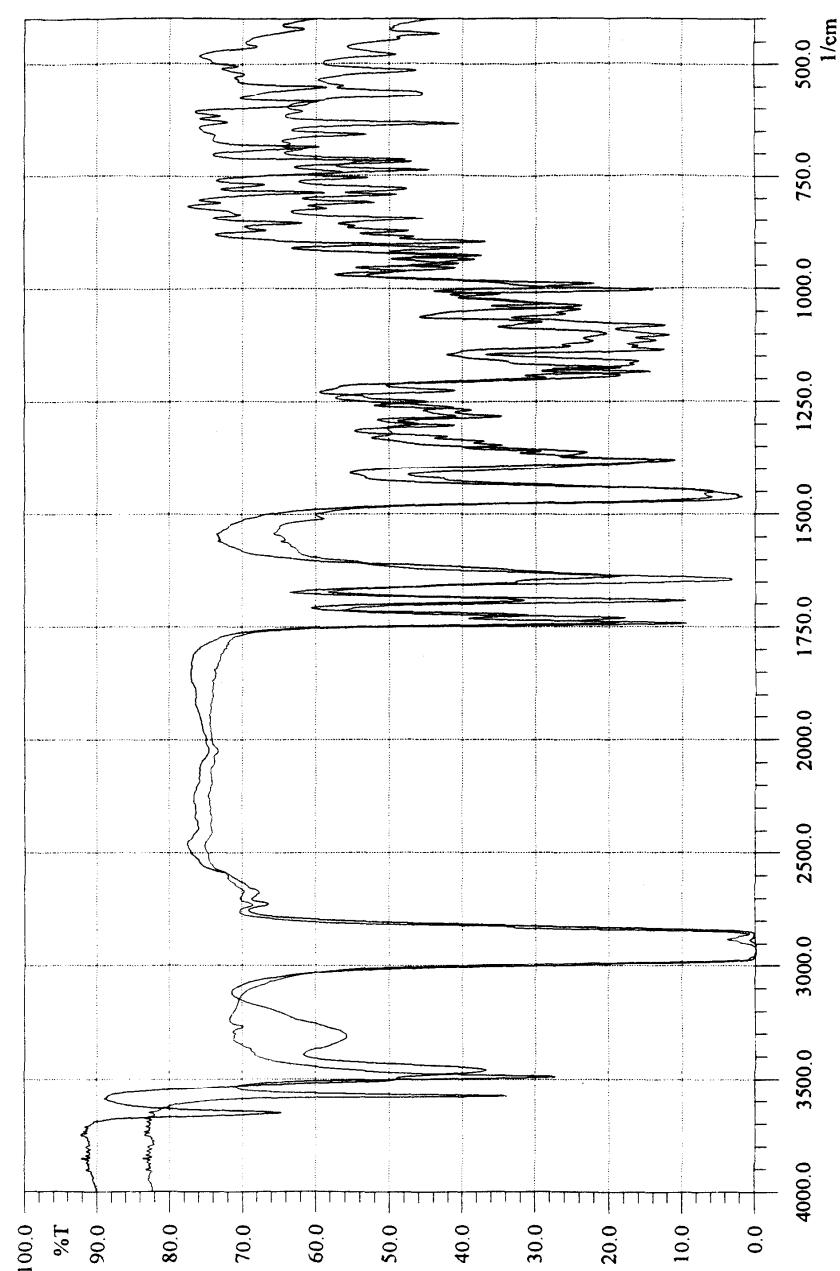
4

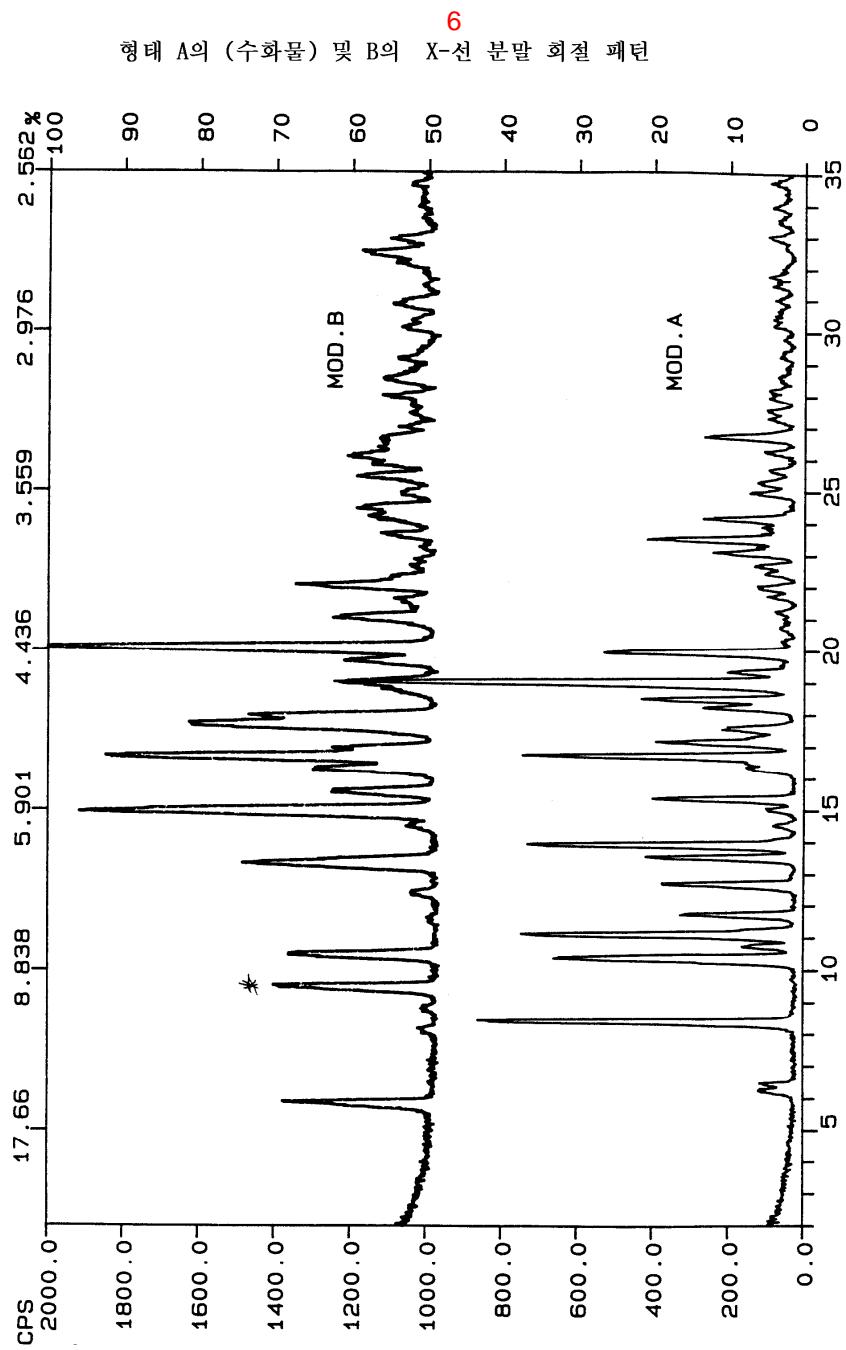
형태 B의 FT-IR스펙트럼



5

형태 A의 (수화물) 및 B FT-IR 스펙트럼 사이의 비교





무정형의 FT-IR 스펙트럼

