Analyse thermique combinée avec l'analyse structurale par XRD-DSC sur un diffractomètre polyvalent Rigaku SmartLab

53ème Journées de Calorimétrie et d'Analyse Thermique, 22-24 Mai 2023

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1. Rigaku
2. Diffractomètre Rigaku SmartLab (XRD)
3. Concept de l'XRD-DSC
4. Exemples d'analyses combinées XRD – DSC
5. Conclusions

Rigaku Corporate Profile

- Business Description: Manufacturing & Sales of Science Instruments
- Address: Headquarters・Tokyo Factory・X-ray research Lab
  Matsubara-cho, 3-9-12 Akishima, Tokyo 196-8666

  Osaka Office & Factory
  Akaoji-cho 14-8, Takatsuki, Osaka 569-1146

  Yamanashi Factory
  Wakamiko 4495-8 Sutama-cho, Hokuto, Yamanashi 408-0112
- Representative: President & CEO Jun KAWAKAMI
- Founded: 6th December 1951
- Capital: 100 Million Japanese Yen
- Employees: Approx. 730 Employees (Approx. 1,400 Group Employees)
- Annual Sales: 37.4 Billion Japanese Yen (as of FY ending March 2016)

Rigaku Analytical Technologies

XRD	XRR	SAXS	XRF	XRT & CT	TA & EGA	Raman
Crystal Structure & Lattice Constant	**Film Thickness, Density & Roughness**	**Particle Size & Shape**	**Elemental Analysis & Thin Film Analysis**	**Internal Structure Defects & Foreign Bodies 3D Observation**	**Thermal Properties (Decomposition, Expansion, Melting, Transition, Oxidation, Crystallization) Evolved Gas**	**Material Identification on Vibration Spectra**
• Ceramics • Nanocarbon • Nanoglass • Battery Materials • Superconductors • Nanometals	• Multilayer Film • Amorphous Films • Patterend Wafers	• Metallic Nanoparticles • Nanoholes • Nanowire • Nanodots • Nanotubes	• Ceramics • Battery Materials • Ferrous/Nonferrous • Platings & Coatings • WEEE, RoHS • Glass	• Bio • Lab Animals • Pharmaceuticals, Rubber • Lightweight Materials • Electronic Components	• Ceramics • Magnetic Material • Glass • Polymers • Thin Films	• Narcotics, Hazardous Substances • Pharmaceutical Raw Materials • Plastics

Micro-area, micro-volume, ultra thin films, high resolution, sensitivity & throughput, complex info systems, in-situ, automation

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2. **Diffractomètre Rigaku SmartLab (XRD)**
3. Concept de l'XRD-DSC
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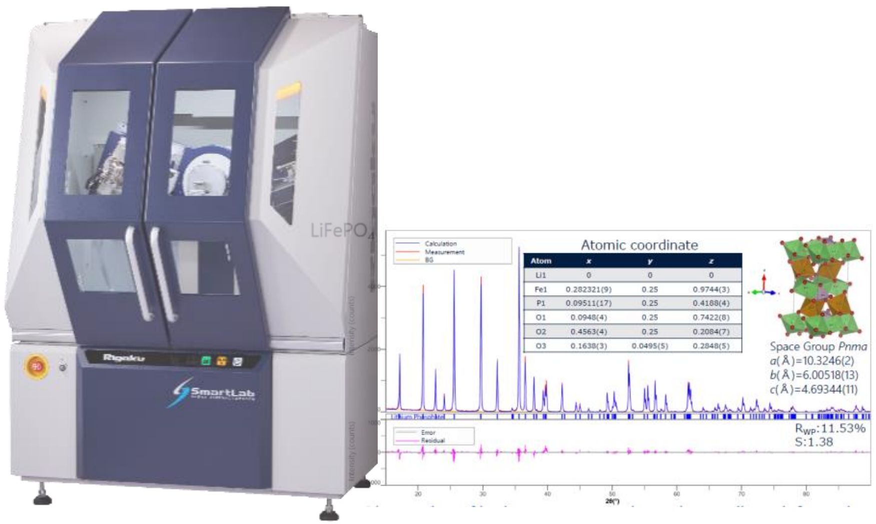
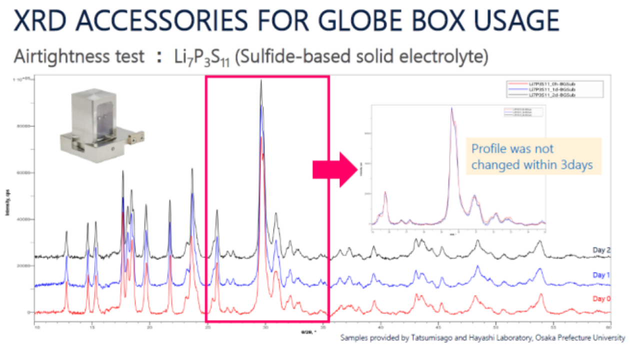
DIFFRACTOMÈTRE POLYVALENT SMARTLAB





- Diffraction des rayons-X sur de la poudre : structure ; concentration ; taux de cristallinité, etc…

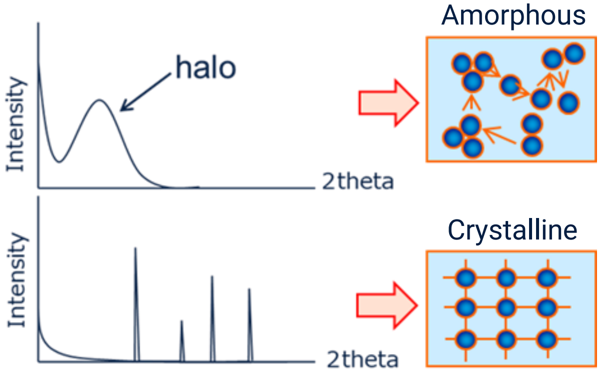
  Géométrie qui permet de maintenir l’échantillon à l’horizontal

- Travail en atmosphère contrôlée

  Permet de passer très rapidement d’une application à une autre (diffusion des rayons-X, analyses combinées en température, analyse de couches minces, etc…

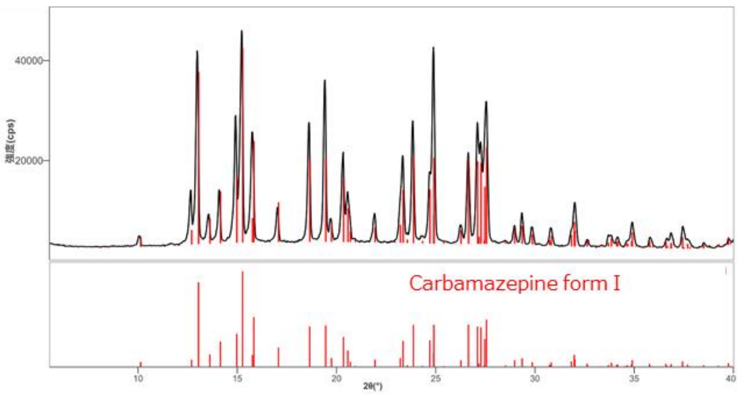
Applications of XRD

Diffraction profile



crystalline or amorphous?

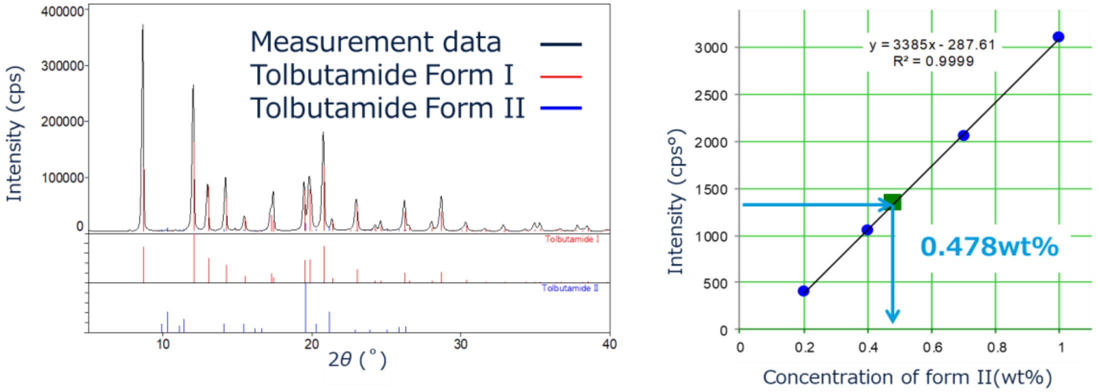
Qualitative analysis



crystal polymorphs?

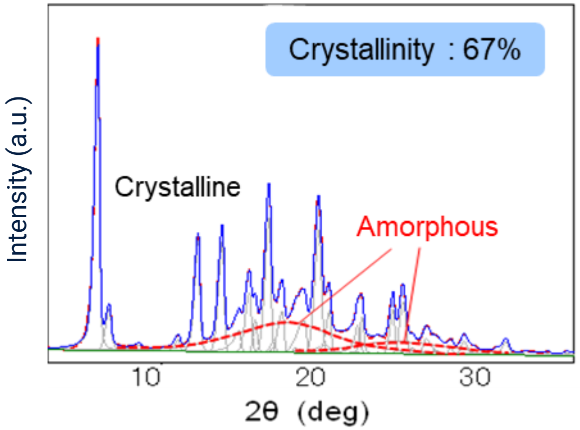
Quantitative analysis

content?

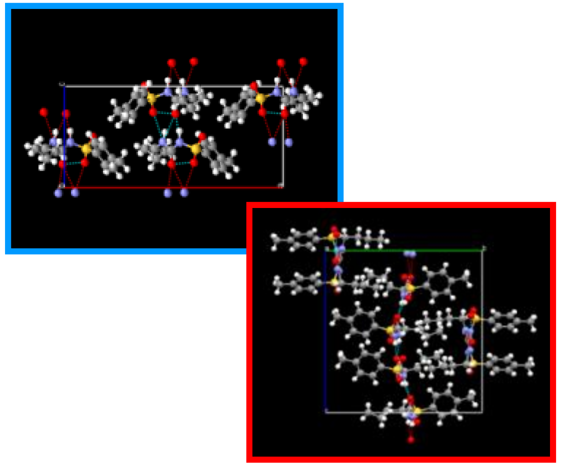


Crystallinity

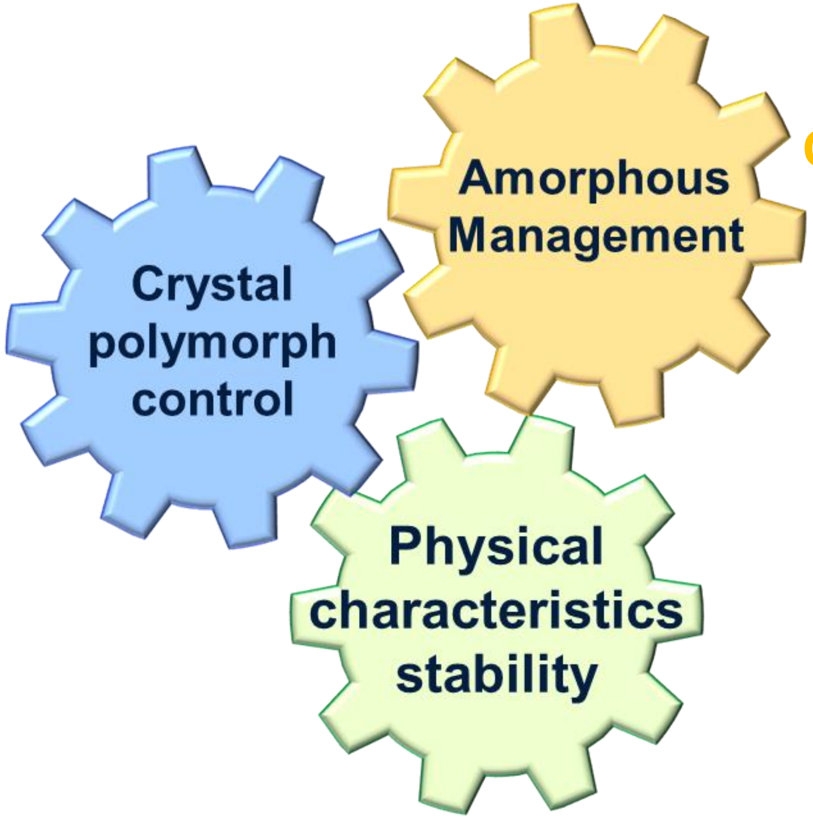
crystallinity?



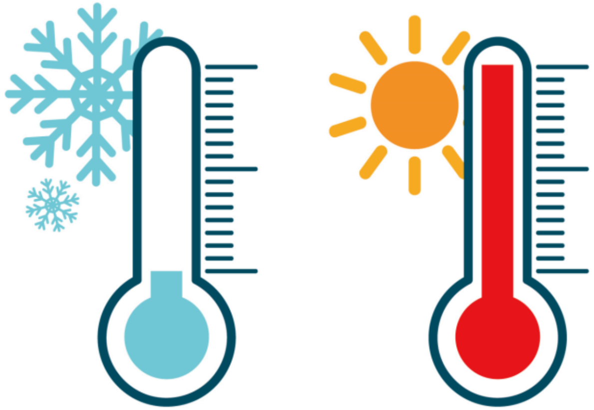
Solid-form screening process



Crystal polymorph
Qualitative / quantitative



Quantification of crystalline and amorphous phases



Temperature / humidity change

XRD and DSC are used as analytical methods

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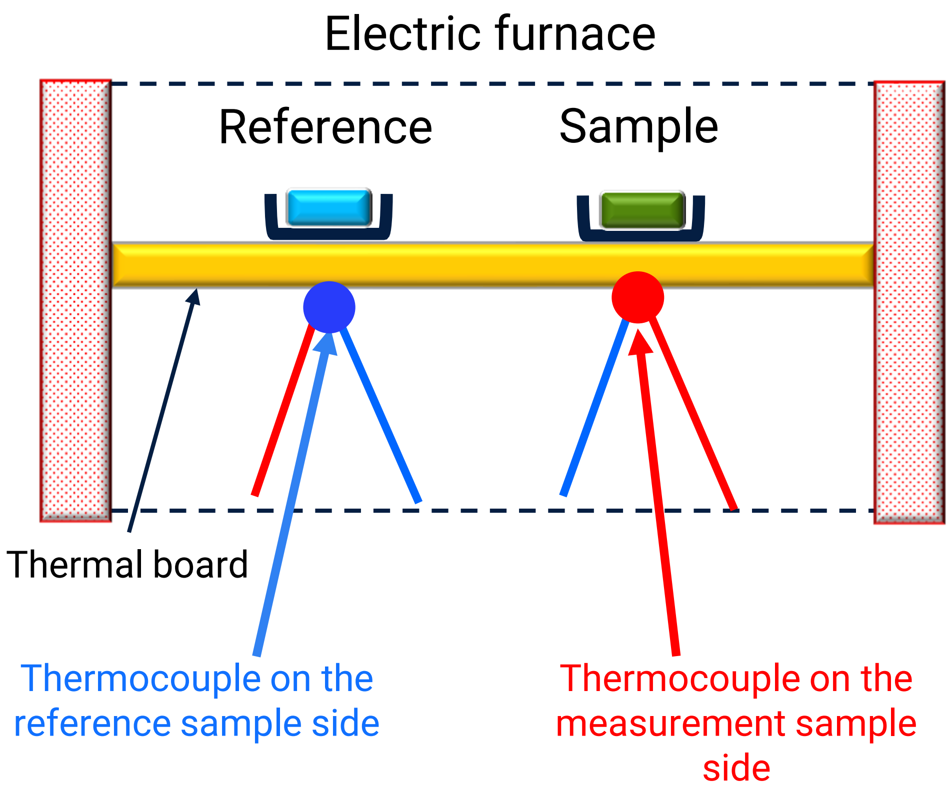
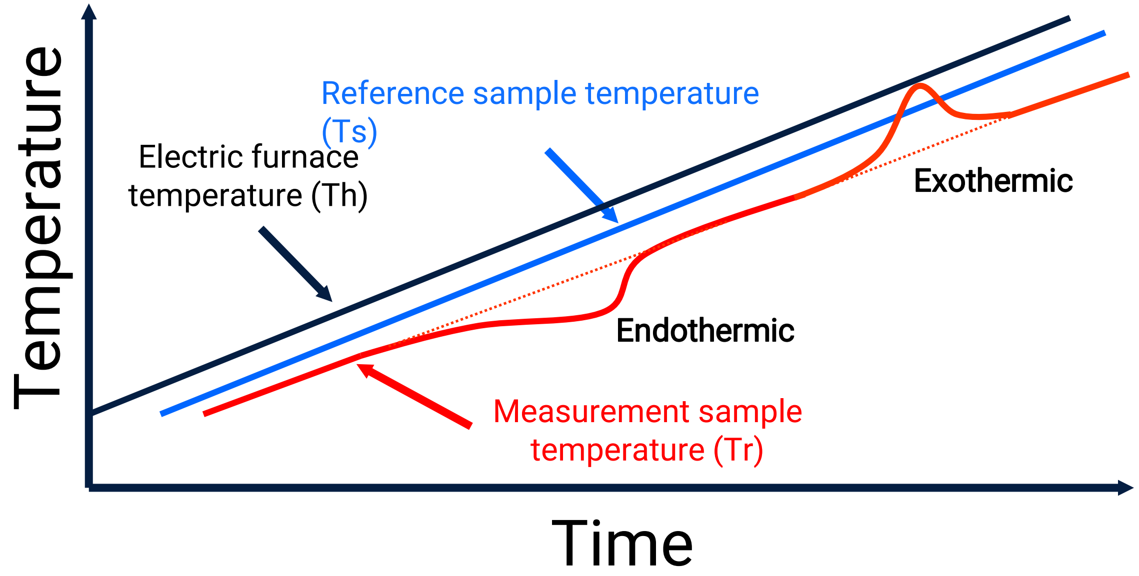
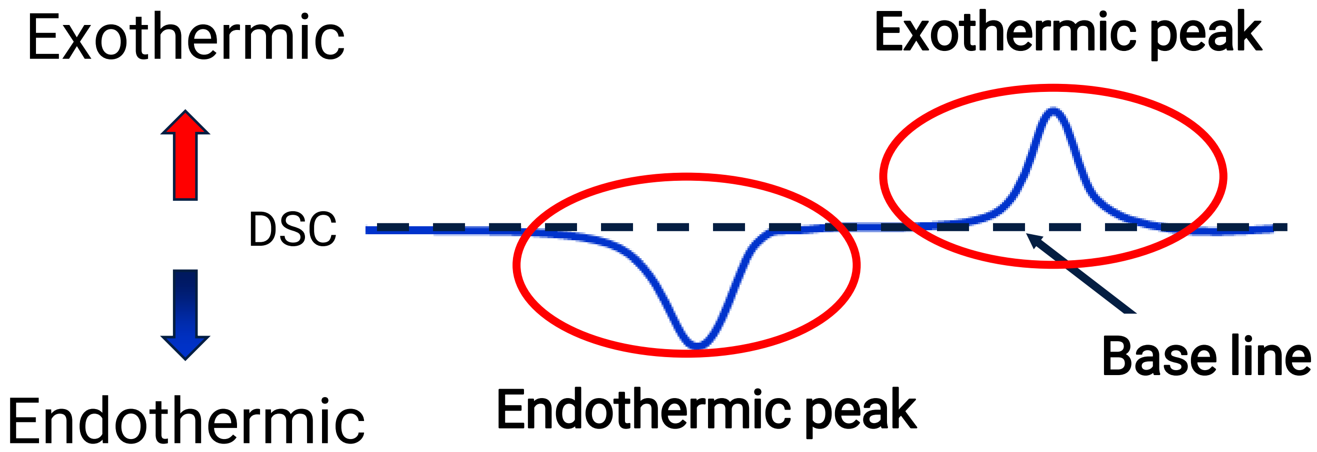
DSC (Differential Scanning Calorimetry)

* Reference sample: A substance that does not change within the measurement temperature range

■ DSC principle



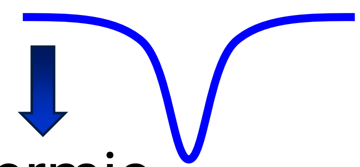




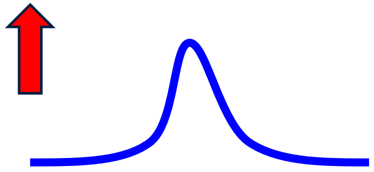
Application of DSC

Exothermic

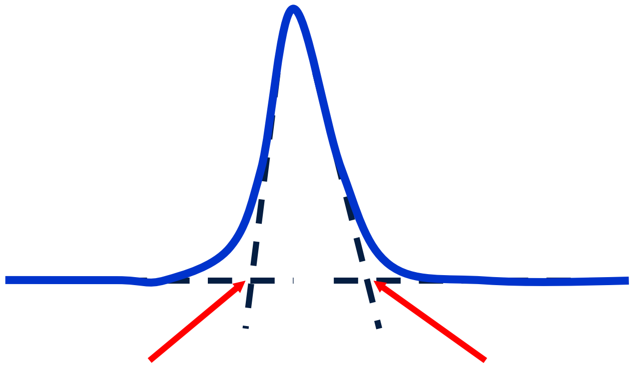
Endothermic

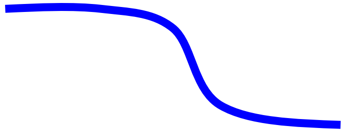


Melting
Crystal phase transition

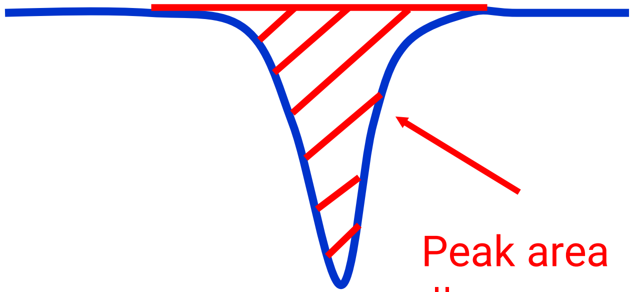


Crystallization
Crystal phase transition

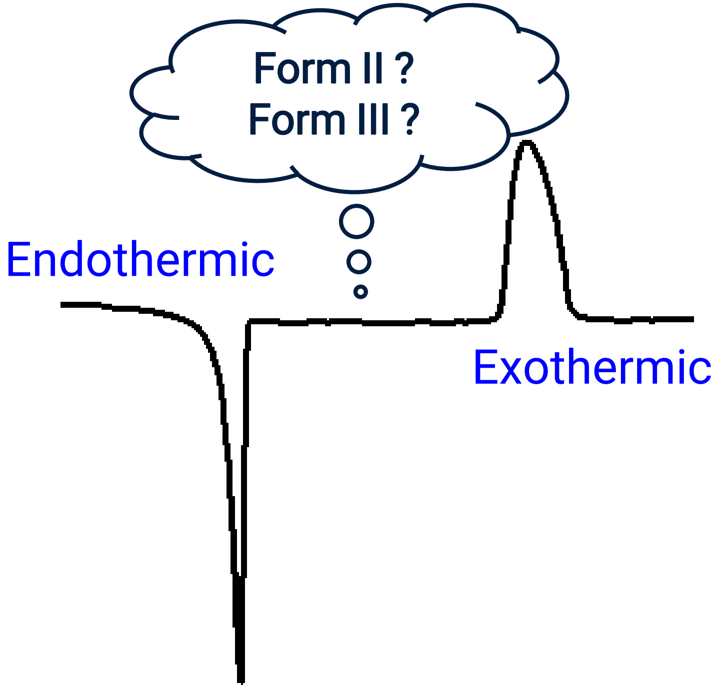




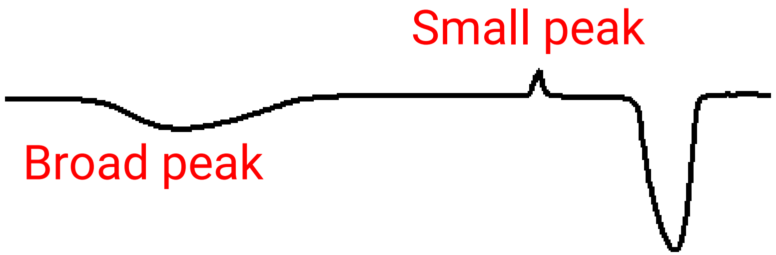
Glass transition



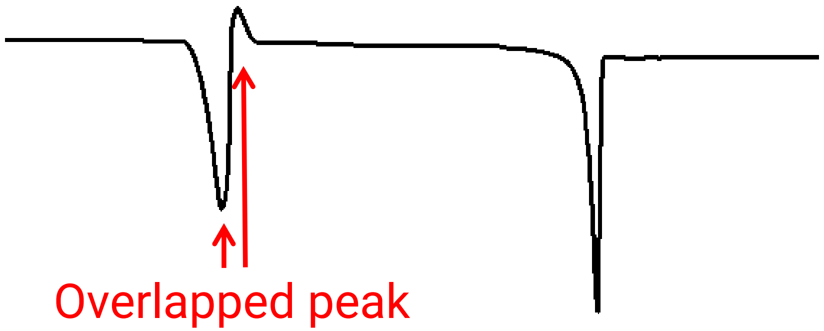
Disadvantages of DSC



- Interpretation of result is often difficult
- Difficult to interpret physical changes of the sample



- Extremely broad peaks and minute peaks may be overlooked



- Analysis of close reactions is difficult

Individual application of XRD and DSC

- Not enough information can be obtained by thermal analysis alone
- Results may differ depending on the potential of the analyzer
- Large quantity of sample is needed, and analysis factors (time and cost) are higher according to the type of analyzer

How to increase the efficiency?

How to solve this problem?

"XRD-DSC" attachment
can measure XRD and DSC simultaneously

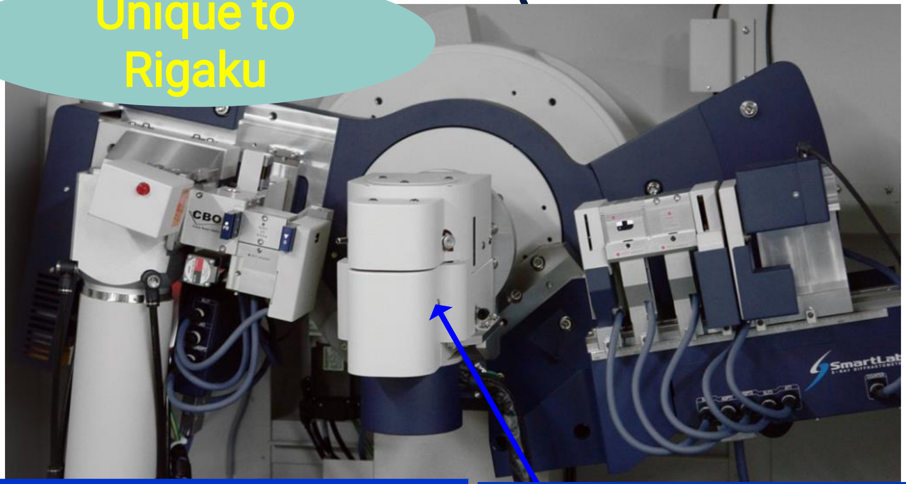
XRD-DSC

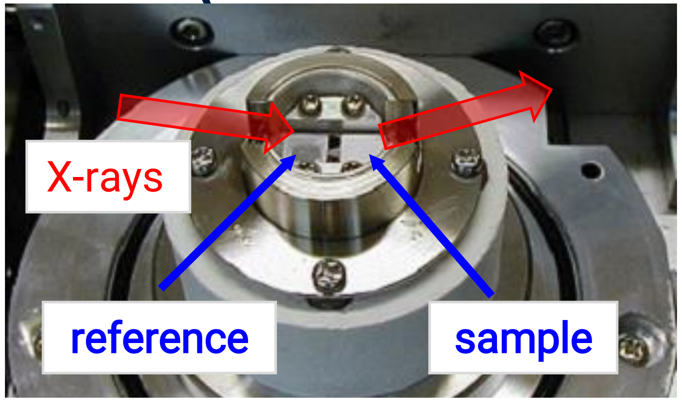
Specifications

❑ Temperature range:	RT to 350 °C - 40 to 350°C (when using the optional low-temperature bath circulator)
❑ Atmosphere:	Air, Nitrogen
❑ Humidity:	RT 5%RH up to 60°C 90%RH
❑ Heating/cooling:	0.5 to 10 °C/min
❑ XRD:	1.5 to 60°/2 theta
❑ Scan speed:	Maximum 100°/min

SIMULTANEOUS XRD AND DSC MEASUREMENT ATTACHMENT (XRD-DSC)

Unique to Rigaku





SmartLab
X-ray Diffractometer

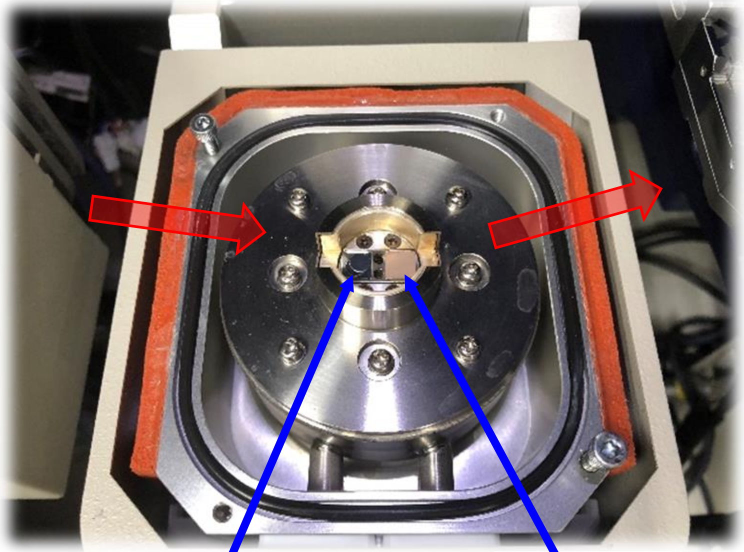
X-ray DSC
XRD-DSC attachment

★**sample amount**	**3 - 10 mg**
★**temp. range**	**RT - 350 ℃(-40 ℃ -*)**
★**atmosphere**	**static air, inert gas, humid gas***
	(- 60 ℃ 90%RH corresponding to 17.9 kPa)
	***…optional**

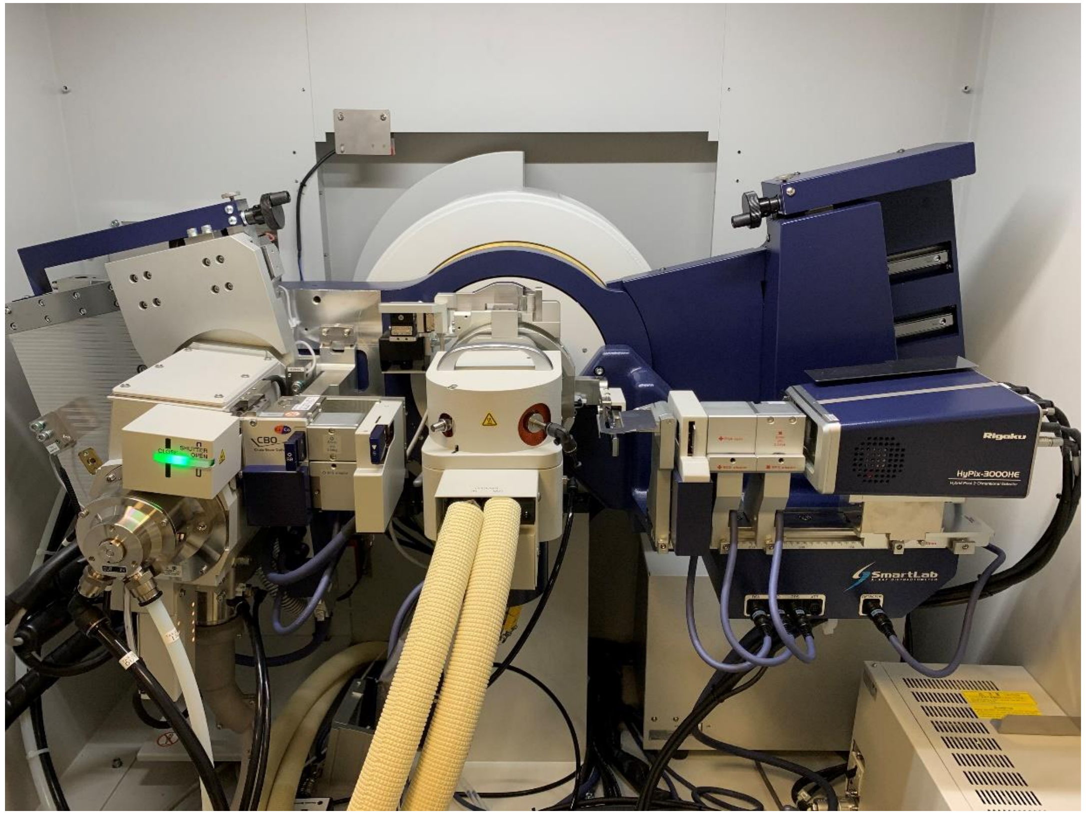
Crystal structural changes and thermal reactions can be observed from one sample in a given atmosphere

XRD-DSC

Sample chamber



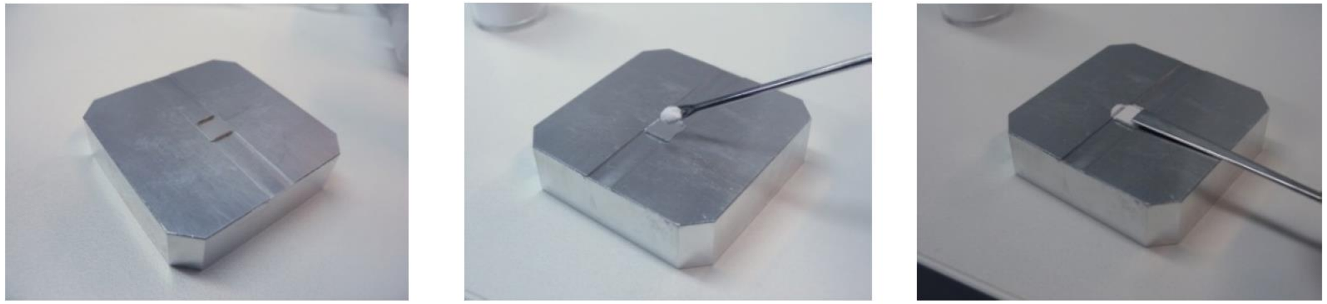
Sample pan: Aluminum sample pan 7 x 7 x 0.9 (0.3) mm
Sample amount: 3 - 10 mg



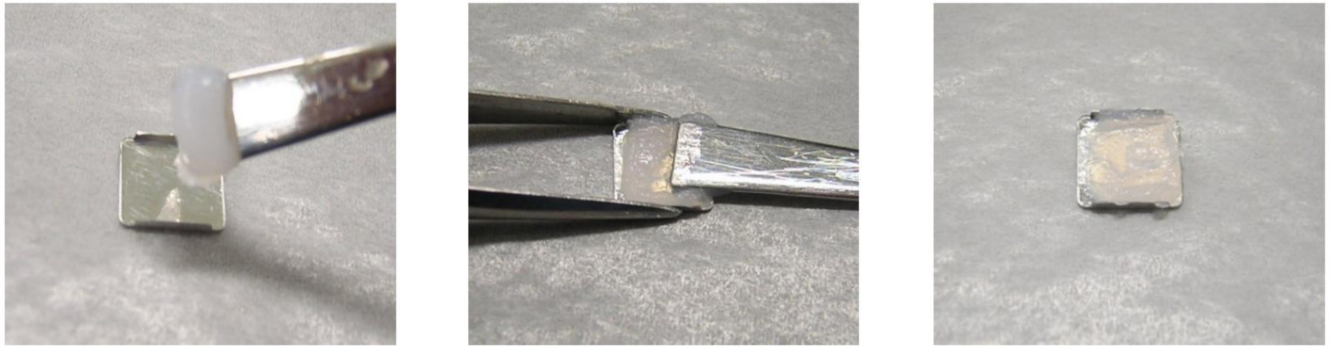
XRD-DSC

Sample preparation

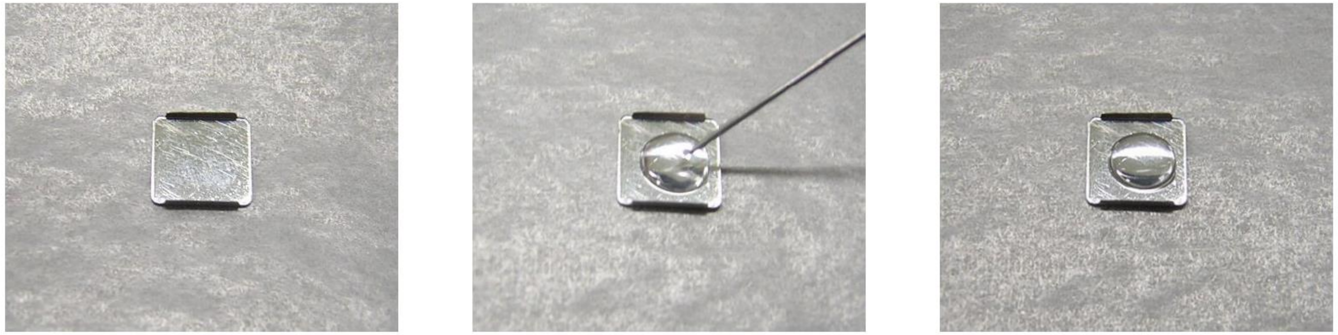
Powder



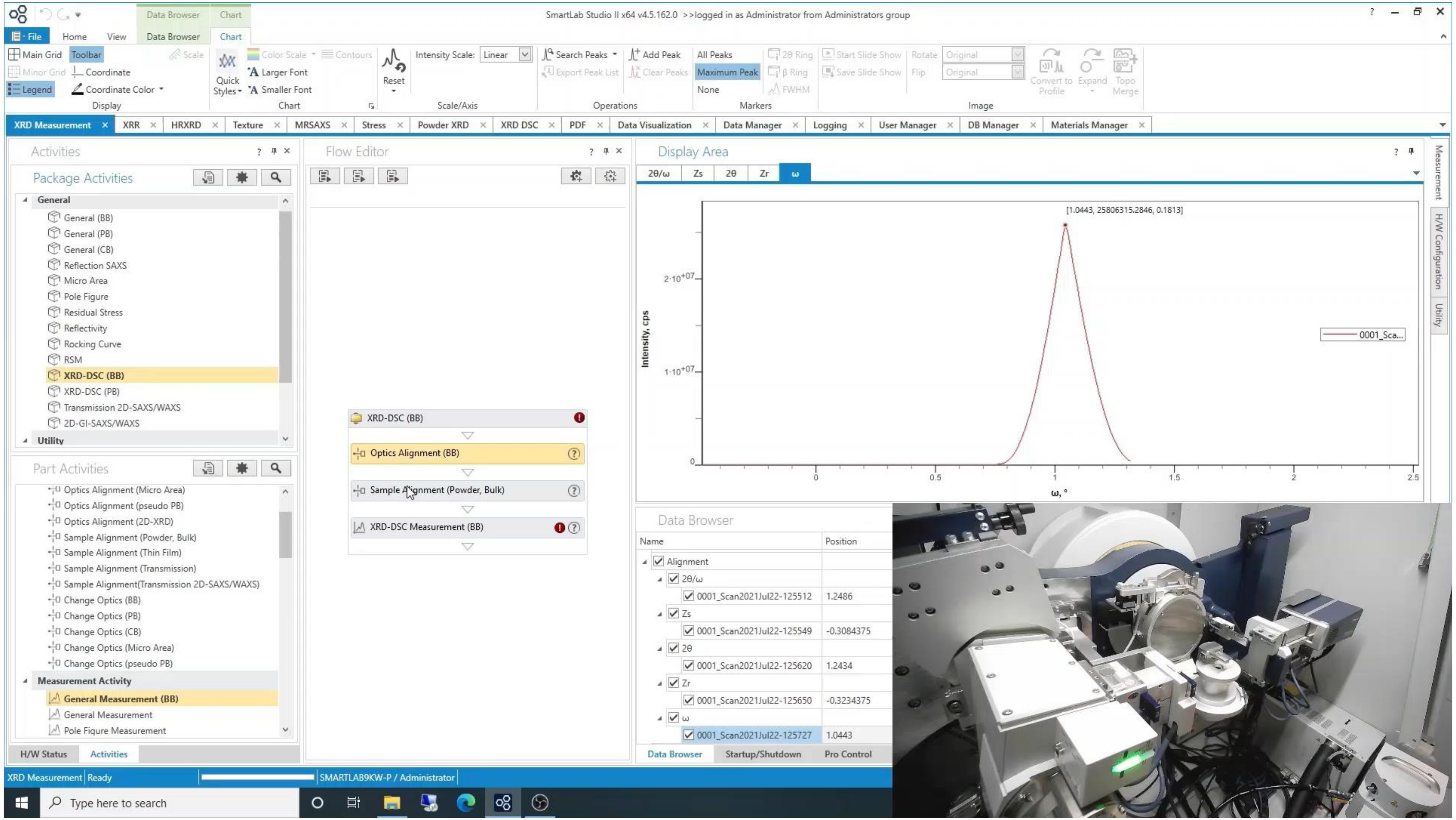
Gel, fat



Liquid



XRD-DSC


SmartLab Studio II x64 v4.5.162.0 >>logged in as Administrator from Administrators group
File
Home
View
Data Browser
Chart
Main Grid
Toolbar
Minor Grid
Coordinate
Legend
Coordinate Color
Display
Quick Styles
Larger Font
Smaller Font
Chart
Reset
Intensity Scale:
Linear
Scale/Axis
Search Peaks
Export Peak List
Add Peak
Clear Peaks
Operations
All Peaks
Maximum Peak
None
Markers
Image
XRD Measurement
XRR
HRXRD
Texture
MRSAXS
Stress
Powder XRD
XRD DSC
PDF
Data Visualization
Data Manager
Logging
User Manager
DB Manager
Materials Manager
Activities
Package Activities
General
General (BB)
General (PB)
General (CB)
Reflection SAXS
Micro Area
Pole Figure
Residual Stress
Reflectivity
Rocking Curve
RSM
XRD-DSC (BB)
XRD-DSC (PB)
Transmission 2D-SAXS/WAXS
2D-GI-SAXS/WAXS
Utility
Part Activities
Optics Alignment (Micro Area)
Optics Alignment (pseudo PB)
Optics Alignment (2D-XRD)
Sample Alignment (Powder, Bulk)
Sample Alignment (Thin Film)
Sample Alignment (Transmission)
Sample Alignment(Transmission 2D-SAXS/WAXS)
Change Optics (BB)
Change Optics (PB)
Change Optics (CB)
Change Optics (Micro Area)
Change Optics (pseudo PB)
Measurement Activity
General Measurement (BB)
General Measurement
Pole Figure Measurement
H/W Status
Activities
Flow Editor
XRD-DSC (BB)
Optics Alignment (BB)
Sample Alignment (Powder, Bulk)
XRD-DSC Measurement (BB)
Display Area
2θ/ω
Zs
2θ
Zr
ω
[1.0443, 25806315.2846, 0.1813]
Intensity, cps
ω, °
0001_Sca...
Data Browser
Name
Position
Alignment
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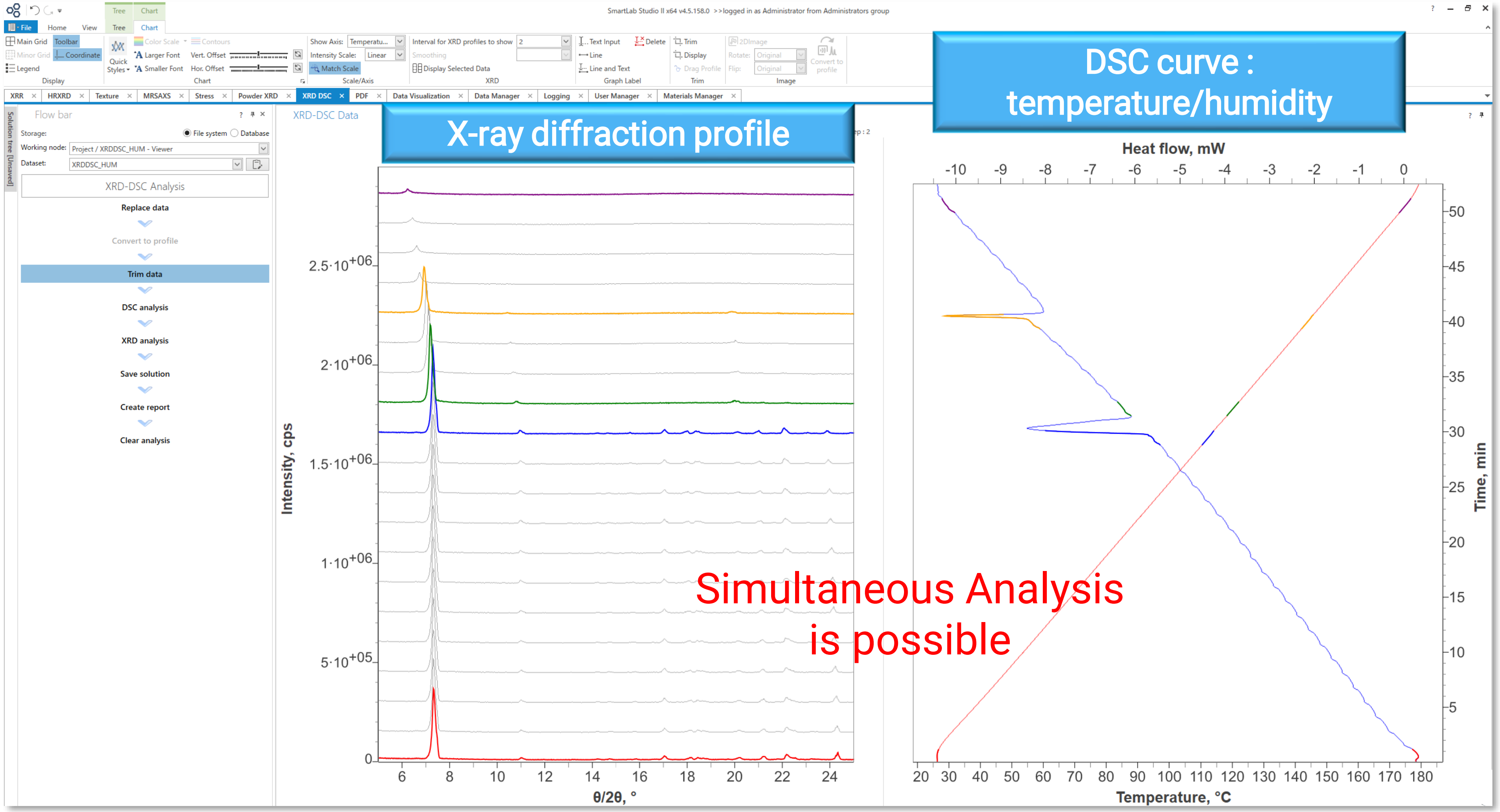
0001_Scan2021Jul22-125620
1.2434
0001_Scan2021Jul22-125650
-0.3234375
0001_Scan2021Jul22-125727
1.0443
Startup/Shutdown
Pro Control
Measurement
H/W Configuration
Utility
XRD Measurement
Ready
SMARTLAB9KW-P / Administrator
Type here to search

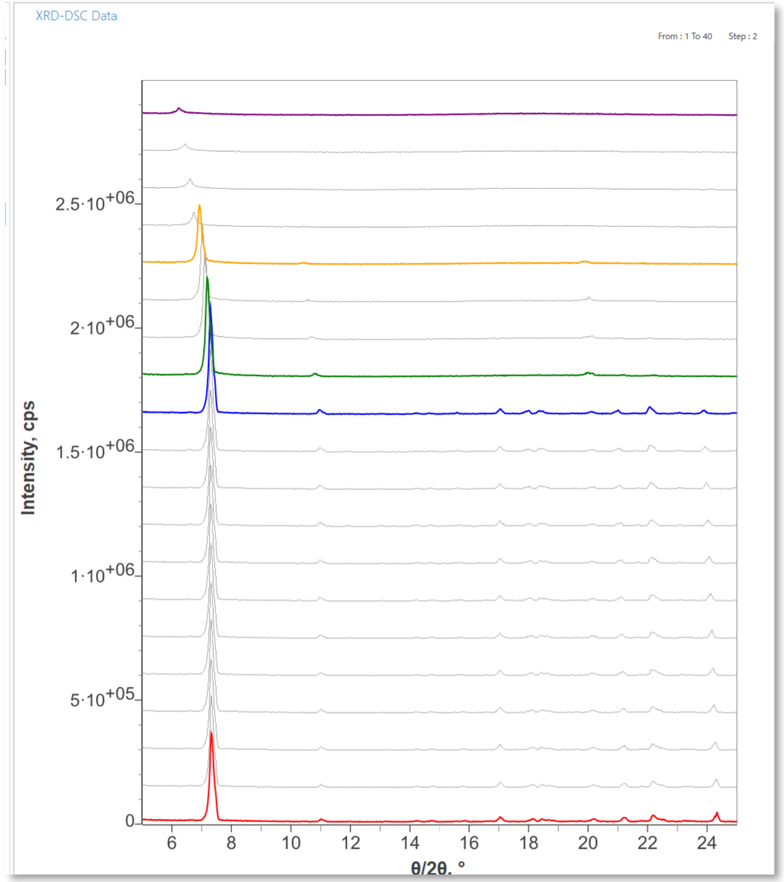
XRD-DSC

XRD-DSC Analysis



XRD-DSC

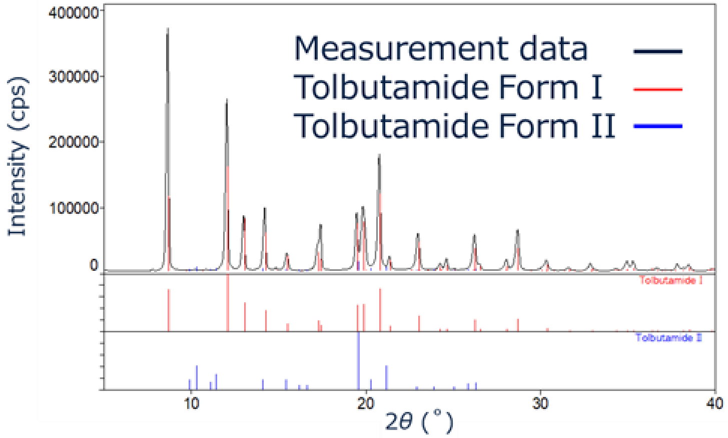
XRD-DSC Analysis



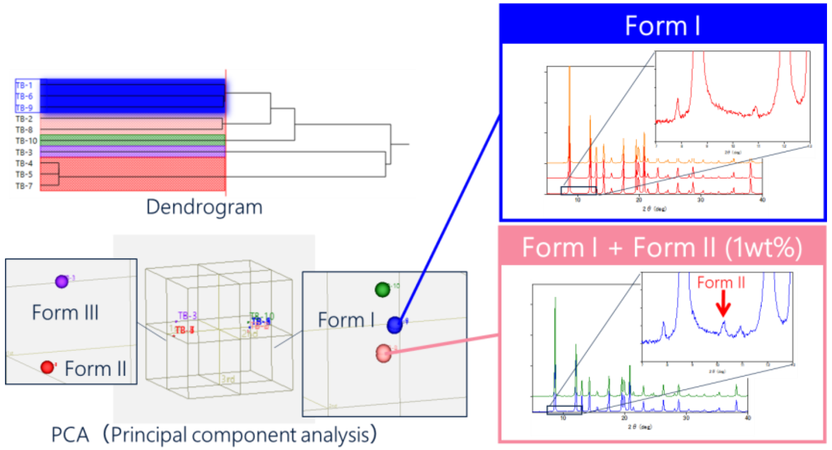
Various analyses are possible

Powder XRD Analysis

Crystal phase identification/ quantification

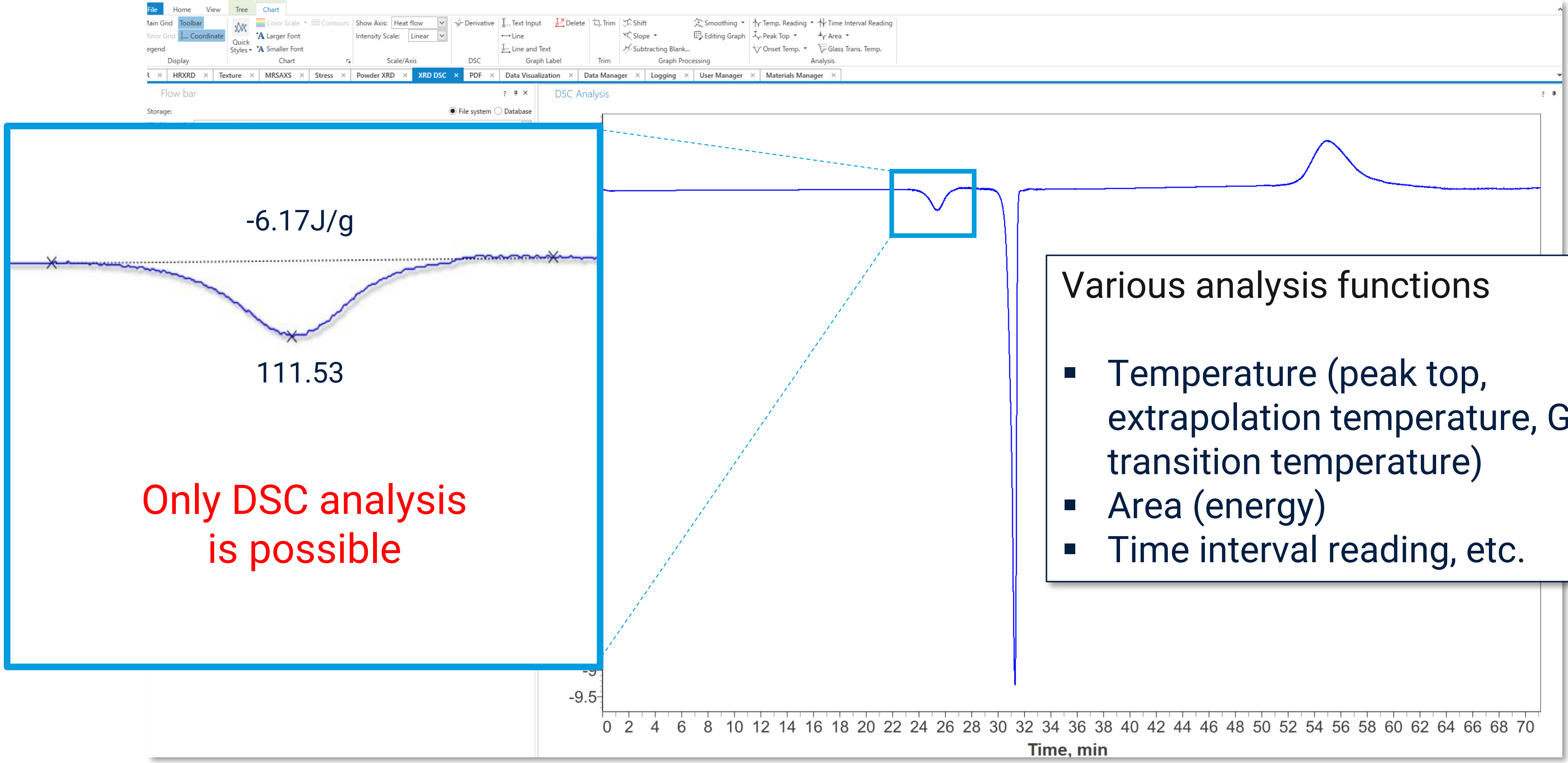


Cluster analysis



XRD-DSC

XRD-DSC Analysis



Only DSC analysis is possible

Various analysis functions

- Temperature (peak top, extrapolation temperature, Glass-transition temperature)
- Area (energy)
- Time interval reading, etc.

SOMMAIRE

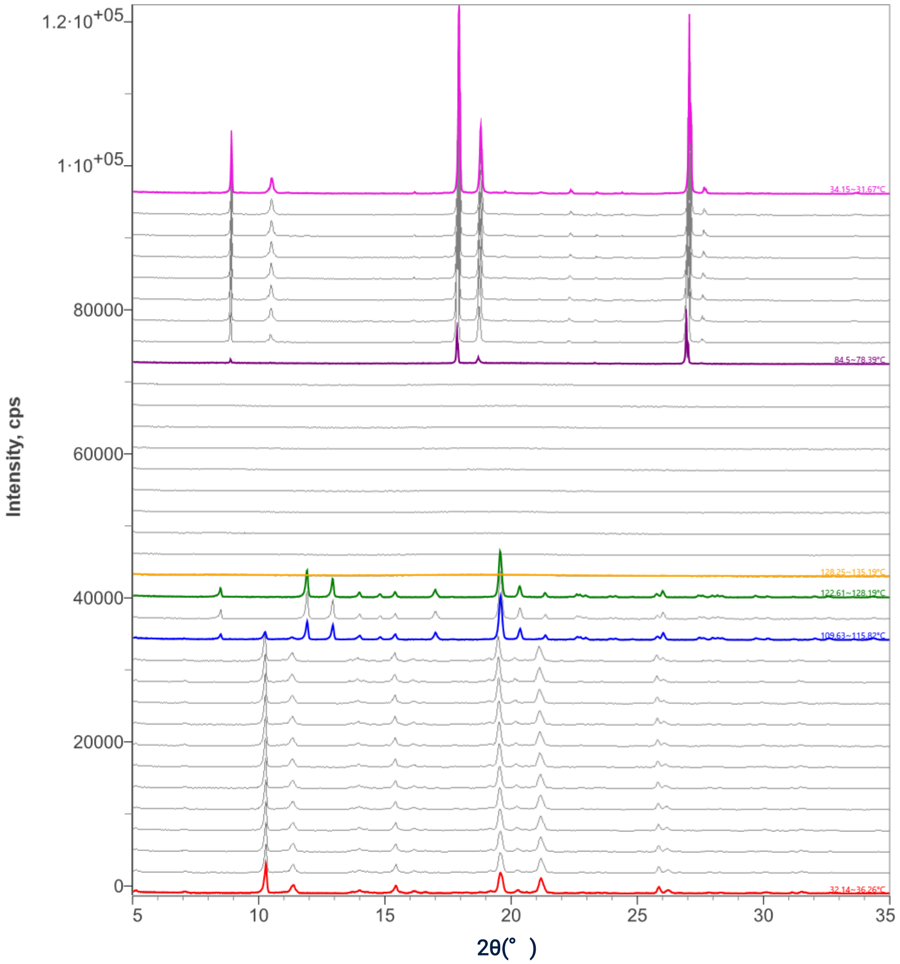
2 EXEMPLES

1. Tolbutamide
2. Lyophilisation d’une solution de d-MANNITOL

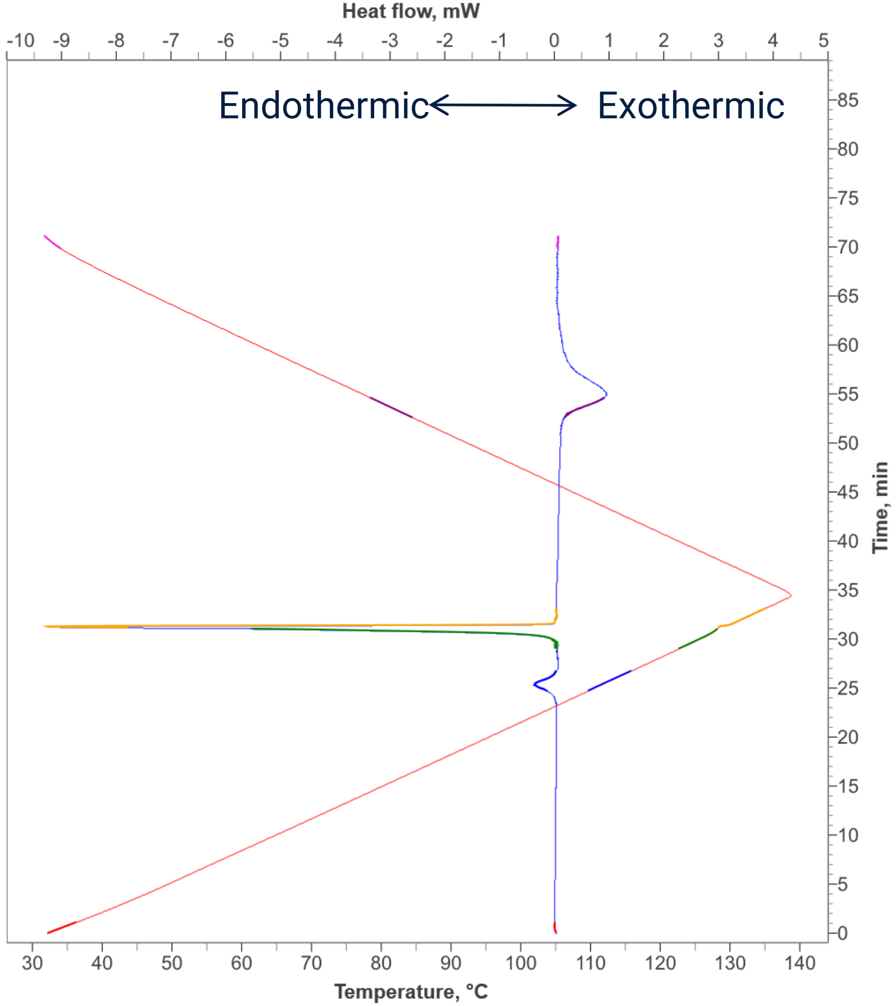
Autres notes d’applications disponibles sur demande

XRD-DSC measurement of Tolbutamide

X-ray diffraction profile



DSC curve and temperature



Heating / cooling measurement

Recrystallization： 30℃

↑

Recrystallization： 78℃

↑

Melting： 129℃

↑

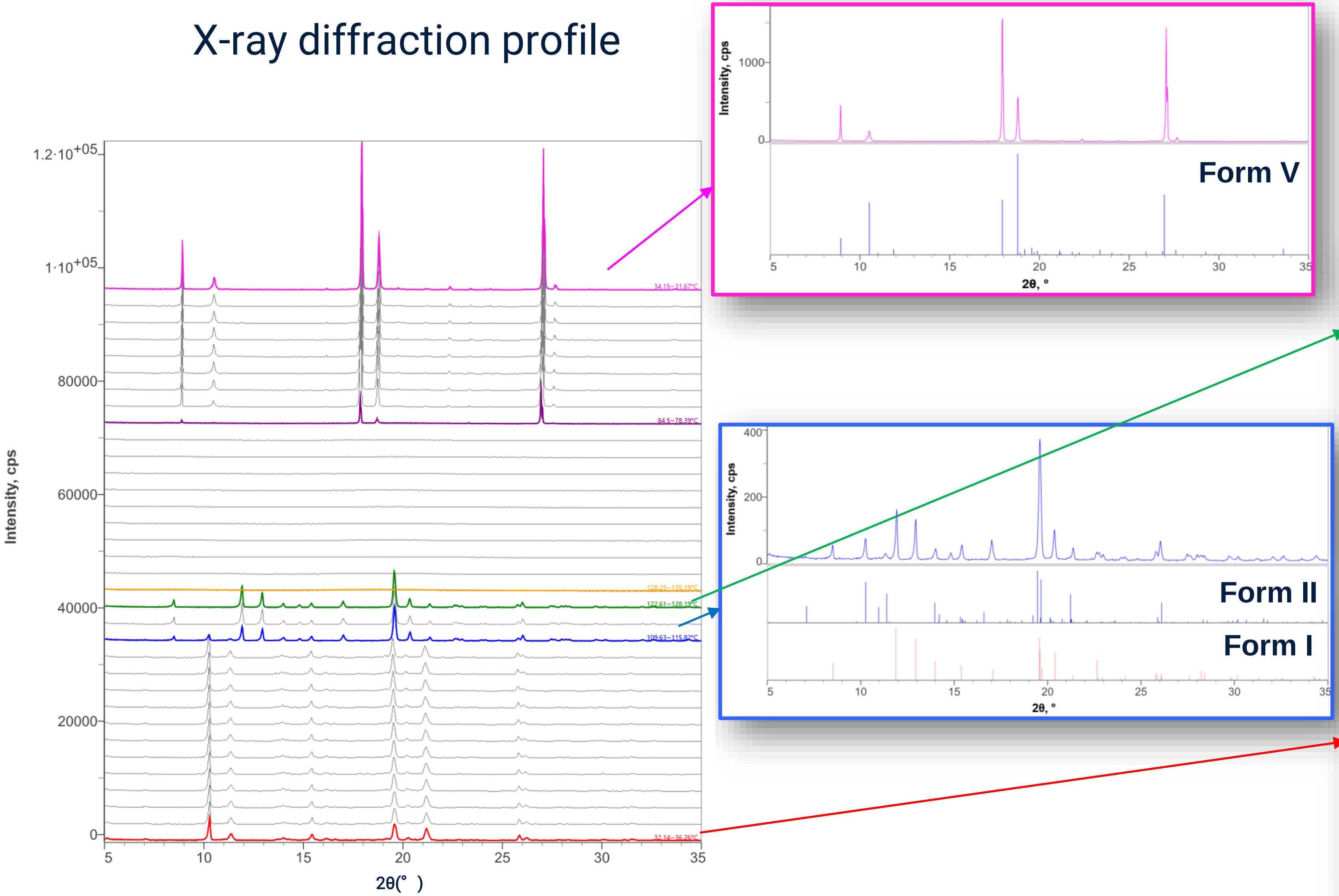
Phase transition： 112℃

↑

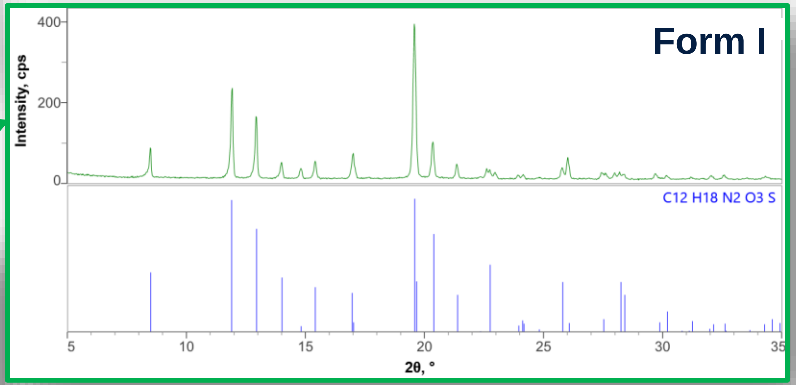
Type II： 30℃

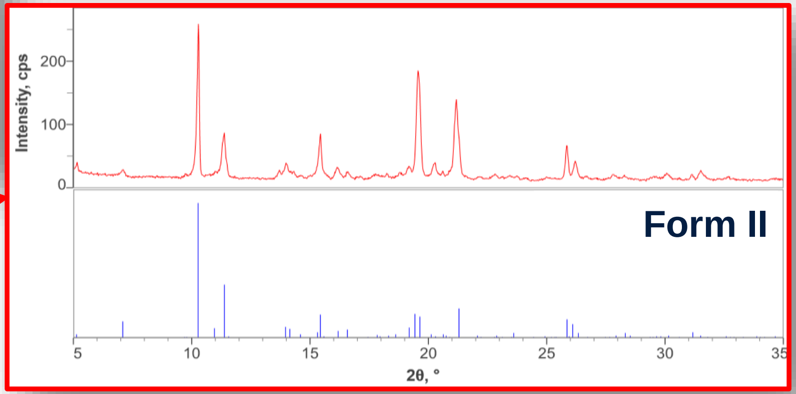
XRD-DSC measurement of Tolbutamide

X-ray diffraction profile

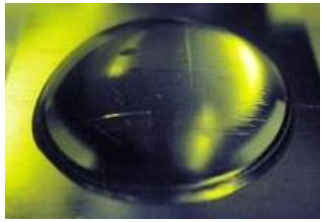


Powder XRD Analysis





FREEZE DRY CONDITION

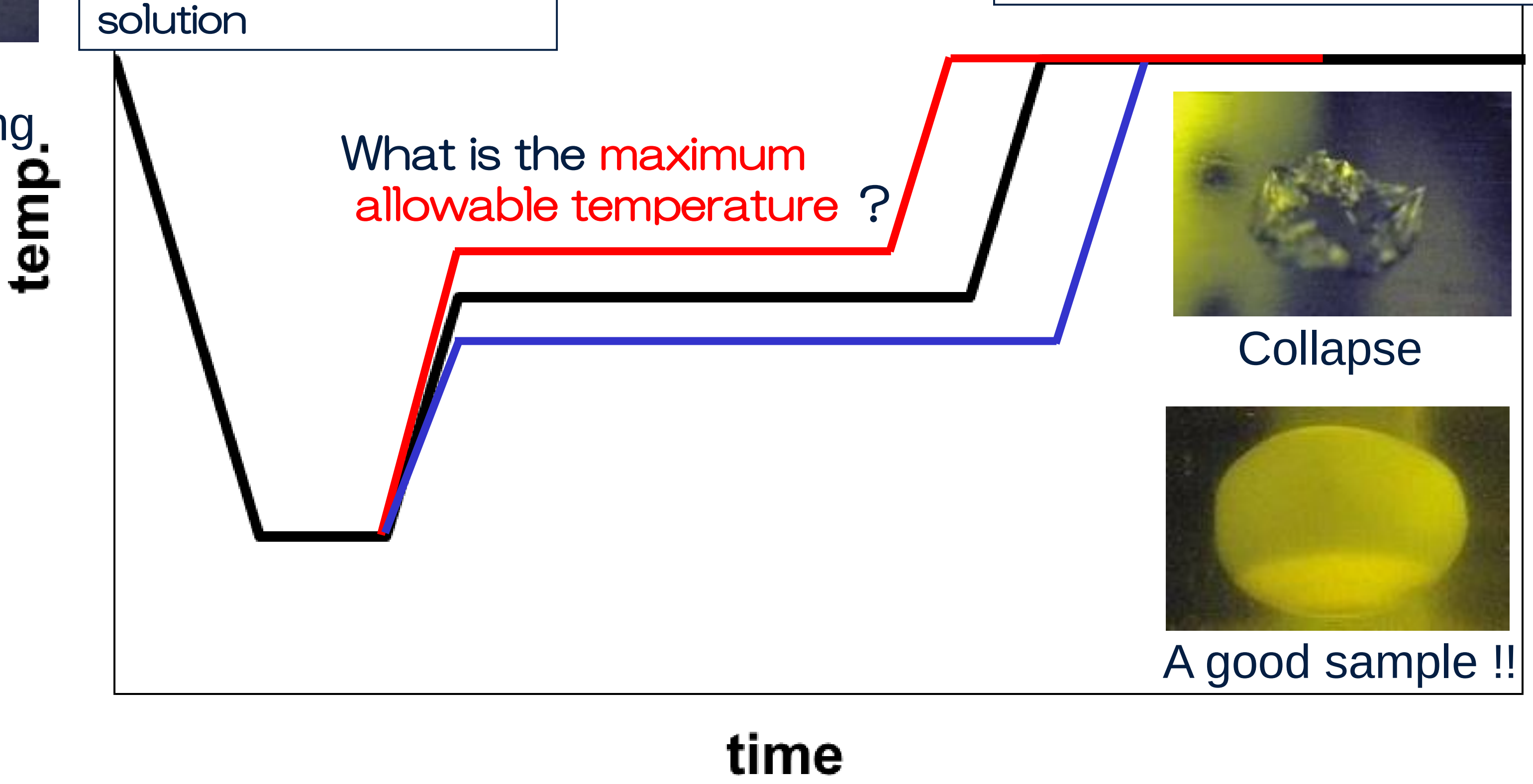


Before
Freeze drying

Freezing
Freezing of water and condensation of the solution

First drying
Sublimation of water

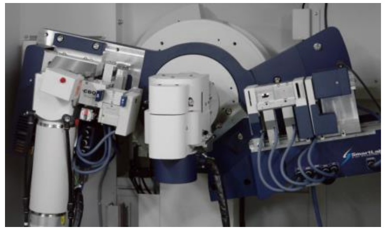
Second drying
Vaporization of water from solid



Crystallization behavior change by contents and concentration.
Development of the correct conditions can be difficult.

XRD-DSC ATTACHMENT AND HIGH AND LOW TEMP. ATTACHMENT

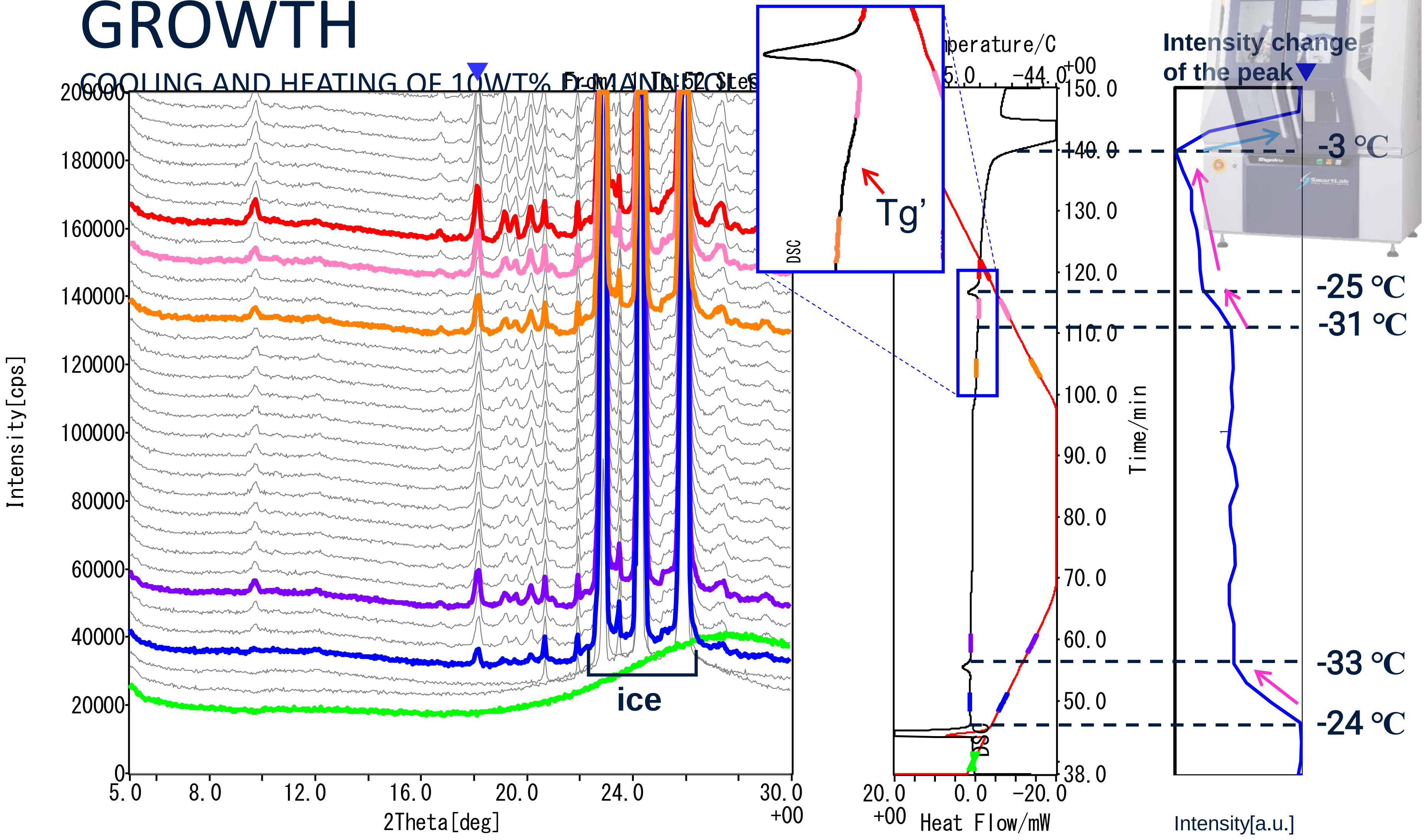
SIMULATION OF THE FREEZE DRYING PROCESS

DSC **XRD-DSC attachment** 	**TTK600** **High and low temp. attachment** 
★Temp. range ：-40～350 ℃ ★Thermal reactions ⇒ Crystallization Glass transition; *T*g’	★Temp. range : -190～600 ℃ ★Vacuum ⇒ for freeze drying

Structurals changes during the freezing and drying process can be observed

THERMAL REACTION AND CRYSTAL GROWTH

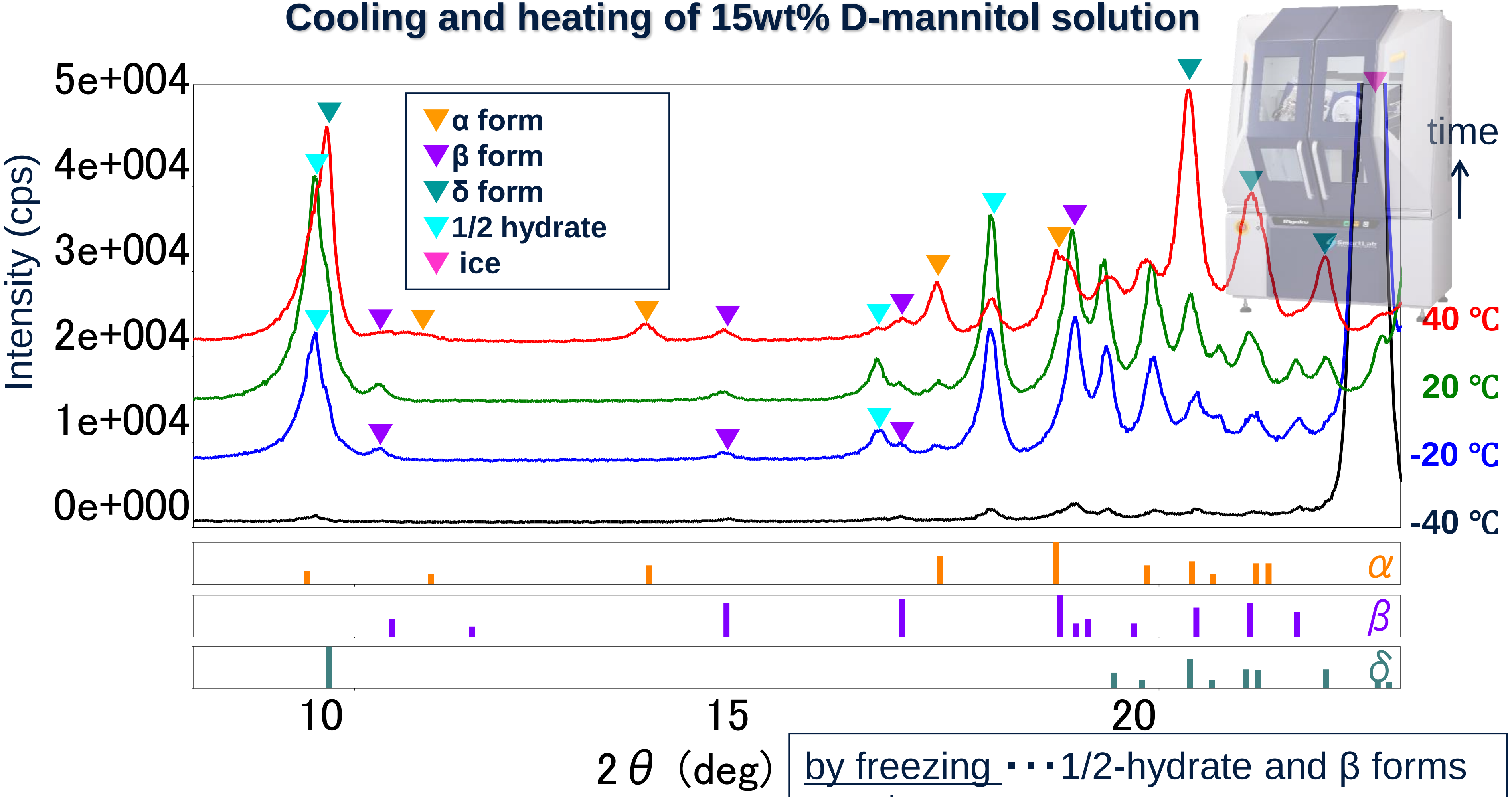
COOLING AND HEATING OF 10WT% MANNITOL



Crystal growth around thermal reaction points can be observed

Crystal growth and phase transformation under vacuum

Cooling and heating of 15wt% D-mannitol solution



by freezing ･･･1/2-hydrate and β forms
in 2nd drying･･･α and δ forms appeared

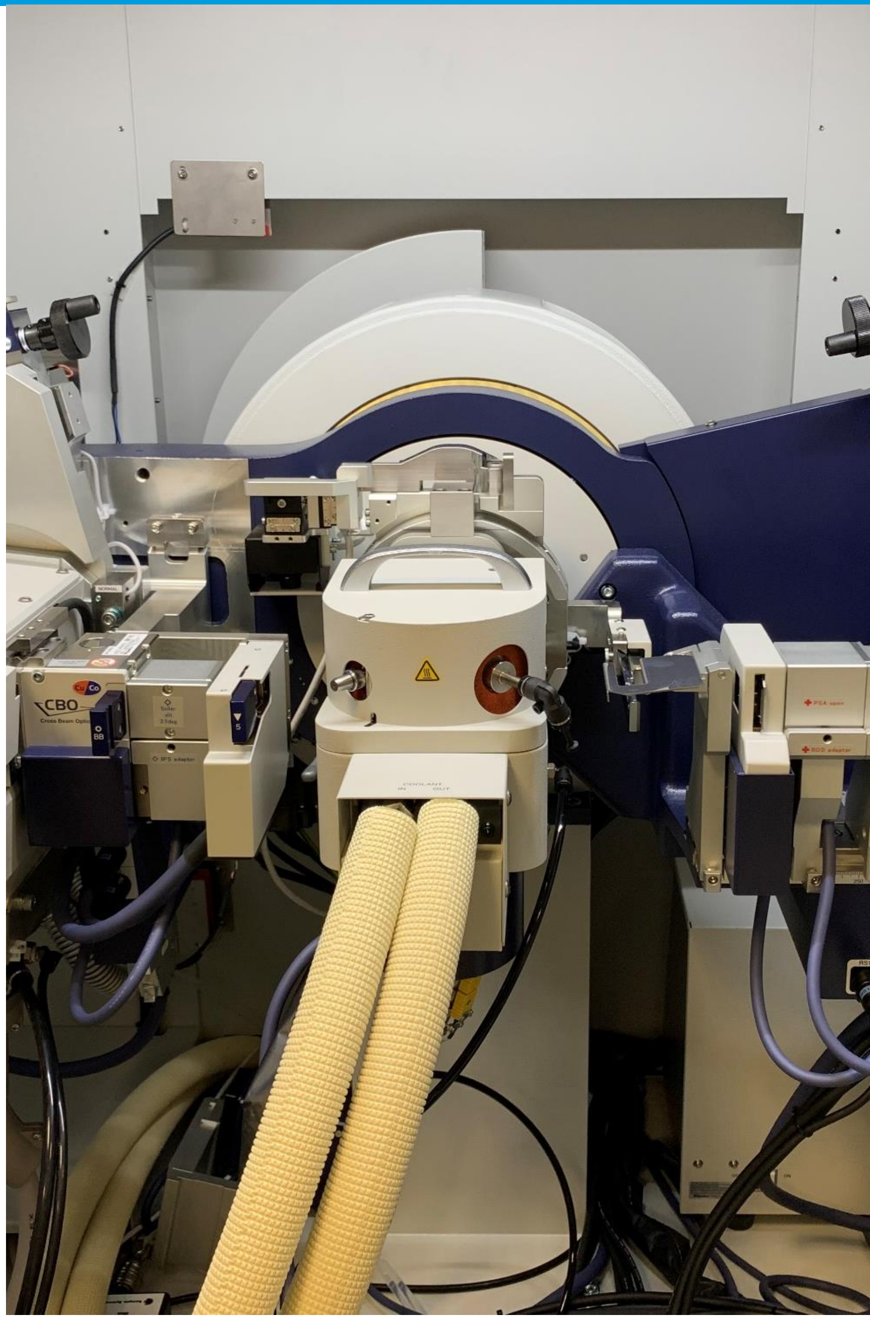
Crystal growth and transitions during the freeze drying process can be observed

SOMMAIRE

XRD-DSC attachment summary

- ✓ simultaneous XRD and DSC measurements under the same conditions
- ✓ easier characterization of the material
- ✓ small sample quantity
- ✓ powder, gel and liquid samples
- ✓ reduction of measurement time and costs
- ✓ Compatible with humidity experiments

A vous d’imaginer les expériences intéressantes pour vos applications et vos recherches



XRD-DSC

Literature examples of using XRD-DSC attachment

CrystEngComm

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

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Cite this: DOI: 10.1039/d0ce00276c

A peculiar dehydration and solid–solid phase transition of the active pharmaceutical ingredient AZD9898 based on *in situ* single crystal-to-single crystal transformations†

Anna Pettersen, *[a] Okky Dwichandra Putra, [b]
Mark E. Light[c] and Yukiko Namatame[d]

Received 25th February 2020,
Accepted 24th March 2020

DOI: 10.1039/d0ce00276c

rsc.li/crystengcomm

AZD9898 has previously been used as a candidate for a potentially active pharmaceutical ingredient. AZD9898 form A hydrate was discovered during development and this form undergoes dehydration upon heating to give anhydrous form B. Further heating results in a solid–solid phase transition to a new anhydrous phase, form C. This study reports the crystal structures of form A, B, and C obtained by heating the single crystal of form A *in situ* on the diffractometer which establish the dehydration and solid–solid phase transition mechanisms. The dehydration from form A hydrate to form B anhydrous is an isostructural process while the solid–solid phase transition from form B to form C requires major structural changes. The relevant thermal profiles and vapour sorption behaviour of these forms are also reported in this study.

A. Pettersen et al., *CrystEngComm*, 2020, 22, 7280-7289

XRD-DSC

Literature examples of using XRD-DSC attachment

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Thermochimica Acta 432 (2005) 70–75

thermochimica acta

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Evaluation of the physical stability and local crystallization of amorphous terfenadine using XRD–DSC and micro-TA

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Abstract

It is very difficult to follow rapid changes in polymorphic transformation and crystallization and to estimate the species recrystallized from the amorphous form. The aim of this study was to clarify the structural changes of amorphous terfenadine and to evaluate the polymorphs crystallized from amorphous samples using XRD–DSC and an atomic force microscope with a thermal probe (micro-TA). Amorphous samples were prepared by grinding or rapid cooling of the melt. The rapid structural transitions of samples were followed by the XRD–DSC system. On the DSC trace of the quenched terfenadine, two exotherms were observed, while only one exothermic peak was observed in the DSC scan of a ground sample. From the in situ data obtained by the XRD–DSC system, the stable form of terfenadine was recrystallized during heating of the ground amorphous sample, whereas the metastable form was recrystallized from the quenched amorphous sample and the crystallized polymorph changed to the stable form. Obtained data suggested that recrystallized species could be related to the homogeneity of samples. When the stored sample surface was scanned by atomic force microscopy (AFM), heterogeneous crystallization was observed. By using micro-TA, melting temperatures at various points were measured, and polymorph forms I and II were crystallized in each region. The percentages of the crystallized form I stored at 120 and 135 °C were 47 and 79%, respectively. This result suggested that increasing the storage temperature increased the crystallization of form I, the stable form, confirming the temperature dependency of the crystallized form. The crystallization behavior of amorphous drug was affected by the annealing temperature. Micro-TA would be useful for detecting the inhomogeneities in polymorphs crystallized from amorphous drug.

Keywords: XRD–DSC; Terfenadine; Amorphous drug; Crystallization; Microthermal analysis

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Dynamics of Polymorphic Transformations in Palm Oil, Palm Stearin and Palm Kernel Oil Characterized by Coupled Powder XRD-DSC

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Abstract: The *in situ* polymorphic forms and thermal transitions of refined, bleached and deodorized palm oil (RBDPO), palm stearin (RBDPS) and palm kernel oil (RBDPKO) were investigated using coupled X-ray diffraction (XRD) and differential scanning calorimetry (DSC). Results indicated that the DSC onset crystallisation temperature of RBDPO was at 22.6℃, with a single reflection at 4.2Å started to appear from 23.4 to 17.1℃, and were followed by two prominent exothermic peaks at 20.1℃ and 8.5℃ respectively. Further cooling to −40℃ leads to the further formation of a β′polymorph. Upon heating, a of β′→β transformation was observed between 32.1 to 40.8℃, before the sample was completely melted at 43.0℃. The crystallization onset temperature of RBDPS was 44.1℃, with the appearance of the α polymorph at the same temperature as the appearance of the first sharp DSC exothermic peak. This quickly changed from α→β′ in the range 25 to 21.7℃, along with the formation of a small β peak at −40℃. Upon heating, a small XRD peak for the β polymorph was observed between 32.2 to 36.0℃, becoming a mixture of (β′+ β) between 44.0 to 52.5℃. Only the β polymorph survived further heating to 59.8℃. For RBDPKO, the crystallization onset temperature was 11.6℃, with the formation of a single sharp exothermic peak at 6.5℃ corresponding to the β′ polymorphic form until the temperature reached -40℃. No transformation of the polymorphic form was observed during the melting process of RBDPKO, before being completely melted at 33.2℃. This work has demonstrated the detailed dynamics of polymorphic transformations of PKO and PS, two commercially important hardstocks used widely by industry and will contribute to a greater understanding of their crystallization and melting dynamics.

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Thank you for your attention

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