

SUPPLEMENTARY MATERIAL

Hydration of Short DNA, RNA, and 2'-OMe Oligonucleotides Determined By Osmotic Stressing

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Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu)
Sucrose									
er058C	0.1		39.3	40.5	39.1	38.5			
er058A	0.2		41.3	40.8	39.6	38.9			
er058C	0.3		40.8	40.5	39.6	39.4			
er058B	0.5		40.3	39.9	39.6	38.7			
er058D	0.5		40.7	40.3	39.8	39.5			
Average		42.6	40.5	40.4	39.5	39.0	62983	63766	176
Standard deviation		0.6	0.7	0.3	0.3	0.4	6800	4792	15

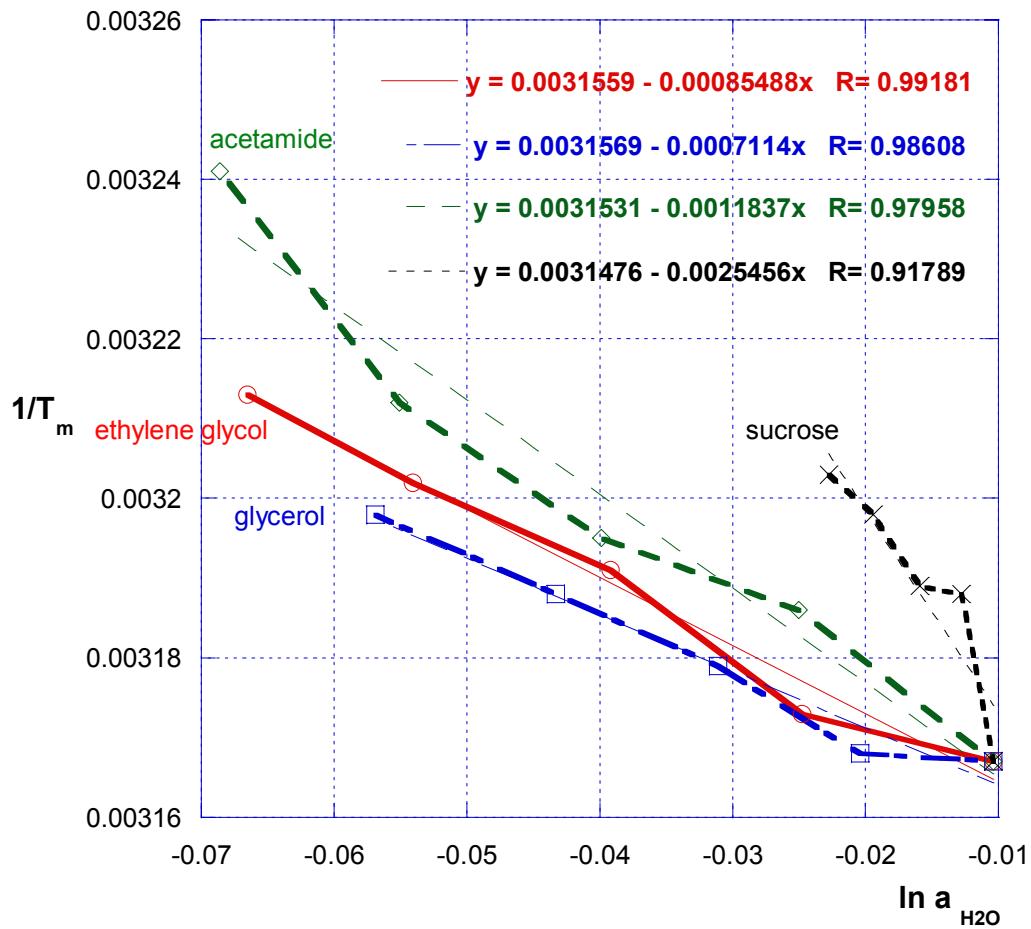


Figure S1. Reciprocal temperature of melting for d(GCGAAUUCGC) **1a** vs. the logarithm of water activity for small cosolutes.

Table S2. Experimental t_m and thermodynamic data for melting of r(GCGAAUUCGC) **1b**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
er050C	0.1	53.2	52.2	50.8	49.5	48.1	95189	102100	286.7
er050C	0.2	53.0	52.2	50.8	49.7	48.4	95246	89000	246.9
er050B	0.3	52.7	52.0	50.8	49.5	48.0	95189	88010	244.2
er050A	0.5	53.3	51.7	51.0	49.7	48.2	99095	97520	272.6
Average			52.0	50.9	49.6	48.2			
Standard deviation			0.2	0.1	0.1	0.2			
Glycerol									
er072A	0.1	54.0	52.9	52.9	51.7	50.6	97692	100600	281.4
er072A	0.2	54.1	53.7	52.5	51.2	50.4	97751	100300	280.4
er072A	0.3	54.0	53.9	52.2	51.4	50.0	99637	99100	276.8
er072B	0.5	53.9	53.5	52.6	51.3	50.4	93350	107000	301.0
er072C	0.5		53.0	52.6	51.2	50.2			
er072C	0.1		53.3	52.5	51.4	50.7			
er072C	0.2		53.4	52.9	51.6	51.0			
Average			53.4	52.6	51.4	50.5			
Standard deviation			0.4	0.2	0.2	0.3			
Acetamide									
er078B	0.1	54.2	52.1	50.1	48.1		93917	95430	265.4
er078B	0.2	54.3	52.2	50.2	48.2	46.0	85609	95240	264.7
er078B	0.3	54.2	51.9	50.0	48.1	46.0	93974	94550	262.7
er078A	0.4	54.2	51.7	49.9	48.0	45.8	83929	96830	269.7
er078A	0.5	54.0	51.7	49.9	48.1	45.7	92139	87360	241.0
Average			51.9	50.0	48.1	45.9			
Standard deviation			0.2	0.1	0.1	0.1			
Sucrose									
er055D	0.1		52.3	51.7	51.4	50.8			
er055C	0.2		52.9	52.6	51.9	51.5			
er055A	0.3		52.6	52.1	51.8	51.2			
er055B	0.5		52.6	52.0	51.6	51.0			
er055D	0.5		52.4	51.8	51.2	50.7			
Average		53.8	52.6	52.0	51.6	51.0	94055	96388	269
Standard deviation		0.5	0.2	0.4	0.3	0.3	4704	5766	17

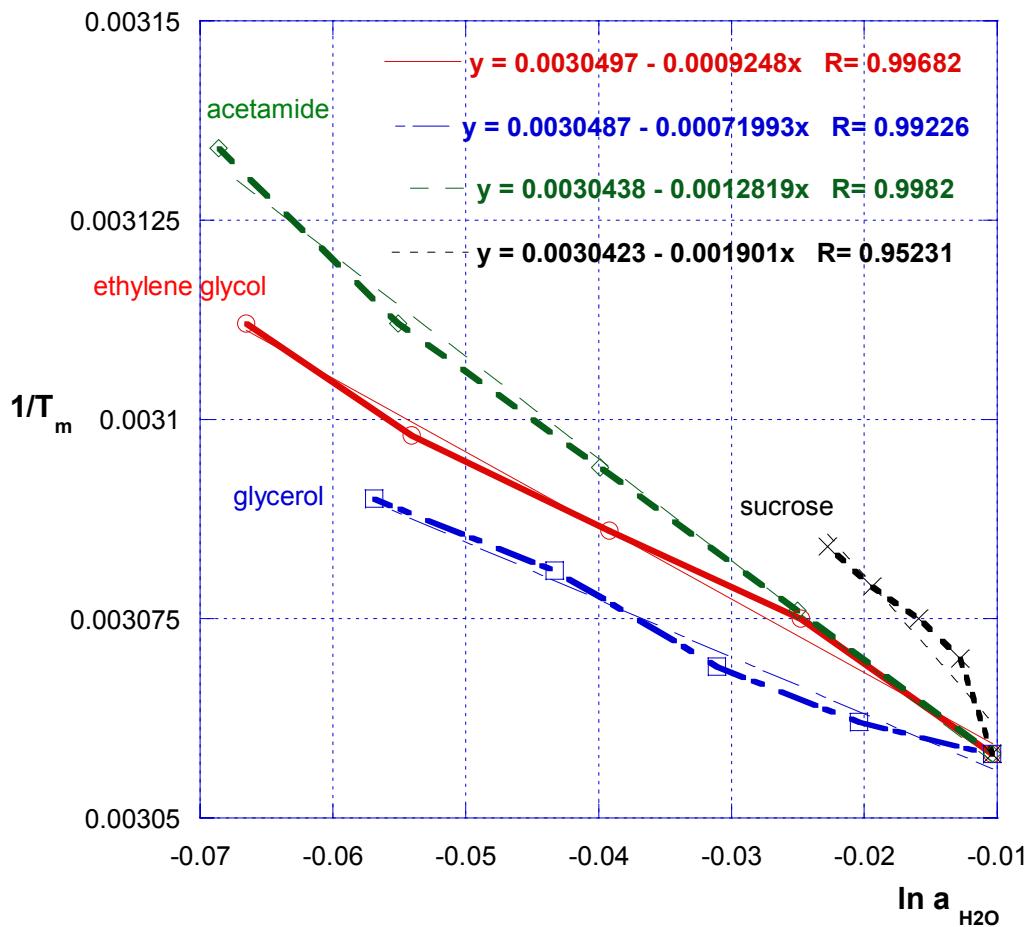


Figure S2. Reciprocal temperature of melting for r(GCGAAUUCGC) **1b** vs. the logarithm of water activity for small cosolutes.

Table S3. Experimental t_m and thermodynamic data for melting of 2'-OMe(GCGAAUUCGC) **1c**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
er118A	0.5	62.3	60.9	59.5	59.2	58.0	94911	88100	236.3
er118B	0.5	62.1	60.9	59.5	59.1	58.0	88145	91900	247.9
er118C	0.4	62.0	61.0	59.6	59.0	57.9	86804	91700	247.6
er118C	0.4	62.4	61.4	59.8	59.2	58.3	88562	88760	238.5
Average			61.1	59.6	59.1	58.1			
Standard deviation			0.2	0.1	0.1	0.2			
Glycerol									
er071B	0.1	61.8	62.4	60.9	60.5	59.4	88354	87100	234.0
er071B	0.2	62.6	62.1	60.9	60.0	59.3	90277	90300	243.0
er071B	0.3		61.6	60.8	60.3	59.2	95415		
er071B	0.4	63.1	61.6	60.9	60.0	58.8	83096	87300	233.5
er071A	0.5	62.1	62.3	60.8	60.7	59.8	poor curve	91900	247.9
er071C	0.3	63.2	62.3	61.5	60.5	59.7	90277	90700	243.5
er071D	0.4	63.4	62.2	61.4	60.2	59.3	85963	90800	243.7
Average			62.1	61.0	60.3	59.4			
Standard deviation			0.3	0.3	0.3	0.3			
Acetamide									
er077A	0.1	62.9		60.0	58.8	57.5	poor curve	80460	240.2
er077B	0.2	63.3	61.3	60.0	58.7	57.3	79130	85100	226.9
er077B	0.3	62.9	61.1	60.1	58.9	56.9	81347	89420	240.0
er077A	0.4	62.5	61.0	59.8	58.6	57.3	88354	88930	238.9
er077A	0.5	62.3	60.9	59.7	58.7	57.2	82608	89380	240.2
er077B	0.5	62.8	61.5	59.8	58.6	57.1	90383	84670	225.9
Average			61.2	59.9	58.7	57.2			
Standard deviation			0.2	0.2	0.1	0.2			
Sucrose									
er060D	0.1		61.7	61.4	60.4	60.1			
er060A	0.2		61.2	60.7	60.1	59.9			
er060B	0.3		61.6	61.0	60.7	60.2			
er060C	0.5		61.7	61.4	60.4	60.1			
Average		62.6	61.6	61.1	60.4	60.1	87575	88533	239
Standard deviation		0.5	0.2	0.3	0.2	0.1	4616	3088	7

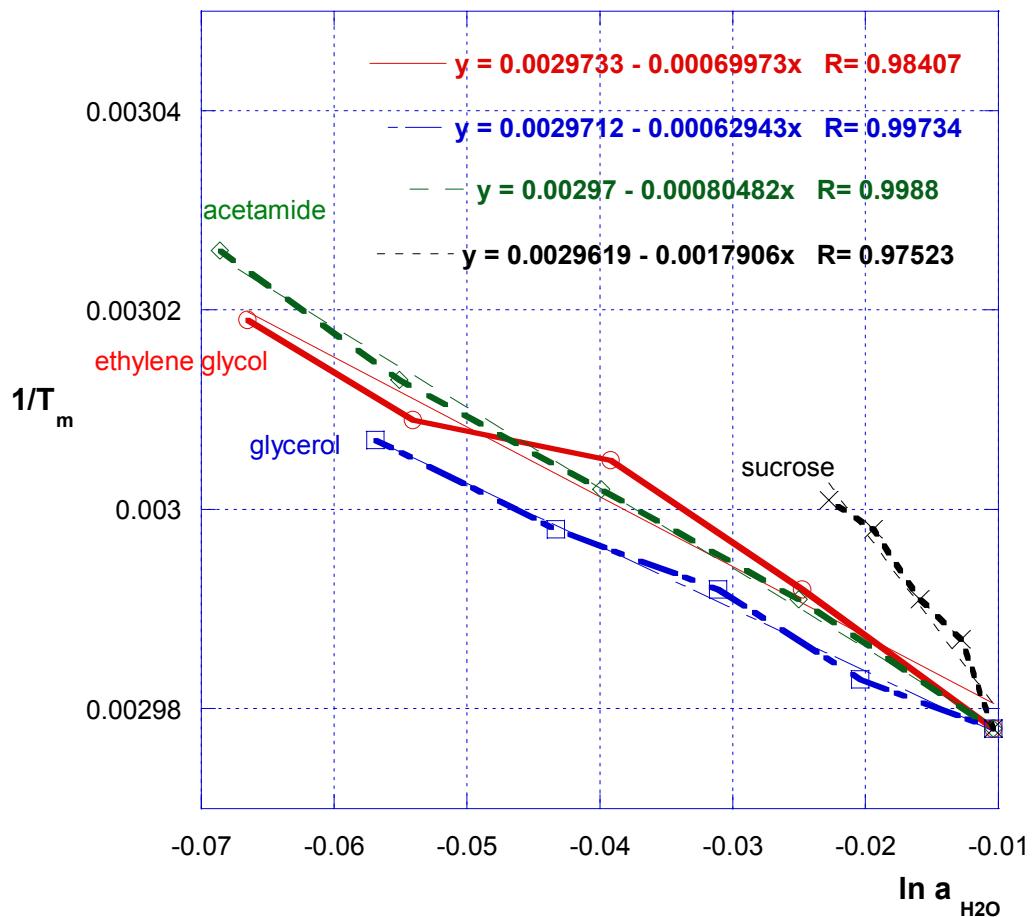


Figure S3. Reciprocal temperature of melting for 2'-OMe(GCGAAUUCGC) **1c** vs. the logarithm of water activity for small cosolutes.

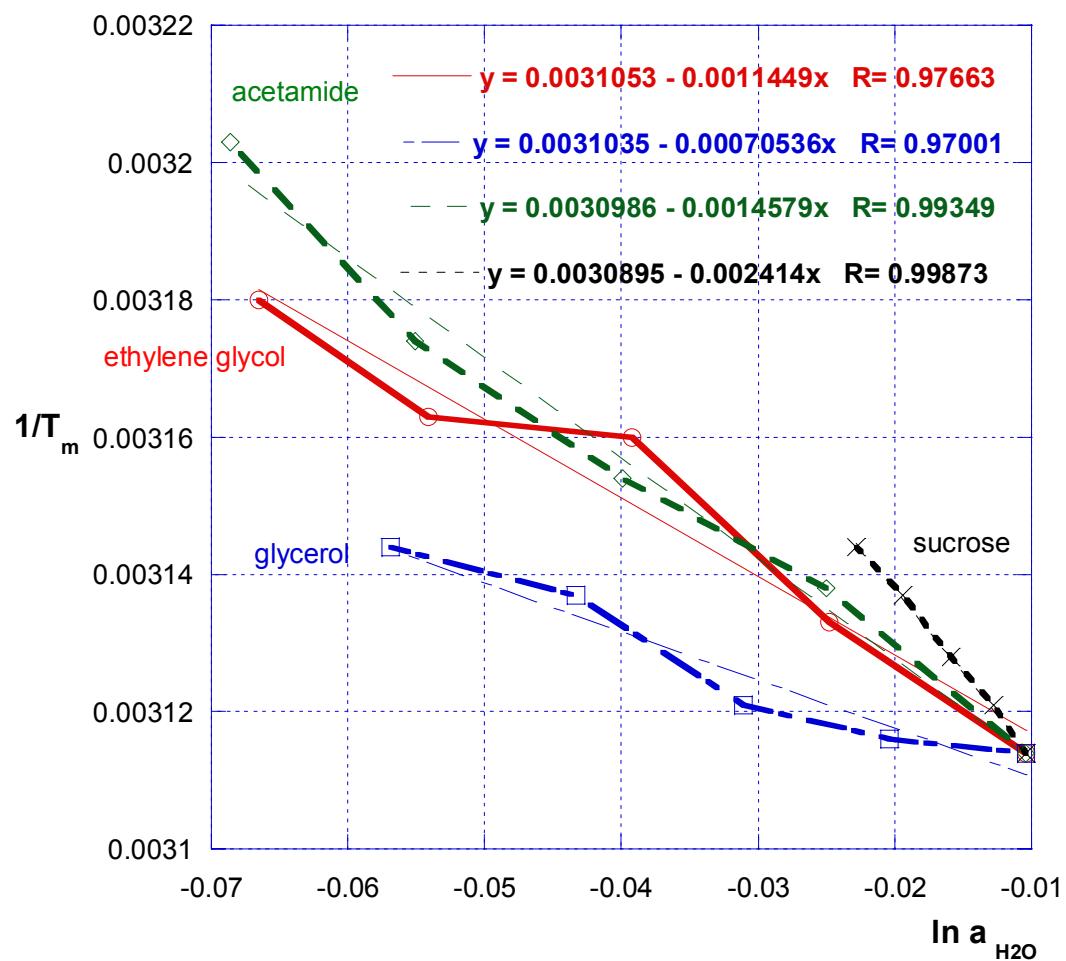


Figure S4. Reciprocal temperature of melting for d(GCGAATTTCGC) **1d** vs. the logarithm of water activity for small cosolutes.

Table S5. Experimental t_m and thermodynamic data for melting of d(UA)₆ **2a**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
er103A	0.5		17.5	16.3	16.1	13.8			
er103C	0.5	18.9		16.4	15.1	14.0	50952	59400	177.1
er103D	0.3	18.7		16.3			52384	60000	179.2
er103E	0.3	17.7	17.5	16.5	16.0	14.7	57270	55200	163.7
er103F	0.3	18.5			16.0	13.6	47686	56600	167.6
er103G	0.3	18.6	17.6	16.8	16.2	14.3	48909	57000	169.0
er103H	0.3	17.1	17.9	16.7	15.9	14.2	49360	58000	173.8
er103I	0.3	18.4	17.0	16.8	16.3		51554	50500	147.2
Average			17.5	16.5	15.9	14.1			
Standard deviation			0.3	0.2	0.4	0.4			
Glycerol									
er104A	0.3		16.1	15.1	14.7	13.3			
er104B	0.3	18.7	17.4	16.3	15.4	13.4	49461	56600	167.9
er104C	0.3	18.1	16.8	14.9	15.6	14.2	56999	54800	161.9
er104D	0.3	17.9	17.3	16.5	16.3	14.6	50027	56800	181.5
er104E	0.3	17.6	16.5	16.0	14.8	14.0	52242	53100	156.4
er104F	0.3	17.6	15.5	15.2	14.2	13.9	52879	54400	161.0
Average			16.6	15.7	15.2	13.9			
Standard deviation			0.7	0.7	0.8	0.5			
Acetamide									
er106A	0.3		15.2	12.9	10.5	9.2			
er106B	0.3		15.4	13.1	9.9	8.4			
er106C	0.3		15.6	13.2	10.9	8.9			
er016D	0.3		15.5	12.8	10.9	8.3			
er016E	0.3		15.9	13.0	11.1	8.2			
Average		18.2	15.5	13.0	10.7	8.6	51644	56608	169
Standard deviation		0.5	0.3	0.2	0.5	0.4	3000	3275	12

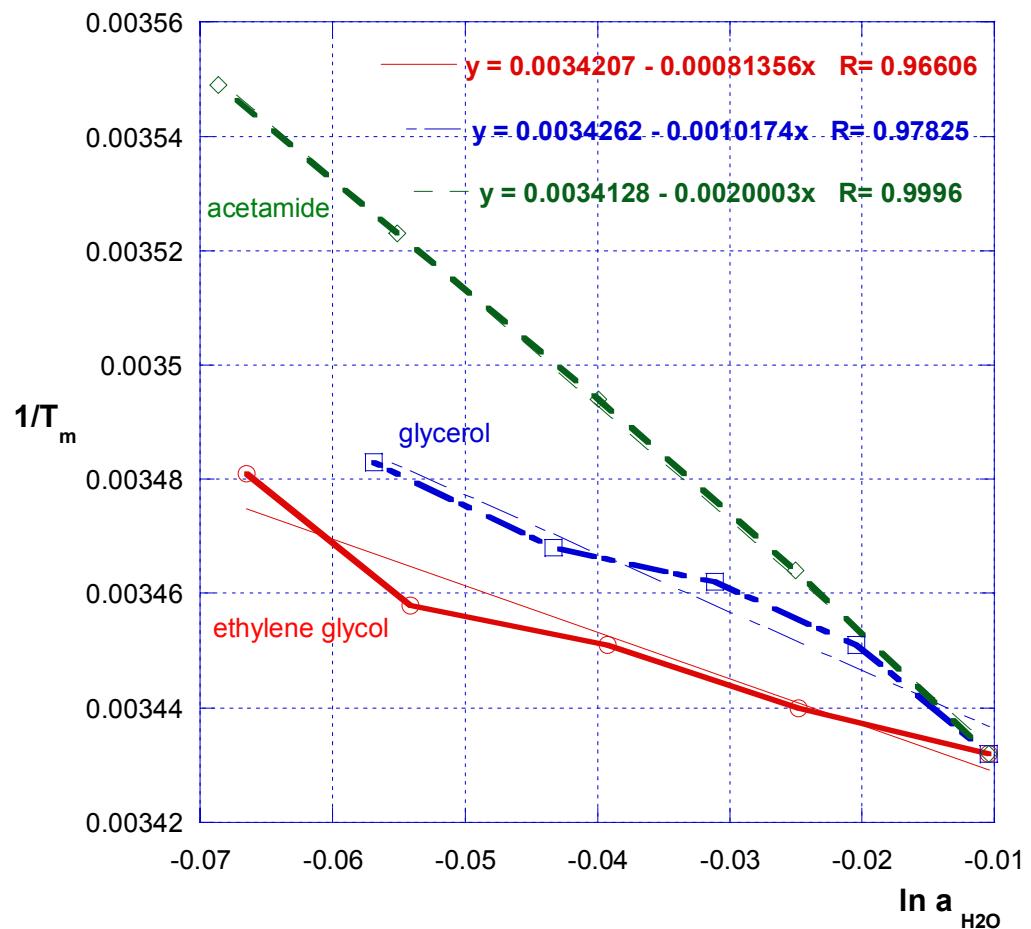


Figure S5. Reciprocal temperature of melting for $d(UA)_6$ **2a** vs. the logarithm of water activity for small cosolutes.

Table S6. Experimental t_m and thermodynamic data for melting of r(UA)₆ **2b**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
jm063A	0.3		29.2	27.2	27.1	25.6			
jm063A	0.3		29.5	27.4	27.3	25.9			
jm063A	0.3		29.9	27.5	27.4	26.2			
er109A	0.5		29.3	27.4	26.4	25.6			
er109B	0.4		29.0	27.8	26.9	25.7			
er109C	0.5		29.2	27.5	26.6	25.2			
er109D	0.5		29.2	27.7	27.1	25.3			
er109E	0.3		29.1	27.8	26.3	25.8			
er109F	0.5		29.2	27.7	27.1	25.1			
er109F	0.5		29.4	27.8	26.9	25.2			
er109G	0.5		29.3	27.8	26.8	25.5			
Average			29.3	27.6	26.9	25.6			
Standard deviation			0.2	0.2	0.4	0.3			
Glycerol									
er107A	0.3	29.8	28.6	28.1	26.9	25.8	87770	70700	207.6
er107B	0.3	29.9	28.8		27.3	25.9	87770	74900	221.1
er107C	0.4	30.4	29.0	28.0	27.0	25.7	84571	73110	214.9
er107D	0.3	30.4	29.2	28.6	26.5	25.5	81360	69500	203.2
er107E	0.3	30.6	28.9	28.6	27.6	26.2	86418	74500	219.3
Average			28.9	28.3	27.1	25.8			
Standard deviation			0.2	0.3	0.4	0.3			
Acetamide									
jm056A	0.3	29.7	27.4	25.4	23.4	22.0	82584	69800	204.6
jm056A	0.3	29.8	27.7	25.9	23.7	21.5	76366	74000	218.5
jm056B	0.3	29.7	27.2	25.5	23.8	21.2	79459	62100	179.4
jm056B	0.3	29.9	27.8	25.6	23.7	21.2	76416	67000	195.4
jm056B	0.3	29.9	27.8	25.8	23.5	21.5	81043	67700	197.6
Average		30.0	27.6	25.6	23.6	21.5	82376	70331	206
Standard deviation		0.3	0.3	0.2	0.2	0.3	4247	4032	13

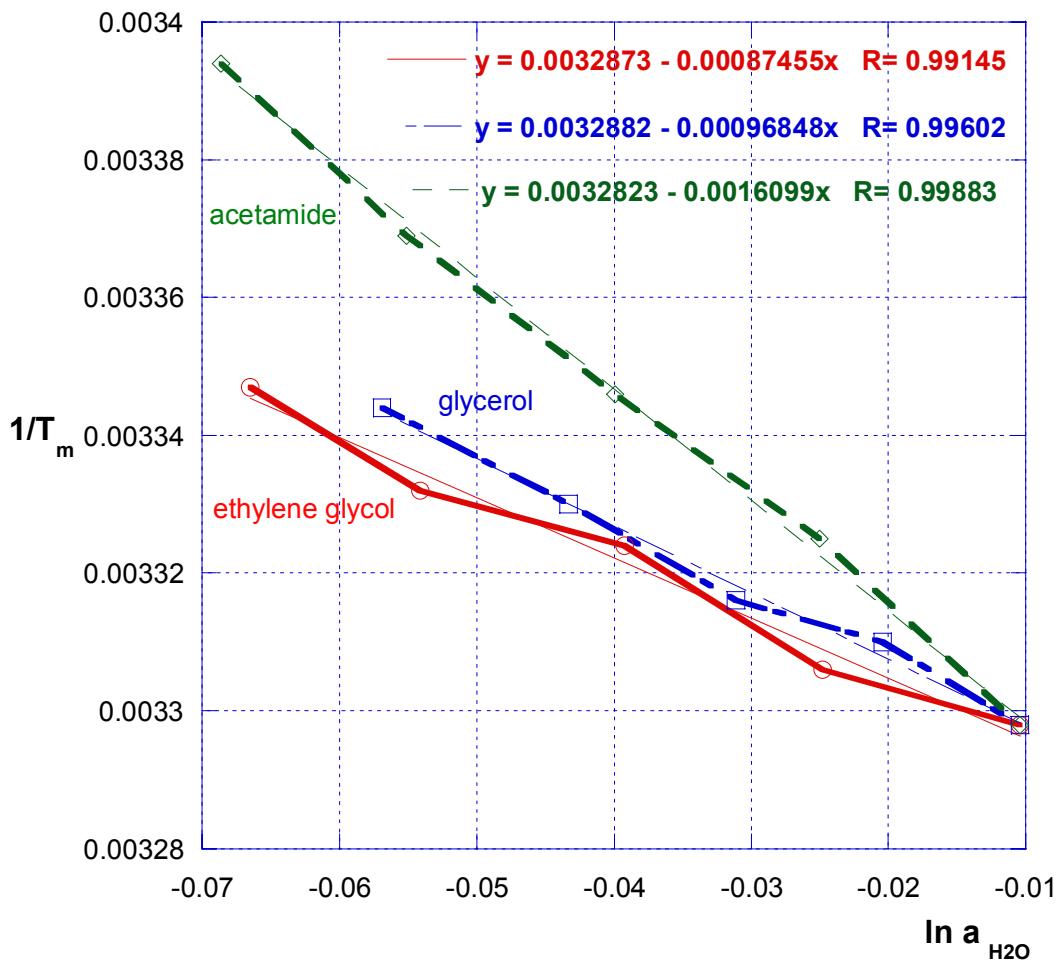


Figure S6. Reciprocal temperature of melting for $r(UA)_6$ **2b** vs. the logarithm of water activity for small cosolutes.

Table S7. Experimental t_m and thermodynamic data for melting of 2'-OMe(UA)₆ **2c**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
jm062A	0.3		41.4	40.4	39.6	38.8			
jm062A	0.3		41.3	40.4	39.8	38.9			
jm062A	0.4		41.6	40.7	40.0	39.0			
jm062A	0.5		41.6	40.8	40.0	39.0			
jm062A	0.3		41.9	40.8	40.2	39.1			
jm062A	0.2		42.2	41.5	40.3	39.1			
jm062B	0.3		41.9	40.8	40.3	39.1			
jm062B	0.3		42.0	40.7	40.4	39.1			
jm062B	0.4		41.9	41.0	40.4	39.0			
jm062B	0.5		41.8	40.9	40.4	39.0			
jm062B	0.3		42.1	41.1	40.6	39.2			
Average			41.8	40.8	40.2	39.0			
Standard deviation			0.3	0.3	0.3	0.1			
Glycerol									
jm060A	0.3		41.5	41.1	39.8	38.7			
jm060A	0.3		41.3	40.9	39.9	38.7			
jm060A	0.4		40.7	40.4	39.4	39.1			
jm060A	0.2		41.5	41.2	40.2	39.4			
jm061A	0.3		41.3	41.0	40.7	39.5			
jm061A	0.3		41.0	40.8	40.2	38.8			
jm061A	0.4		42.0			38.8			
jm061A	0.5		41.0	40.8	39.7	38.6			
Average			41.3	40.9	40.0	39.0			
Standard deviation			0.4	0.3	0.4	0.3			
Acetamide									
jm058A	0.4	41.8	40.3	38.7	36.6	36.1	85950	60700	167.3
jm058B	0.3	42.1	40.1	38.8	37.0	35.9	89389	70240	194.3
jm058B	0.3	42.3	40.3	38.6	37.0	36.0	99602	68500	191.5
jm058B	0.3	42.3	40.2	38.7	37.0	35.7	99602	69600	195.1
jm058B	0.3	42.3	40.2	38.4	36.9	35.8	101898	68200	190.8
jm058B	0.5		40.5	38.7	36.9	35.8			
Average		42.2	40.3	38.7	36.9	35.9	95288	67448	188
Standard deviation		0.2	0.1	0.1	0.2	0.1	7122	3861	12

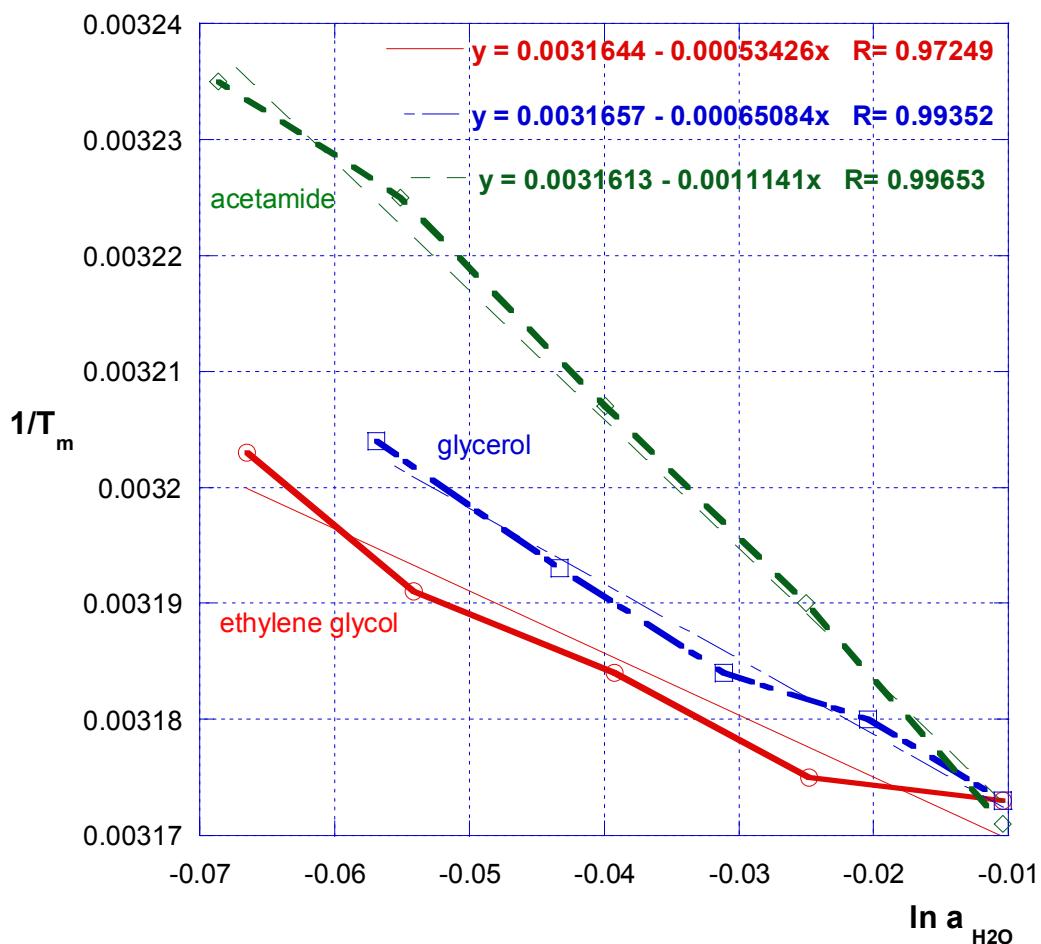


Figure S7. Reciprocal temperature of melting for 2'-OMe(UA)₆ **2c** vs. the logarithm of water activity for small cosolutes.

Table S8. Experimental t_m and thermodynamic data for melting of d(TA)₆ **2d**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
er097A	0.5	22.1	21.3	19.9	18.1	16.7	34966	35300	93.5
er097B	0.4		20.8	20.8	19.2	18.5			
er097C	0.3	22.0	21.4	21.0	17.1	18.7	42823	48200	137.2
er097D	0.3	23.8	21.5	21.5	19.3	17.8	43512	39400	106.4
er097F	0.2		23.0	21.0					
er097F	0.3	23.1	22.3	20.7	20.5		poor curve	42400	116.7
er097E	0.2	24.0	22.6	21.4			poor curve	48000	135.2
er097E	0.3	24.0	23.3	22.8	18.5		43339	45100	125.4
Average			22.0	21.1	18.8	17.9			
Standard deviation			0.9	0.8	1.2	0.9			
Glycerol									
er105A	0.3		19.8	19.7	17.8	17.4			
er105B	0.3			18.5		16.9			
er105C	0.3			19.8	17.9	17.5			
er105C	0.2		20.1	20.3	18.3	16.7			
er105D	0.3		22.6	21.3	18.3	17.8			
er105E	0.3		22.7	19.4	18.9	19.6			
er105F	0.3			20.4	19.9	17.6			
Average			21.3	19.9	18.5	17.6			
Standard deviation			1.6	0.9	0.8	0.9			
Acetamide									
er110A	0.5		19.2	17.2	15.6	13.5			
er110B	0.5	22.7	20.1	18.1		13.7	37678	39100	105.8
er110C	0.3	22.5	19.7	18.3		13.6	40147	39400	106.9
er110D	0.5	22.3	19.6	17.5	14.8	12.9	37956	39100	105.7
er110E	0.5	22.1	20.0	17.8	15.4	13.1	36081	37000	98.9
er110F	0.4	23.4	20.1		15.9	12.9	41856	43970	121.7
er110G	0.4	22.9	19.8	18.1	15.7	12.2	36379	39940	108.5
Average		22.9	19.8	17.8	15.5	13.1	39474	41409	113
Standard deviation		0.7	0.3	0.4	0.4	0.5	3258	4138	14

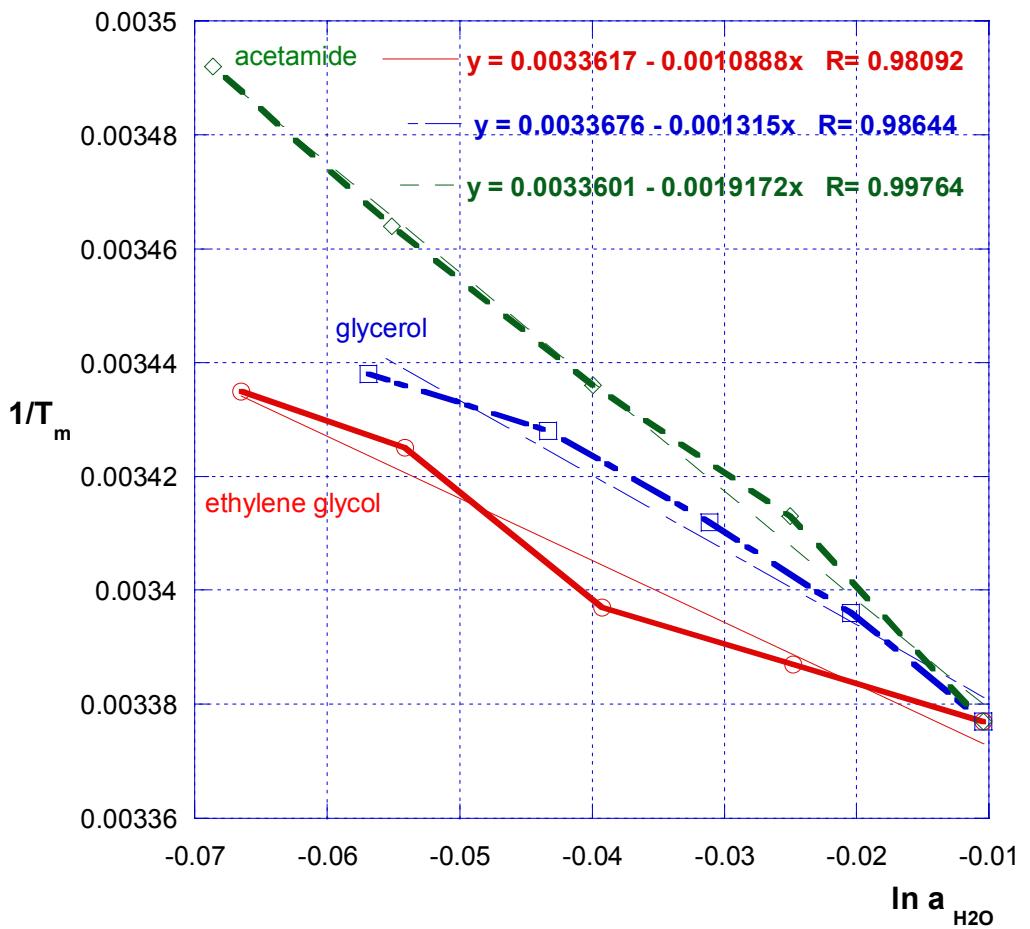


Figure S8. Reciprocal temperature of melting for $d(TA)_6$ **2d** vs. the logarithm of water activity for small cosolutes.

Table S9. Experimental t_m and thermodynamic data for melting of d(CG)₃ **3a**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	$-\Delta H$ (cal/mol) $\delta\alpha/\delta T_m$	$-\Delta H$ (cal/mol) van't Hoff	$-\Delta S$ (eu) van't Hoff
Ethylene glycol									
er134A	0.5	39.3	37.6	36.8	35.6	34.4	60590	66200	185.6
er134B	0.5	38.3	37.2	35.7	35.1		57558	60300	167.3
er134B	0.5	38.5	36.9	36.4	35.3	33.4	54749	58600	161.8
er134C	0.3	39.1	37.2	36.7	35.4	33.0	60590	55900	152.7
er134C	0.4	39.7	38.0	36.7	35.8	33.8	59011	55500	151.2
er134C	0.4	39.5	38.0	37.4	35.2	33.2	56093	56600	154.9
er134D	0.5	39.4	37.1	36.9	35.0	33.7	54776	59300	163.5
er134D	0.5	39.9	38.7	37.2	36.1		poor curve	58800	161.8
er134E	0.5	39.1	37.8	37.3	36.1	33.9	poor curve	58000	159.8
Average			37.6	36.8	35.5	33.6			
Standard deviation			0.6	0.5	0.4	0.5			
Glycerol									
er124G	0.5		37.7						
er124H	0.5		37.4	36.0	35.1	34.2			
er124H	0.4		37.5	36.0	35.1				
er124I	0.4		37.3	36.2	35.1	33.9			
er124K	0.3		37.5	36.4	35.6	34.9			
er124K	0.3		37.9	36.9	35.8	34.7			
Average			37.6	36.3	35.3	34.4			
Standard deviation			0.2	0.4	0.3	0.5			
Acetamide									
er124D	0.5	39.6	37.1	34.2	32.9	29.8	poor curve	60500	167.2
er124E	0.5	39.3	36.9	35.4	32.8	30.7	56093	58500	160.9
er124F	0.5	38.8	36.8	33.2	31.7	29.8	59011	60300	167.0
er124F	0.4	38.8	37.5	34.9	34.0		61413	60200	166.9
er124F	0.3	38.9	36.8	34.5	32.2		60590	60300	196.6
er124G	0.5			33.4		29.0			
er124H	0.5					29.9			
er124H	0.5					29.6			
er124I	0.4					28.6			
er124K	0.5					29.3			
er124K	0.4					29.7			
er129A	0.5	39.1	36.8	33.4	31.2	29.6	59377	67400	189.5
er129A	0.5	39.3	36.9	34.0	31.5	29.5	66870	63400	176.7
er129B	0.3	39.4	37.5	34.4	30.9	29.7	62297	63500	177.1
Average		39.2	37.0	34.2	32.2	29.6	59216	60194	168
Standard deviation		0.4	0.3	0.7	1.0	0.5	3289	3314	13

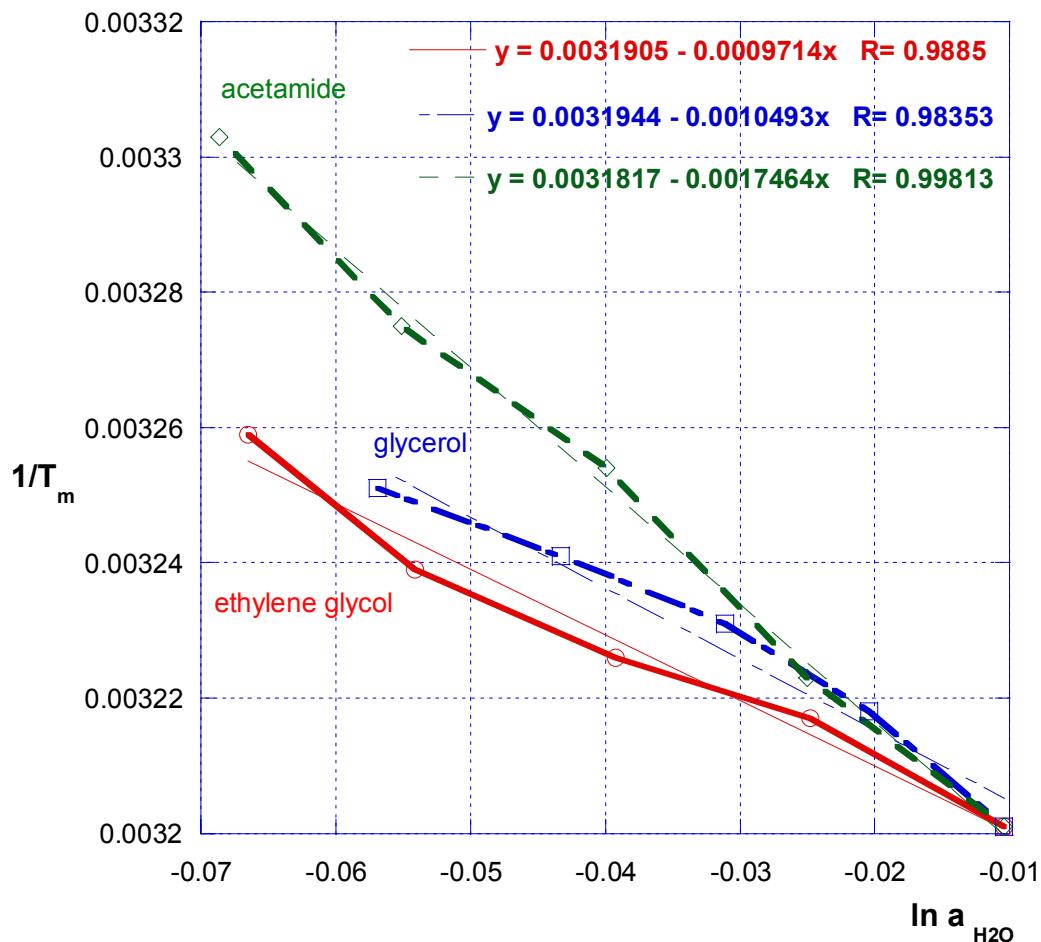


Figure S9. Reciprocal temperature of melting for d(CG)₃ **3a** vs. the logarithm of water activity for small cosolutes.

Table S10. Experimental t_m and thermodynamic data for melting of r(CG)₃ **3b**.

Experiment	Ramp °C/min	0%	5%	10%	15%	20%	−ΔH (cal/mol) $\delta\alpha/\delta T_m$	−ΔH (cal/mol) van't Hoff	−ΔS (eu) van't Hoff
Ethylene glycol									
er128H	0.5	43.3	41.7	40.2	39.8	38.2		61830	169.8
er128I	0.4	43.0	41.2	40.5	38.9	37.9	55710	62000	169.9
er128I	0.3	43.1	41.4	40.5	39.0	37.3	56459	63800	175.7
er128I	0.3	43.2	41.7	40.6	39.2	37.8	63757	69100	191.2
er128L	0.5		41.2	39.8	39.0	37.7			
er128L	0.4		41.1	40.2	38.9	38.1			
er128L	0.3		41.8	40.7	39.1	38.2			
er128K	0.5	42.3	40.7	39.8	38.4	37.6	56836	62900	173.0
er128K	0.4	42.8	41.4	40.1	39.3	37.9	56801	62200	170.8
Average			41.4	40.3	39.1	37.9			
Standard deviation			0.4	0.3	0.4	0.3			
Glycerol									
er128A	0.5	42.8	40.7	39.9	39.8	38.9	56459	65200	180.2
er128B	0.5	43.0	41.5	40.5	39.3		57156	62900	172.8
er128B	0.4	43.1	41.6	40.4	39.5	38.8	50059	63400	174.4
er128B	0.3	43.2	41.9	41.4	39.4	38.1	58605	64800	178.8
er128B	0.3	42.8	41.5	40.6	40.0	38.9	52290	65900	182.5
er128C	0.5	42.9	41.8	41.1	39.6	38.9	57871	65500	181.0
er128C	0.5	43.1	41.8	40.8	40.5	38.7	58605	66700	184.9
er128D	0.5	42.7	42.0	41.0	39.8	39.1	57835	57400	155.5
Average		43.0	41.6	40.7	39.7	38.8			
Standard deviation		0.3	0.4	0.5	0.4	0.3			
Acetamide									
er128E	0.5	41.5	40.0	38.4	36.4	34.4	59756	63200	174.8
er128F	0.5	41.9	40.3	38.2	37.0	35.2	56836	63900	176.8
er128F	0.4	42.0	40.0	39.0	36.9	34.4	61355	62600	172.4
er128F	0.3	41.8	40.3	38.1	37.0	35.0	53469	62900	173.7
er128G	0.5	41.3	40.0	38.9	36.6	35.5	60545	61200	168.4
er128G	0.4	42.3	40.2	38.3	36.8	35.7	66218	65200	180.4
er128G	0.4	41.5	40.3	38.7	36.7	34.5	poor curve	67800	189.1
er135A	0.5	42.6	40.7	38.8	37.1	35.4	poor curve	65100	180.0
Average		41.9	40.2	38.6	36.8	35.0	57717	63888	176
Standard deviation		0.4	0.2	0.3	0.2	0.5	3740	2469	8

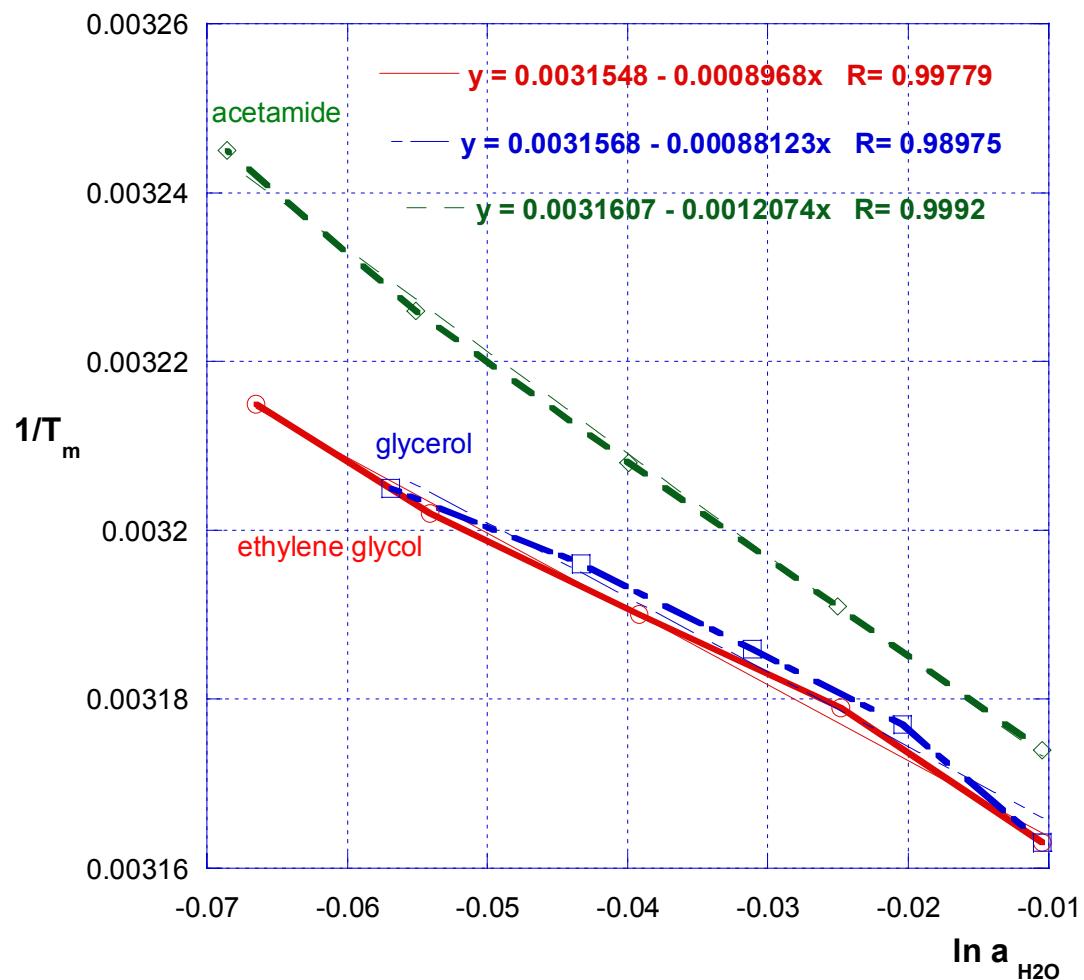


Figure S10. Reciprocal temperature of melting for r(CG)₃ **3b** vs. the logarithm of water activity for small cosolutes.

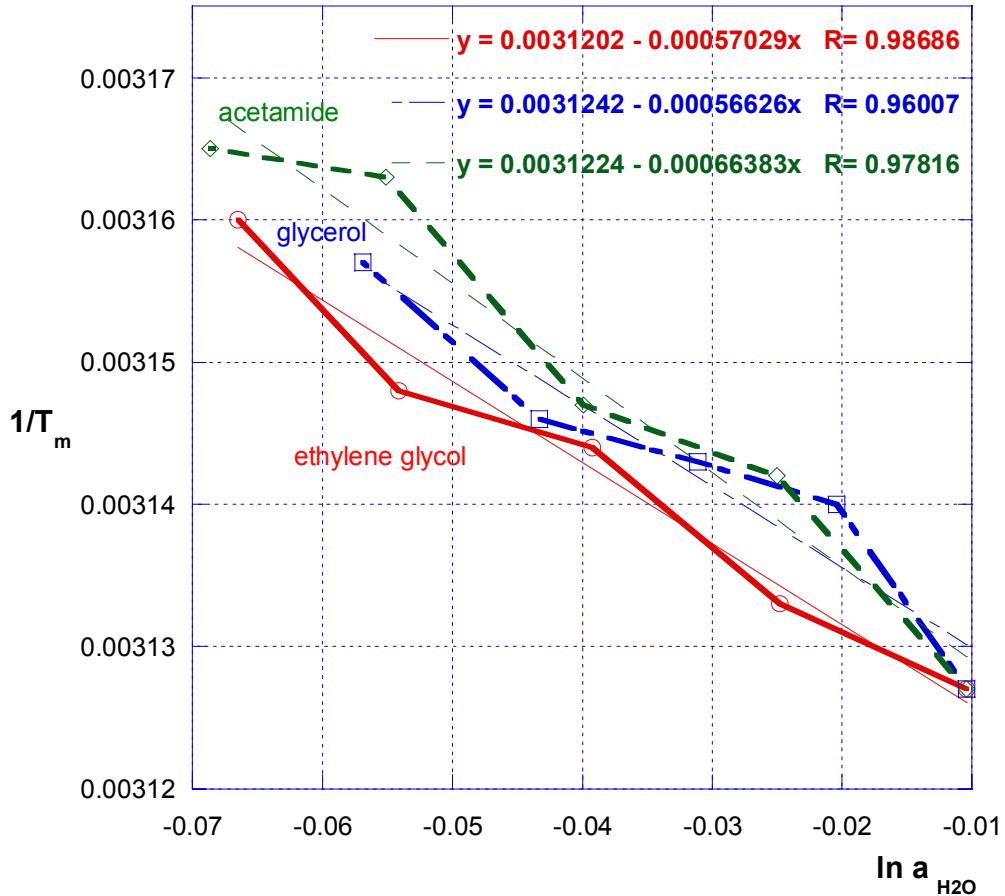


Figure S11. Reciprocal temperature of melting for 2'-OMe(CG) **3c** vs. the logarithm of water activity for small cosolutes.

Table S12 continued). Experimental t_m at different concentrations of (GCGAAUUCGC) 1.

Experiment	Ramp °C/min	Concentration (μmol)						
		1	2	4	8	16	32	64
1d d(GCGAATTTCGC)								
er152A/50C	0.5	44.1	46.4	49.9	51.5	53.4	57.2	58.0
er152A/50C	0.5	43.6	46.5		52.3	54.0	57.3	
er152A/50C	0.4	44.9	47.4		52.6	54.4	57.1	58.7
er152B	0.4	44.6	46.7					
er152B	0.5		47.2					
er152A/51F	0.5	43.7	46.6	49.6	51.0	53.2	56.6	58.1
er152A/51F	0.5				51.9		56.2	58.4
er152A/51F	0.5			49.7	52.1	54.2	56.7	58.3
er152A/51G	0.5				51.4	53.2	56.8	
er152A/51G	0.4	44.8	47.6	50.2	51.0	53.9	57.2	58.1
er150B	0.4	44.6	47.0		52.1	54.2	57.0	58.3
Average		44.3	46.9	49.9	51.8	53.8	56.9	58.3
Standard deviations		0.5	0.4	0.3	0.6	0.5	0.4	0.2

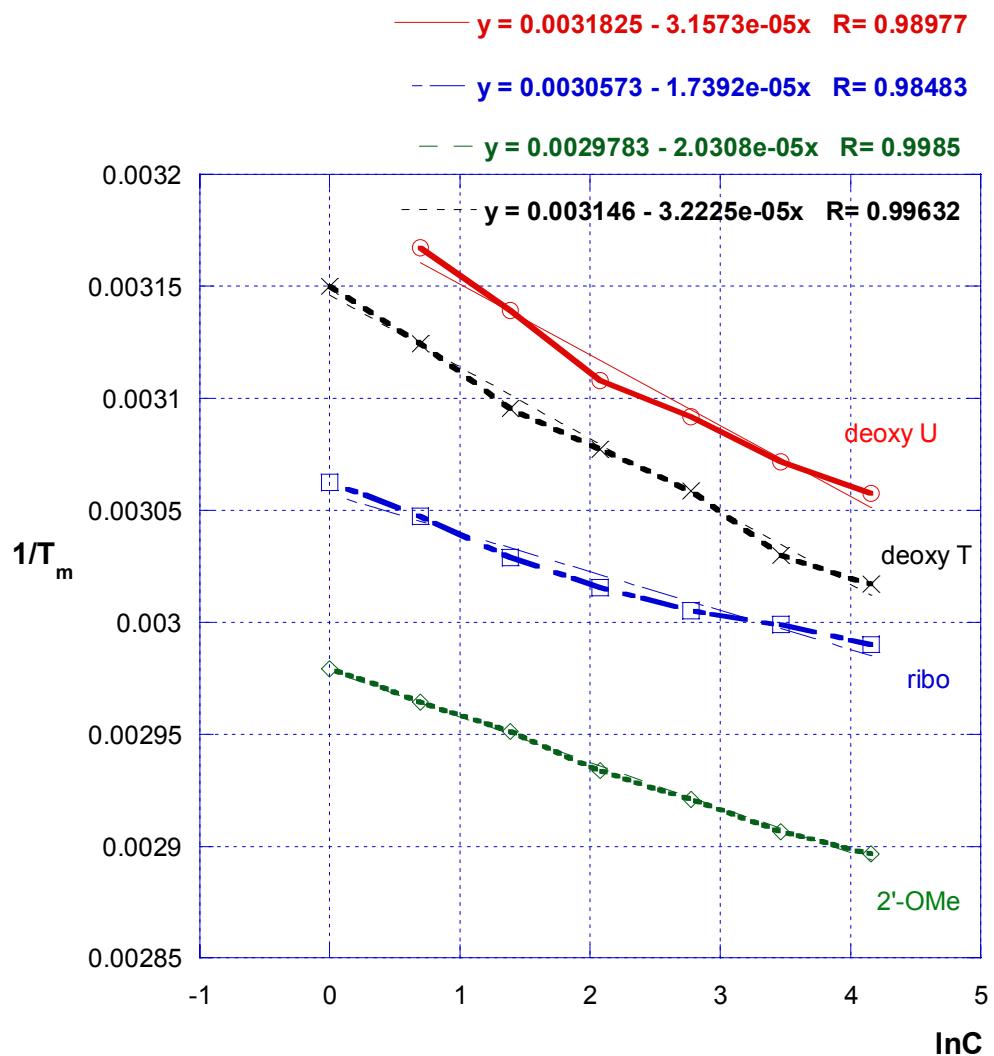


Figure S12. Reciprocal temperature of melting for (GCGAAUUCGC) 1 vs. the logarithm of oligonucleotide concentration.

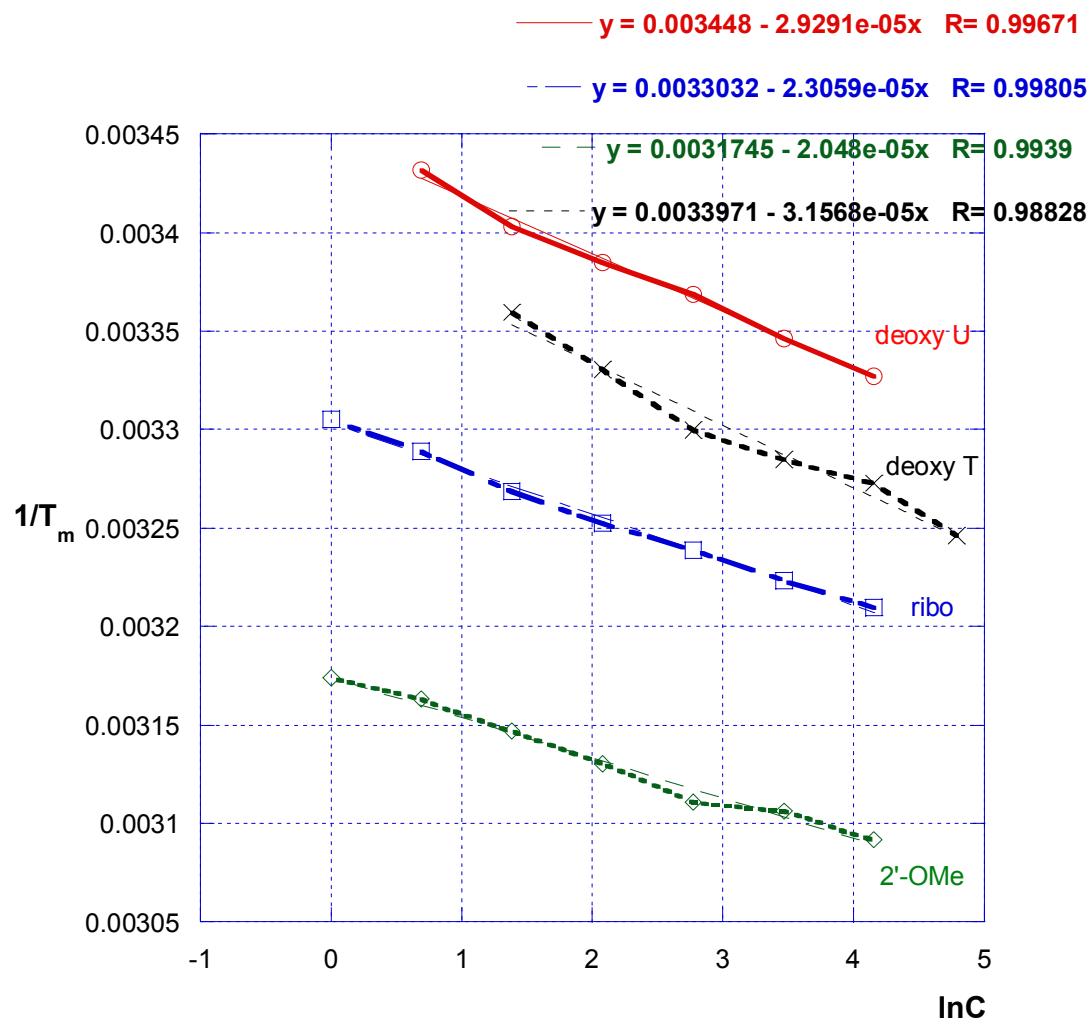


Figure S13. Reciprocal temperature of melting for $(\text{UA})_6$ **2** vs. the logarithm of oligonucleotide concentration.

Table S14. Experimental t_m at different concentrations of $(CG)_3$ **3**.

Experiment	Ramp °C/min	Concentration (μmol)					
		2	4	8	16	32	64
3a d(CG)3							
er147A	0.5		41.9	44.7	46.9	49.3	51.6
er147A	0.5		42.0	45.1	47.0	49.0	51.6
er147B	0.4			44.2	47.0	48.1	51.8
er147B	0.5		42.1	45.0	46.6	49.3	51.7
er147B	0.4		42.7				51.7
er147B	0.4		42.0	45.9			52.3
Average		39.2	42.1	45.0	46.9	48.9	51.8
Standard deviations		0.4	0.3	0.6	0.2	0.6	0.3
3b ribo(CG)3							
er147E	0.5		46.2	48.5	50.3	52.7	54.7
er147E	0.5		46.4	48.5	51.6	53.3	54.9
er147E	0.4			49.6	52.3		55.6
er147E	0.4		46.7	48.4	51.7		55.5
er147F	0.5		46.2	48.6	51.7	52.7	55.1
er147F	0.5		46.7	49.5	51.5	53.2	56.5
er147G	0.5		46.4	49.0	51.8	52.9	56.0
er147G	0.4					52.8	55.9
er147G	0.4					53.2	56.6
Average		43.0	46.4	48.9	51.6	53.0	55.6
Standard deviations		0.3	0.2	0.5	0.6	0.3	0.7
3c 2'-OMe(CG)3							
er147C	0.4		49.3		54.4	56.6	60.4
er147C	0.5		49.7	52.3	55.6	57.3	60.4
er147C	0.4		50.0	53.0	56.3	58.6	60.2
er147C	0.4		50.0	53.1	57.0	58.0	60.0
er147D	0.5		50.5	52.9	56.7	58.3	60.8
er147D	0.5		50.1	52.7	56.5	59.0	61.4
Average		46.6	49.9	52.8	56.1	58.0	60.5
Standard deviations		0.5	0.4	0.3	0.9	0.9	0.5

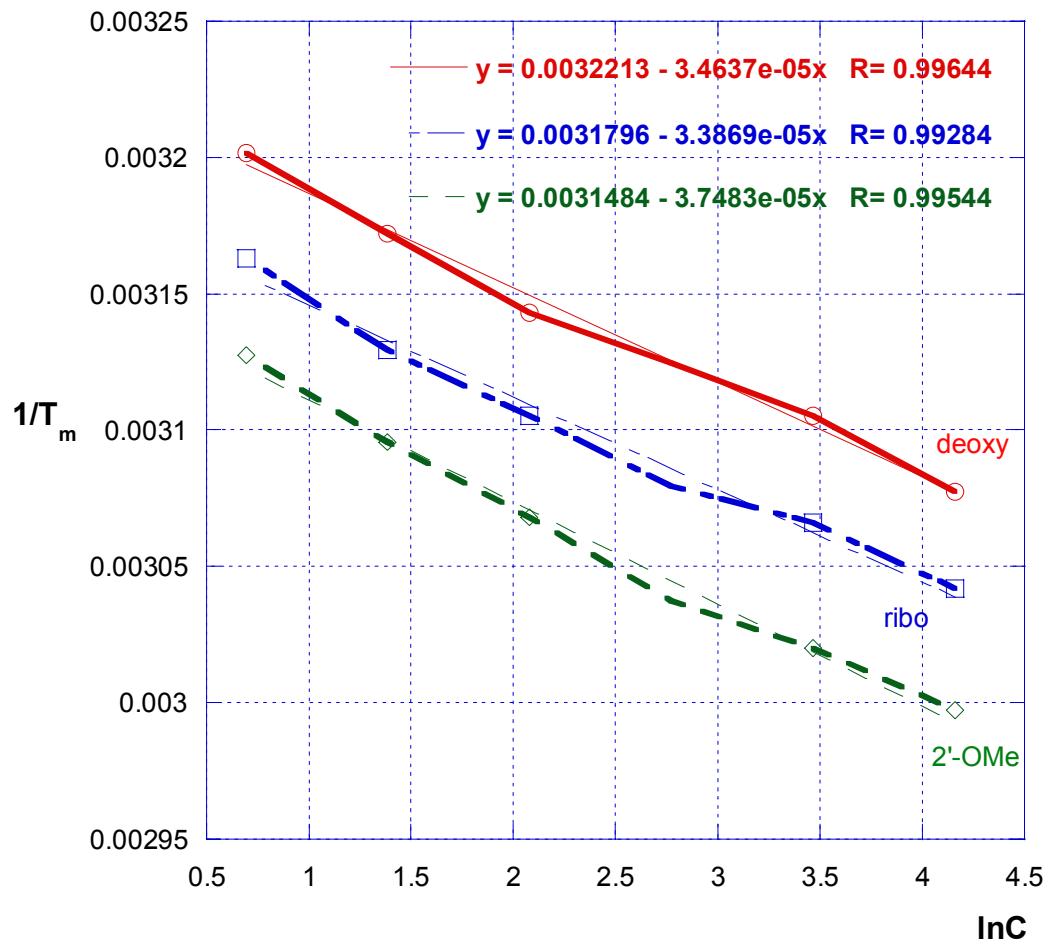


Figure S14. Reciprocal temperature of melting for $(CG)_3$ **3** vs. the logarithm of oligonucleotide concentration.

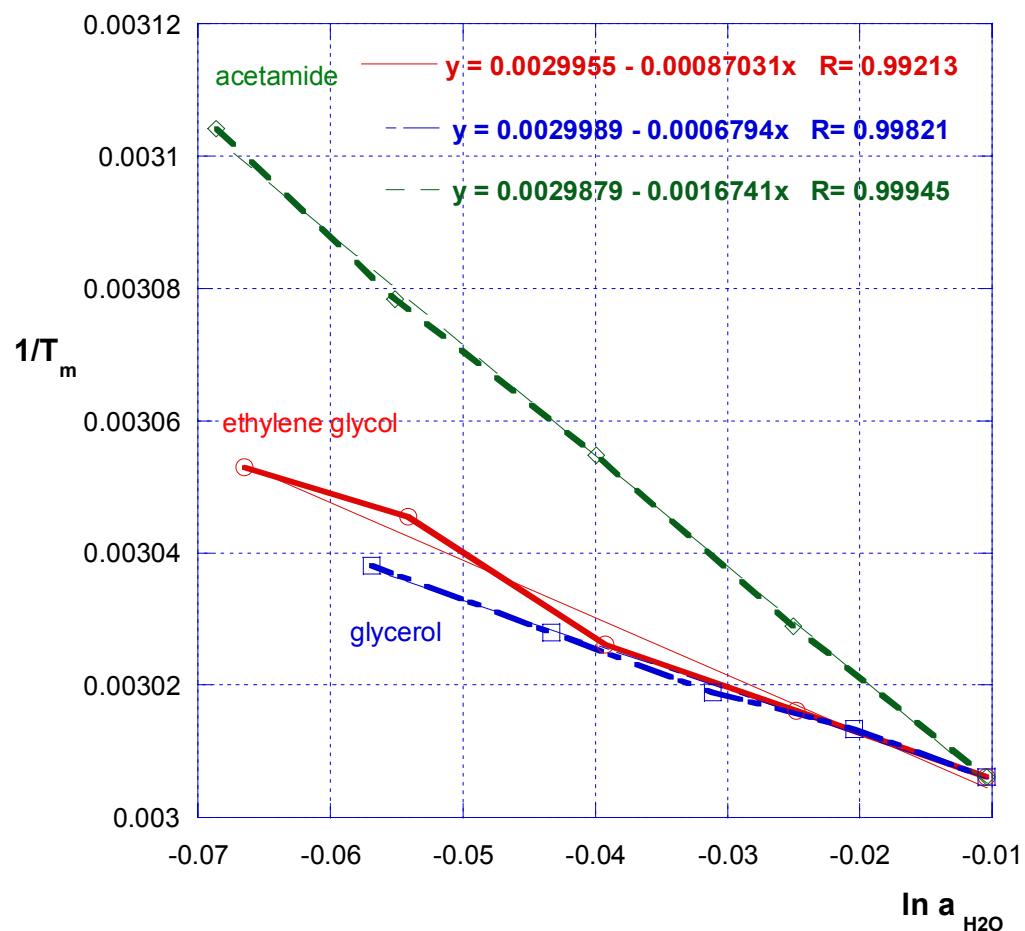


Figure S15. Reciprocal temperature of melting for r(CGCAAUUUGCG) **4b** vs. the logarithm of water activity for small cosolutes.

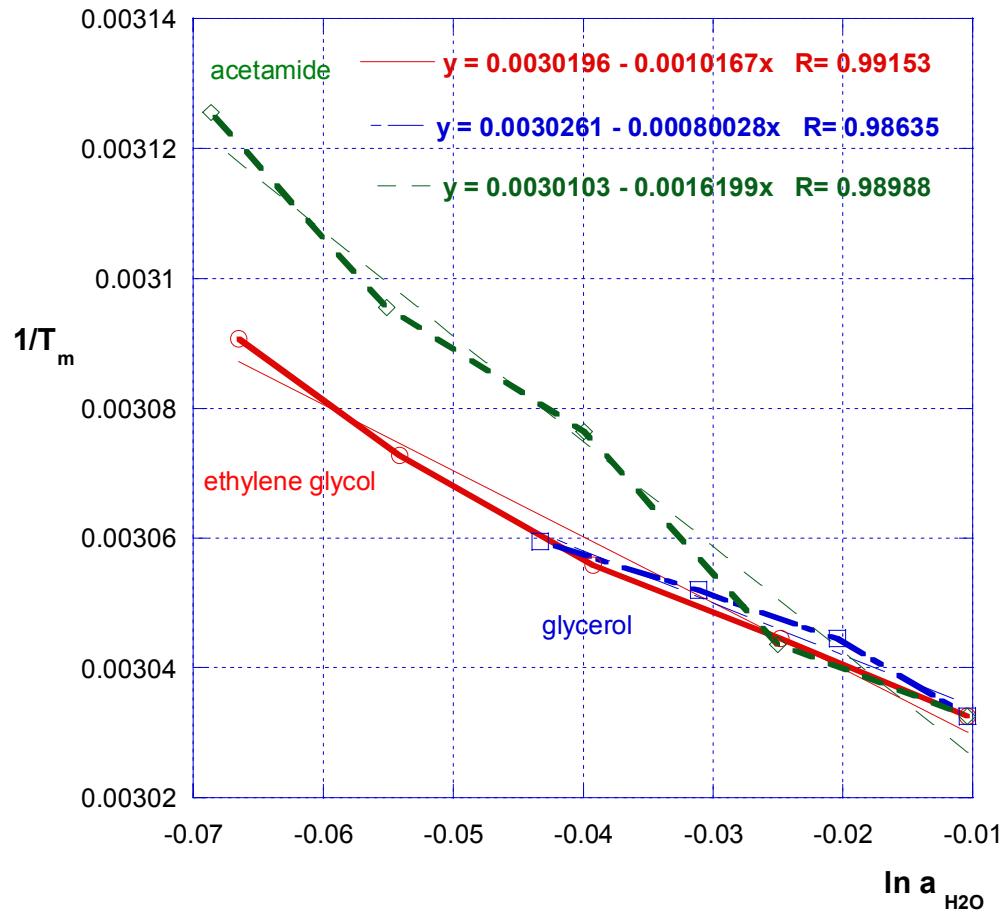


Figure S16. Reciprocal temperature of melting for d(CGCAAATTCGCG) **4d** vs. the logarithm of water activity for small cosolutes.

Table S17. Experimental t_m at different concentrations of r(CGCAAAUUUGCG) **4b** and d(CGCAAATTGCG) **4d**.

Experiment	Ramp °C/min	Concentration (μmol)					
		1	2	4	8	16	32
4b r(CGCAAAUUUGCG)							
er156A	0.5	57.2		58.2	61	60.8	
er156A	0.5	56.2		59.4	59.7	61.3	
er156A	0.4	58.6		59	59.6	60.7	
er156A	0.4	59.3		59.1	59.4	61	
er156B	0.5	59		58.4	60.4	61.2	
er156B	0.5	58.3		57.8	59.7	61.1	
Average		58.1	59.5	58.7	60.0	61.0	
Standard deviations		1.2	0.7	0.6	0.6	0.2	
4d d(CGCAAATTGCG)							
er157A	0.5	52.6		56.5	58.5		61.7
er157A	0.5	55		57.5	59.4	60	62.5
er157B	0.5	54.9		58.1	59.7	59.1	61.9
er157B	0.5	53.8		57.7	59.3	59.2	61.8
er157B	0.4	55		56.4	58.3	61.2	62.5
er157B	0.4	54.6		57.4	59.2		
er157C	0.5	54.4		56.8	57.8	60.6	
er157C	0.5	53.6		56.7		60.6	
Average		54.2		57.1	58.9	60.1	62.1
Standard deviations		0.8		0.6	0.7	0.8	0.4

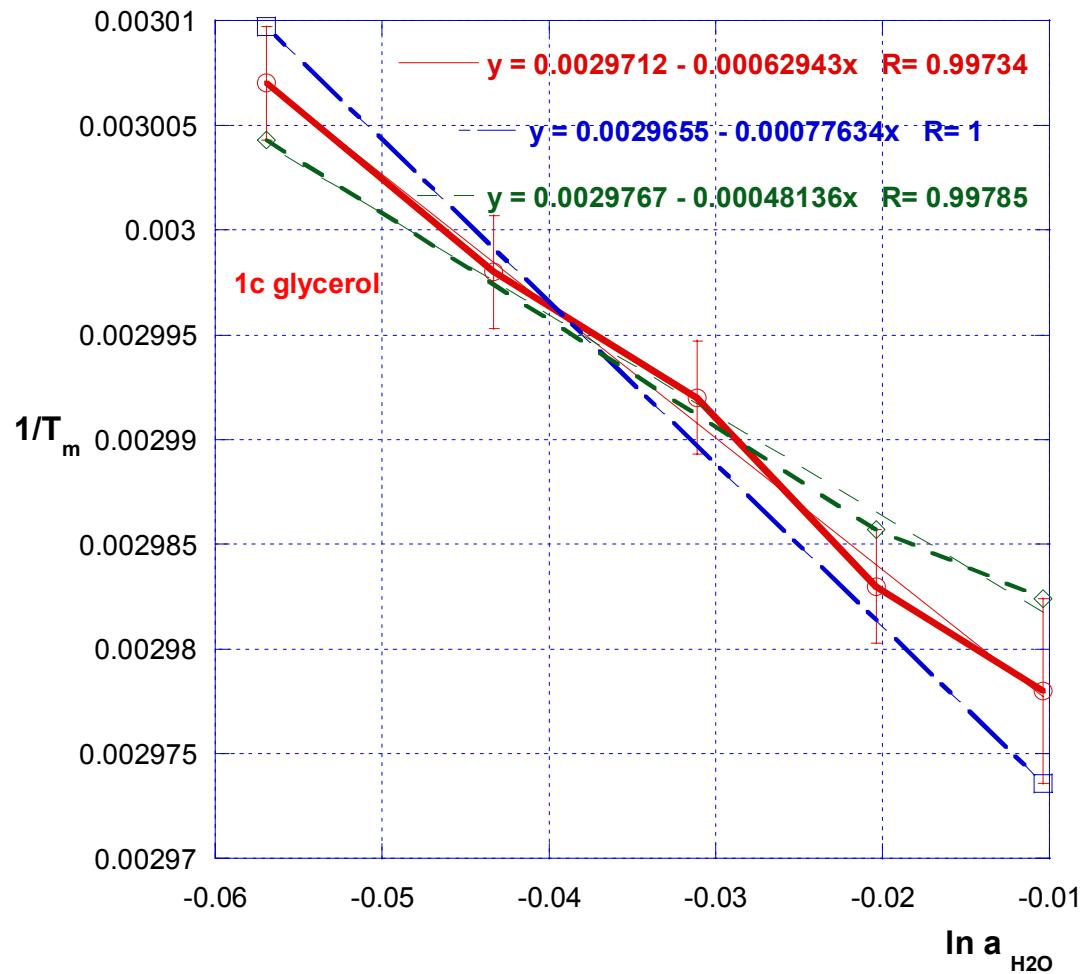


Figure S18. Uncertainty estimates using error bars to construct alternative plots of reciprocal temperature of melting for 2'-OMe(GCGAAUUCGC) **1c** vs. the logarithm of water activity for glycerol.

$$\sigma(d(1/T_m)/d(\ln a_{H_2O})) = ((0.0006294 - 0.0004814) + (0.0007763 - 0.0004814))/2 = 0.0001474$$