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Preparation of solubility curve using Paracetamol

Experiment

Using Crystal16, we created a solubility curve (Van't Hoff curve) using Paracetamol as a sample compound.

*Information on sample compound

Paracetamol (Acetaminophen)

CAS No.: 103-90-2 Chemical formula : C8H9NO2 Molecular weight: 151.169 Solubility: 14 mg/mL (25°C); Literature value



1. Preparation of measurement sample

The following four samples (solvent: water) for measurement were prepared. The basis (weight) value should be the amount by which a solution can be obtained within the measurement temperature range (2°C to 85°C), with reference to the solubility mentioned above.

The temperature at the precipitation time is also measured so the precipitation should also be detected within the above temperature range.

After the preparation was completed, the sample was set in Reactor A of Crystal16.

1.40.0 mg/mL	2.70.0 mg/mL	3.100.0 mg/mL	4.150.0 mg/mL
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2. Selection of measurement conditions

Start at 2°C. Raise the temperature at 5°C/min to 85°C. Then, lower the temperature 4°C/min. Agitation speed: 700 rpm. Measurement time is 55 minutes. The actual measurement was carried out using an inert gas with a dew point indication at -10°C.

** Crystal16						-	
File Edit Connection View Help							
G Back to overview			Finished				
	Reactor A					Experiment	program
	Pre-step Type:	Temperature:	Heating rate:	Bottom stirring sp	red:	Top stirring speed:	
CopyOfAcetaminophen-001B by: M.T	Ide v	3 .	¢ °C/min		rpm ↓	\$	rpm
B	Program	1- 12 B					
100% 200% 3100% 4100%	Action Type Start Linear	End temp (*C) Heating rate (*C/min) Dura	tion (hh:mm:ss) Sampling interv	val (secs.) Bottom stirring speed	(rpm) Top stirring speed 700	(rpm) Evaporation 700 Off	Message 🔨
Reactor available	Hold Hold Ramp Linear Tune Tune		0:05:00 0:16:36 0:00:01	1	700 700	700 Off 700 Off 700 Off 700 Off	
C	Hold Hold		0:05:00	1	700	700 Off 700 Off	
100% 2100% 3100% 4100%	< Post-step Type:	Temperature:	Heating rate:	Bottom stiming speed:	Top stirring speed:		> Evaporation:
Reactor available	Idle 🗸	¢ċ	C/min	ç, ipm	¢	rpm	
D	Temperat	ure	85℃			Agitatio	on speed
1 100% 2 100% 3 100% 4 100%						(rpm)	- 1000 Stirring s
Reactor available	19 40 - 						- 500 geed (17
Dew point temperature: -10 °C Dew point	nt 2°C -						
Case temperature: 24.0 °C	0	5 10 15	20 25 Estimated run time	30 35 (minutes)	40 45	50	55 minute
Heat sink temperature: 23.5 °C		Tempera	ture Bottom stirr	ring speed —— Top stirring s	peed		
							TCP/IP

Figure 1: Measurement condition selection screen





3. Measurement results

The dissolution and precipitation phenomena of the samples at 4 concentrations in a 55minute measurement are shown here.



Figure 2: Display screen of measurement results

4. Data analysis (Crystalclear)

The raw data from the main unit was sent to the dedicated analysis software (Crystalclear) where data analysis was performed. Below are the results for the first of the four vials. The dissolution temperature and the precipitation start temperature were obtained. The same procedure was conducted for the remaining vials.



Figure 3 : Display screen of vial 1 data analysis



Figure 4 : Solubility curve for Paracetamol

Report (Word format)



Figure 5 : Solubility and Meta-Stable Limit Curves



NVT Application Note 03-CR 21st Jan.2022

Sample

concentration



Reporting

EXPERIMENT SUMMARY

The following experiments were used to create the presented solubility and/or meta-stable limit curves.

Experiment	Vial	Concentration [mg/ml]	Solvent	1
201904117Acetaminophen-001A	1	40		
201904117Acetaminophen-001A	2	70		
201904117Acetaminophen-001A	3	100		8
201904117Acetaminophen-001A	4	150		

TRANSITION POINTS

Clear

Concentration [mg/ml]	Temperature [°C]	Experiment	Vial	Time [min]
40	47.5	201904117Acetaminophen-001A	1	26.07
70	64.6	201904117Acetaminophen-001A	2	29.50
100	72.5	201904117Acetaminophen-001A	3	31.07
150	77.5	201904117Acetaminophen-001A	4	32.04
Cloud				

Concentration [mg/ml]	Temperature [°C]	Experiment	Vial	Time [min]
40	20.6	201904117Acetaminophen-001A	1	54.76
70	39.4	201904117Acetaminophen-001A	2	50.06
100	47.6	201904117Acetaminophen-001A	3	48.00
150	55.8	201904117Acetaminophen-001A	4	45.95

FITTED CURVES

- Clear			
Function	Van't Hoff		
Coefficients	exp(18.1932+(-4667.9117)/(x+273))	->	Dissolution
Colour			
- Cloud			
Function	Van't Hoff		
Coefficients	exp(15.6429+(-3526.0165)/(x+273))		Dracinitation
Colour			Precipitation

CRYSTAL 16 SOURCE FILES

The following table presents a summary of the Crystal 16 source files for this project:					
[Experiment	User	Date/Time	Filename	
ſ	201904117Acetaminophen-001A	M.T	17-Apr-2019 10:32:15	201904117Acetaminophen-001A.csv	

REPORT GENERATION

This report was generated by the CrystalClear software package, a product of Avantium Technologies. For support and purchasing queries related to CrystalClear please contact Avantium at <u>www.avantium.com</u> CrystalClear and Crystal 16 are Trademarks of Avantium Technologies.















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