

# Supporting Information

## Sustainable Mechano-synthesis of Novel Tetraol Monomers and Their Enzymatic Polymerization

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**Table S1.** E-factors at mg scale

Entry	Diamine	Masse diamine (mg)	Masse 2H-HBO 1 (mg)	Yield %	Masse 2a-d (mg)	E-factor (ideal value = 0)
1	Diaminohexane	80,6	144,1	76 (2a)	162,6	0,38
2	Spermidine	116,1	169,4	62 (2b)	170,2	0,68
3	Spermine	106,6	111	53 (2c)	109,9	0,98
4	4,9-dioxadodecandiamine	159,6	164,9	80 (2d)	246	0,32

**Table S2.** E-factors at g scale

Entry	Diamine	Masse diamine (g)	Masse 2H-HBO 1 (g)	Yield %	Masse 2a-d (g)	E-factor (ideal value = 0)
1	Diaminohexane	0,9	1,7	67 (2a)	1,7	0,53
2	Spermidine	1,5	2,2	72 (2b)	2,53	0,46
3	Spermine	1,9	2	60 (2c)	2,23	0,75
4	4,9-dioxadodecandiamine	1,7	1,7	73 (2d)	2,35	0,45

**Table S3.** EcoScale at g and mg scales for compound **2a**

Parameters	Penalty points	Synthesis for 2a (mg scale)	Explanations	Synthesis for 2a (g scale)	Explanations
1. Yield	(100 - yield)/2	12	Yield : 76 %	17	Yield : 67 %
2. Reactant price (to obtain 10 mmol of final product)	Total =	0		0	
Inexpensive (< 10 €)	0	0	2H-HBO (3,07 g), diaminohexane (1,72 g)	0	2H-HBO (3,47 g), diaminohexane (1,84 g)
Expensive (>10 € et <50 €)	3	0		0	
Very expensive (> 50 €)	5	0		0	
3.Safety	Total =	10		10	
N (dangerous for the environment)	5	0		0	
Corrosive	5	5	Diaminohexane	5	Diaminohexane
T (toxic)	5	5	Diaminohexane	5	Diaminohexane
F (highly flammable)	5	0		0	
E (explosive)	10	0		0	
F+ (extremely flammable)	10	0		0	
T+ (extremely toxic)	10	0		0	
4. Technical setup	Total =	2		2	
Common setup	0	0		0	
Instrument for controlled addition (dropping funnel, etc. )	1	0		0	
Unconventional activation technique (microwave, etc. )	2	2	Ball-milling	2	Ball-milling
Pressur equipment > 1 atm	3	0		0	
Any additional special glassware	1	0		0	
(Inert) gas atmosphere	1	0		0	
Glove box	3	0		0	
5. Temperature/time	Total =	1		1	
Room temperature, < 1 h	0	0		0	
Room temperature, < 24 h	1	1		1	
Heating, < 1 h	2	0		0	
Heating, > 1 h	3	0		0	
Cooling to 0 °C	4	0		0	
Cooling < 0 °C	5	0		0	
6. Workup/purification	Total =	10		10	
None	0	0		0	
Cooling to room temperature	0	0		0	
Adding solvent	0	0	MeOH to remove the crude product from the jar	0	MeOH to remove the crude product from the jar
Simple filtration	0	0		0	
Removal of solvent with bp < 150 °C	0	0	MeOH before purification	0	MeOH before purification
Crystallization and filtration	1	0		0	
Removal of solvent with bp > 150 °C	2	0		0	
Solid phase extraction	2	0		0	
Distillation	3	0		0	
Sublimation	3	0		0	
Liquid-liquid extraction	3	0		0	
Classical chromatography	10	10	Yes	10	Yes
Total		35		40	
Ecoscale (/100)		65		60	

**Table S4. EcoScale at g and mg scales for compound 2b**

Parameters	Penalty points	Synthesis of 2b (mg scale)	Explanations	Synthesis for 2b (g scale)	Explanations
1. Yield	(100-yield)/2	19	Yield : 62 %	14	Yield : 72 %
2. Reactant price (to obtain 10 mmol of final product)	Total =	5		5	
Inexpensive (< 10 €)	0	0	2H-HBO (3,76 g)	0	2H-HBO (3,29 g)
Expensive (>10 € et <50 €)	3	0		0	
Very expensive (> 50 €)	5	5	Spermidine (2,58 g)	5	Spermidine (2,24 g)
3.Safety	Total =	5		5	
N (dangerous for the environment)	5	0		0	
Corrosive	5	5	Spermidine	5	Spermidine
T (toxic)	5	0		0	
F (highly flammable)	5	0		0	
E (explosive)	10	0		0	
F+ (extremely flammable)	10	0		0	
T+ (extremely toxic)	10	0		0	
4. Technical setup	Total =	2		2	
Common setup	0	0		0	
Instrument for controlled addition (dropping funnel, etc.)	1	0		0	
Unconventional activation technique (microwave, etc.)	2	2	Ball-milling	2	Ball-milling
Pressur equipment > 1 atm	3	0		0	
Any additional special glassware	1	0		0	
(Inert) gas atmosphere	1	0		0	
Glove box	3	0		0	
5. Temperature/time	Total =	1		1	
Room temperature, < 1 h	0	0		0	
Room temperature, < 24 h	1	1		1	
Heating, < 1 h	2	0		0	
Heating, > 1 h	3	0		0	
Cooling to 0 °C	4	0		0	
Cooling < 0 °C	5	0		0	
6. Workup/purification	Total =	10		10	
None	0	0		0	
Cooling to room temperature	0	0		0	
Adding solvent	0	0	MeOH to remove the crude product from the jar	0	MeOH to remove the crude product from the jar
Simple filtration	0	0		0	
Removal of solvent with bp < 150 °C	0	0	MeOH before purification	0	MeOH before purification
Crystallization and filtration	1	0		0	
Removal of solvent with bp > 150 °C	2	0		0	
Solid phase extraction	2	0		0	
Distillation	3	0		0	
Sublimation	3	0		0	
Liquid-liquid extraction	3	0		0	
Classical chromatography	10	10	Yes	10	Yes
Total		42		37	
Ecoscale (/100)		58		63	

**Table S5.** EcoScale at g and mg scales for compound **2c**

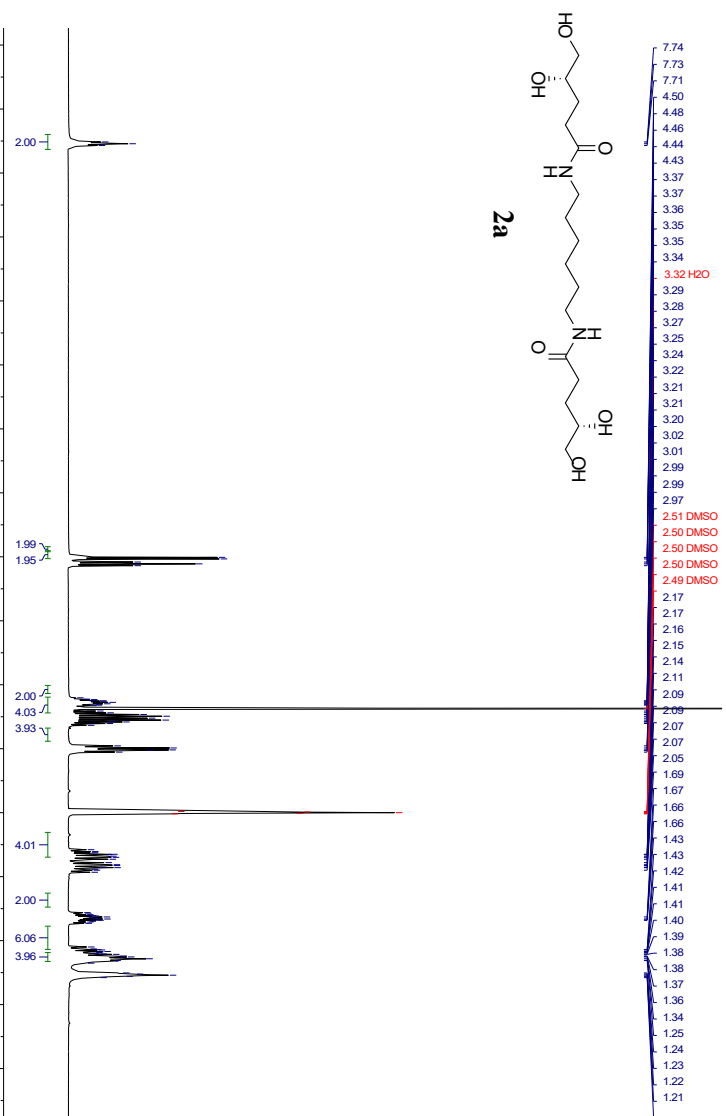
Parameters	Penalty points	Synthesis of 2c (mg scale)	Explanations	Synthesis for 2c (g scale)	Explanations
1. Yield	(100 - yield)/2	24	Yield : 53 %	20	Yield : 60 %
2. Reactant price (to obtain 10 mmol of final product)	Total =	5		5	
Inexpensive (< 10 €)	0	0	2H-HBO (4,44 g)	0	2H-HBO (3,90 g)
Expensive (>10 € et <50 €)	3	0		0	
Very expensive (>50 €)	5	5	Spermine (4,26 g)	5	Spermine (3,71 g)
3. Safety	Total =	5		5	
N (dangerous for the environment)	5	0		0	
Corrosive	5	5	Spermine	5	Spermine
T (toxic)	5	0		0	
F (highly flammable)	5	0		0	
E (explosive)	10	0		0	
F+ (extremely flammable)	10	0		0	
T+ (extremely toxic)	10	0		0	
4. Technical setup	Total =	2		2	
Common setup	0	0		0	
Instrument for controlled addition (dropping funnel, etc.)	1	0		0	
Unconventional activation technique (microwave, etc.)	2	2	Ball-milling	2	Ball-milling
Pressur equipment > 1 atm	3	0		0	
Any additional special glassware	1	0		0	
(Inert) gas atmosphere	1	0		0	
Glove box	3	0		0	
5. Temperature/time	Total =	1		1	
Room temperature, < 1 h	0	0		0	
Room temperature, < 24 h	1	1		1	
Heating, < 1 h	2	0		0	
Heating, > 1 h	3	0		0	
Cooling to 0 °C	4	0		0	
Cooling < 0 °C	5	0		0	
6. Workup/purification	Total =	10		10	
None	0	0		0	
Cooling to room temperature	0	0		0	
Adding solvent	0	0	Water to remove the crude product from the jar	0	MeOH to remove the crude product from the jar
Simple filtration	0	0		0	
Removal of solvent with bp < 150 °C	0	0		0	MeOH before purification
Crystallization and filtration	1	0		0	
Removal of solvent with bp > 150 °C	2	0		0	
Solid phase extraction	2	0		0	
Distillation	3	0		0	
Sublimation	3	0		0	
Liquid-liquid extraction	3	0		0	
Classical chromatography	10	10	Yes	10	Yes
Total		47		43	
Ecoscale (/100)		53		57	

**Table S6.** EcoScale at g and mg scales for compound **2d**

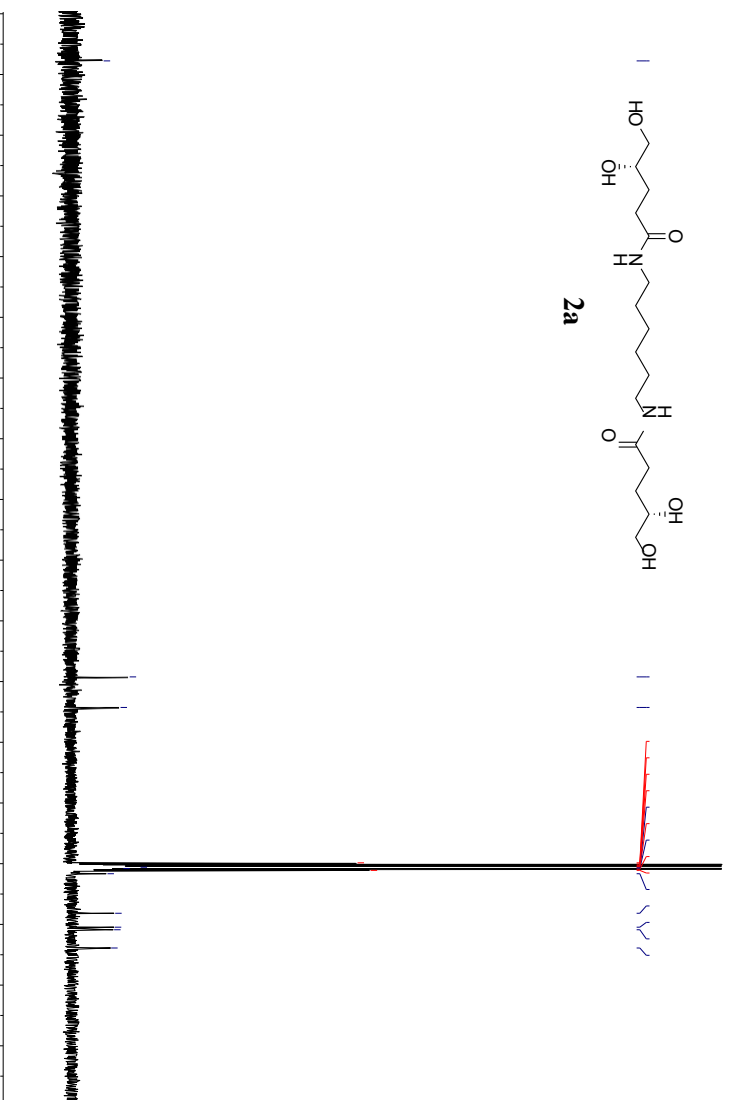
Parameters	Penalty points	Synthesis of 2d (mg scale)	Explanations	Synthesis for 2d (g scale)	Explanations
1. Yield	(100 - yield)/2	10	Yield : 80 %	14	Yield : 73%
2. Reactant price (to obtain 10 mmol of final product)	Total =	0		0	
Inexpensive (< 10 €)	0	0	2H-HBO (2,95 g), 4,9-dioxadodecandiamine (2,86 g)	0	2H-HBO (3,22 g), 4,9-dioxadodecandiamine (3,11 g)
Expensive (>10 € et <50 €)	3	0		0	
Very expensive (> 50 €)	5	0		0	
3.Safety	Total =	5		5	
N (dangerous for the environment)	5	0		0	
Corrosive	5	5	4,9-dioxadodecandiamine	5	4,9-dioxadodecandiamine
T (toxic)	5	0		0	
F (highly flammable)	5	0		0	
E (explosive)	10	0		0	
F+ (extremely flammable)	10	0		0	
T+ (extremely toxic)	10	0		0	
4. Technical setup	Total =	2		2	
Common setup	0	0		0	
Instrument for controlled addition (dropping funnel, etc.)	1	0		0	
Unconventional activation technique (microwave, etc.)	2	2	Ball-milling	2	Ball-milling
Pressur equipment > 1 atm	3	0		0	
Any additional special glassware	1	0		0	
(Inert) gas atmosphere	1	0		0	
Glove box	3	0		0	
5. Temperature/time	Total =	1		1	
Room temperature, < 1 h	0	0		0	
Room temperature, < 24 h	1	1		1	
Heating, < 1 h	2	0		0	
Heating, > 1 h	3	0		0	
Cooling to 0 °C	4	0		0	
Cooling < 0 °C	5	0		0	
6. Workup/purification	Total =	10		1	
None	0	0		0	
Cooling to room temperature	0	0		0	
Adding solvent	0	0	MeOH to remove the crude product from the jar	0	MeOH to remove the crude product from the jar
Simple filtration	0	0		0	
Removal of solvent with bp < 150 °C	0	0	MeOH before purification	0	MeOH before purification
Crystallization and filtration	1	0		1	Trituration in hot acetone and filtration
Removal of solvent with bp > 150 °C	2	0		0	
Solid phase extraction	2	0		0	
Distillation	3	0		0	
Sublimation	3	0		0	
Liquid-liquid extraction	3	0		0	
Classical chromatography	10	10	Yes	0	
Total		28		23	
Ecoscale (/100)		72		77	

**Table S7.** Failed polymerization reactions using the described reaction conditions.

Entry	Tetraol	Tetraol/DMS	Enz. wt%	Solv.	T (°C)	t (h)
19	<b>2a</b>	1	5	-	90	24
20	<b>2a</b>	1	5	Cyrene™	90	24
21	<b>2a</b>	1	5	DMI	90	24
22	<b>2a</b>	1	5	DPE	40	24
23	<b>2b</b>	1	20	DPE	90	24
24	<b>2b</b>	1	5	DPE	90	24
25	<b>2b</b>	0.5	20	DPE	90	24
26	<b>2b</b>	1	20	Cyrene™	90	24
27	<b>2b</b>	1	20	DMI	90	24
28	<b>2c</b>	1	20	DPE	90	24
29	<b>2c</b>	1	5	DPE	90	24
30	<b>2c</b>	0.5	20	DPE	90	24
31	<b>2c</b>	1	20	Cyrene™	90	24
32	<b>2c</b>	1	20	DMI	90	24



**Figure S1.** <sup>1</sup>H NMR (Table 1, Entry 3) spectrum of **2a**.



**Figure S2.** <sup>13</sup>C NMR (Table 1, Entry 3) spectrum of **2a**.



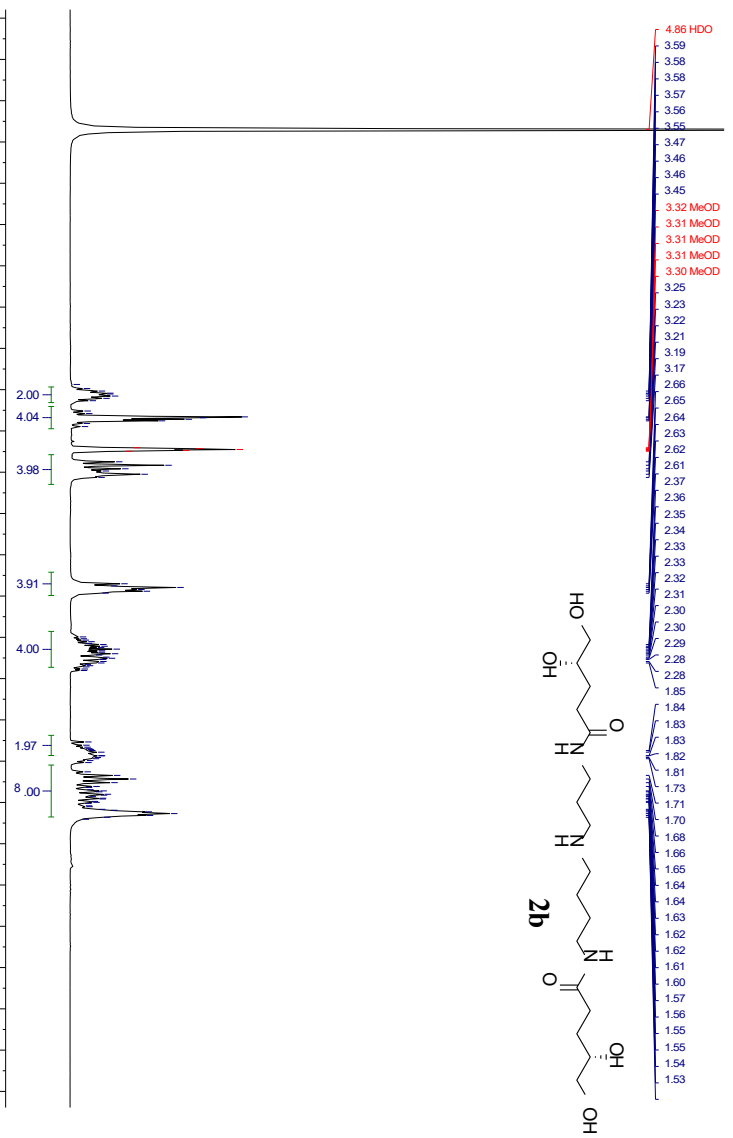


Figure S3. <sup>1</sup>H NMR (Table 1, Entry 4) spectrum of **2b**.

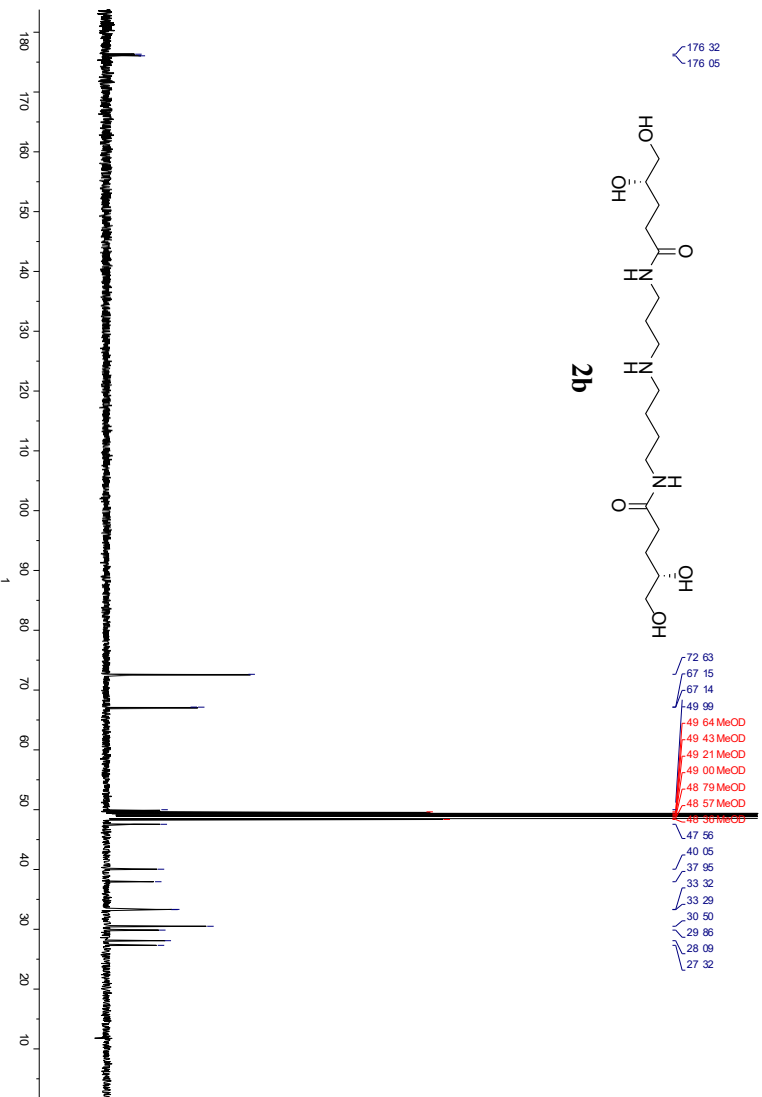


Figure S4. <sup>13</sup>C NMR (Table 1, Entry 4) spectrum of **2b**.



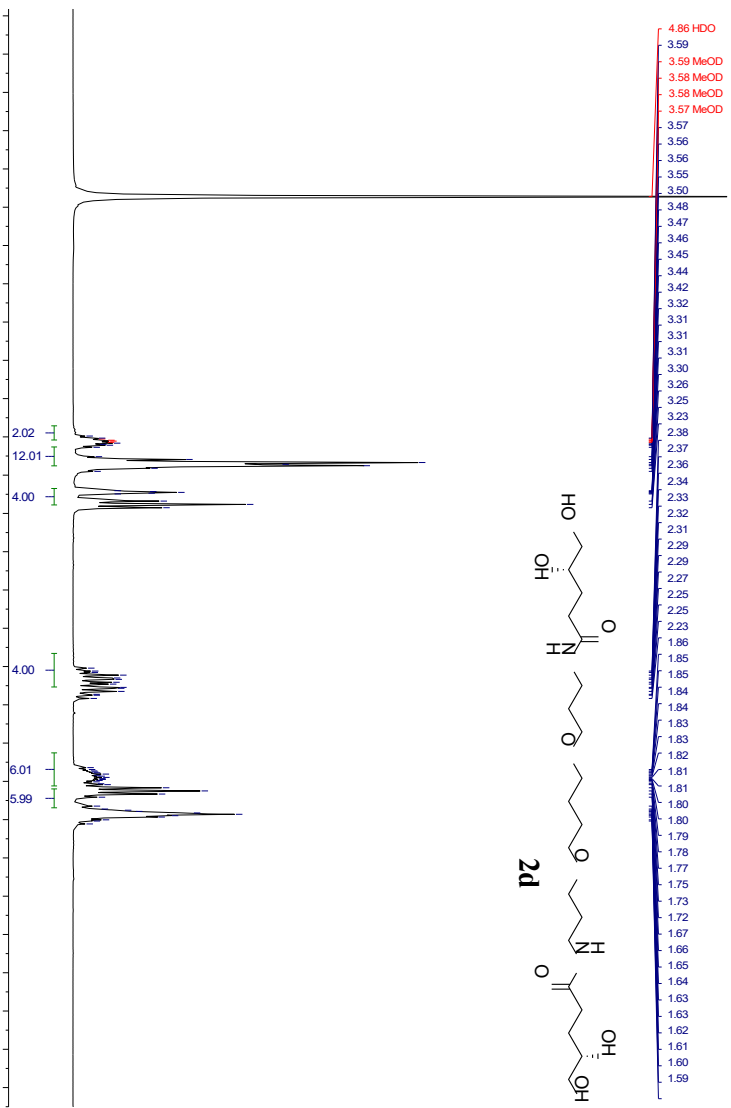


Figure S7.  $^1\text{H}$  NMR (Table 1, Entry 6) spectrum of **2d**.

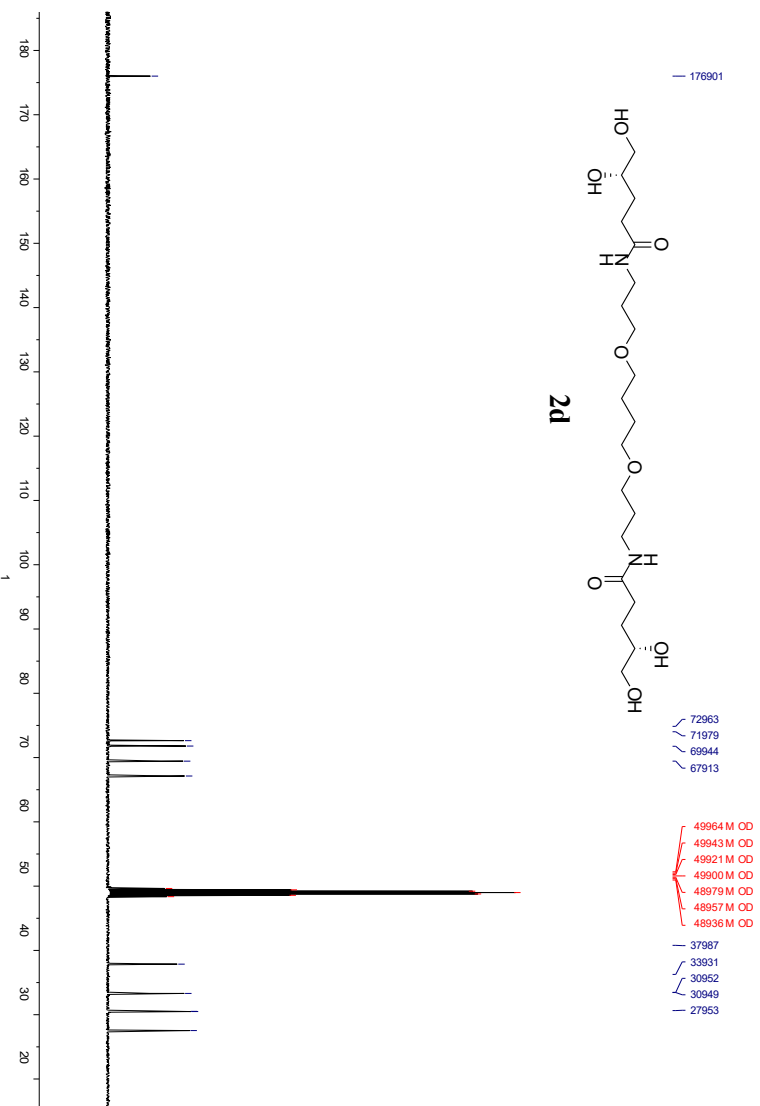
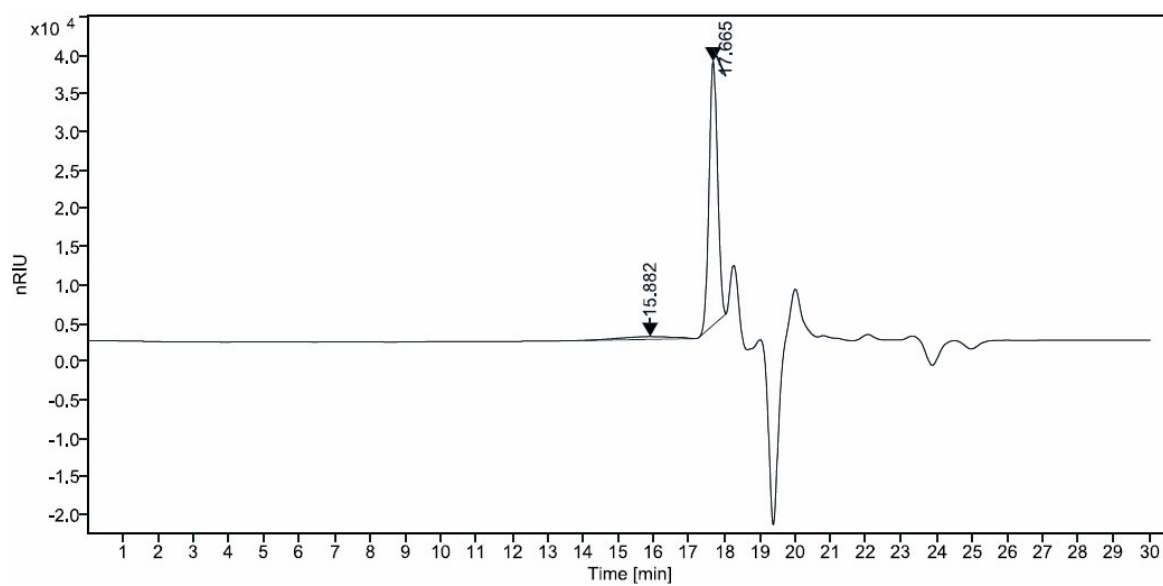
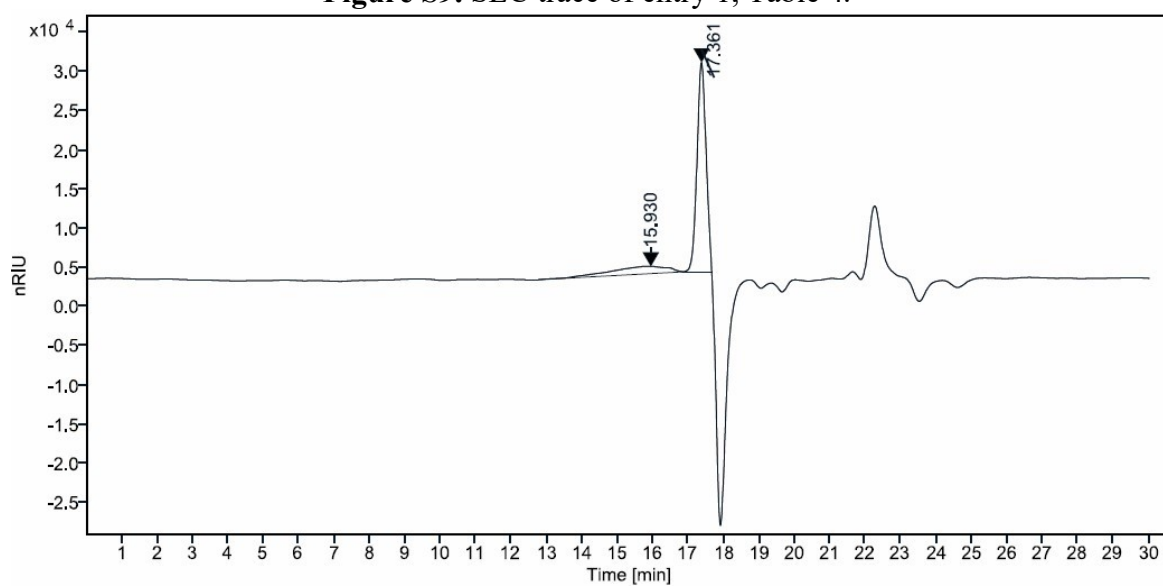


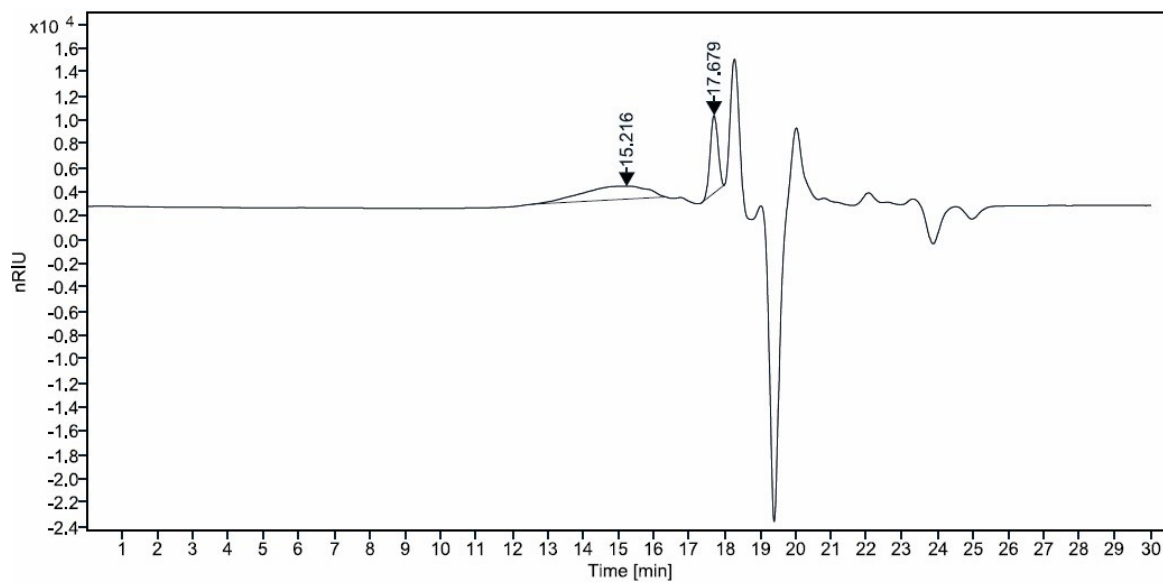
Figure S8.  $^{13}\text{C}$  NMR (Table 1, Entry 6) spectrum of **2d**.



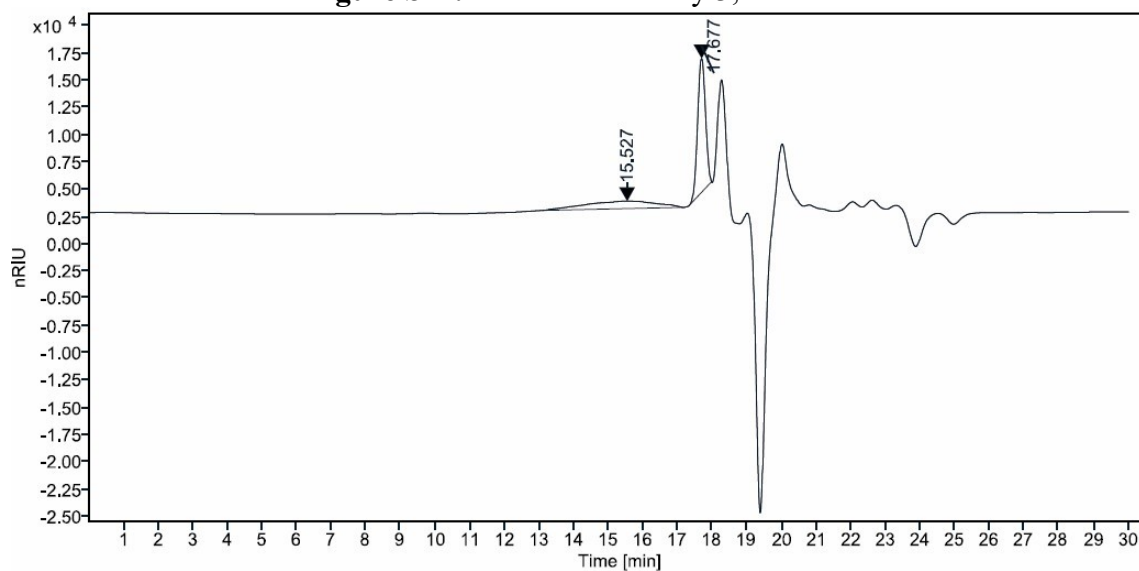
**Figure S9.** SEC trace of entry 1, Table 4.



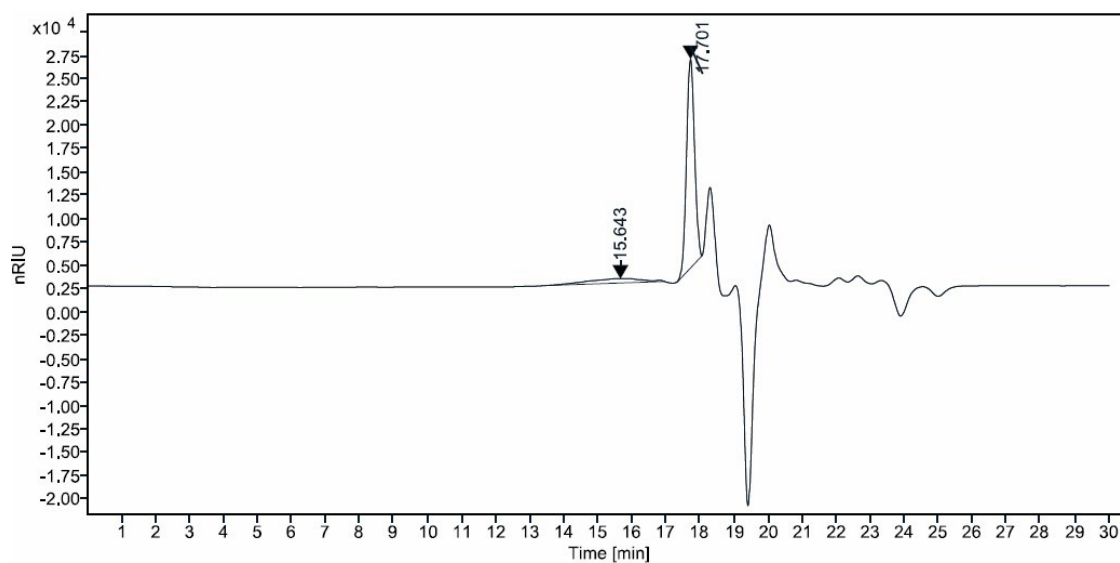
**Figure S10.** SEC trace of entry 2, Table 4.



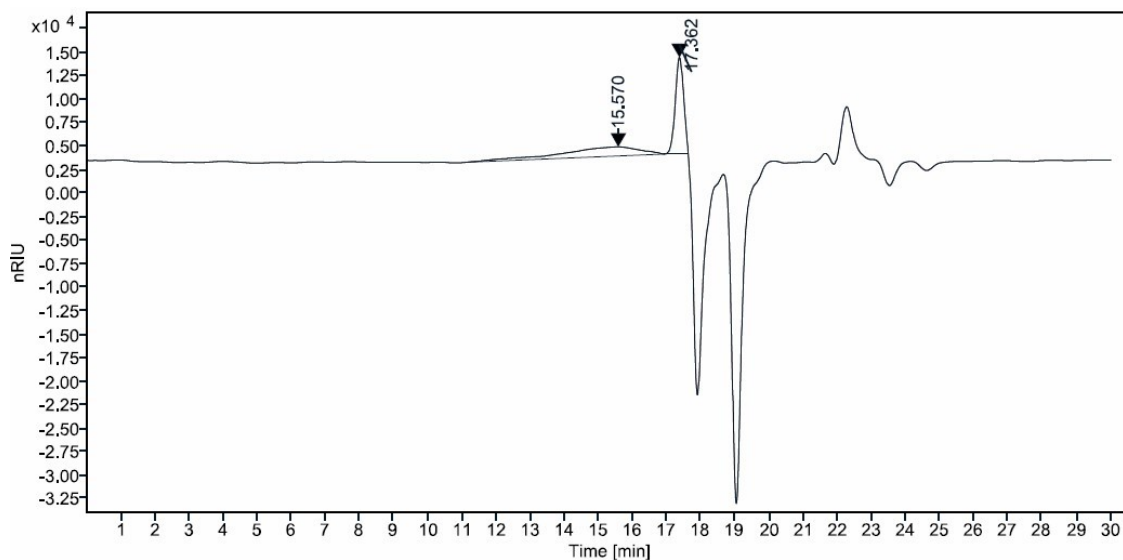
**Figure S11.** SEC trace of entry 3, Table 4.



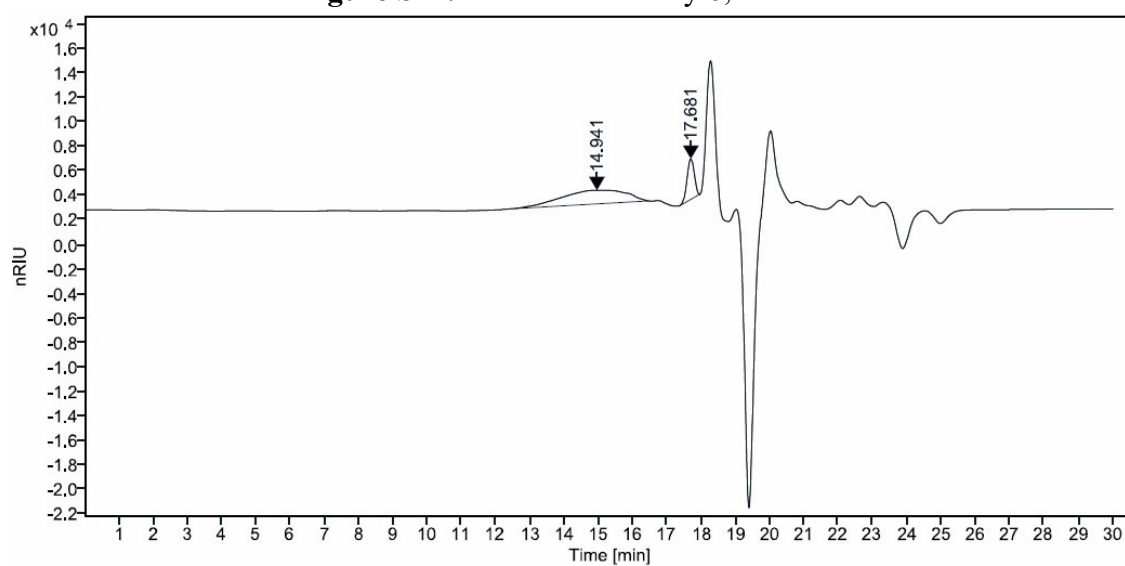
**Figure S12.** SEC trace of entry 4, Table 4.



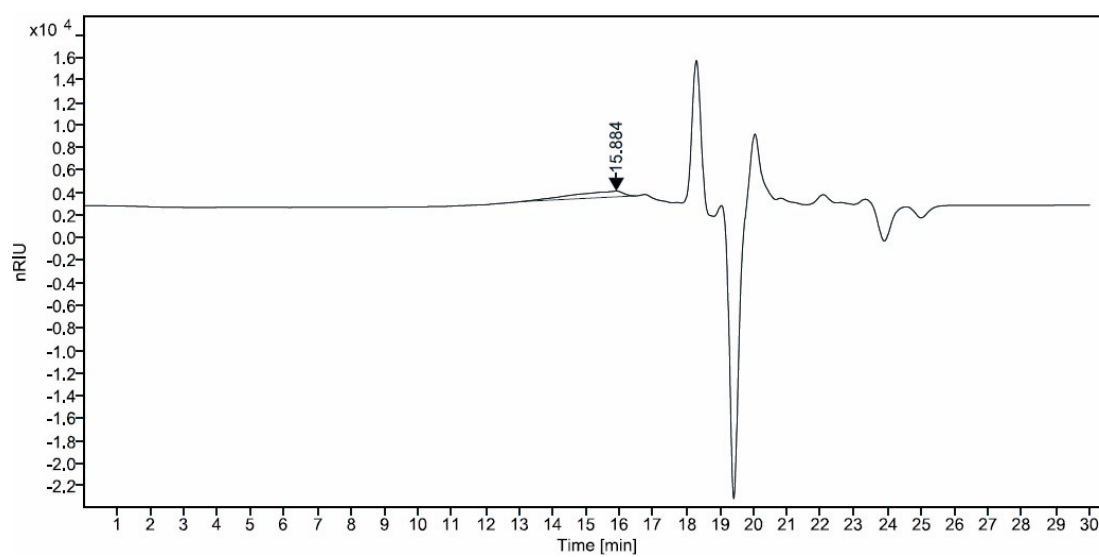
**Figure S13.** SEC trace of entry 8, Table 4.



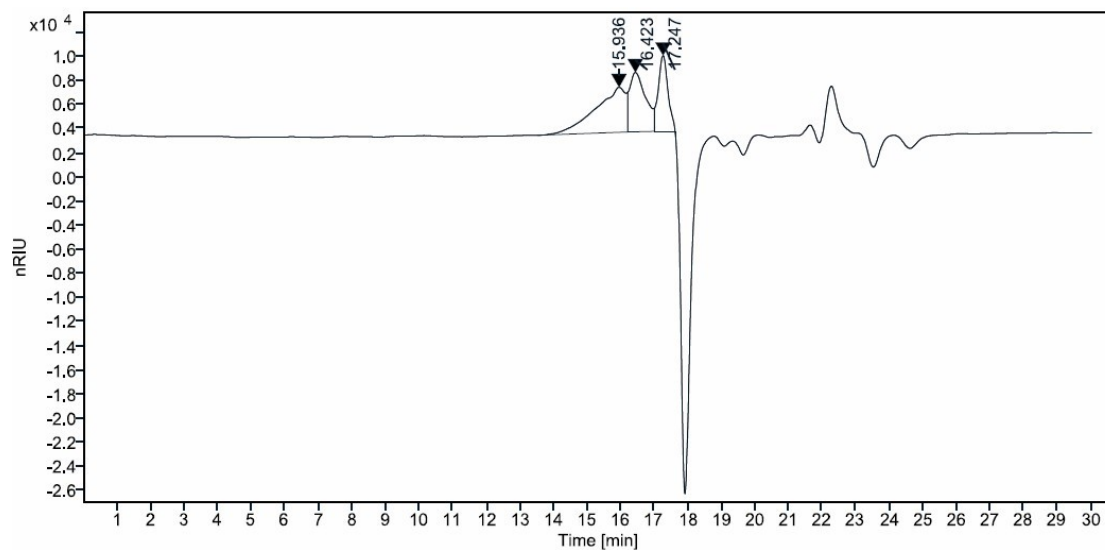
**Figure S14.** SEC trace of entry 6, Table 4.



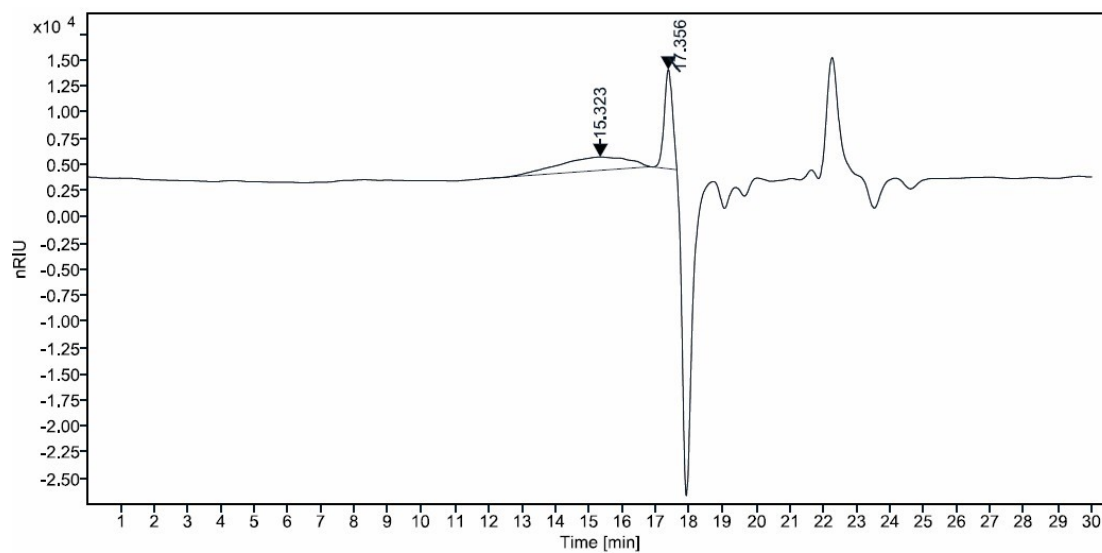
**Figure S15.** SEC trace of entry 7, Table 4.



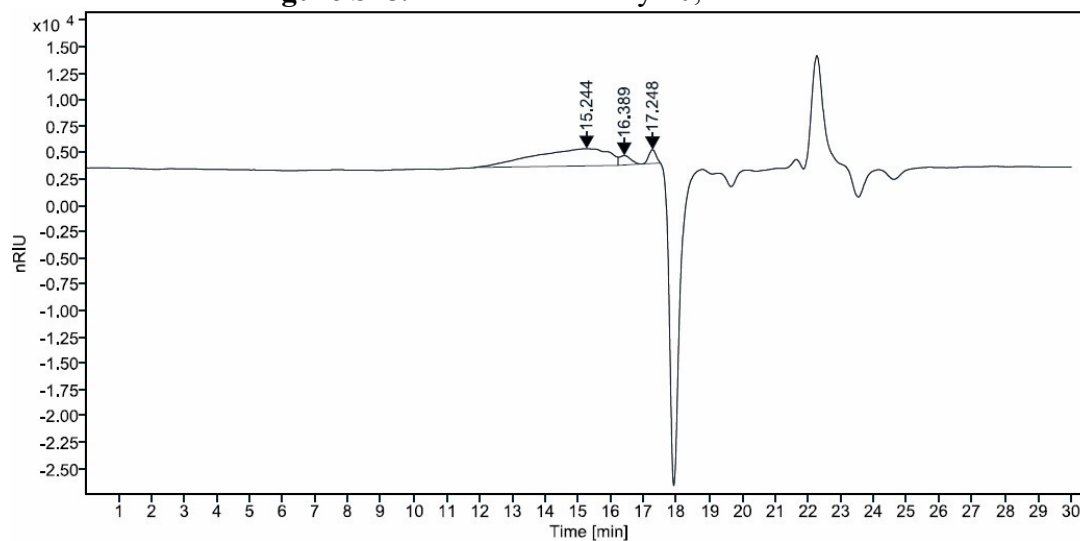
**Figure S16.** SEC trace of entry 8, Table 4.



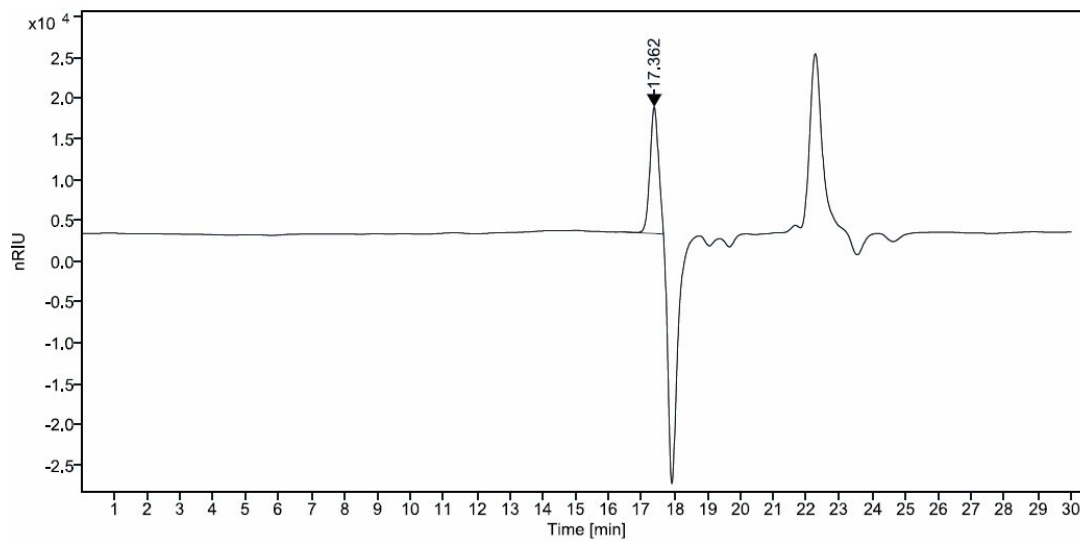
**Figure S17.** SEC trace of entry 9, Table 4.



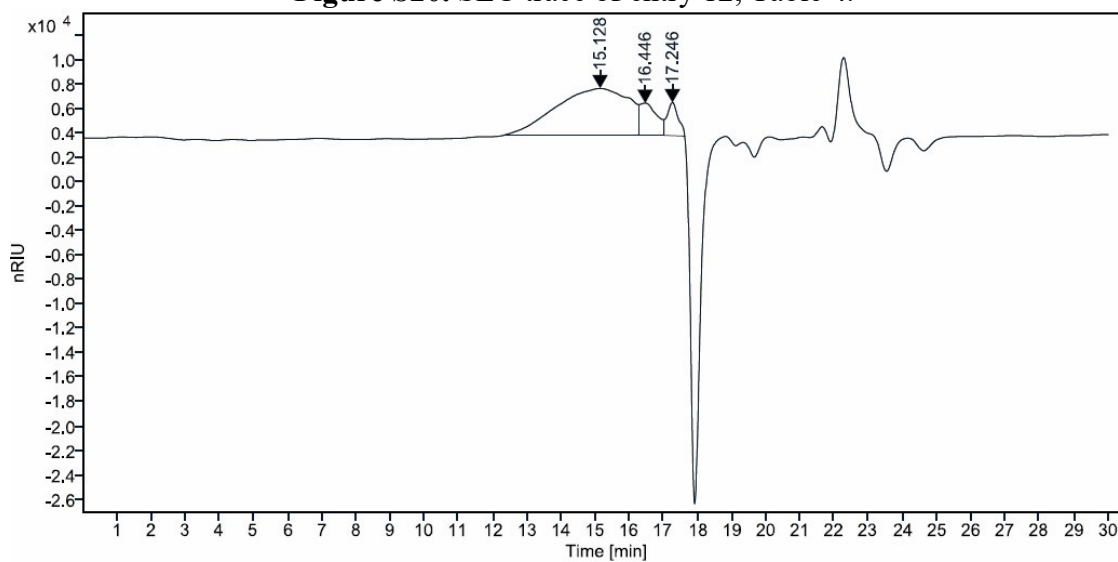
**Figure S18.** SEC trace of entry 10, Table 4.



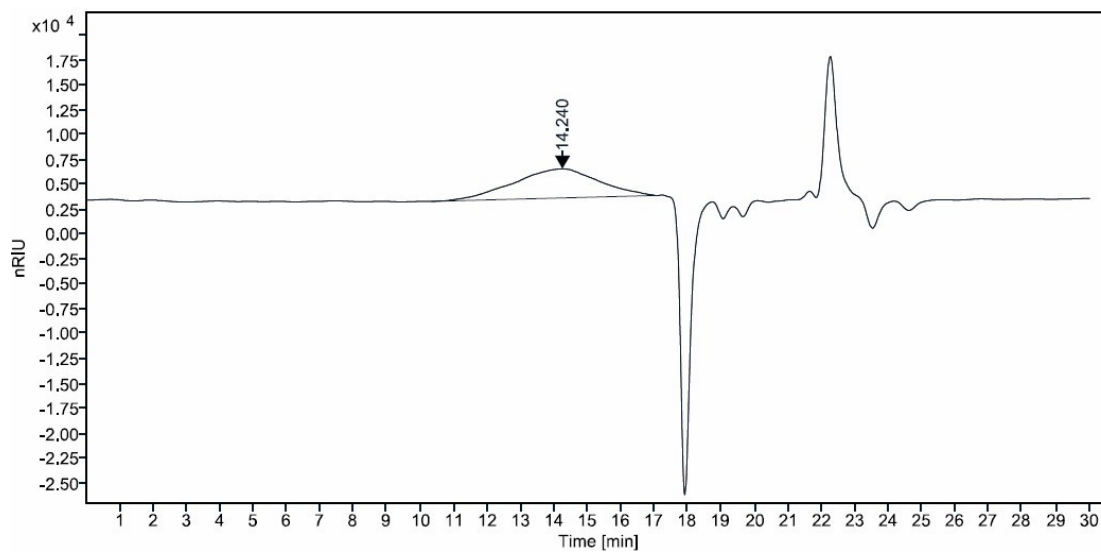
**Figure S19.** SEC trace of entry 11, Table 4.



**Figure S20.** SEC trace of entry 12, Table 4.

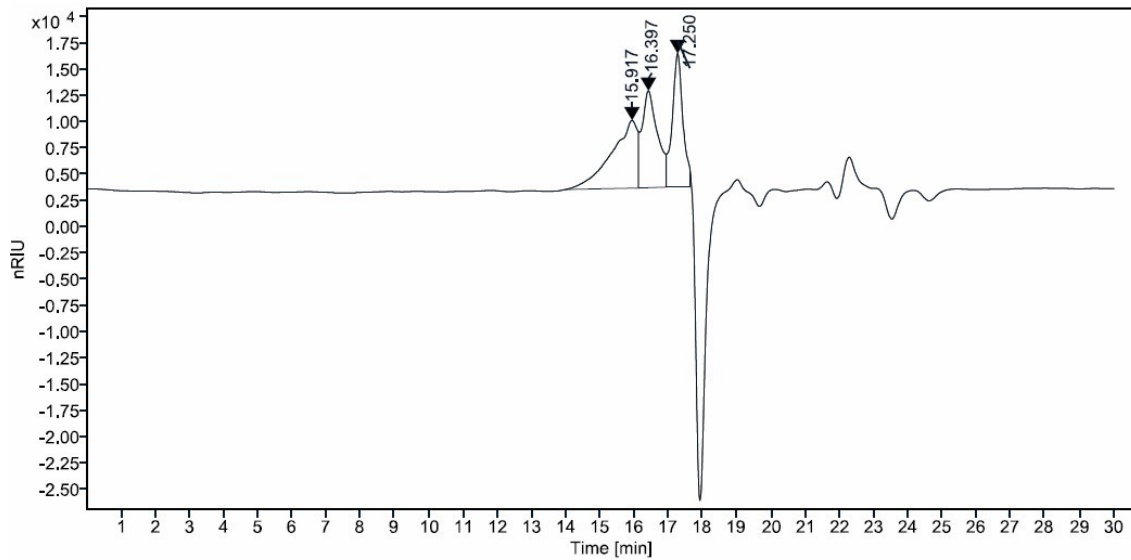


**Figure S21.** SEC trace of entry 13, Table 4.

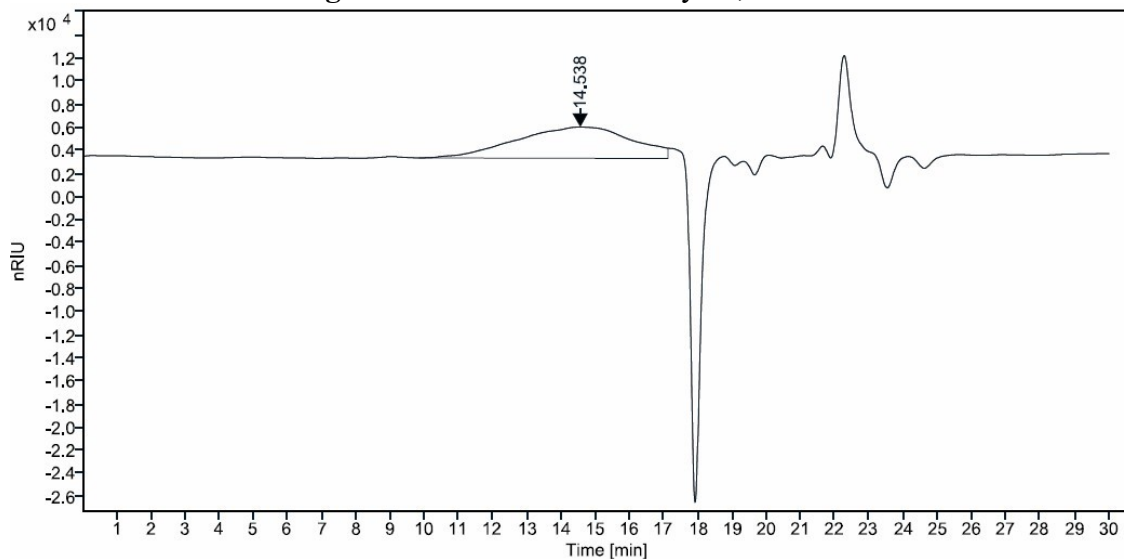


**Figure S22.** SEC trace of entry 14, Table 4.

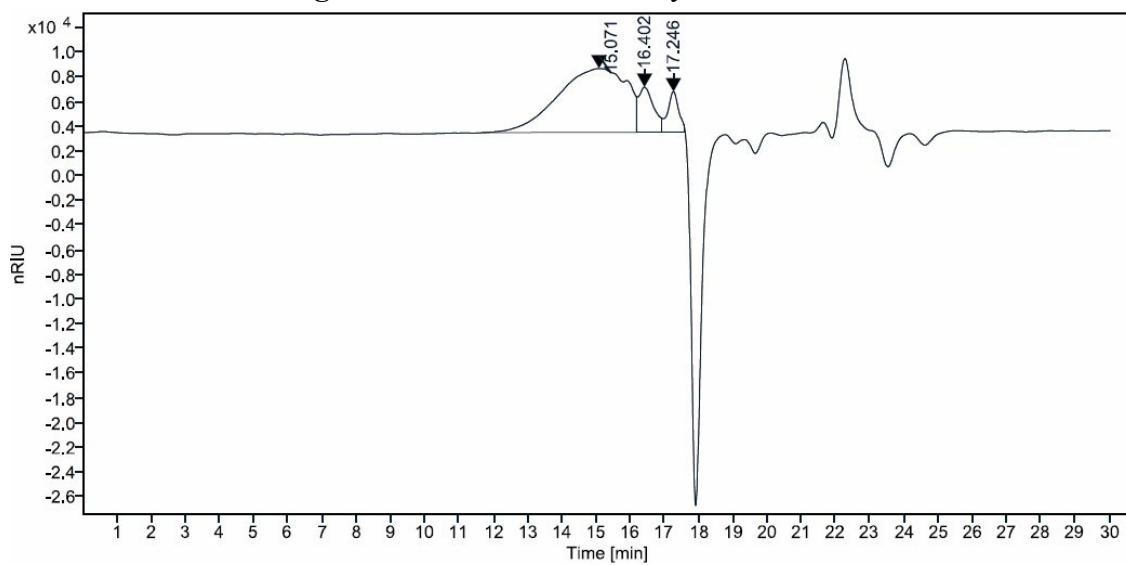




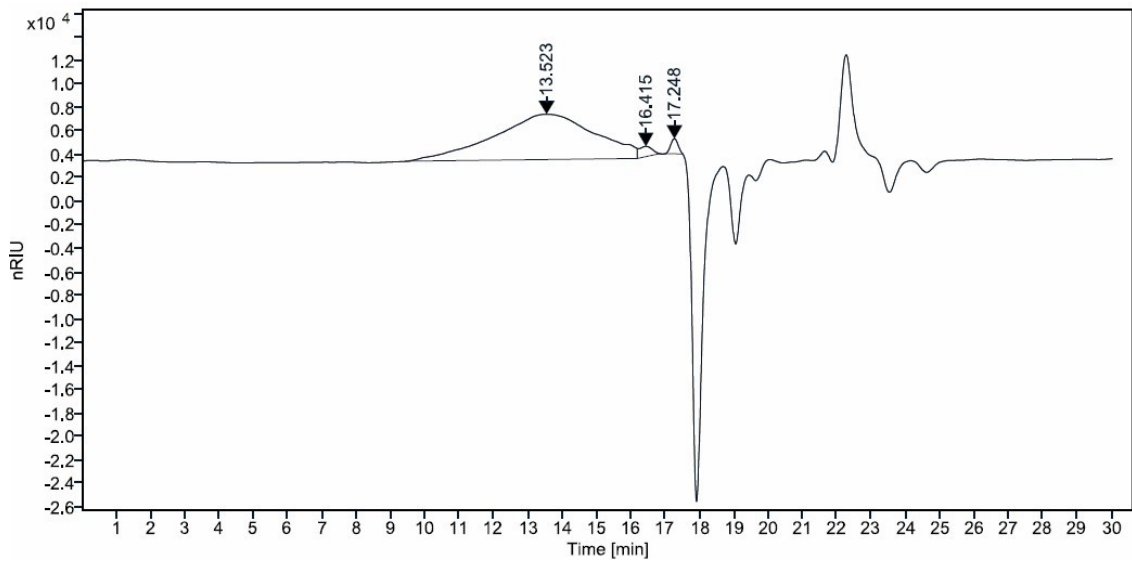
**Figure S23.** SEC trace of entry 15, Table 4.



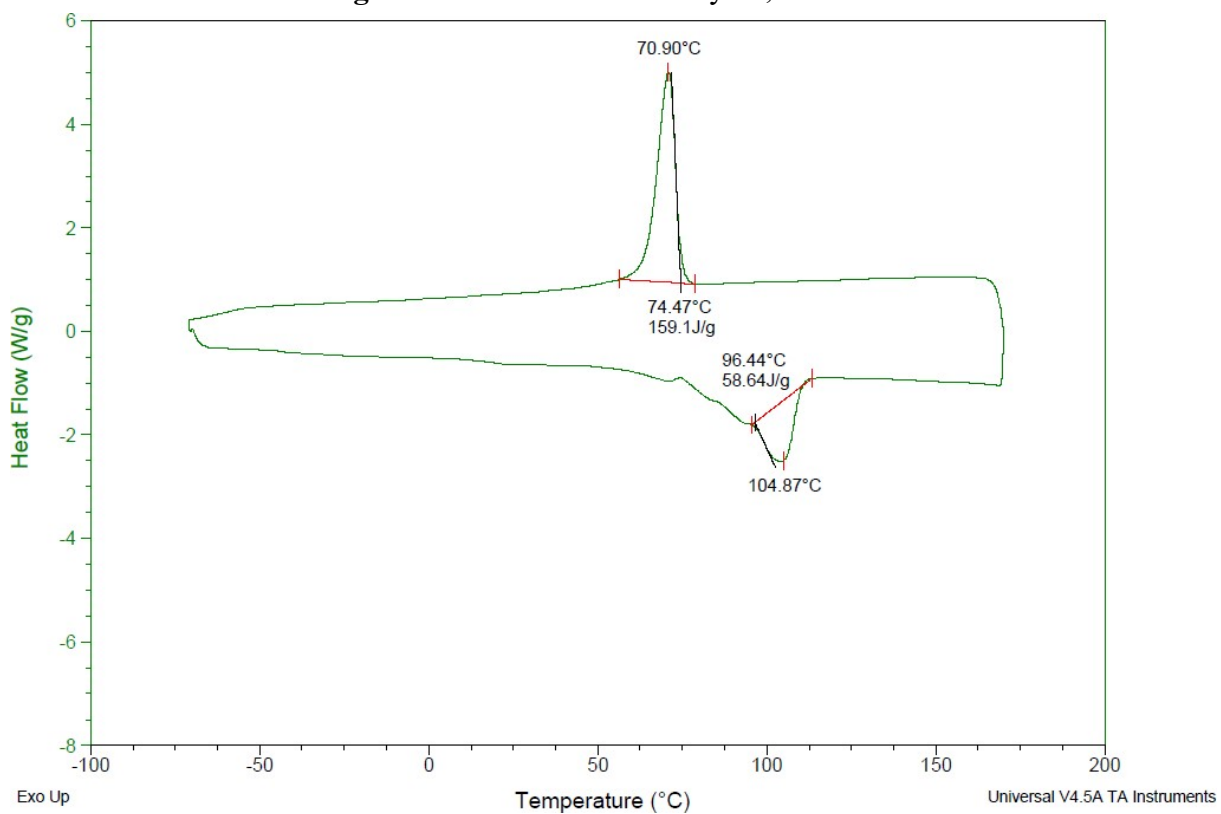
**Figure S24.** SEC trace of entry 16, Table 4.



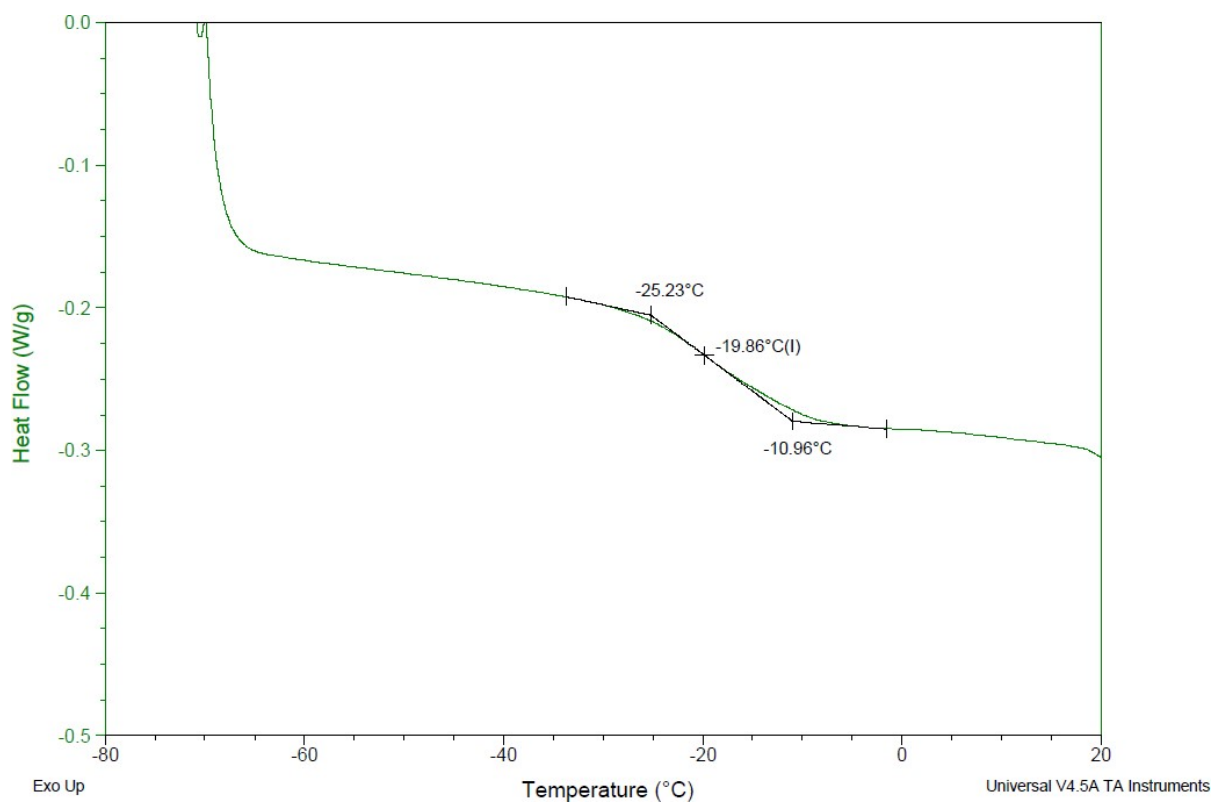
**Figure S25.** SEC trace of entry 17, Table 4.



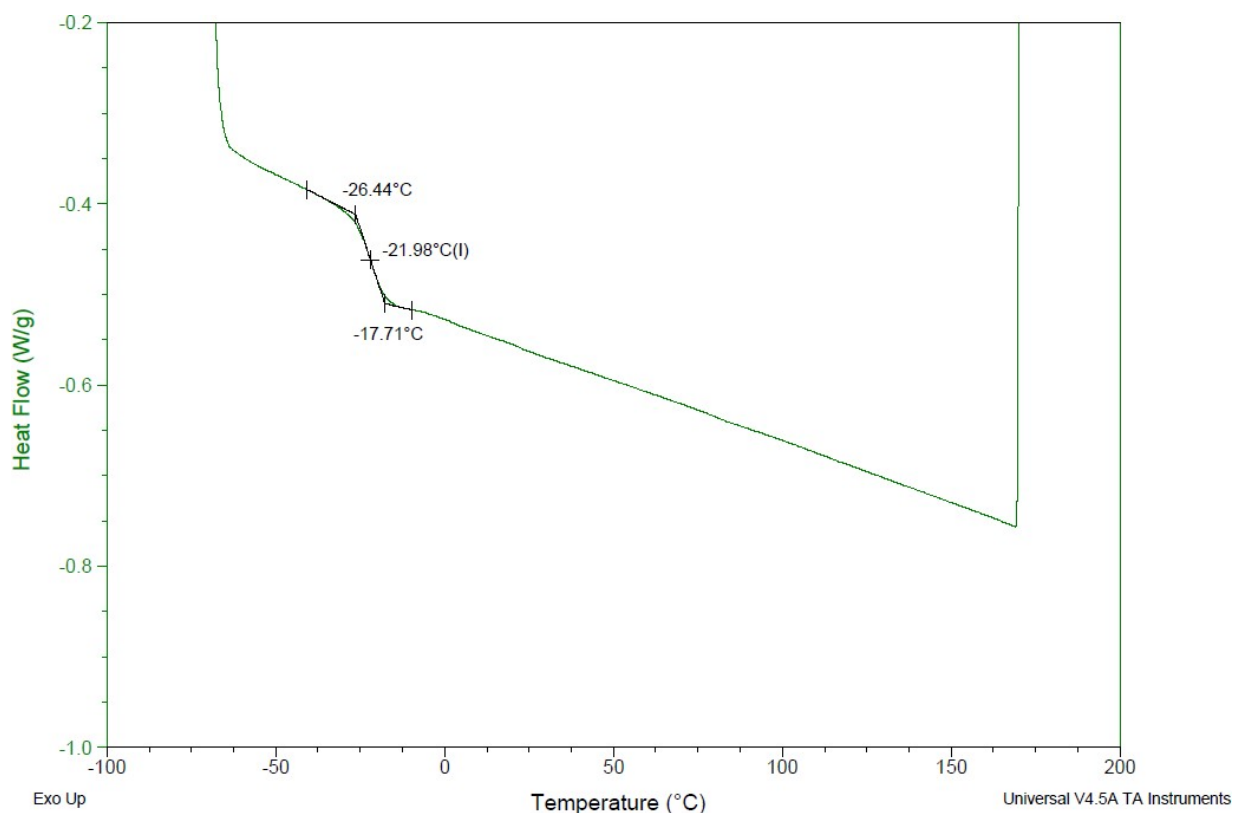
**Figure S26.** SEC trace of entry 18, Table 4.



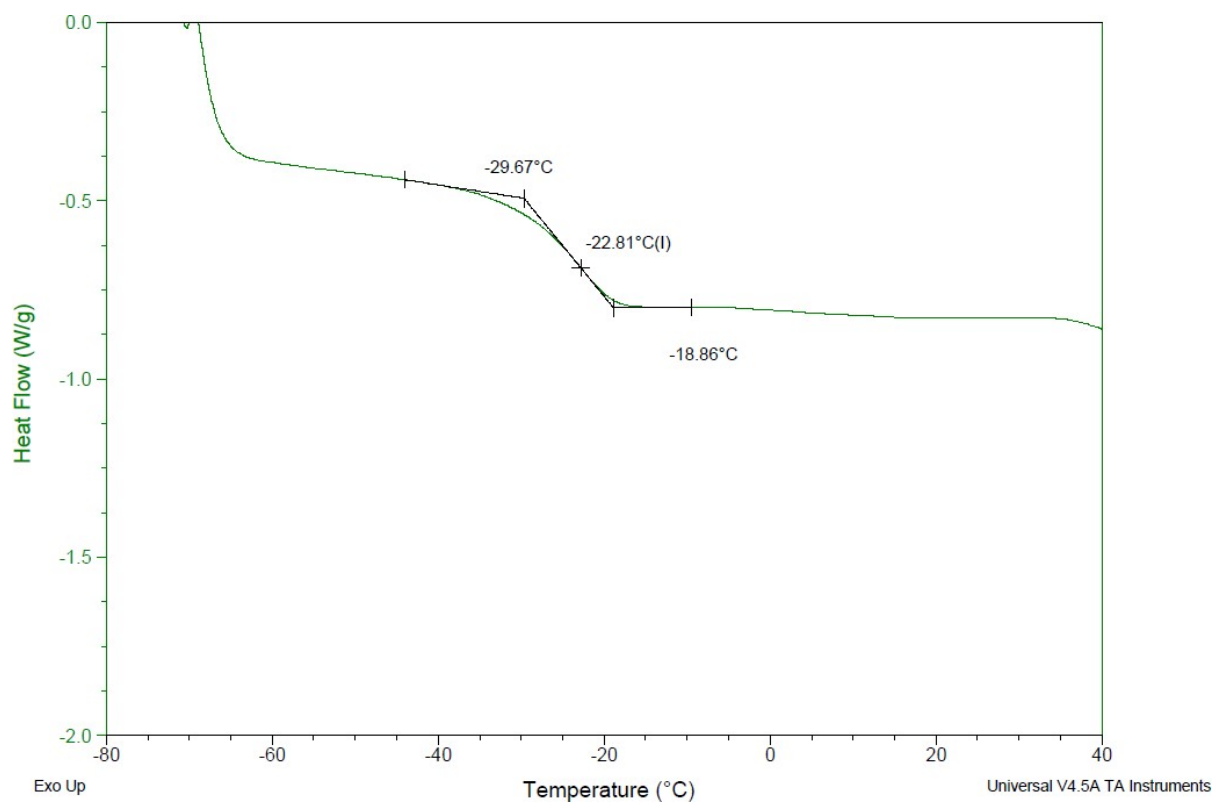
**Figure S27.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 1, Table 4.



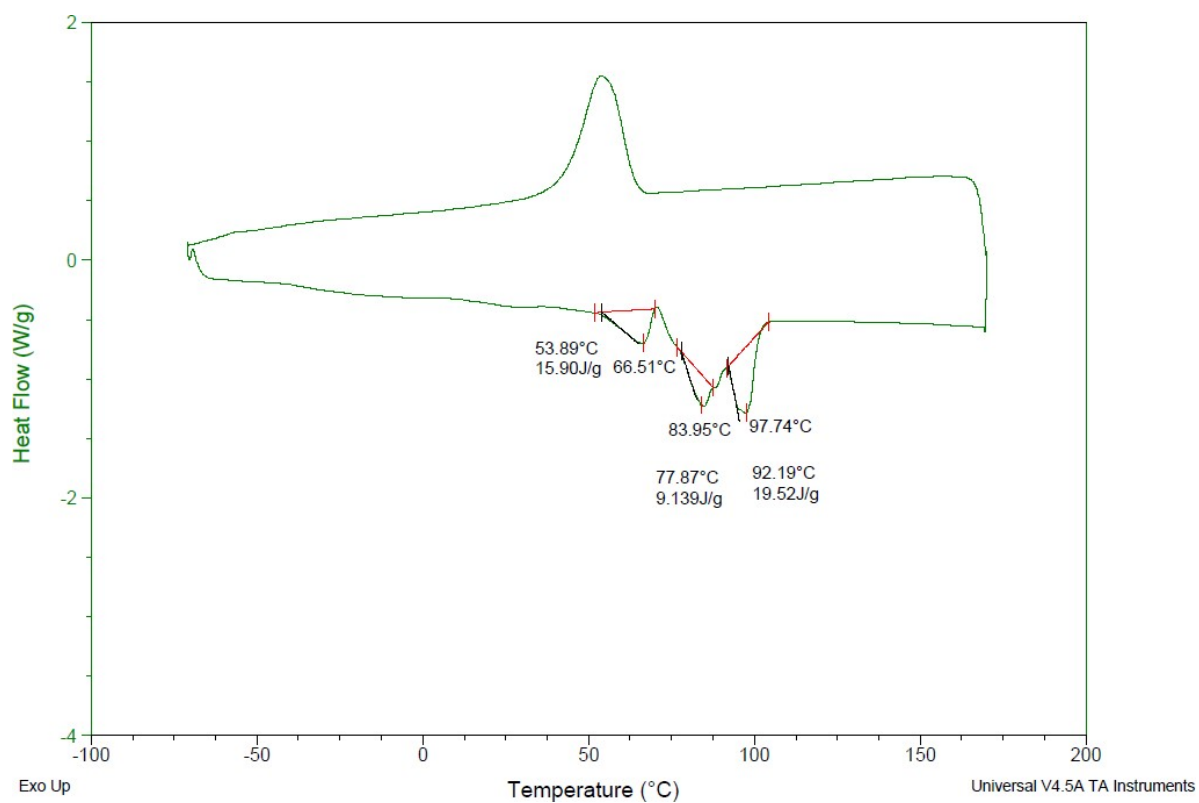
**Figure S28.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 2, Table 4.



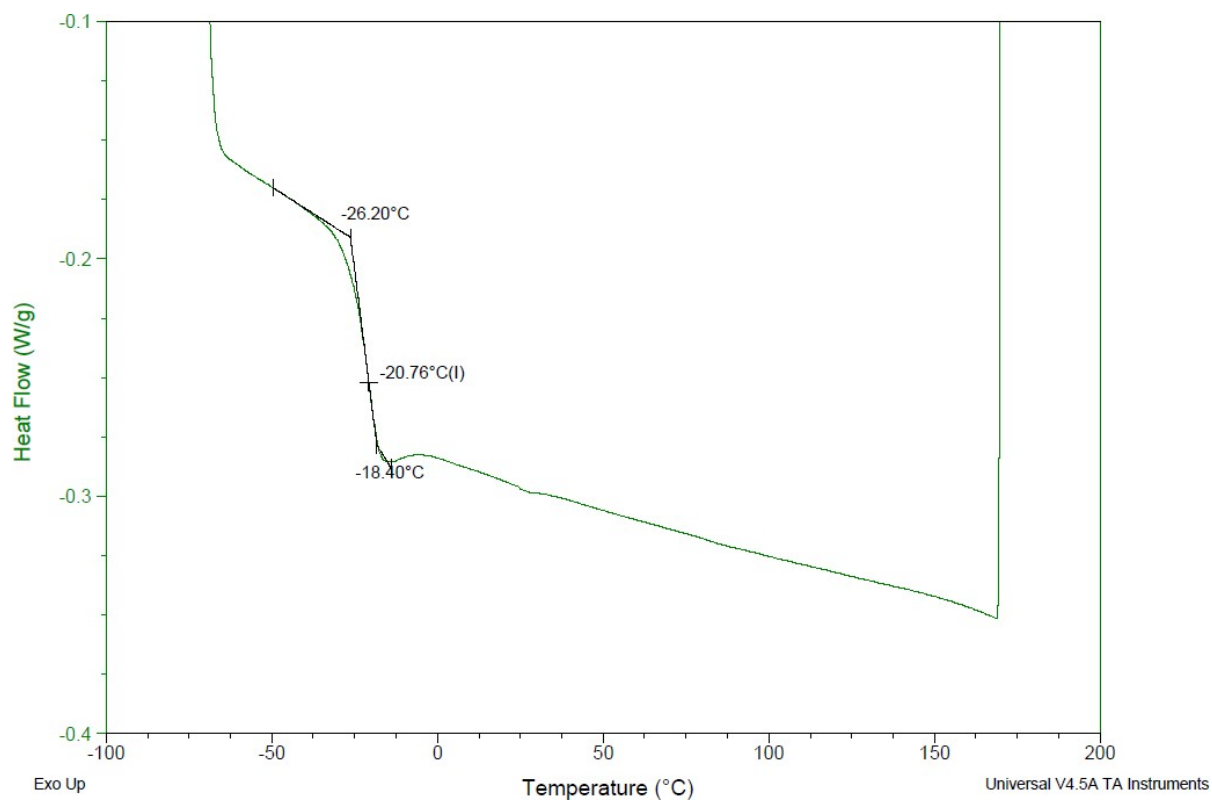
**Figure S29.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 3, Table 4.



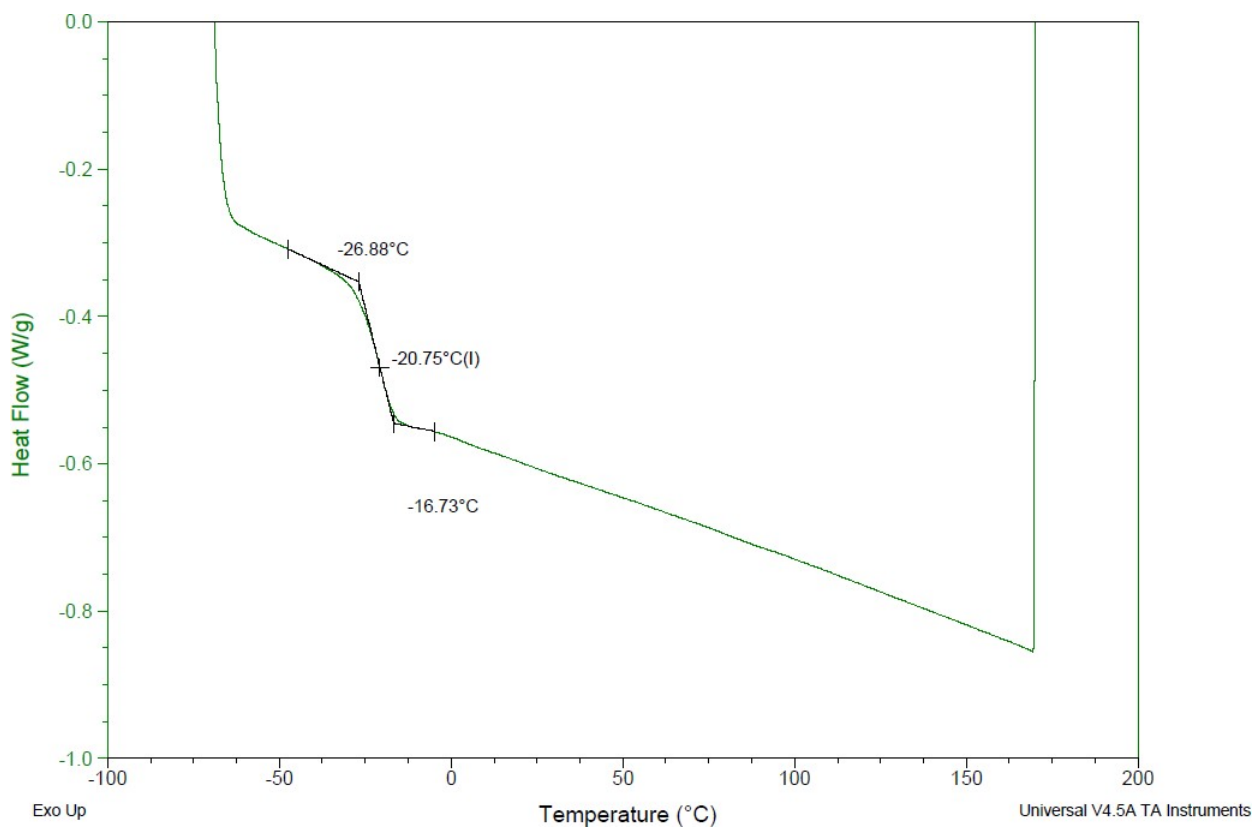
**Figure S30.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 4, Table 4.



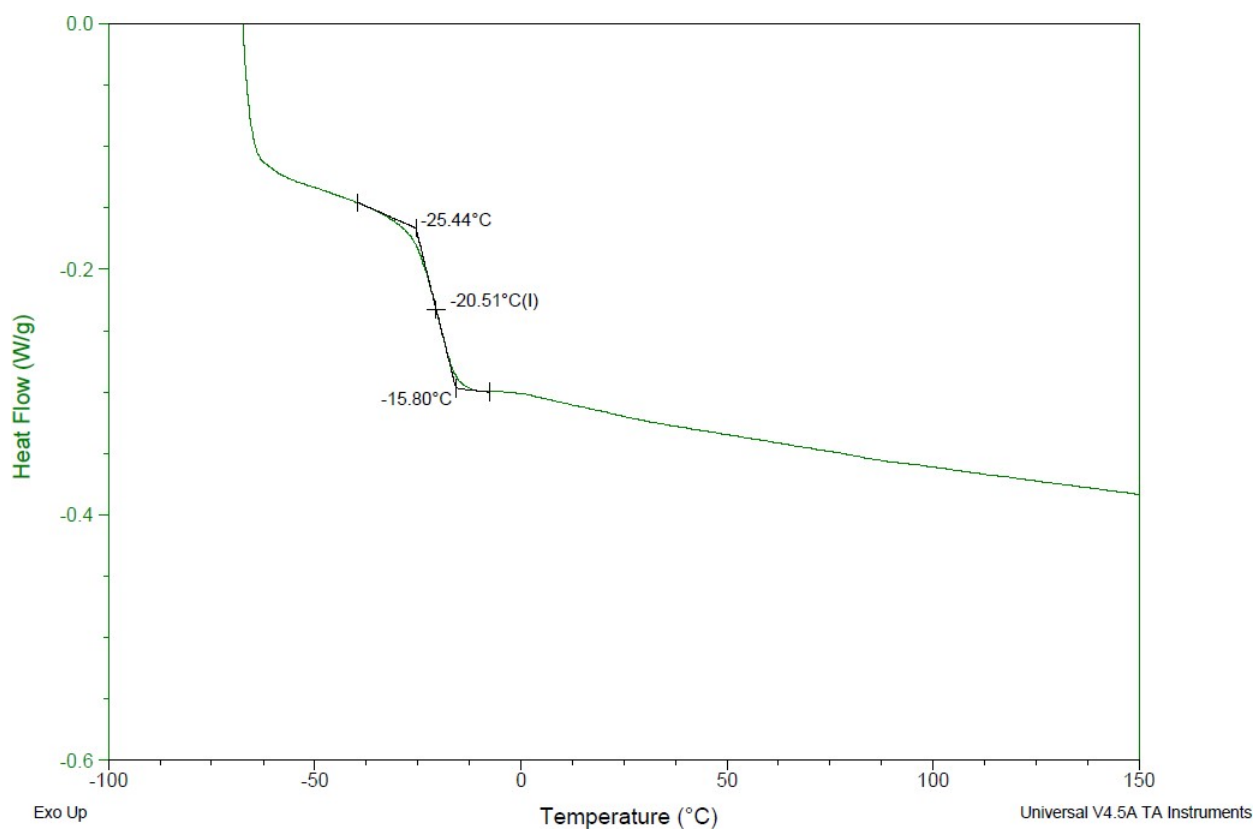
**Figure S31.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 5, Table 4.



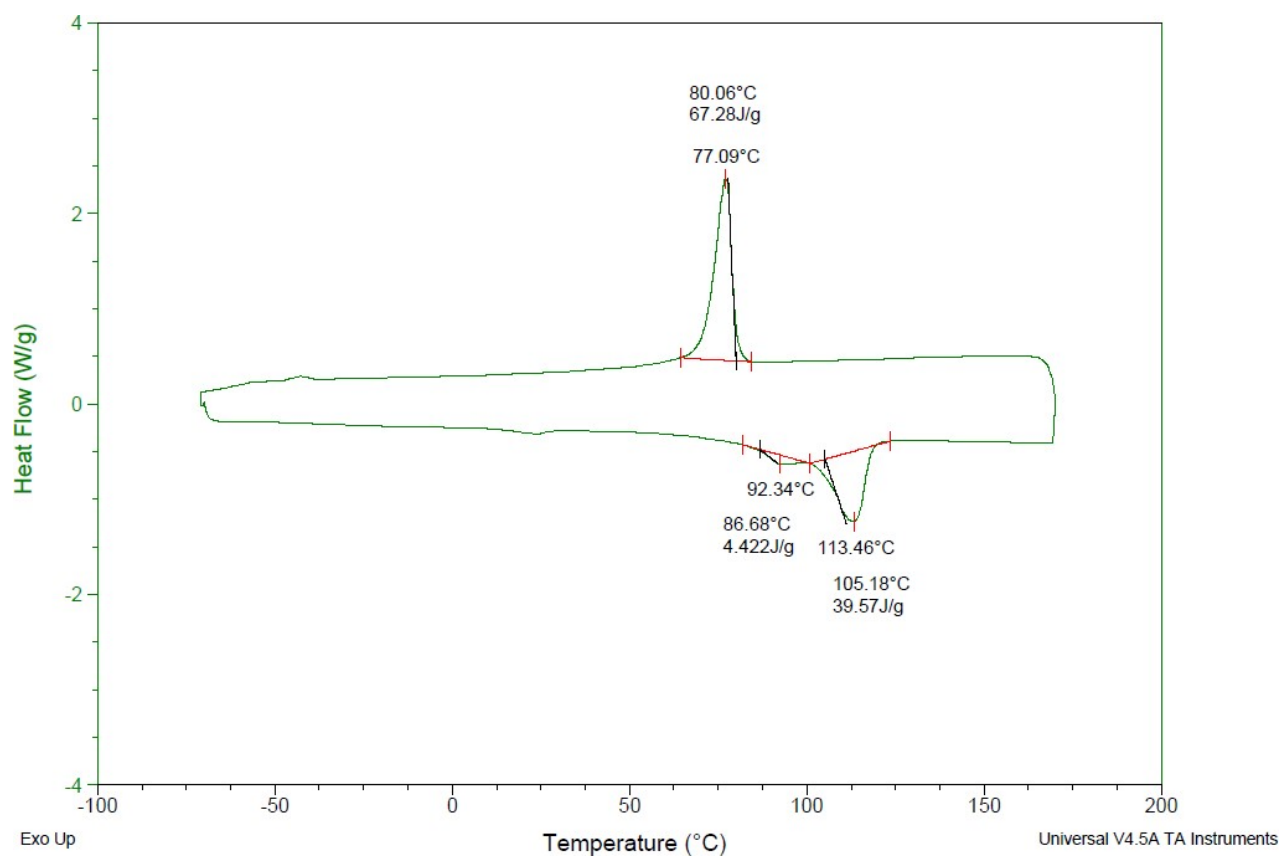
**Figure S32.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 6, Table 4.



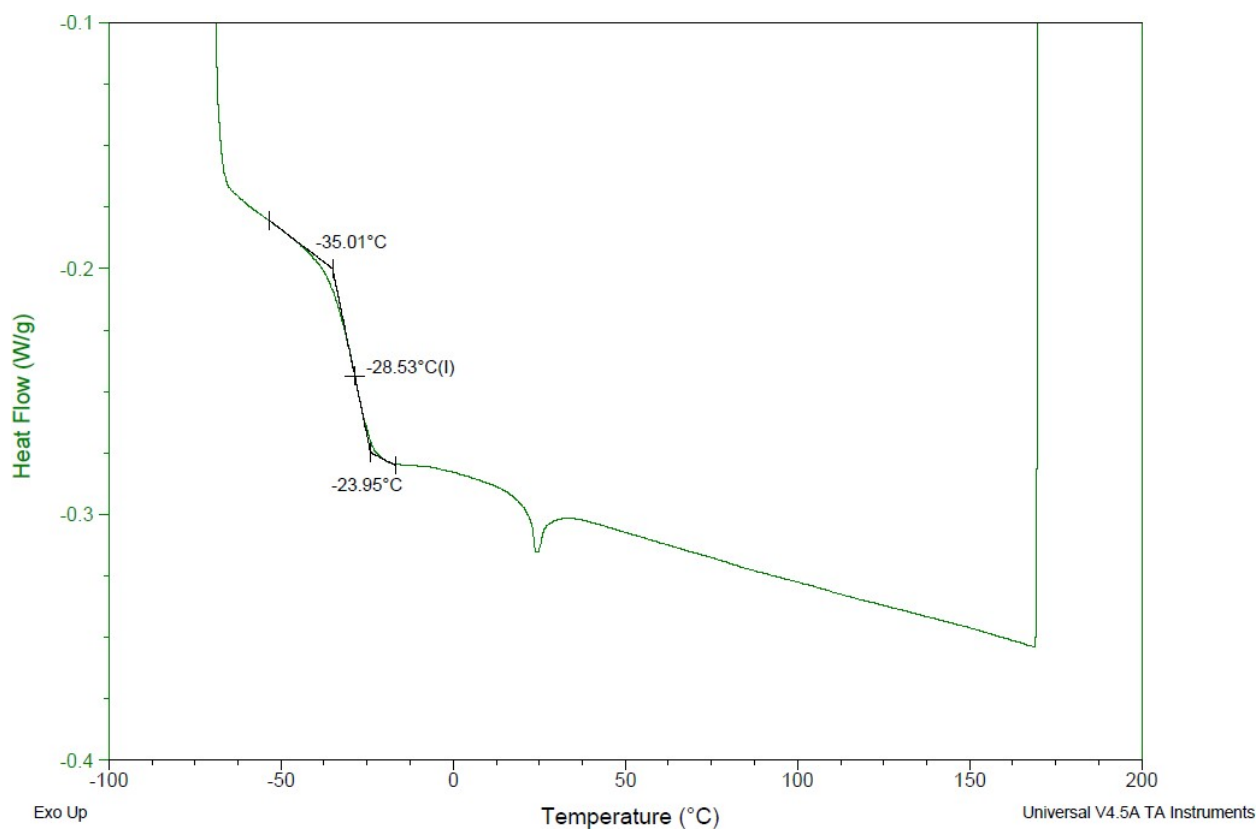
**Figure S33.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 7, Table 4.



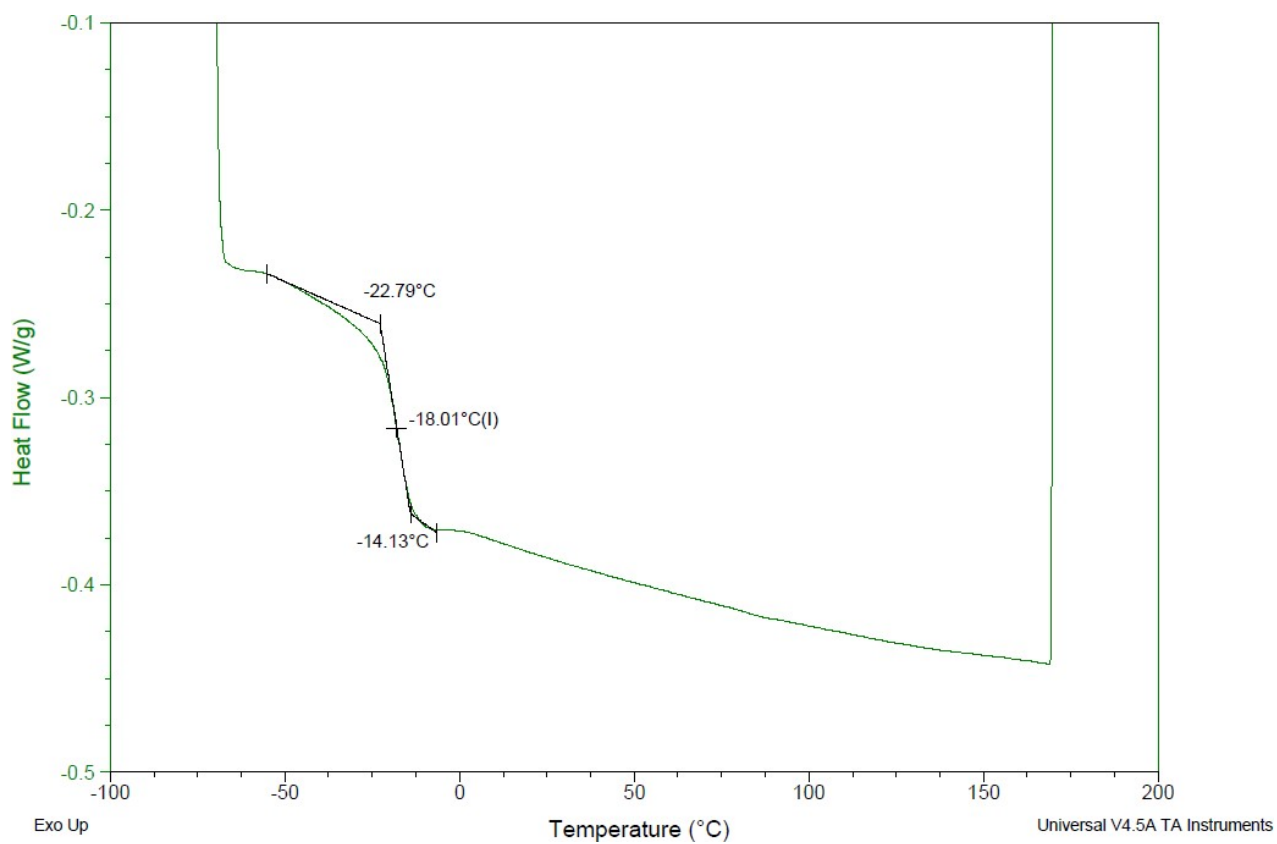
**Figure S34.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 8, Table 4.



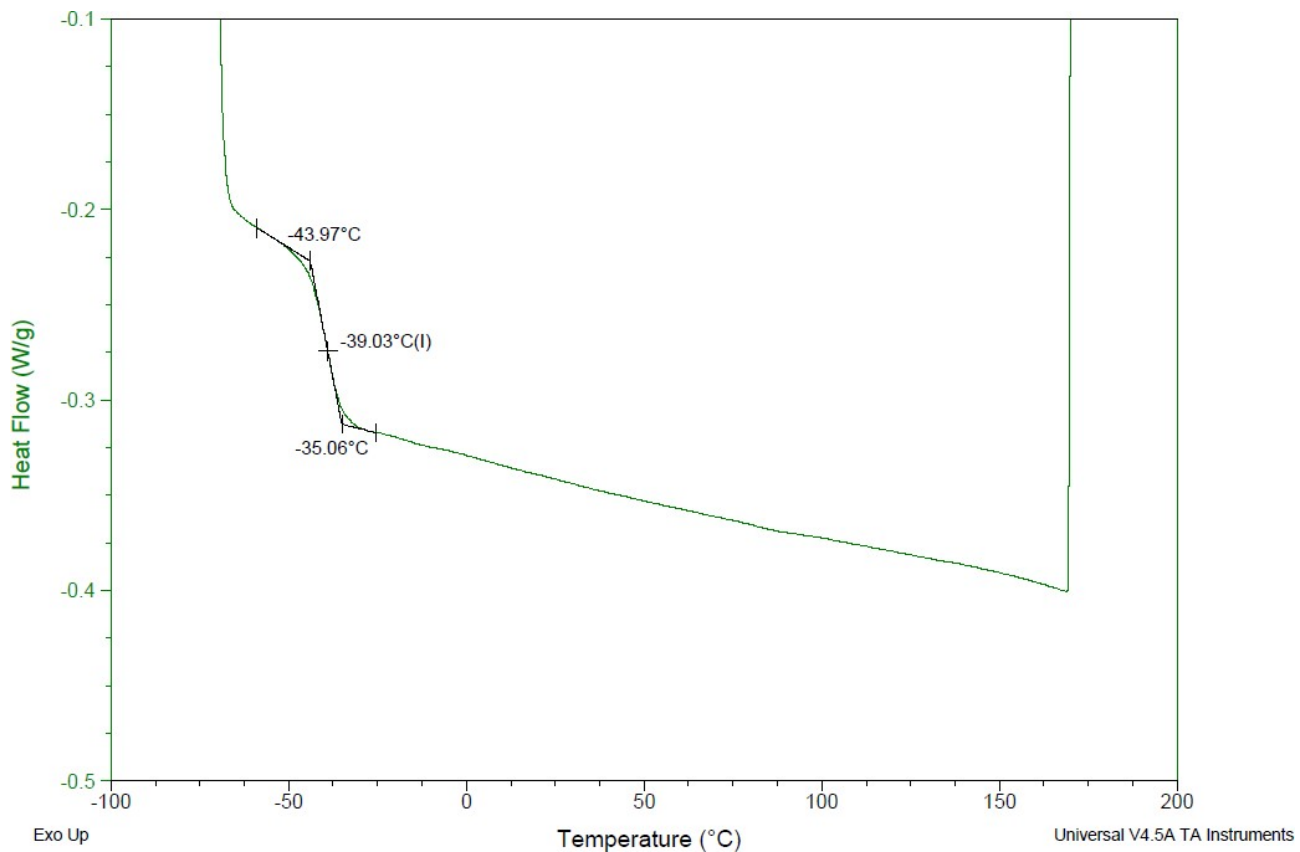
**Figure S35.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 9, Table 4.



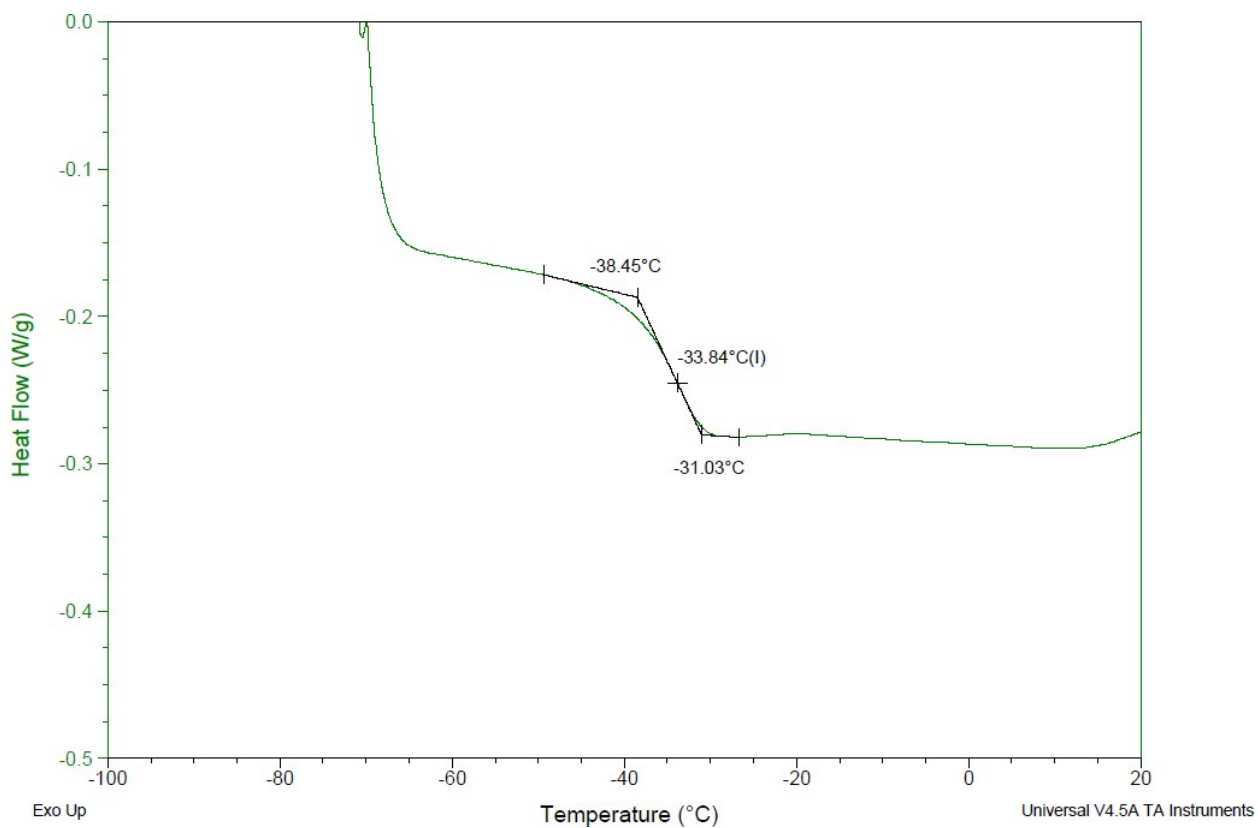
**Figure S36.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 10, Table 4.



**Figure S37.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 11, Table 4.

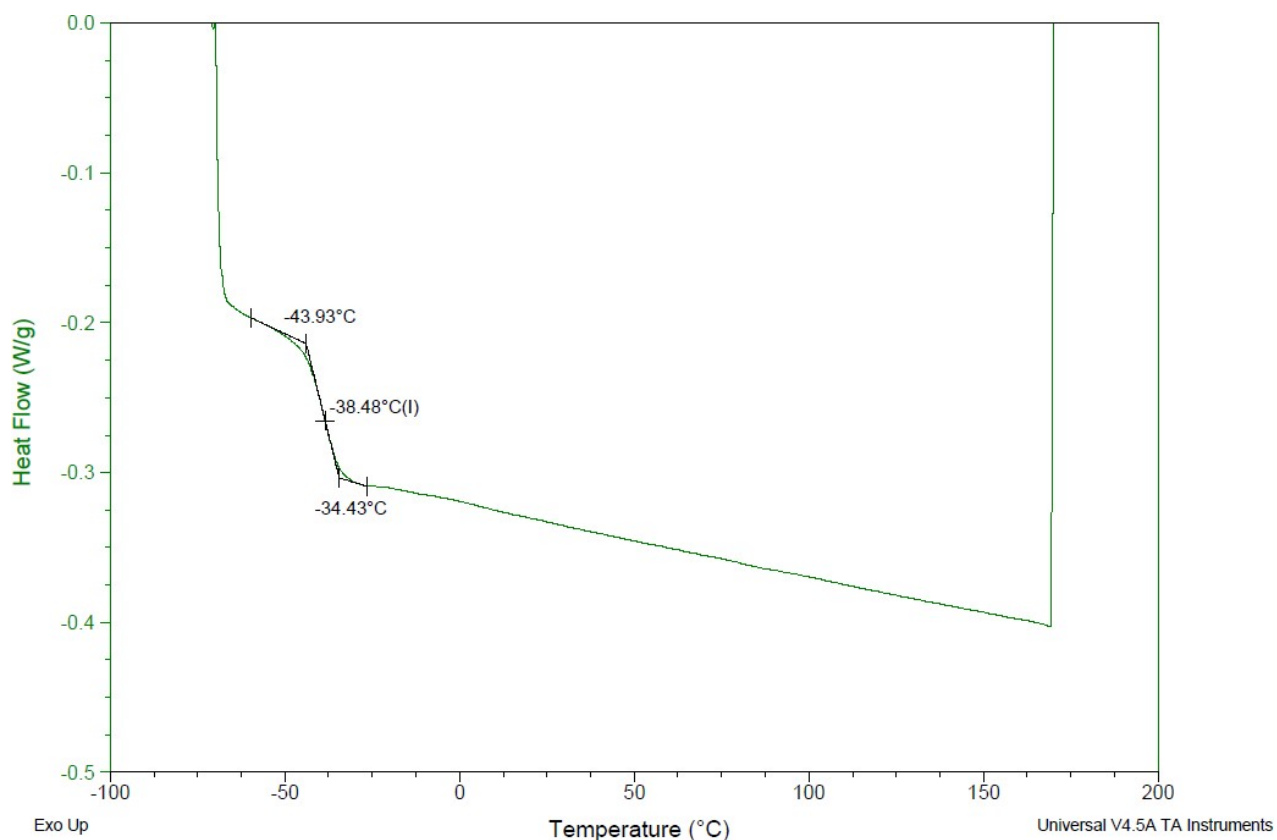


**Figure S38.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 12, Table 4.

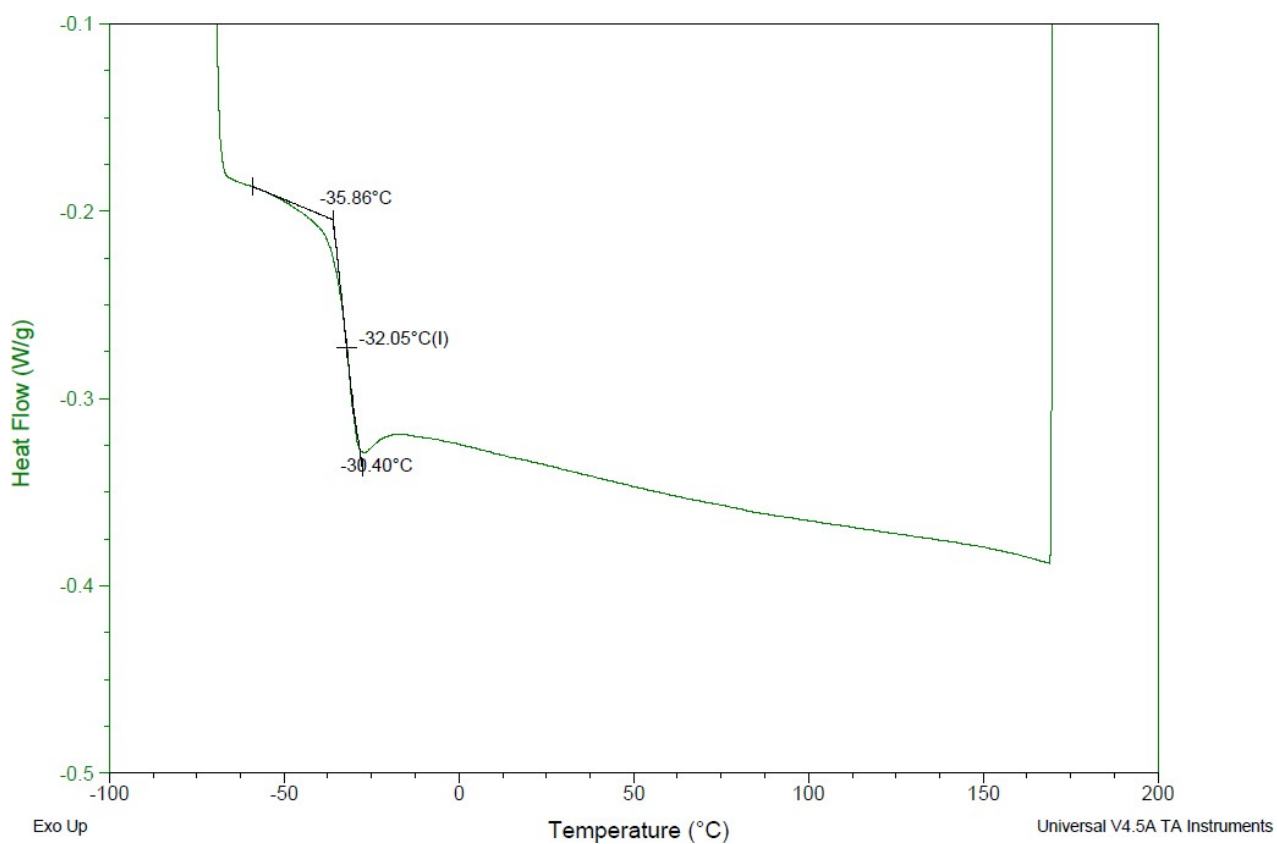


**Figure S39.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 13, Table 4.

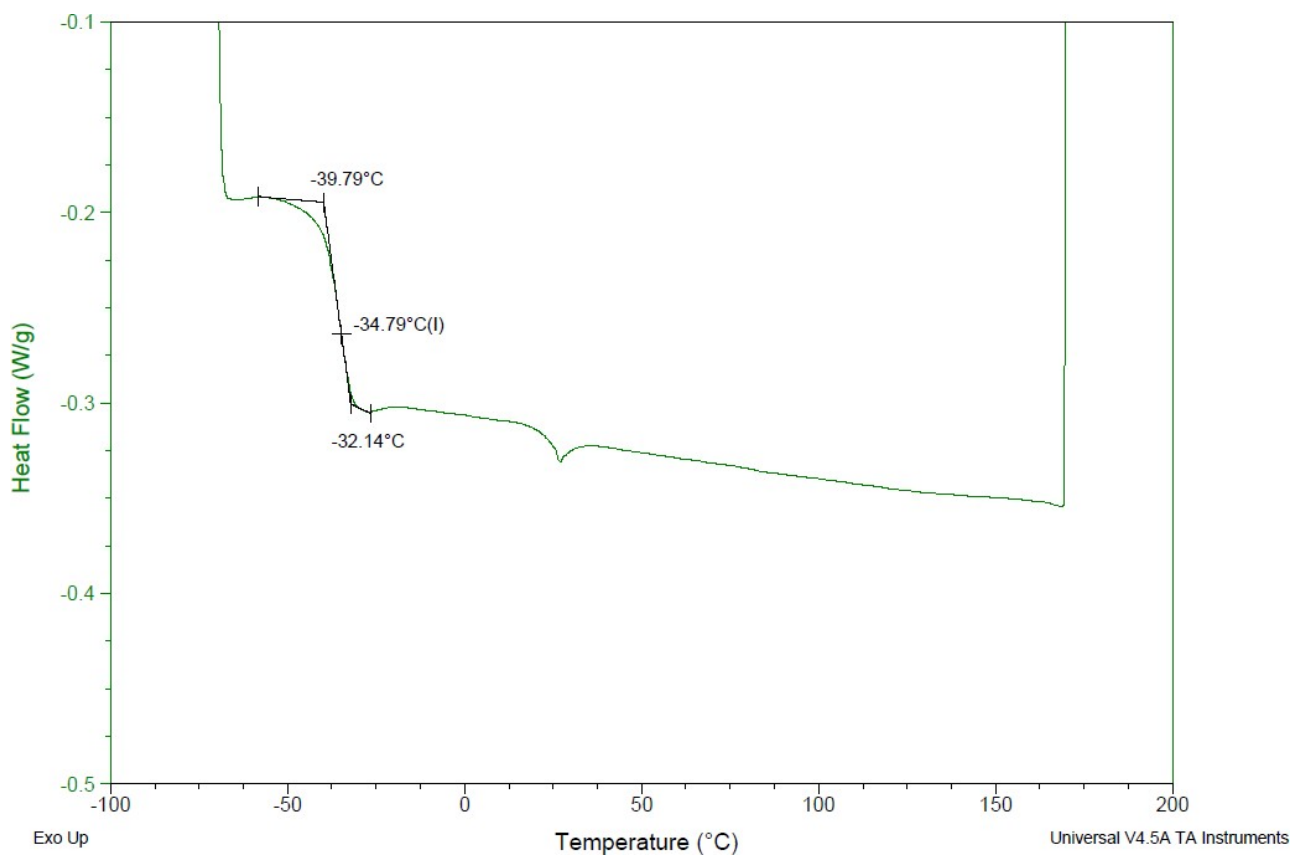




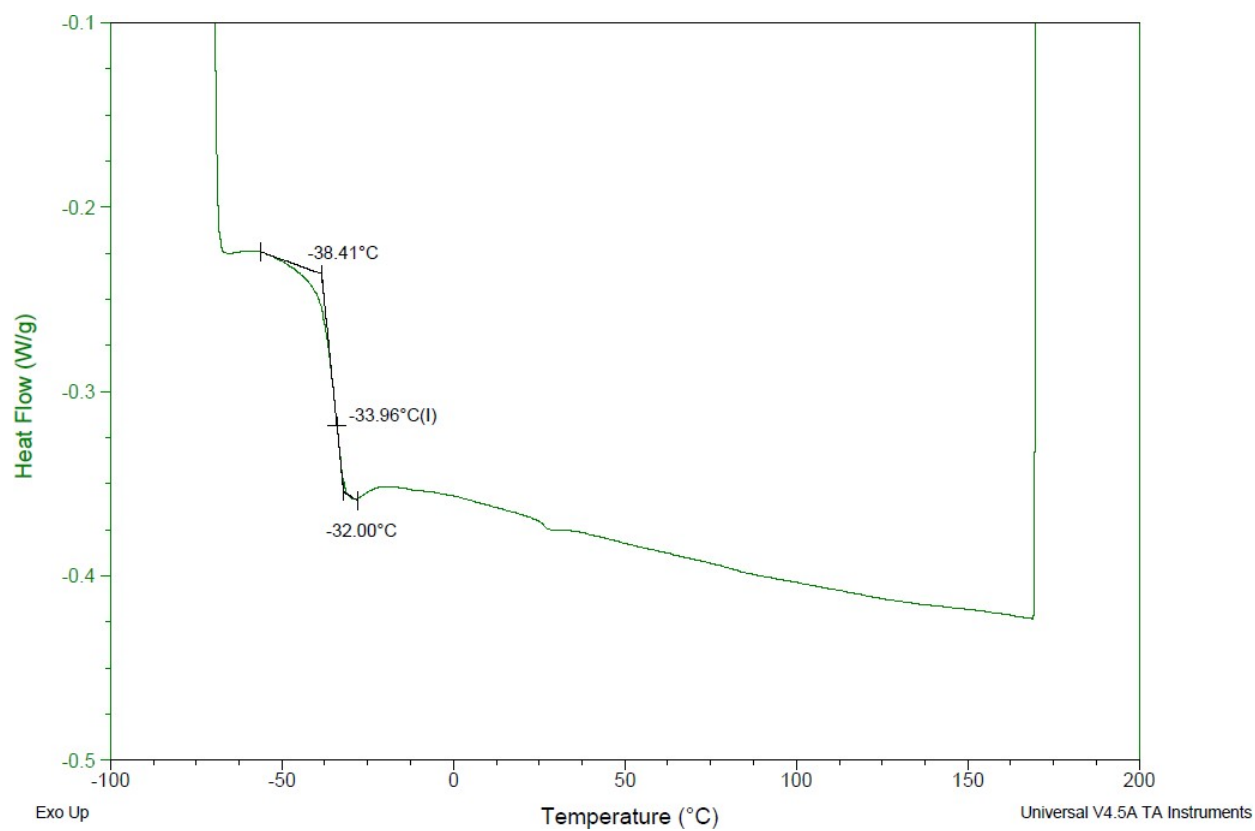
**Figure S40.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 14, Table 4.



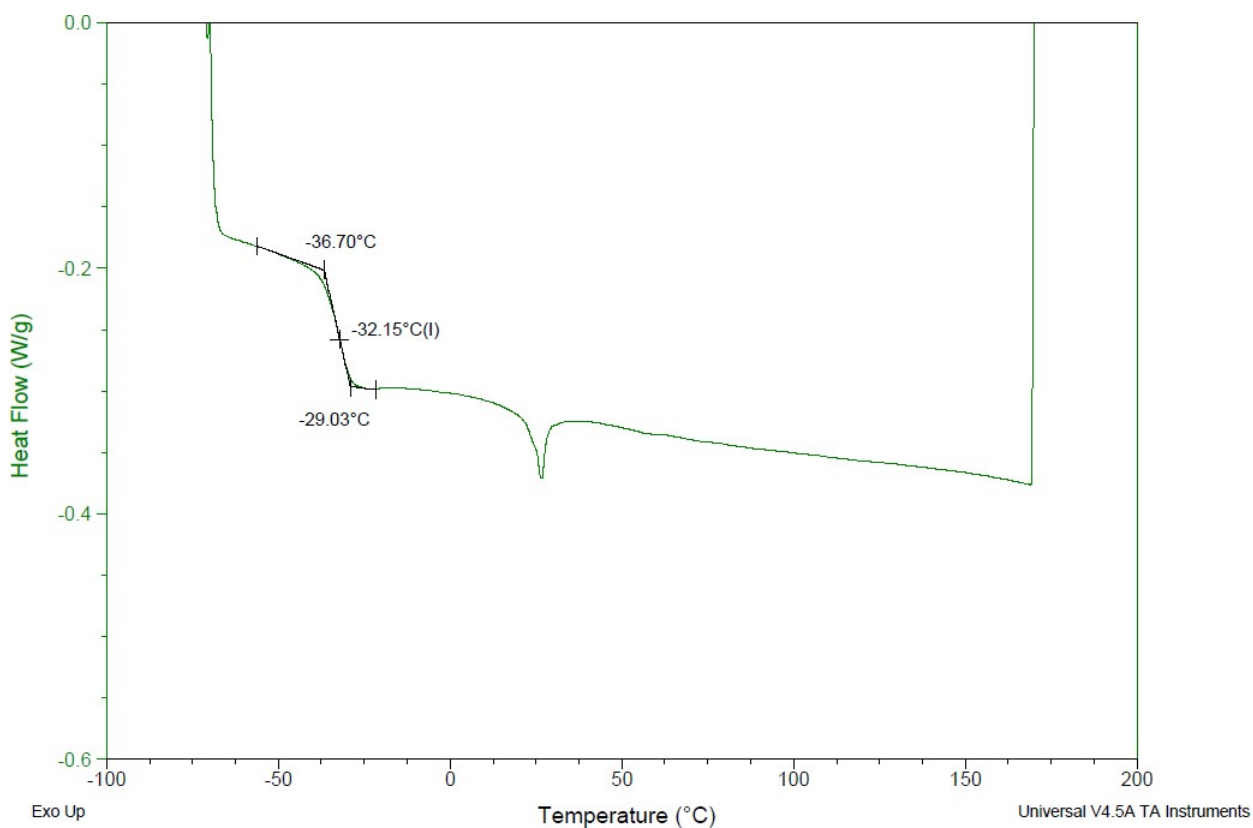
**Figure S41.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 15, Table 4.



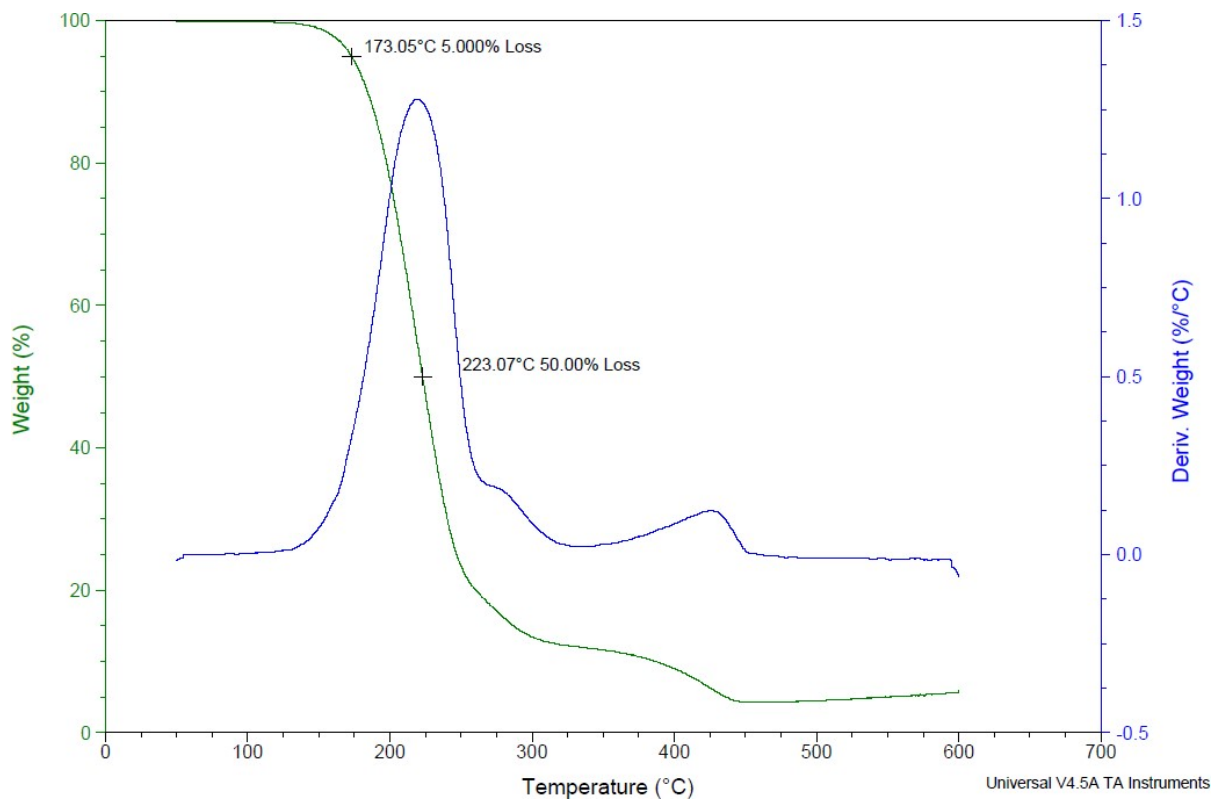
**Figure S42.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 16, Table 4.



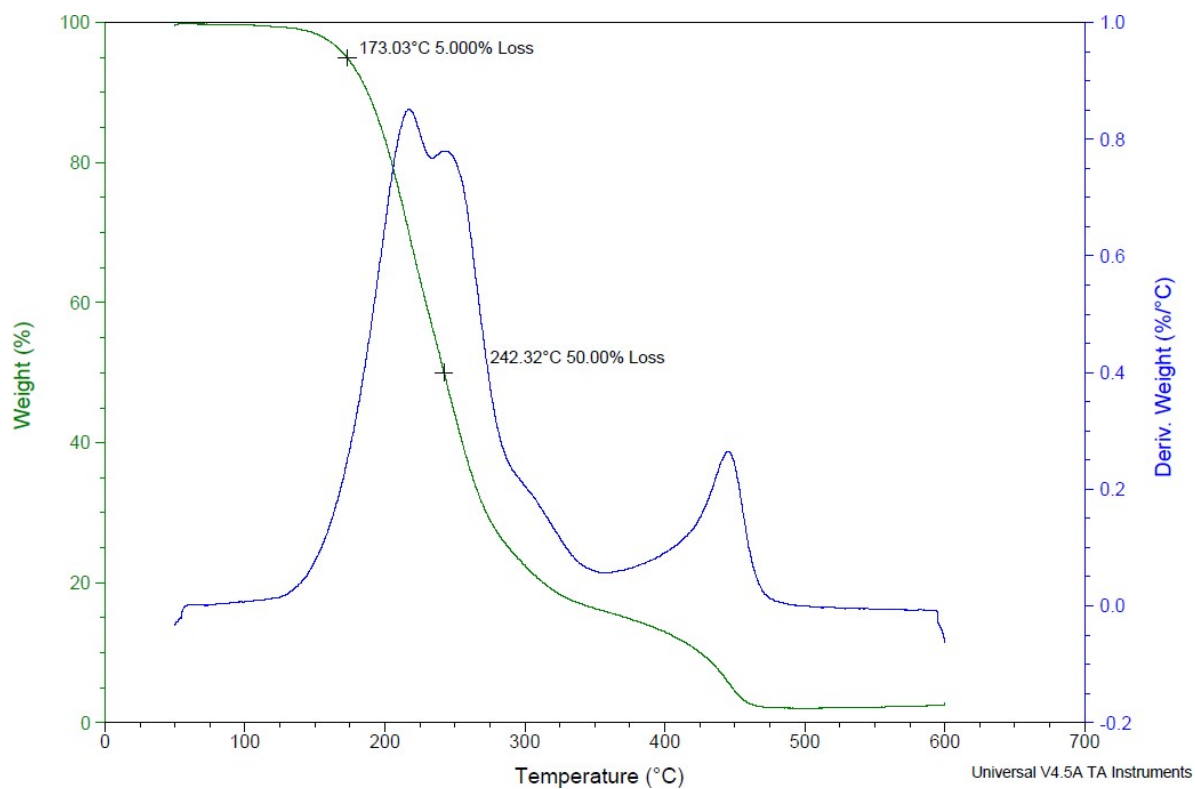
**Figure S43.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 17, Table 4.



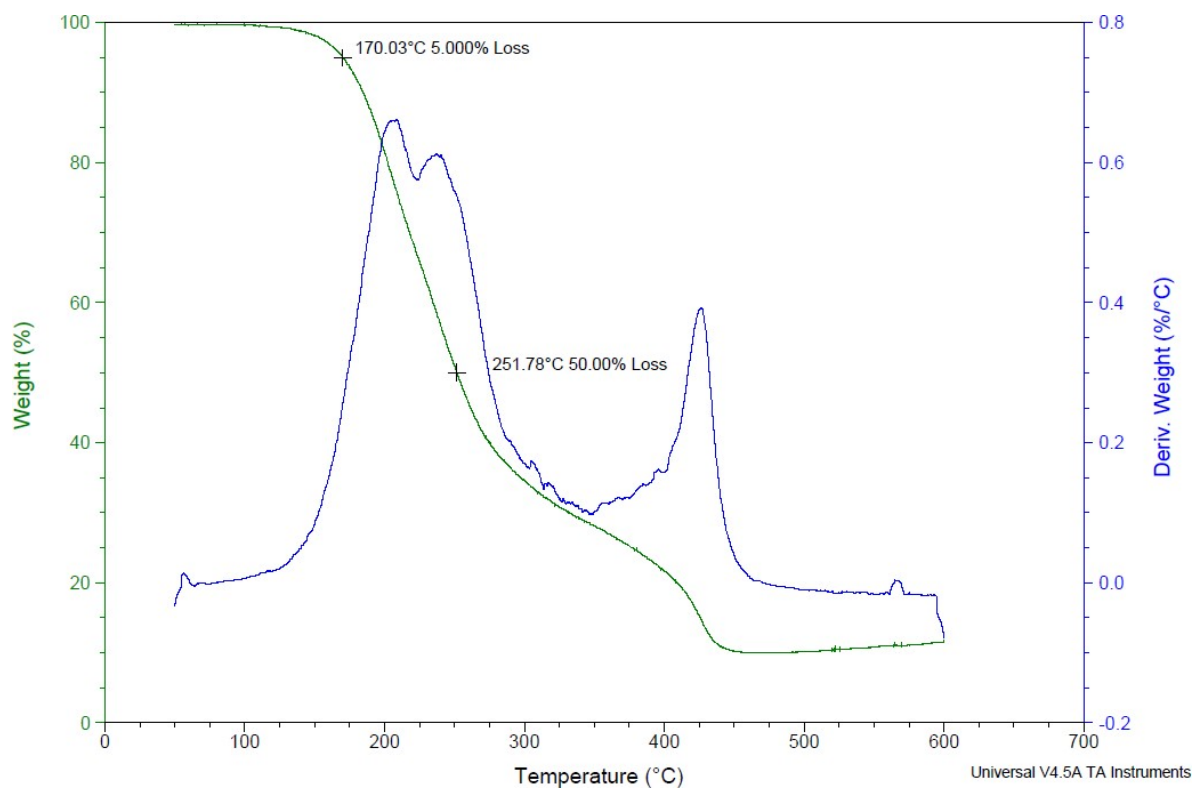
**Figure S44.** DSC thermogram (3<sup>rd</sup> heat cycle) of entry 18, Table 4.



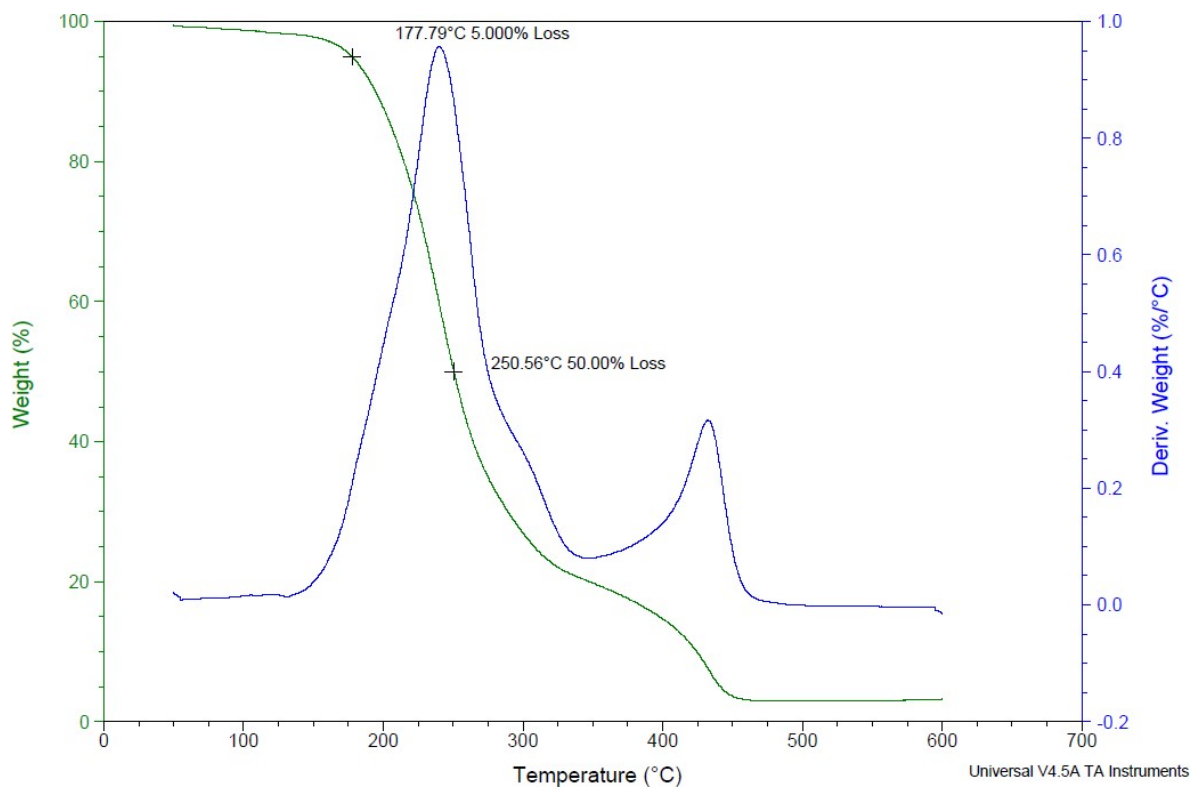
**Figure S45.** TGA thermogram of entry 1, Table 4.



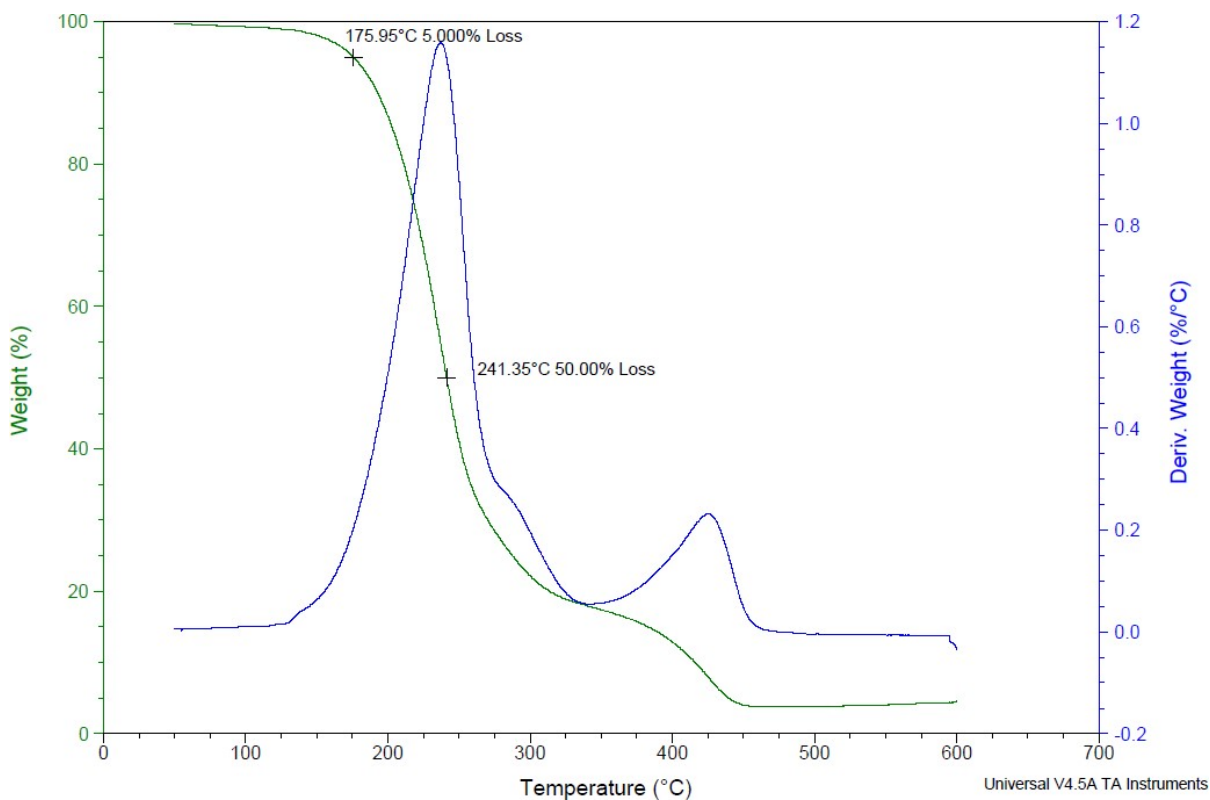
**Figure S46.** TGA thermogram of entry 2, Table 4.



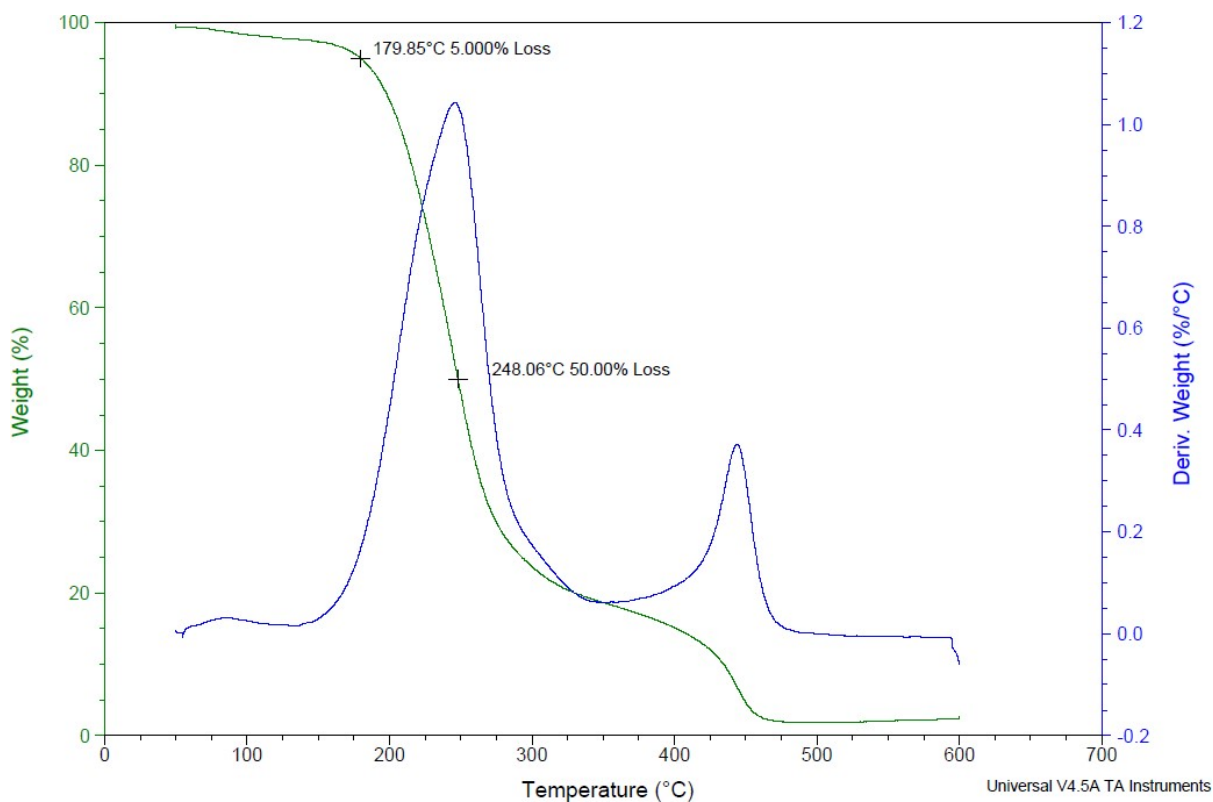
**Figure S47.** TGA thermogram of entry 3, Table 4.



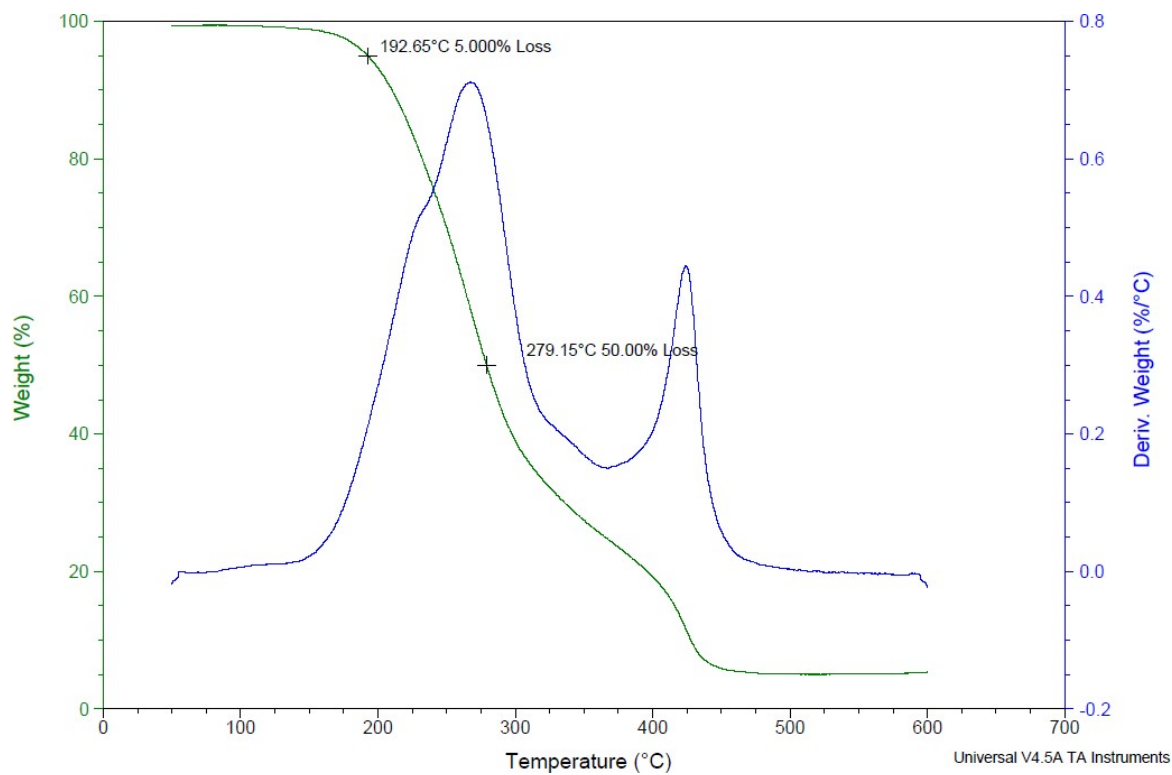
**Figure S48.** TGA thermogram of entry 4, Table 4.



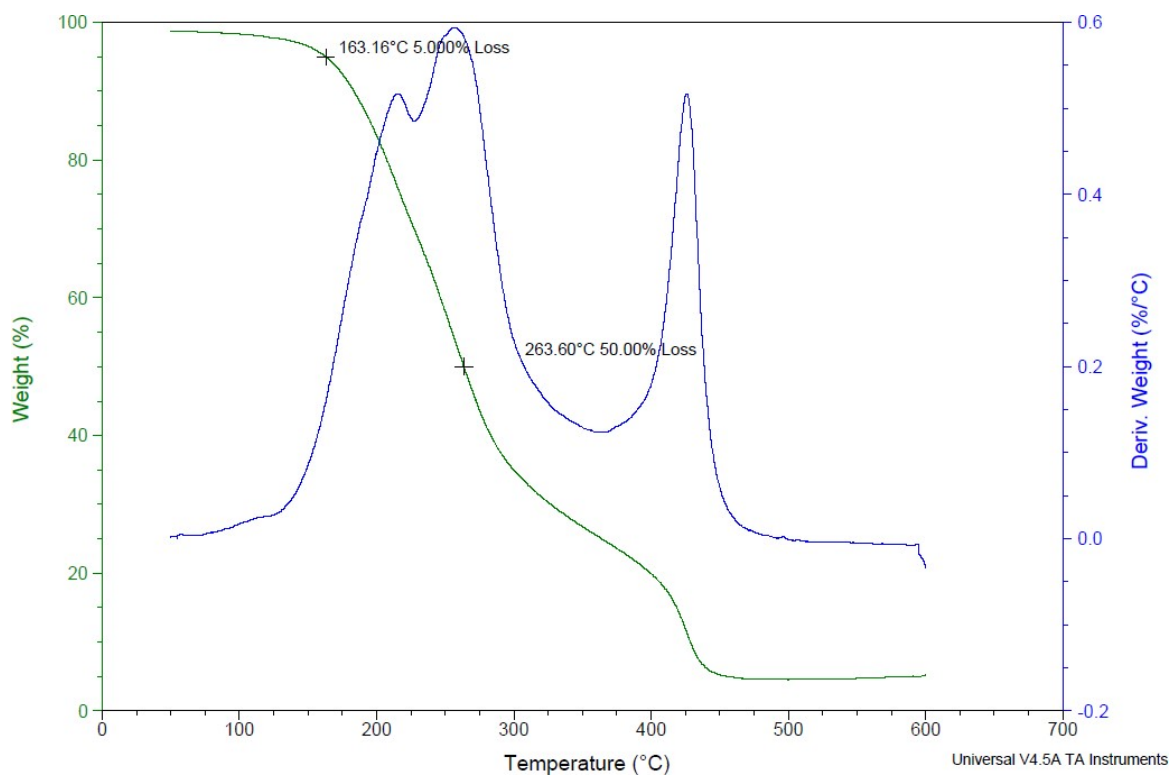
**Figure S49.** TGA thermogram of entry 5, Table 4.



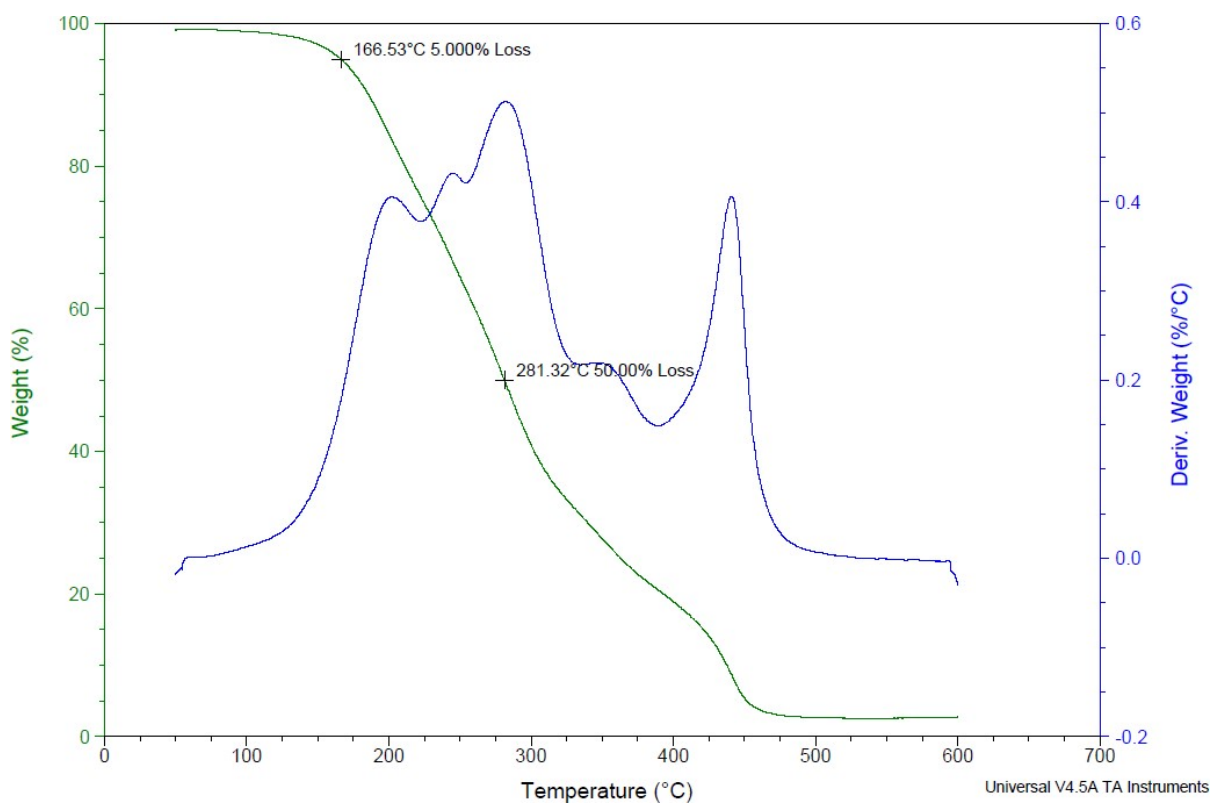
**Figure S50.** TGA thermogram of entry 6, Table 4.



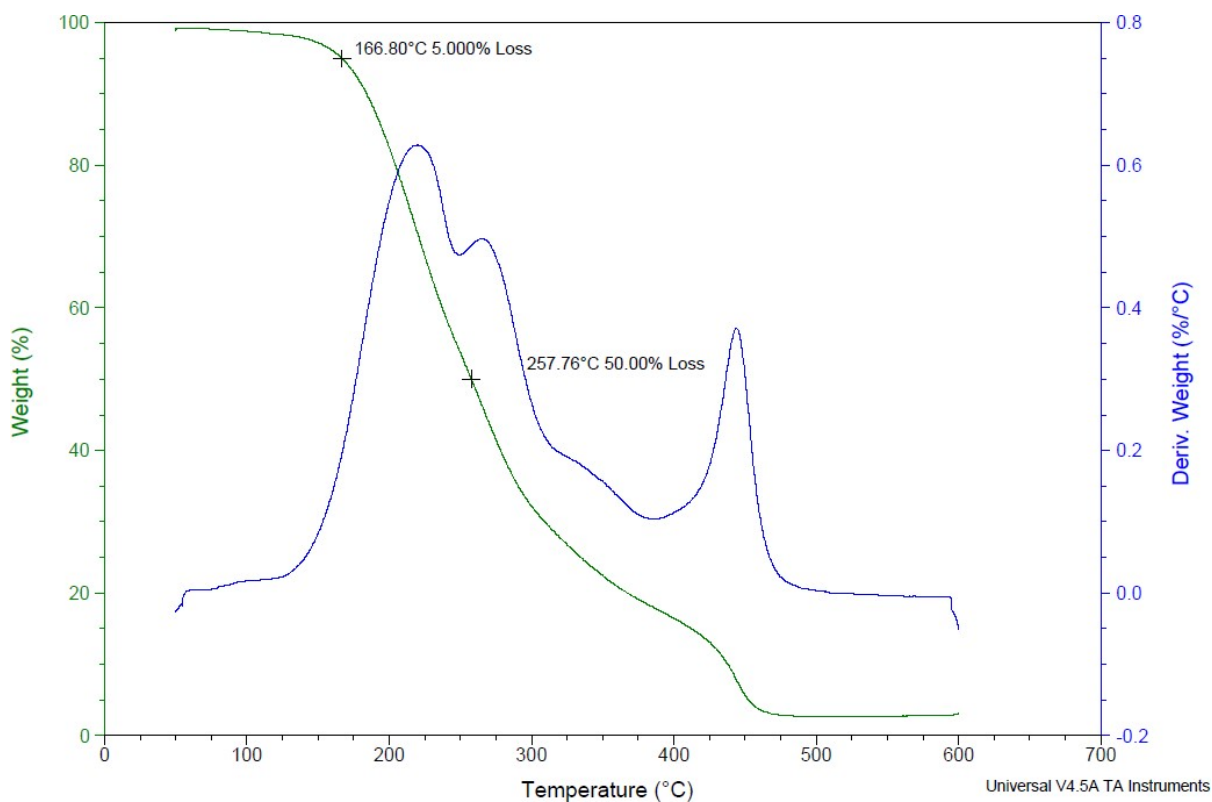
**Figure S51.** TGA thermogram of entry 7, Table 4.



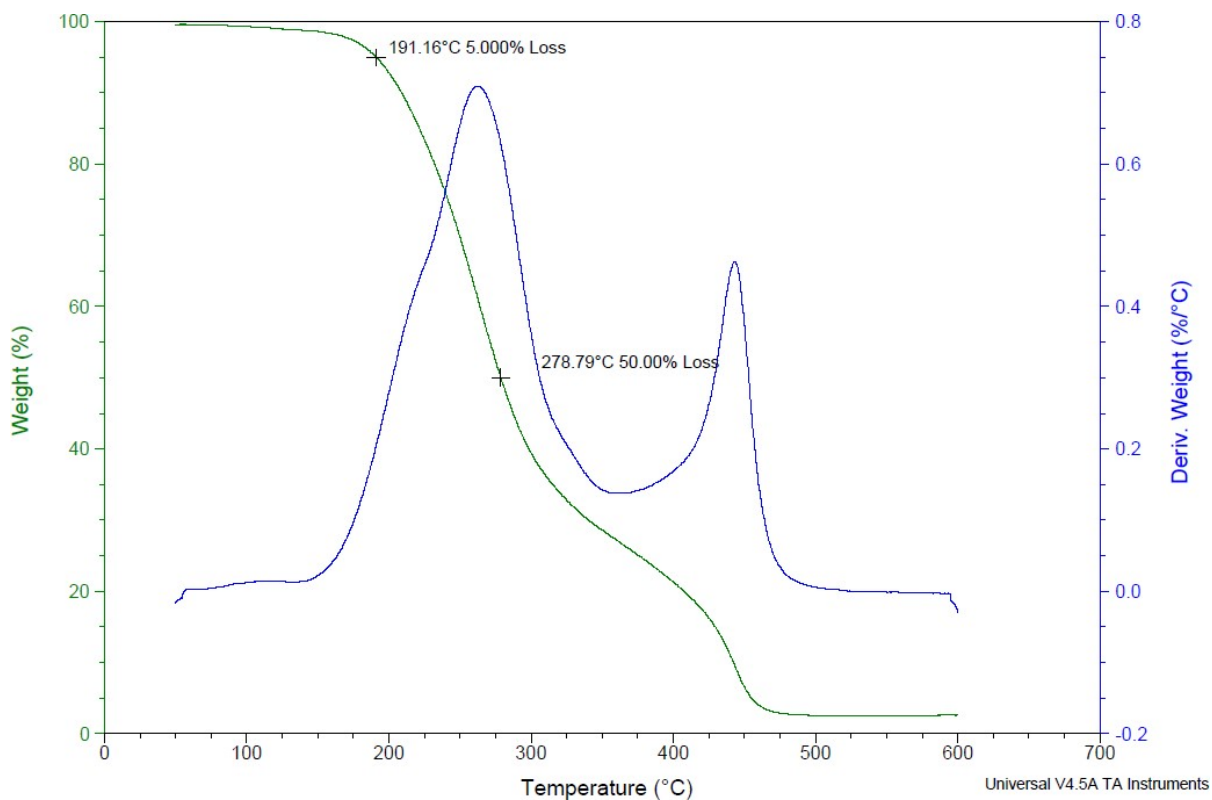
**Figure S52.** TGA thermogram of entry 8, Table 4.



**Figure S53.** TGA thermogram of entry 9, Table 4.

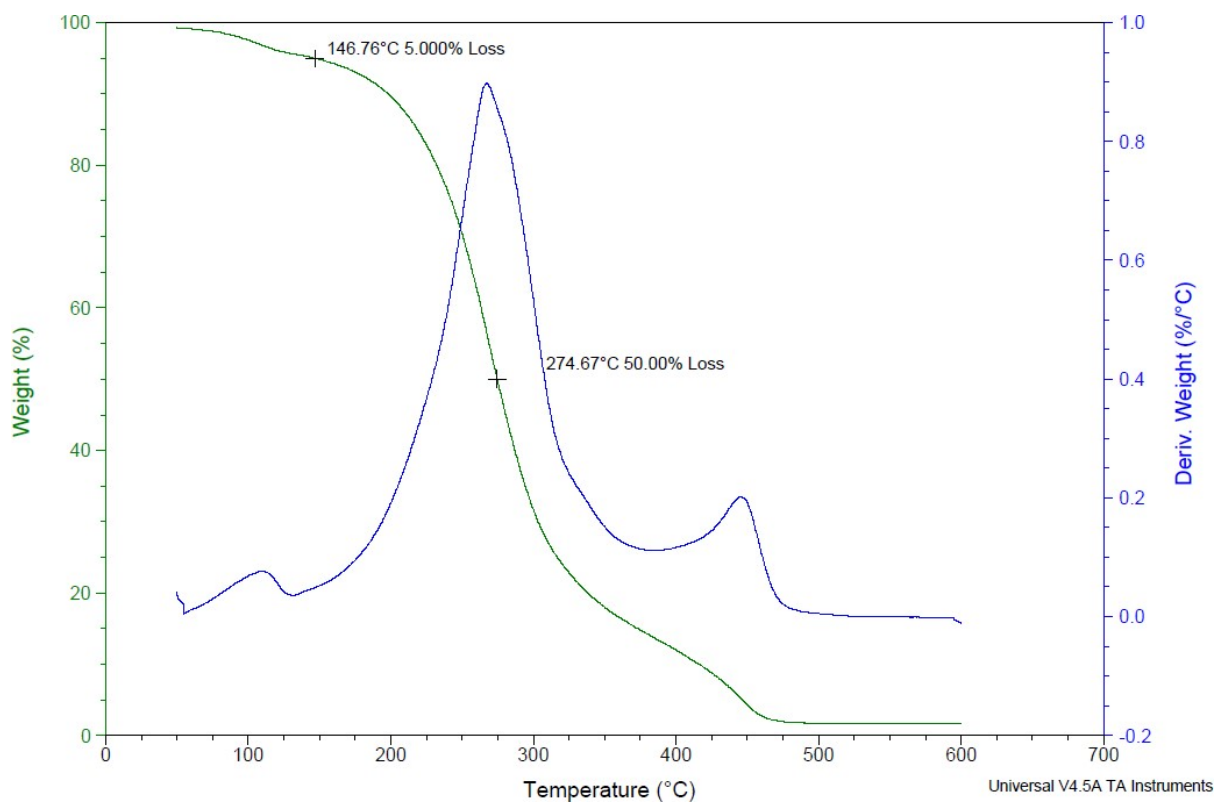


**Figure S54.** TGA thermogram of entry 10, Table 4.

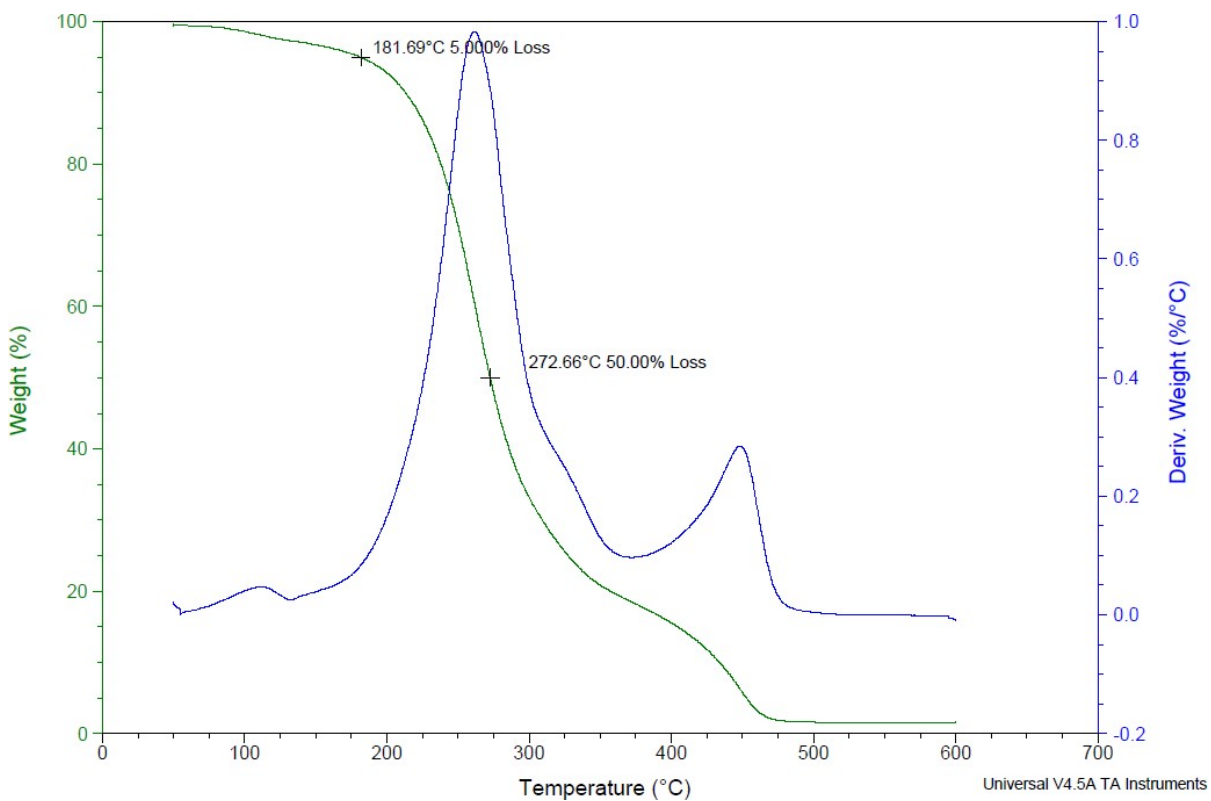


**Figure S55.** TGA thermogram of entry 11, Table 4.

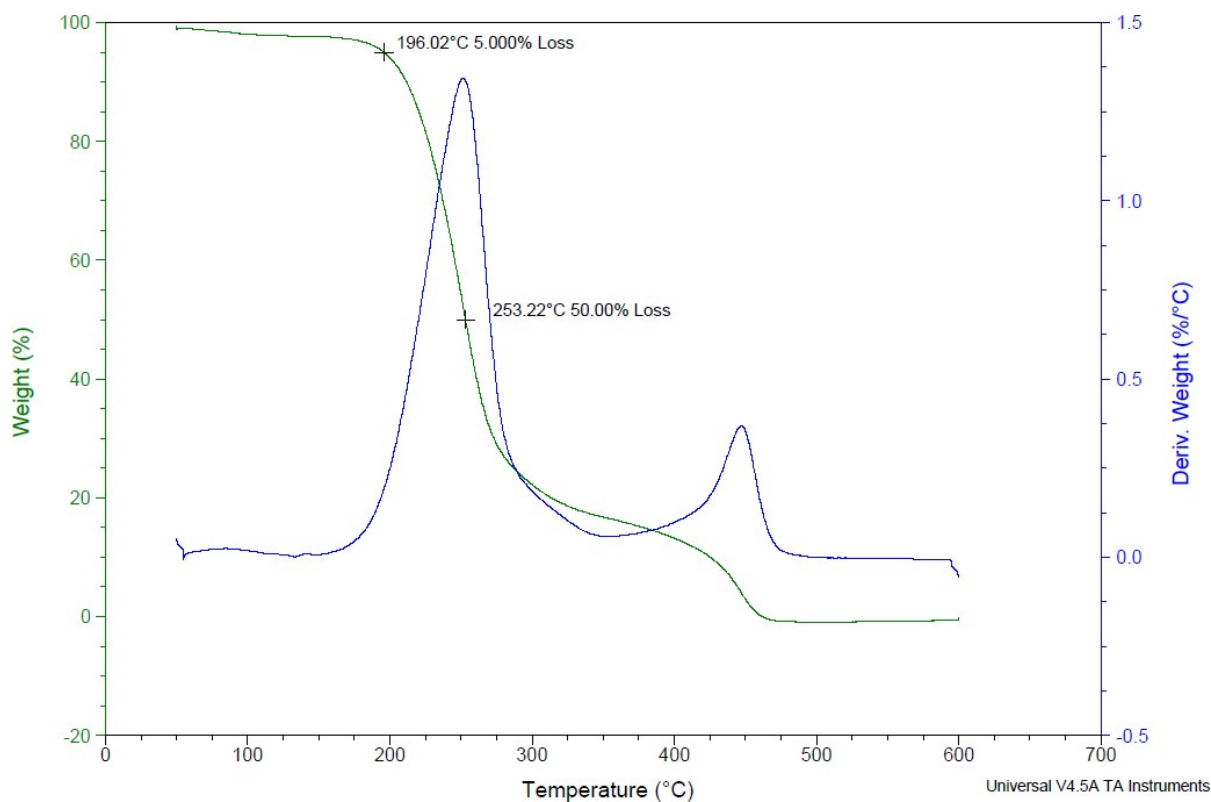




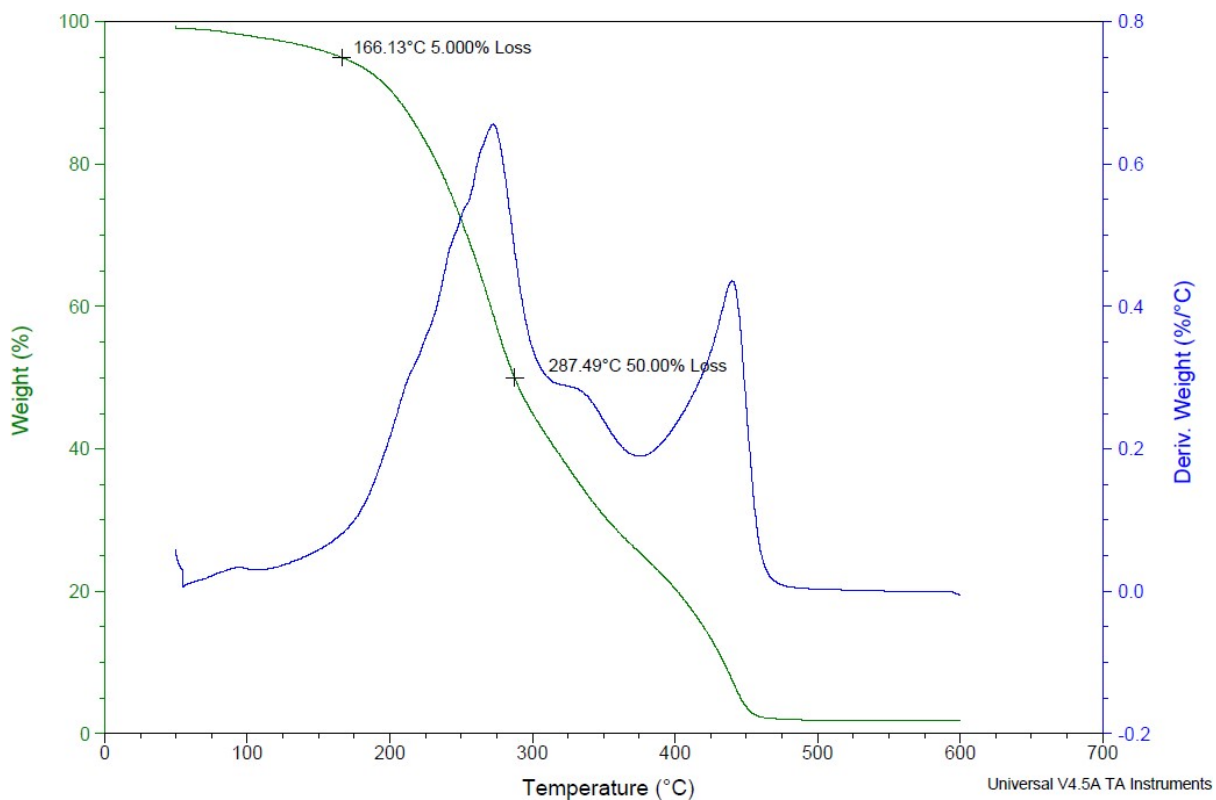
**Figure S56.** TGA thermogram of entry 12, Table 4.



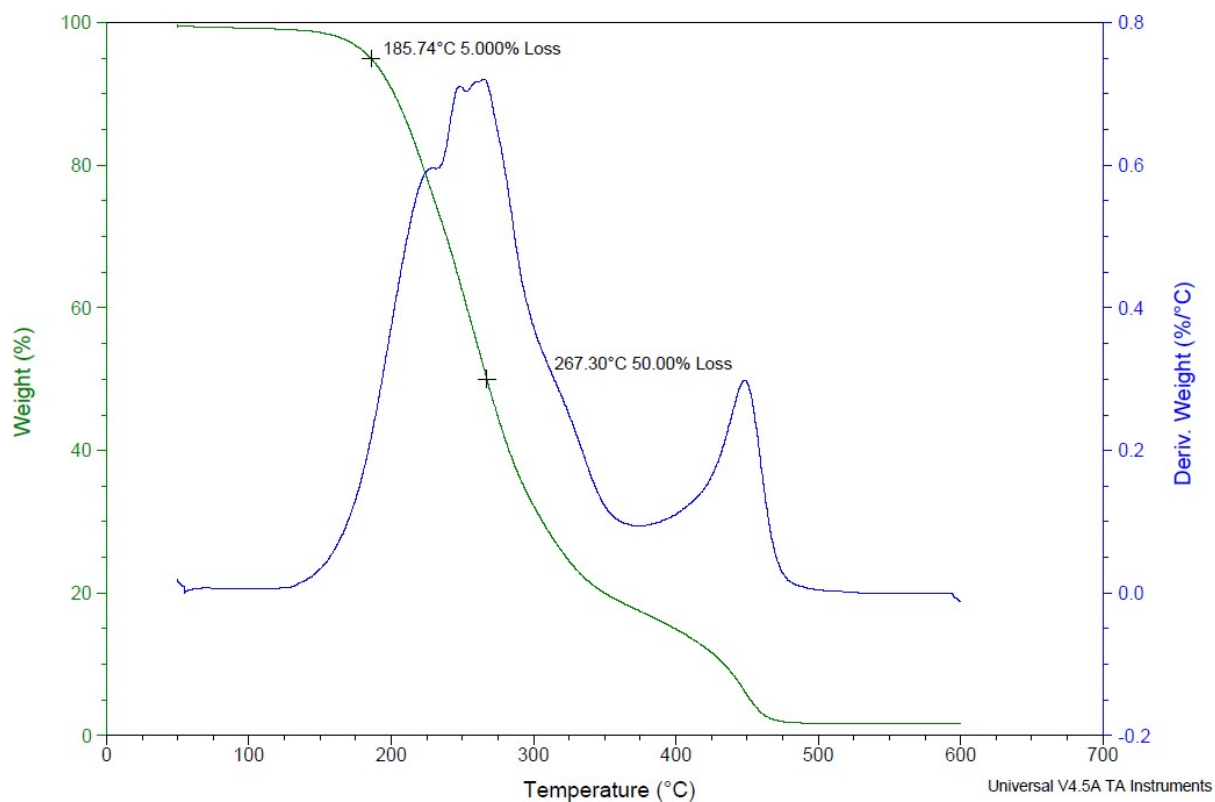
**Figure S57.** TGA thermogram of entry 13, Table 4.



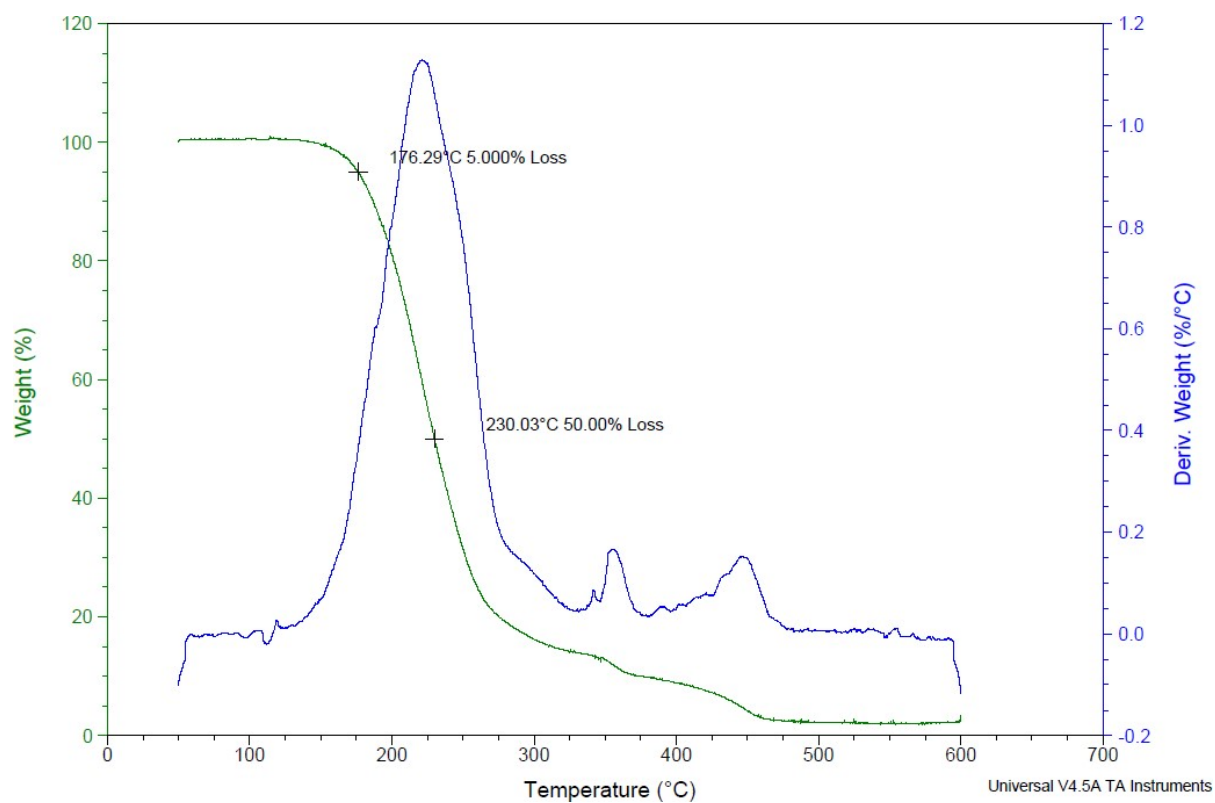
**Figure S58.** TGA thermogram of entry 14, Table 4.



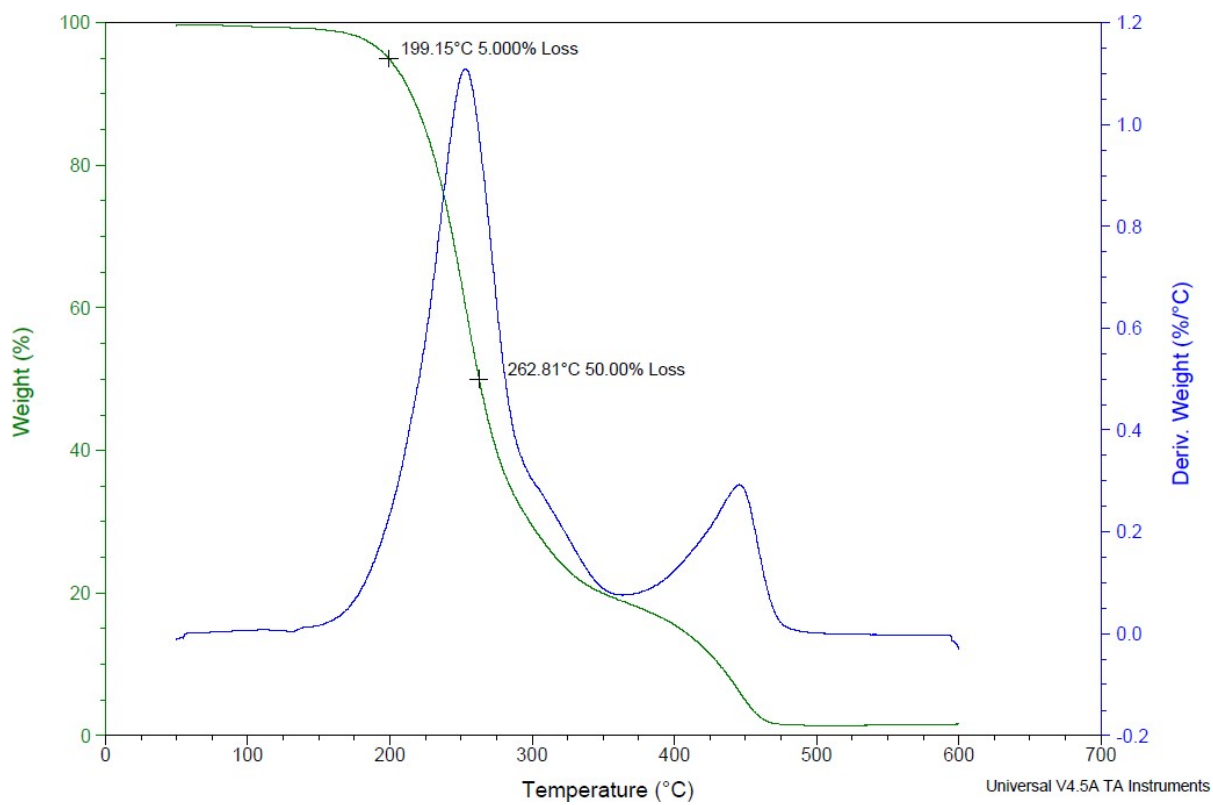
**Figure S59.** TGA thermogram of entry 15, Table 4.



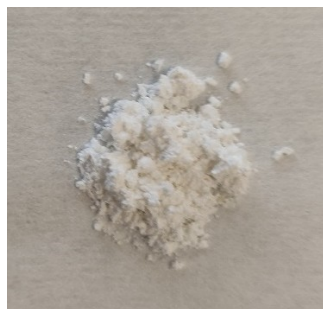
**Figure S60.** TGA thermogram of entry 16, Table 4.



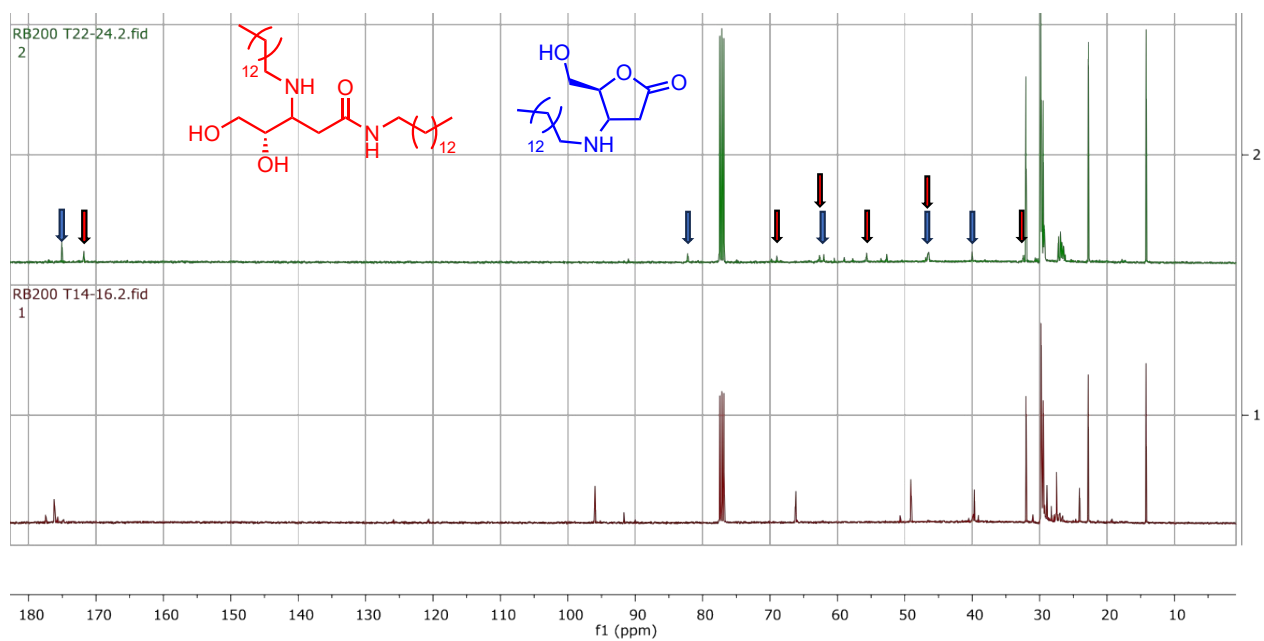
**Figure S61.** TGA thermogram of entry 17, Table 4.



**Figure S62.** TGA thermogram of entry 18, Table 4.



**Figure S63.** A typical polymer sample, entry 1, Table 4.



**Figure S64.**  $^{13}\text{C}$  NMR spectra of two partially purified samples from the mecanochemistry reaction onto HBO suggesting the aza-Michael addition.