METODOS TERMICOS – I: PRINCIPIOS DE TGA y DSC PRACTICO DE DSC

Programa de Actualización en

Caracterización Estructural y Análisis de Propiedades de Sólidos Cristalinos: Polimorfos, Solvatos, Cocristales y Sales

DQIAQF - FCEN – UBA

2º cuatrimestre 2018

Miércoles 5/8/2018

Temario

Caracterización de Sólidos

Clase I – miércoles 5/9

1) **PRESENTACION DE METODOS TERMICOS**
2) **CALORIMETRIA Y TERMODINAMICA DE TRANSICIONES**
3) **TP LABORATORIO: Seguimiento de transiciones polimórficas en un fármaco: Paracetamol**

Clase II – miércoles 12/9

1) **METODOS TERMICOS Y TRANSICIONES DE FASE**
2) **METODOS TERMICOS EN ESTUDIOS DE POLIMORFOS:**
   a) **Ejemplos de la química de materiales**
   b) **Ejemplos de la química de fármacos**

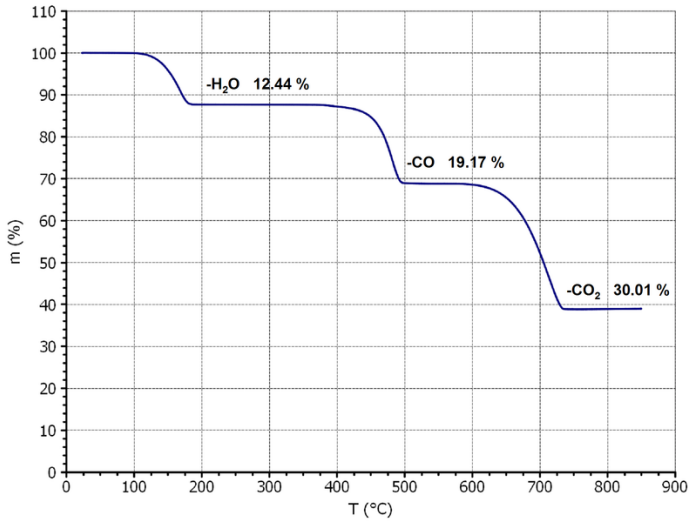
ANALISIS TERMOGRAVIMETRICO

ANALISIS TERMICO DIFERENCIAL

CALORIMETRIA DIFERENCIAL DE BARRIDO

ANALISIS TERMOGRAVIMETRICO (TGA)

$CaC_2O_4 \cdot H_2O$



ANALISIS TERMOGRAVIMETRICO (TGA)

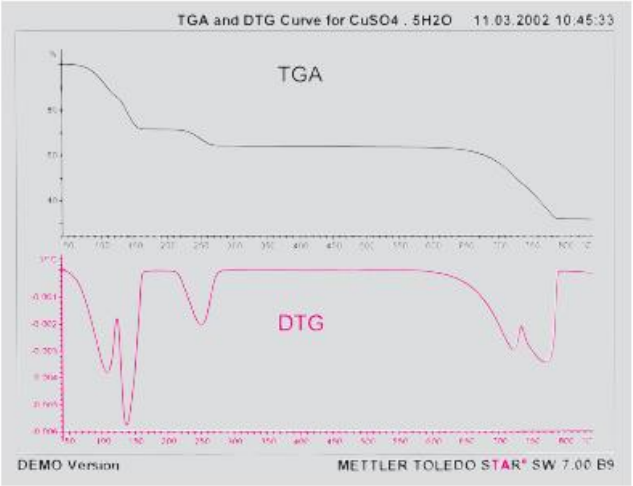


Fig. 1. TGA curve of the thermal decomposition of $CuSO_4 \cdot 5\ H_2O$ in the temperature range 40 °C to 840 °C.

ANALISIS TERMOGRAVIMETRICO (TGA)

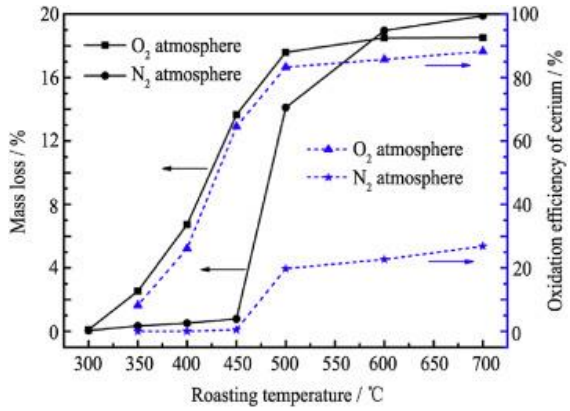
Thermal analysis and decomposition kinetics of the dehydration of copper sulfate pentahydrate

Long Cheng, Wen Li, Yifan Li, Yue Yang, Yanchun Li, Yi Cheng, Dongming Song

The thermal decomposition kinetics of individual stages of copper sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$) was investigated by TG–DSC, and the kinetic parameters were calculated by Ozawa method and multivariate nonlinear regression.It is found that $CuSO_4 \cdot 5H_2O$ decomposes to $CuSO_4$ in two stages, three steps. The first and the second steps are continuous processes of dehydration reaction; the temperature range of the two steps is from 50 to 150 °C. The first step lost two water molecules which rely on the copper ion as center by coordinate bonds, activation energy of the reaction is 71.26 kJ mol^{-1}, the pre-exponential factor log*A* is 8.40, and reaction order is 0.09. The second step lost other two water molecules which are not only relying on combination of coordination bonds, but also on hydrogen bonding. Activation energy of the reaction is 112.12 kJ mol^{-1}, the pre-exponential factor is 13.23, and reaction order is 0.18. The third step lost the fifth water molecule which forms hydrogen bonds and is based on sulfate ion binding, activation energy is 165.23 kJ mol^{-1}, the pre-exponential factor is 15.09, and reaction order is 0.90. Reaction mechanism of the above three steps is *Fn* (*n*-order reaction).

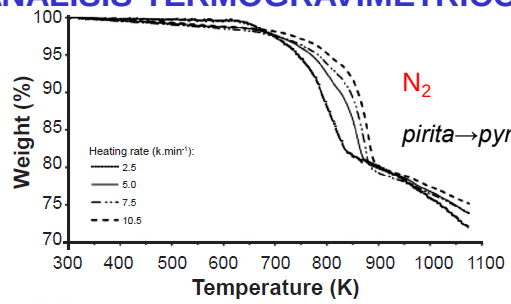
J. Therm. Anal. Calorim. https://doi.org/10.1007/s10973-018-7595-y. Published online: 19 aug 2018

ANALISIS TERMOGRAVIMETRICO (TGA)



$(REE)CO_3F$

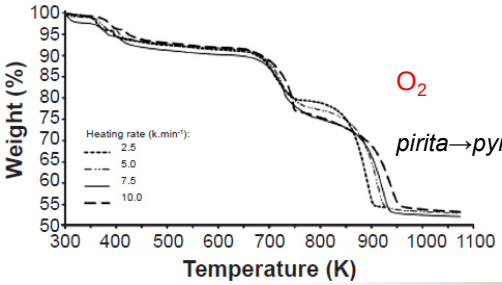
ANALISIS TERMOGRAVIMETRICO (TGA)



Pirita
Esencialmente FeS_2

N_2

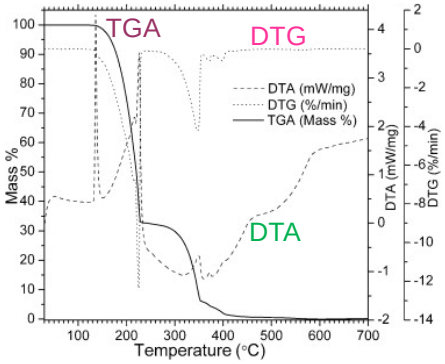
pirita→pyrrhotita→troilita→Fe

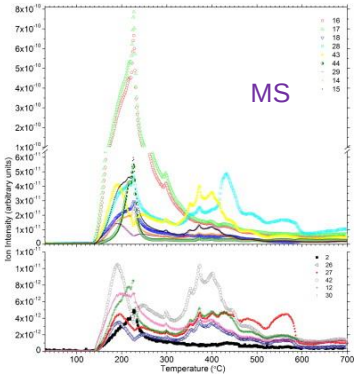


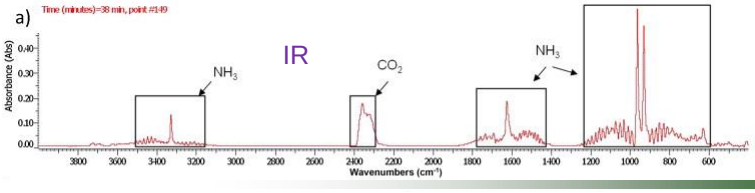
O_2

pirita→pyrrhotita→magnetita, hematita

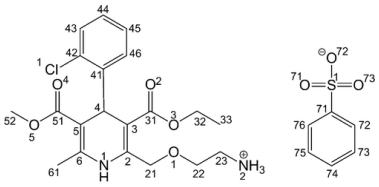
ANALISIS TERMOGRAVIMETRICO (TGA)

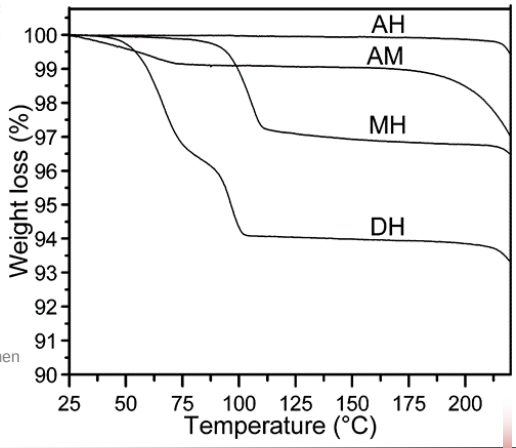






ANALISIS TERMOGRAVIMETRICO (TGA)



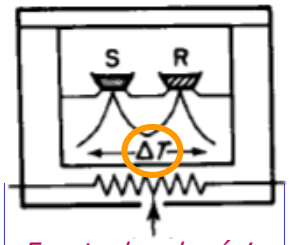


Solid Forms of Amlodipine Besylate: Physicochemical, Structural, and Thermodynamic Characterization

V. Koradia, H. Lopez de Diego, K. Frydenvang, M. Ringkjøbing-Elema, A. Müllertz, A. D. Bond, J. Rantanen

Cryst. Growth Des., **2010**, *10*, 5279–5290

METODOS DIFERENCIALES CALORIMETRICOS



Fuente de calor única

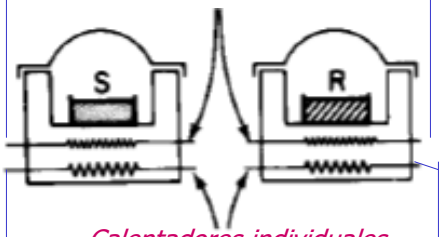
Control de rampa de temperatura

ANALISIS TERMICO DIFERENCIAL (DTA)

CALORIMETRIA DIFERENCIAL DE BARRIDO (DSC)

Control de rampa de temperatura

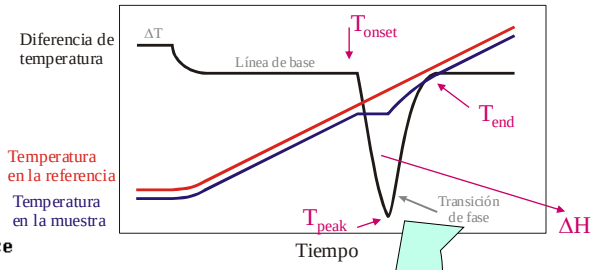
Termocuplas independientes

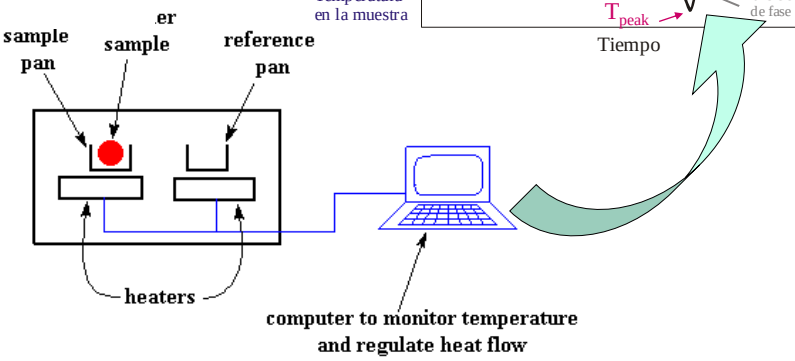


Calentadores individuales

Control de compensación por diferencias de temperatura

METODOS DIFERENCIALES CALORIMETRICOS





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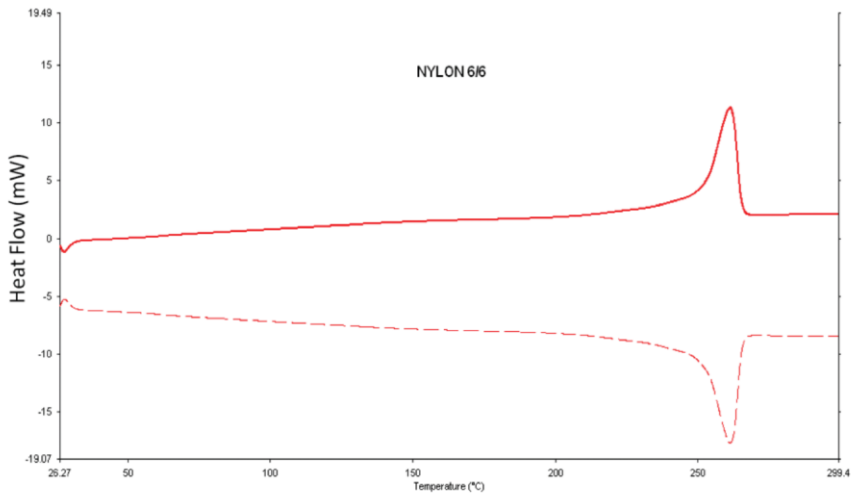


METODOS DIFERENCIALES CALORIMETRICOS

	compensación de potencia	flujo de calor
	Heat Flow	**Heat Flux**
Fast Heating (250 °C/min plus)	Yes	No
Modulated Techniques	Yes	Yes
Accuracy of Cp Values	High	Moderate
Delta H Accuracy	High	Moderate
Ease of cleaning	Very	Moderate
OIT Testing	Moderate	Easy
Isotherm Performance	Excellent	Affected by sample

Perkin Elmer – Differential Scanning Calorimetry (DSC) – A begginer´s guide

1º PRINCIPIO TERMODINAMICA

$$\Delta U = q + w$$

$\Delta U = q - p_{ext}\Delta V$ si $V = cte$ $\Delta U = q_v$

$$H = U + pV$$

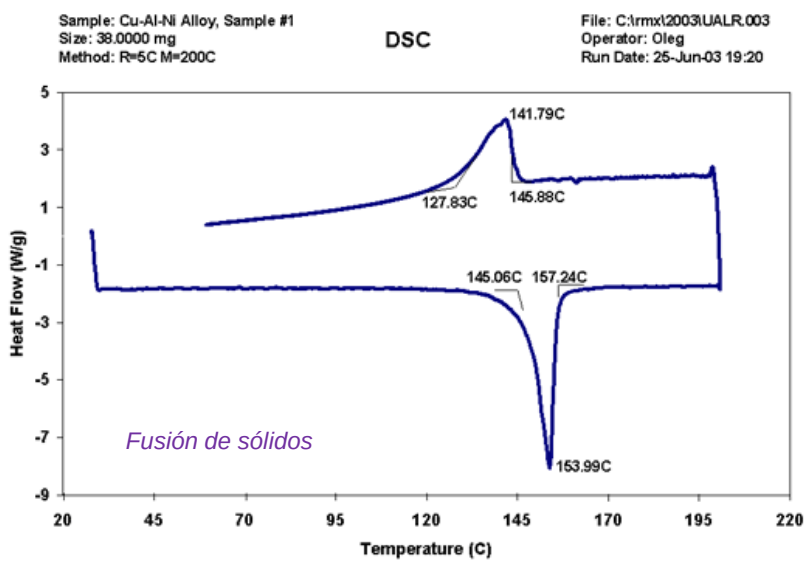
$$\Delta H = \Delta U + \Delta (pV) = q + w + p\,\Delta V + V\,\Delta p$$

$\Delta H = q - p\,\Delta V + p\,\Delta V + V\,\Delta p$ si $p = cte$: $\Delta H = q_p$

En general (p cte): $\Delta H = \Delta U + p\Delta V$

En fases condensadas: $\Delta H \approx \Delta U$

TRANSICIONES DE FASE



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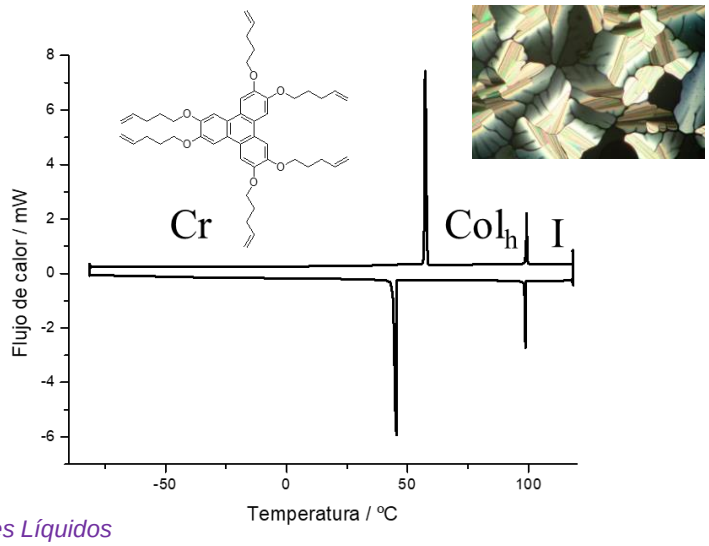
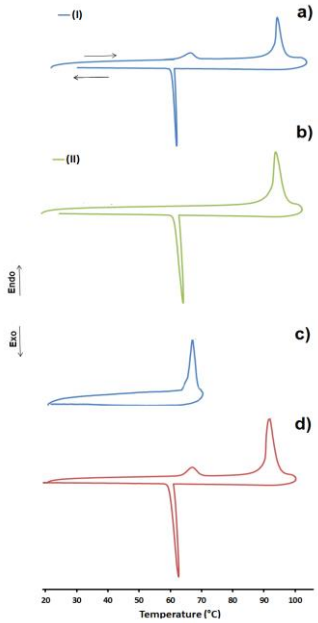


Cristales Líquidos

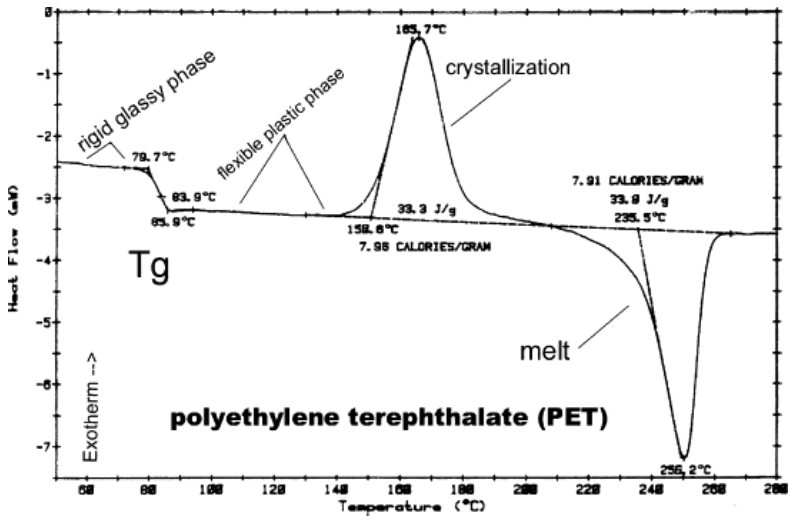
TRANSICIONES DE FASE

Entre polimorfos



TRANSICIONES DE FASE

Polímeros



TRANSICIONES DE FASE

TP Laboratorio:

Estudio por DSC de transiciones polimórficas en un fármaco

Shimadzu DSC-50

Ciclado térmico

Al – N_2(g)

METODOS TERMICOS – II: TRANSICIONES DE FASE Y POLIMORFOS

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a) Ejemplos de la química de materiales

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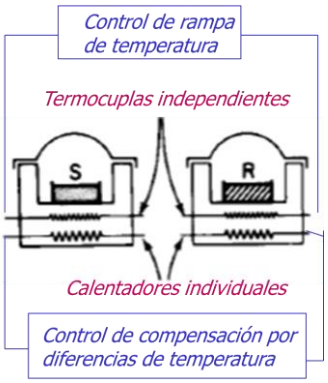
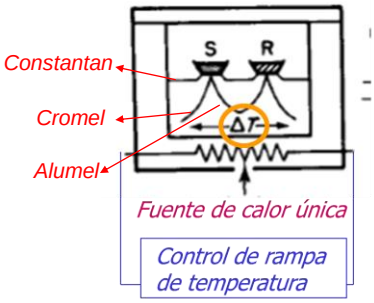
TGA

ATD

DSC *Compensacion de potencia* *Flujo de calor*





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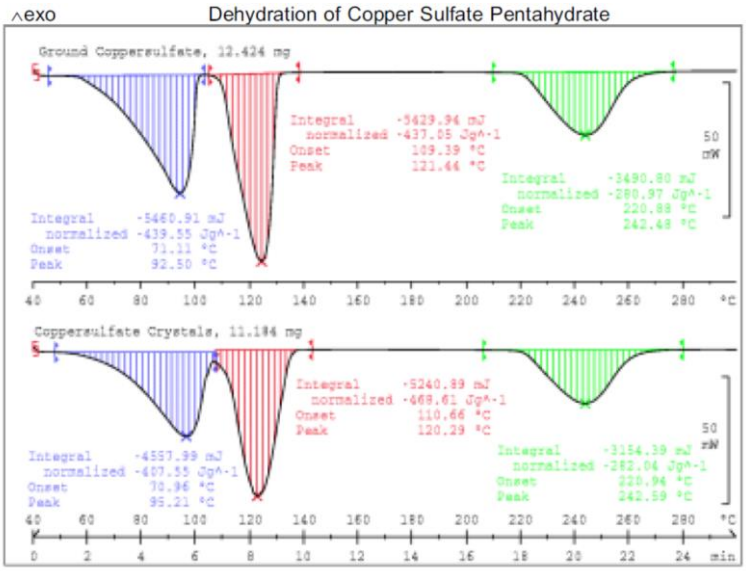
DSC



DSC

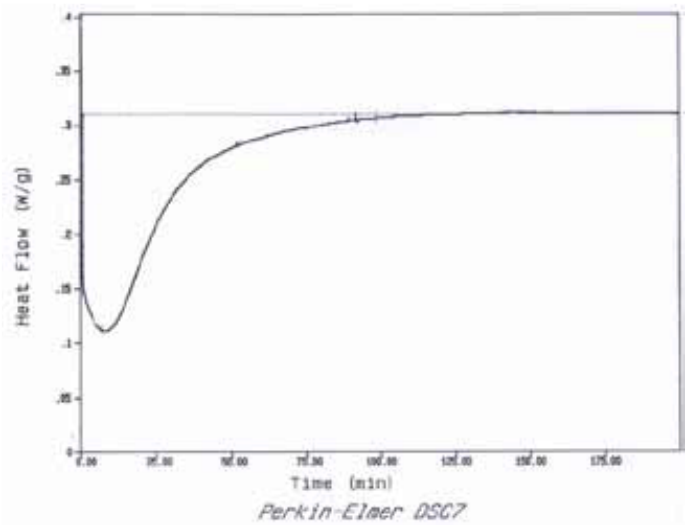


FOTO-DSC

Influence of temperature and light intensity on the photocuring process and kinetics parameters of a pigmented UV curable system

Pooneh Kardar, Morteza Ebrahimi, Saeed Bastani

Journal of Thermal Analysis and Calorimetry (2014) *118, pp 541–549*

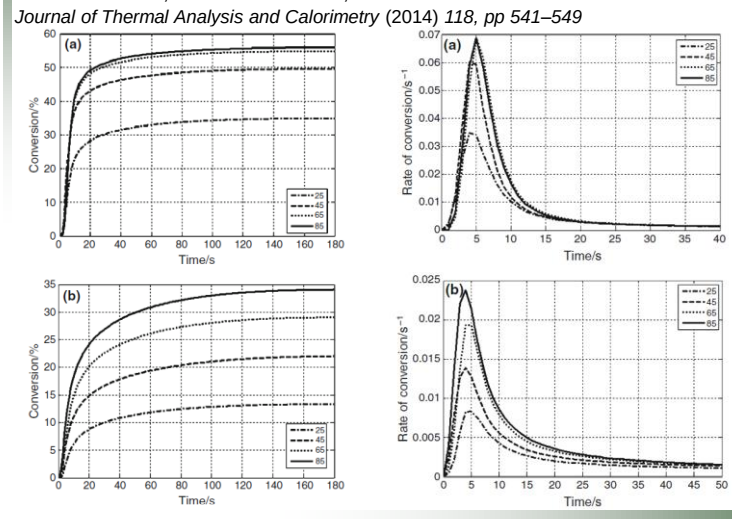
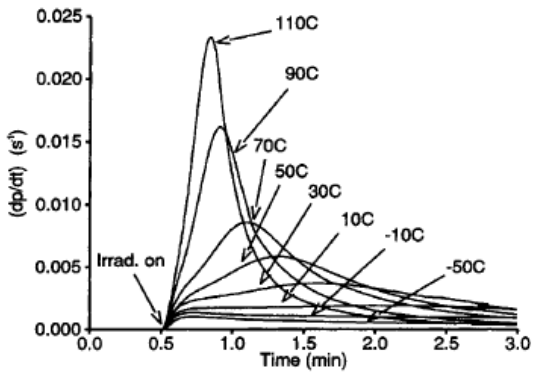


FOTO-DSC

CH2=C(CH3)COOCH2CH2OCOC(CH3) =CH2



The photopolymerization kinetics were monitored with a DSC7 differential scanning calorimeter (Perkin Elmer, USA) that was fitted with an Intracooler cooling system in some cases. The DSC was calibrated with indium, azobenzene, and water standards. Because the DSC pans were to be used unsealed during the photopolymerization experiments, and because the temperature difference between the DSC heat sink block and the sample pan holder was up to 100°C, a large thermal gradient was expected across the sample pan. To minimize this problem, disks of transparent PET film were used as covers for the sample pan holders in place of the original Pt pan covers. The DSC was also modified to allow for irradiation of the sample and reference pans by use of a bifurcated fiber optic lead, thus minimizing the thermal heating effect of the photocuring source.

DSC + SONDAS

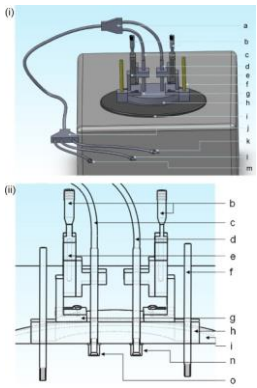
ELSEVIER

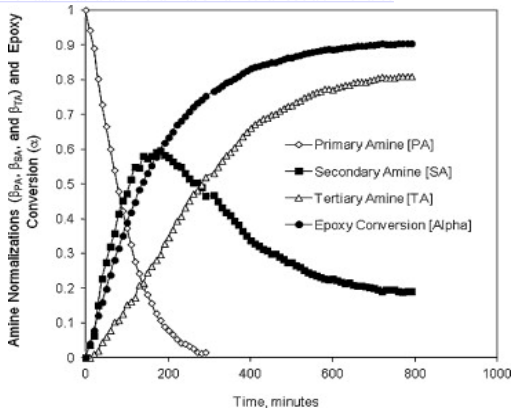
Thermochimica Acta
Volume 543, 10 September 2012, Pages 9-17

Simultaneous DSC-FTIR spectroscopy: Comparison of cross-linking kinetics of an epoxy/amine resin system

Surya D.PanditaLiweiWangRamani S.MahendranVenkata R.MachavaramMuhammad S.IrfanDeeHarrisGerard F.Fernando

https://doi.org/10.1016/j.tca.2012.04.024





Métodos Térmicos: ¿qué se puede medir?

Caracterización de Sólidos

DSC + TGA

STA 449 ***F1*** *Jupiter*

PE-SDT650

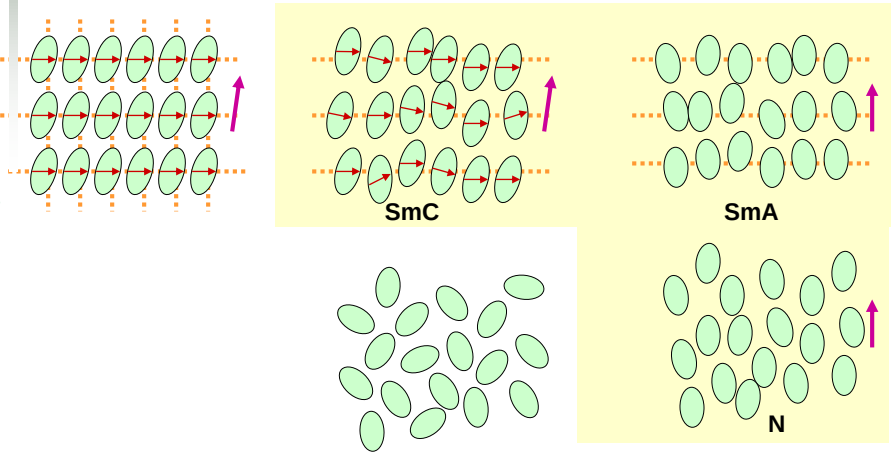
Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

CRISTALES LIQUIDOS

1 – Aproximación al concepto

Polimorfismo Liquido-cristalino



CRISTALES LIQUIDOS
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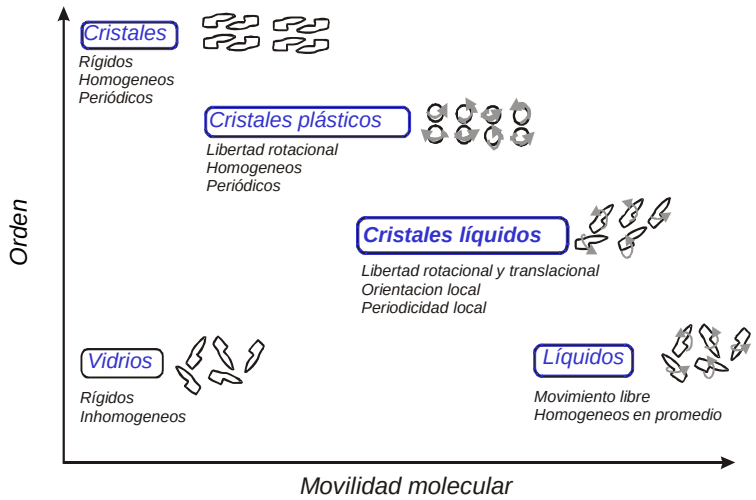
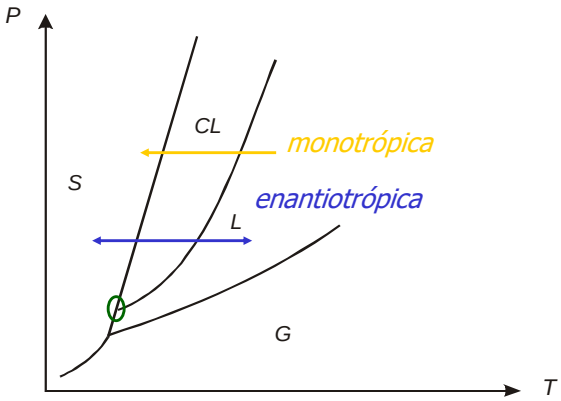


Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

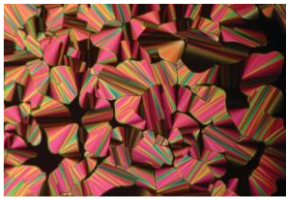
CRISTALES LIQUIDOS
1 – Aproximación al concepto

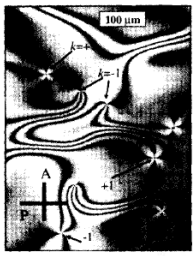


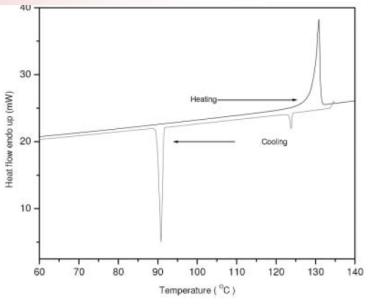
CRISTALES LIQUIDOS

2 – ¿Cómo se estudian?

MOLP

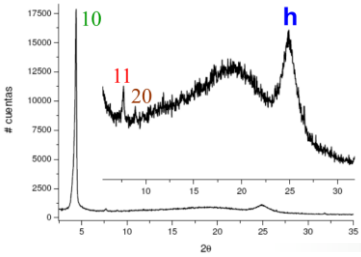


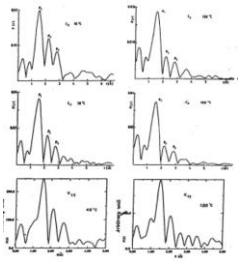


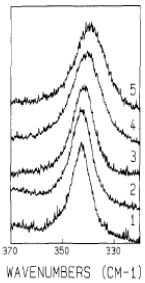


DSC

Tvar-DRX



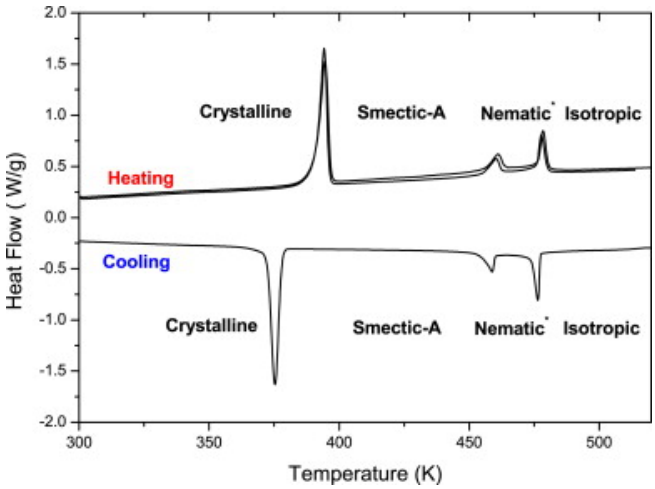




Sondas locales

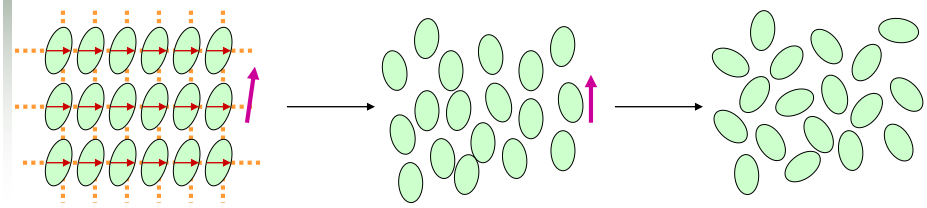
CRISTALES LIQUIDOS

3 – Transiciones de fase en CL calamíticos



CRISTALES LIQUIDOS

3 – Transiciones de fase en CL calamíticos



ΔH_m >> ΔH_{cl}

ΔS_m >> ΔS_{cl}

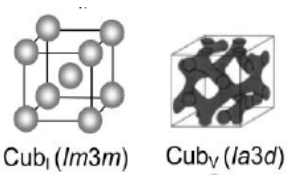
Transiciones de fase y polimorfismo en materiales

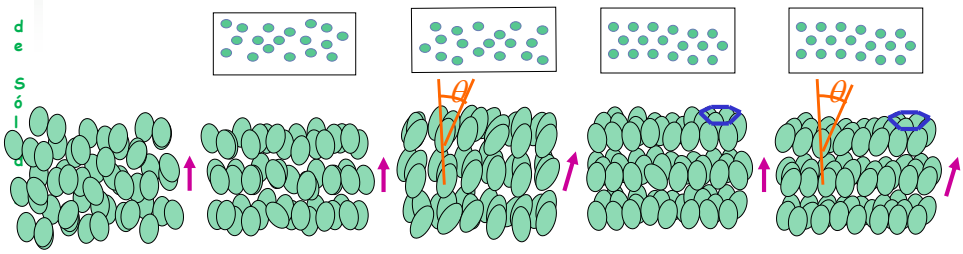
Caracterización de Sólidos

CRISTALES LIQUIDOS

4 – Amplio polimorfismo CL

Mesógenos discóticos



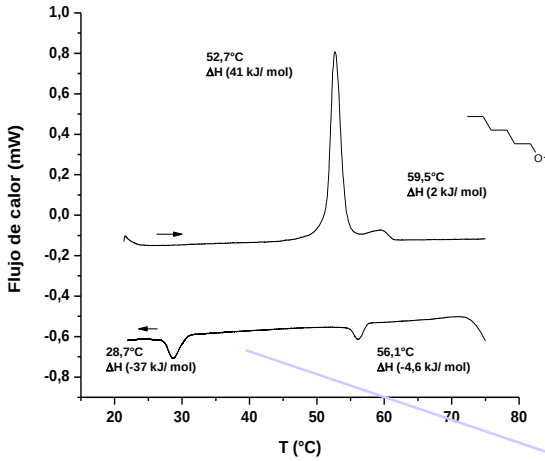


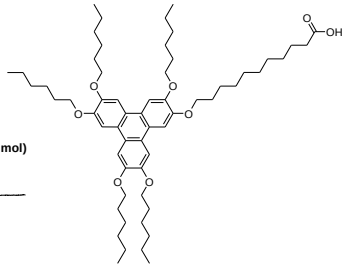
N SmA SmC SmB SmI

Mesógenos calamíticos

CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares



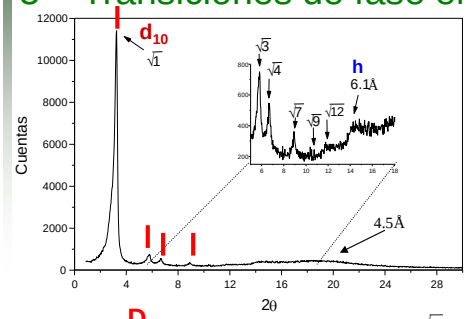


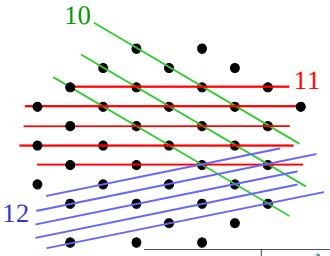
Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

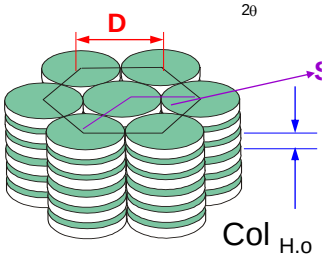
CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares





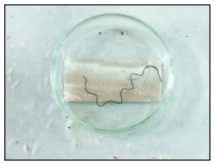
Hk	$(h^2 + k^2 + h*k)^{1/2}$
10	√1
11	√3
20	√4
21	√7
30	√9
22	√12
31	√13
40	√16
32	√19
41	√21

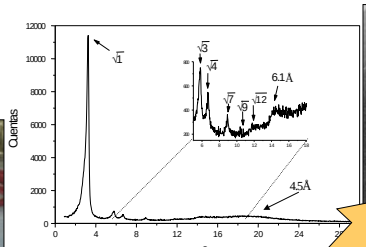


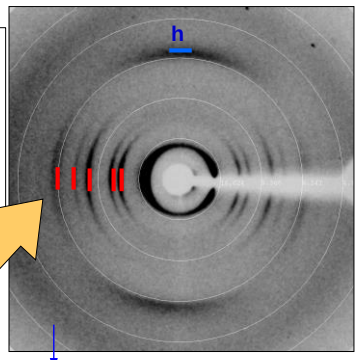
$$d_{hk} = \frac{\sqrt{3}}{2} * \frac{a}{\sqrt{(h^2 + k^2 + h*k)}}$$

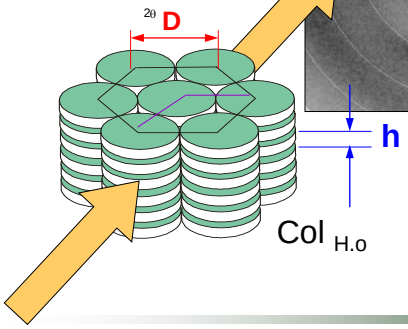
CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares







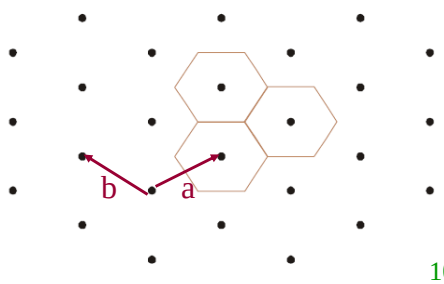


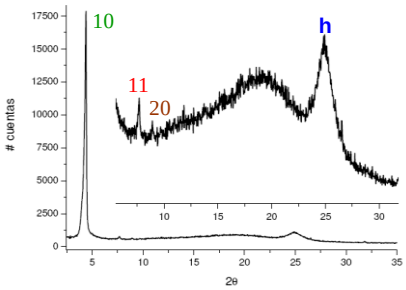
Transiciones de fase y polimorfismo en materiales

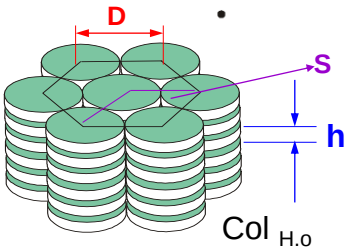
Caracterización de Sólidos

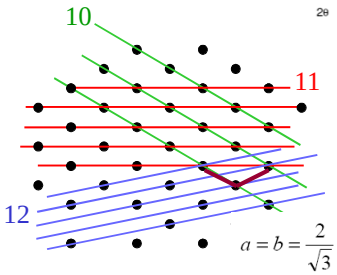
CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares







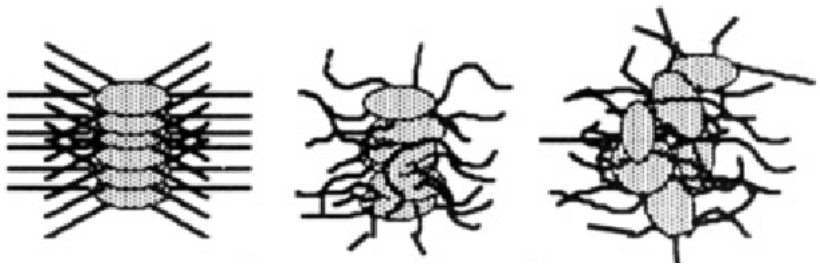


$$a = b = \frac{2}{\sqrt{3}} d_{10}$$

$$S = \frac{\sqrt{3}}{2} a^2$$

Métodos Térmicos en el Estudio de Sólidos Cristalinos: Transiciones de Fase y Polimorfismo 3/50

CRISTALES LIQUIDOS
5 – Transiciones de fase en CL columnares



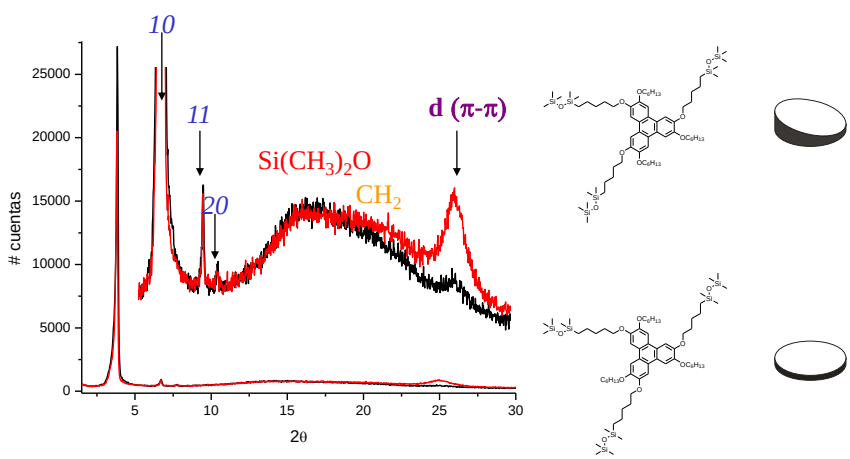
Fase cristalina $\xrightarrow{T_f}$ Mesofase columnar $\xrightarrow{T_i}$ Líquido isotrópico

Fontes et al .Phys. Rev. **A 137**, 8577 (1980)
Collard, Lyllia J. Am. Chem. Soc.**37**, 8577 (1991)

Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

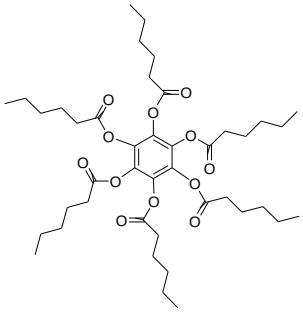
CRISTALES LIQUIDOS
5 – Transiciones de fase en CL columnares



Métodos Térmicos en el Estudio de Sólidos Cristalinos: Transiciones de Fase y Polimorfismo 3/50

CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares



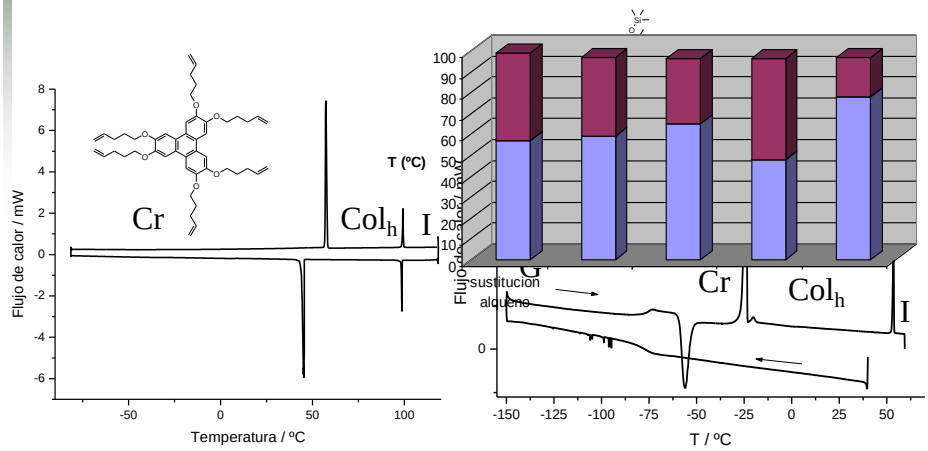
n	Cr	T (ºC)	ΔH (kJ/mol)	Col_H			I
5	•	106	(6)	--			•
6	•	68	(5)	•	86	(5)	•
7	•	80	(7)	•	86	(5)	•
8	•	79	(10)	•	84	(4)	•

Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

CRISTALES LIQUIDOS

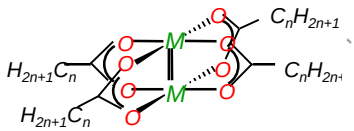
5 – Transiciones de fase en CL columnares

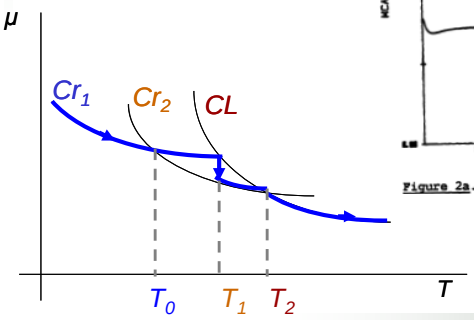


Caracterización de Sólidos

CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares





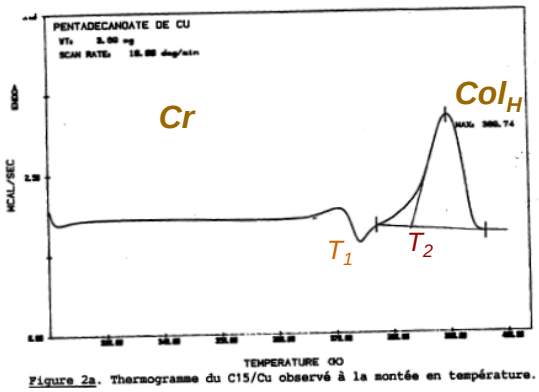


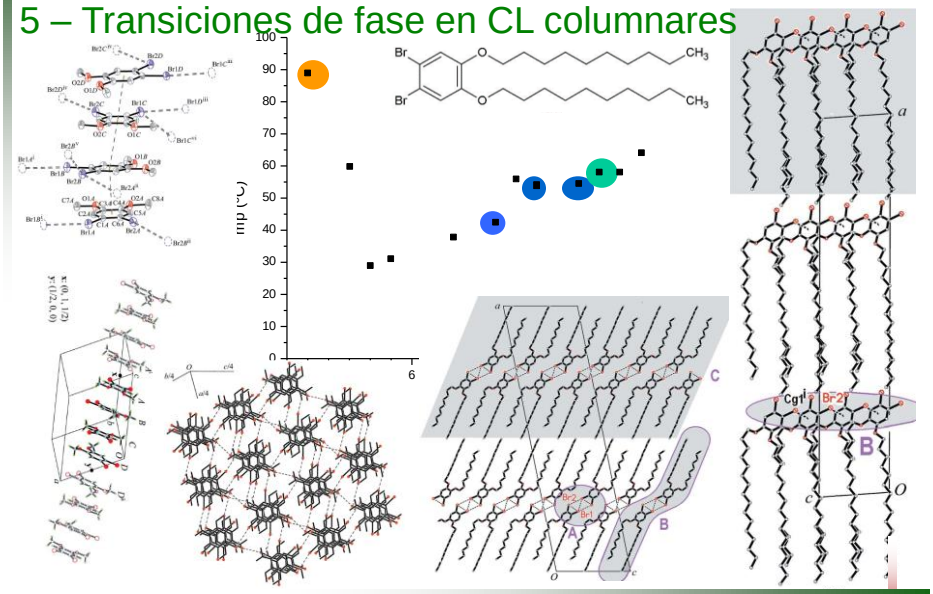
Figure 2a. Thermogramme du C15/Cu observé à la montée en température.

Transiciones de fase y polimorfismo en materiales

Caracterización de Sólidos

CRISTALES LIQUIDOS

5 – Transiciones de fase en CL columnares



Métodos Térmicos en el Estudio de Sólidos Cristalinos: Transiciones de Fase y Polimorfismo 3/50

Supramoleculares – ej. de polimorfos independientes

Polymorphism of a widely used building block for halogen-bonded assemblies: 1,3,5-trifluoro-2,4,6-triiodobenzene

Pablo A. Raffo, Sebastián Suárez, Adolfo C. Fantoni, Ricardo Baggio and Fabio D. Cukiernik *Acta Cryst.* (2017). C73, 667–673

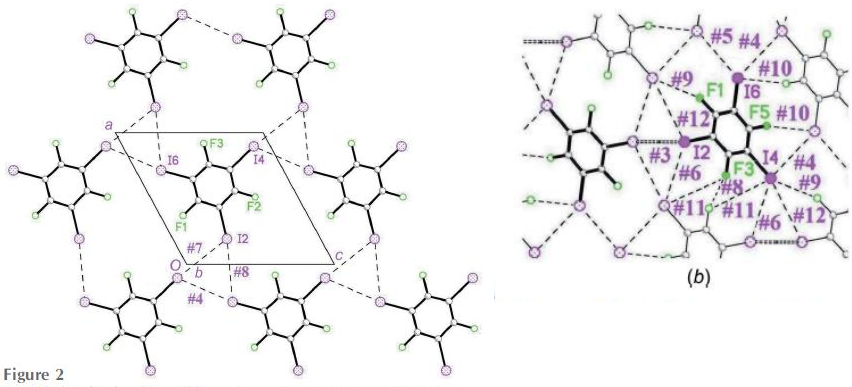
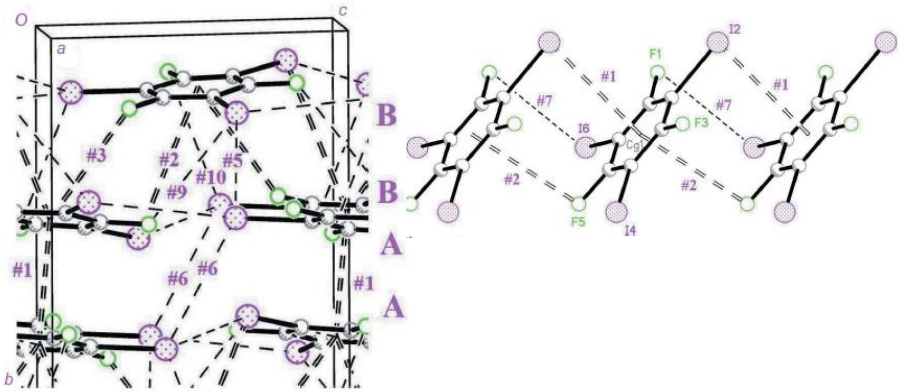


Figure 2
View of the (010) plane in (I). Interaction codes are as in Table 4.

Supramoleculares – ej. de polimorfos independientes



Supramoleculares – ej. de polimorfos independientes

C—X···π interactions for (I) (X = F, I).

Code	Type	C—X···Cg	X···Cg (Å)	X/perp (Å)	X···Cg/perp (°)	C—X/perp (°)	$100*\rho(r_{CP})$ (a.u.)	$100*\nabla^2\rho(r_{CP})$ (a.u.)
#2	**B–B**	C6—I6···$Cg1^{ii}$	4.308 (3)	3.797 (3)	28.1 (2)	69.8 (2)	0.50	0.14
#3	**B–B**	C3—F3···$Cg1^{iii}$	3.663 (6)	3.109 (7)	30.8 (2)	111.3 (3)	0.49	0.20

C—X···X'—C′ interactions for (I) (X = F, I).

Code	Type	C—X···(X—C)′	X···X' (Å)	<C—X···X'> (°)	<X···X'—C′> (°)	$100*\rho(r_{CP})$ (a.u.)	$100*\nabla^2\rho(r_{CP})$ (a.u.)
#4	***X***	C4—I4···(I6—C6)^{iv}	3.8341 (15)	111.3 (3)	157.4 (3)	0.93	0.22
#5	**B–B**	C2—I2···(I4—C4)^{v}	3.9264 (14)	143.3 (3)	100.3 (3)	0.86	0.20
#6	**A–A**	C4—I4···(I4—C4)^{vi}	4.0610 (12)	118.1 (3)	118.1 (3)	0.73	0.17
#7	***X***	C2—I2···(I4—C4)^{vii}	3.9617 (11)	113.0 (3)	176.6 (3)	0.70	0.18
#8	***X***	C2—I2···(I6—C6)^{viii}	4.1271 (15)	152.3 (4)	106.5 (4)	0.42	0.11
#9	**B–B**	C2—I2···(F1—C1)^{iii}	3.7852 (13)	83.2 (4)	126.1 (4)	0.38	0.12
#10	**B–B**	C4—I4···(F5—C5)^{iii}	3.8683 (14)	109.6 (3)	86.9 (3)	0.36	0.12

C—X···π interactions for (II) (X = F, I).

Code	Type	C—X···Cg	X···Cg (Å)	X/perp (Å)	X···Cg/perp (°)	C—X/perp (°)	$100*\rho(r_{CP})$ (a.u.)	$100*\nabla^2\rho(r_{CP})$ (a.u.)
#1	***X***	C2—I2···$Cg1^{i}$	3.728 (3)	3.642	12.29	83.1 (2)	0.69	0.21
#2	***X***	C5—F5···$Cg1^{ii}$	3.663 (6)	3.575	12.66	82.7 (4)	0.48	0.19

C—X···X'—C′ interactions for (II) (X = F, I).

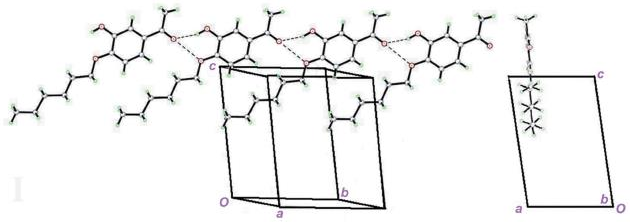
Code	Type	C—X···(X—C)′	X···X'	<C—X···X'> (°)	<X···X'—C′> (°)	$100*\rho(r_{CP})$ (a.u.)	$100*\nabla^2\rho(r_{CP})$ (a.u.)
#3	**Y**	C2—I2···(I2—C2)^{iii}	3.774 (2)	171.1 (2)	100.7 (2)	1.02	0.24
#4	**Z**	C4—I4···(I6—C6)^{iv}	3.957 (2)	80.5 (5)	146.8 (5)	0.80	0.19
#5	**Z**	C6—I6···(I6—C6)^{v}	4.101 (2)	138.4 (2)	138.4 (2)	0.57	0.14
#6	**Z**	C2—I2···(I4—C4)^{vi}	4.241 (5)	126.9 (4)	123.2 (4)	0.55	0.13
#7	***X***	C1—F1···(I6—C6)^{i}	3.656 (5)	87.3 (4)	90.4 (4)	0.53	0.17
#8	**Z**	C3—F3···(F3—C3)^{vii}	2.851 (8)	157.4 (5)	157.4 (5)	0.52	0.28
#9	**Z**	C1—F1···(I4—C4)^{vii}	3.584 (5)	145.5 (4)	126.1 (4)	0.49	0.17
#10	**Z**	C5—F5···(I6—C6)^{viii}	3.530 (5)	167.3 (4)	74.2 (4)	0.41	0.13
#11	**Z**	C3—F3···(I4—C4)^{vi}	3.979 (6)	111.9 (5)	79.0 (5)	0.35	0.11
#12	**Z**	C2—I2···(I4—C4)^{vii}	4.044 (2)	105.6 (2)	157.5 (2)	0.24	0.06

Transiciones entre polimorfos

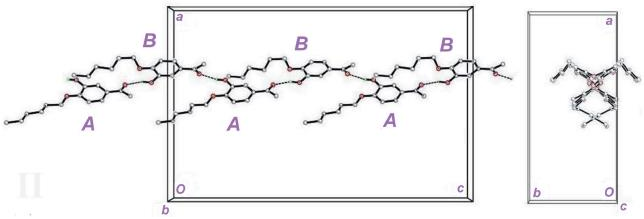
A combined crystallographic, thermal, Raman and computational study on polymorphism and phase transition in 1-(4-hexyloxy-3-hydroxyphenyl)ethanone

Acta Cryst. (2017). C73, 1137–1143

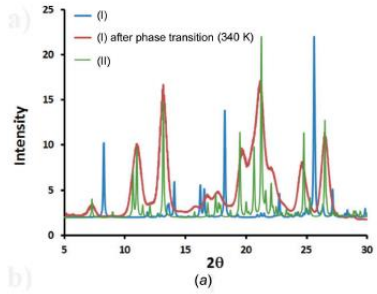
Sebastián Suárez, Veronica E. Manzano, Adolfo C. Fantoni, Emilia Halac, Ricardo Baggio and Fabio D. Cukiernik

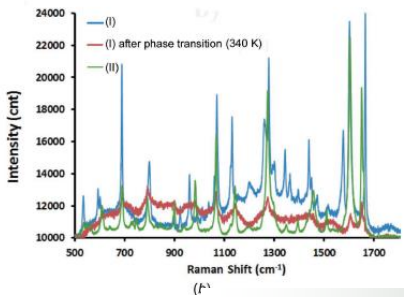


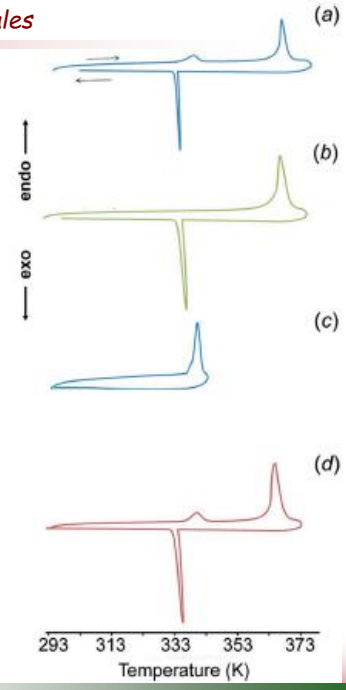
(a)



Transiciones entre polimorfos





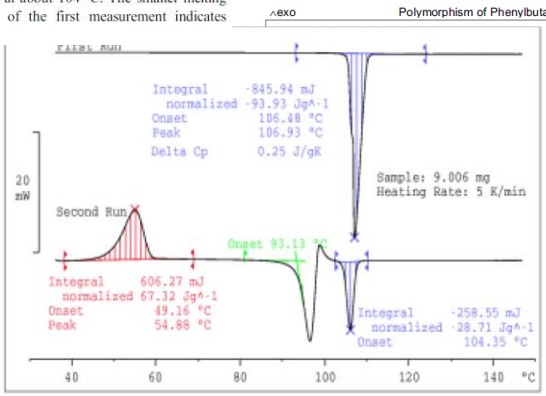


Fenilbutazona

5 Polymorphism of Phenylbutazone

Sample	Phenylbutazone	
Conditions	Measuring cell:	DSC821^e
	Pan:	Aluminum standard 40 µl, hermetically sealed
	Sample preparation:	Phenylbutazone, pressed into the pan with a PTFE rod, total weight 9.006 mg
	DSC measurement:	Heating from 30 °C to 150 °C, cooling to 30 °C and a second heating run to 150 °C; All heating and cooling runs at 5 K/min
	Atmosphere:	Air, stationary environment, no flow

Phenylbutazone can exist in stable and metastable modifications (polymorphism). The stable form melts at about 106 °C (upper curve). On cooling, the melt solidifies to a glassy state. On heating again, the amorphous sample begins to crystallize at about 50 °C to the metastable modification (lower curve, exothermic peak). The metastable form melts at about 93 °C. At the same time, the stable modification crystallizes from the resulting melt (endothermic peak followed by an exothermic peak). The stable modification melts afterwards at about 104 °C. The smaller melting peak area in comparison with that of the first measurement indicates incomplete crystallization.



Estearato de magnesio

ORGANIC PROCESS RESEARCH & DEVELOPMENT
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Identification of Pseudopolymorphism of Magnesium Stearate by Using Low-Frequency Raman Spectroscopy

Tatsuo Koide,[*,†] Toshiro Fukami,[‡] Hiroshi Hisada,[‡,§] Motoki Inoue [+]
Noriko Katori,[†] Haruhiro Okuda,[†] and Yukihiro Goda[†]

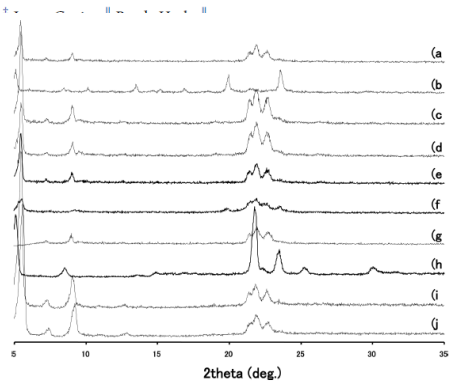
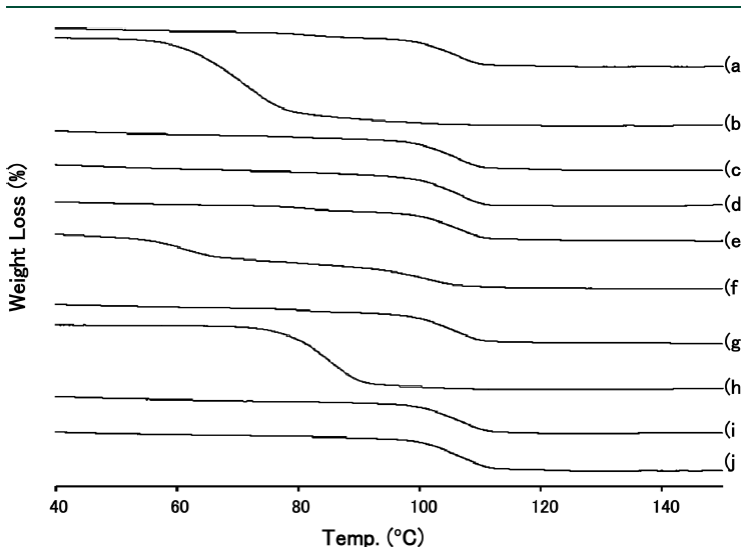


Figure 1. Powder X-ray diffraction patterns of Mg-St samples: (a) WM, (b) W1, (c) WP, (d) SG, (e) KT, (f) AL, (g) TH, (h) M2, (i) MP, and (j) MM.

Transiciones de fase y polimorfismo en fármacos

Caracterización de Sólidos

Estearato de magnesio



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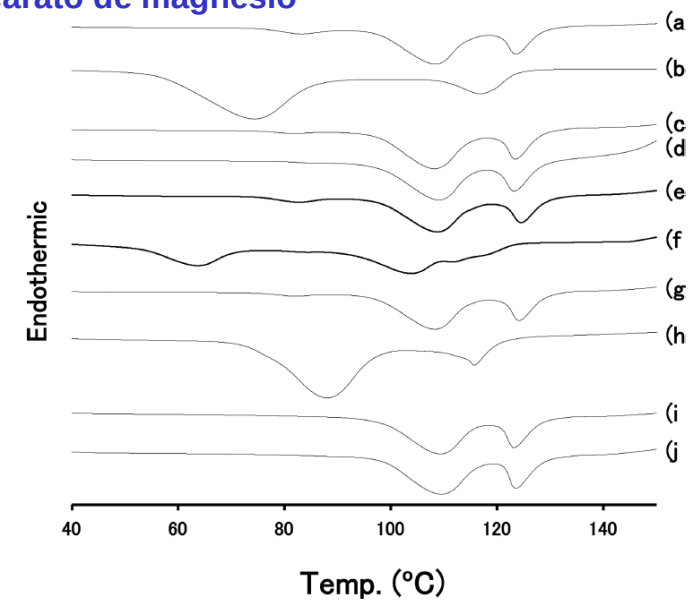
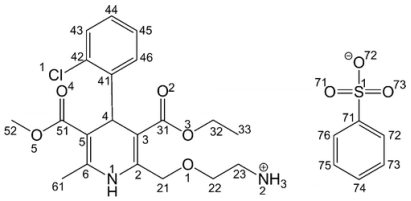


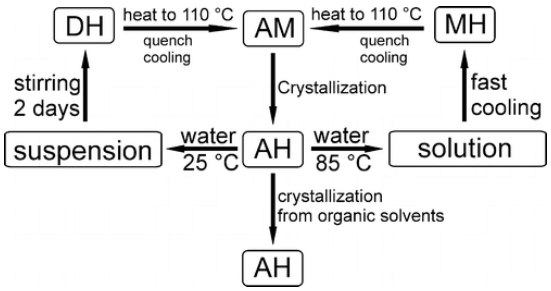
Amlodipina



Solid Forms of Amlodipine Besylate: Physicochemical, Structural, and Thermodynamic Characterization

V. Koradia, H. Lopez de Diego, K. Frydenvang, M. Ringkjøbing-Elema, A. Müllertz, A. D. Bond, J. Rantanen

Cryst. Growth Des., **2010**, *10*, 5279–5290



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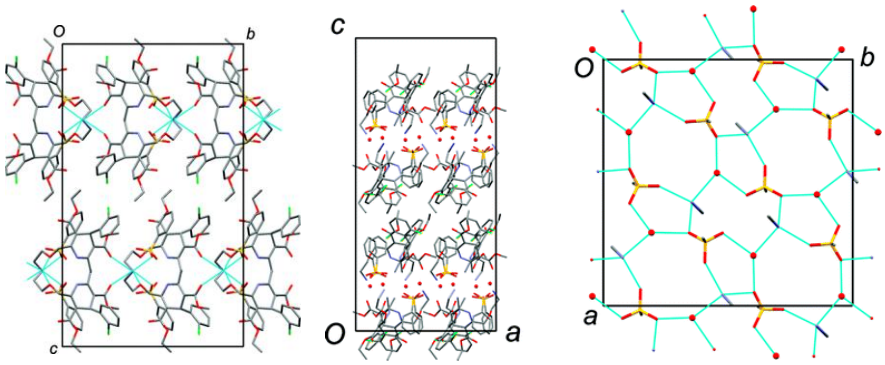
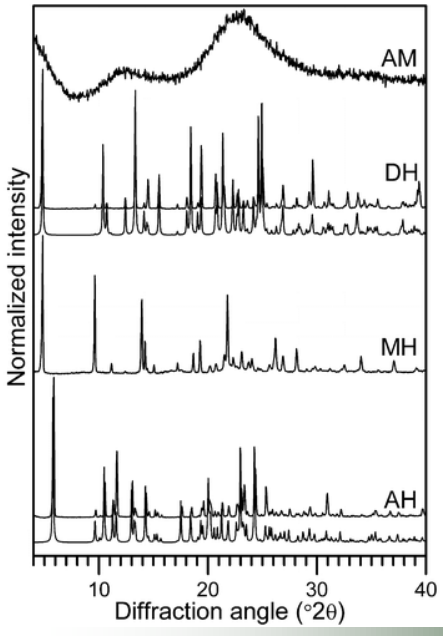


Transiciones de fase y polimorfismo en fármacos

Caracterización de Sólidos

Amlodipina



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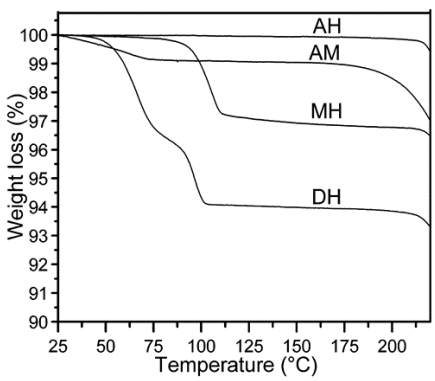
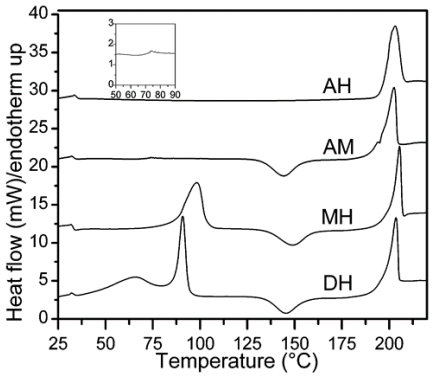
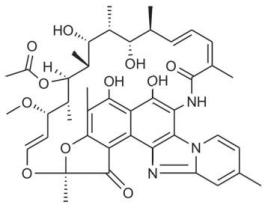
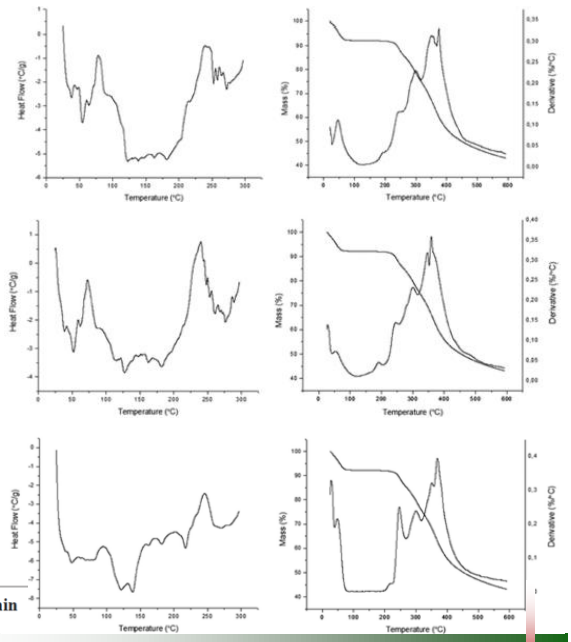




Rifaximina





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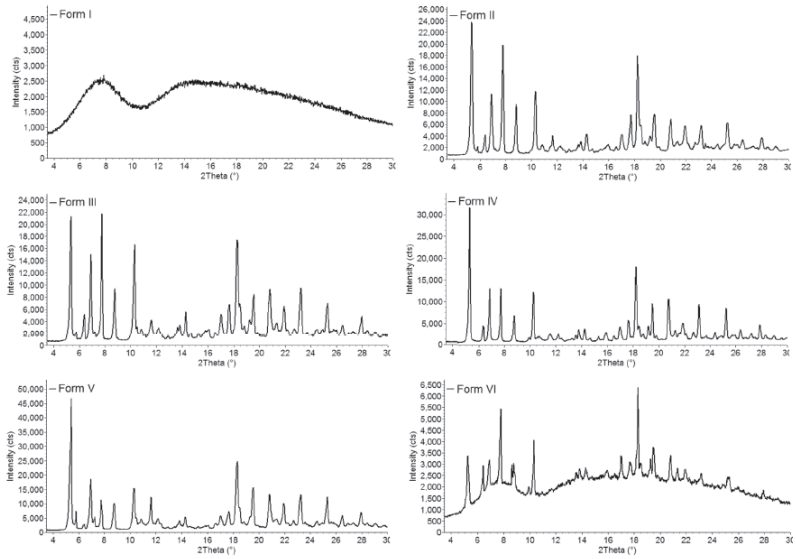
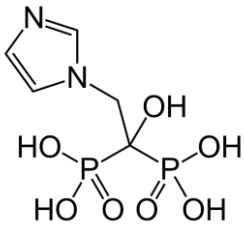
DRUG FORMULATIONS AND CLINICAL METHODS

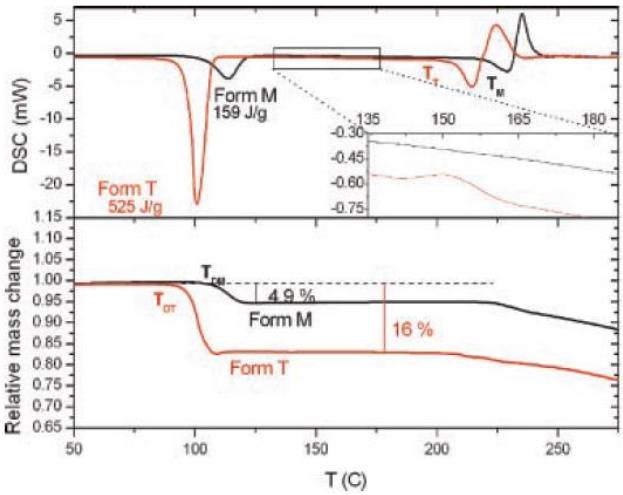
Characterization of Polymorphic Forms of Rifaximin

Rifaximina



Acido Zoledrónico





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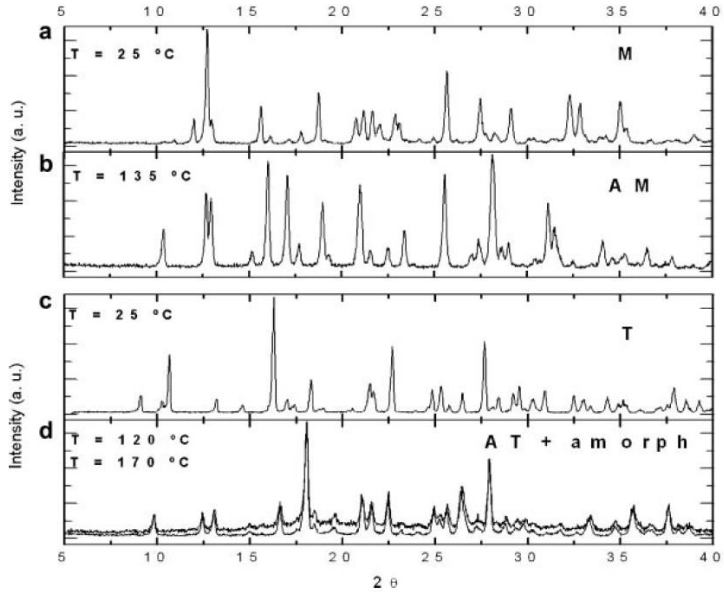
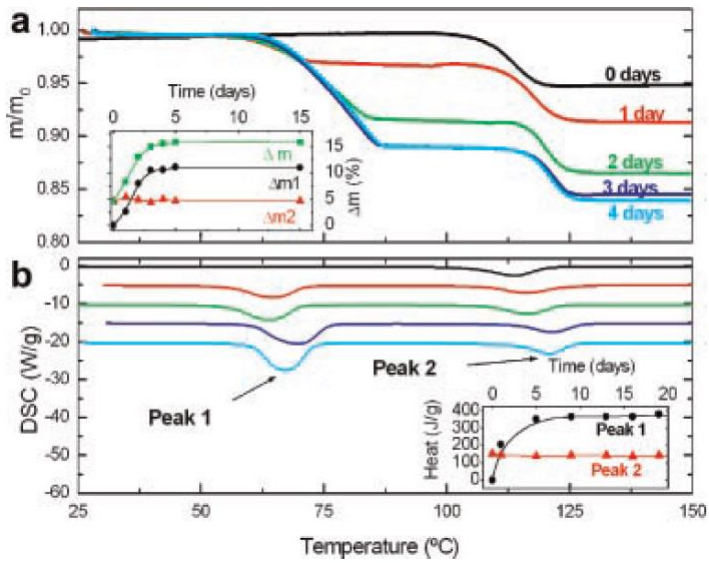


Transiciones de fase y polimorfismo en fármacos

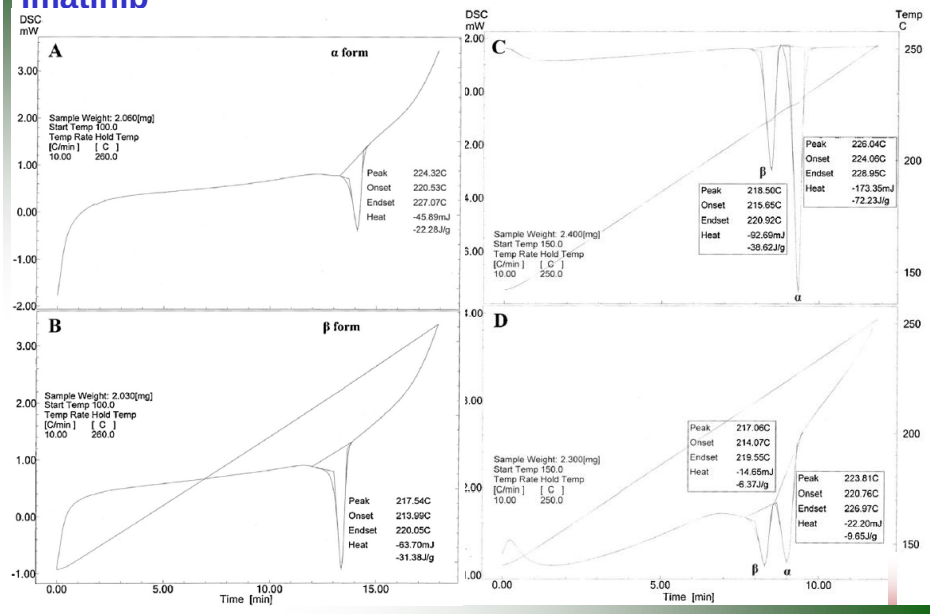
Caracterización de Sólidos

Acido Zoledrónico



Métodos Térmicos en el Estudio de Sólidos Cristalinos: Transiciones de Fase y Polimorfismo 3/50

Imatinib


A
α form
Sample Weight: 2.060[mg]
Start Temp 100.0
Temp Rate Hold Temp
[C/min] [C]
10.00 260.0
Peak 224.32C
Onset 220.53C
Endset 227.07C
Heat -45.89mJ
-22.28J/g
B
β form
Sample Weight: 2.030[mg]
Start Temp 100.0
Temp Rate Hold Temp
[C/min] [C]
10.00 260.0
Peak 217.54C
Onset 213.99C
Endset 220.05C
Heat -63.70mJ
-31.38J/g
DSC mW
Time [min]
C
Sample Weight: 2.400[mg]
Start Temp 150.0
Temp Rate Hold Temp
[C/min] [C]
10.00 250.0
β
Peak 218.50C
Onset 215.65C
Endset 220.92C
Heat -92.69mJ
-38.62J/g
α
Peak 226.04C
Onset 224.06C
Endset 228.95C
Heat -173.35mJ
-72.23J/g
D
Sample Weight: 2.300[mg]
Start Temp 150.0
Temp Rate Hold Temp
[C/min] [C]
10.00 250.0
Peak 217.06C
Onset 214.07C
Endset 219.55C
Heat -14.65mJ
-6.37J/g
β
α
Peak 223.81C
Onset 220.76C
Endset 226.97C
Heat -22.20mJ
-9.65J/g
Temp C