



-4104

28

-79576

11

-79589

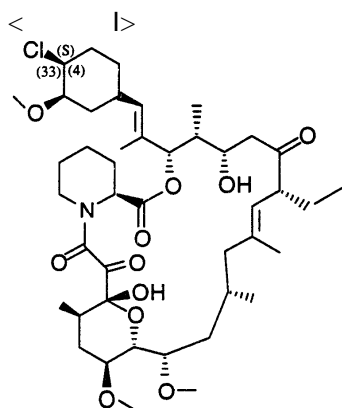
78

(74)

:

(54)

, A B (I) 33- -33-



I

A A , B

(I)

, B

(I)

,

-

.

,

,

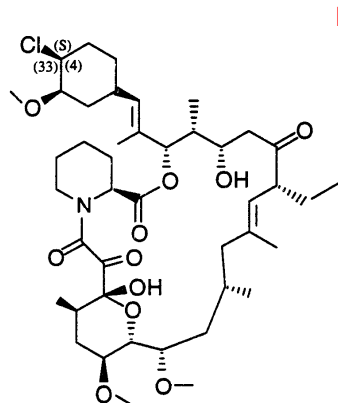
.

, 33-

-33-

I

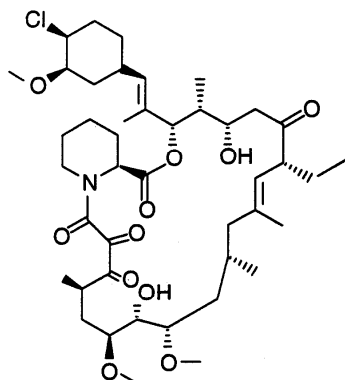
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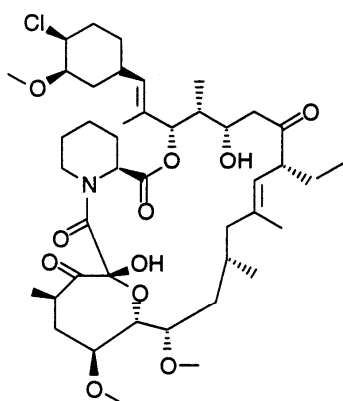
I

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

Ia



Ia



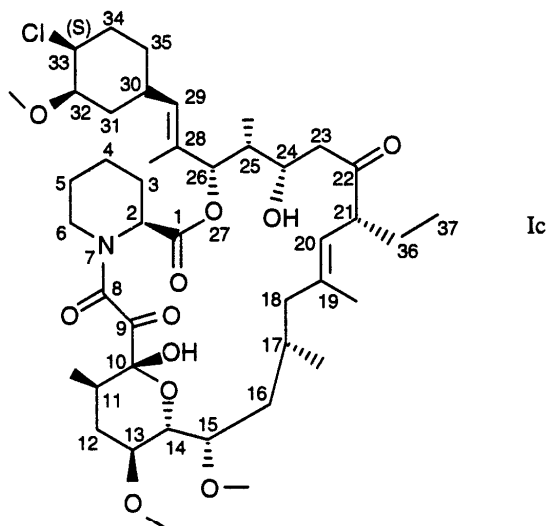
Ib

(I) EP 427 680 66a ( <sup>1</sup> H-NMR=  
 4.56(m, H-33)] , EP 480 623 53( 가 )  
 (I) 가  
 4 ( I Ic 33 가 )  
 , EP 427 680  
 , NMR

가 , 480 62  
3 , ; ,  
가 ; , 4-  
가 , (Fisons) WO 91/13889,  
42a), 42b) 가 49a) :  
, FK 506 23-  
2 , 가 , WO 97/818  
(I) 가  
(I)  
(I)  
가  
(I)  
(I)  
(I)  
(I)  
가  
10  
10  
30 1 %  
30 0.01 %  
10 가 가  
0 1 % 3  
30 0.01 % 가 , 10  
0 가 , 1  
10 60 10  
10  
가  
10  
(I) " " 가  
"A " 가  
"A " "B " 가  
A B 가

- : ( / );  
- 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 μm);  
- ( ): 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 -

- 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<sup>-1</sup>);
- X : 6 (Scintag XDS 2000 ; 0.5 ° 1 ° / (2 );
- 3) , FT-IR 7 ;
- : [ ]<sub>D</sub><sup>20</sup> = -48.0 ° (± 0.2 °)(CDCl<sub>3</sub>);
- TLC: R<sub>f</sub> = 0.18 ( ; / 2:1)
- R<sub>f</sub> = 0.62 ( ; / 1:1)
- <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 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<sub>1/2</sub> = 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);
- <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 두 배좌 이성체 (Z:E = 1:2). 주 배좌이성체 d에 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) :



\_\_\_\_\_:

DMSO:

DSC:

FT-IR: Fourier

m.p.:

r.h.:

SEM:

T:

TG:

THF:

TLC:

1: A	DSC	( )
2: B	DSC	( )
3: A	FT-IR	( )
(% T =	%)	
4: B	FT-IR	( )
(% T =	%)	
5: A	( )	B FT-IR
(% T =	%)	
A	( )	: 90 %T
B		: 82 %T
6: A	( )	B X
A: A	( )	
B: B		
	:	(cps= )
	:	(%= )
	:	
	: 2	( )
7:	FT-IR	(%= )
	(I)	
	,	
	,	
	,	
	,	
	(I)	-
	,	
	,	
	,	
	A	10
	,	
	A	B
	B	6
	,	
	A	,
	,	
	B	
	:	

- ;  
- 가 ;  
- ,  
- .

(I) 가 A B (I)  
, , (I)

**1: 33- -33- (A )**  
( 180 ml 33- -33- ) 27 g  
가 ( 65 ml). 4 16  
. 10 ml 가 4 4  
, 1:1(v/v) , (12 mm  
Hg) 20 ( : 18 g; 135-136 ; 98%,  
HPLC ; ).

**2: 1% A B 가**  
a) A 1% , 60-75  
1% , 가  
. 10 5 , 25 40  
. 3  
(1%) 25 -  
1% A 100%  
b) B 가  
(I) B 0%, 1%, 5% 10% 가 (1% )  
, B A  
, 6 , 3 , 6 9

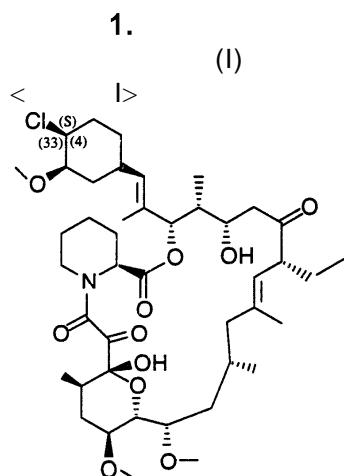
**3: 33- -33- A**  
( / / )  
33- -33- B ( A ) 10 g /  
/ 9:0.5:0.5 (v/v) 10g 70 1:5(w/w) , 가 0.5  $\mu$ m  
(germ) 10 25  
% w/w) A 0.06 g ( ) 10  
4 가 ( 7.5 ), 2  
. 9.3g  
가 A B 20% A B 2%  
A B : , A B 1:1  
0 A 75%

**4: 33- -33- B**  
( / / )  
33- -33- A ( ) ( B , ) 25 g /  
/ 9:0.5:0.5 (v/v) 75g 70 1:7(w/w) ,  
30 B 0.1 g 3.5 )  
4 가 24.6g

**5: 33- -33- B**  
( 1500 ml 33- -33- ) (A /  
B / ) 94.5 g 48-52 (400-50 mbar)

50 mbar) / 9.5:0.5 (v/v) 500 ml 48-52 (400-  
 (70-75 ) 0.45  $\mu$ m / 9.5:0.5 (v/v) 400 ml  
 가 A 30-40 20-25 , 200 ml  
 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 ( ; )

(57)



( )

3.

( )

4.

(I)

1

5.

( )

6.

( )

7.

1

8.

( )

9.

4

1

10.

11.

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  $\mu\text{m}$ );  
 - ( ): 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  $\text{cm}^{-1}$  );  
 - 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 , 가 10 ° K/ );

- FT - IR : 4 5 (PE FT - IR 1725X; KBr, ; 4000 - 400  $\text{cm}^{-1}$  );  
 - X : 6 (Scintag XDS 2000 ; 0.5 ° 1 ° / (2 ).

**13.**

(I) , 가 ,  
 (I)

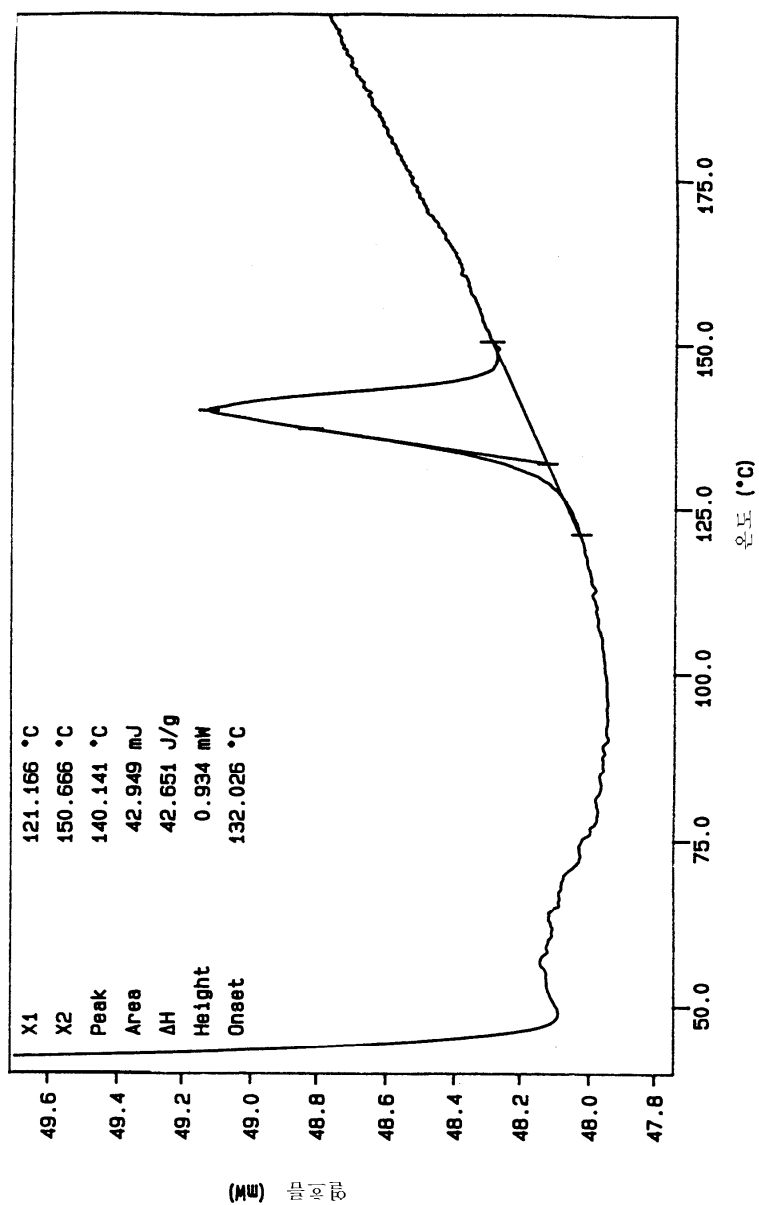
1

**14.**

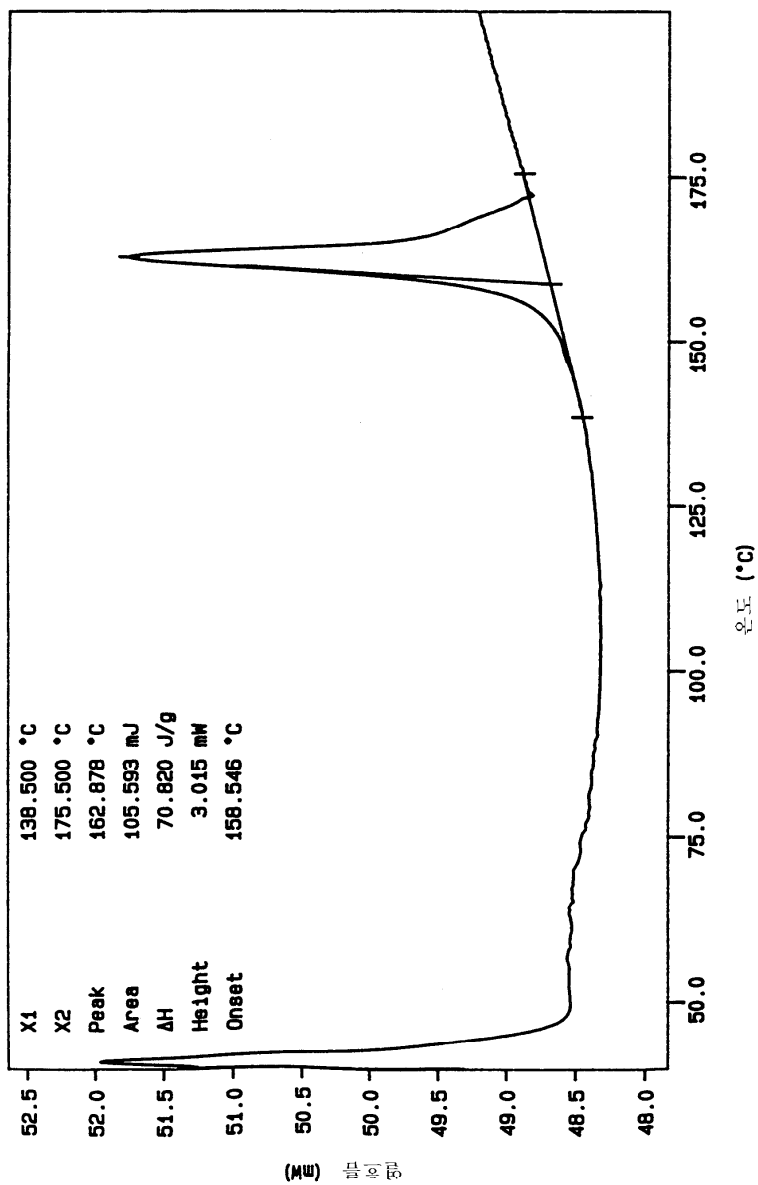
(I) (I) ,  
 (I)

1

1  
형태 A의 DSC 곡선 (수화물)

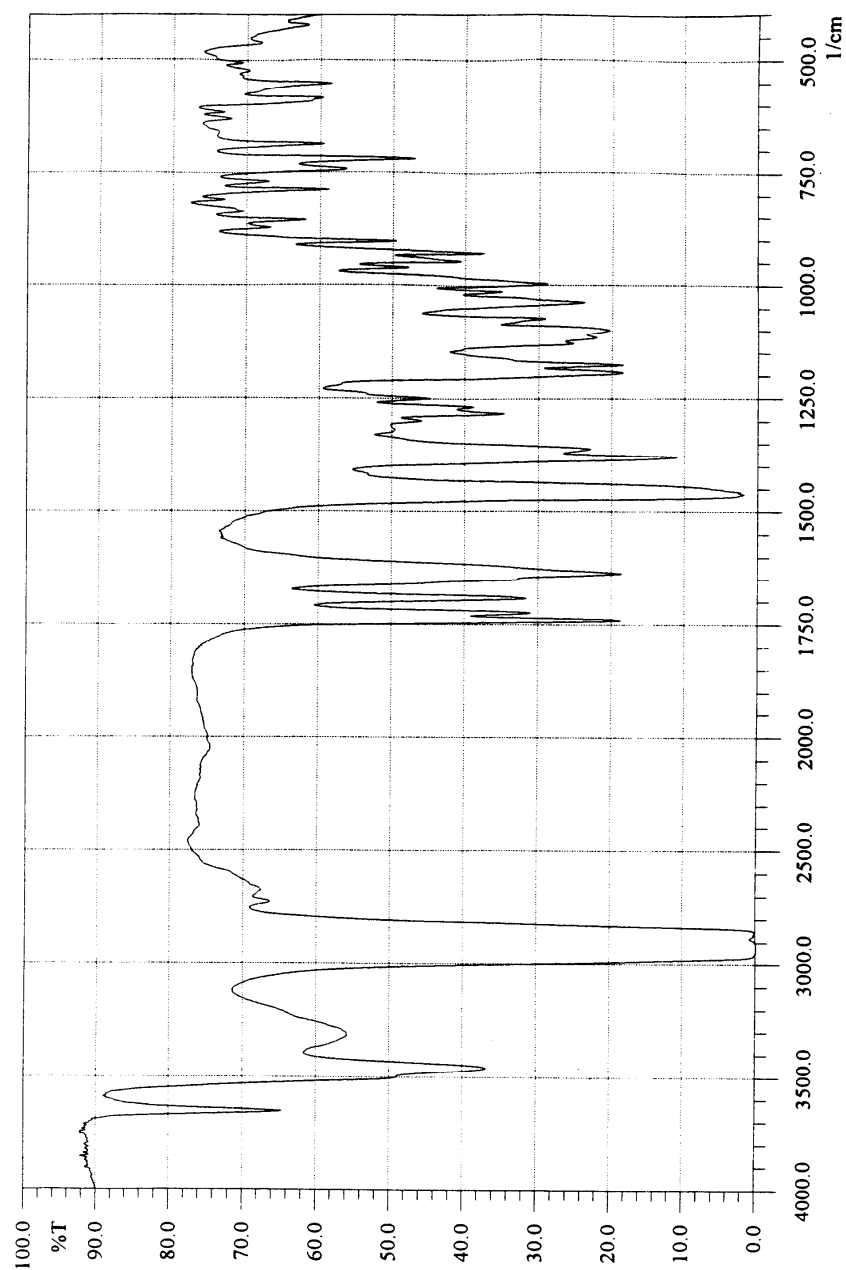


2  
형태 B의 DSC 곡선



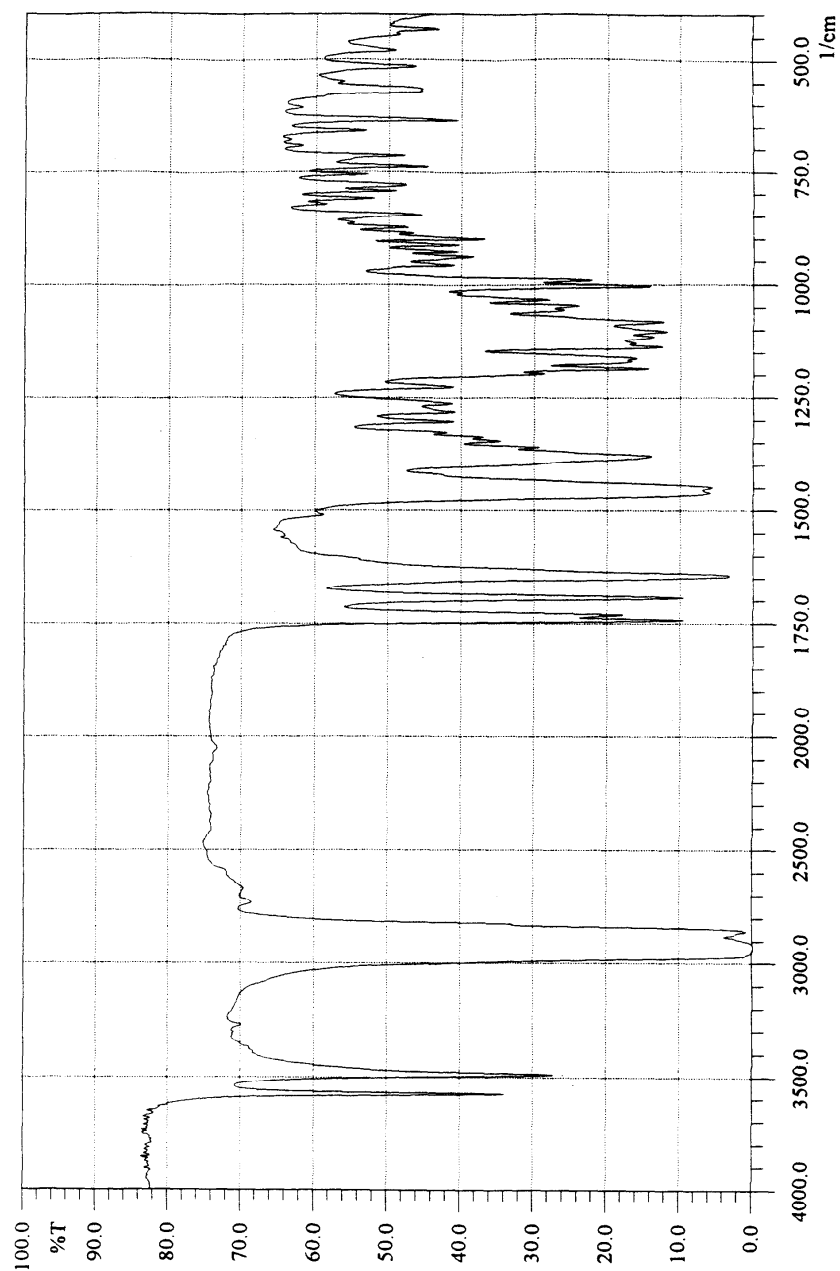
3

형태 A의 FT-IR 스펙트럼 (수화물)



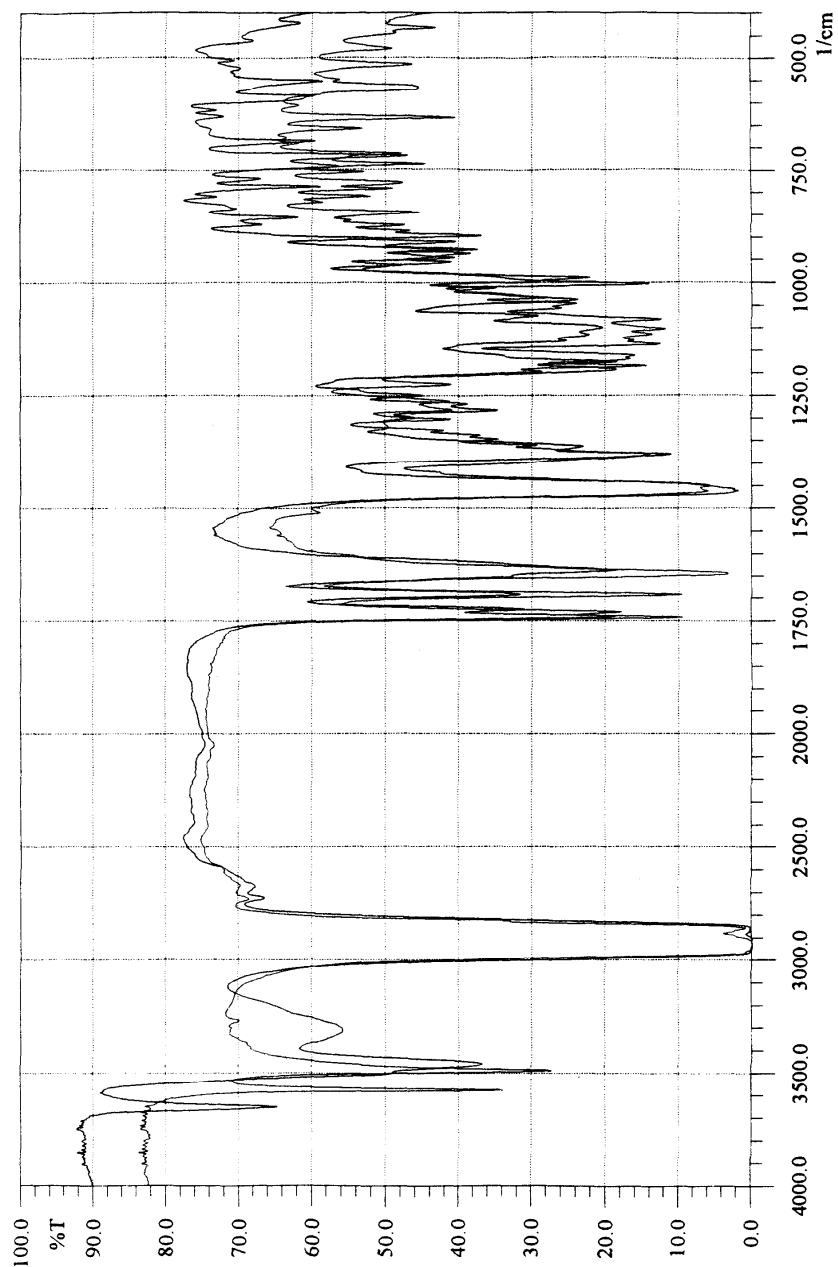
4

형태 B의 FT-IR 스펙트럼



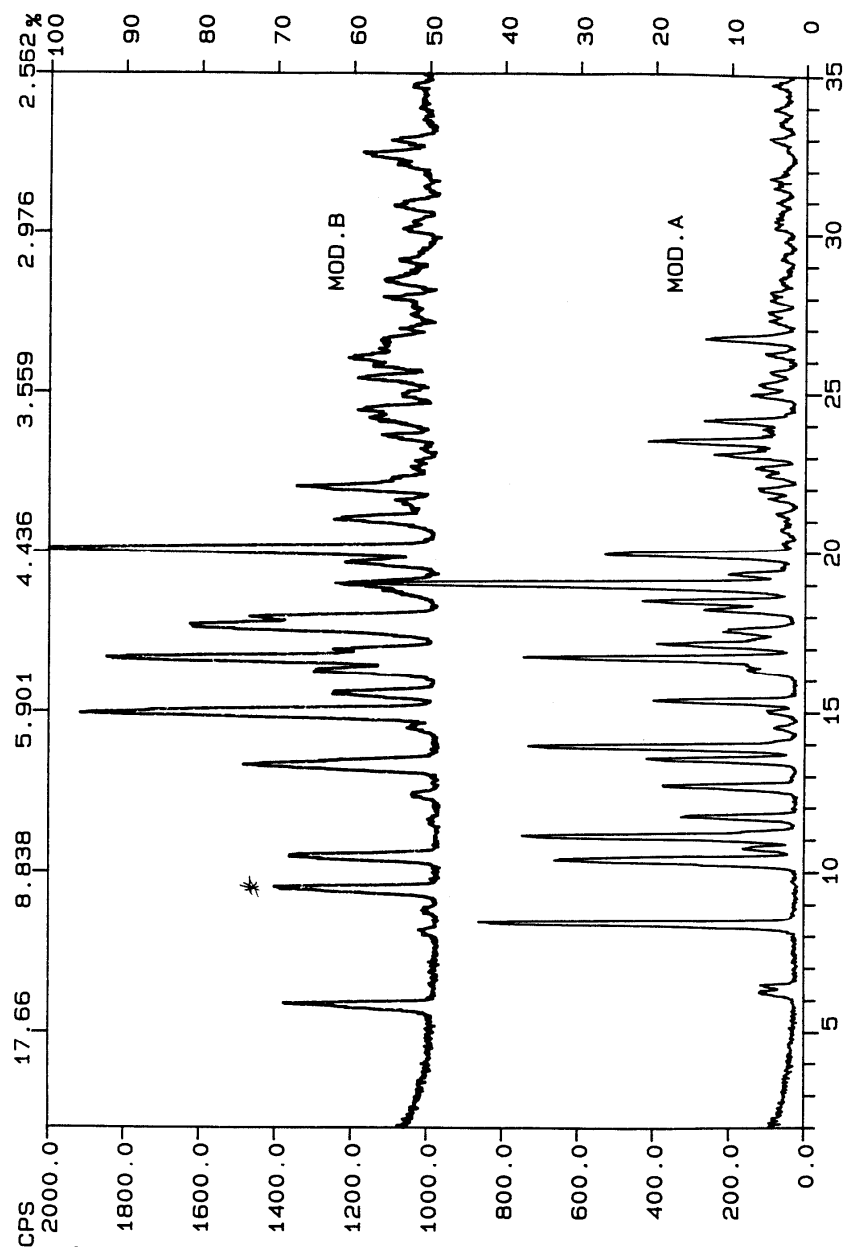
5

형태 A의 (수화물) 및 B FT-IR 스펙트럼 사이의 비교



6

형태 A의 (수화물) 및 B의 X-선 분말 회절 패턴



7  
무정형의 FT-IR 스펙트럼

