

Controlling the Exothermicity of O-arylation by Evaporative Cooling during the Process Development of Fluoxetine Hydrochloride[†]

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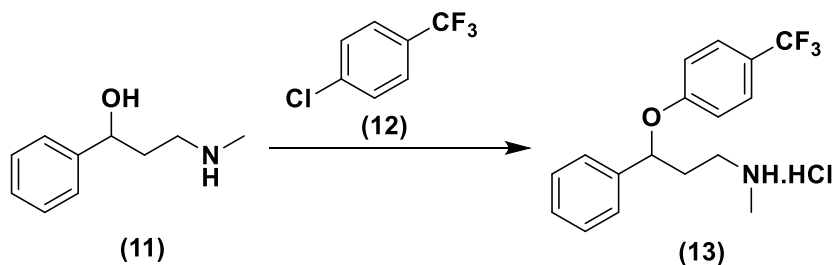
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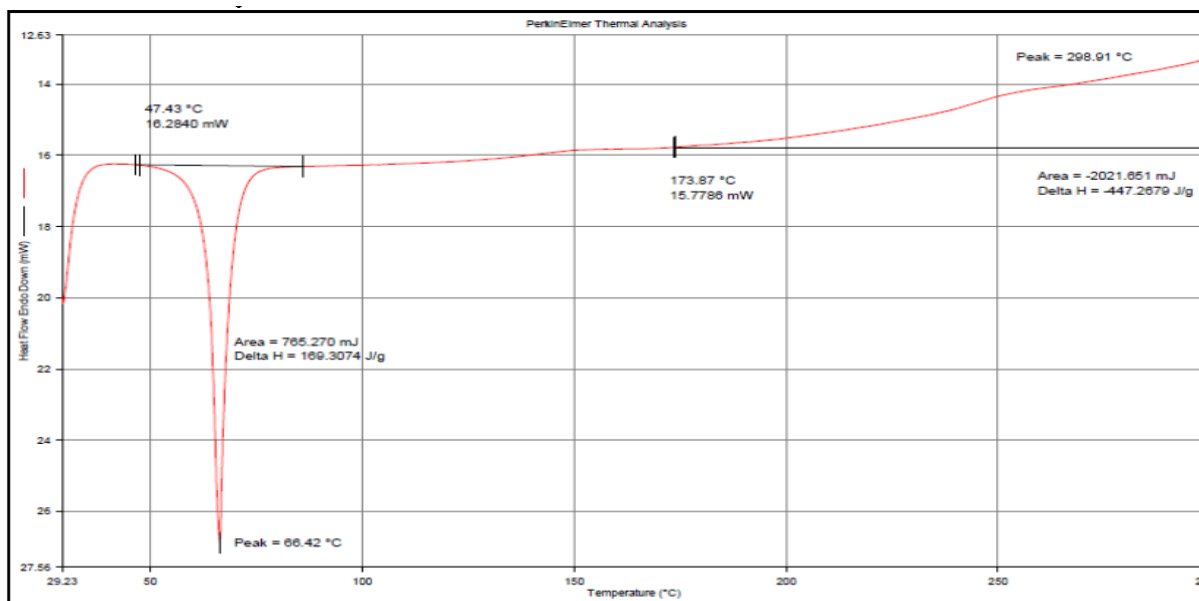
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[†]Dr. Reddy's Communication no: IPDO IPM-00379

Scheme 3.



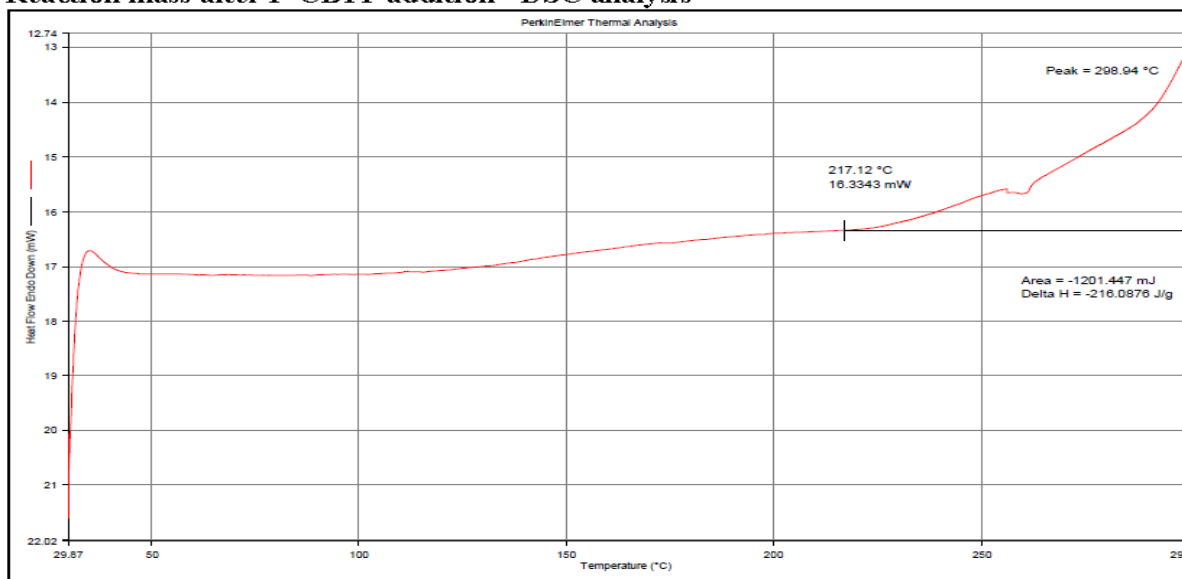
Experiment 1: 3-(methylamino)-1-phenylpropan-1-ol (4): DSC Analysis



- Endotherm starts at 47.43°C with heat of endotherm 169.31J/g.
- Exotherm starts at 173.87°C with heat of exotherm -447.27J/g.

Experiment 2: Reaction mass after 3-(methylamino)-1-phenylpropan-1-ol (4): DSC Analysis

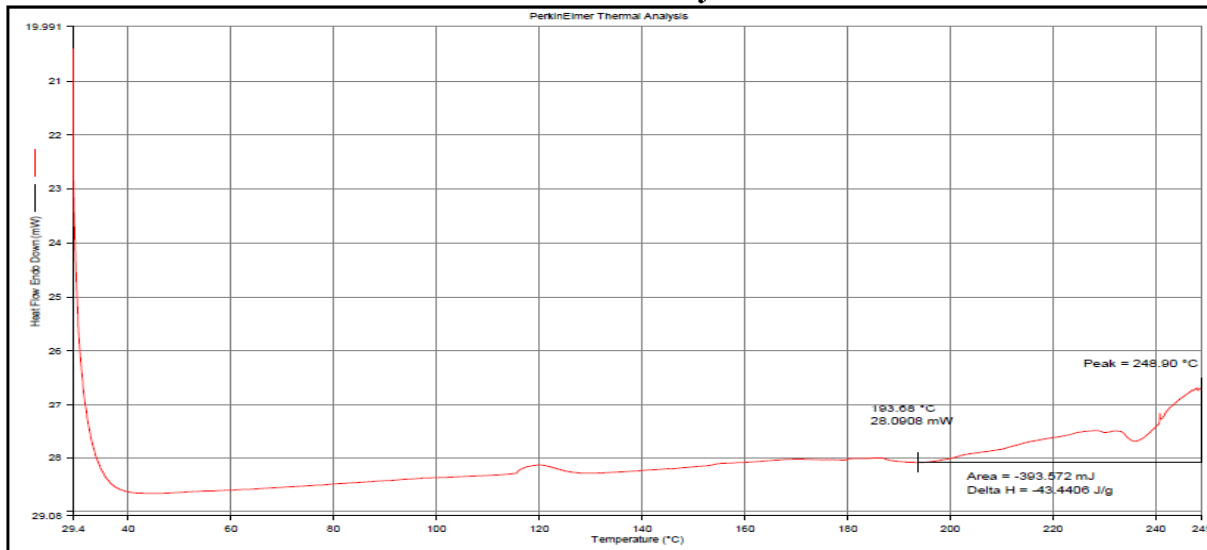
Reaction mass after P-CBTF addition - DSC analysis



- Exotherm starts at 217.21°C with heat of exotherm -216.1 J/g. The initial heat (drift in line at around 100°C) may correspond to desired heat of reaction, as the reaction is happening at 105-110°C.

Experiment 3: Reaction mass after KOH addition: DSC Analysis

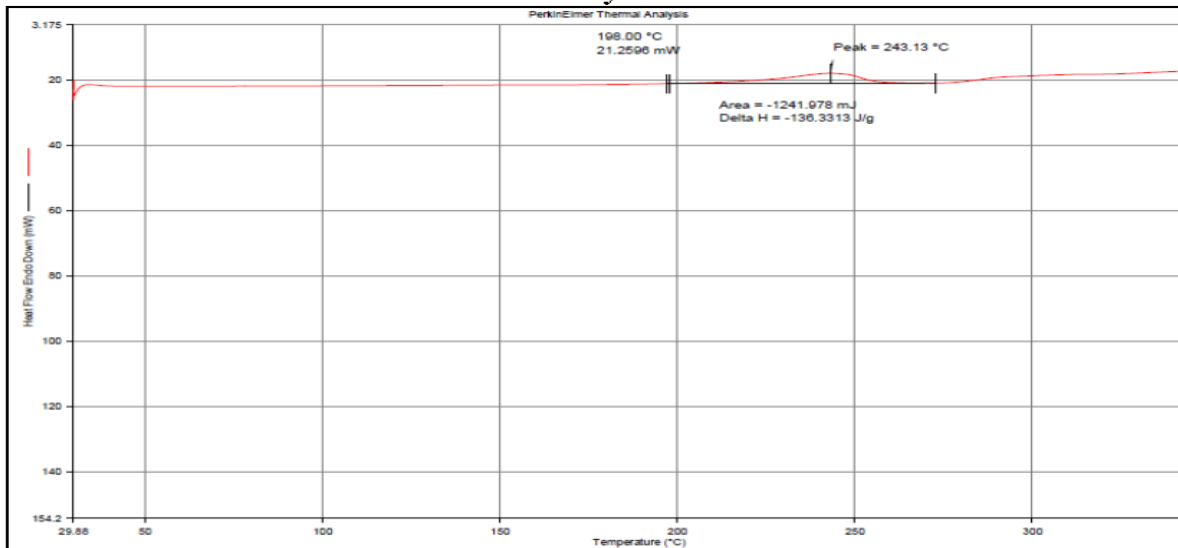
Reaction mass after KOH flakes addition - DSC analysis



- Exotherm starts at 193.68°C with heat of exotherm -43.44 J/g.

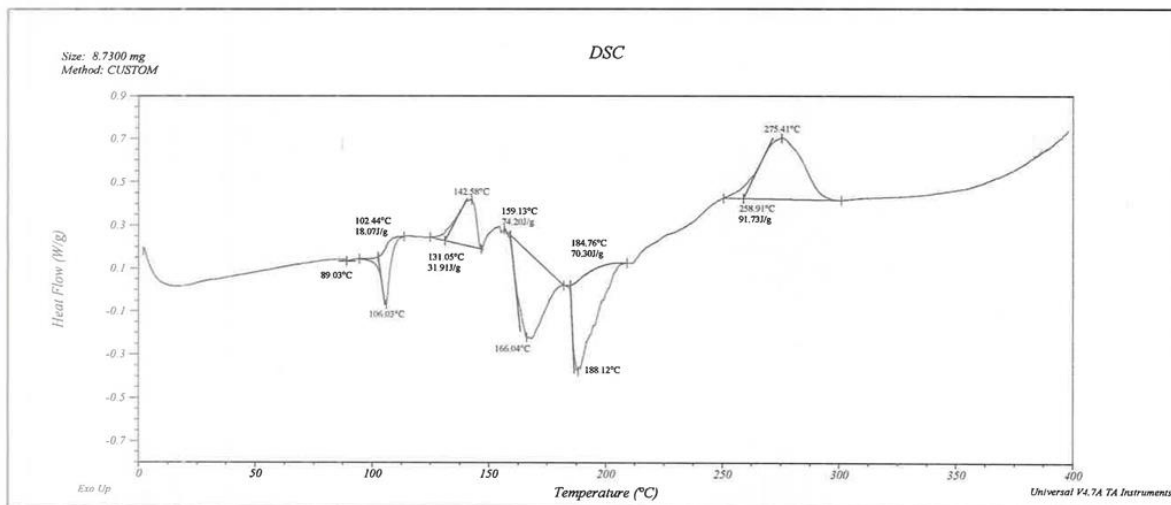
Experiment 5: DSC for reaction mass after water addition

Reaction mass after water addition - DSC analysis



- Exotherm starts at 198°C with heat of exotherm -136.33 J/g.

Experiment 5: DSC for reaction mass in gold pan (reaction mass made uniform by grinding before DSC analysis without toluene).

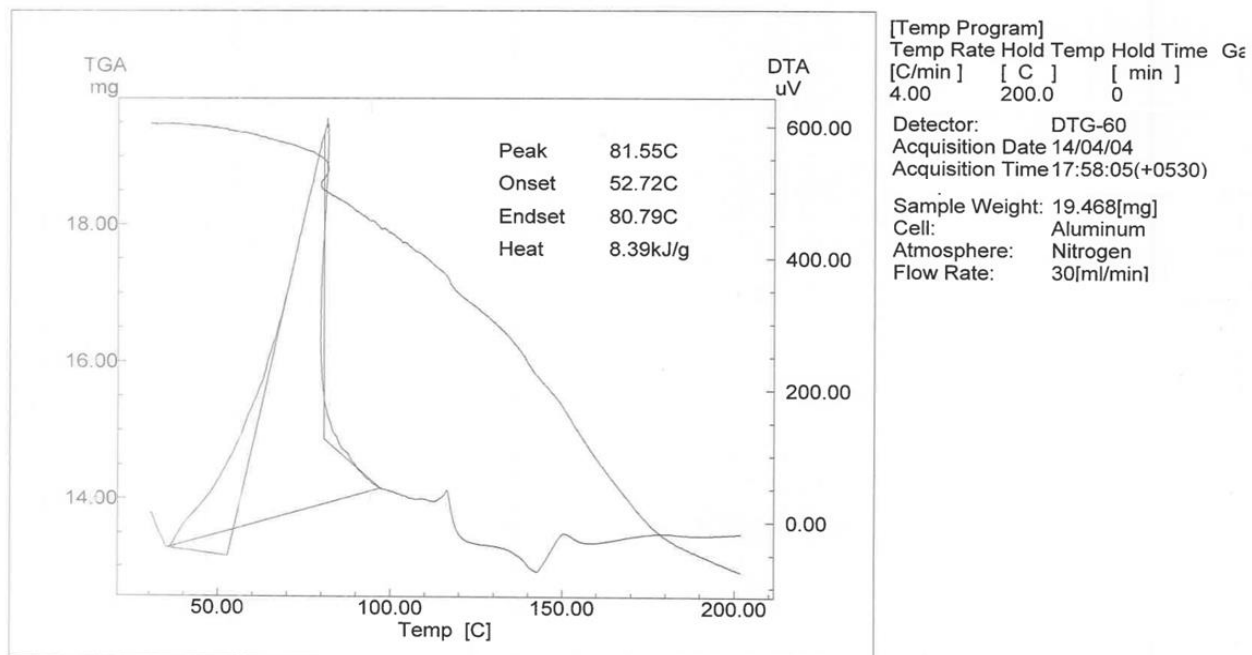


Method Log:

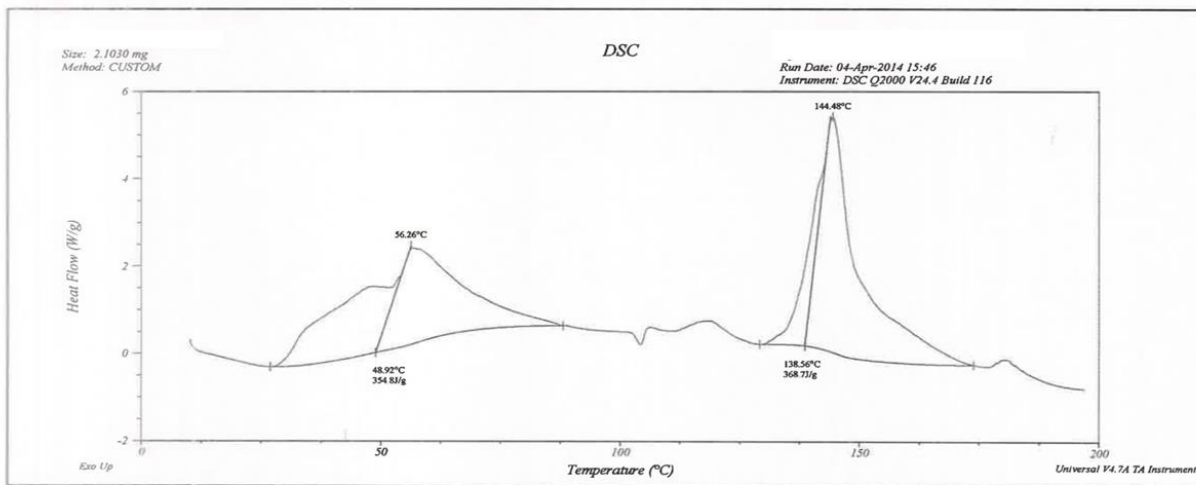
1: Equilibrate at 0.00°C

2: Ramp 4.00°C/min to 400.00°C

Experiment 6: TGA for reaction mass in gold pan (reaction mass made uniform by grinding before DSC analysis without toluene).



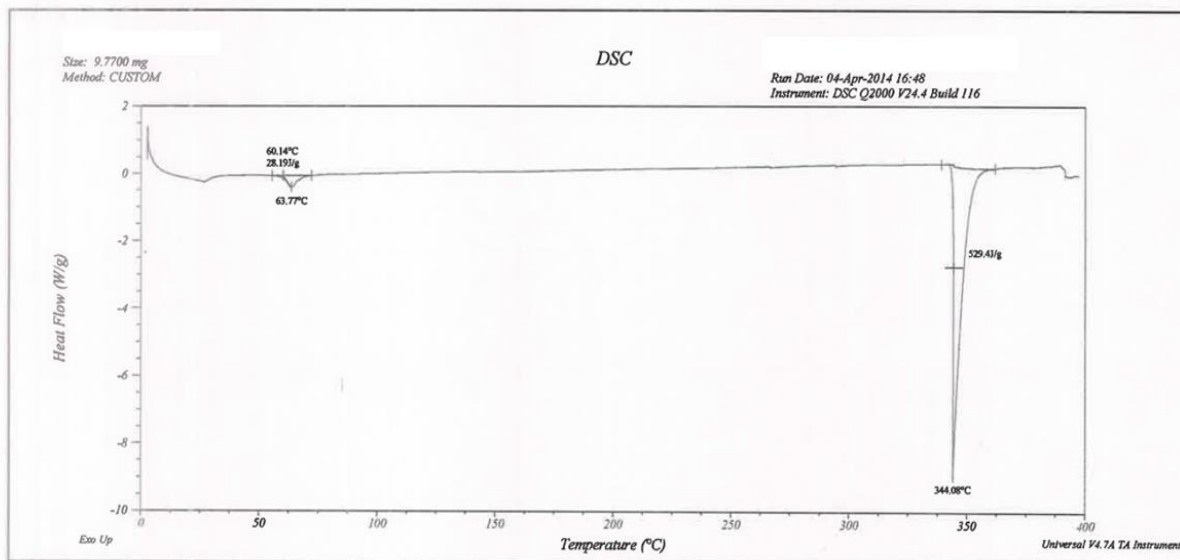
Experiment 7: DSC of reaction mass (paste) in Aluminum pan without solvent.



Method Log:

- 1: Equilibrate at 10.00°C
- 2: Ramp 10.00°C/min to 200.00°C
- 3: End of method

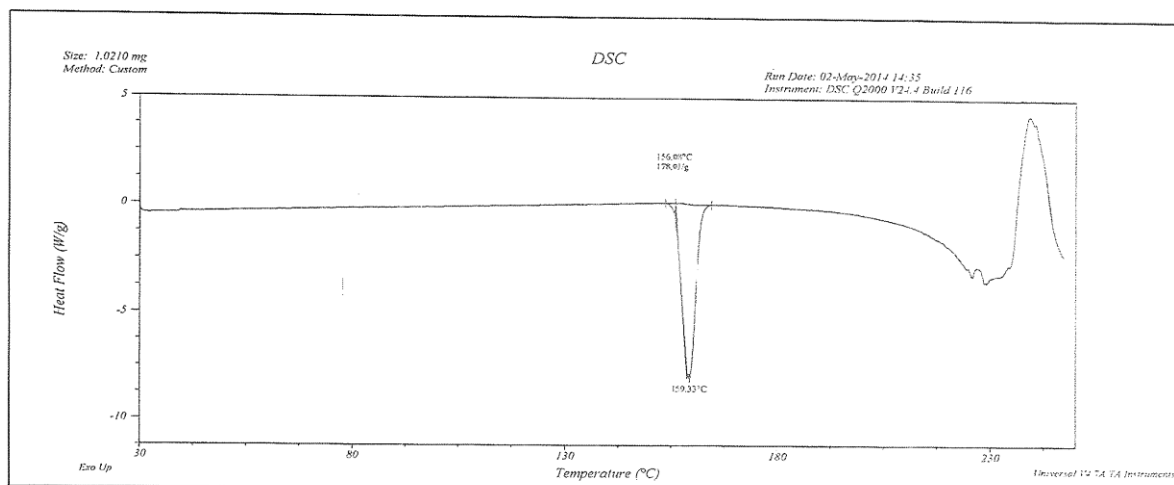
Experiment 8. DSC of the reaction Mass Paste in Gold pan without solvent.



Method Log:

- 1: Equilibrate at 0.00°C
- 2: Ramp 4.00°C/min to 400.00°C
- 3: End of method

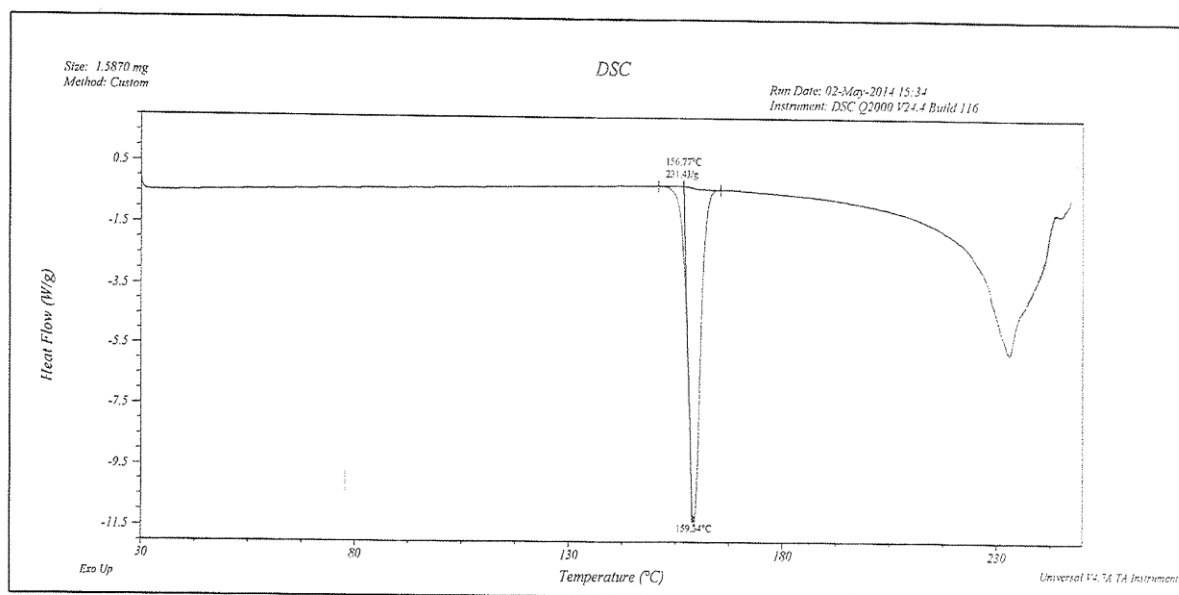
Fluoxetine Hydrochloride (1) Working Standard DSC



Method Log:

- 1: Equilibrate at 30.00°C
- 2: Ramp 10.00°C/min to 250.00°C
- 3: End of method

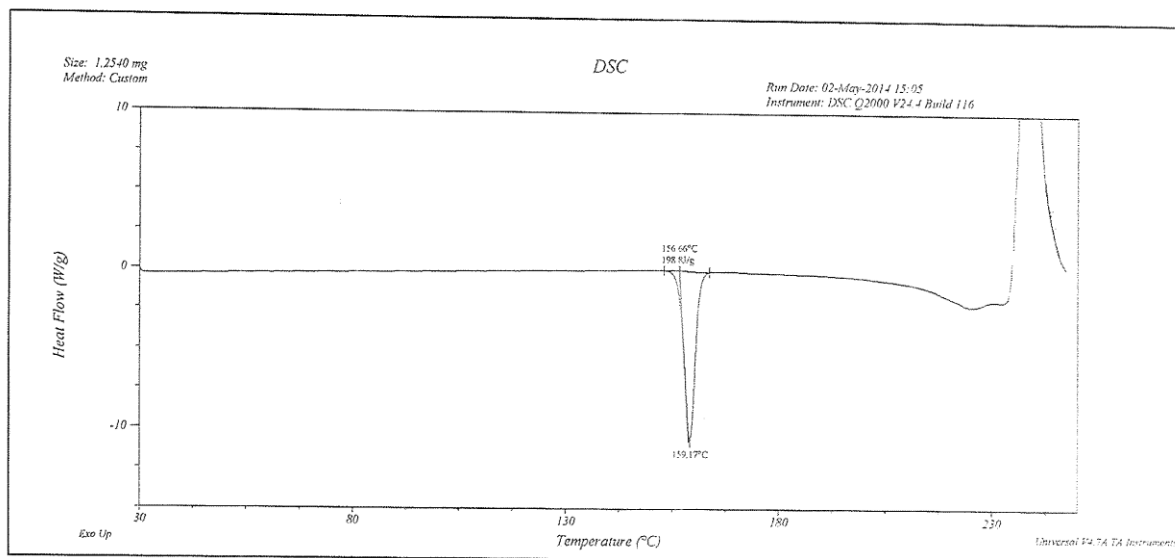
Fluoxetine Hydrochloride (1) Lab. Batch DSC



Method Log:

- 1: Equilibrate at 30.00°C
- 2: Ramp 10.00°C/min to 250.00°C
- 3: End of method

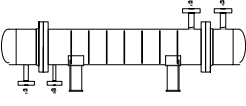
Fluoxetine Hydrochloride (1) commercial lot DSC

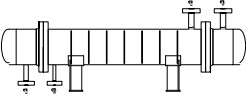


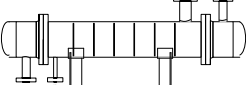
Method Log:

- 1: Equilibrate at 30.00°C
- 2: Ramp 10.00°C/min to 250.00°C
- 3: End of method

	Batch size	kg	70		225	
		UOM	Case I	Case II	Case III	Case IV
Hot fluid	Boil up	kg/hr	220	220	700	700
	Inlet T	C	110.67	110.67	110.67	110.67
	Outlet T	C				
Cold fluid	Type	-	Ch Brine	CT water	Ch Brine	CT water
	Flow rate	kg/hr	5745	5257	18230	16271
	Inlet T	C	-8	30	-8	30
	Outlet T	C	-4	34	-4	34
Condenser	Heat exchanged	kcal/hr	19471	19471	61952	61952
	Area	m2	3.5	3.5	3.5	3.5

Item No.: condenser 2		Your Reference: Nikhil											
Date:		Rev No.:		Job No.:									
Size	203 /	1219 mm		Type	BEM	Hor	Connected in		1	parallel	1	series	
Surf/unit(eff.)	3.5	m2		Shells/unit	1	Surf/shell (eff.)		3	m2				
PERFORMANCE OF ONE UNIT													
Fluid allocation				Shell Side				Tube Side					
Fluid name				hot				cold					
Fluid quantity, Total				kg/h				220					
Vapor (In/Out)				kg/h				220		0		0	
Liquid				kg/h				0		220		5257	
Noncondensable				kg/h				0		0		0	
Temperature (In/Out)				C				111		107		30	
Dew / Bubble point				C				111		111		134	
Density (Vap / Liq)				kg/m3				3 /		/ 785		/ 989	
Viscosity				cp				0 /		/ 0		/ 1	
Molecular wt, Vap								92					
Molecular wt, NC													
Specific heat				kcal/(kg*C)				0 /		/ 1		/ 1	
Thermal conductivity				kcal/(h*m*C)				0 /		/ 0		/ 1	
Latent heat				kcal/kg				86		87			
Pressure (abs)				bar				1		1		3	
Velocity				m/s				3		0			
Pressure drop, allow./calc.				kgf/cm2				0		0		1	
Fouling resistance (min)				m2*h*C/kcal				0		0		0	
Heat exchanged				19471 kcal/h				MTD corrected				78 C	
Transfer rate, Service				83				Dirty		262		Clean	
										480		W/(m2*K)	
CONSTRUCTION OF ONE SHELL													
				Shell Side				Tube Side					
Design/vac/test pressure:g				bar				3 /		/			
Design temperature				C				71		71			
Number passes per shell								1		1			
Corrosion allowance				mm				3		0			
Connections		In	mm	1	32	/	-	1	25	/	-		
Size/rating		Out		1	13	/	-	1	32	/	-		
Nominal		Intermediate			/	-	-		/	-	-		
Tube No.	51	OD	19	Tks-	Avg	1.65	mm	Length	1219	mm	Pitch	24	
Tube type	Plain			Material				SS 304		Tube pattern			
Shell	Carbon Steel		ID	205	OD	219	mm	Shell cover		-			
Channel or bonnet				Carbon Steel				Channel cover		-			
Tubesheet-stationary				Carbon Steel				Tubesheet-floating		-			
Floating head cover				-				Impingement protection		None			
Baffle-cross	Carbon Steel		Type	Single segme		Cut(%d)	40	V	Spacing: c/c	133	mm		
Baffle-long	-		Seal type						Inlet	171	mm		
Supports-tube				U-bend				Type					
Bypass seal				Tube-tubesheet joint				Exp.					
Expansion joint				-				Type					
RhoV2-Inlet nozzle	1371	Bundle entrance				166	Bundle exit		1	kg/(m*s2)			
Gaskets - Shell side				-				Tube Side		Flat Metal Jacket Fibe			
Floating head				-									
Code requirements				ASME Code Sec VIII Div 1				TEMA class		R - refinery service			
Weight/Shell	215	Filled with water				251	Bundle		78	kg			
Remarks													

Item No.: condenser 2		Your Reference: Nikhil											
Date:		Rev No.:		Job No.:									
Size	203 /	1219 mm		Type	BEM	Hor	Connected in		1	parallel	1	series	
Surf/unit(eff.)	3.5	m2		Shells/unit	1	Surf/shell (eff.)		3	m2				
PERFORMANCE OF ONE UNIT													
Fluid allocation				Shell Side				Tube Side					
Fluid name				hot				cold					
Fluid quantity, Total				kg/h				220					
Vapor (In/Out)				kg/h				220		0		0	
Liquid				kg/h				0		220		5257	
Noncondensable				kg/h				0		0		0	
Temperature (In/Out)				C				111		107		30	
Dew / Bubble point				C				111		111		134	
Density (Vap / Liq)				kg/m3				3 /		/ 785		/ 989	
Viscosity				cp				0 /		/ 0		/ 1	
Molecular wt, Vap								92					
Molecular wt, NC													
Specific heat				kcal/(kg*C)				0 /		/ 1		/ 1	
Thermal conductivity				kcal/(h*m*C)				0 /		/ 0		/ 1	
Latent heat				kcal/kg				86		87			
Pressure (abs)				bar				1		1		3	
Velocity				m/s				3		0			
Pressure drop, allow./calc.				kgf/cm2				0		0		1	
Fouling resistance (min)				m2*h*C/kcal				0		0		0	
Heat exchanged				19471 kcal/h				MTD corrected				78 C	
Transfer rate, Service				83				Dirty		262		Clean	
										480		W/(m2*K)	
CONSTRUCTION OF ONE SHELL													
				Shell Side				Tube Side					
Design/vac/test pressure:g				bar				3 /		/			
Design temperature				C				71		71			
Number passes per shell								1		1			
Corrosion allowance				mm				3		0			
Connections		In	mm	1	32	/	-	1	25	/	-		
Size/rating		Out		1	13	/	-	1	32	/	-		
Nominal		Intermediate			/	-	-		/	-	-		
Tube No.	51	OD	19	Tks-	Avg	1.65	mm	Length	1219	mm	Pitch	24	
Tube type	Plain			Material				SS 304		Tube pattern			
Shell	Carbon Steel		ID	205	OD	219	mm	Shell cover		-			
Channel or bonnet				Carbon Steel				Channel cover		-			
Tubesheet-stationary				Carbon Steel				Tubesheet-floating		-			
Floating head cover				-				Impingement protection		None			
Baffle-cross	Carbon Steel		Type	Single segme		Cut(%d)	40	V	Spacing: c/c	133	mm		
Baffle-long	-		Seal type						Inlet	171	mm		
Supports-tube				U-bend				Type					
Bypass seal				Tube-tubesheet joint				Exp.					
Expansion joint				-				Type					
RhoV2-Inlet nozzle	1371	Bundle entrance				166	Bundle exit		1	kg/(m*s2)			
Gaskets - Shell side				-				Tube Side		Flat Metal Jacket Fibe			
Floating head				-									
Code requirements				ASME Code Sec VIII Div 1				TEMA class		R - refinery service			
Weight/Shell	215	Filled with water				251	Bundle		78	kg			
Remarks													

Date:	Rev No.:	Job No.:																				
Size	203	/	1219	mm	Type	BEM	Hor	Connected in	1	parallel	1	series										
Surf/unit(eff.)	3.5	m2	Shells/unit	1	Surf/shell (eff.)	3	m2															
PERFORMANCE OF ONE UNIT																						
Fluid allocation				Shell Side				Tube Side														
Fluid name				Toluene vapors				CHB														
Fluid quantity, Total				kg/h				700														
Vapor (In/Out)				kg/h				700														
Liquid				kg/h				0														
Noncondensable				kg/h				0														
Temperature (In/Out)				C				111														
Dew / Bubble point				C				111														
Density (Vap / Liq)				kg/m3				3 /														
Viscosity				mPa*s				0 /														
Molecular wt, Vap								92														
Molecular wt, NC																						
Specific heat				kJ/(kg*K)				1 /														
Thermal conductivity				W/(m*K)				0 /														
Latent heat				kJ/kg				362														
Pressure (abs)				bar				1														
Velocity				m/s				9														
Pressure drop, allow./calc.				bar				0														
Fouling resistance (min)				m2*K/W				0														
Heat exchanged				72				kW				MTD corrected	78	C								
Transfer rate, Service				280				Dirty				378	Clean	957	W/(m2*K)							
CONSTRUCTION OF ONE SHELL																						
				Shell Side				Tube Side														
Design/vac/test pressure:g				bar				3 /														
Design temperature				C				71														
Number passes per shell								1														
Corrosion allowance				mm				3														
Connections				In				mm														
Size/rating				Out				mm														
Nominal				Intermediate				mm														
Tube No.				48				OD				19	Tks-	Avg	2.11	mm	Length	1219	mm	Pitch	24	mm
Tube type				Plain				Material				Carbon Steel				Tube pattern				30		
Shell				Carbon Steel				ID				205	OD	219	mm	Shell cover				-		
Channel or bonnet				Carbon Steel				Channel cover				-										
Tubesheet-stationary				Carbon Steel				Tubesheet-floating				-										
Floating head cover				-				Impingement protection				None										
Baffle-cross				Carbon Steel				Type				Single segme				Cut(%d)	40	V	Spacing: c/c	152	mm	
Baffle-long				-				Seal type				Inlet				190	mm					
Supports-tube				U-bend				Type														
Bypass seal				Tube-tubesheet joint				Exp.														
Expansion joint				-				Type														
RhoV2-Inlet nozzle				568				Bundle entrance				358				Bundle exit	2	kg/(m*s2)				
Gaskets - Shell side				-				Tube Side				Flat Metal Jacket Fibe										
Floating head				-																		
Code requirements				ASME Code Sec VIII Div 1				TEMA class				R - refinery service										
Weight/Shell				232				Filled with water				270				Bundle	85	kg				
Remarks																						