Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Electronic Supplementary Information

Hyaluronan Derivatives Bearing Variable Densities of Ferulic Acid Residues

Andrea Cappelli,[*,a] Giorgio Grisci,[a] Marco Paolino,[a] Germano Giuliani,[a] Alessandro Donati,[a] Raniero Mendichi,[b] Roberto Artusi,[c] Mario Demiranda,[c] Andrea Zanardi,[c] Gianluca Giorgi,[a] Salvatore Vomero.[a]

[a]Dipartimento di Biotecnologie, Chimica e Farmacia and European Research Centre for Drug Discovery and Development, Università degli Studi di Siena, Via A. Moro 2, 53100 Siena, Italy

[b]Istituto per lo Studio delle Macromolecole (CNR), Via E. Bassini 15, 20133 Milano, Italy

[c]Rottapharm Madaus, Via Valosa di Sopra 7, 20900 Monza, Italy

Content:

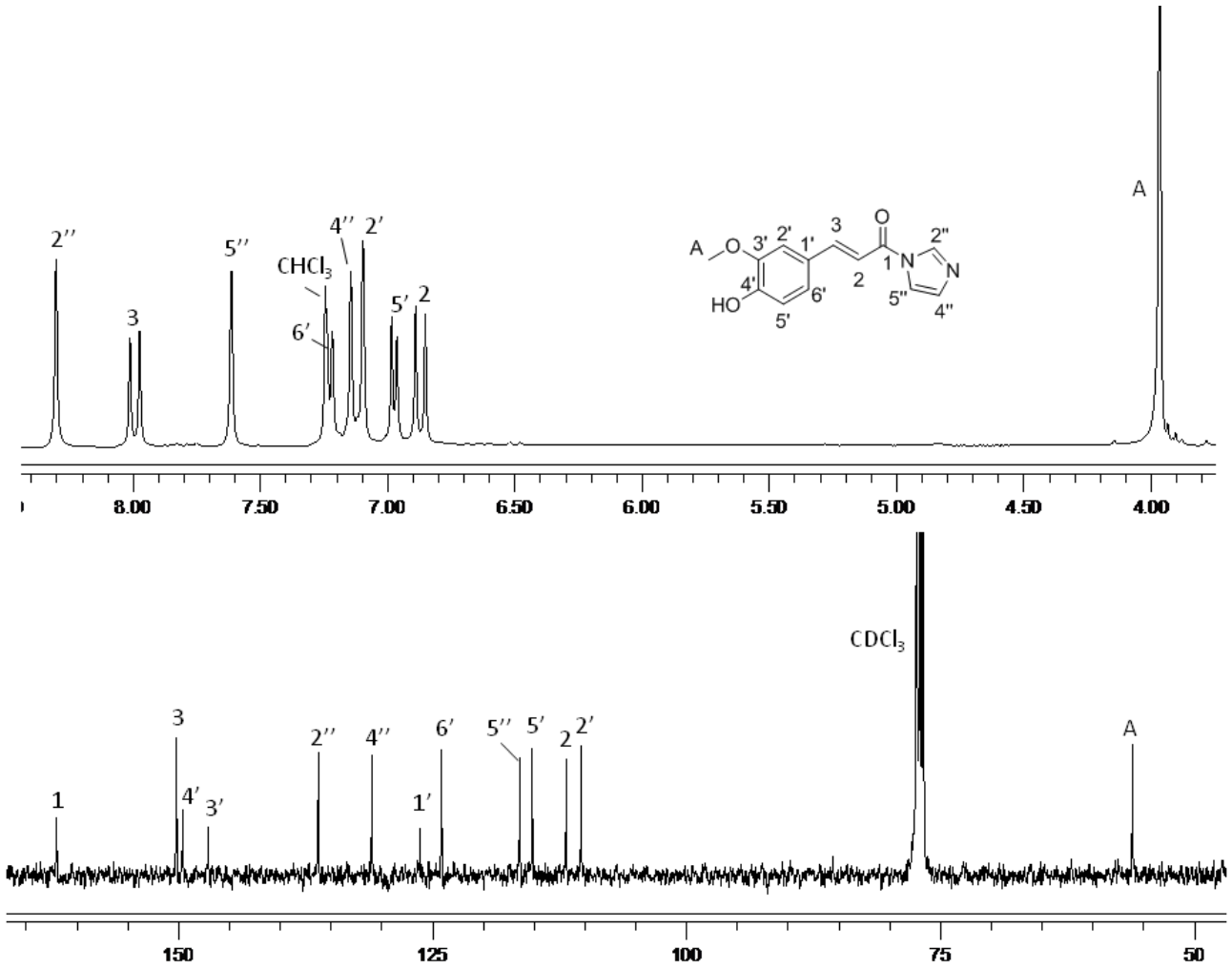

Figure ESI-1. NMR spectra of compound **2** in $CDCl_3$. $CHCl_3$ and $CDCl_3$indicate the solvent peaks.

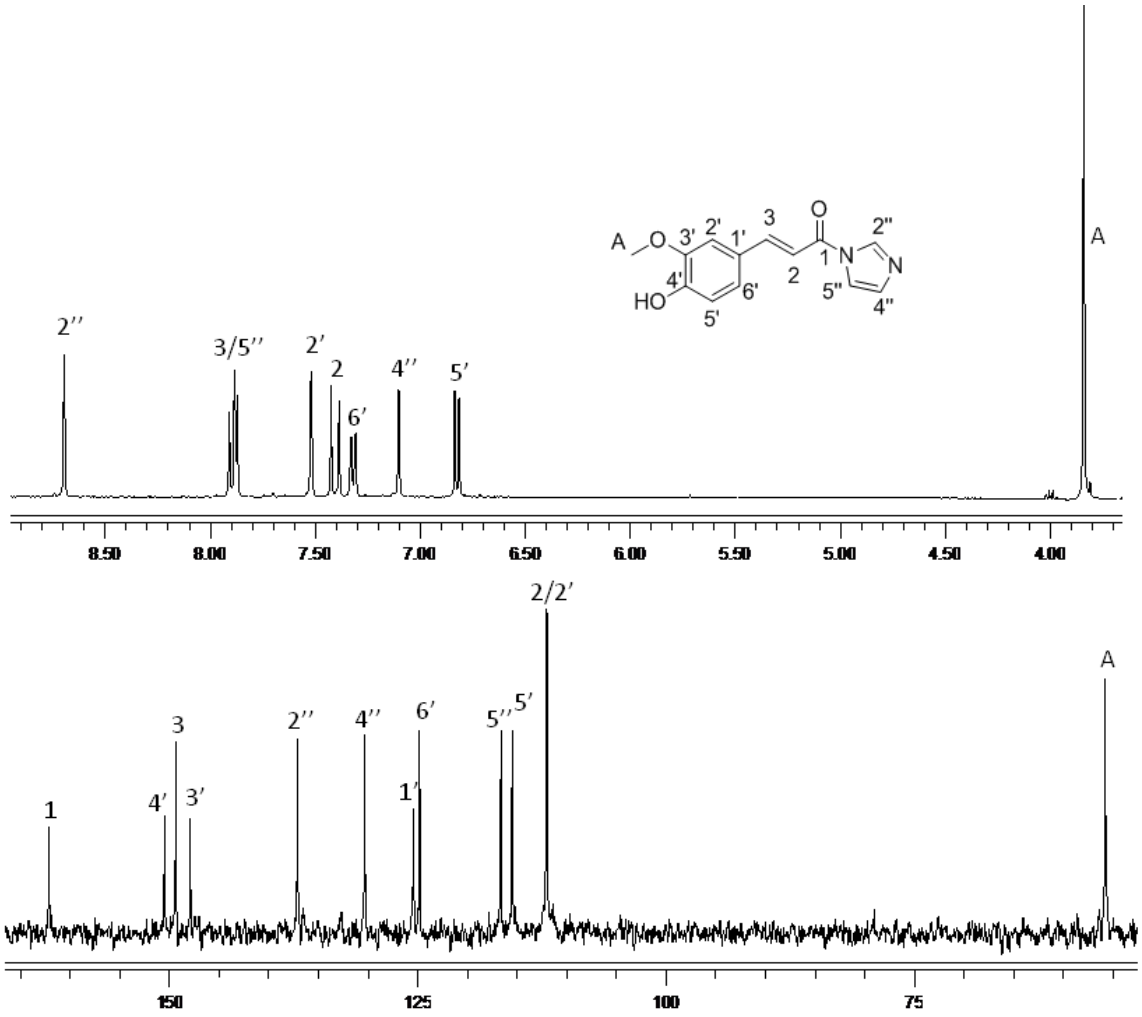

Figure ESI-2. NMR spectra of compound **2** in DMSO-d_6.

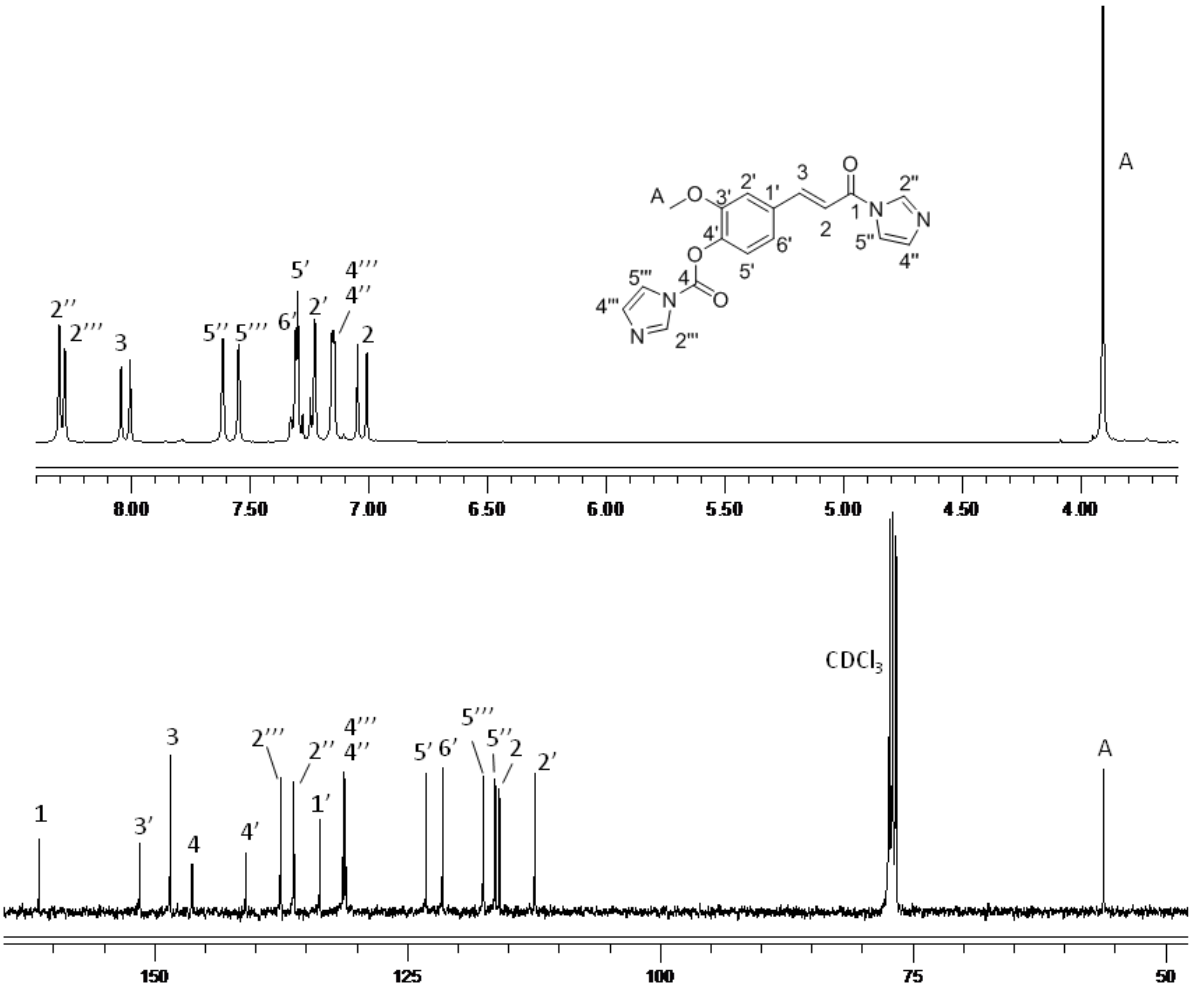

Figure ESI-3. NMR spectra of compound **3** in $CDCl_3$. $CDCl_3$ indicates the solvent peak.

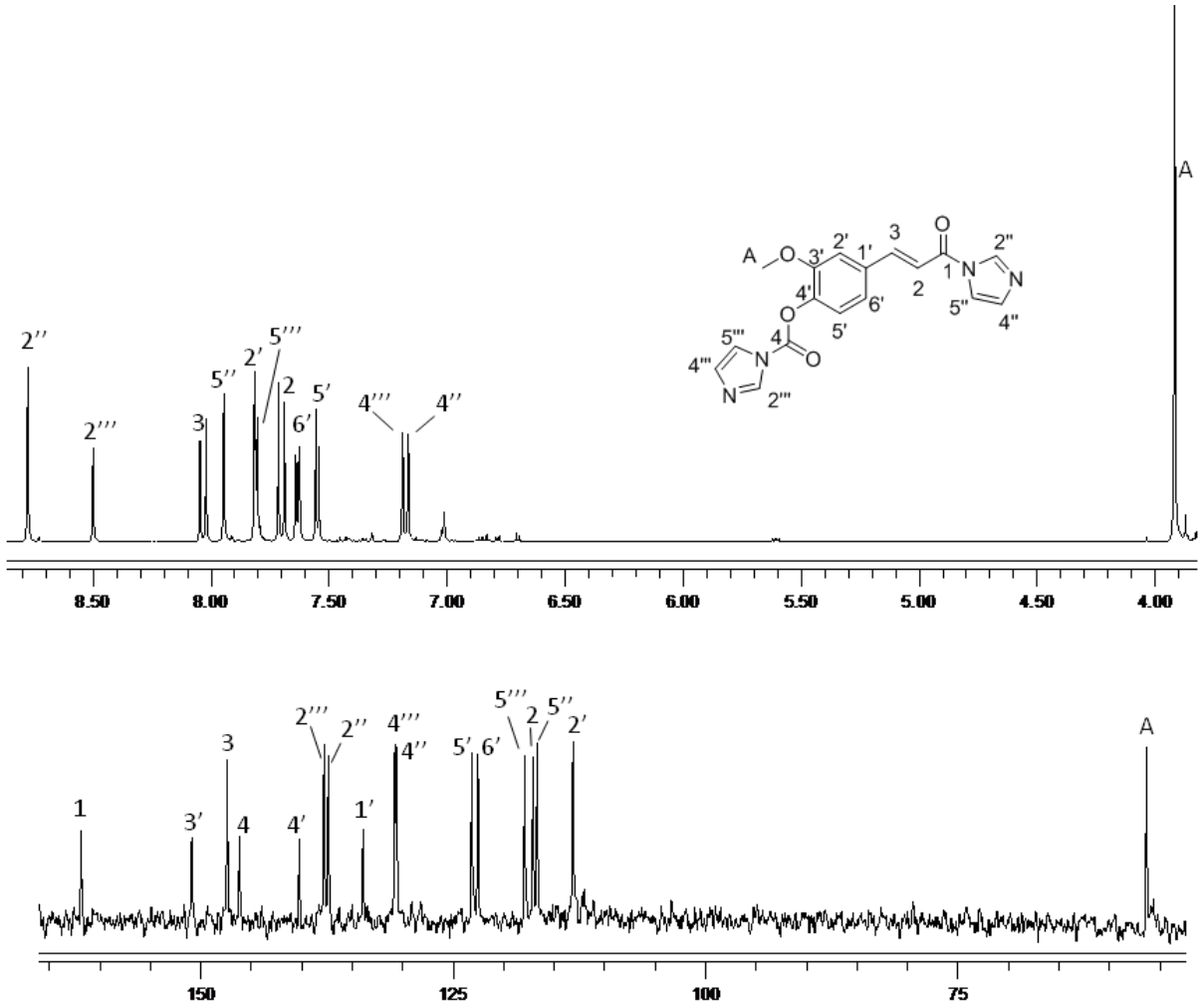

Figure ESI-4. NMR spectra of compound **3** in DMSO-d_6.

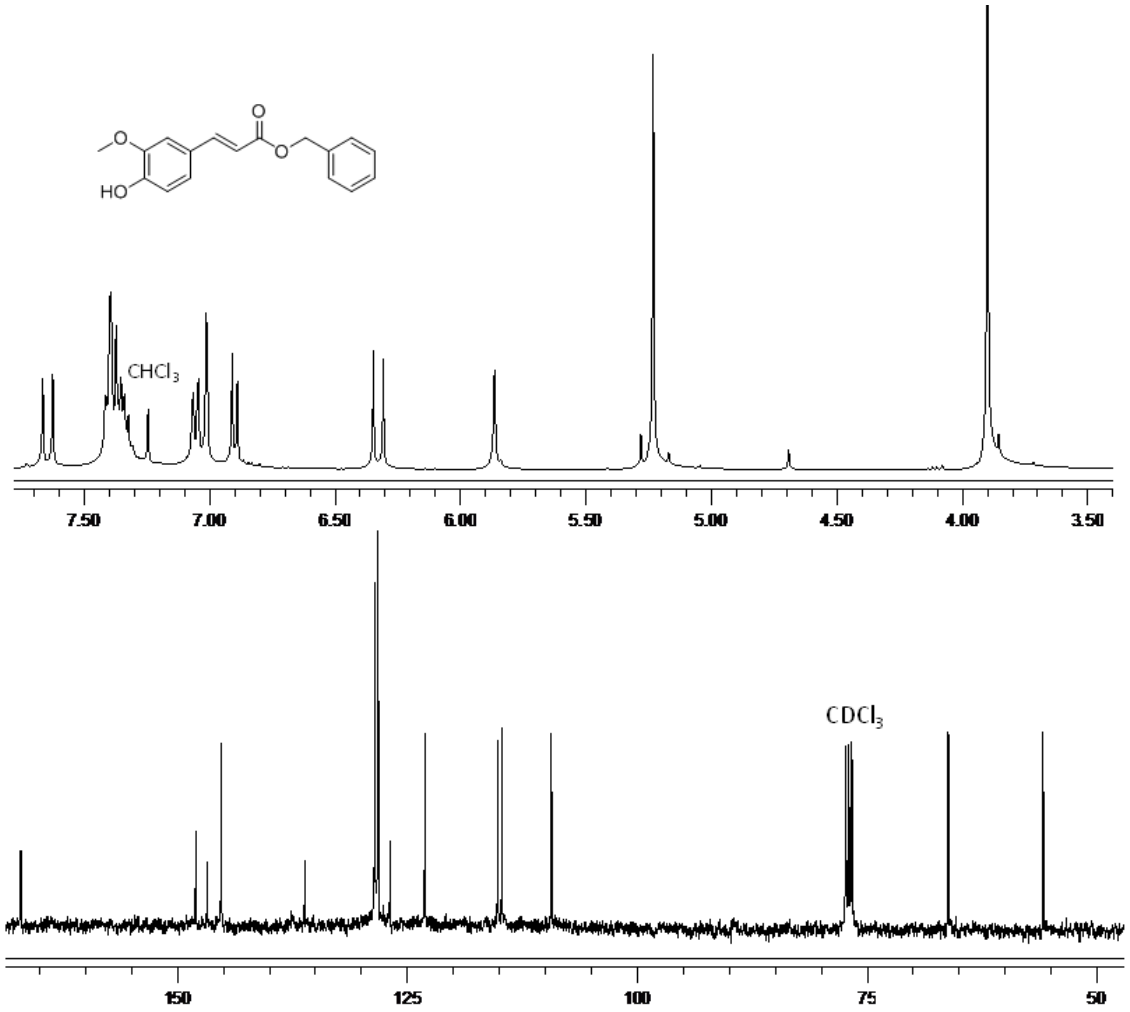

Figure ESI-5. NMR spectra of benzyl ferulate **5** in $CDCl_3$. $CHCl_3$ and $CDCl_3$indicate the solvent peaks.

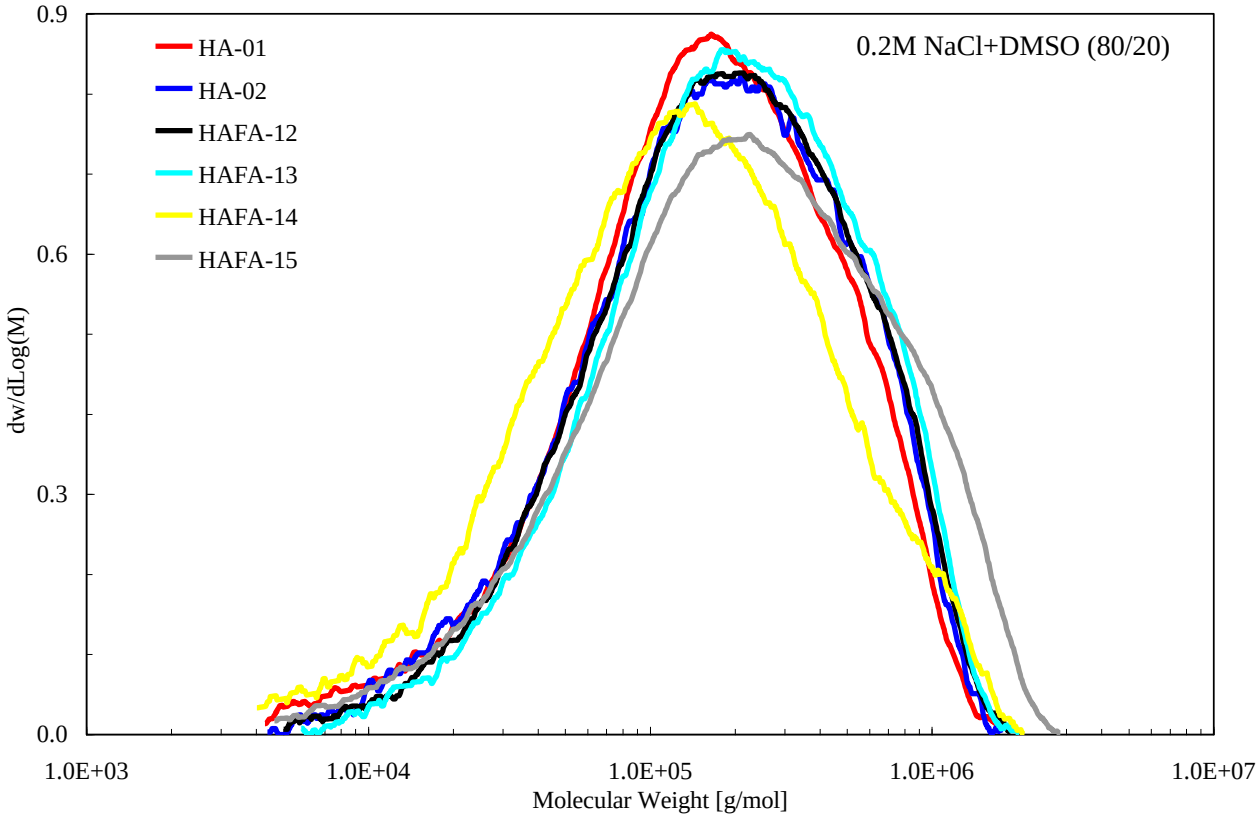

Figure ESI-6. Comparison of differential MWD of the two native **HA** and of four **HAFA** derivatives.

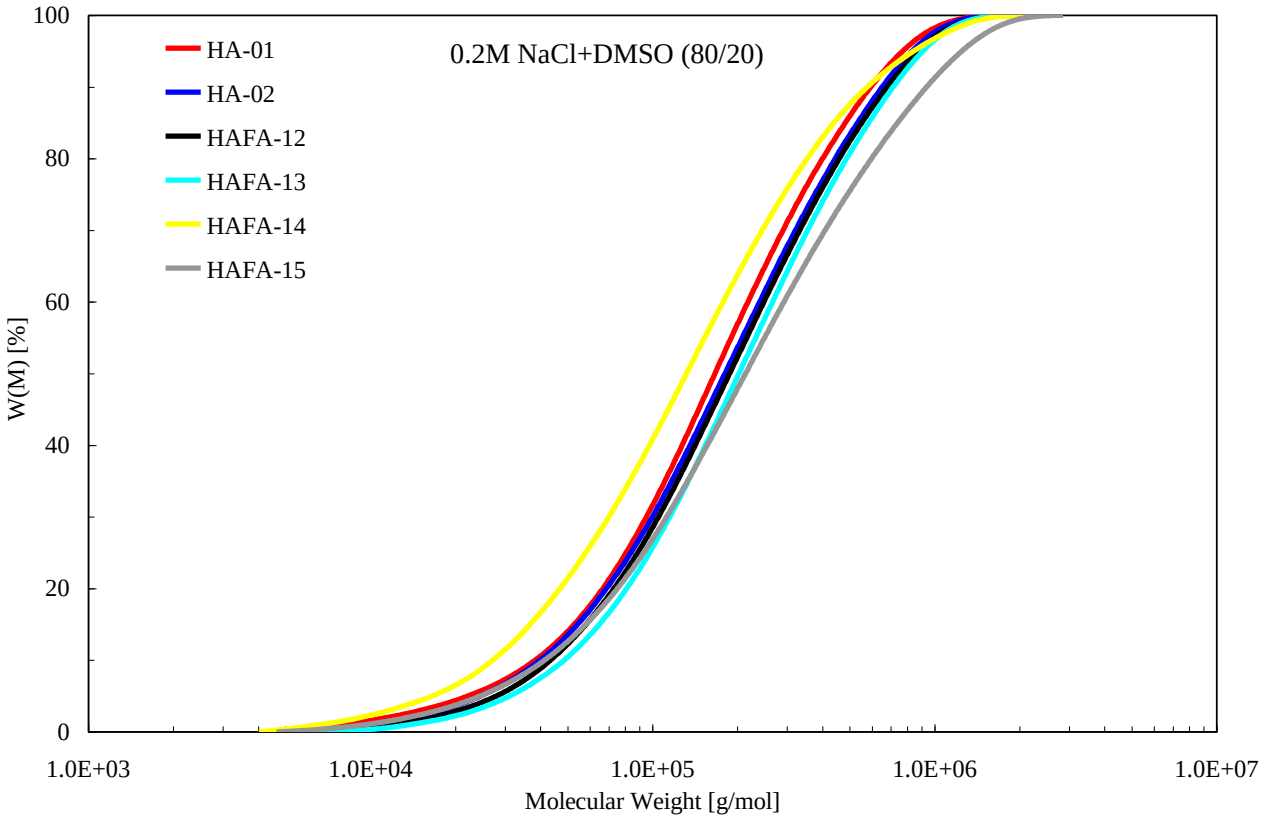

Figure ESI-7. Comparison of the cumulative MWD of the two native **HA** and of four **HAFA** derivatives.

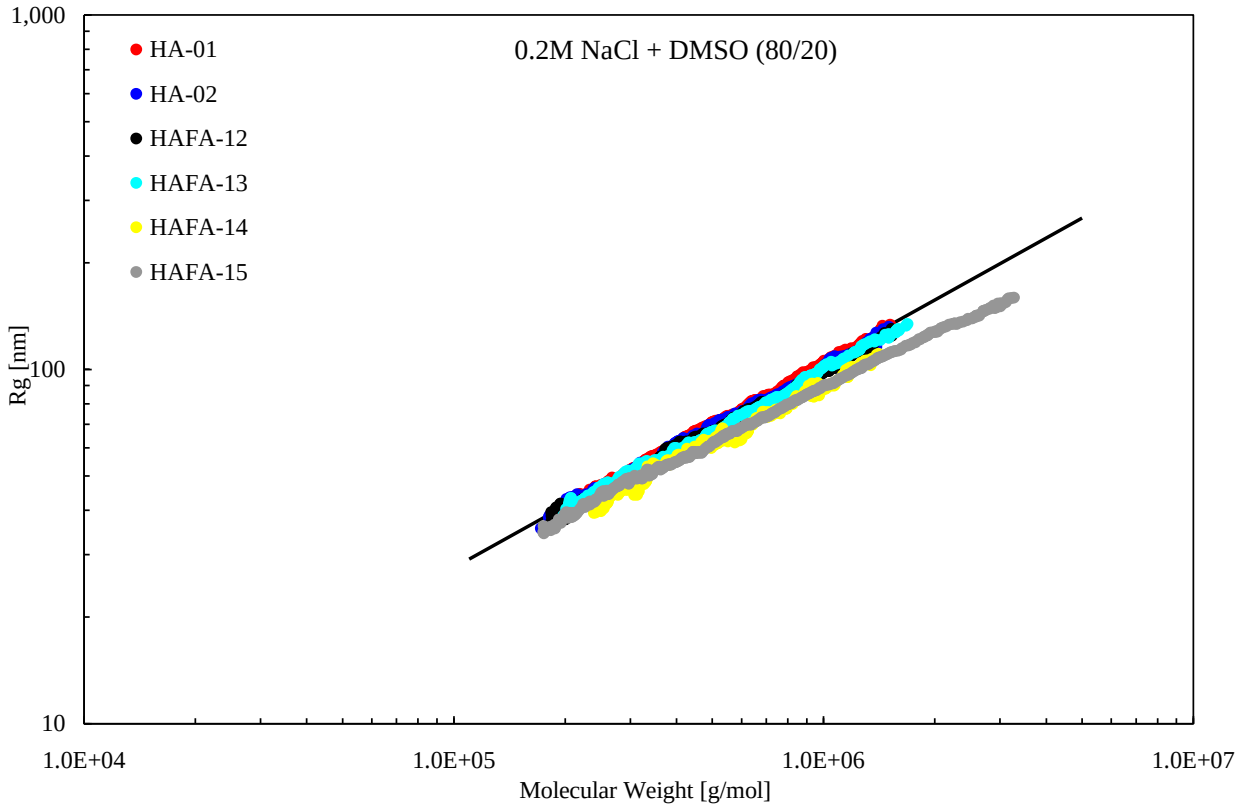

Figure ESI-8. Comparison of the conformation plots of native **HA** and selected **HAFA** derivatives.

Table ESI-1. Crystal data and structure refinement for compound **2**.

Empirical formula	C13 H12 N2 O3	
Formula weight	244.25	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 9.1833(10) Å	α= 90°.
	b = 10.8772(10) Å	β= 106.907(11)°.
	c = 12.2834(16) Å	γ = 90°.
Volume	1173.9(2) $Å^3$	
Z	4	
Density (calculated)	1.382 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	512	
Crystal size	0.5 × 0.5 × 0.3 mm^3	
Theta range for data collection	2.46 to 29.11°.	
Index ranges	-8≤h≤12, -14≤k≤13, -16≤l≤16	
Reflections collected	8625	
Independent reflections	2752 [R(int) = 0.0970]	
Completeness to theta = 29.11°	87.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.66873	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2752 / 0 / 165	
Goodness-of-fit on F^2	1.002	
Final R indices [I>2sigma(I)]	R1 = 0.0769, wR2 = 0.1065	
R indices (all data)	R1 = 0.2189, wR2 = 0.1454	
Largest diff. peak and hole	0.169 and -0.168 e.$Å^{-3}$	

Table ESI-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **2**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
N(1)	799(3)	2082(2)	1401(2)	46(1)
C(2)	-569(4)	1657(3)	731(3)	51(1)
N(3)	-1573(3)	2518(3)	406(2)	59(1)
C(4)	-816(4)	3572(3)	886(3)	76(1)
C(5)	611(4)	3335(3)	1494(3)	71(1)
C(6)	2122(4)	1340(3)	1796(3)	45(1)
O(1)	2022(2)	248(2)	1552(2)	59(1)
C(7)	3513(4)	1950(3)	2459(3)	49(1)
C(8)	4873(4)	1469(3)	2561(3)	49(1)
C(1')	6351(4)	1981(3)	3162(3)	43(1)
C(2')	7676(4)	1328(3)	3197(2)	48(1)
C(3')	9098(4)	1768(3)	3766(3)	45(1)
C(4')	9233(4)	2929(3)	4280(3)	50(1)
C(5')	7949(4)	3583(3)	4256(3)	53(1)
C(6')	6521(4)	3106(3)	3723(3)	50(1)
O(2)	10455(3)	1171(2)	3902(2)	63(1)
C(9)	10403(4)	-97(3)	3643(3)	69(1)
O(3)	10608(3)	3417(2)	4838(2)	75(1)

Table ESI-3. Bond lengths [Å] and angles [°] for non-H atoms of compound **2**.

N(1)-C(2)	1.367(3)	C(2)-N(1)-C(5)	105.6(3)
N(1)-C(5)	1.383(4)	C(2)-N(1)-C(6)	123.9(3)
N(1)-C(6)	1.421(4)	C(5)-N(1)-C(6)	130.3(3)
C(2)-N(3)	1.293(4)	N(3)-C(2)-N(1)	112.8(3)
N(3)-C(4)	1.381(4)	C(2)-N(3)-C(4)	104.2(3)
C(4)-C(5)	1.331(4)	C(5)-C(4)-N(3)	111.7(3)
C(6)-O(1)	1.222(3)	C(4)-C(5)-N(1)	105.7(3)
C(6)-C(7)	1.460(4)	O(1)-C(6)-N(1)	118.2(3)
C(7)-C(8)	1.327(4)	O(1)-C(6)-C(7)	124.7(3)
C(8)-C(1')	1.454(4)	N(1)-C(6)-C(7)	117.0(3)
C(1')-C(6')	1.391(4)	C(8)-C(7)-C(6)	121.3(3)
C(1')-C(2')	1.399(4)	C(7)-C(8)-C(1')	127.6(3)
C(2')-C(3')	1.376(4)	C(6')-C(1')-C(2')	117.4(3)
C(3')-O(2)	1.371(4)	C(6')-C(1')-C(8)	122.8(3)
C(3')-C(4')	1.401(4)	C(2')-C(1')-C(8)	119.7(3)
C(4')-O(3)	1.357(4)	C(3')-C(2')-C(1')	121.8(3)
C(4')-C(5')	1.370(4)	O(2)-C(3')-C(2')	126.2(3)
C(5')-C(6')	1.385(4)	O(2)-C(3')-C(4')	114.5(3)
O(2)-C(9)	1.414(3)	C(2')-C(3')-C(4')	119.3(3)
		O(3)-C(4')-C(5')	118.5(3)
		O(3)-C(4')-C(3')	121.8(3)
		C(5')-C(4')-C(3')	119.7(3)
		C(4')-C(5')-C(6')	120.4(3)
		C(5')-C(6')-C(1')	121.2(3)
		C(3')-O(2)-C(9)	117.7(3)

Table ESI-4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for compound **2**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	27(2)	41(2)	61(2)	-2(1)	-4(1)	-2(1)
C(2)	31(2)	41(2)	73(2)	-2(2)	1(2)	-6(2)
N(3)	33(2)	52(2)	80(2)	-1(2)	-4(2)	0(2)
C(4)	43(3)	48(2)	117(3)	-12(2)	-8(2)	7(2)
C(5)	45(3)	43(2)	108(3)	-19(2)	-3(2)	-2(2)
C(6)	31(2)	48(2)	53(2)	2(2)	7(2)	-2(2)
O(1)	40(2)	41(1)	87(2)	0(1)	2(1)	-1(1)
C(7)	35(2)	43(2)	60(2)	-4(2)	-1(2)	-4(2)
C(8)	36(2)	43(2)	60(2)	5(2)	4(2)	1(2)
C(1')	26(2)	39(2)	56(2)	4(2)	0(2)	1(2)
C(2')	39(2)	40(2)	57(2)	-6(2)	3(2)	-5(2)
C(3')	29(2)	44(2)	58(2)	3(2)	7(2)	7(2)
C(4')	35(2)	41(2)	63(2)	-2(2)	-2(2)	-2(2)
C(5')	39(3)	40(2)	68(2)	-8(2)	-3(2)	6(2)
C(6')	33(2)	48(2)	61(2)	-1(2)	1(2)	7(2)
O(2)	34(2)	51(2)	100(2)	-15(1)	11(1)	1(1)
C(9)	66(3)	52(2)	83(3)	-15(2)	14(2)	7(2)
O(3)	37(2)	54(2)	117(2)	-25(2)	-7(2)	-2(1)