Synthesis and Evaluation of Radiopharmaceuticals for Imaging Bacterial Infection

Supplementary Data

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Chapter 2

Figure S 2.1 IR spectrum of **2** (KBr pellet).

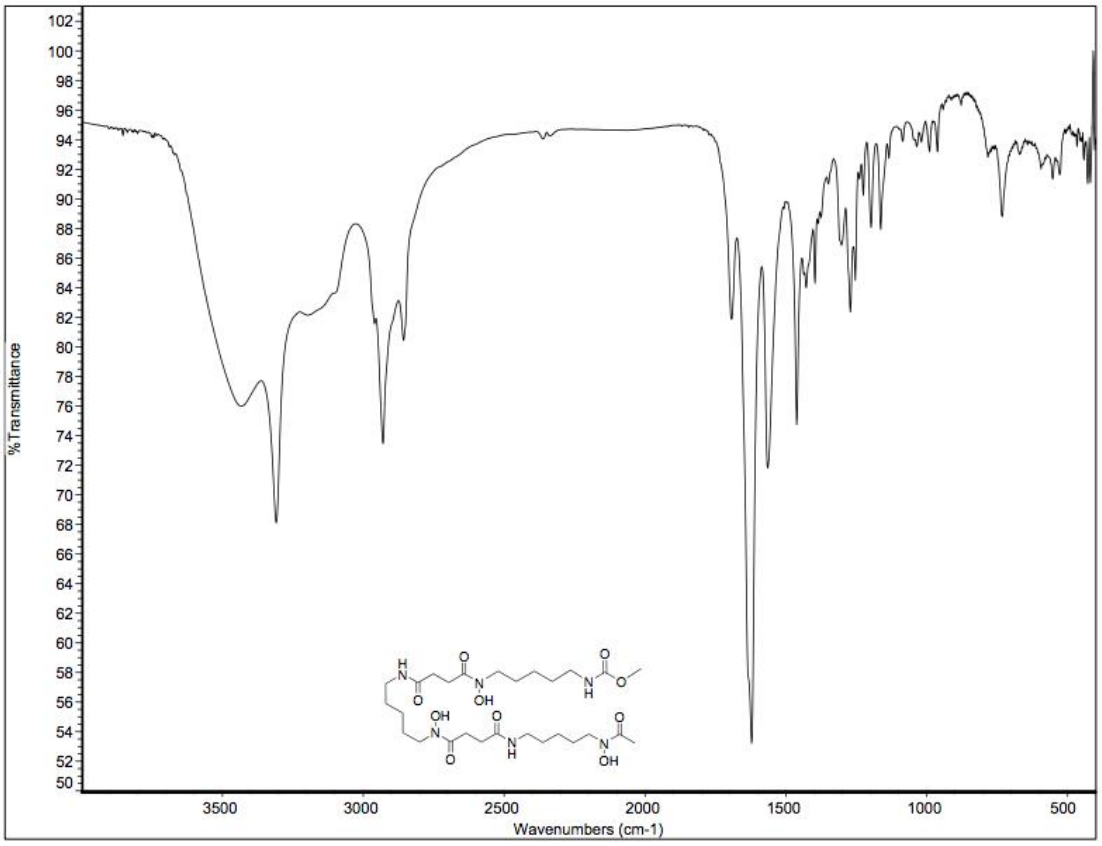


Figure S 2.2 ^{1}H NMR spectrum of **2** in DMSO-d_6 at 300 K.

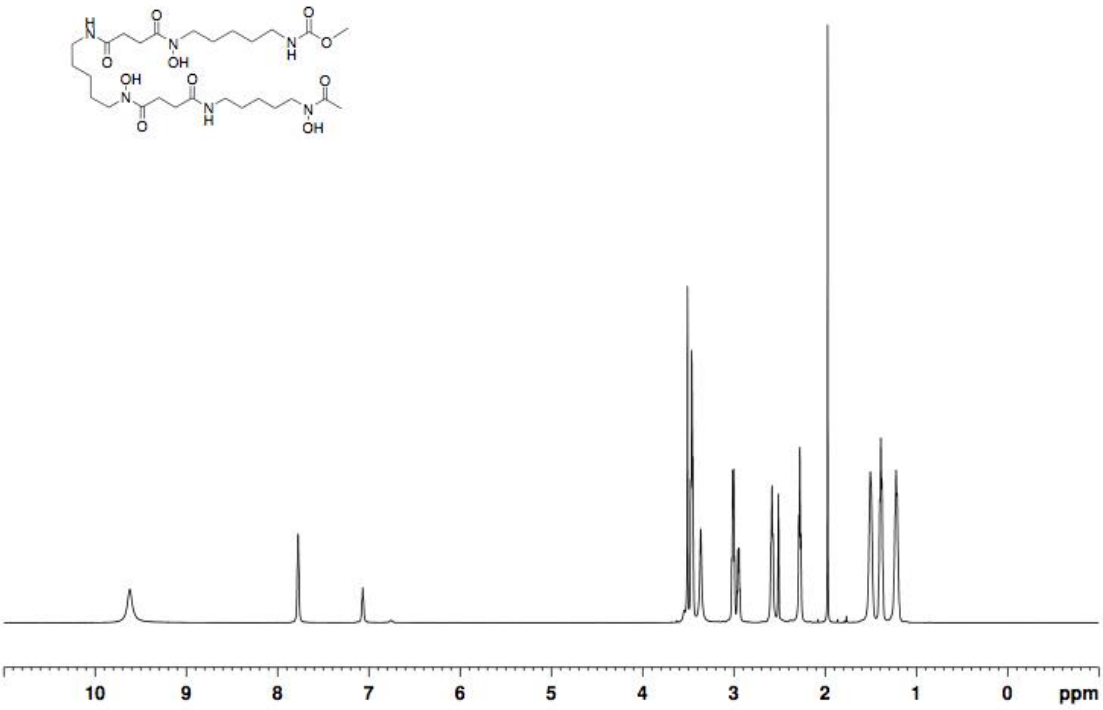


Figure S 2.3 ^{13}C NMR spectrum of **2** in DMSO-d_6 at 300 K.

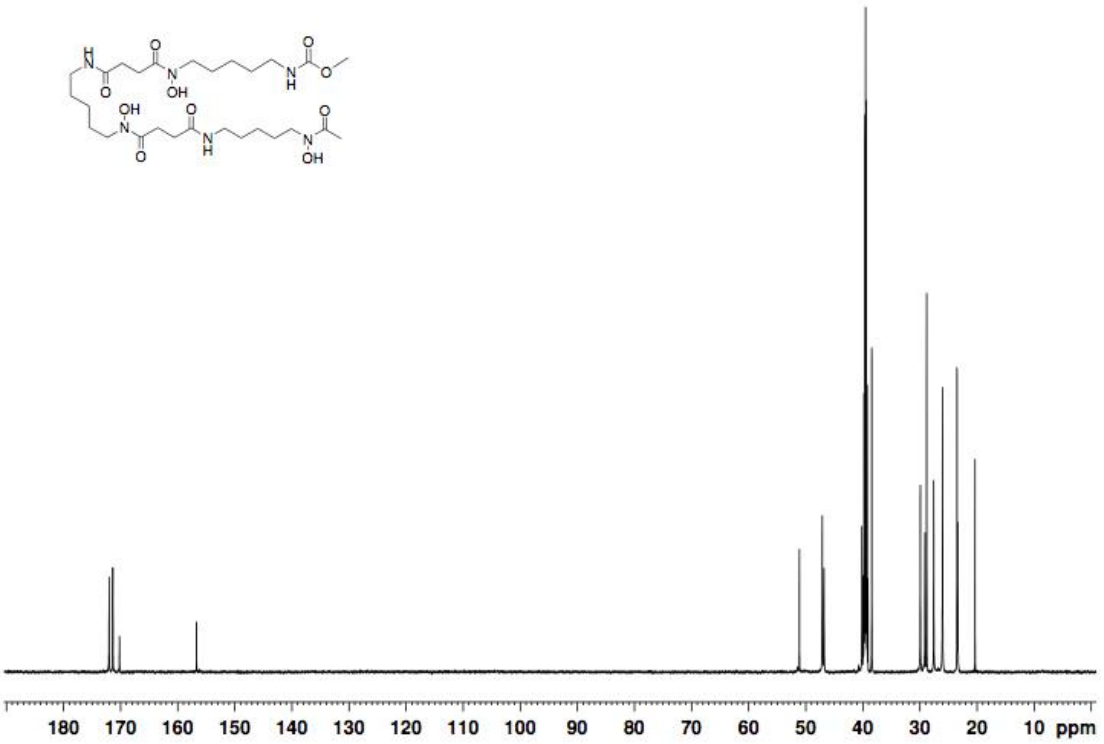


Figure S 2.4 High-resolution mass spectrum of **2**.

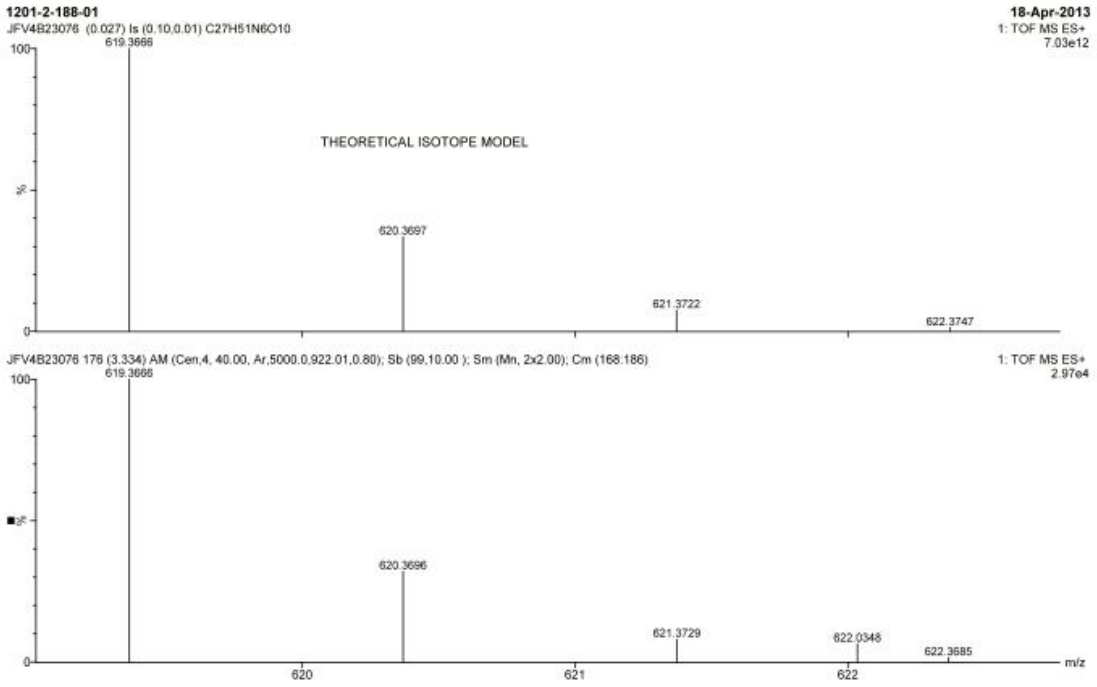


Figure S 2.5 HPLC chromatogram of **2**. UV peak at λ = 220 nm

(Note injection volume contains DMSO).

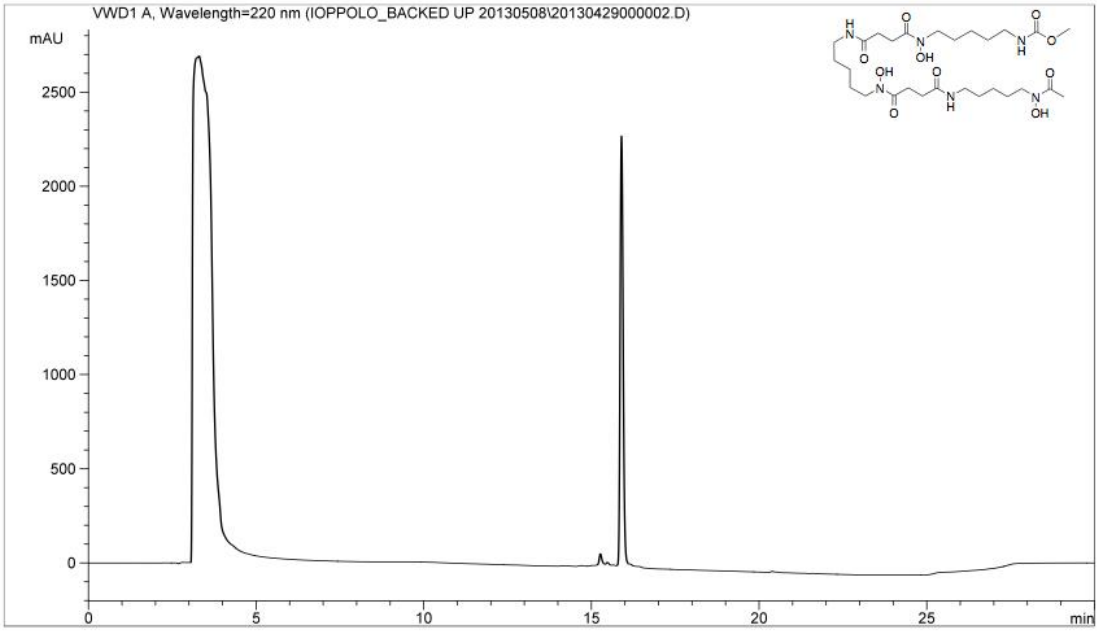


Figure S 2.6 IR spectrum of **3** (KBr pellet).

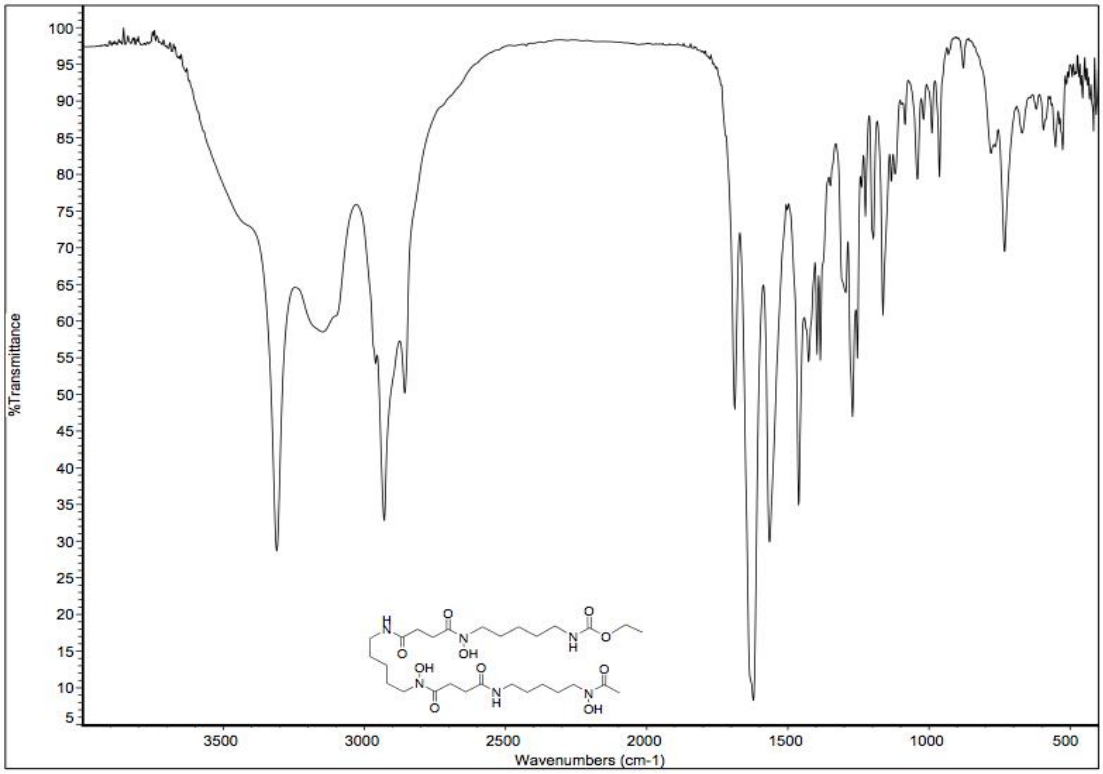


Figure S 2.7 ^{1}H NMR spectrum of **3** in DMSO-d_6 at 300 K.

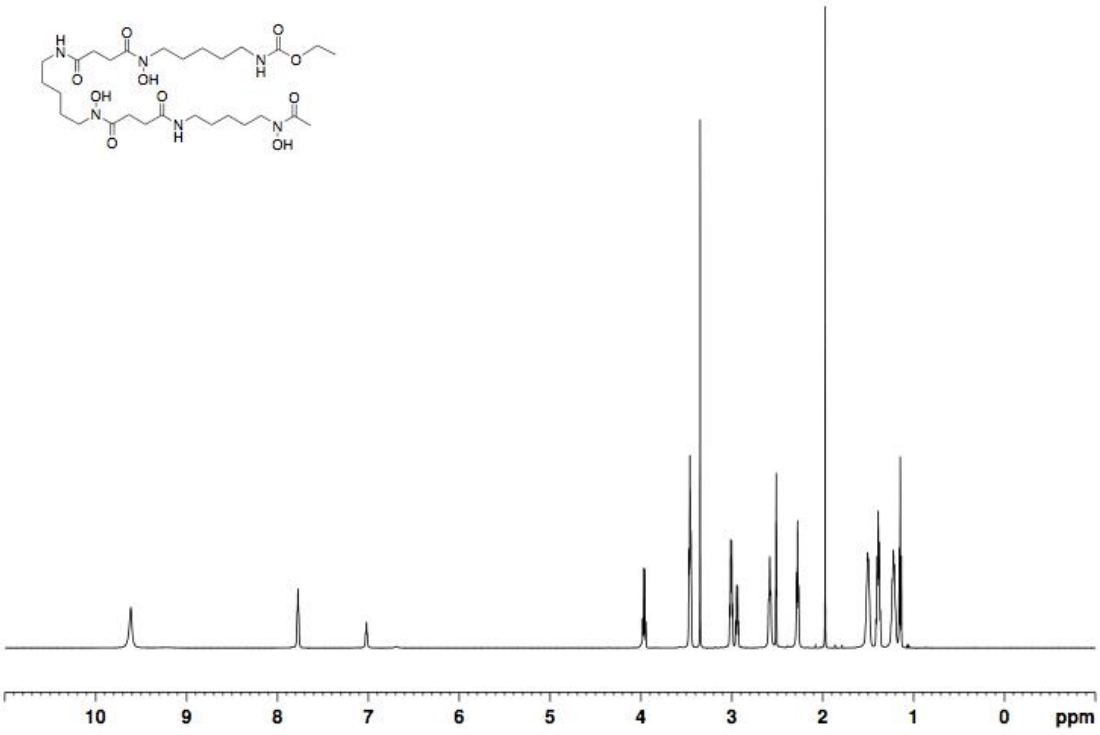


Figure S 2.8 ^{13}C NMR spectrum of **3** in DMSO-d_6 at 300 K.

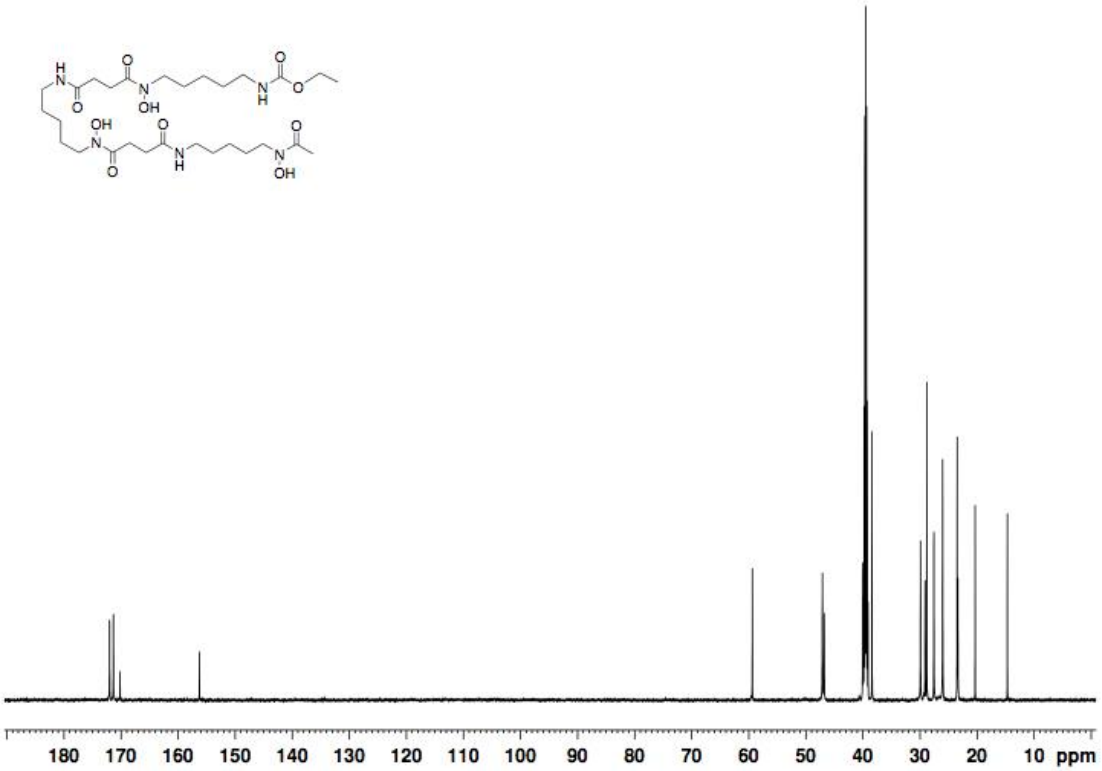
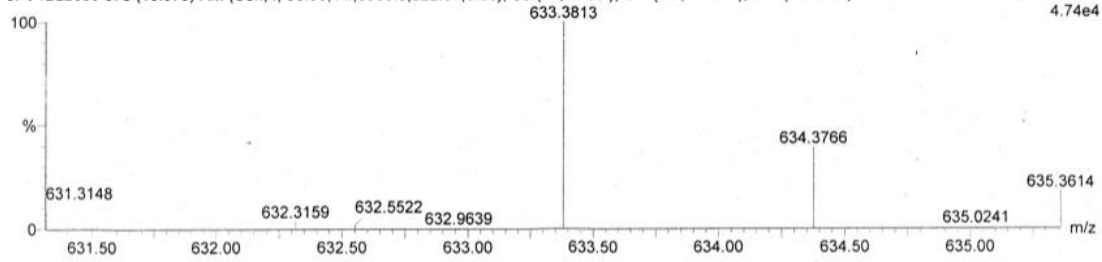


Figure S 2.9 High-resolution mass spectrum of **3**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
22 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

1201-2-85-01
JFV4B22589 578 (10.979) AM (Cen,4, 80.00, Ar,6000.0,922.01,0.80); Sb (99,10.00); Sm (Mn, 3x3.00); Cm (475:641)
05-Dec-2012
1: TOF MS ES+
4.74e4



Minimum:				-1.5		
Maximum:		10.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
633.3813	633.3823	-1.0	-1.6	5.5	1	C28 H53 N6 O10

Figure S 2.10 HPLC chromatogram of **3**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

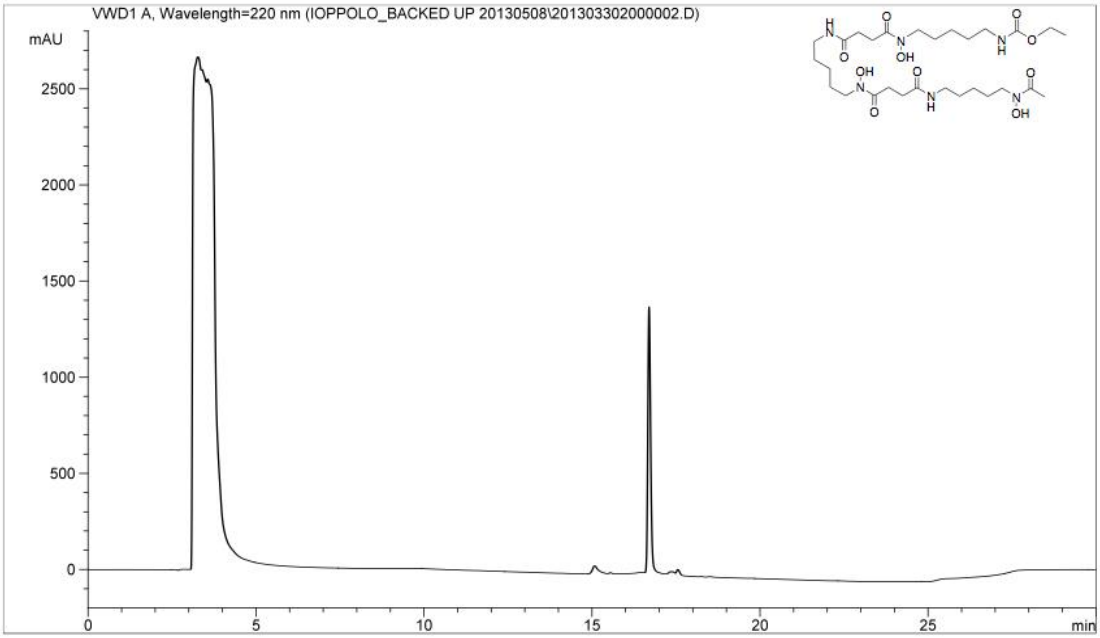


Figure S 2.11 IR spectrum of **4** (KBr pellet).

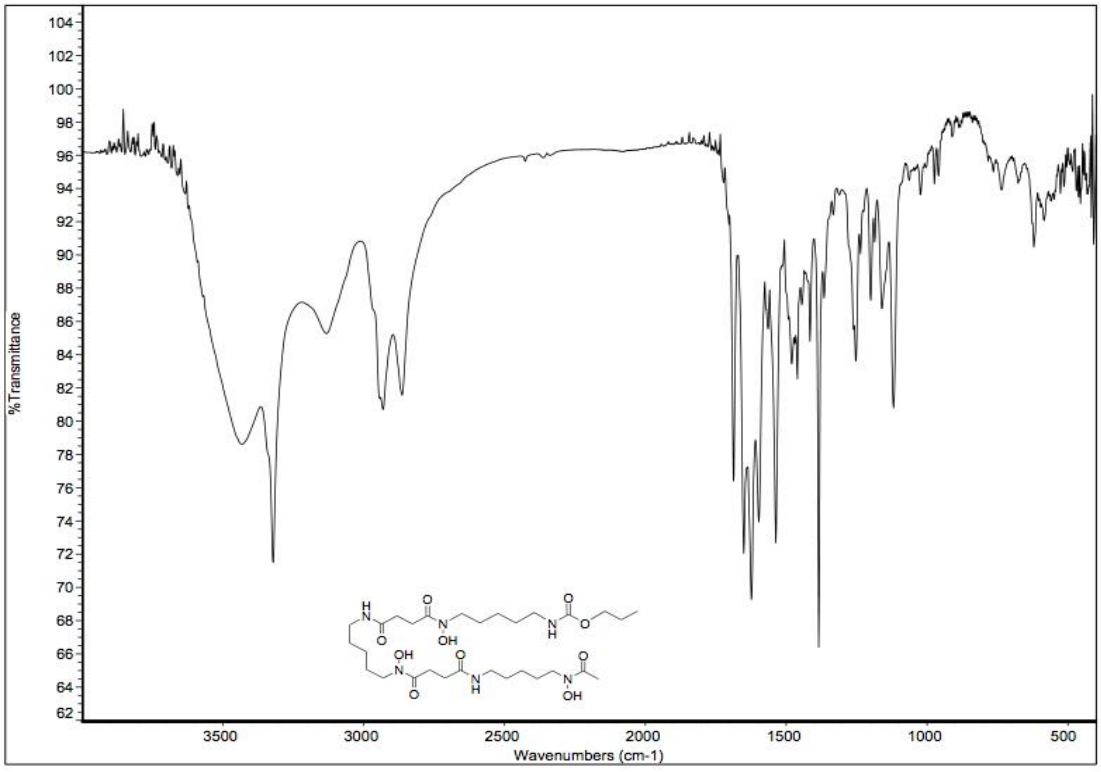


Figure S 2.12 ^{1}H NMR spectrum of **4** in DMSO-d_6 at 300 K.

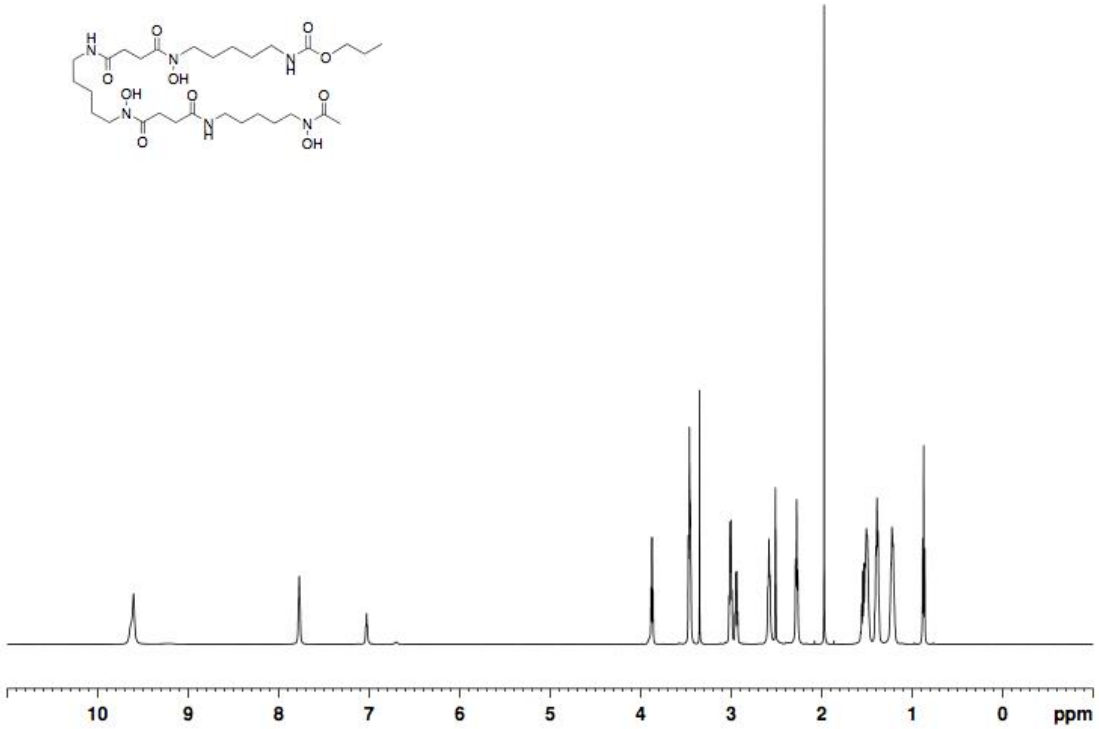


Figure S 2.13 ^{13}C NMR spectrum of **4** in DMSO-d_6 at 300 K.

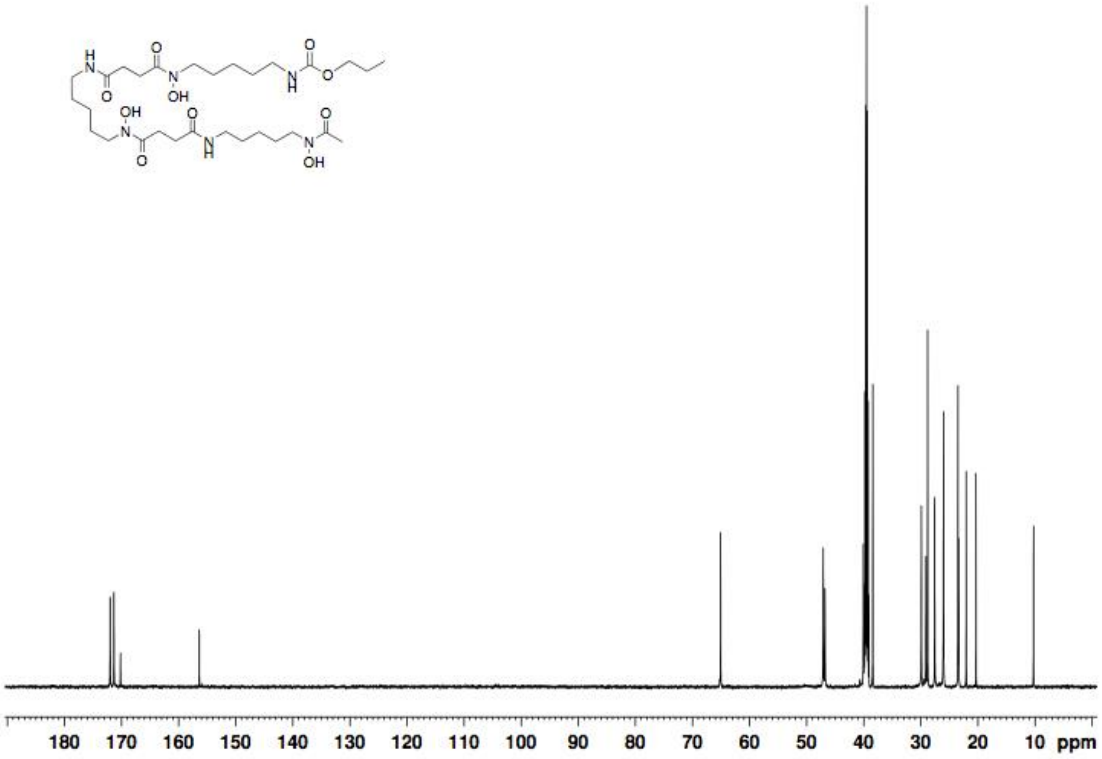


Figure S 2.14 High-resolution mass spectrum of **4**.

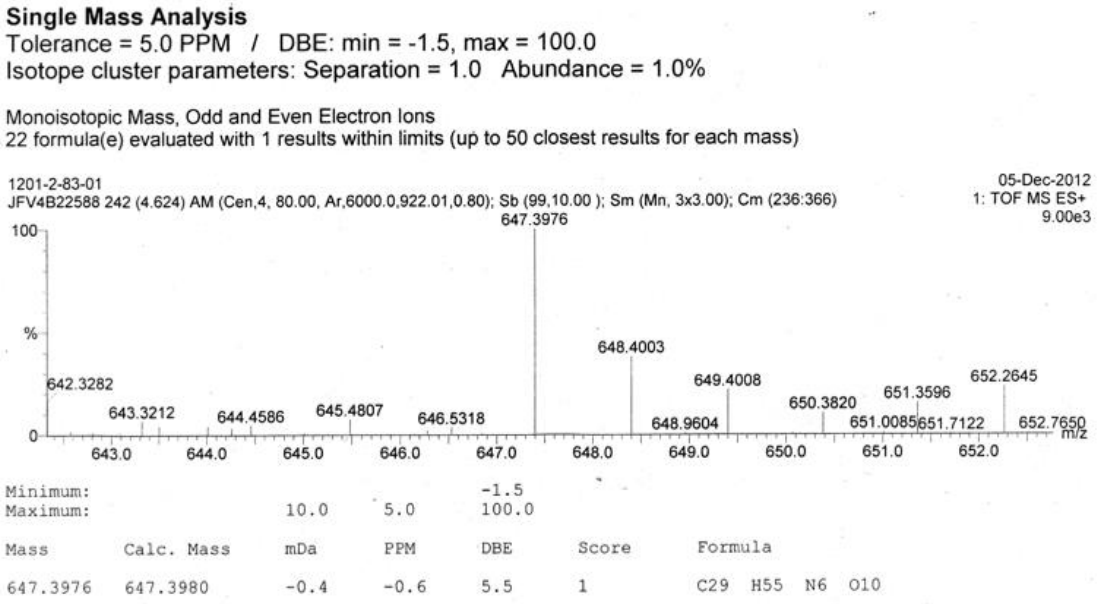


Figure S 2.15 HPLC chromatogram of **4**. UV peak at $\lambda = 220$ nm.

(Note injection volume contains DMSO).

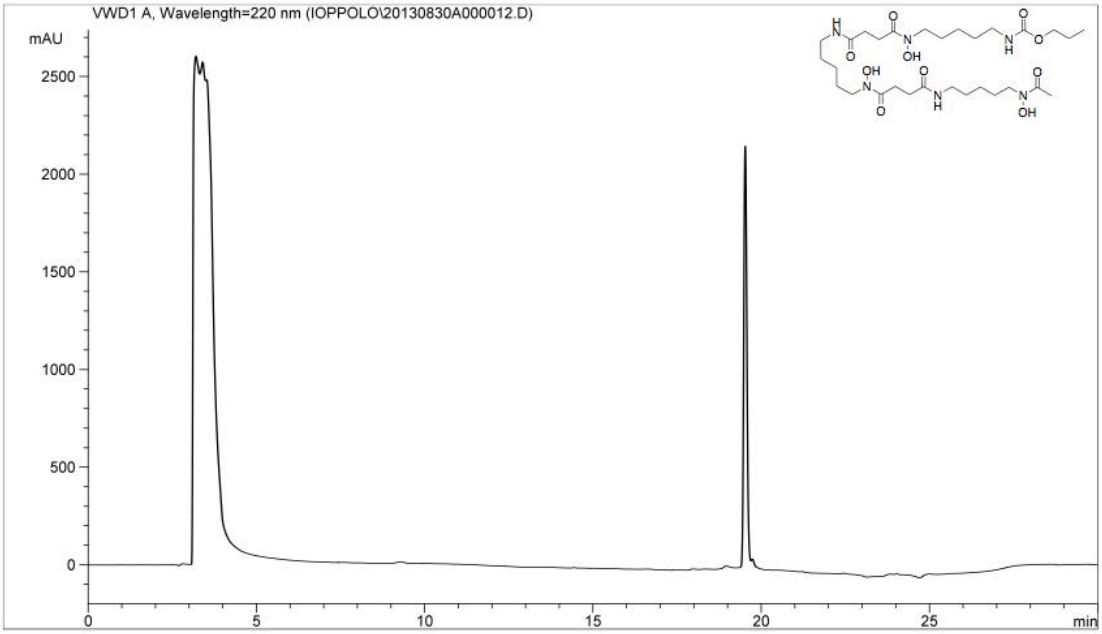


Figure S 2.16 IR spectrum of **5** (KBr pellet).

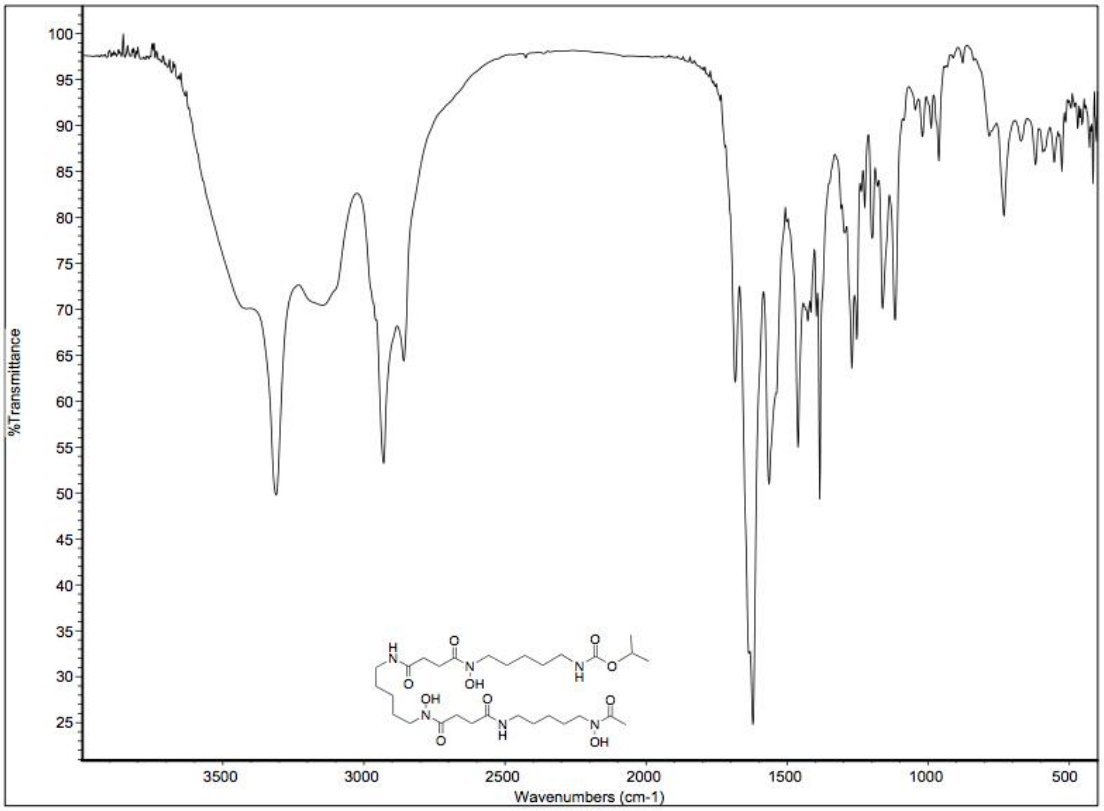


Figure S 2.17 ^{1}H NMR spectrum of **5** in DMSO-d_6 at 300 K.

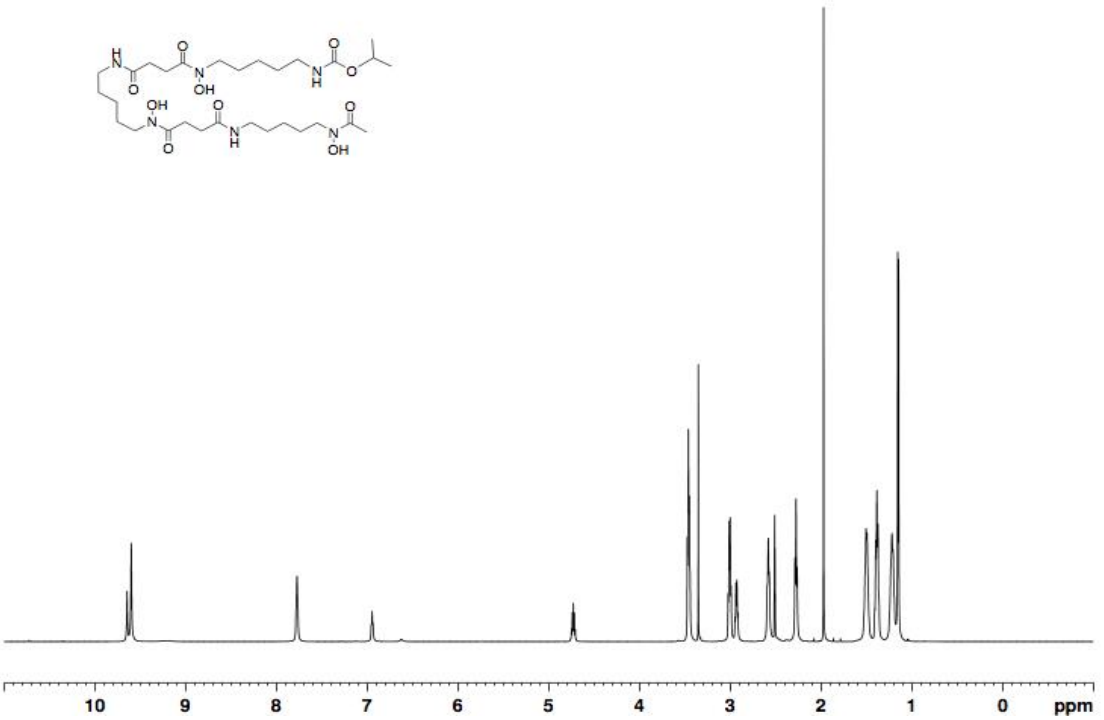


Figure S 2.18 ^{13}C NMR spectrum of **5** in DMSO-d_6 at 300 K.

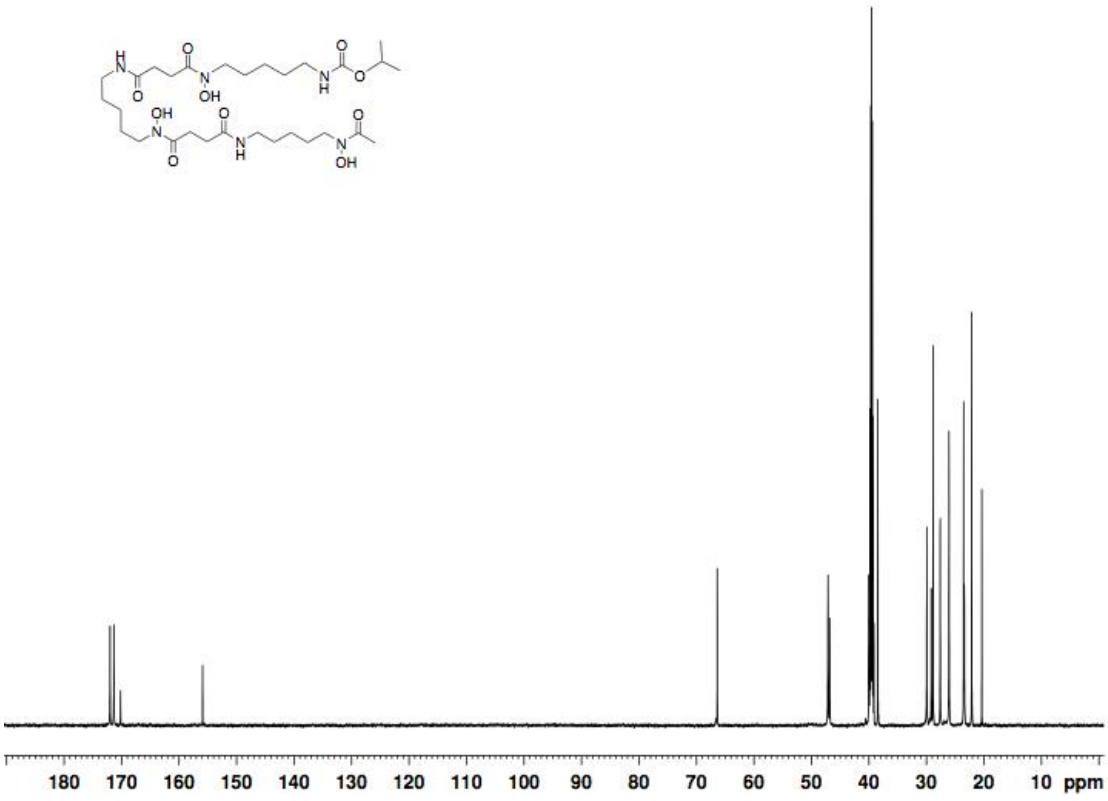
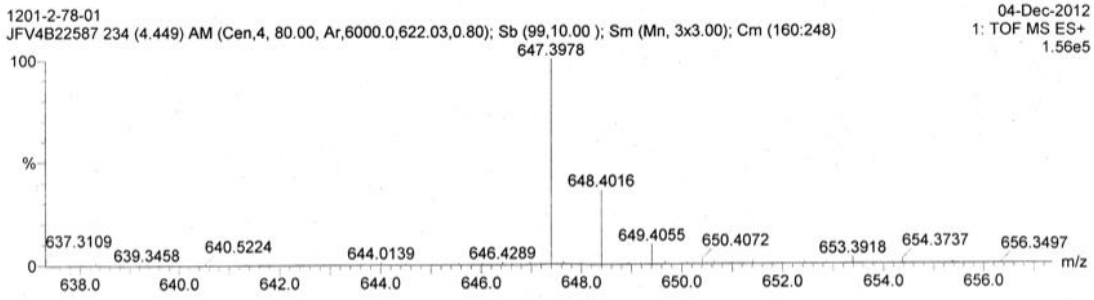


Figure S 2.19 High-resolution mass spectrum of **5**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
22 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		10.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
647.3978	647.3980	-0.2	-0.3	5.5	1	C29 H55 N6 O10

Figure S 2.20 HPLC chromatogram of **5**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO)

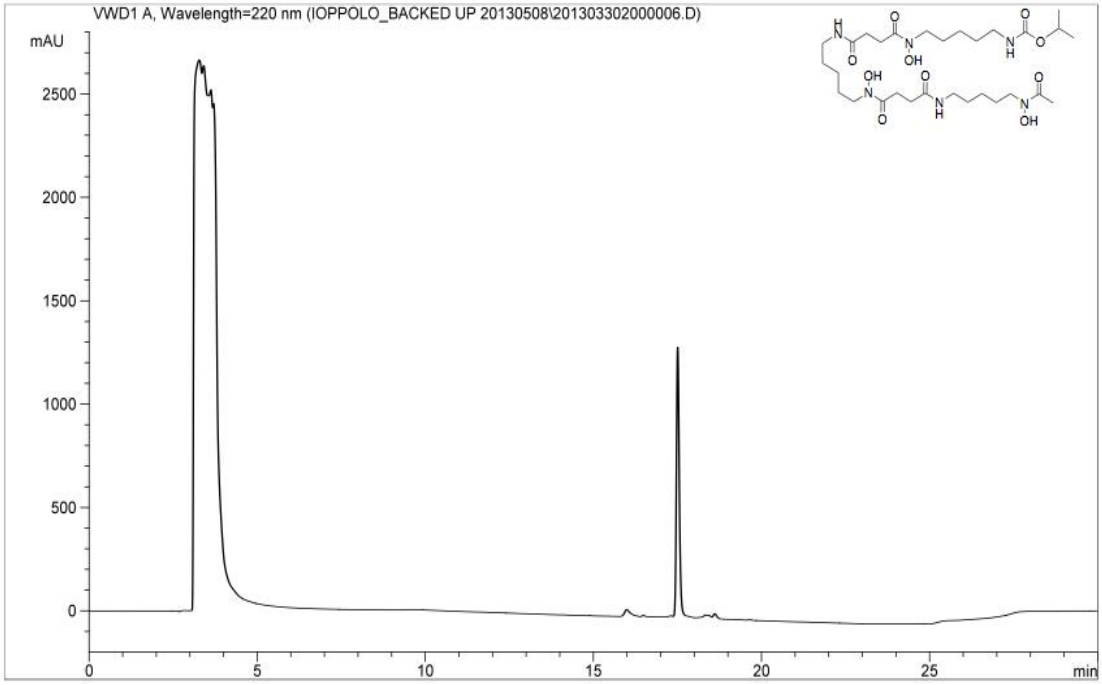


Figure S 2.21 IR spectrum of **6** (KBr pellet).

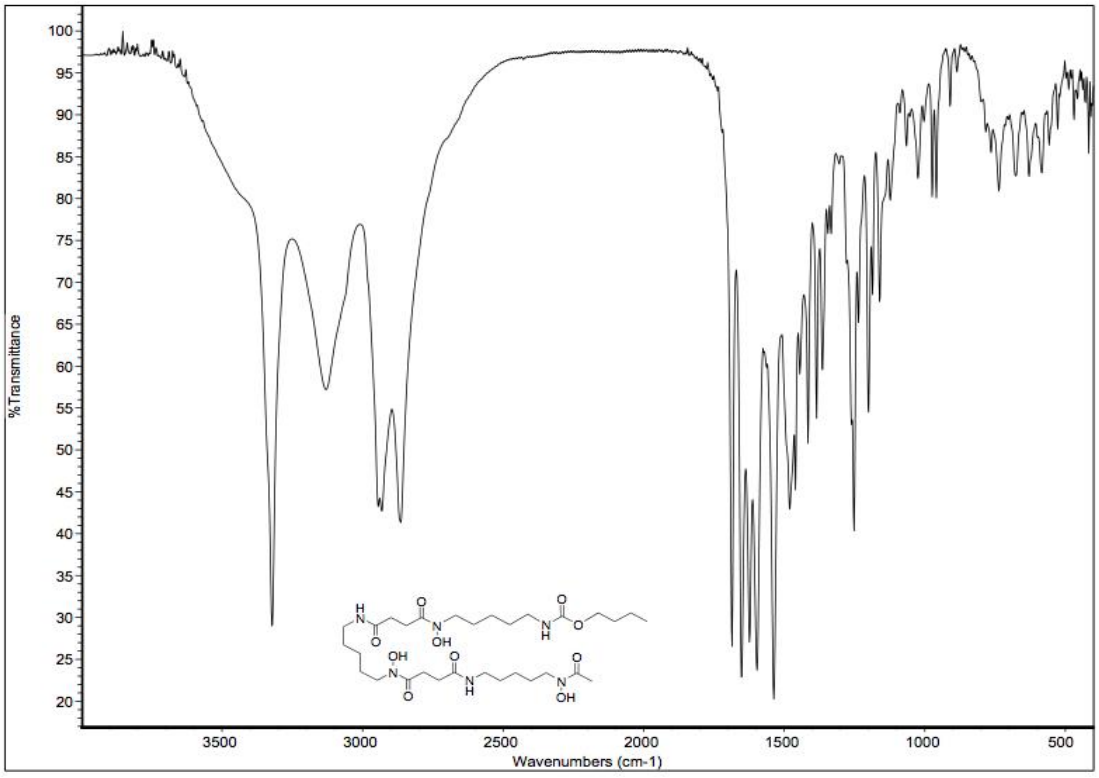


Figure S 2.22 ^{1}H NMR spectrum of **6** in DMSO-d_6 at 300 K.

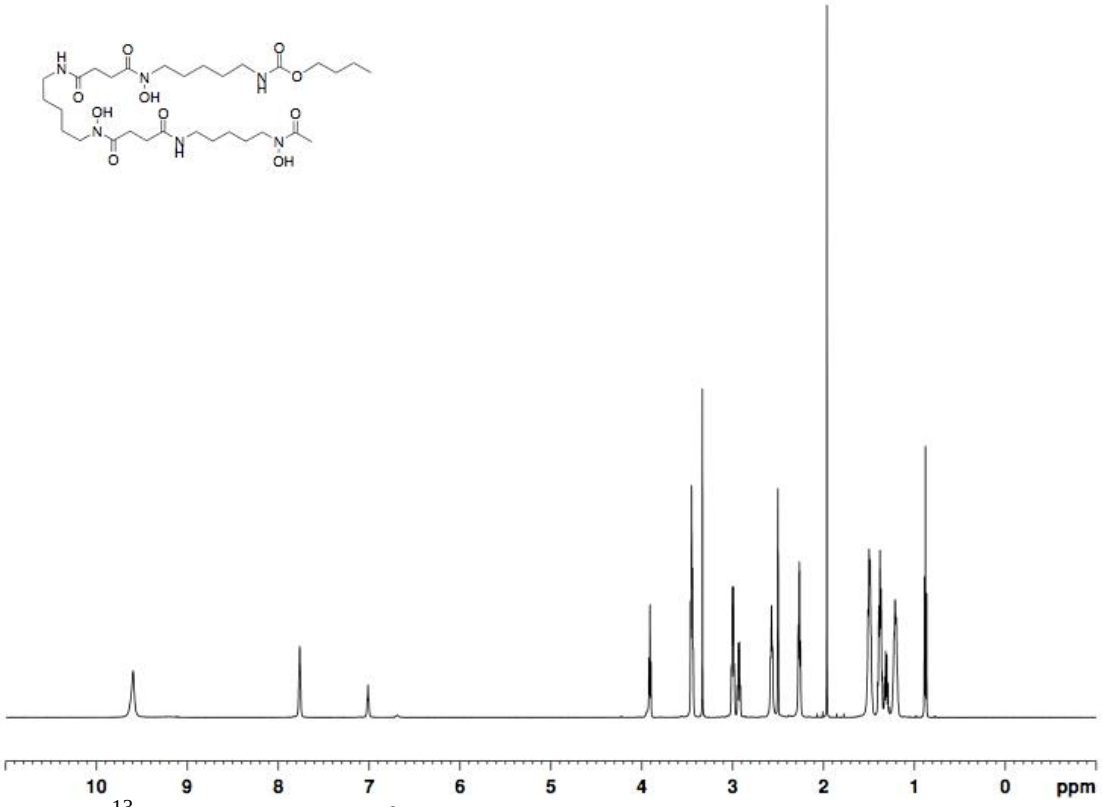


Figure S 2.23 ^{13}C NMR spectrum of **6** in DMSO-d_6 at 300 K.

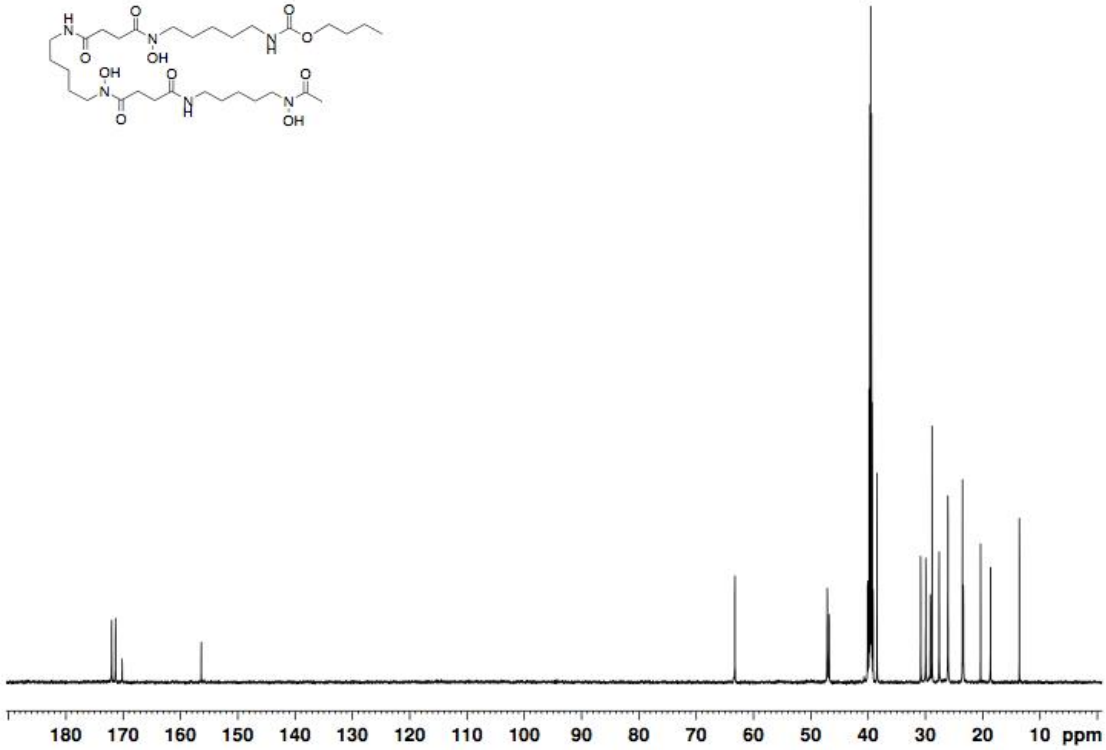


Figure S 2.24 High-resolution mass spectrum of **6**.

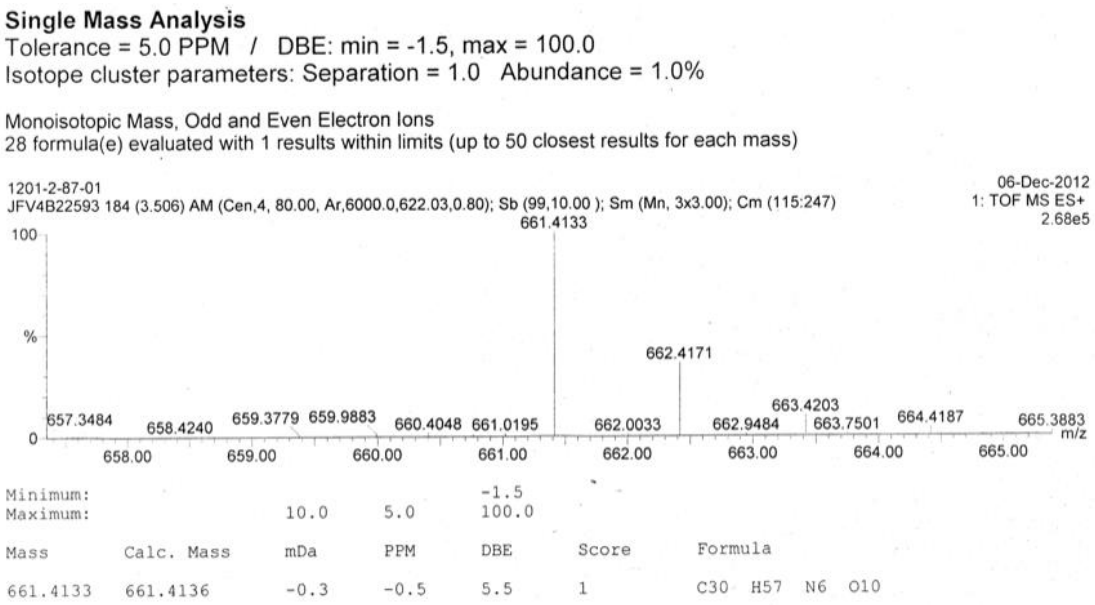


Figure S 2.25 HPLC chromatogram of **6**. UV peak at $\lambda = 220$ nm.

(Note injection volume contains DMSO).

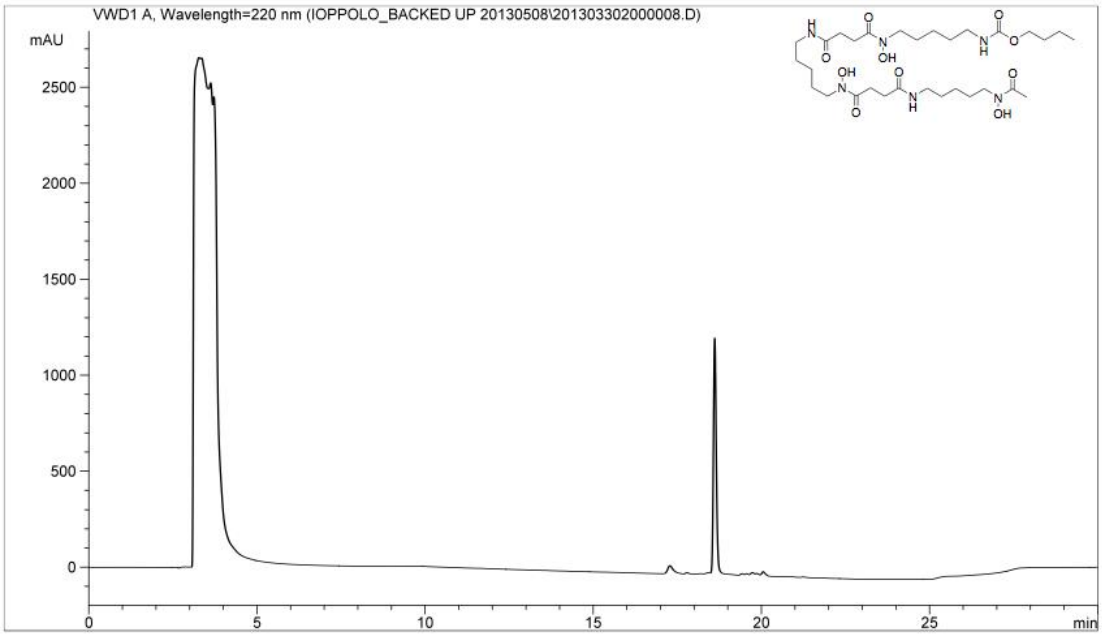


Figure S 2.26 IR spectrum of **7** (KBr pellet).

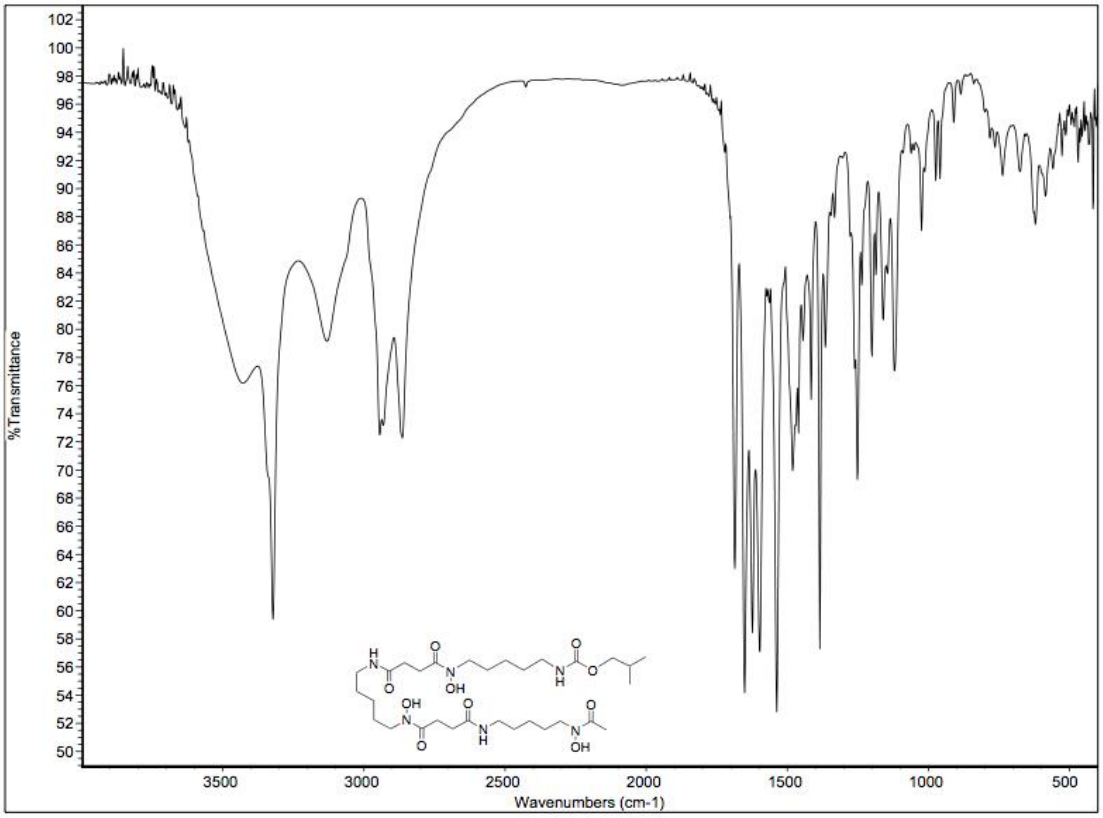


Figure S 2.27 ^{1}H NMR spectrum of **7** in DMSO-d_6 at 300 K.

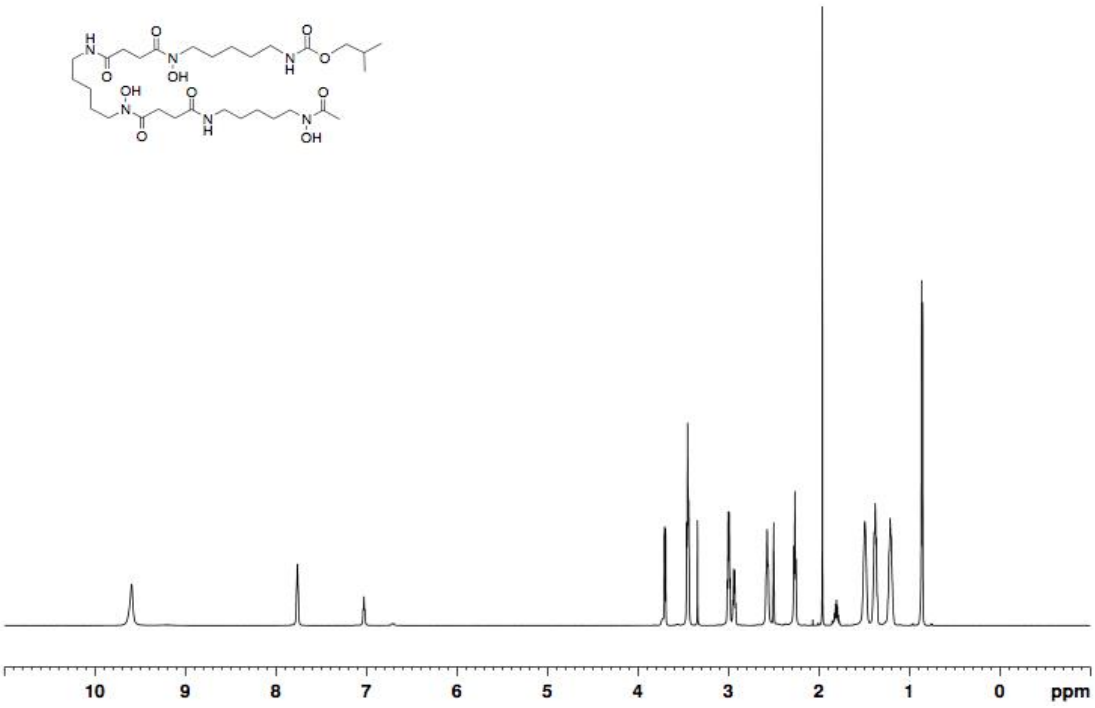


Figure S 2.28 ^{13}C NMR spectrum of **7** in DMSO-d_6 at 300 K.

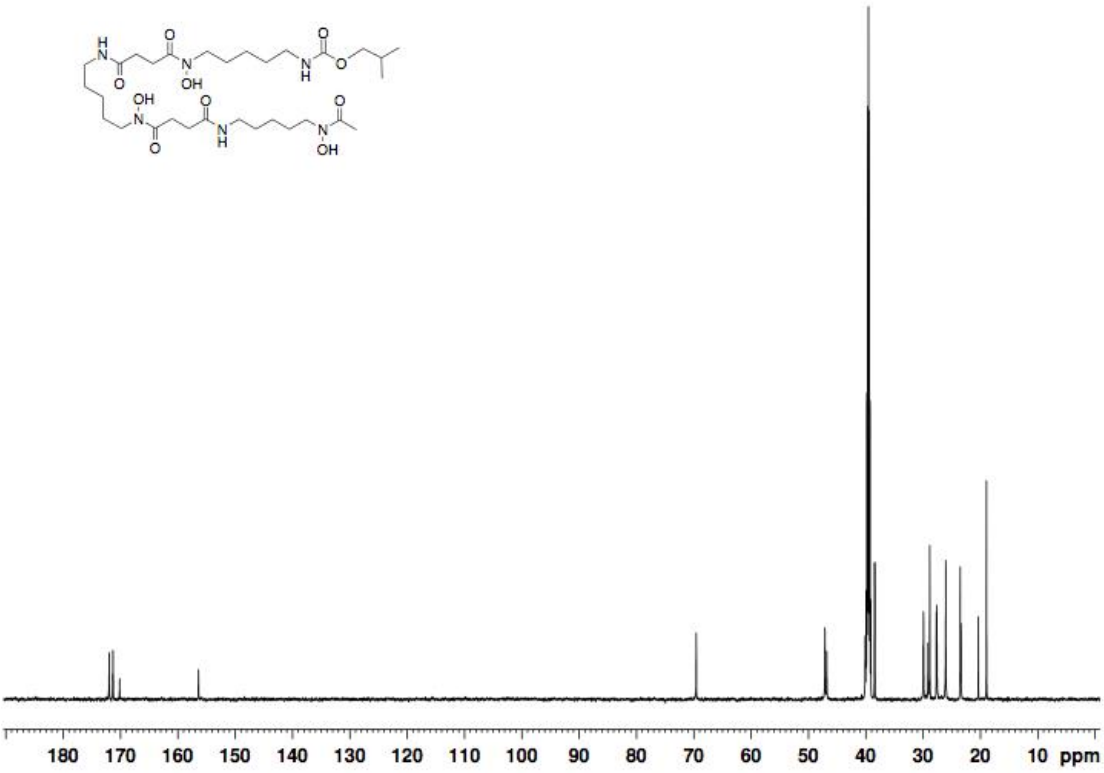


Figure S 2.29 High-resolution mass spectrum of **7**.

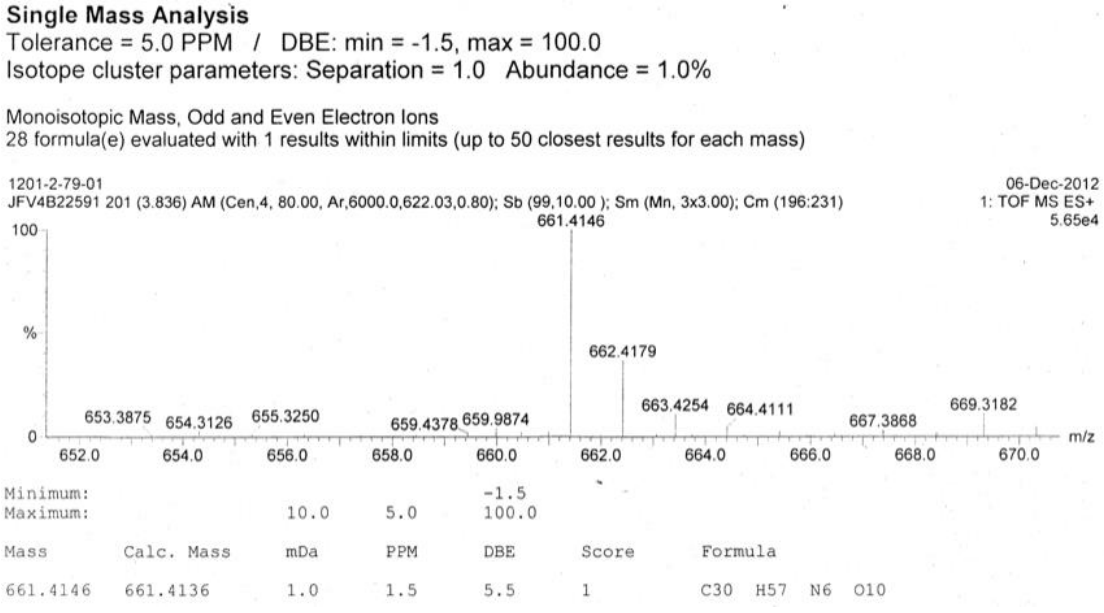


Figure S 2.30 HPLC chromatogram of **7**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

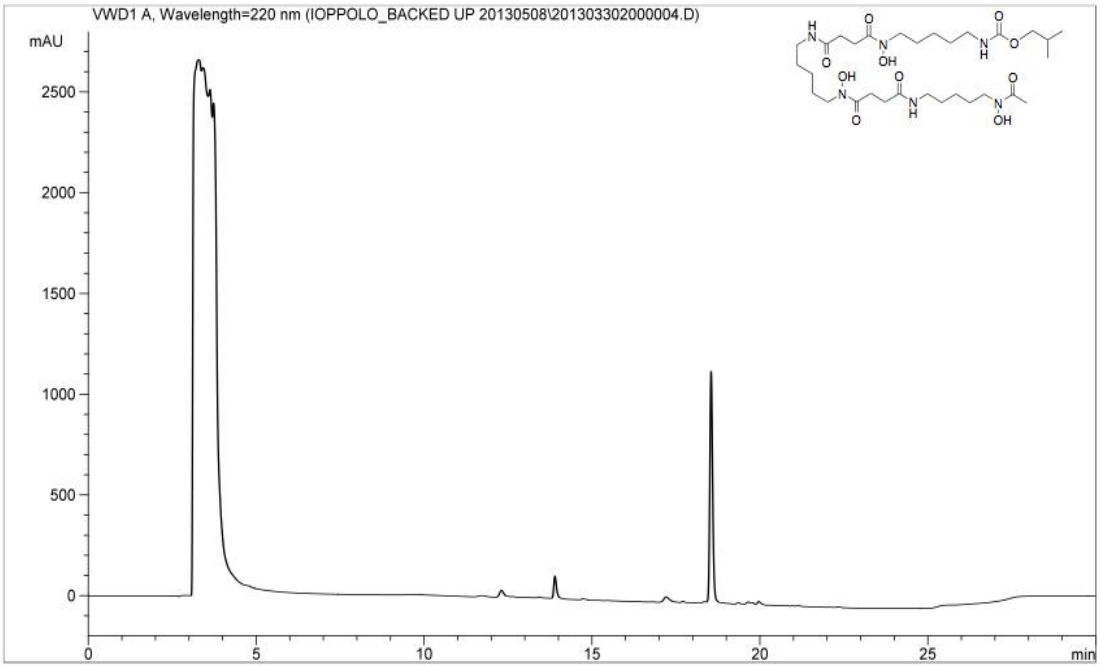


Figure S 2.31 IR spectrum of **8** (KBr pellet).

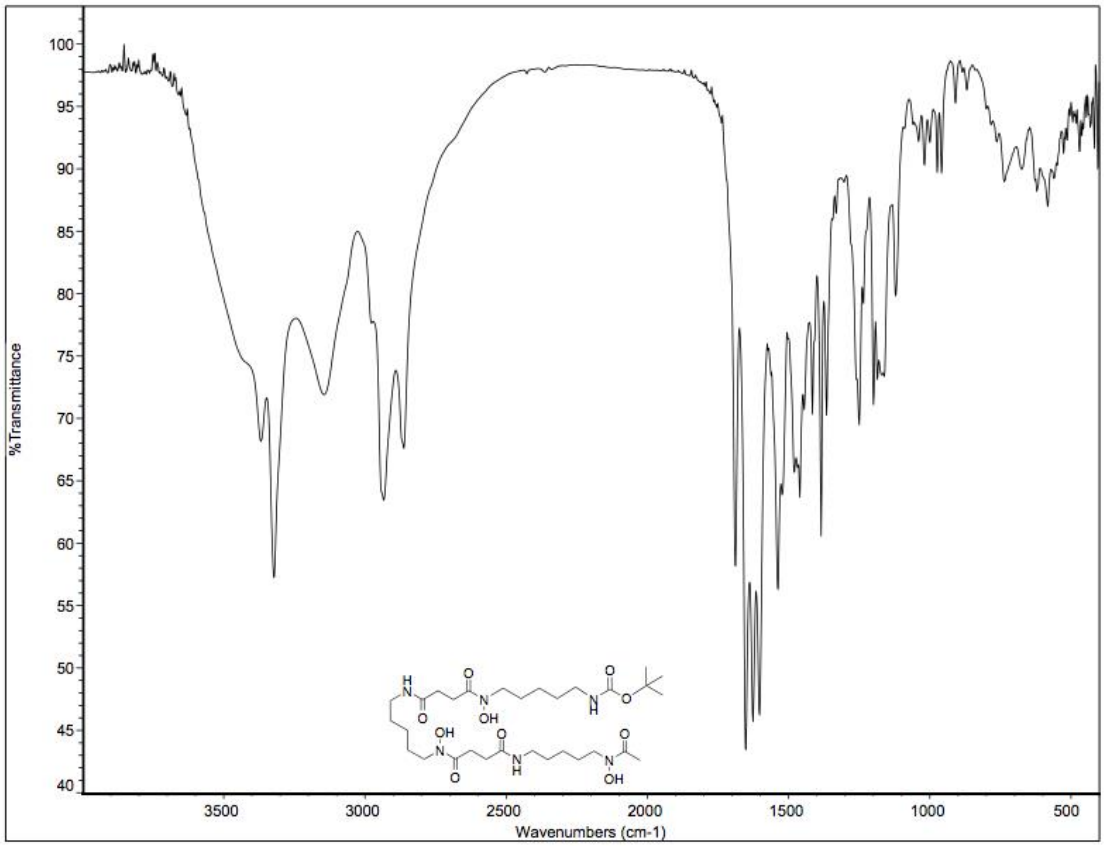


Figure S 2.32 ^{1}H NMR spectrum of 8 in DMSO-d6 at 300 K.

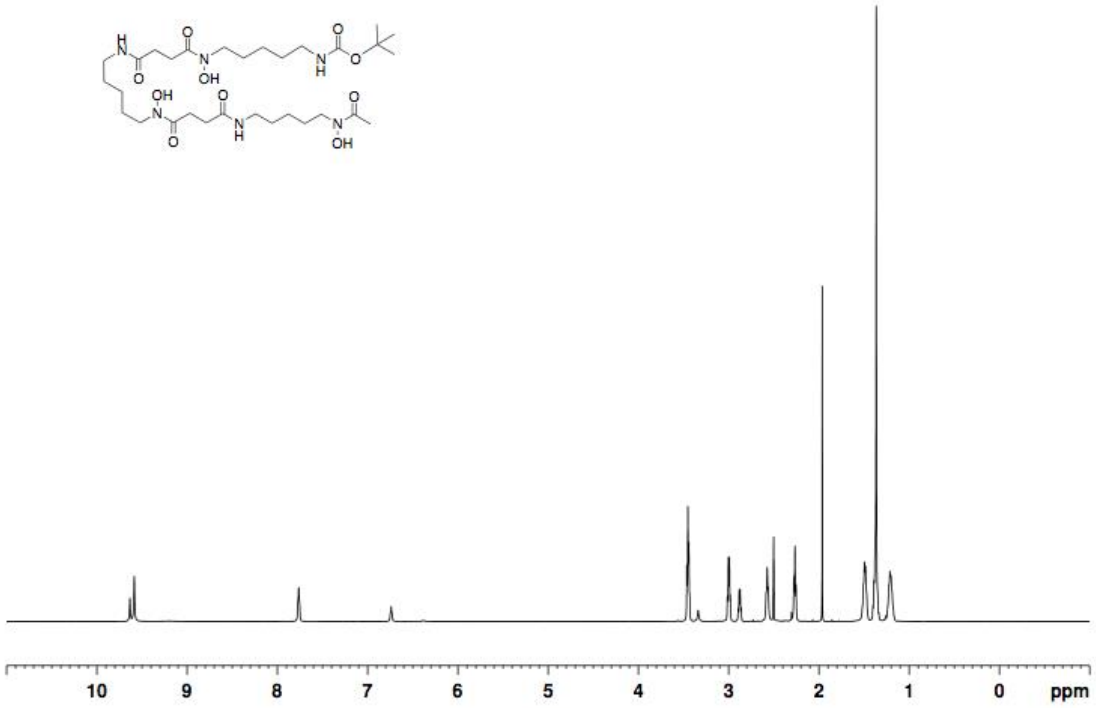


Figure S 2.33 ^{13}C NMR spectrum of **8** in DMSO-d_6 at 300 K.

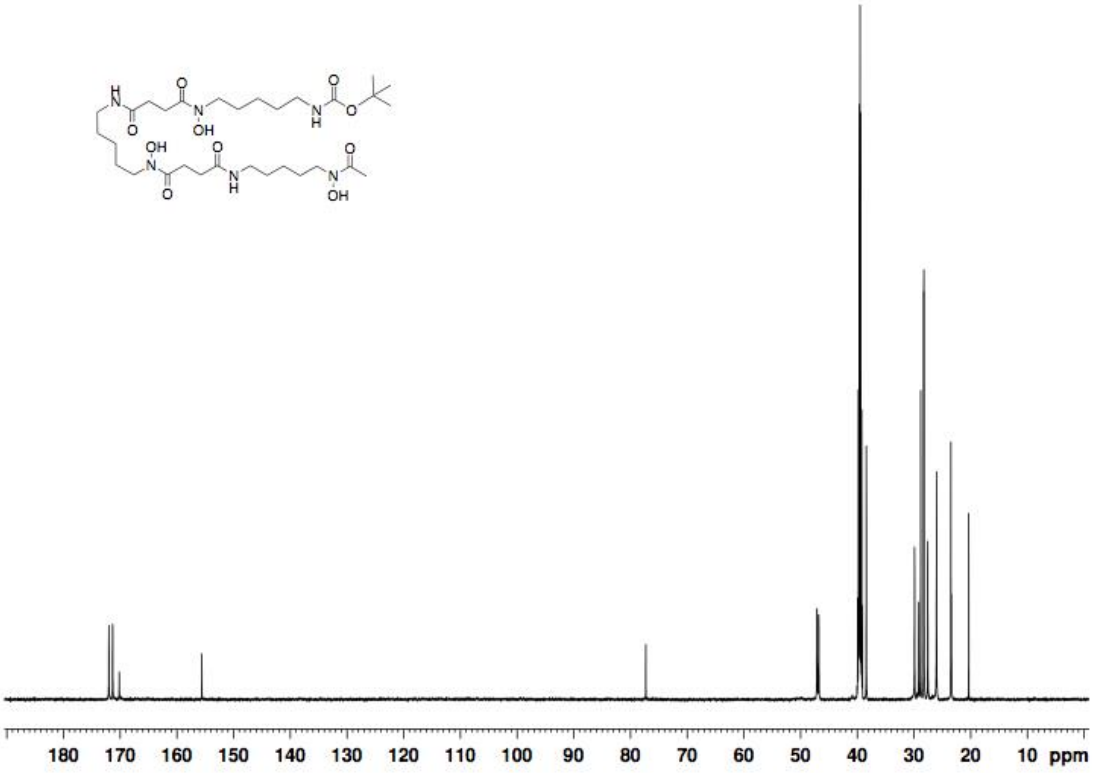


Figure S 2.34 High-resolution mass spectrum of **8**.

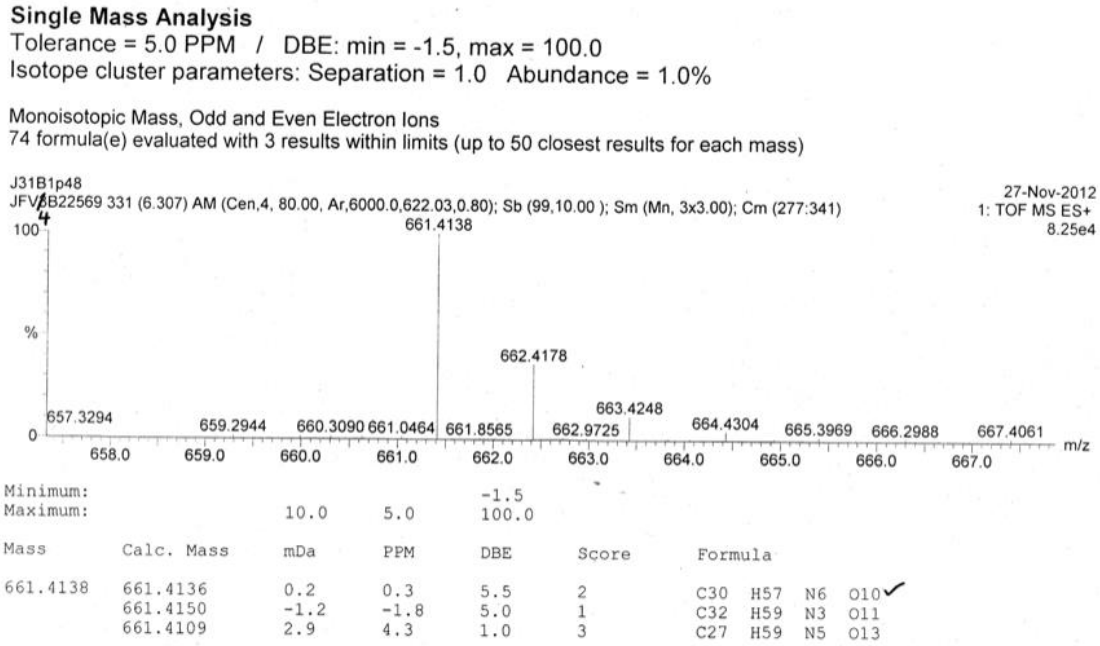


Figure S 2.35 HPLC chromatogram of **8**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

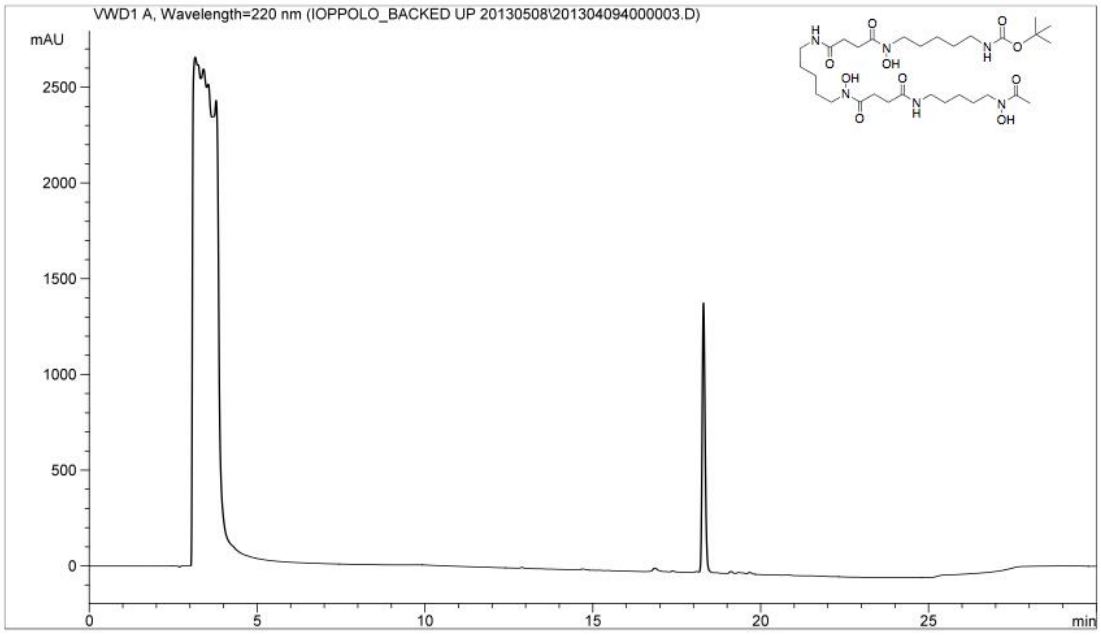


Figure S 2.36 IR spectrum of **9** (KBr pellet).

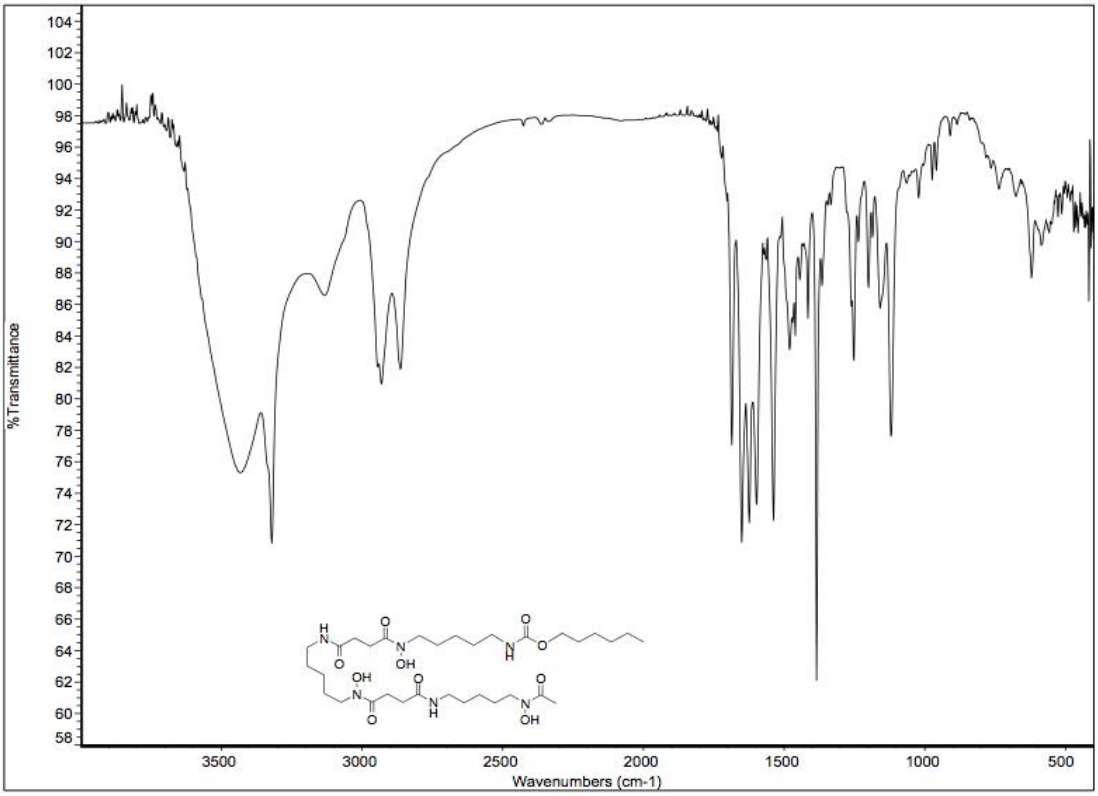


Figure S 2.37 ^{1}H NMR spectrum of **9** in DMSO-d_6 at 300 K.

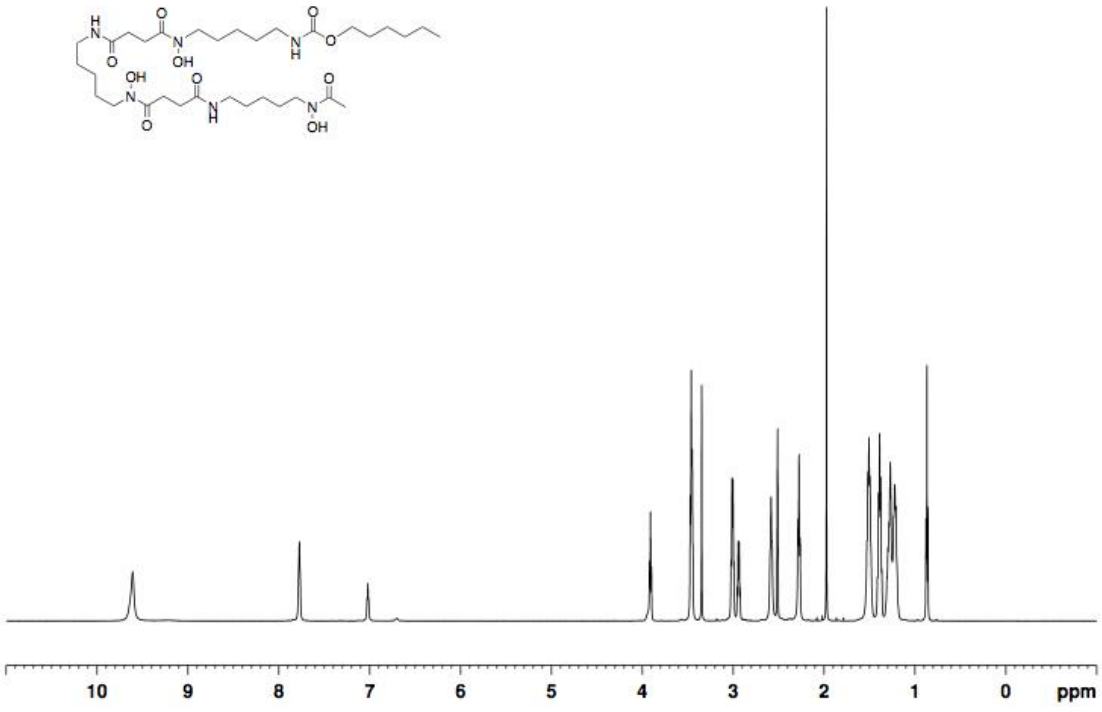


Figure S 2.38 ^{13}C NMR spectrum of **9** in DMSO-d_6 at 300 K.

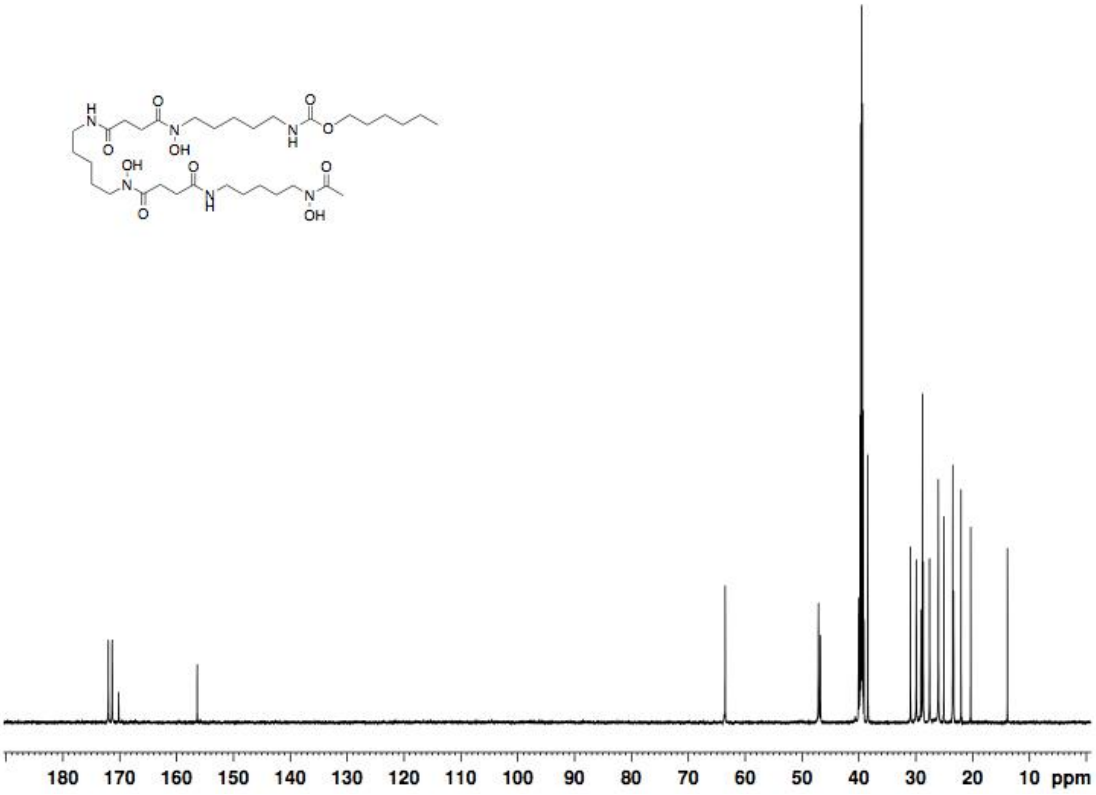


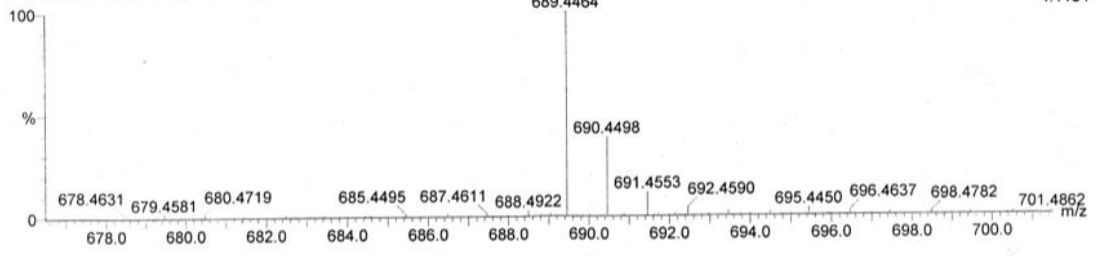
Figure S 2.39 High-resolution mass spectrum of **9**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
26 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

1201-2-81-01
JFV4B22590 133 (2.538) AM (Cen,4, 80.00, Ar,6000.0,622.03,0.80); Sb (99,10.00); Sm (Mn, 3x3.00); Cm (111:145)

06-Dec-2012
1: TOF MS ES+
4.11e4



Minimum:				-1.5		
Maximum:		10.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
689.4464	689.4449	1.5	2.1	5.5	1	C32 H61 N6 O10

Figure S 2.40 HPLC chromatogram of **9**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

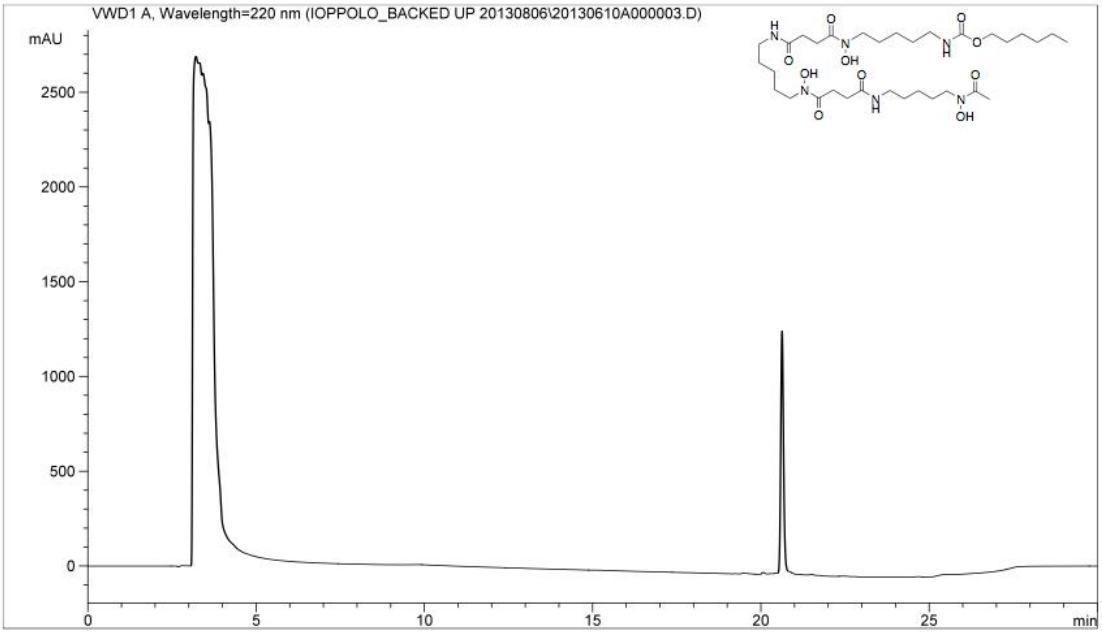


Figure S 2.41 IR spectrum of **10** (KBr pellet)

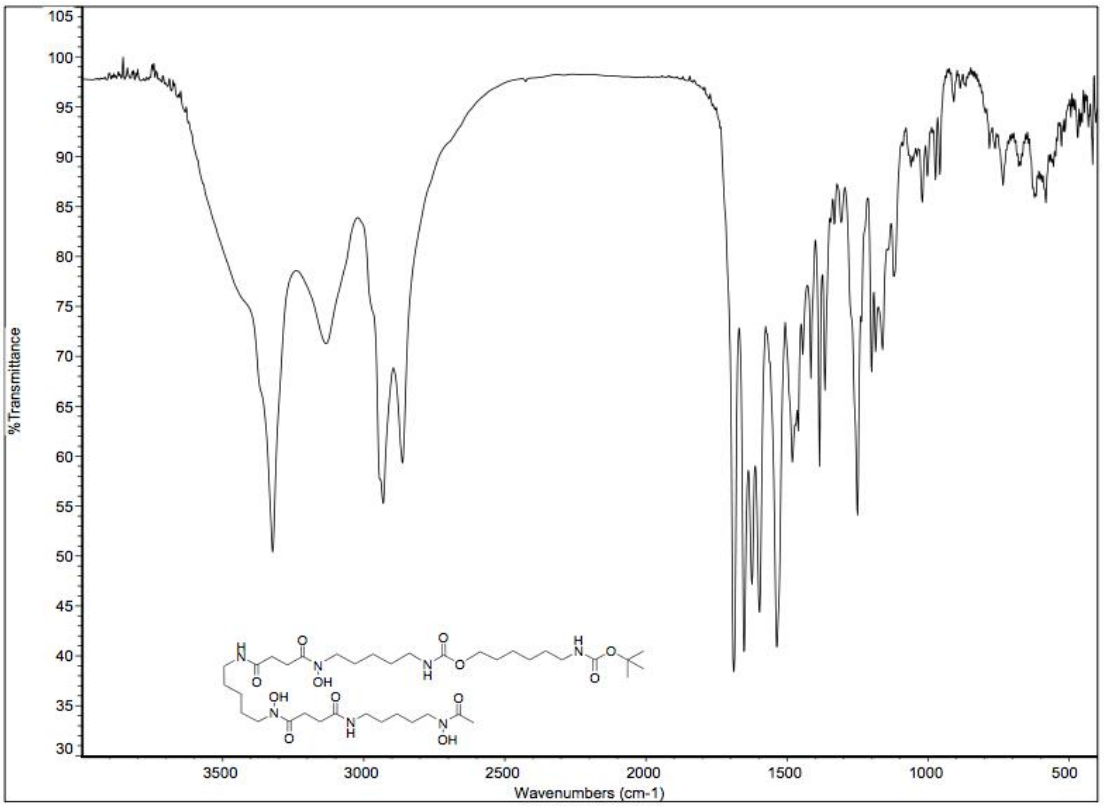


Figure S 2.42 ^{1}H NMR spectrum of **10** in DMSO-d_6 at 300 K.

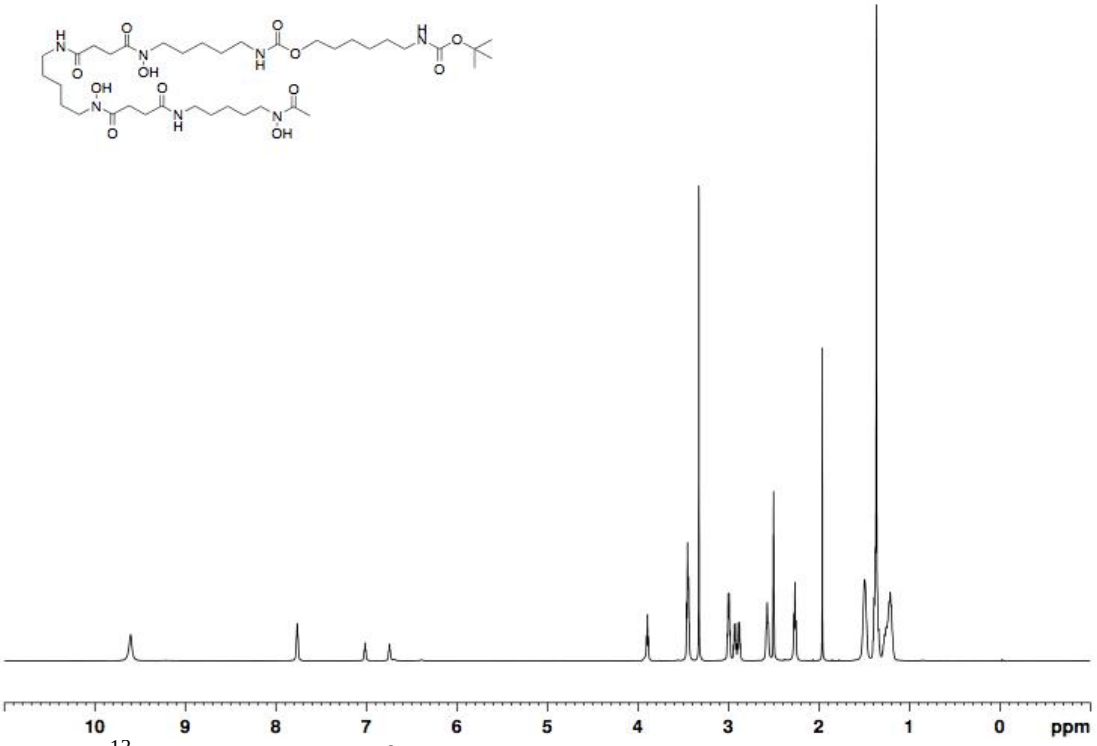


Figure S 2.43 ^{13}C NMR spectrum of **10** in DMSO-d_6 at 300 K.

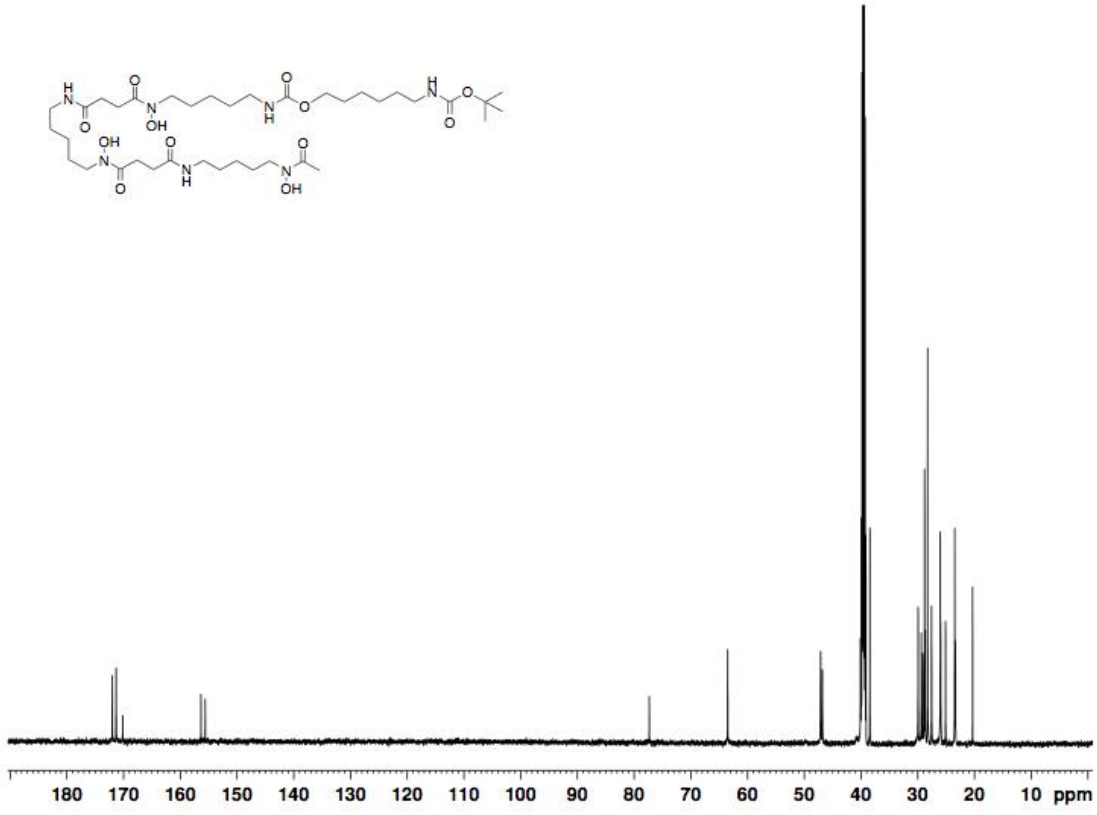


Figure S 2.44 High-resolution mass spectrum of **10**.

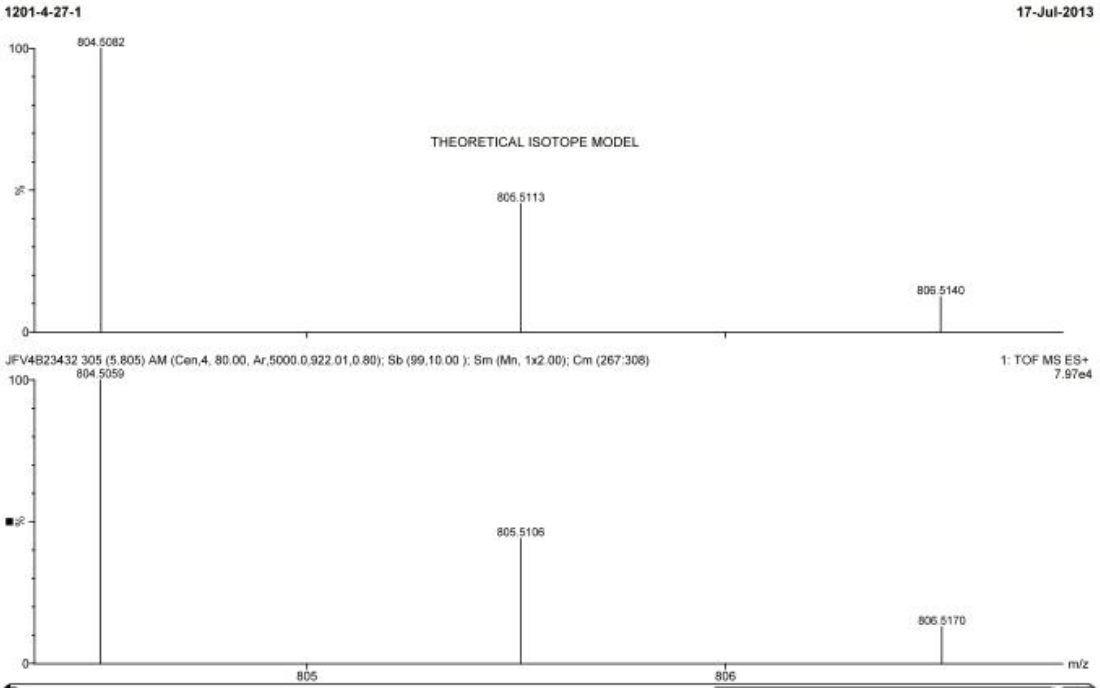


Figure S 2.45 HPLC chromatogram of **10**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

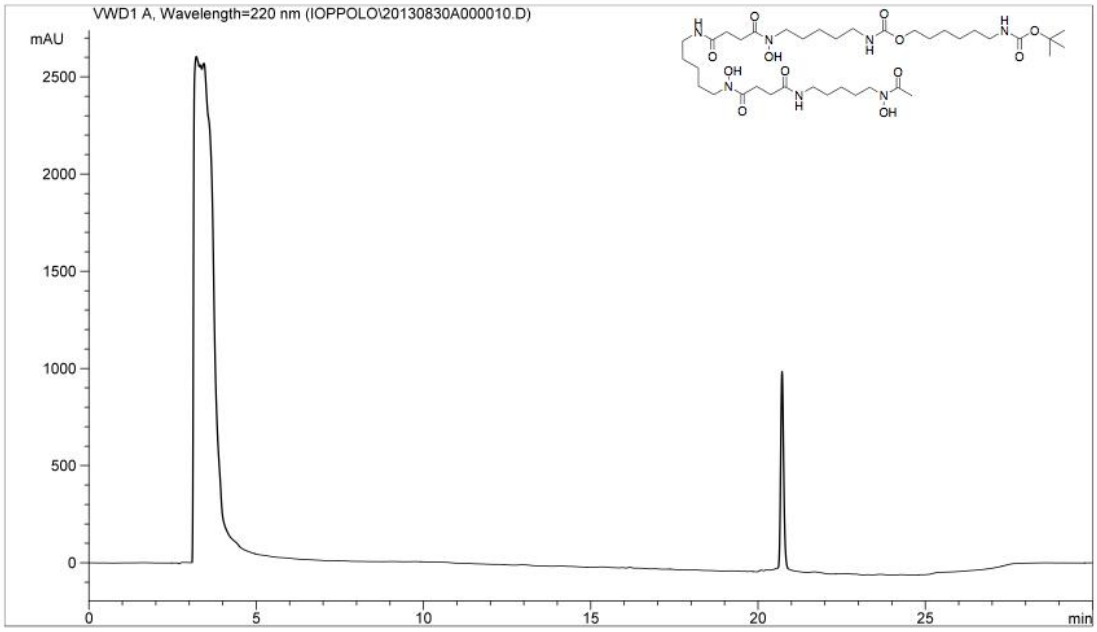


Figure S 2.46 IR spectrum of **11** (KBr pellet).

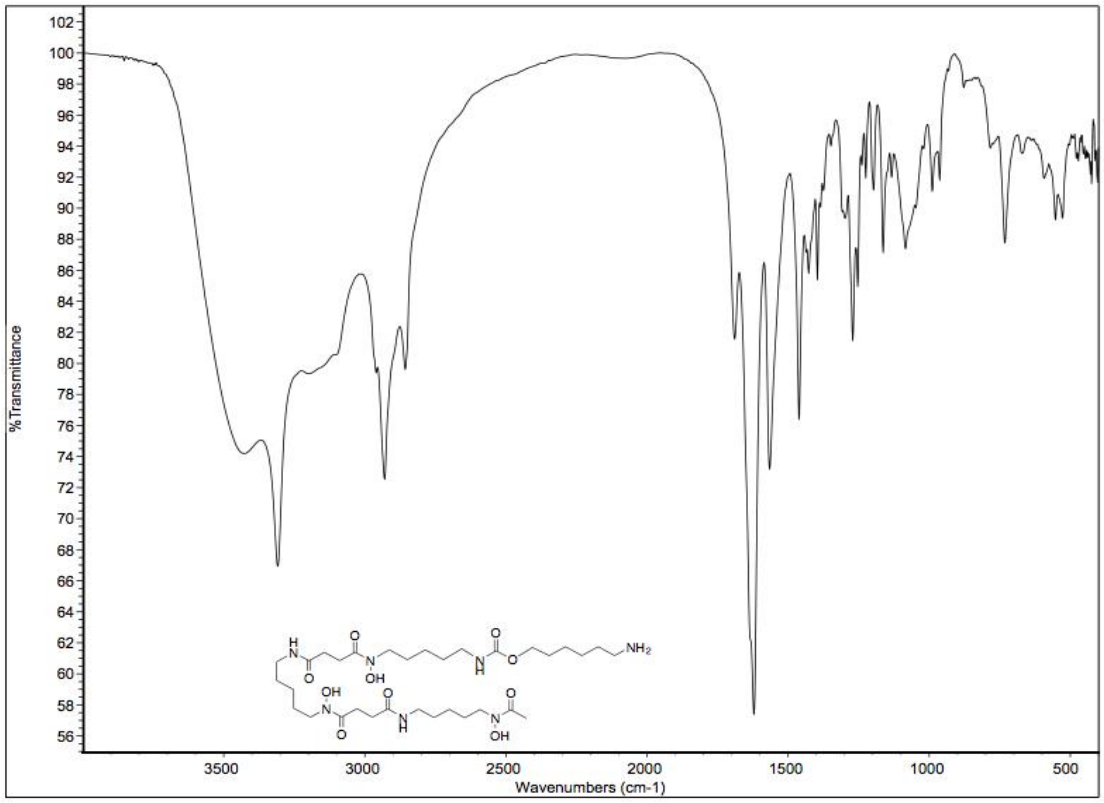


Figure S 2.47 ^{1}H NMR spectrum of **11** in DMSO-d_6 at 300 K.

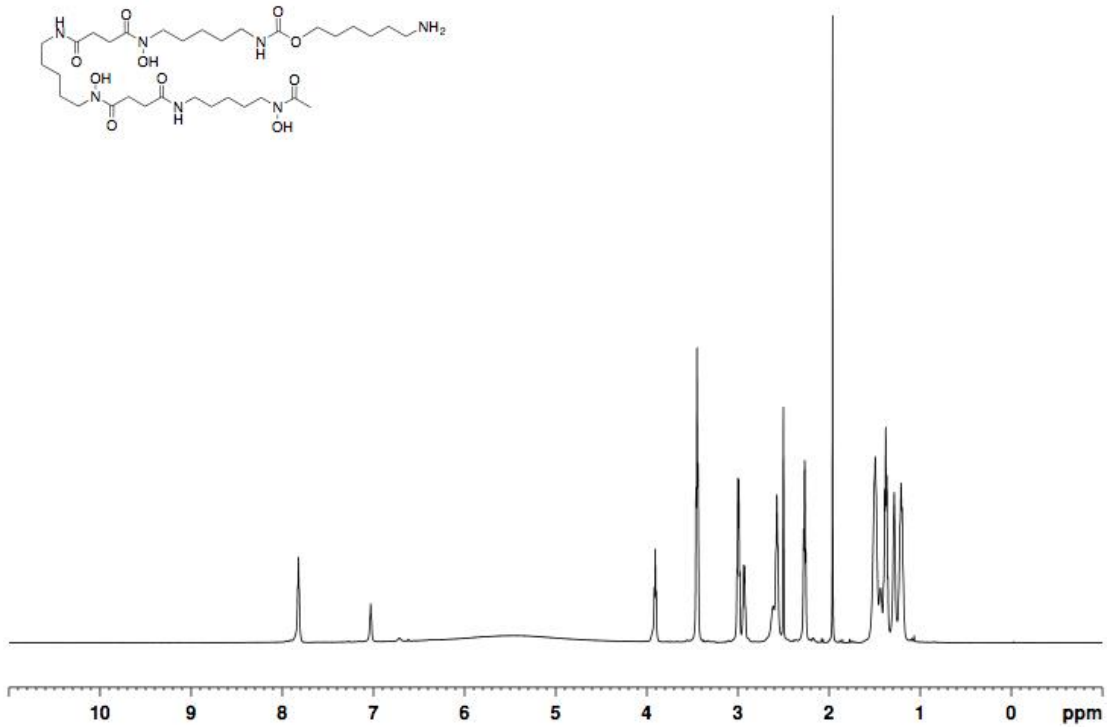


Figure S 2.48^{13}C NMR spectrum of **11** in DMSO-d_6 at 300 K.

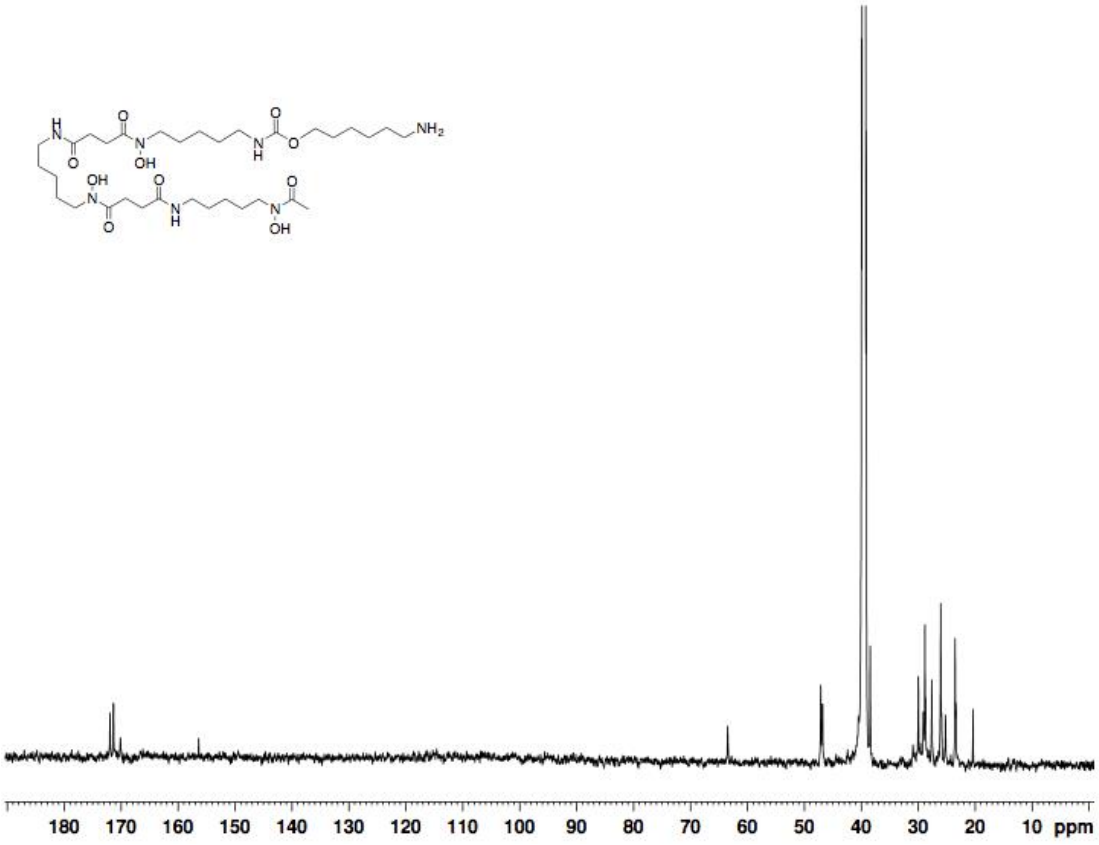


Figure S 2.49 High-resolution mass spectrum of **11**.

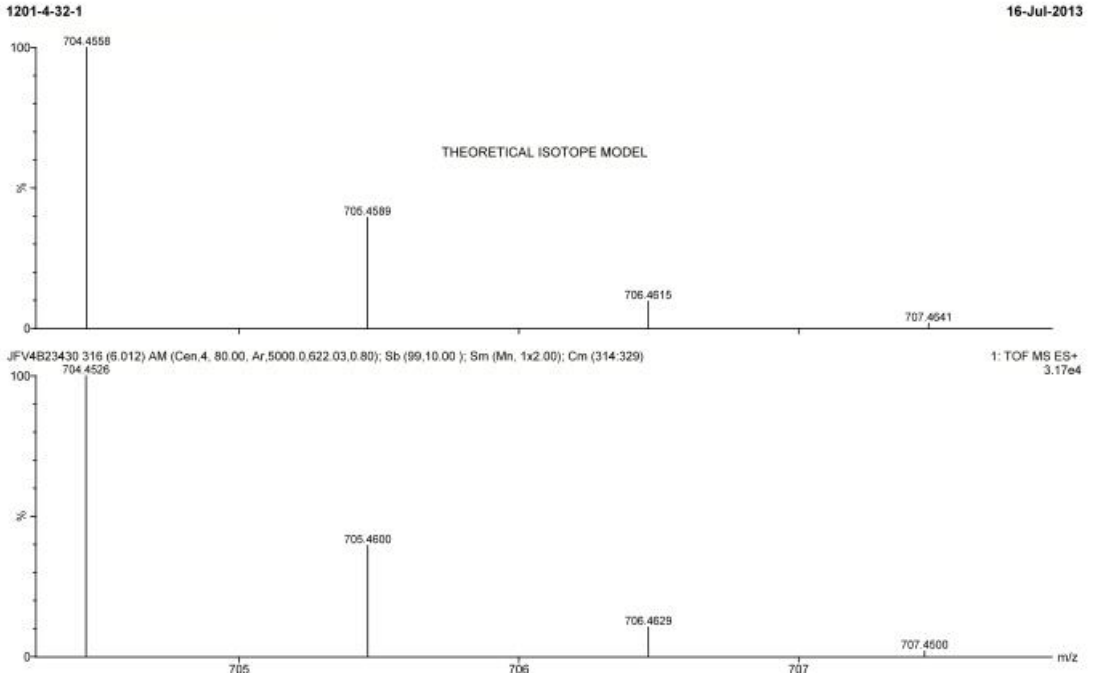


Figure S 2.50 HPLC chromatogram of **11**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

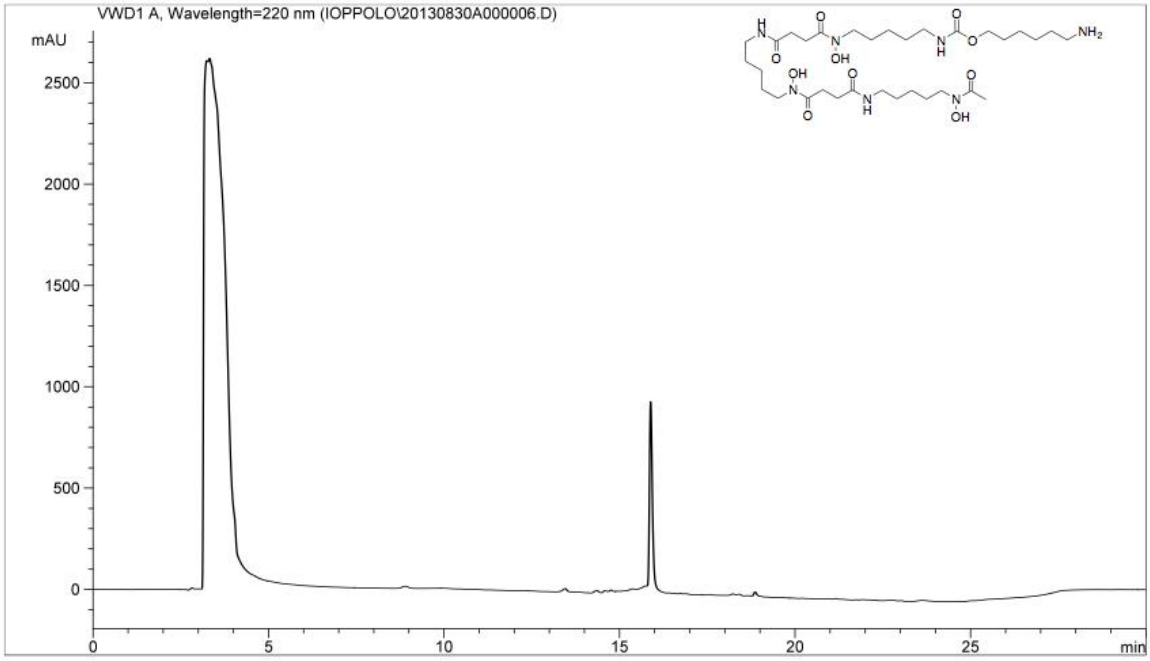


Figure S 2.51 IR spectrum of **12** (KBr pellet).

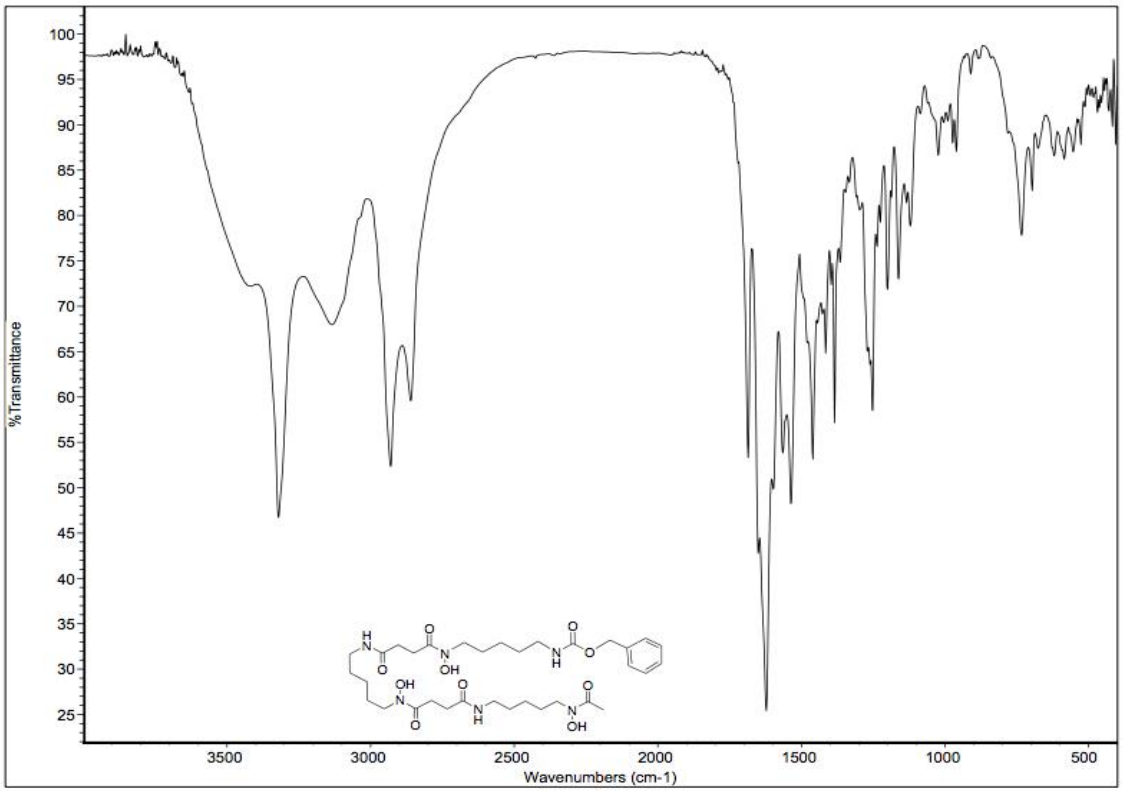


Figure S 2.52 ^{1}H NMR spectrum of **12** in DMSO-d_6 at 300 K.

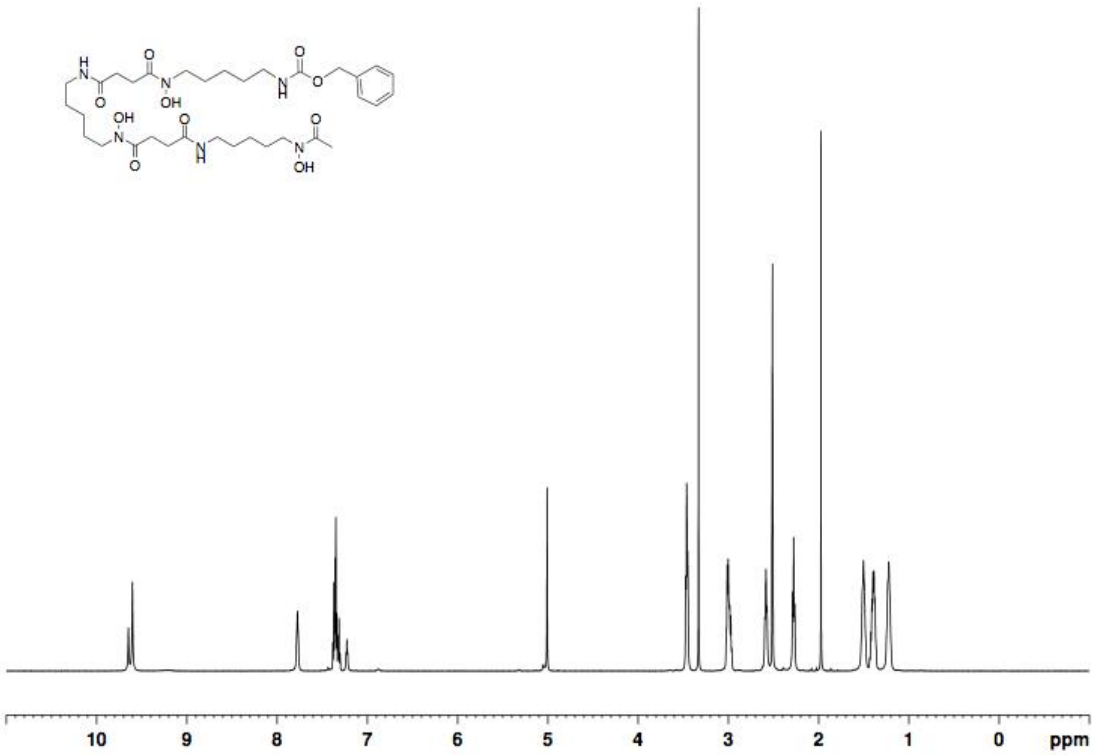


Figure S 2.53 ^{13}C NMR spectrum of **12** in DMSO-d_6 at 300 K.

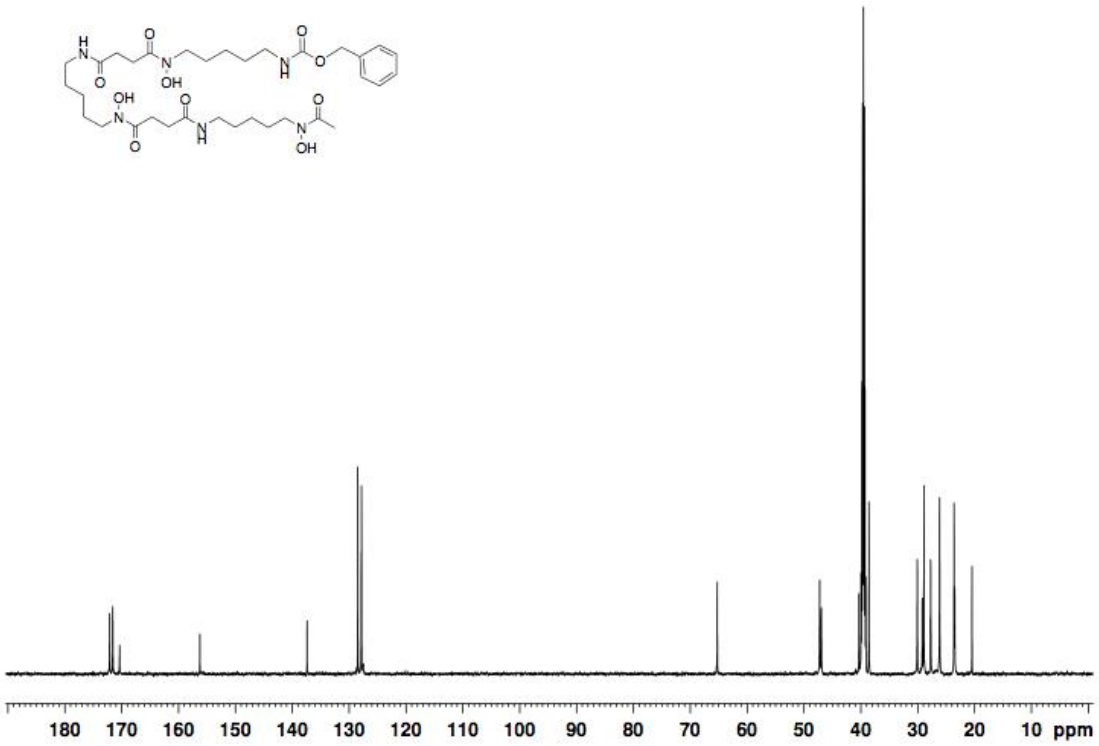


Figure S 2.54 High-resolution mass spectrum of **12**.

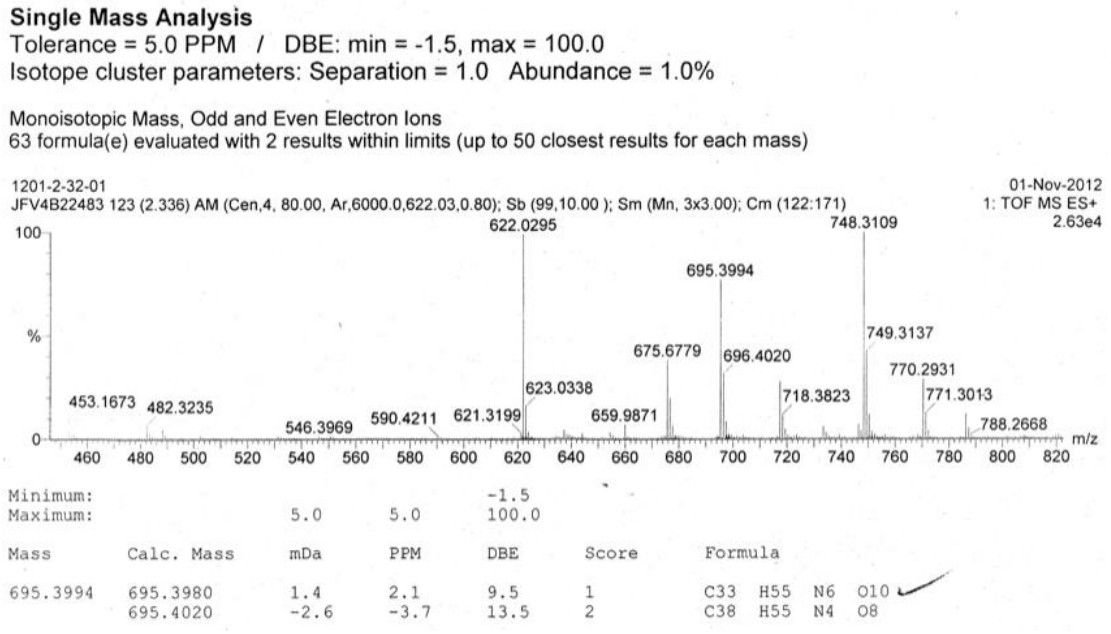


Figure S 2.55 HPLC chromatogram of **12**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

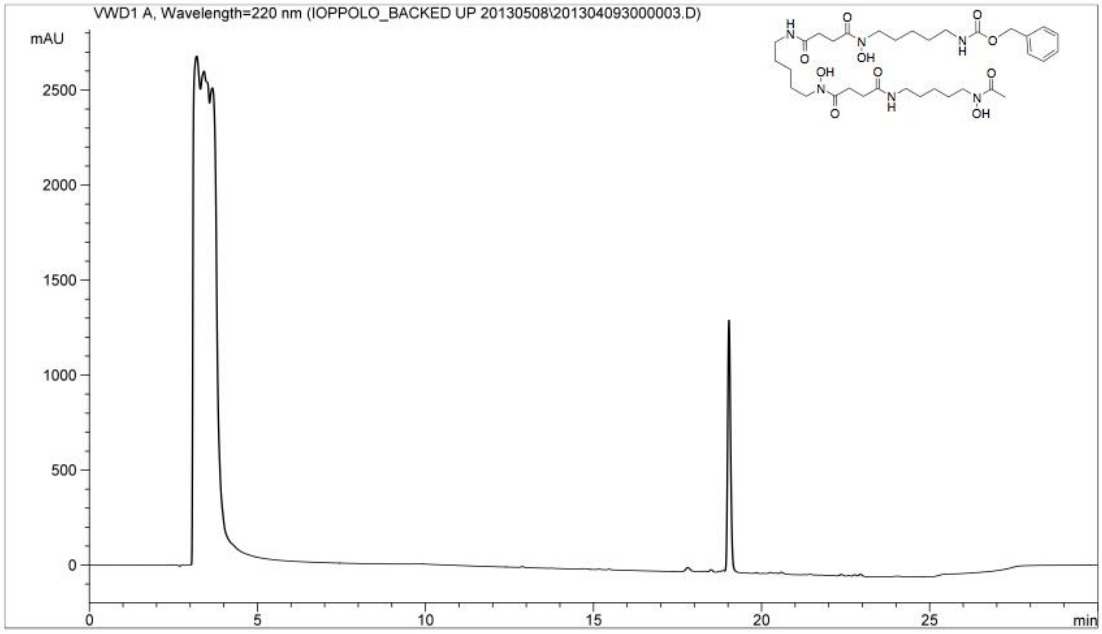


Figure S 2.56 IR spectrum of **15** (KBr pellet).

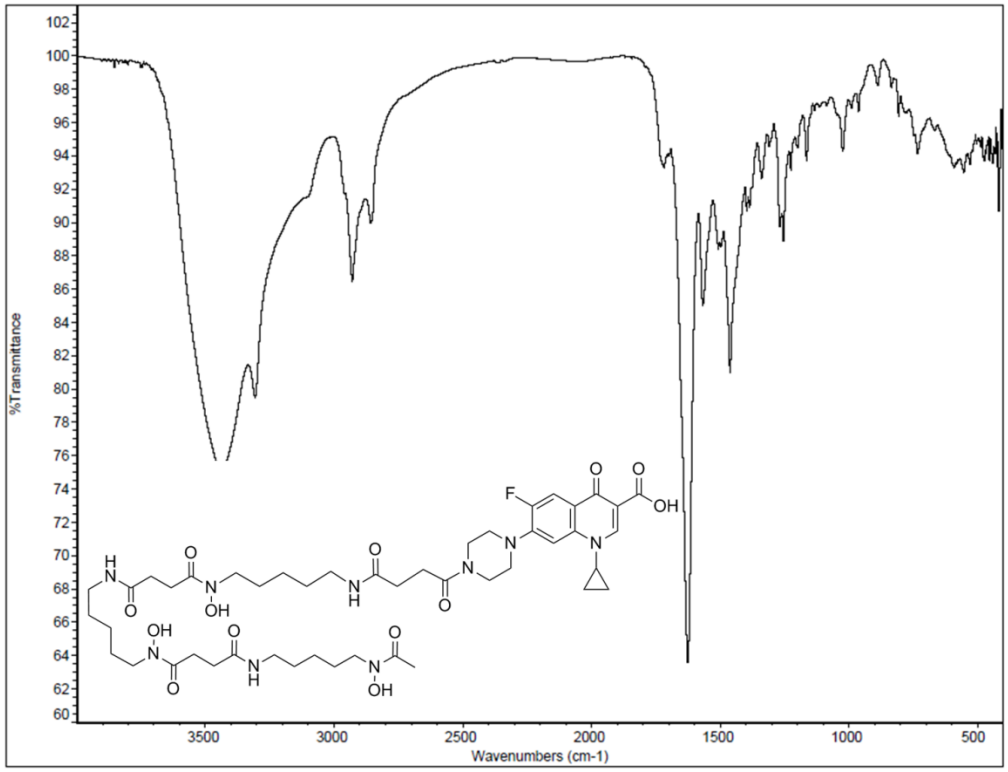


Figure S 2.57 ^{1}H NMR spectrum of **15** in DMSO-d_6 at 300 K.

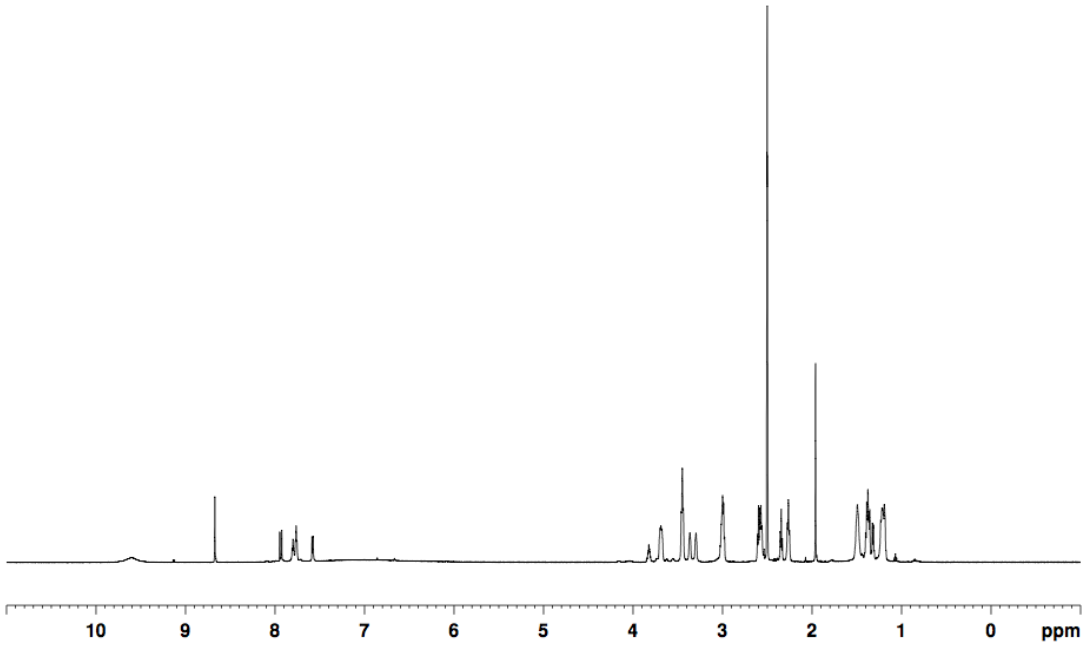


Figure S 2.58 ^{19}F NMR spectrum of **15** in DMSO-d_6 at 300 K.

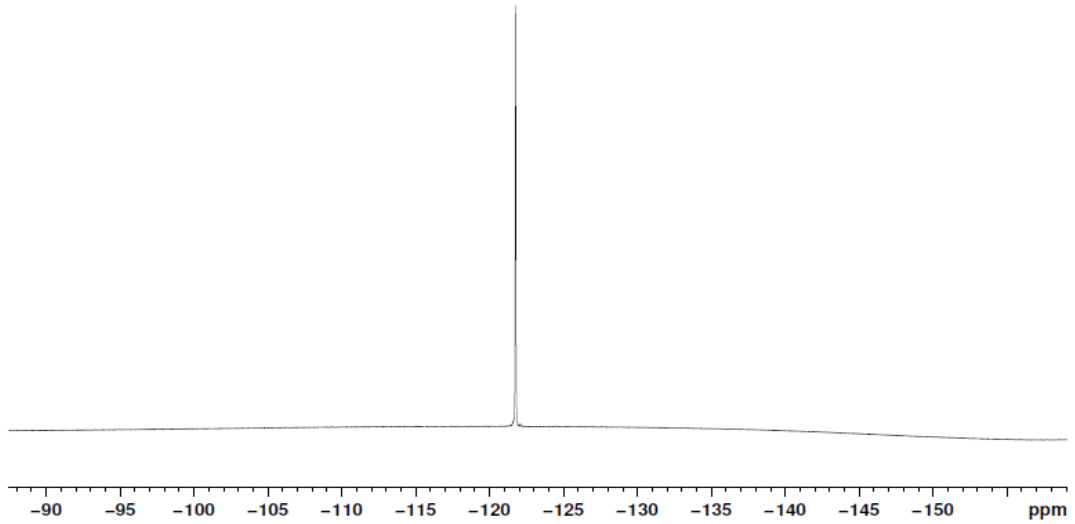


Figure S 2.59 High-resolution mass spectrum of **15**.

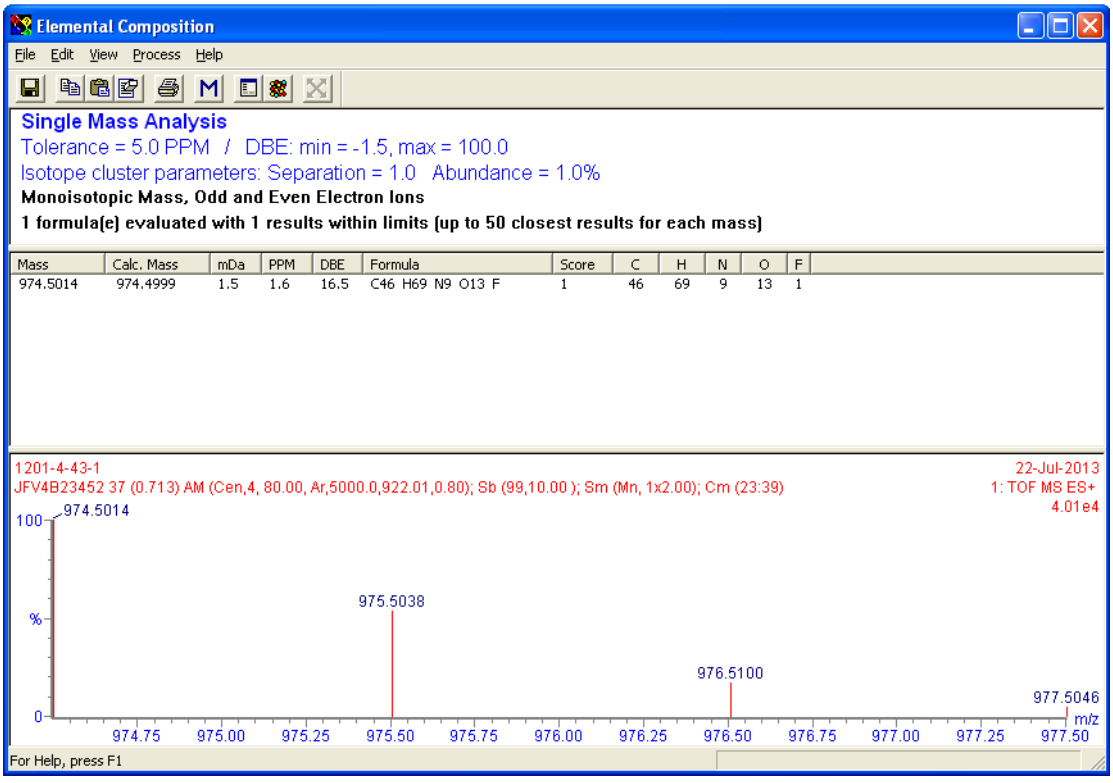


Figure S 2.60 HPLC chromatogram of **15**. UV peak at λ = 220 nm.

(Note injection volume contains DMSO).

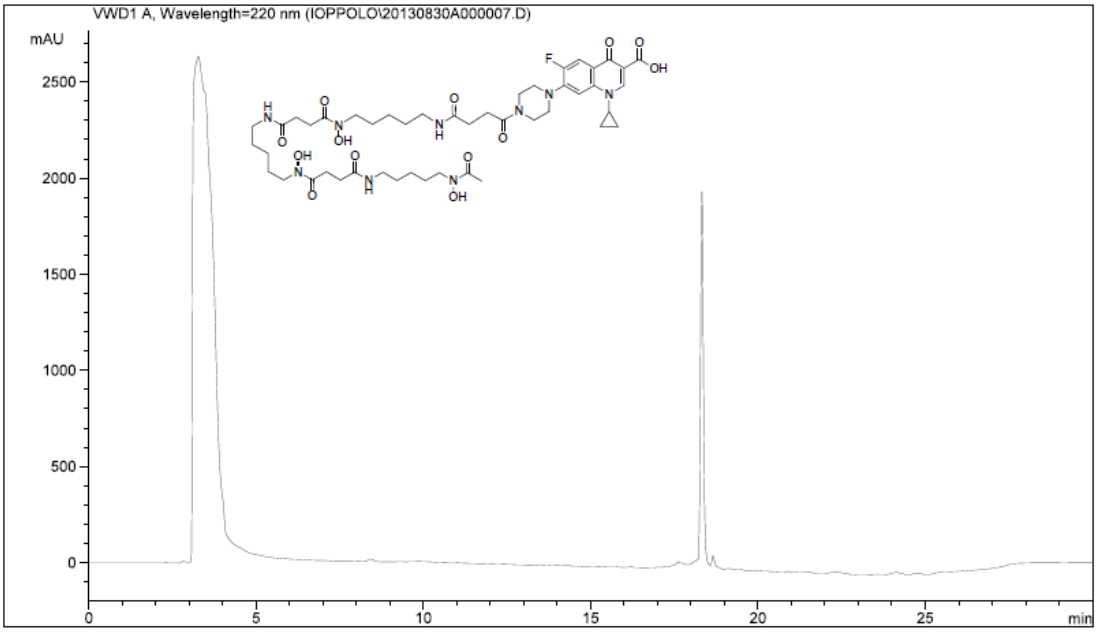


Figure S 2.61 IR spectrum of **17** (KBr pellet).

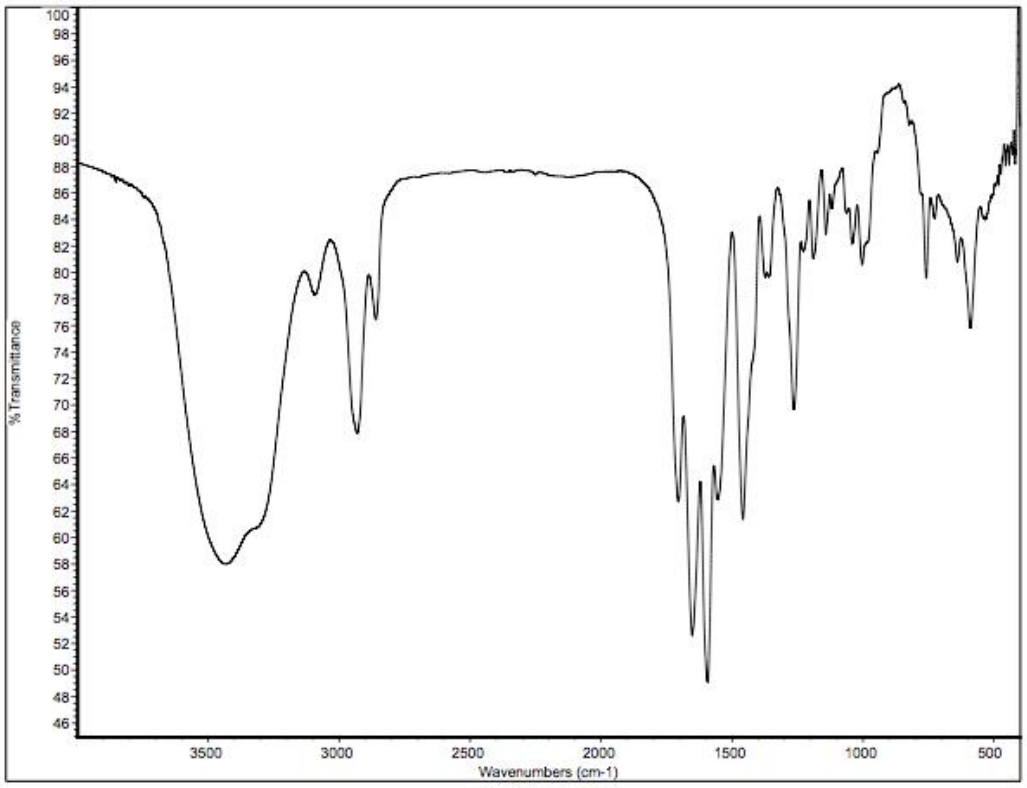


Figure S 2.62 ^{1}H NMR spectrum of **17** in DMSO-d_6 at 300 K.

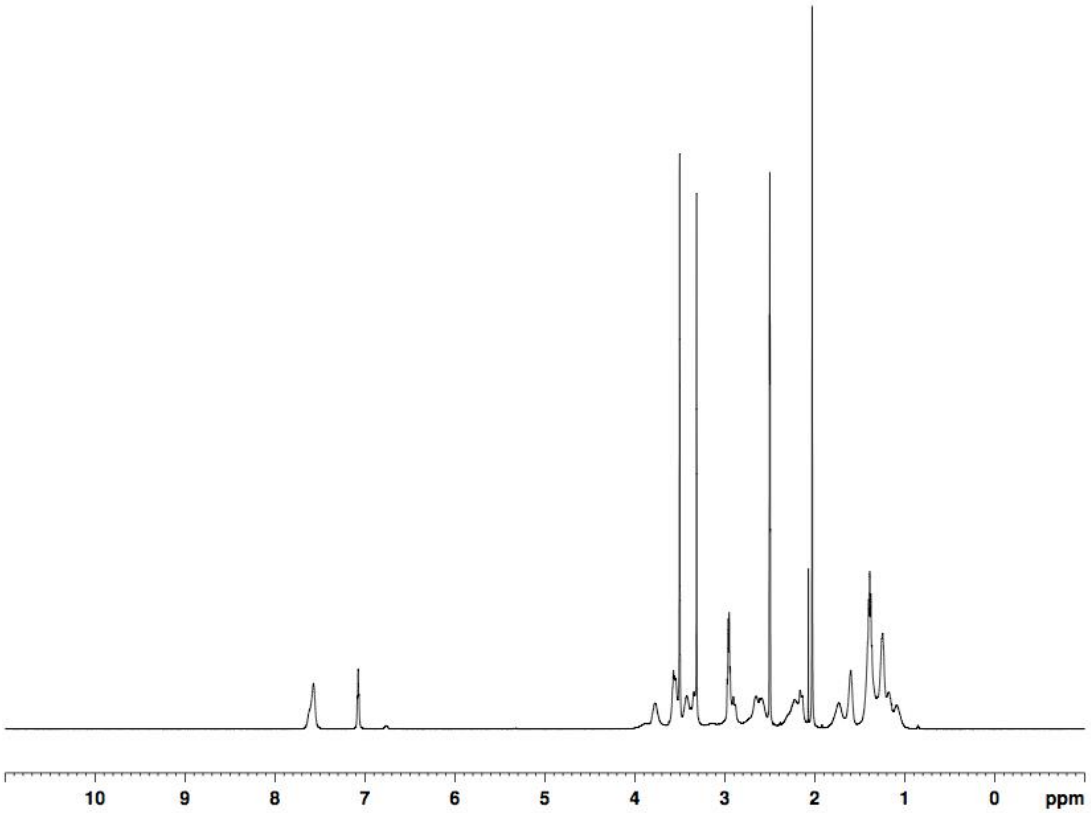


Figure S 2.63 High-resolution mass spectrum of **17**.

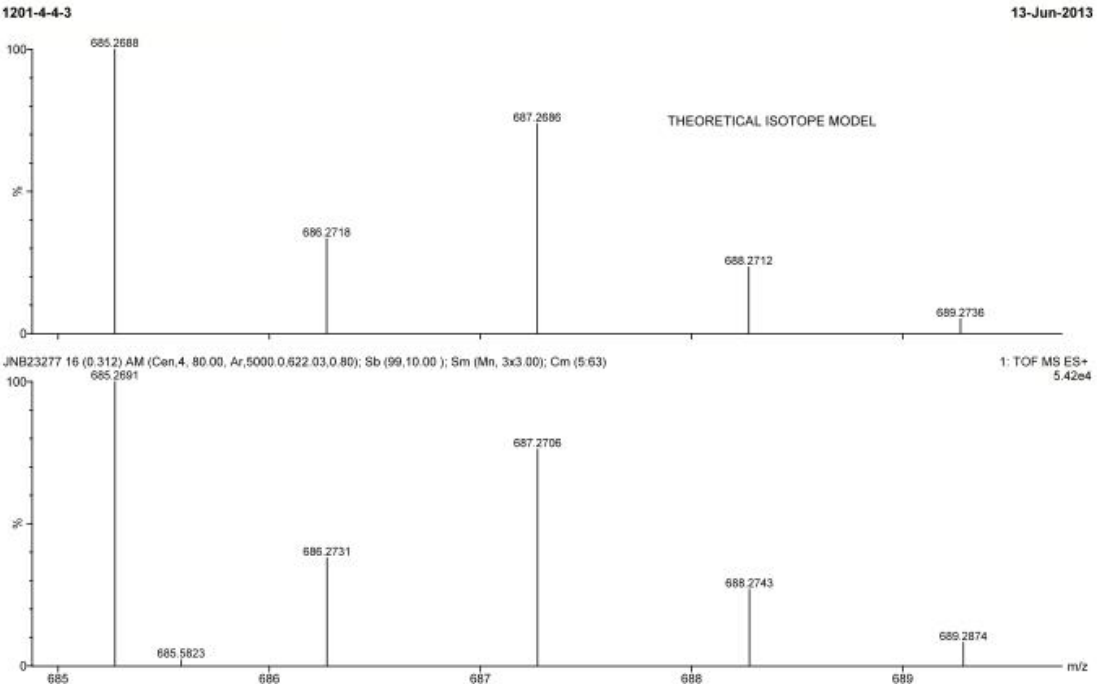


Figure S 2.64 HPLC chromatogram of **17**. UV peak at λ = 240 nm.

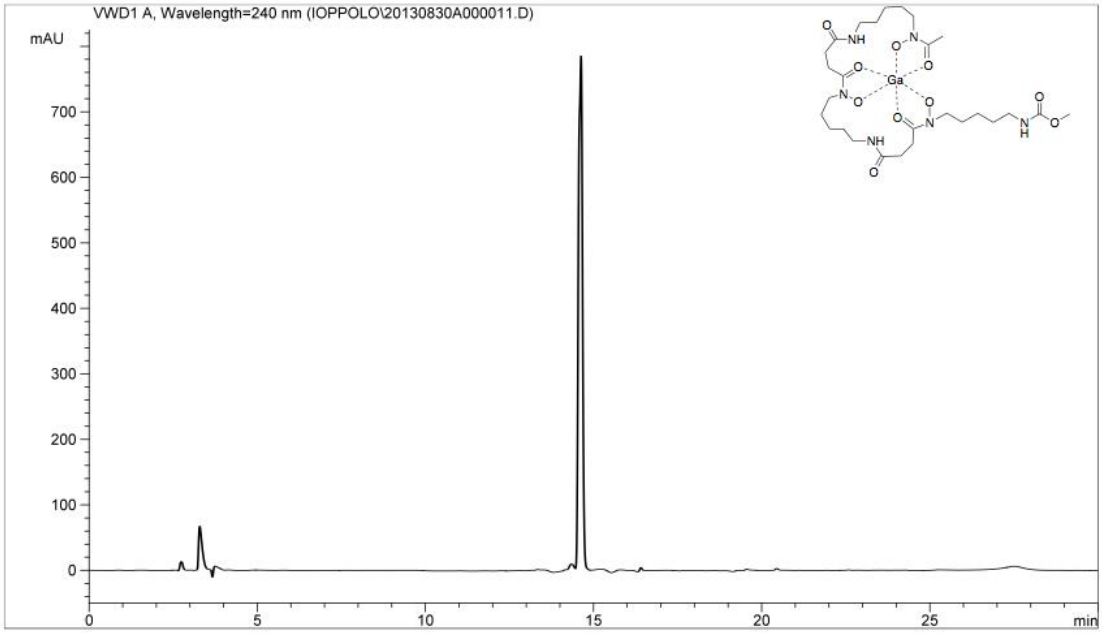


Figure S 2.65 IR spectrum of **18** (KBr pellet).

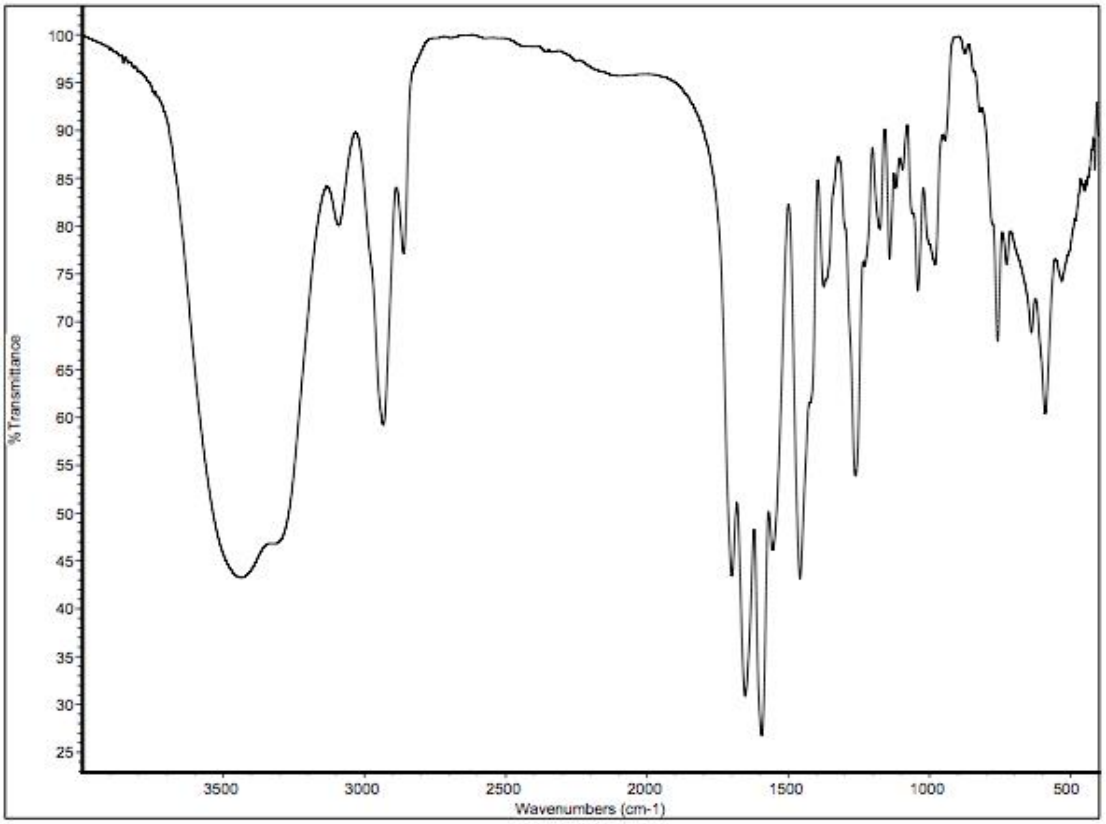


Figure S 2.66 ^{1}H NMR spectrum of **18** in DMSO-d_6 at 300 K.

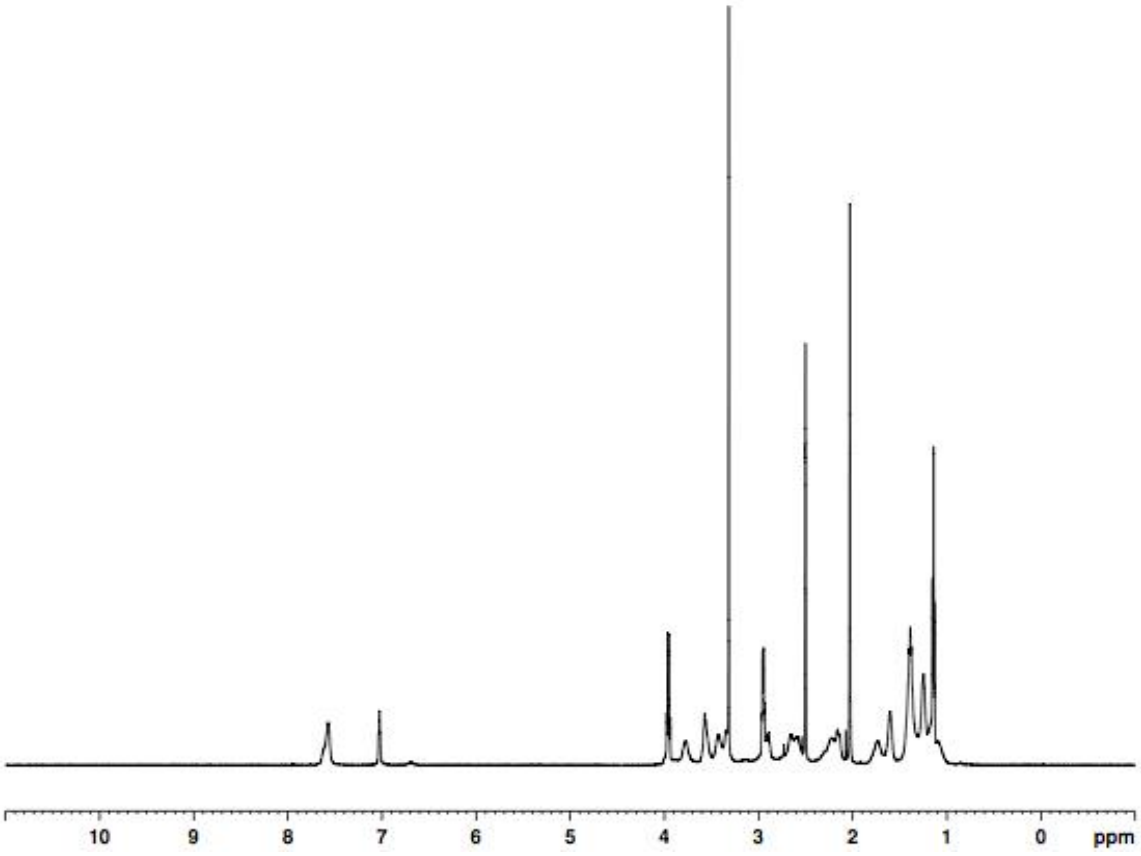


Figure S 2.67 High-resolution mass spectrum of **18**.

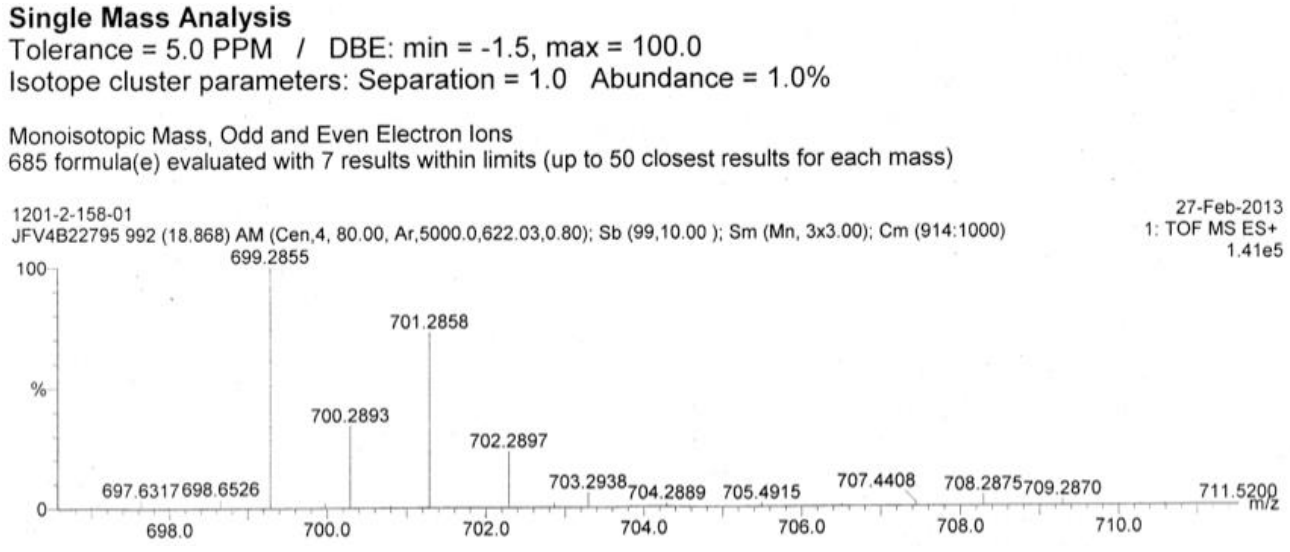


Figure S 2.68 HPLC chromatogram of **18**. UV peak at λ = 240 nm.

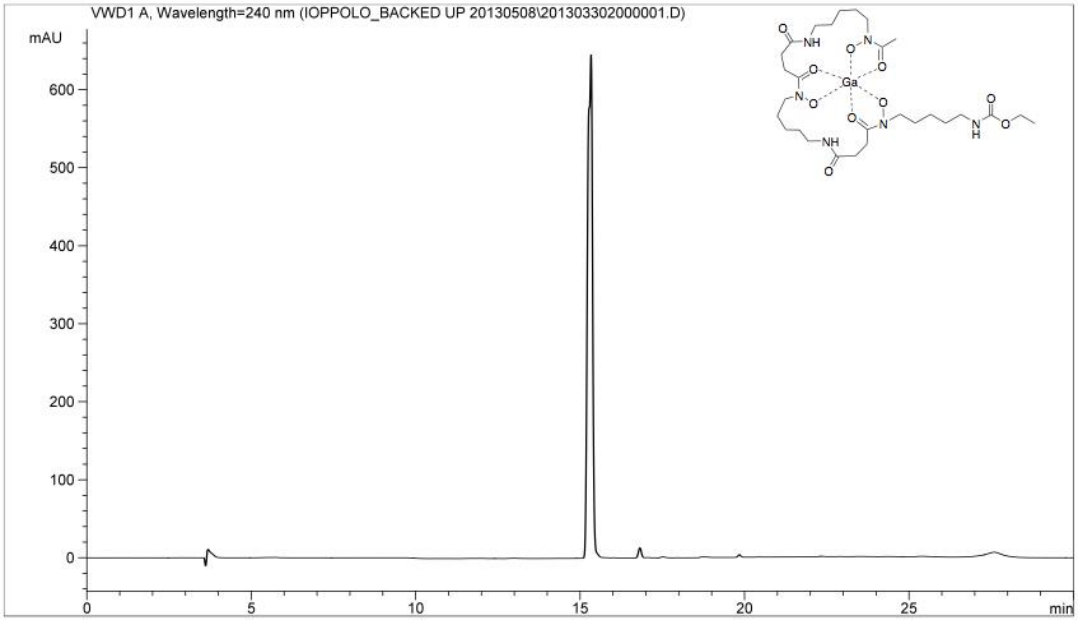


Figure S 2.69 IR spectrum of **19** (KBr pellet).

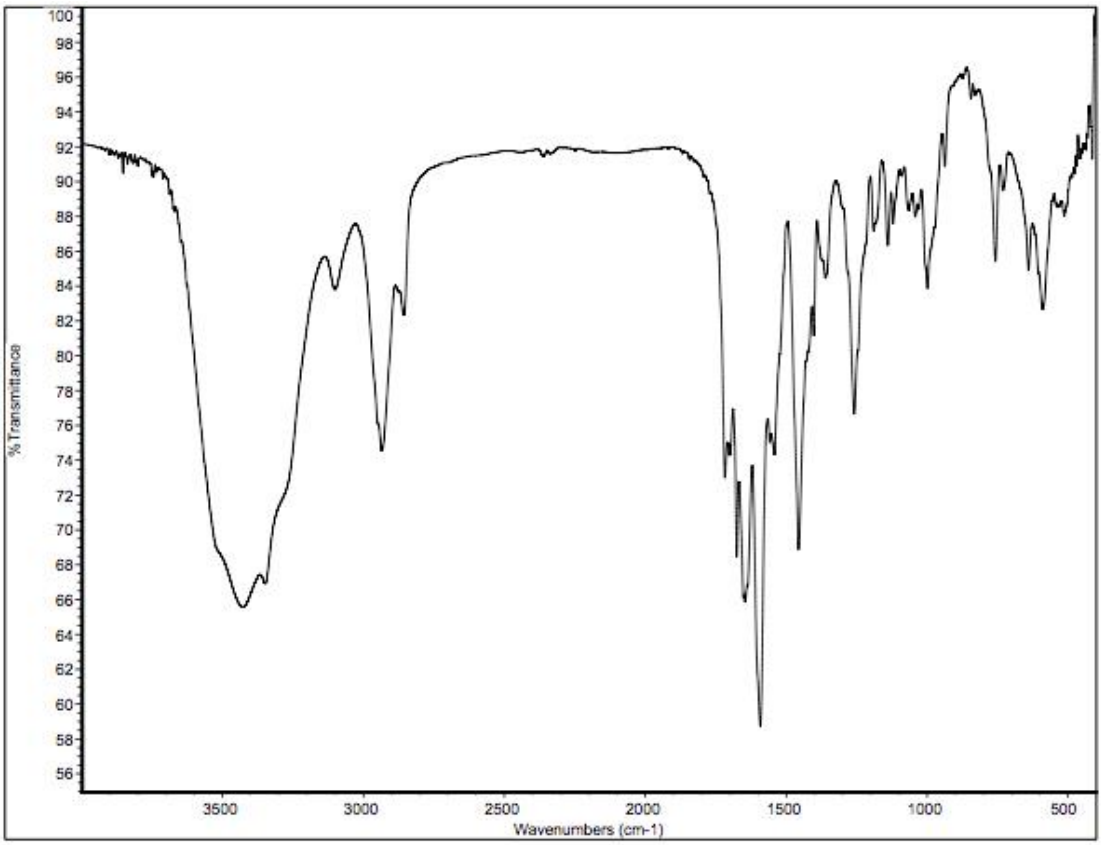


Figure S 2.70 ^{1}H NMR spectrum of **19** in DMSO-d_6 at 300 K.

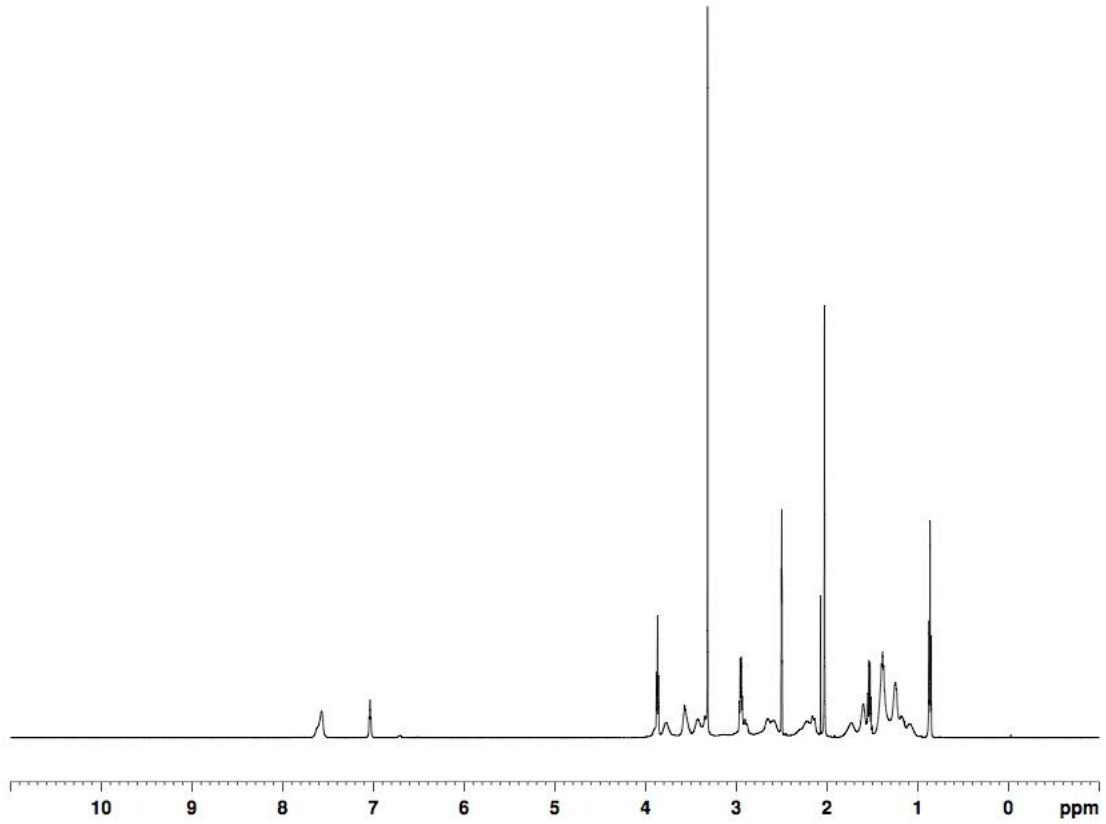


Figure S 2.71 High-resolution mass spectrum of **19**.

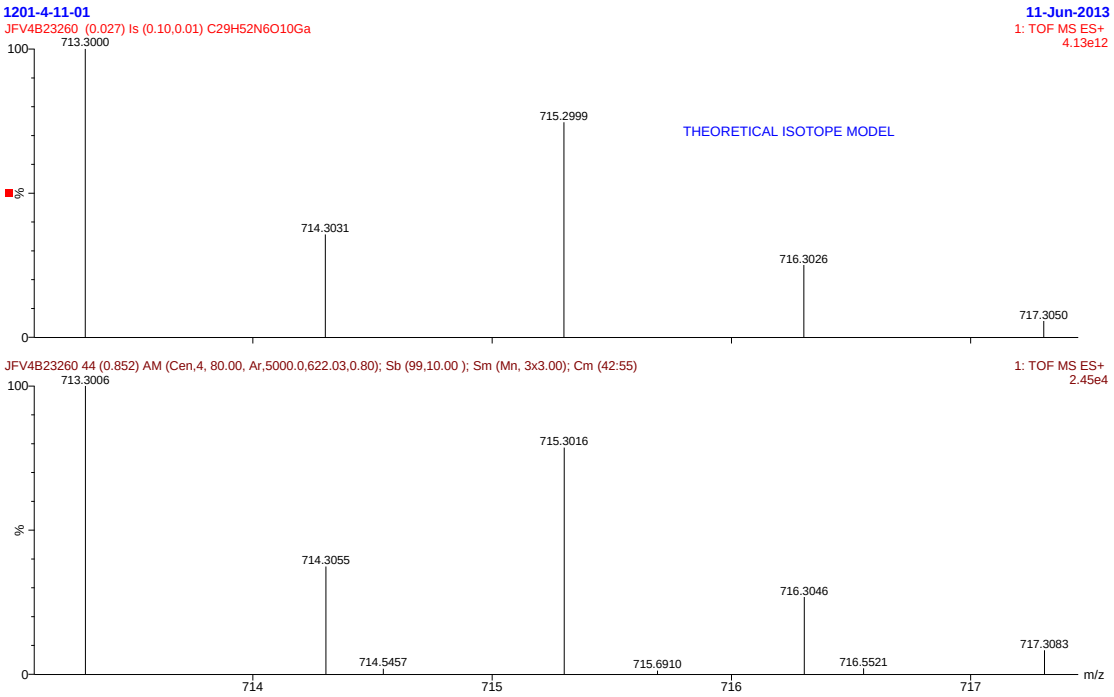


Figure S 2.72 HPLC chromatogram of 19. UV peak at λ = 240 nm.

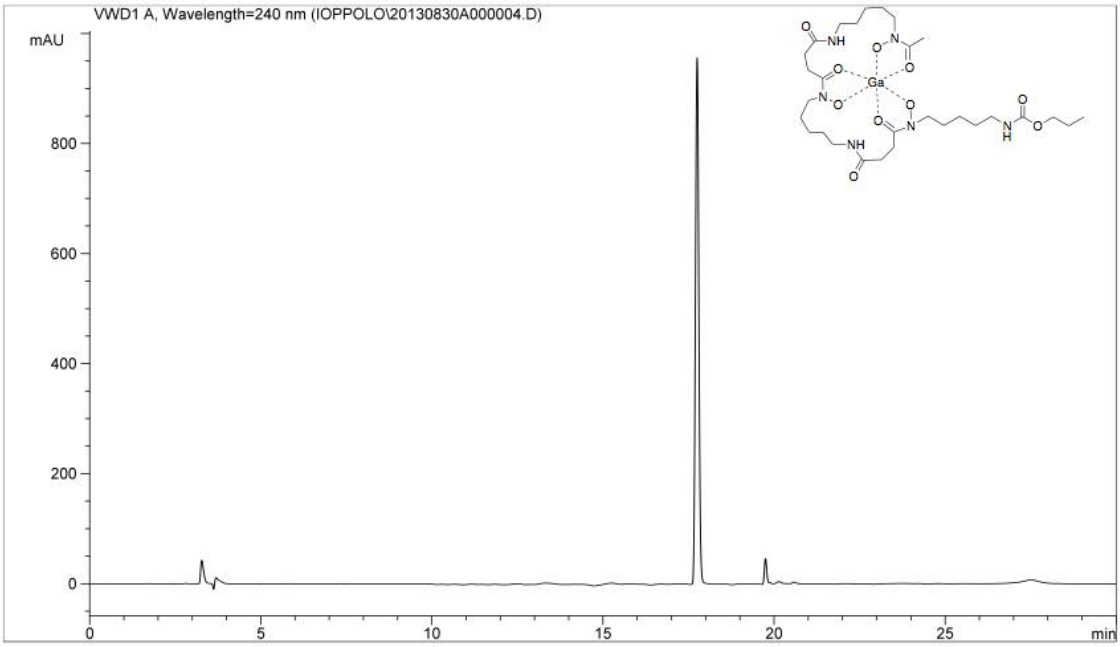


Figure S 2.73 IR spectrum of **20** (KBr pellet).

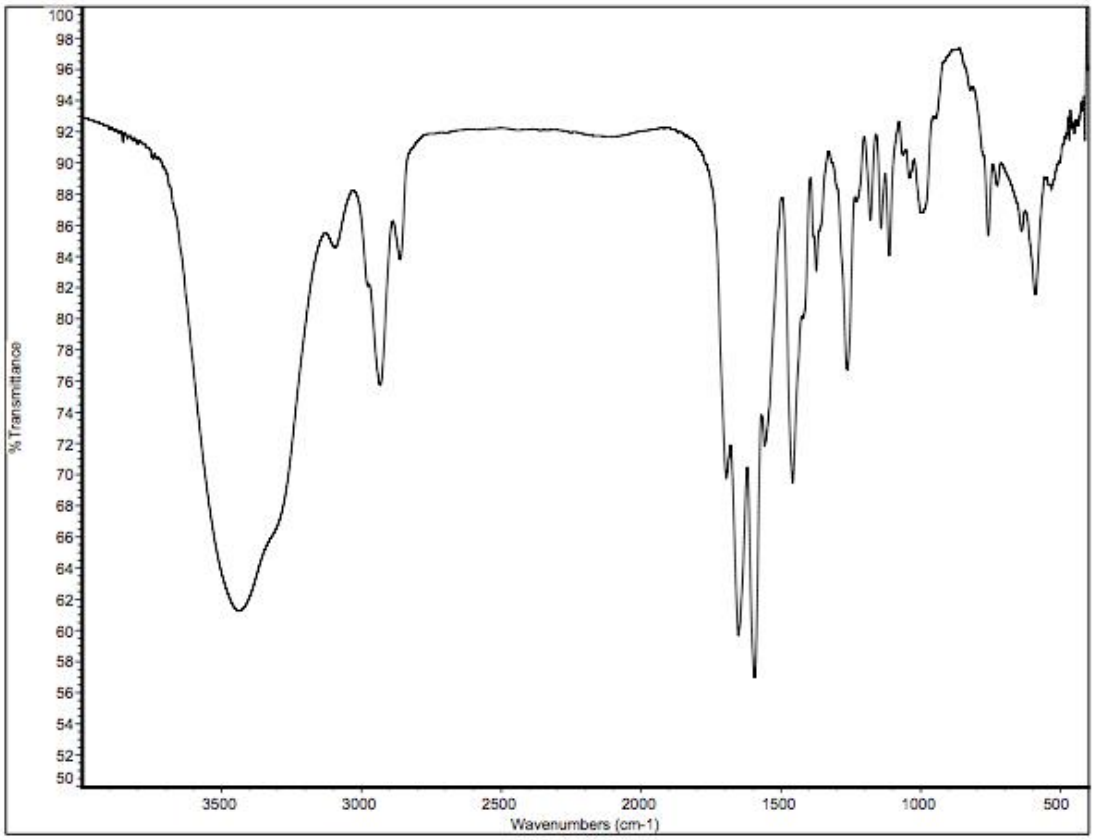


Figure S 2.74 ^{1}H NMR spectrum of **20** in DMSO-d_6 at 300 K.

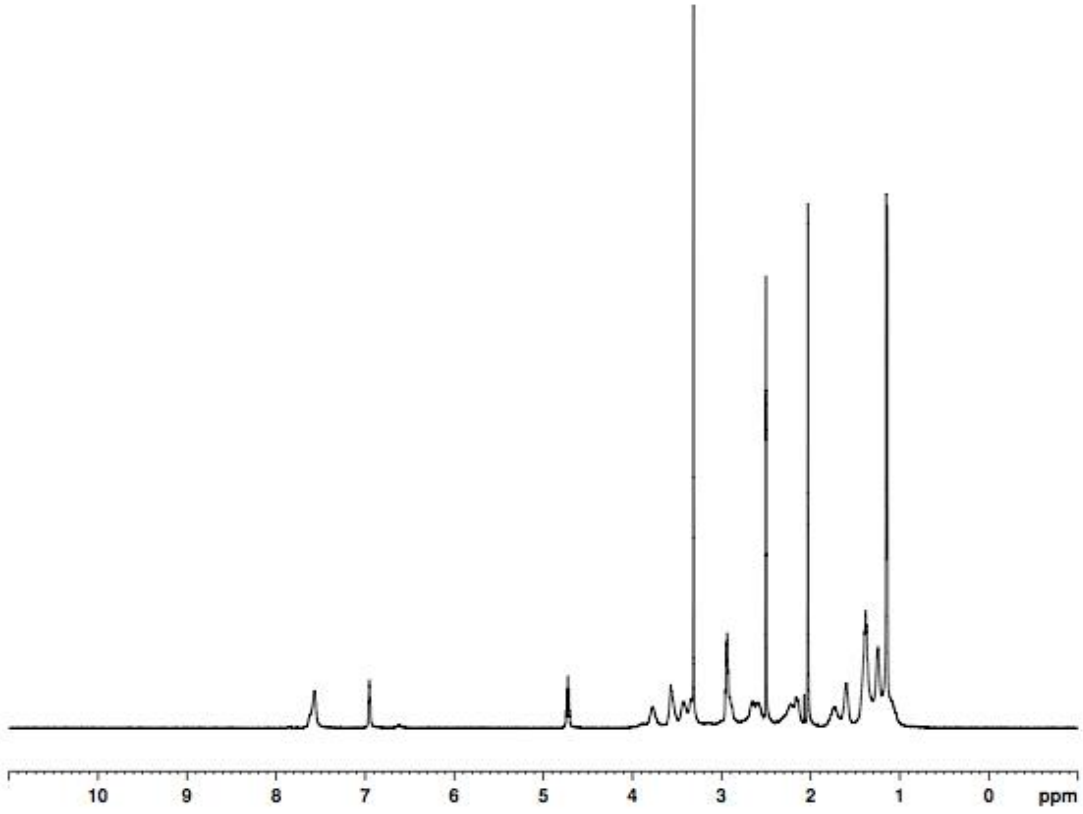
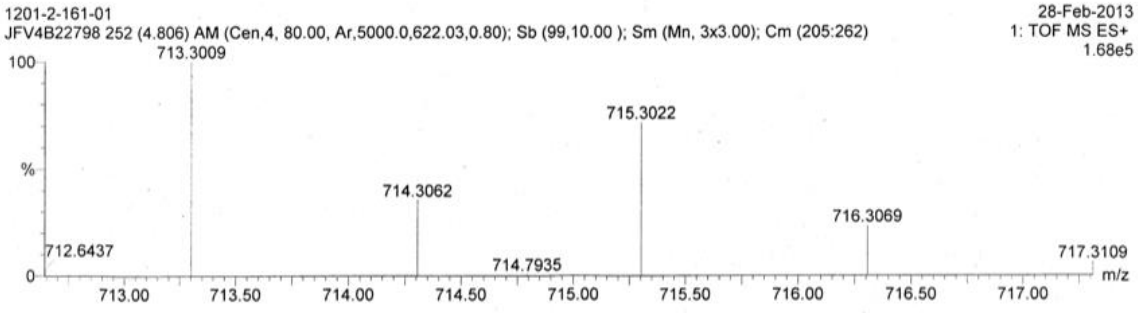


Figure S 2.75 High-resolution mass spectrum of **20**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
440 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		2.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
713.3009	713.3001	0.8	1.2	7.5	1	C29 H52 N6 O10 Ga✔

Figure S 2.76 HPLC chromatogram of **20**. UV peak at λ = 240 nm.

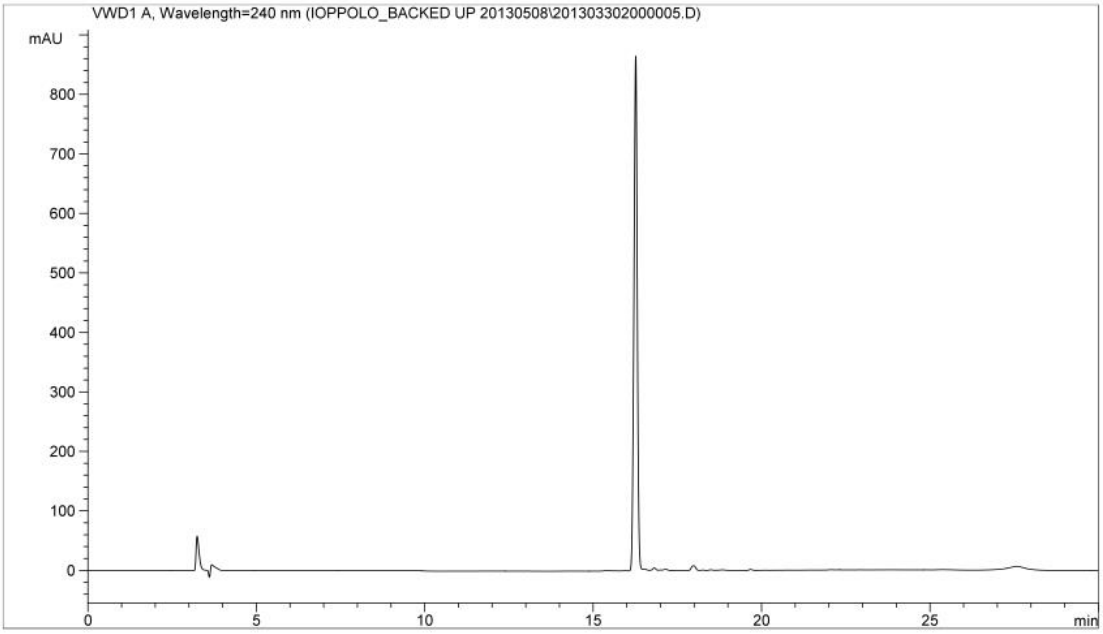


Figure S 2.77 IR spectrum of **21** (KBr pellet).

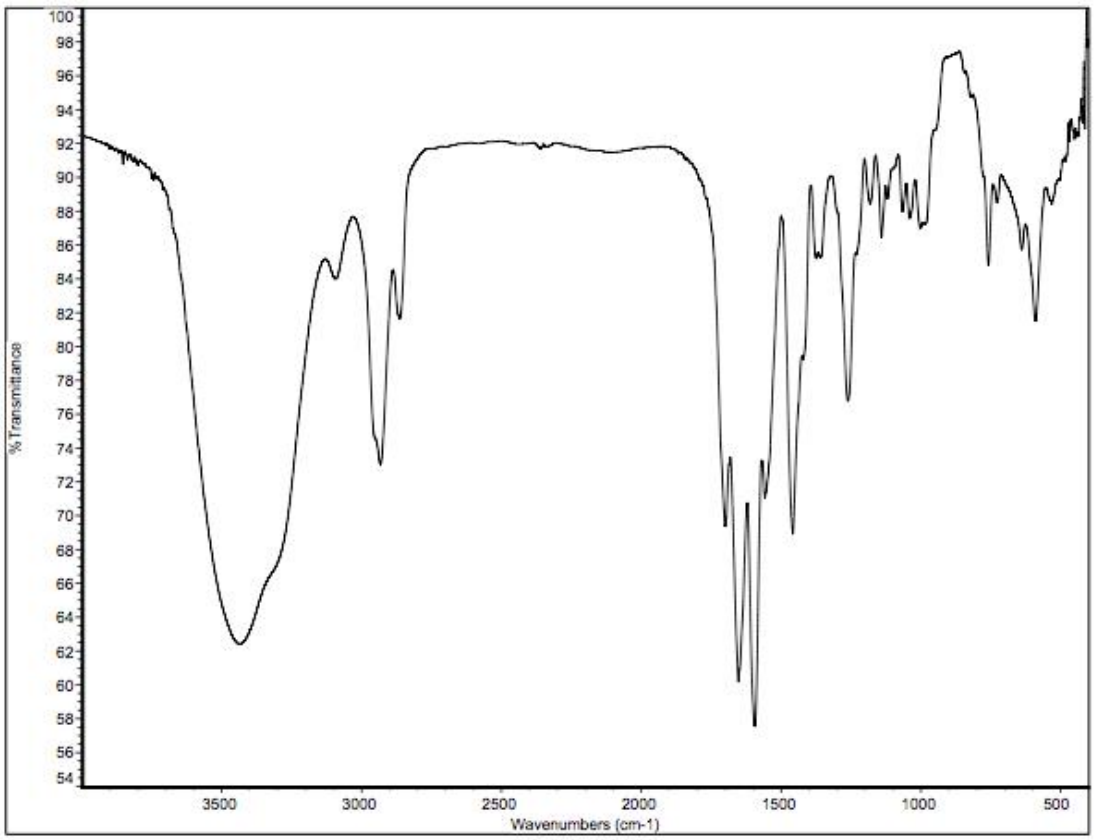


Figure S 2.78 ^{1}H NMR spectrum of **21** in DMSO-d_6 at 300 K.

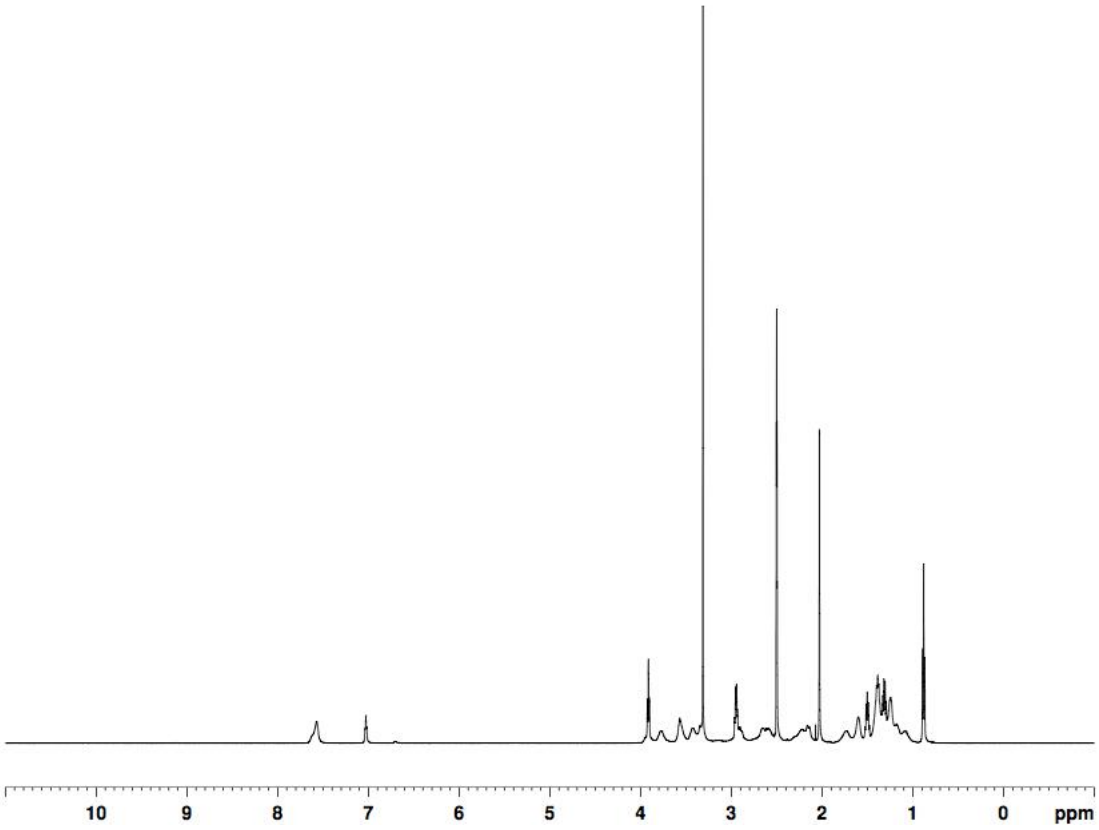
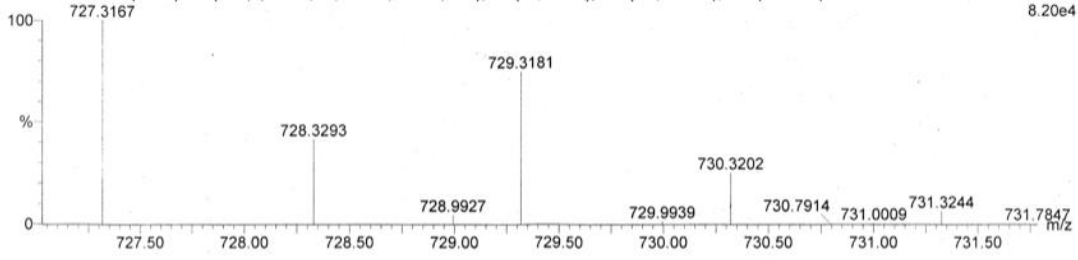


Figure S 2.79 High-resolution mass spectrum of **21**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
547 formula(e) evaluated with 6 results within limits (up to 50 closest results for each mass)

1201-2-159-01
JFV4B22796 371 (7.050) AM (Cen,4, 80.00, Ar,5000.0,622.03,0.80); Sb (99,10.00); Sm (Mn, 3x3.00); Cm (336:408)
27-Feb-2013
1: TOF MS ES+
8.20e4



Minimum:				-1.5		
Maximum:		2.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
727.3167	727.3164	0.3	0.5	16.5	6	C32 H43 N10 O10
	727.3171	-0.4	-0.5	12.5	1	C31 H50 N10 O6 Ga
	727.3157	1.0	1.3	7.5	4	C30 H54 N6 O10 Ga ✓

Figure S 2.80 HPLC chromatogram of 21. UV peak at λ = 240 nm.

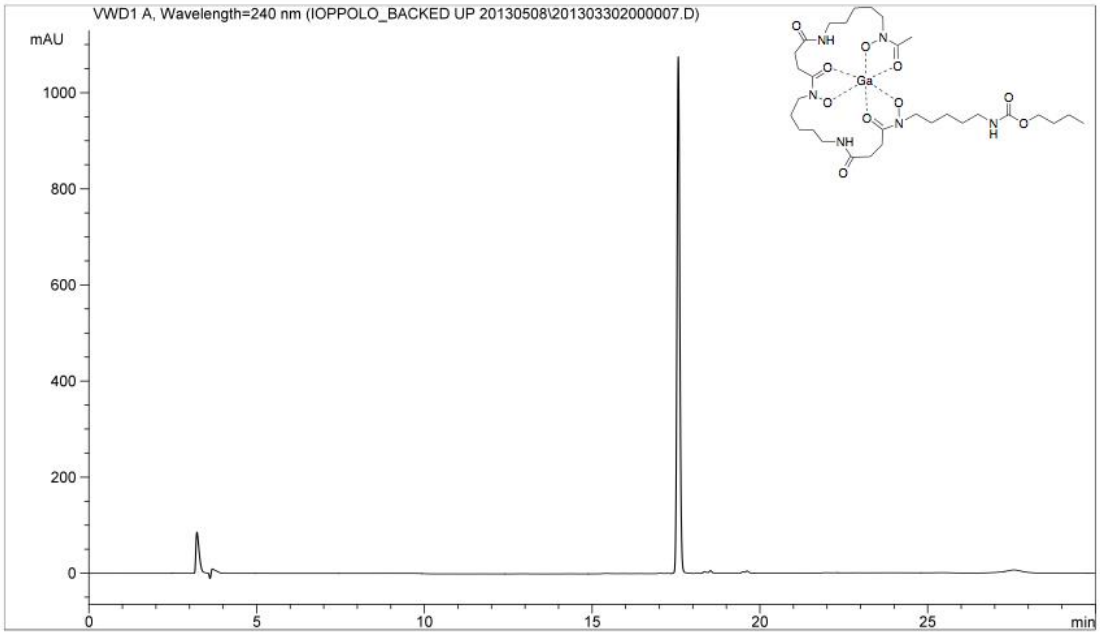


Figure S 2.81IR spectrum of 22 (KBr pellet).

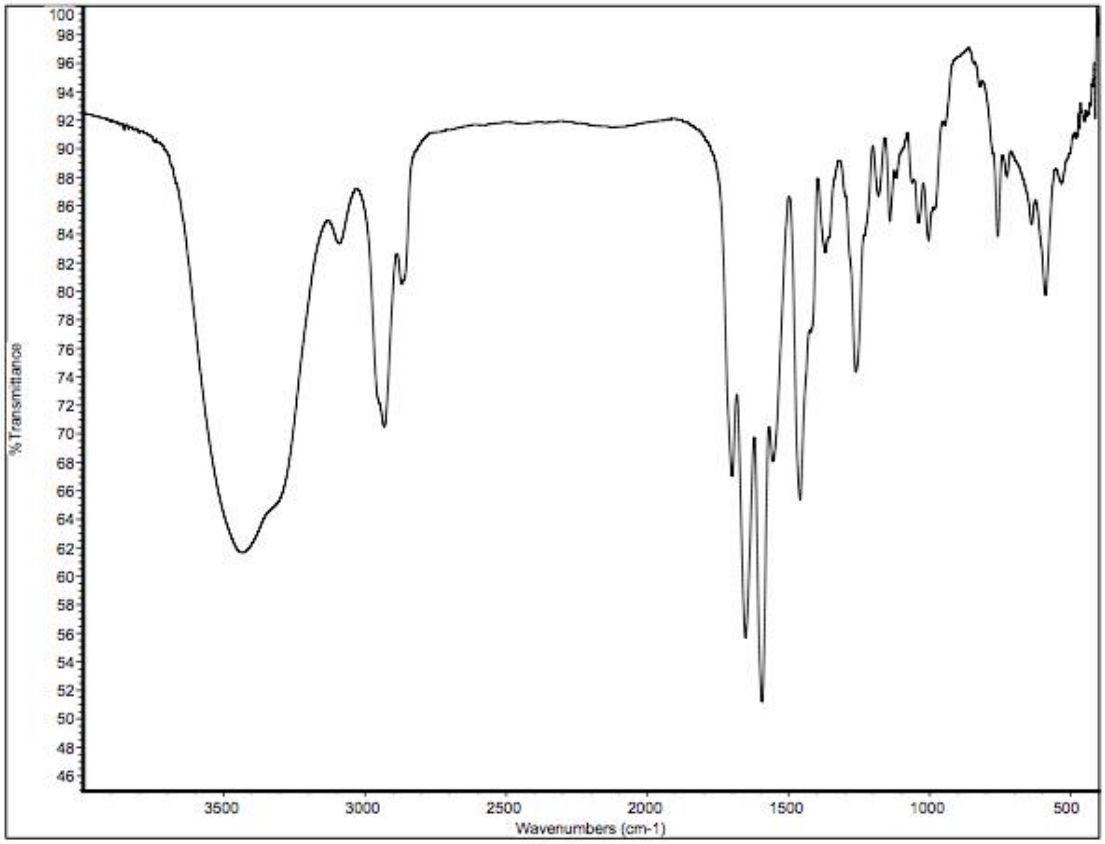


Figure S 2.82 ^{1}H NMR spectrum of **22** in DMSO-d_6 at 300 K.

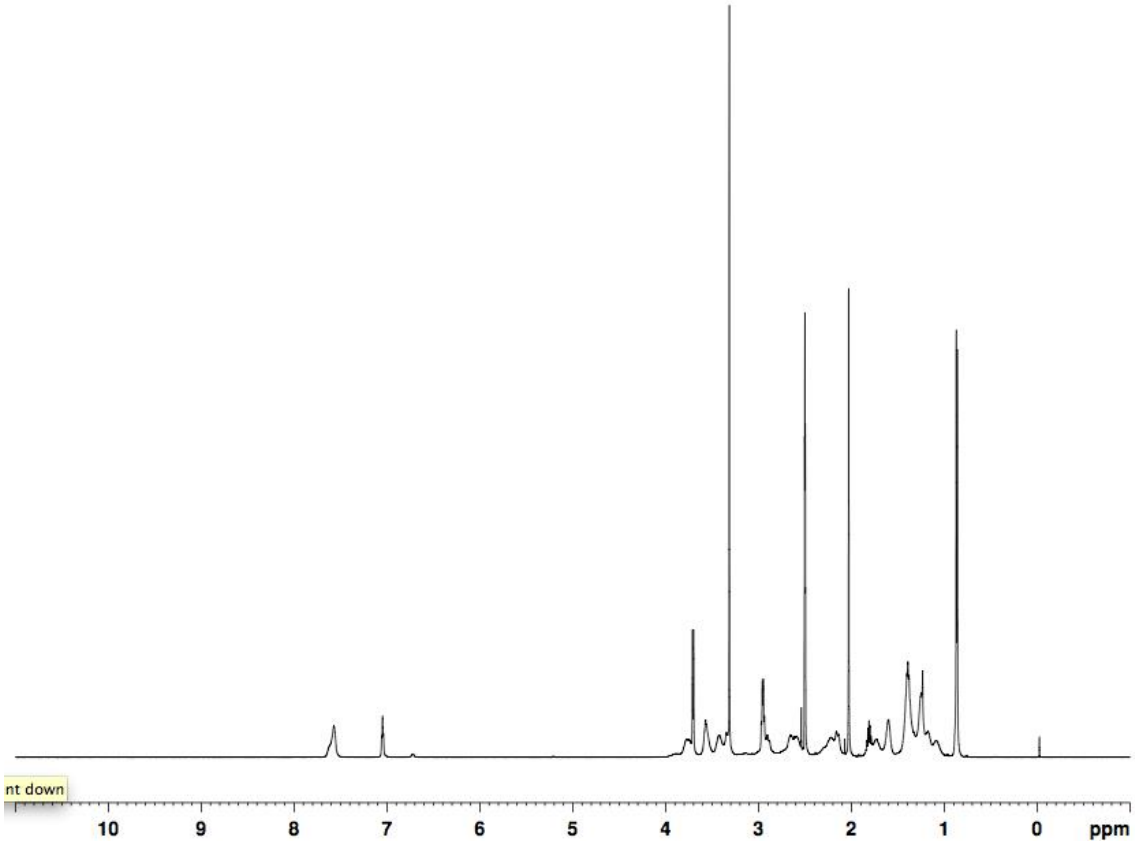


Figure S 2.83 High-resolution mass spectrum of **22**.

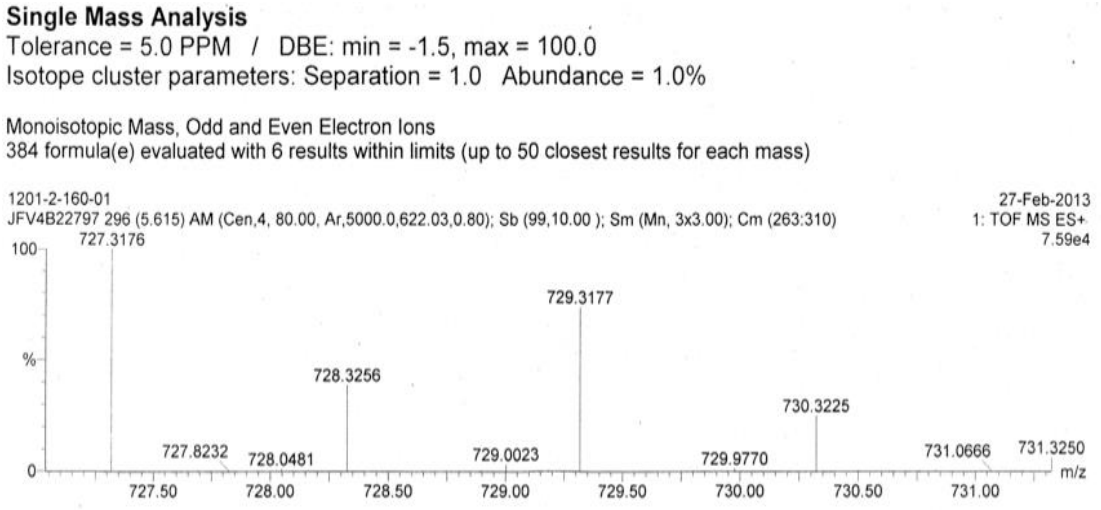


Figure S 2.84 HPLC chromatogram of 22. UV peak at λ = 240 nm.

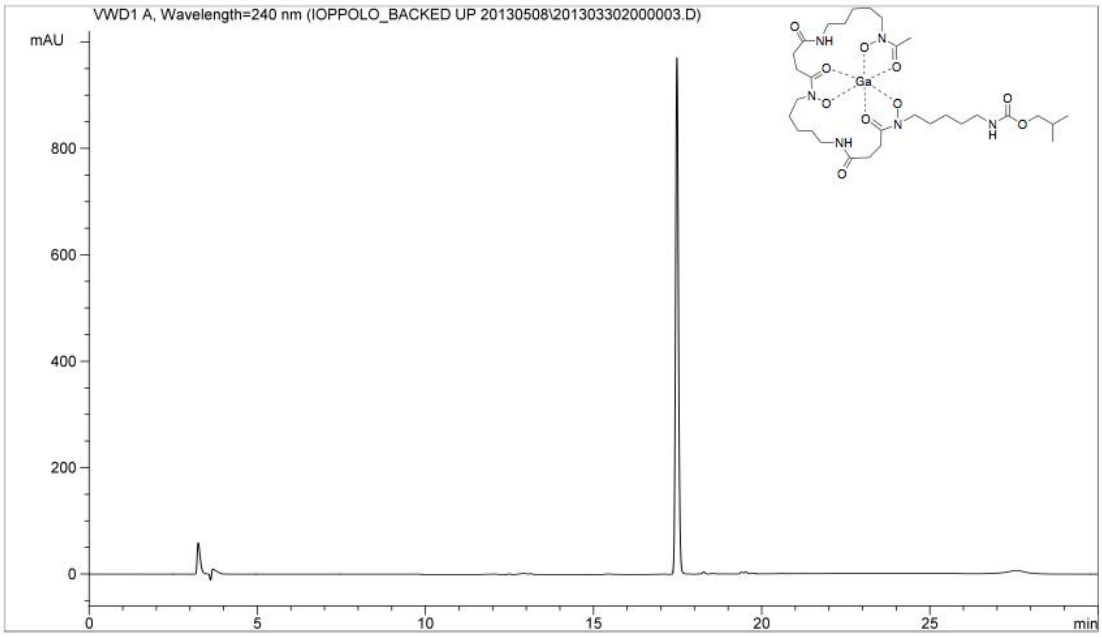


Figure S 2.85 IR spectrum of 23 (KBr pellet).

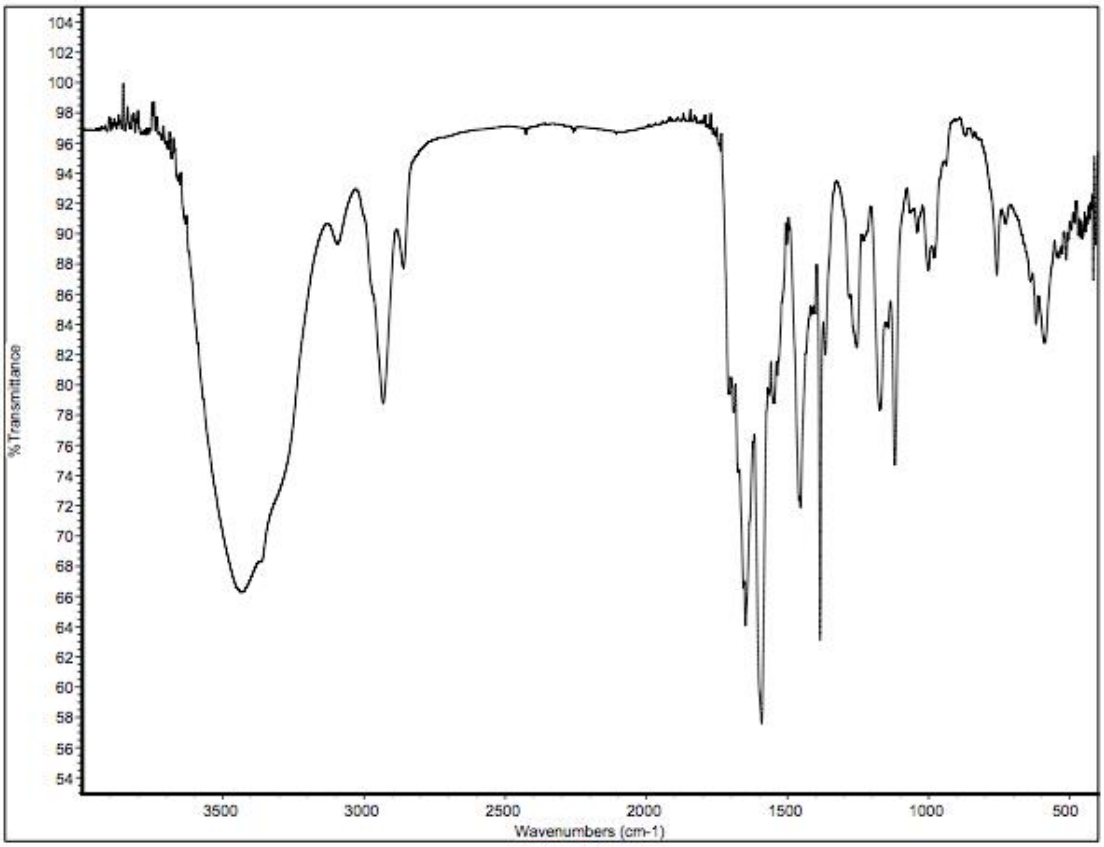


Figure S 2.86 ^{1}H NMR spectrum of **23** in DMSO-d_6 at 300 K.

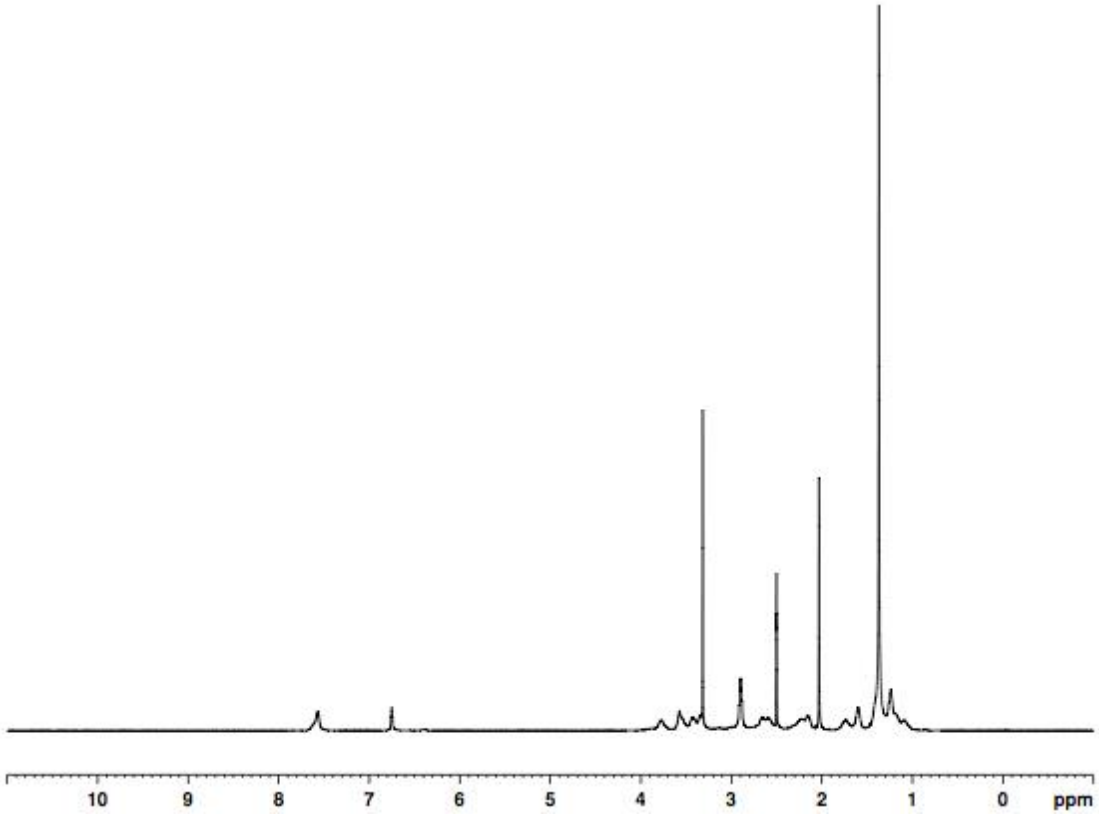


Figure S 2.87 High-resolution mass spectrum of **23**.

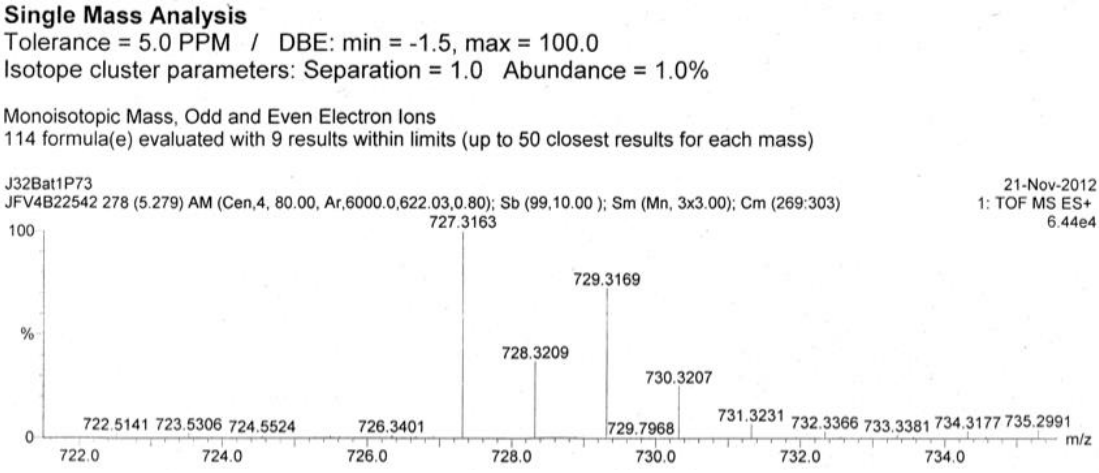


Figure S 2.88 HPLC chromatogram of **23**. UV peak at λ = 240 nm.

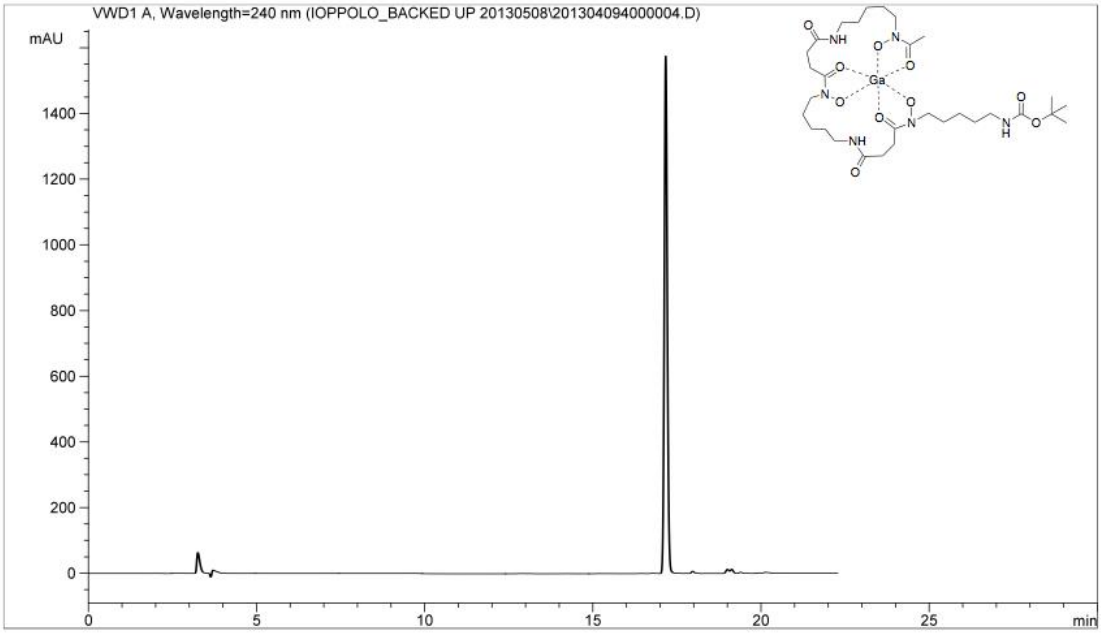


Figure S 2.89 IR spectrum of 24 (KBr pellet).

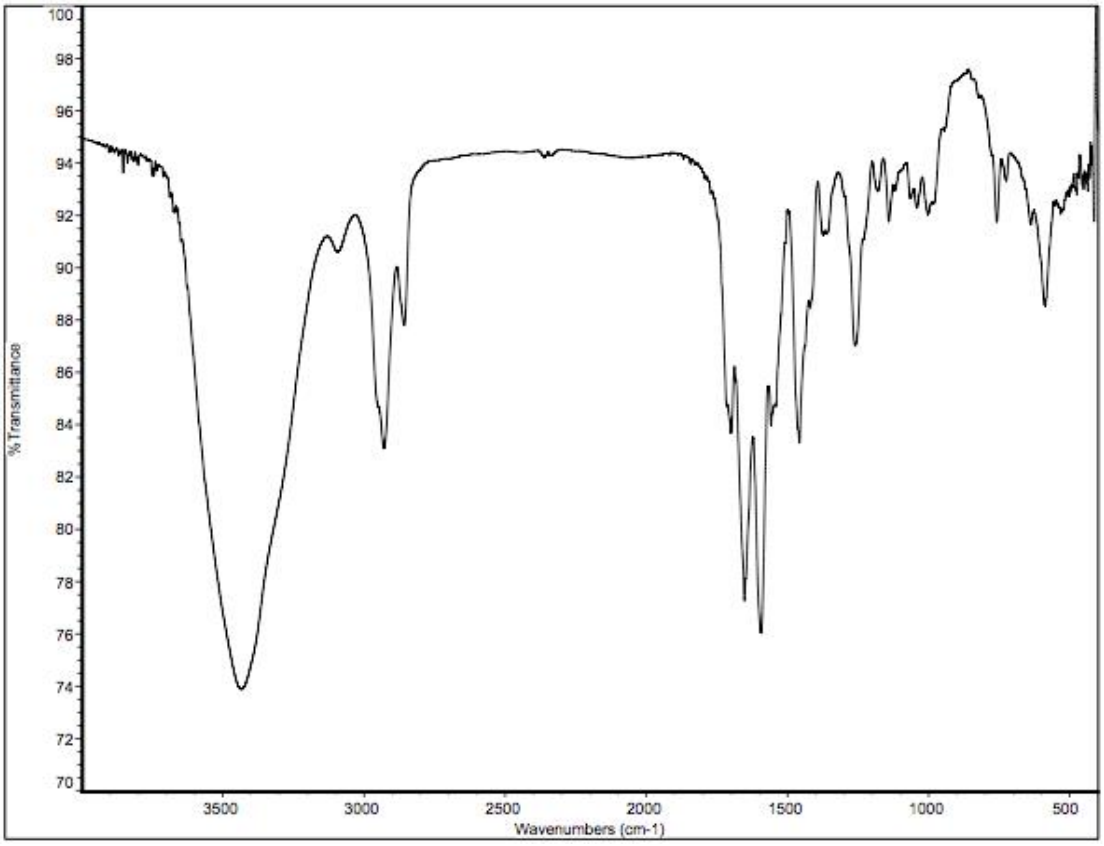


Figure S 2.90 ^{1}H NMR spectrum of **24** in DMSO-d_6 at 300 K.

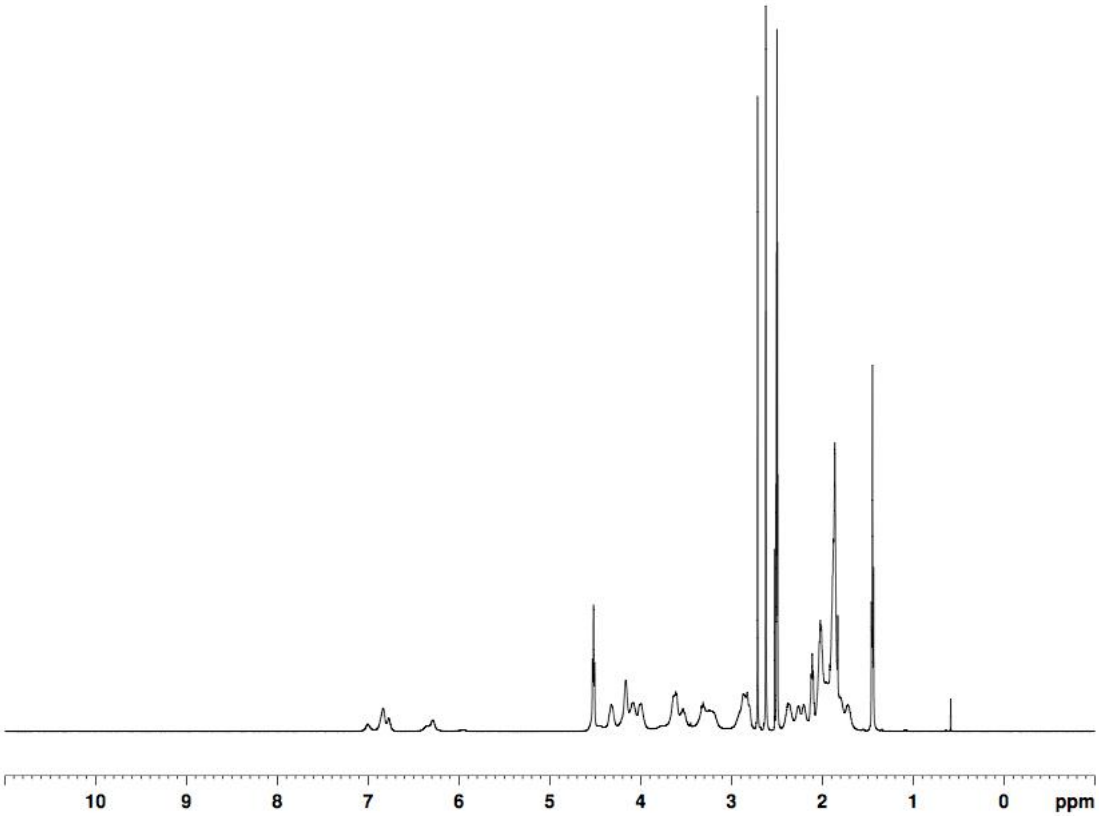
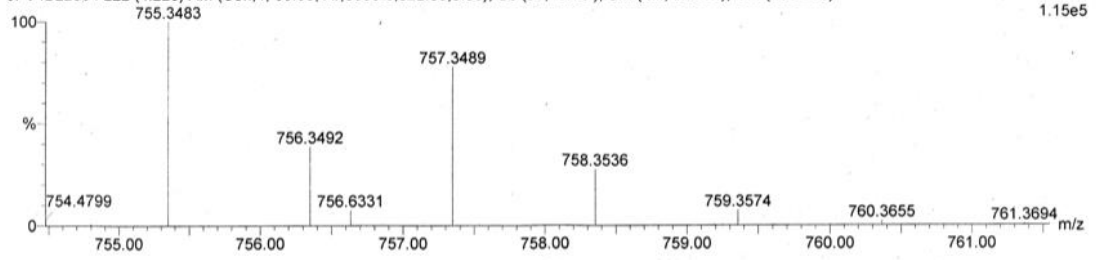


Figure S 2.91 High-resolution mass spectrum of **24**.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
296 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)

1201-2-162-01
JFV4B22804 222 (4.220) AM (Cen,4, 80.00, Ar,5000.0,622.03,0.80); Sb (99,10.00); Sm (Mn, 3x3.00); Cm (208:263)
28-Feb-2013
1: TOF MS ES+
1.15e5



Minimum:				-1.5		
Maximum:		2.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
755.3483	755.3470	1.3	1.7	7.5	1	C32 H58 N6 O10 Ga
	755.3497	-1.4	-1.9	12.0	2	C35 H56 N7 O7 Ga
	755.3510	-2.7	-3.6	11.5	3	C37 H58 N4 O8 Ga
	755.3517	-3.4	-4.5	20.5	4	C39 H47 N8 O8

Figure S 2.92HPLC chromatogram of 24. UV peak at λ = 240 nm.

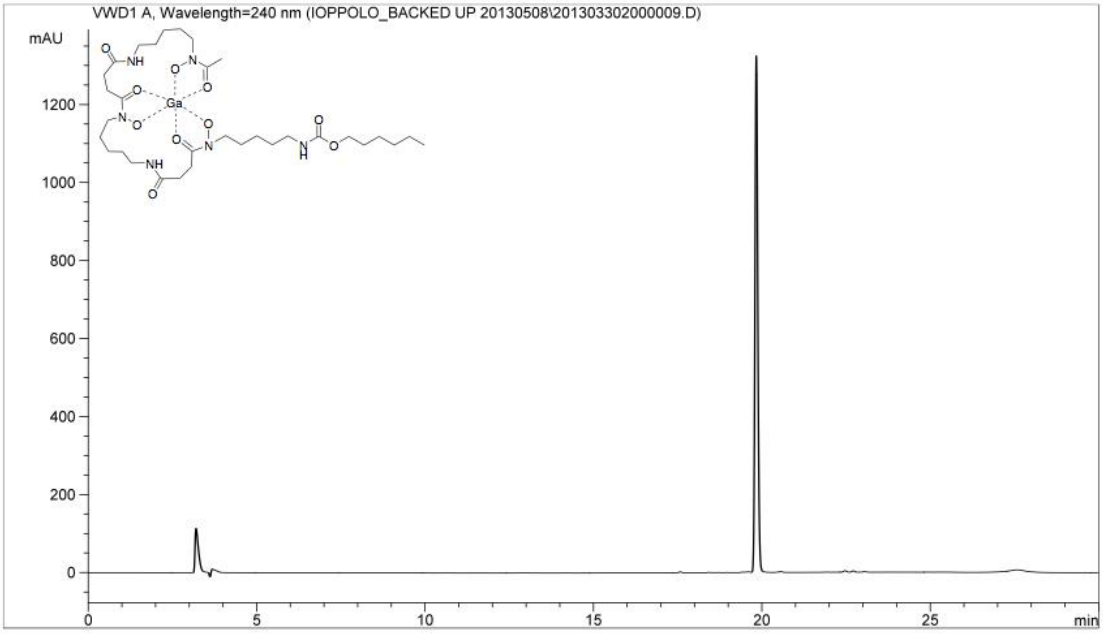


Figure S 2.93 IR spectrum of 25 (KBr pellet).

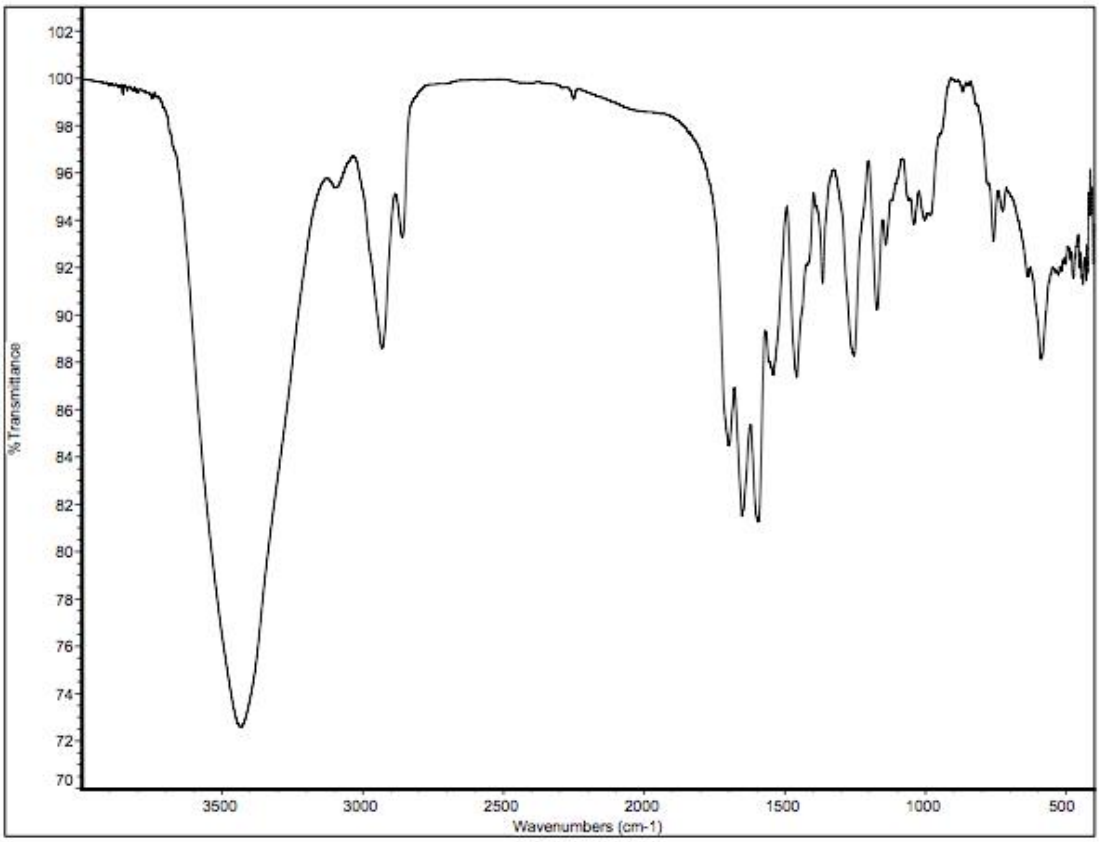


Figure S 2.94 ^{1}H NMR spectrum of 25 in DMSO-d_6 at 300 K.

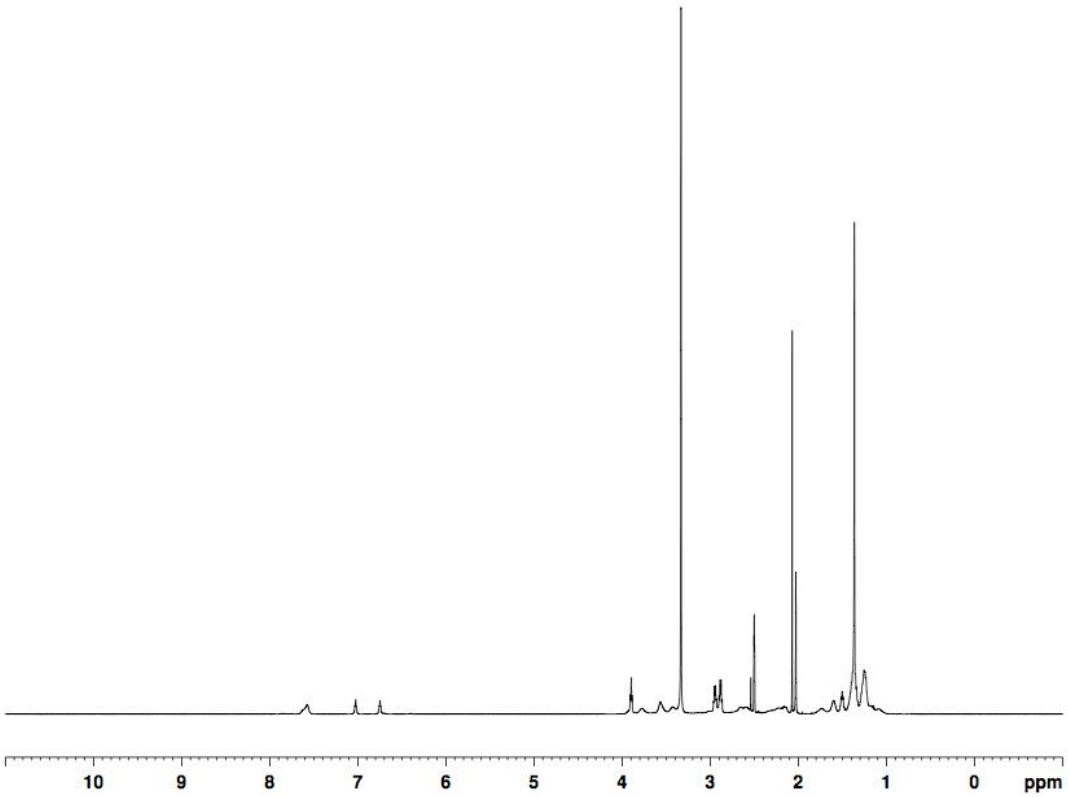


Figure S 2.95 High-resolution mass spectrum of **25**.

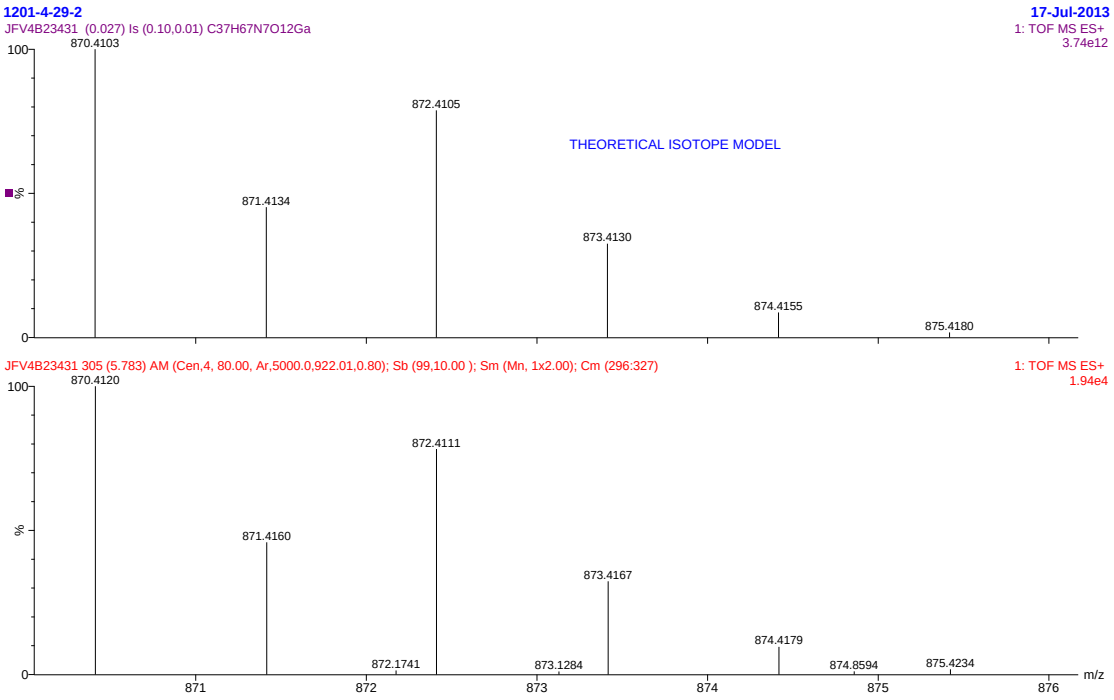


Figure S 2.96 HPLC chromatogram of 25, UV peak at λ = 240 nm.

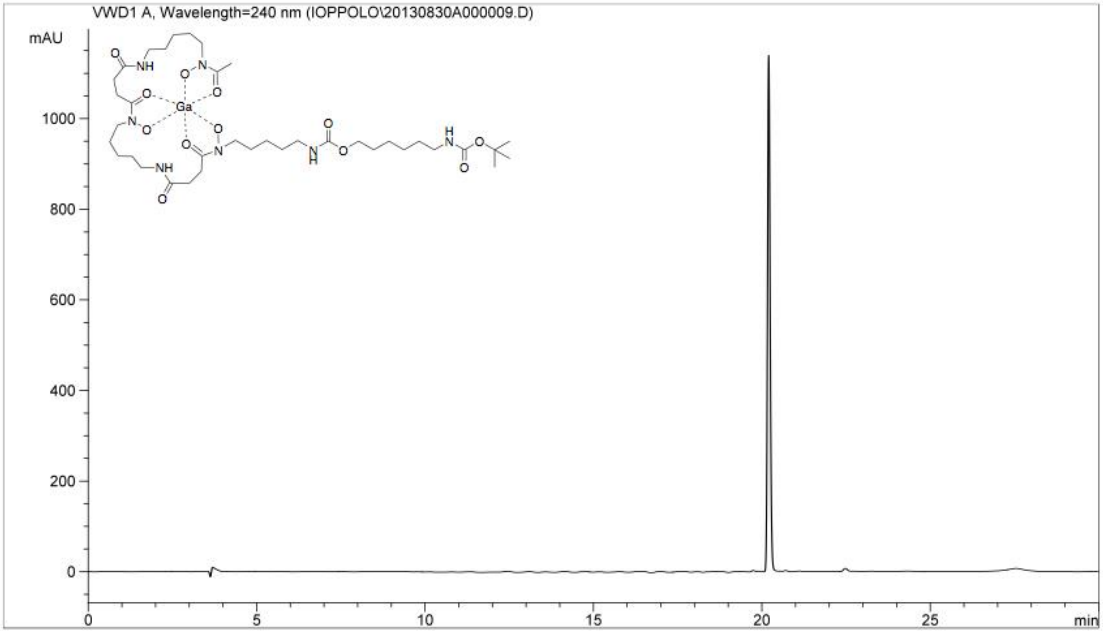


Figure S 2.97 IR spectrum of **26** (KBr pellet).

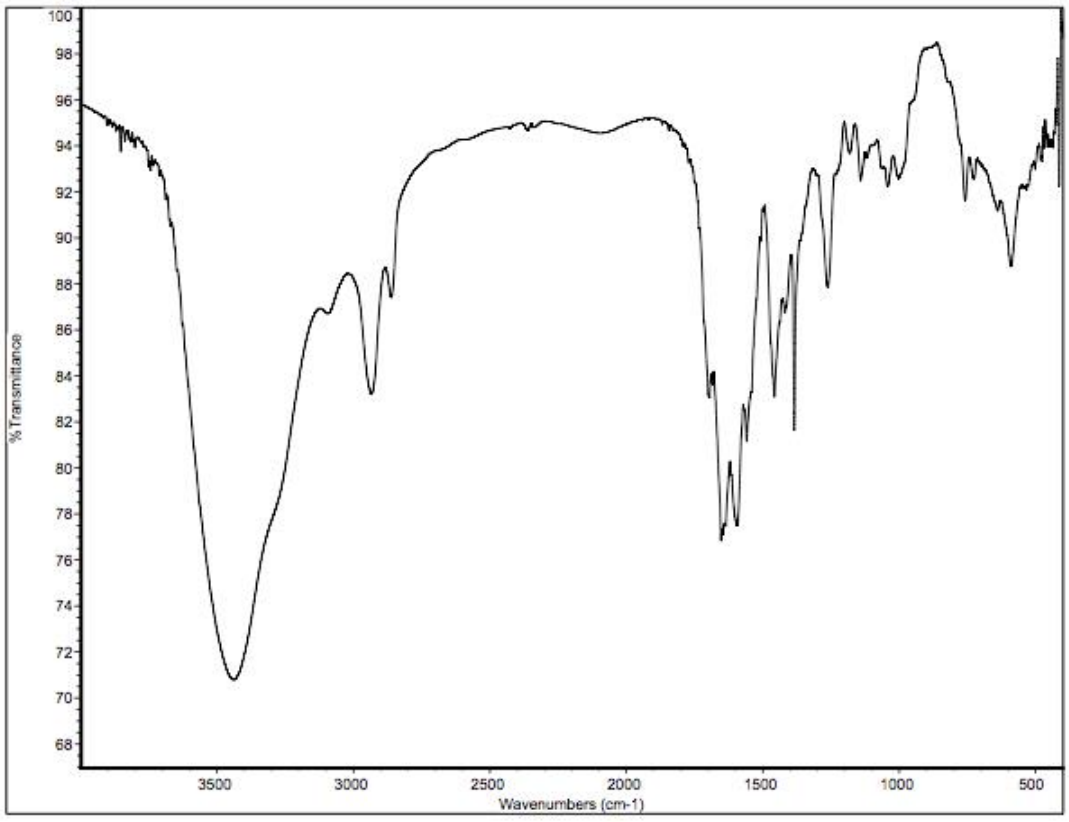


Figure S 2.98 ^{1}H NMR spectrum of **26** in DMSO-d_6 at 300 K.

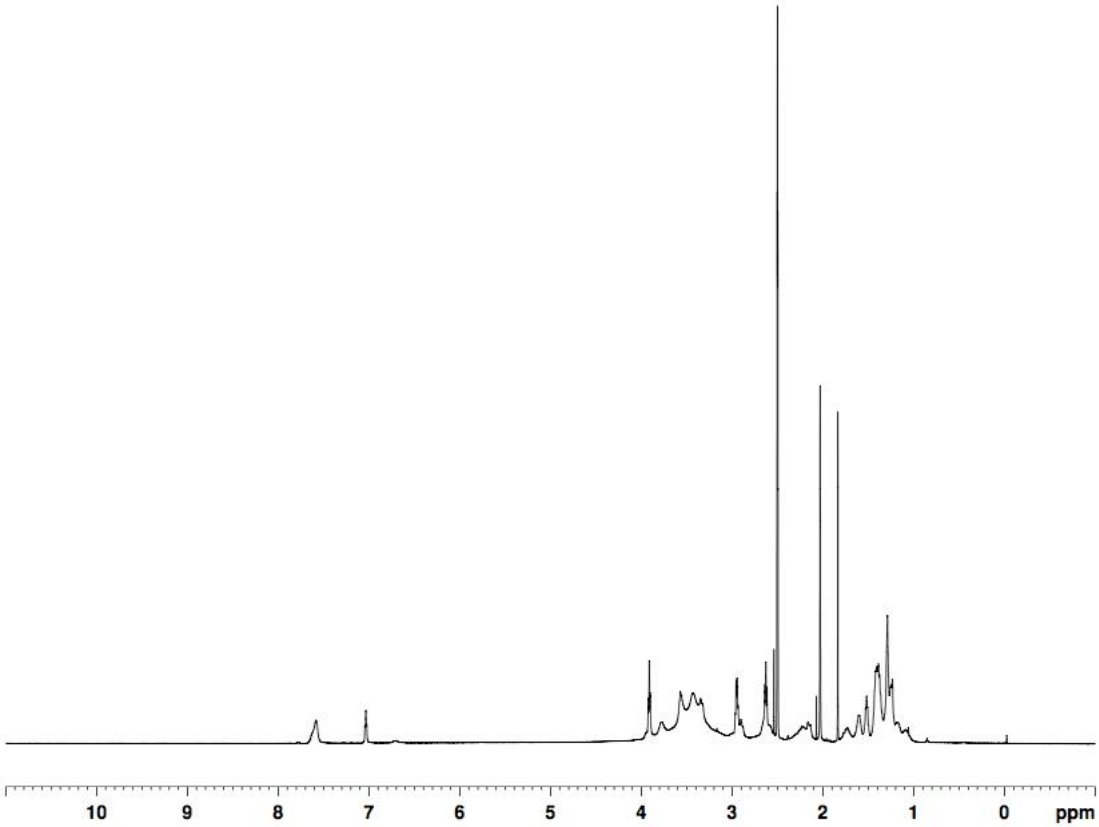


Figure S 2.99 High-resolution mass spectrum of **26**.

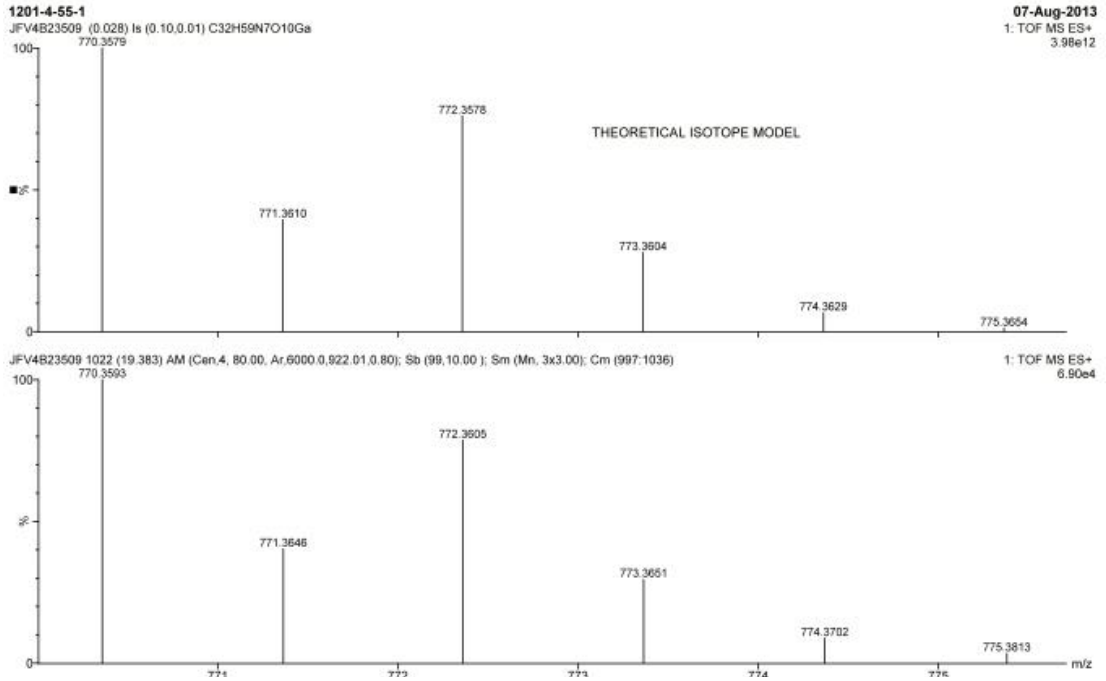


Figure S 2.100 HPLC chromatogram of **26**, UV peak at λ = 240 nm.

(Note: Injection volume contains DMSO).

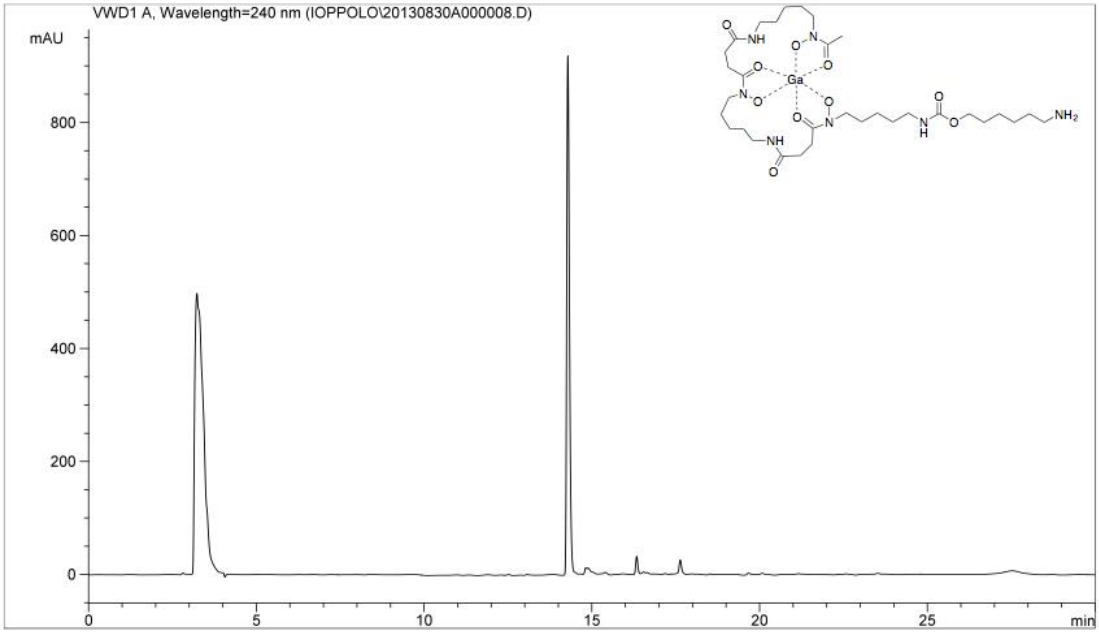


Figure S 2.101 IR spectrum of **27** (KBr pellet).

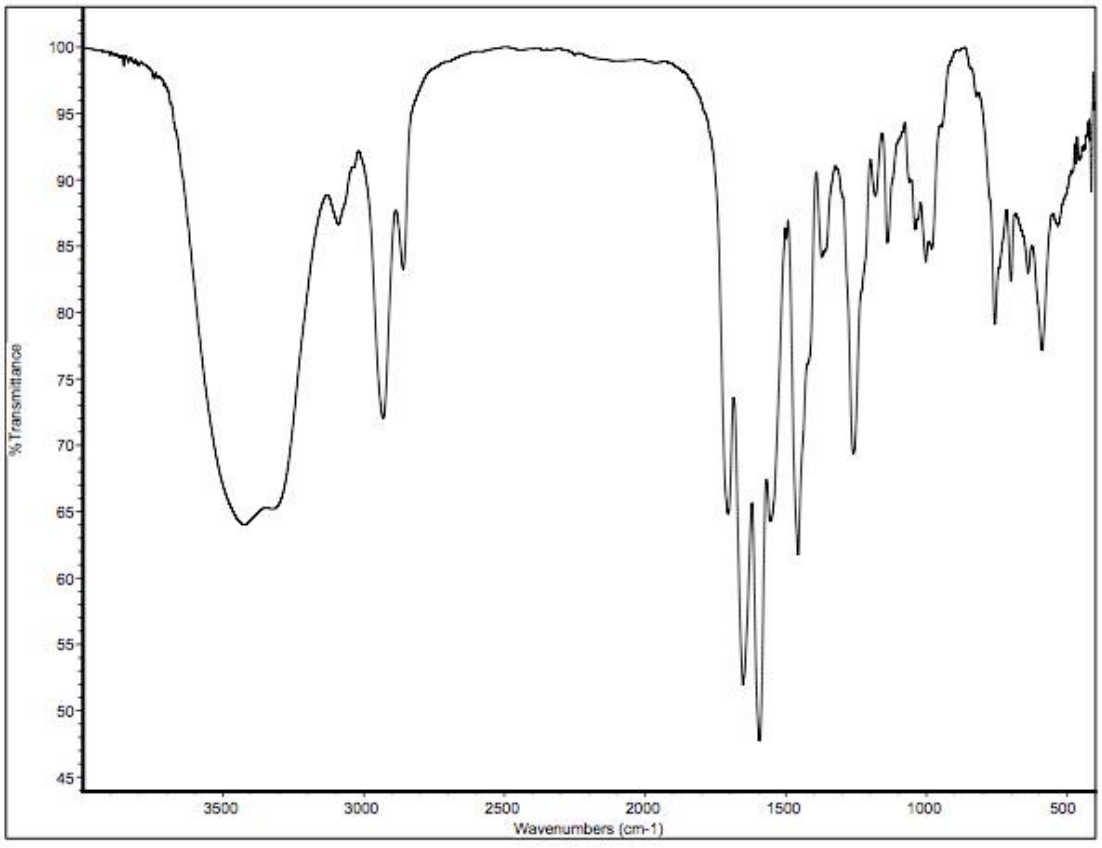


Figure S 2.102 ^{1}H NMR spectrum of **27** in DMSO-d_6 at 300 K.

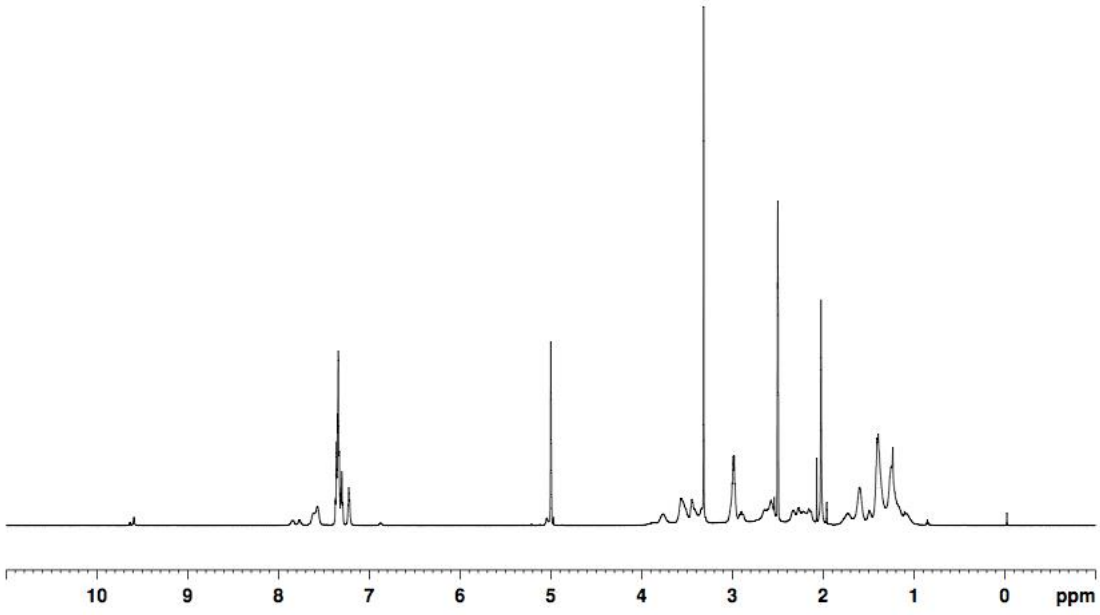


Figure S 2.103 High-resolution mass spectrum of **27**.

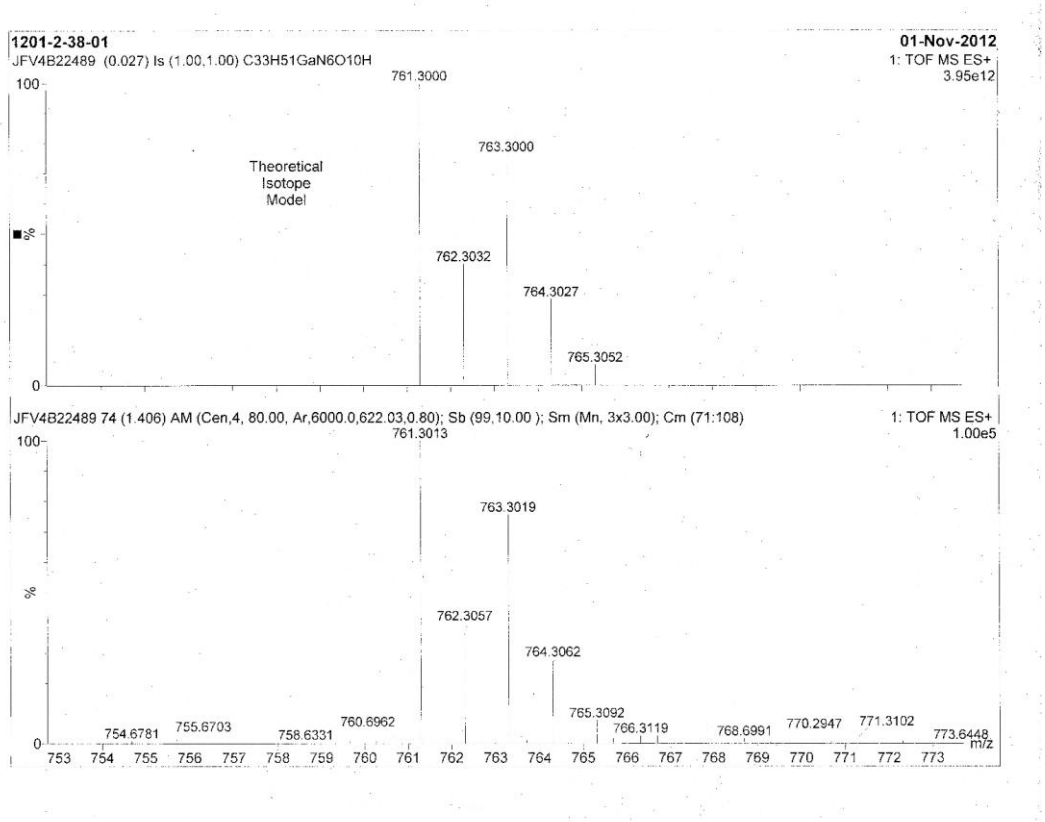


Figure S 2.104 HPLC chromatogram of 27. UV peak at λ = 240 nm.

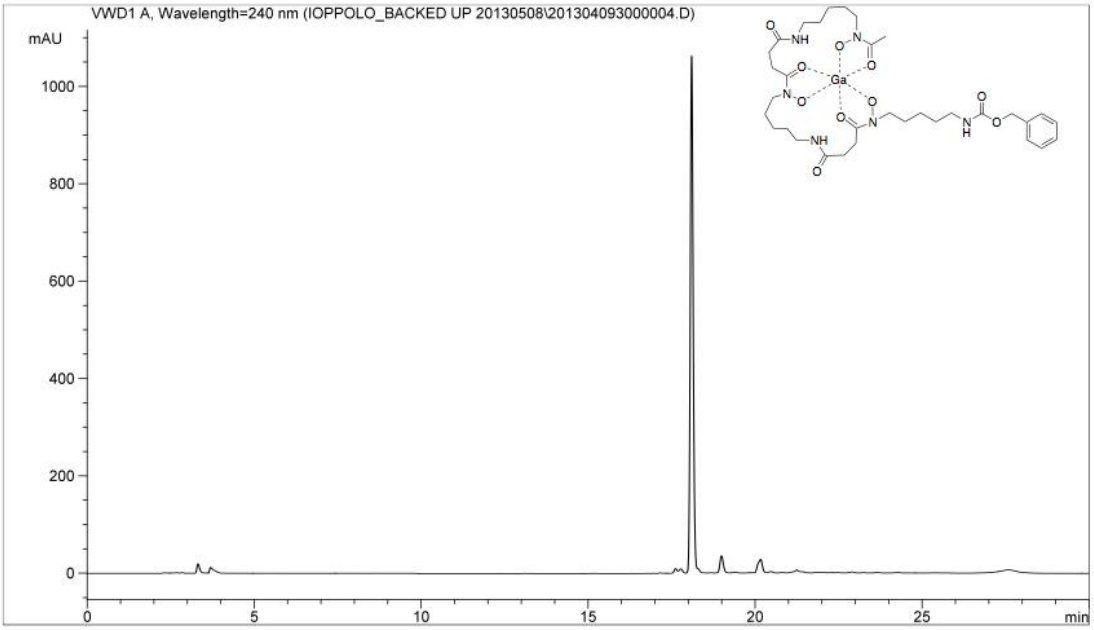


Figure S 2.105 IR spectrum of 28 (KBr pellet).

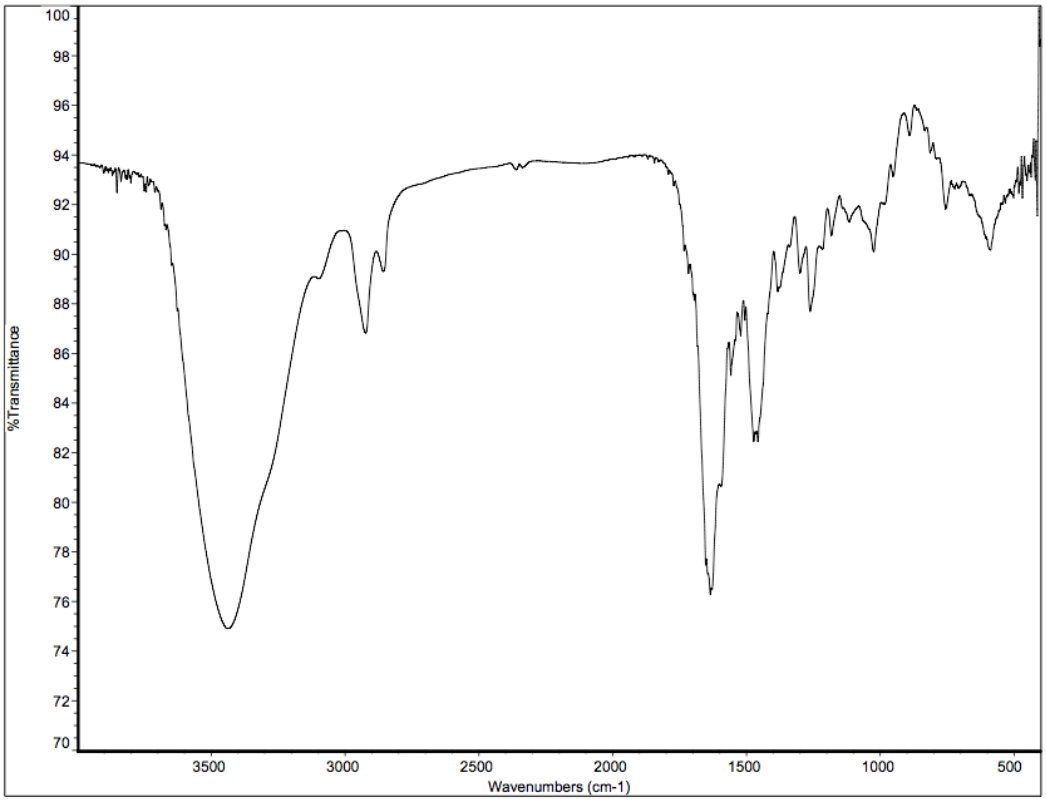


Figure S 2.106 ^{1}H NMR spectrum of 28 in DMSO-d_6 at 300 K.

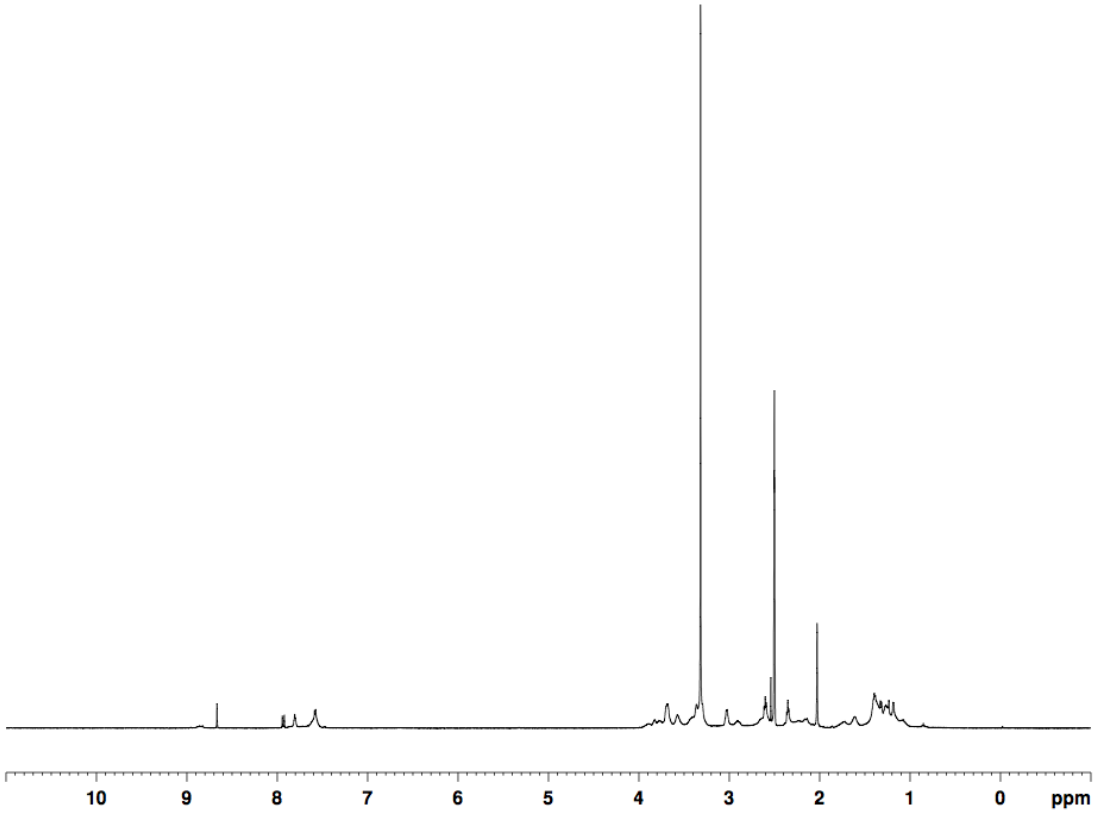


Figure S 2.107 High-resolution mass spectrum of **28**.

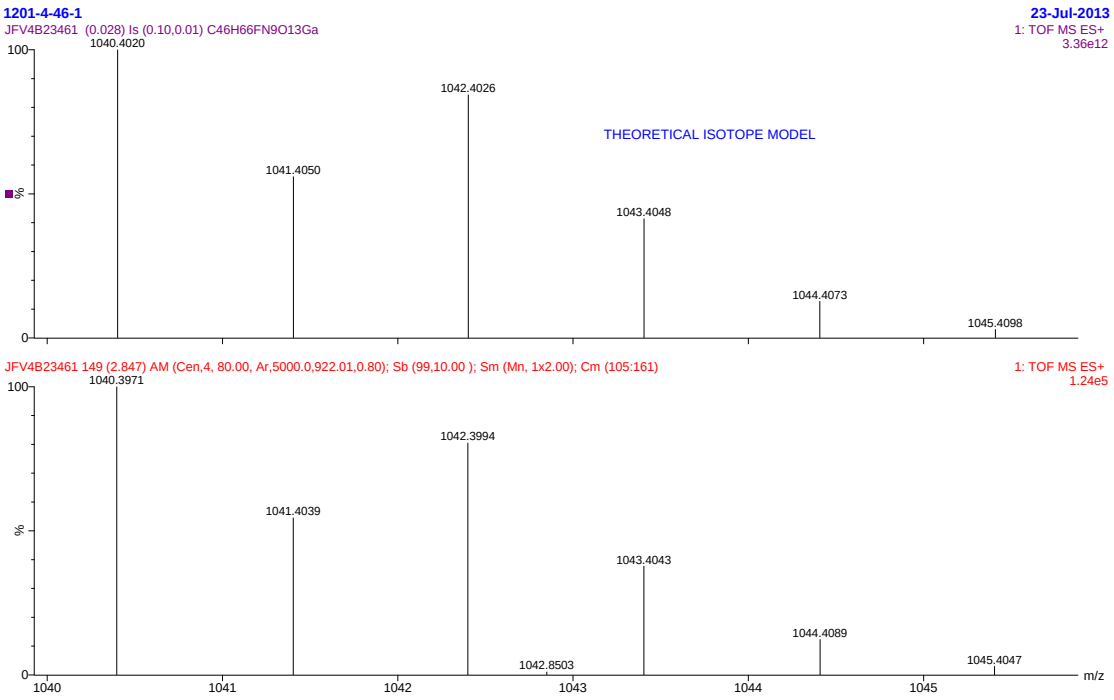


Figure S 2.108 HPLC chromatogram of 28, UV peak at λ = 240 nm.

(Note: Injection volume contains DMSO).

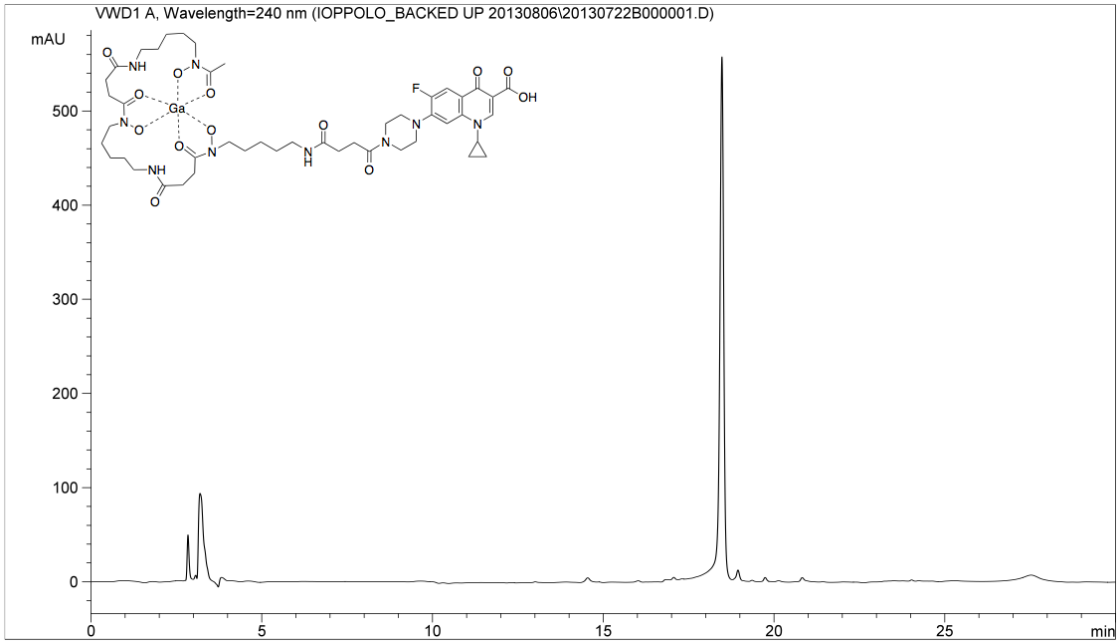


Figure S 2.109 HPLC chromatograms of [^{67}Ga]-**16** with cold **16** co-injection.
Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

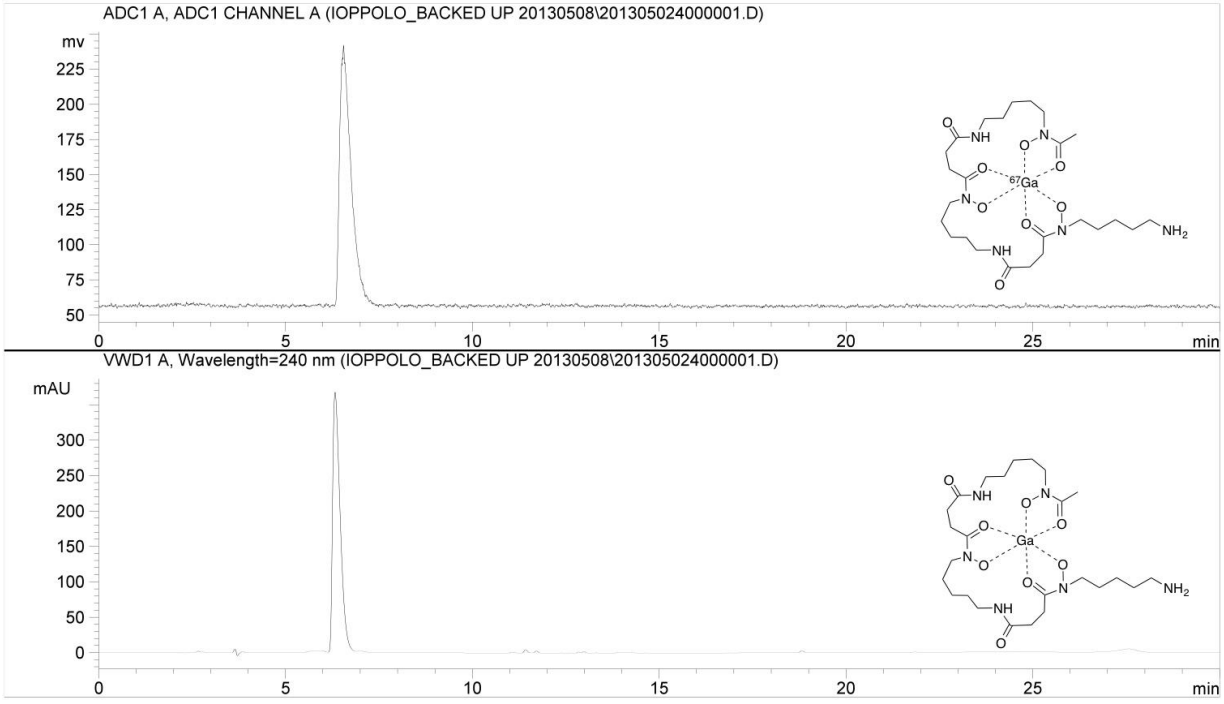


Figure S 2.110 HPLC chromatograms of [^{67}Ga]-**17** with cold **17** co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

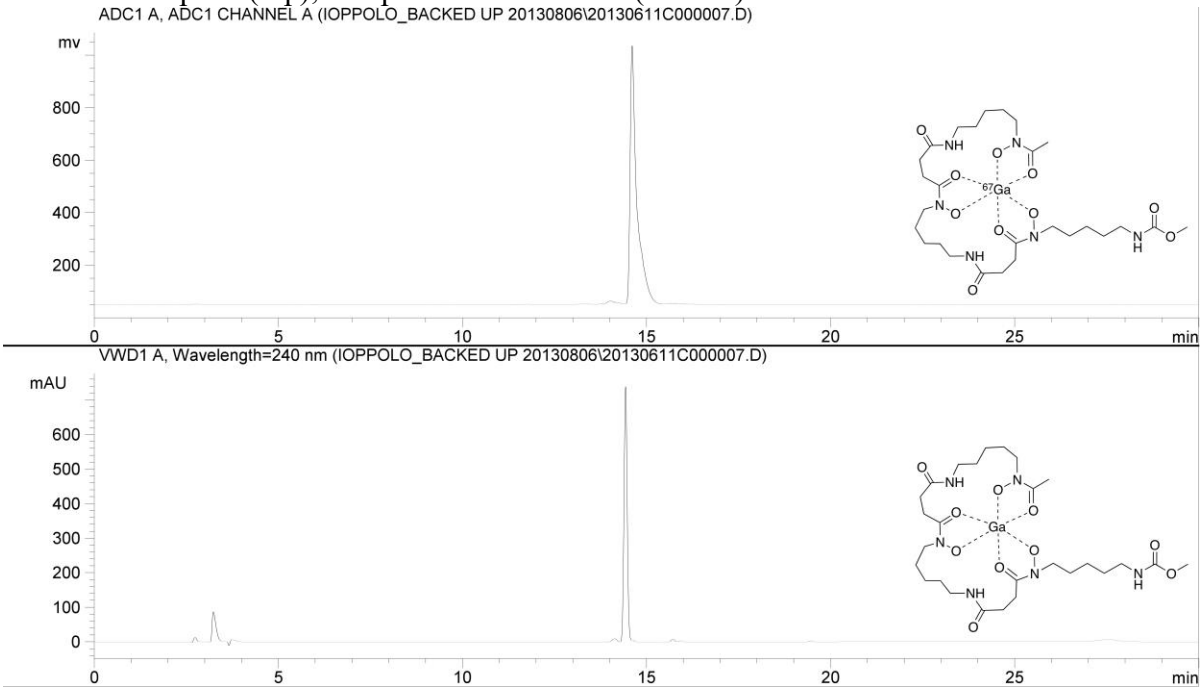


Figure S 2.111 HPLC chromatograms of [^{67}Ga]-18 with 18 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

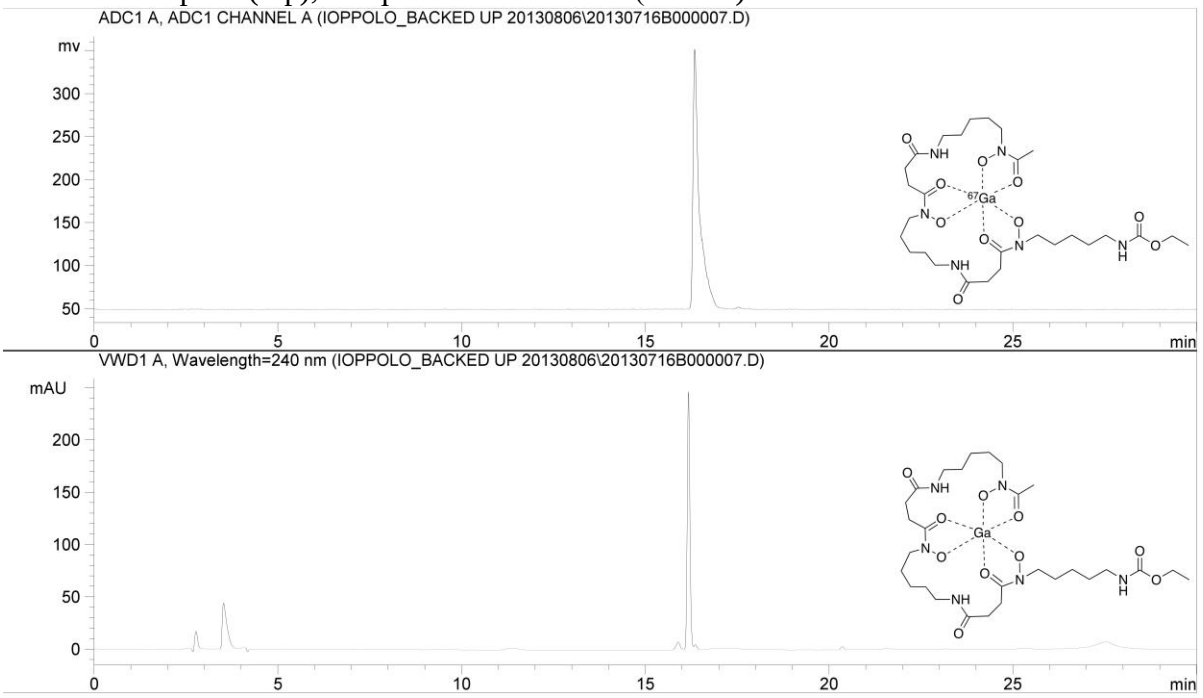


Figure S 2.112 HPLC chromatograms of [^{67}Ga]-**19** with cold **19** co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

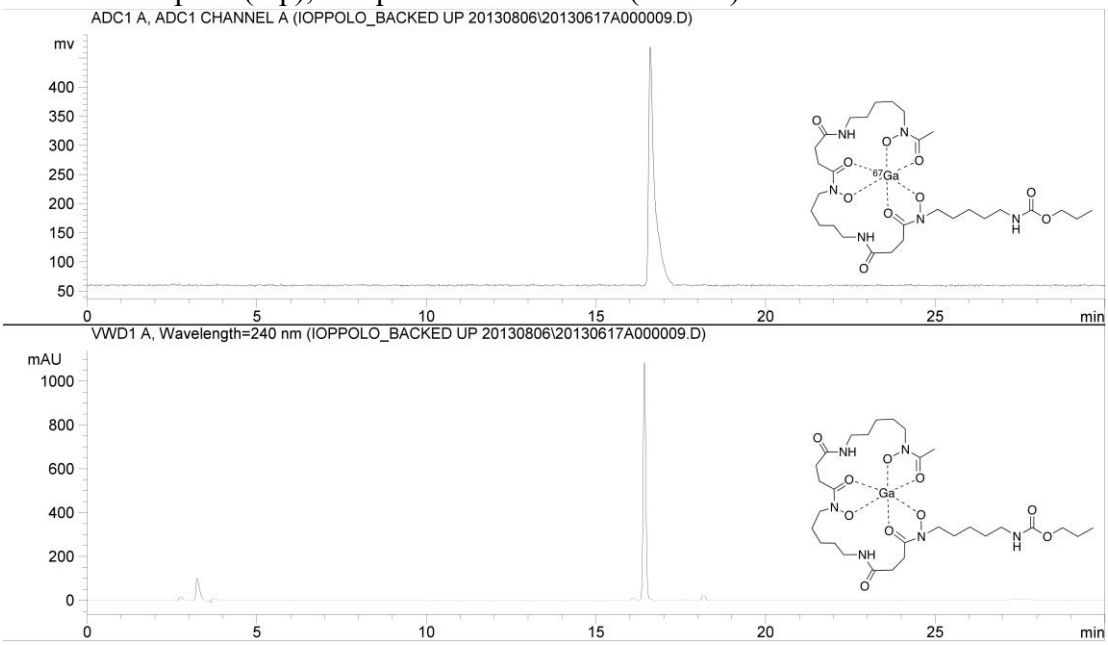


Figure S 2.113 HPLC chromatograms of [^{67}Ga]-20 with cold 20 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

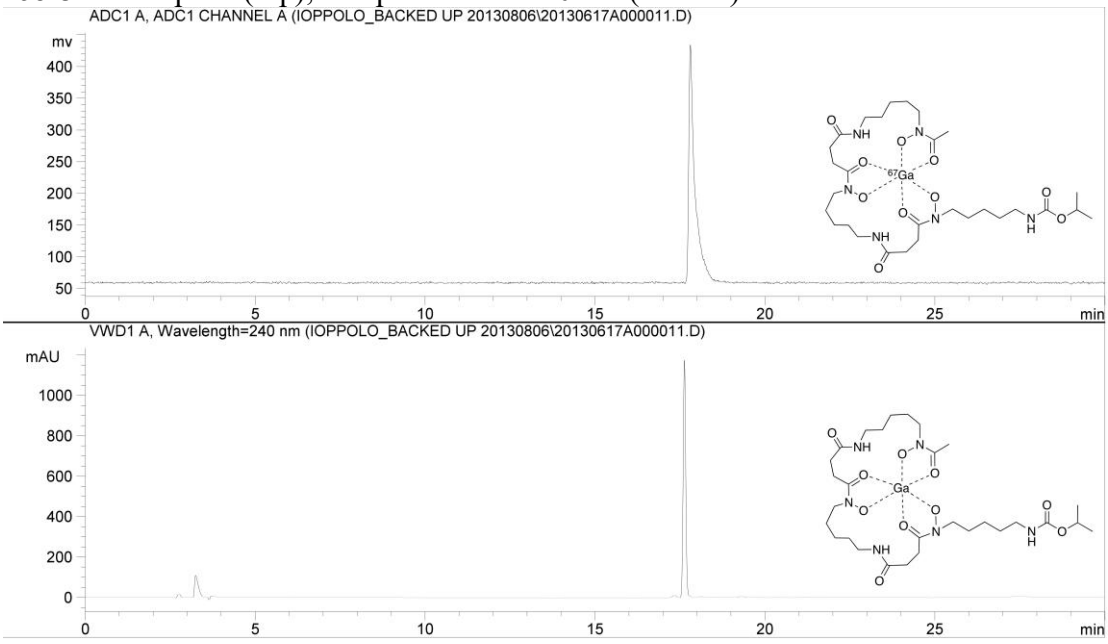


Figure S 2.114 HPLC chromatograms of [^{67}Ga]-**21** with cold **21** co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

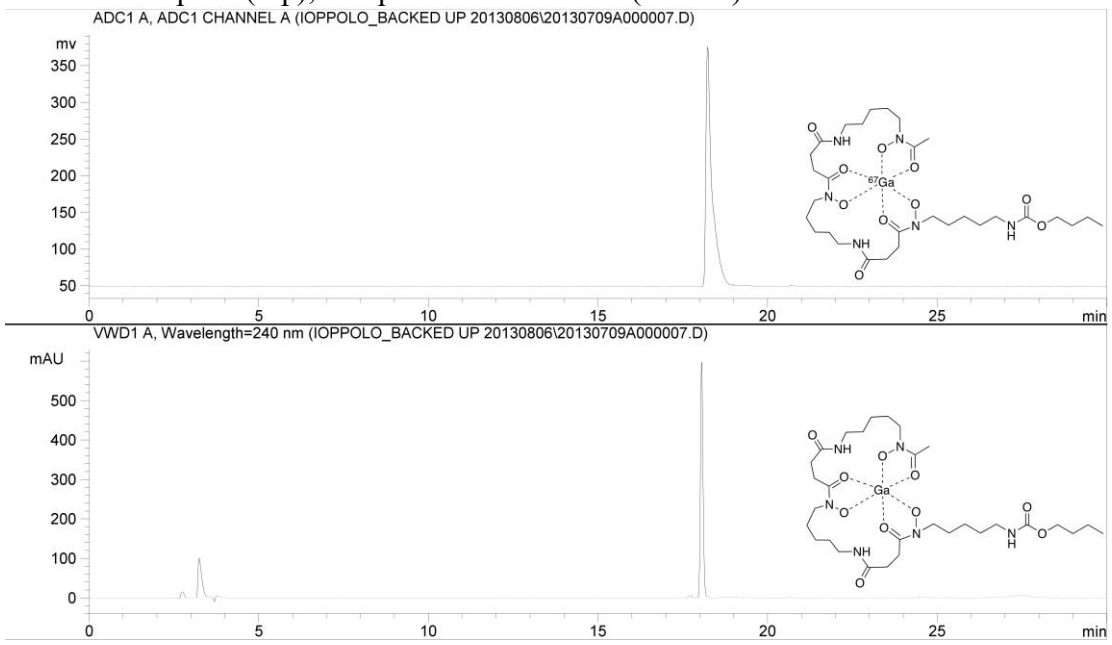


Figure S 2.115 HPLC chromatograms of [^{67}Ga]-22 with cold 22 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

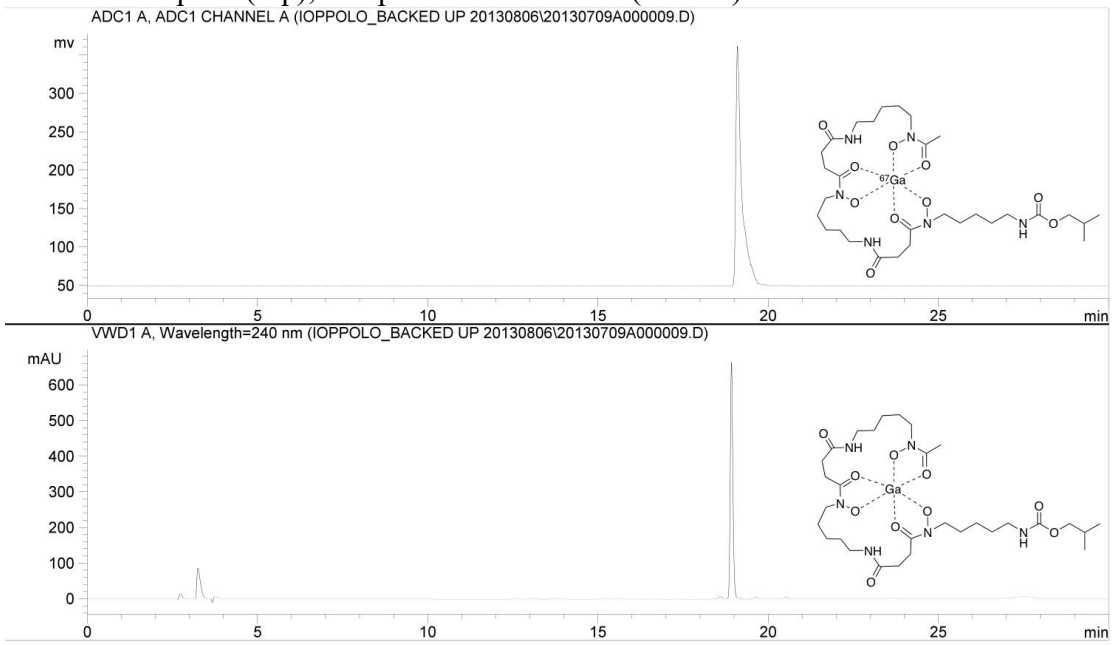


Figure S 2.116 HPLC chromatograms of [^{67}Ga]-23 with cold 23 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

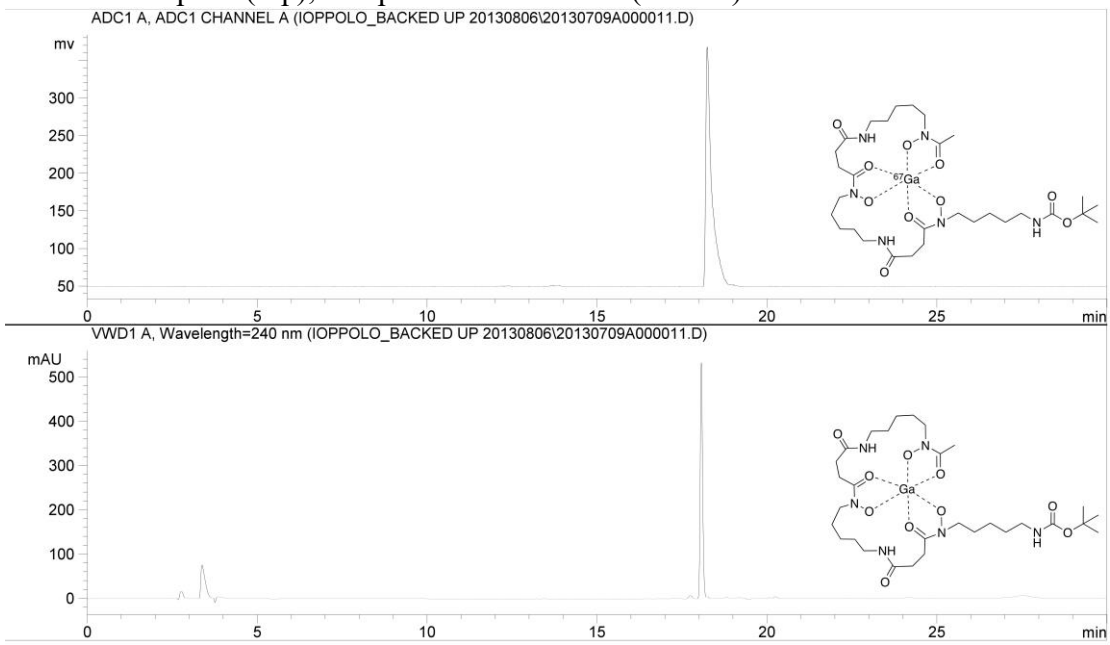


Figure S 2.117 HPLC chromatograms of [^{67}Ga]-**24** with cold **24** co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

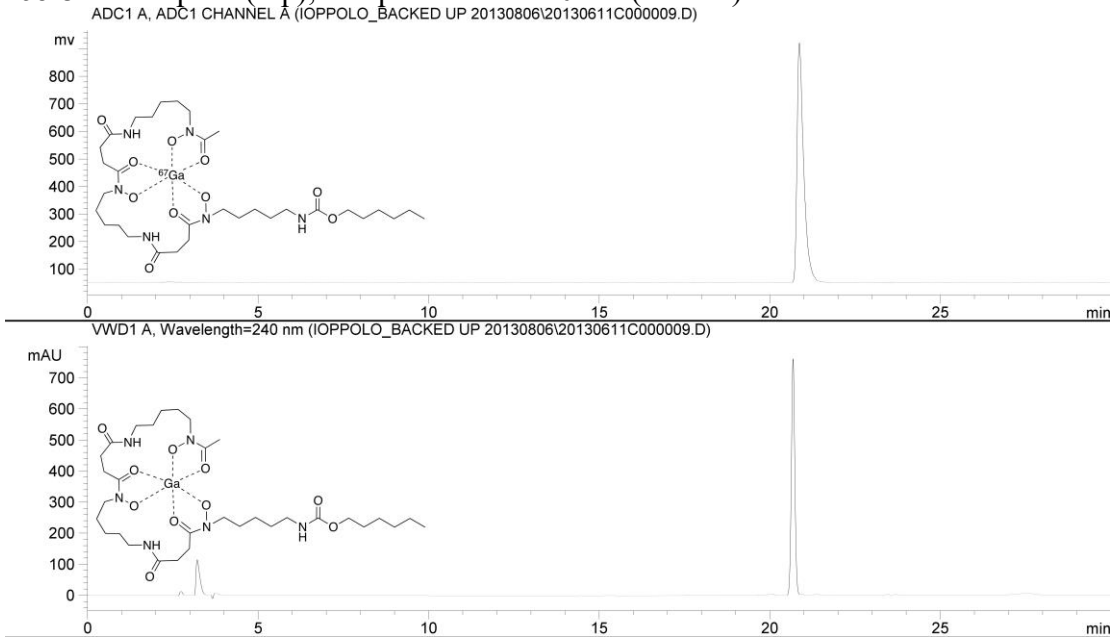


Figure S 2.118 HPLC chromatograms of [^{67}Ga]-**25** with cold **25** co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

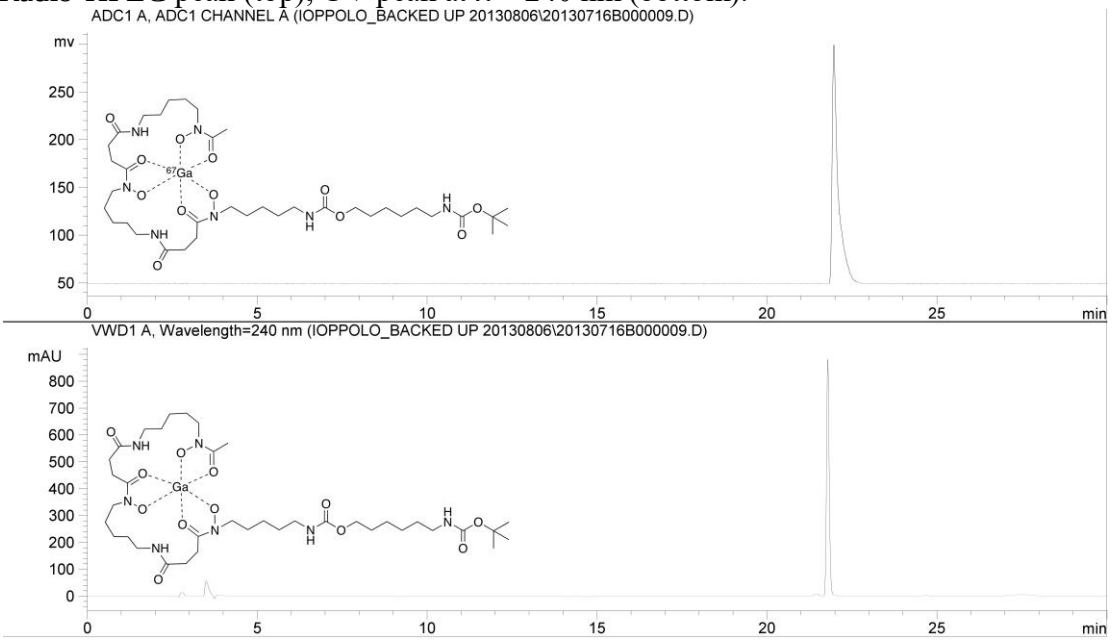


Figure S 2.119 HPLC chromatograms of [^{67}Ga]- 26 with cold 26 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

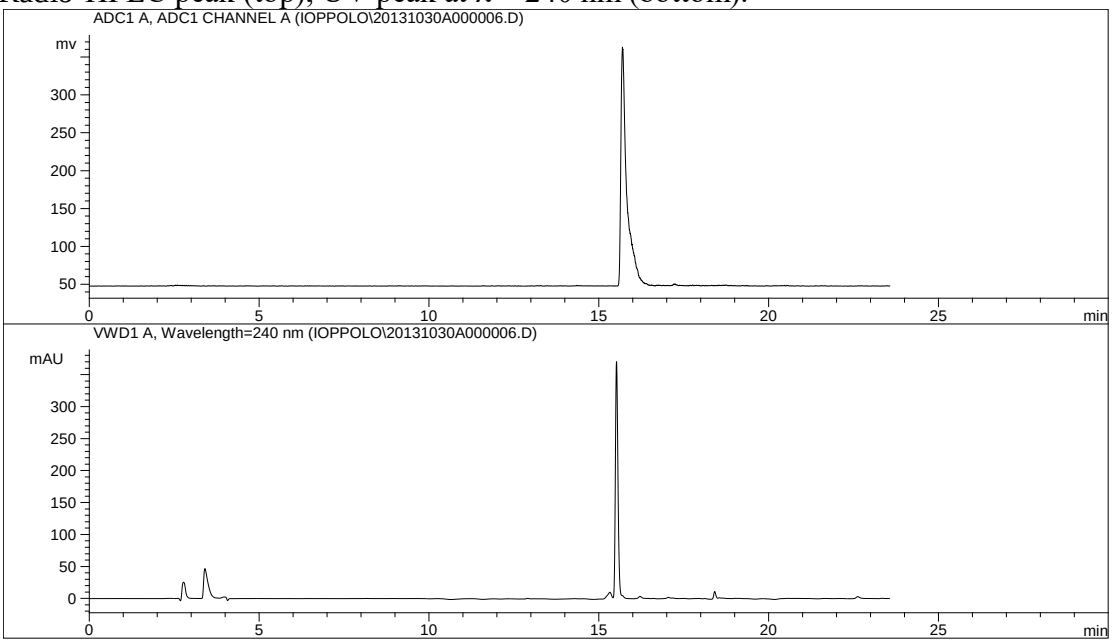


Figure S 2.120 HPLC chromatograms of [^{67}Ga]- 27 with cold 27 co-injection.

Radio-HPLC peak (top), UV peak at λ = 240 nm.

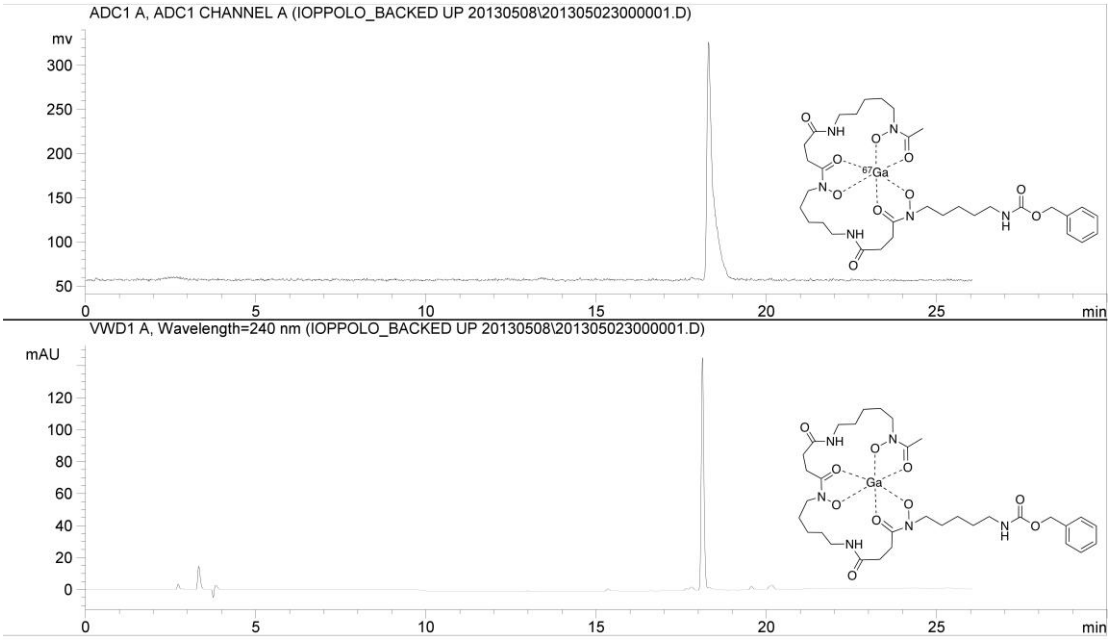


Figure S 2.121 HPLC chromatograms of [^{67}Ga]- 28 with cold 28 co-injection.

Radio-H PLC peak (top), UV peak at λ = 240 nm.

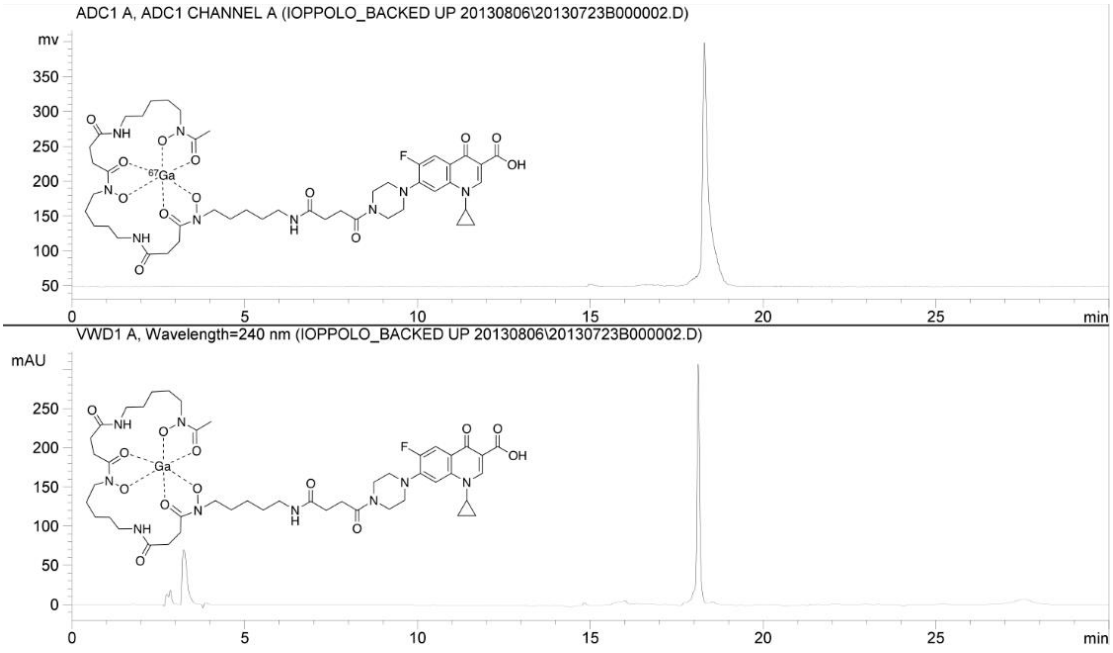


Figure S 2.122 *In vitro* uptake of ^{67}Ga-deferoxamine compounds by *S. aureus* over time.

Note that time zero represents samples processed immediately following the addition of the radioactive material. All experiments were performed in duplicate.

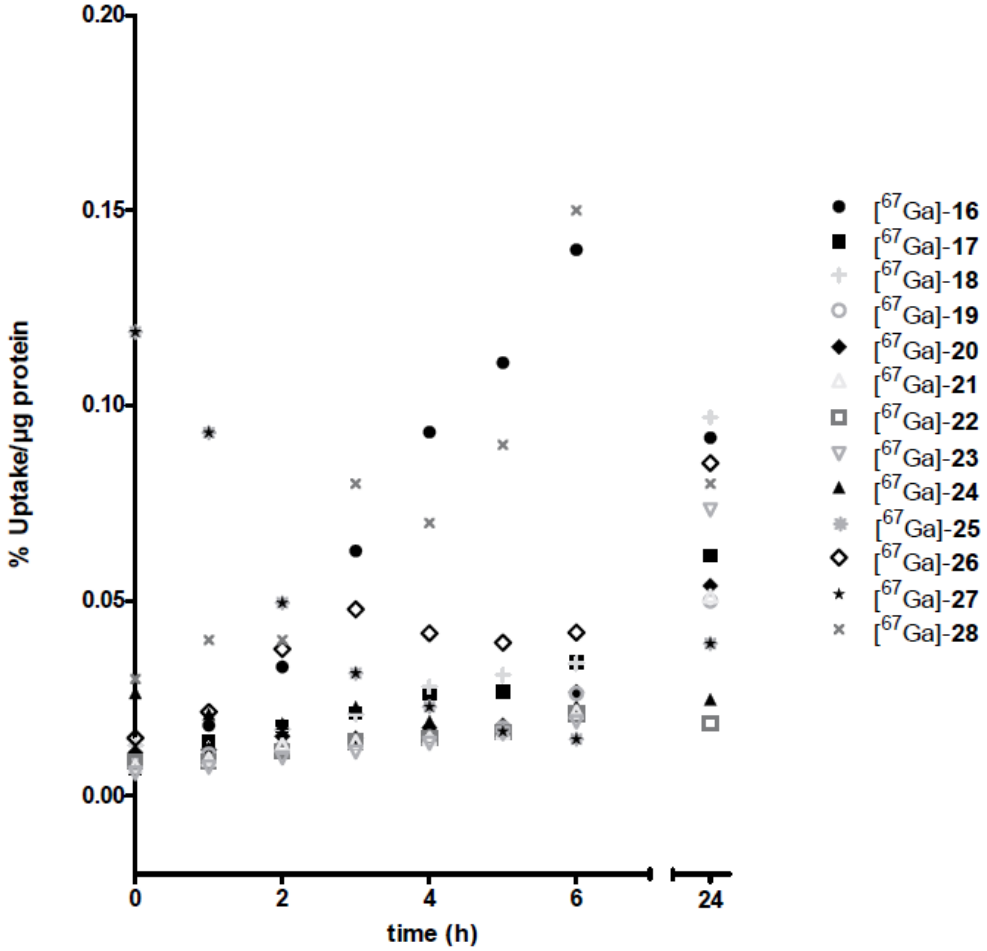


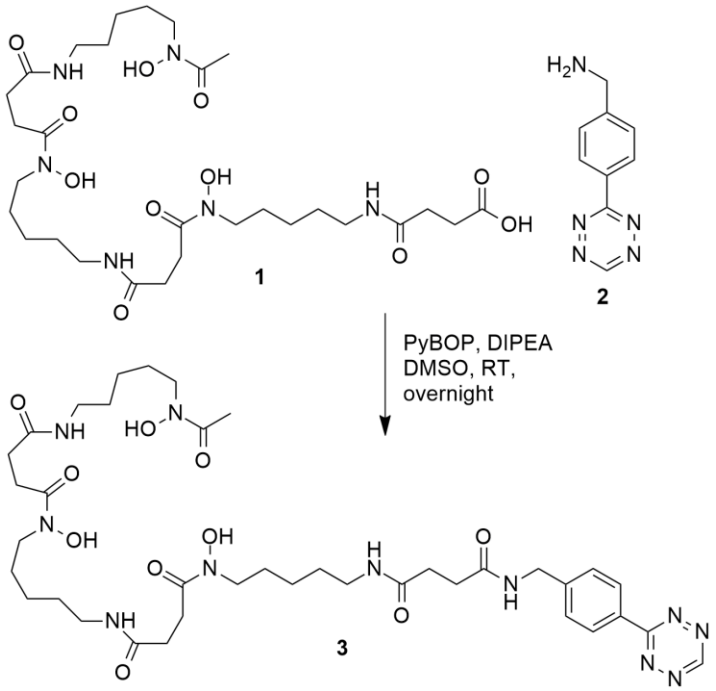
Table S 2-1Percent injected dose per gram (%ID/g) for select tissues and fluids obtained from the biodistribution of [^{67}Ga]-16, [^{67}Ga]-18, [^{67}Ga]- 26 and [^{67}Ga]- 28 in *S. aureus* murine models at 1 h p.i.

Data are expressed as mean ± SEM (n=3).

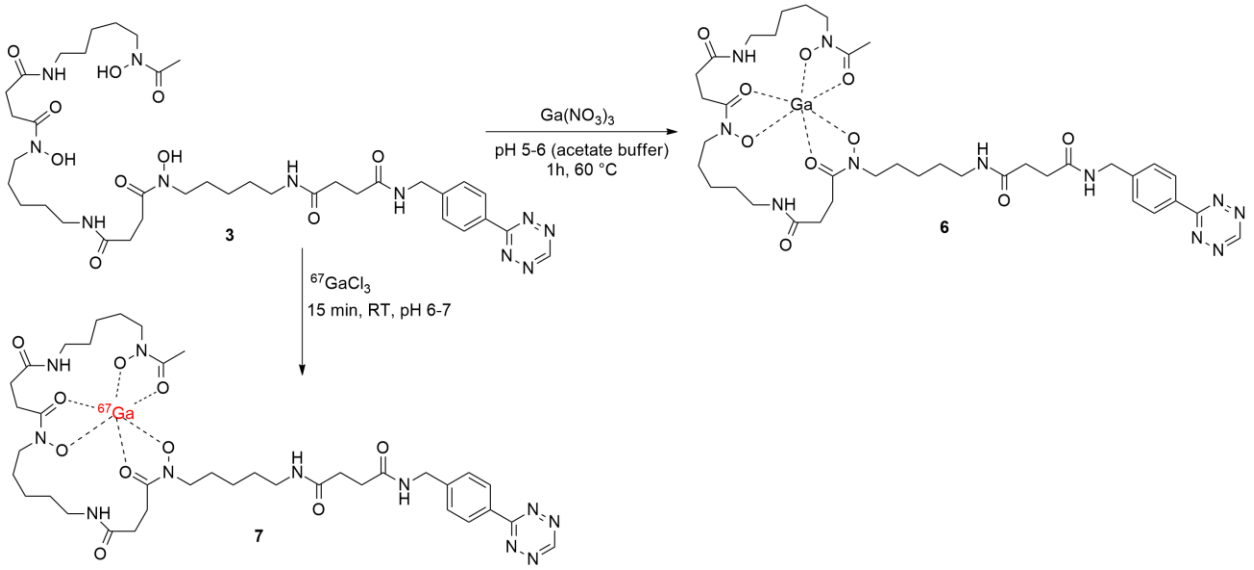
Organs	^{67}Ga-**16**	^{67}Ga-**18**	^{67}Ga-**26**	^{67}Ga-**28**
Blood	0.07 ± 0.01	0.05 ± 0.00	0.06 ± 0.00	0.47 ± 0.37
Kidneys + Adrenals	1.75 ± 0.25	0.10 ± 0.01	4.38 ± 0.06	0.39 ± 0.05
Liver + Gall Bladder	0.11 ± 0.01	2.95 ± 0.57	3.49 ± 0.73	2.33 ± 1.08
Lymph Nodes	0.32 ± 0.16	0.06 ± 0.03	1.65 ± 0.27	0.19 ± 0.06
Small Intestine	0.63 ± 0.11	30.04 ± 2.45	46.24 ± 3.02	46.27 ± 2.69
Spleen	0.12 ± 0.01	0.04 ± 0.00	0.10 ± 0.02	0.11 ± 0.02
Calf Muscle (Left)	0.07 ± 0.01	0.02 ± 0.00	0.13 ± 0.03	0.14 ± 0.03
Calf Muscle (Right)	0.46 ± 0.12	0.28 ± 0.11	0.30 ± 0.07	0.26 ± 0.05
Urine + Bladder	381.75 ± 107.15	229.96 ± 64.17	862.37 ± 355.58	255.65 ± 85.39

Chapter 3

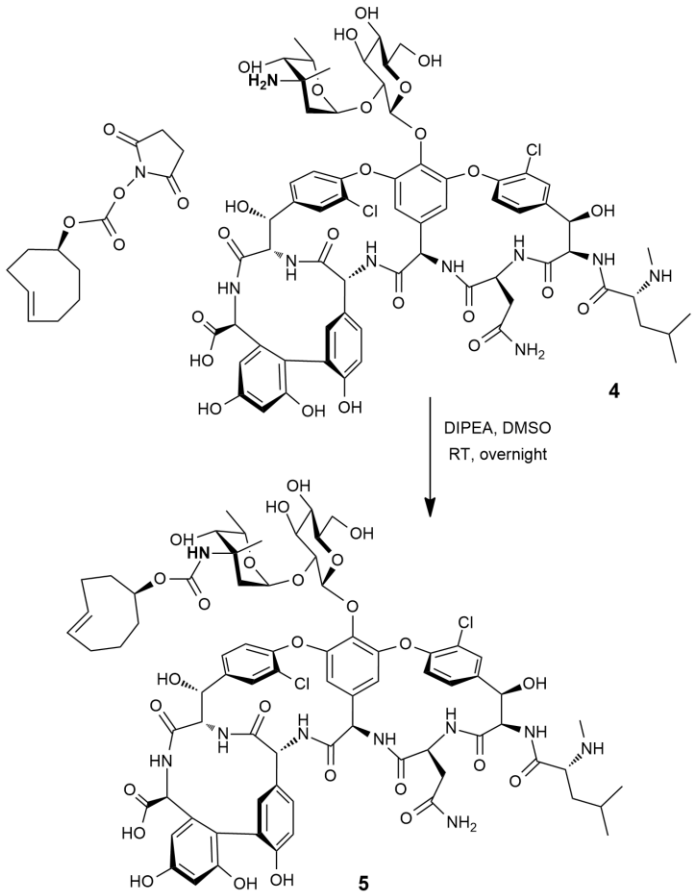
Scheme S 3-1 Preparation of DFOTz



Scheme S 3-2 Preparation of GaDFO-Tz **6** and ^{67}GaDFO-Tz **7** complexes.



Scheme S 3-3 Preparation of Vanco-TCO **5**.



Scheme S 3-4 Preparation of ^{67}GaDFO-Tz conjugate **8** complex.

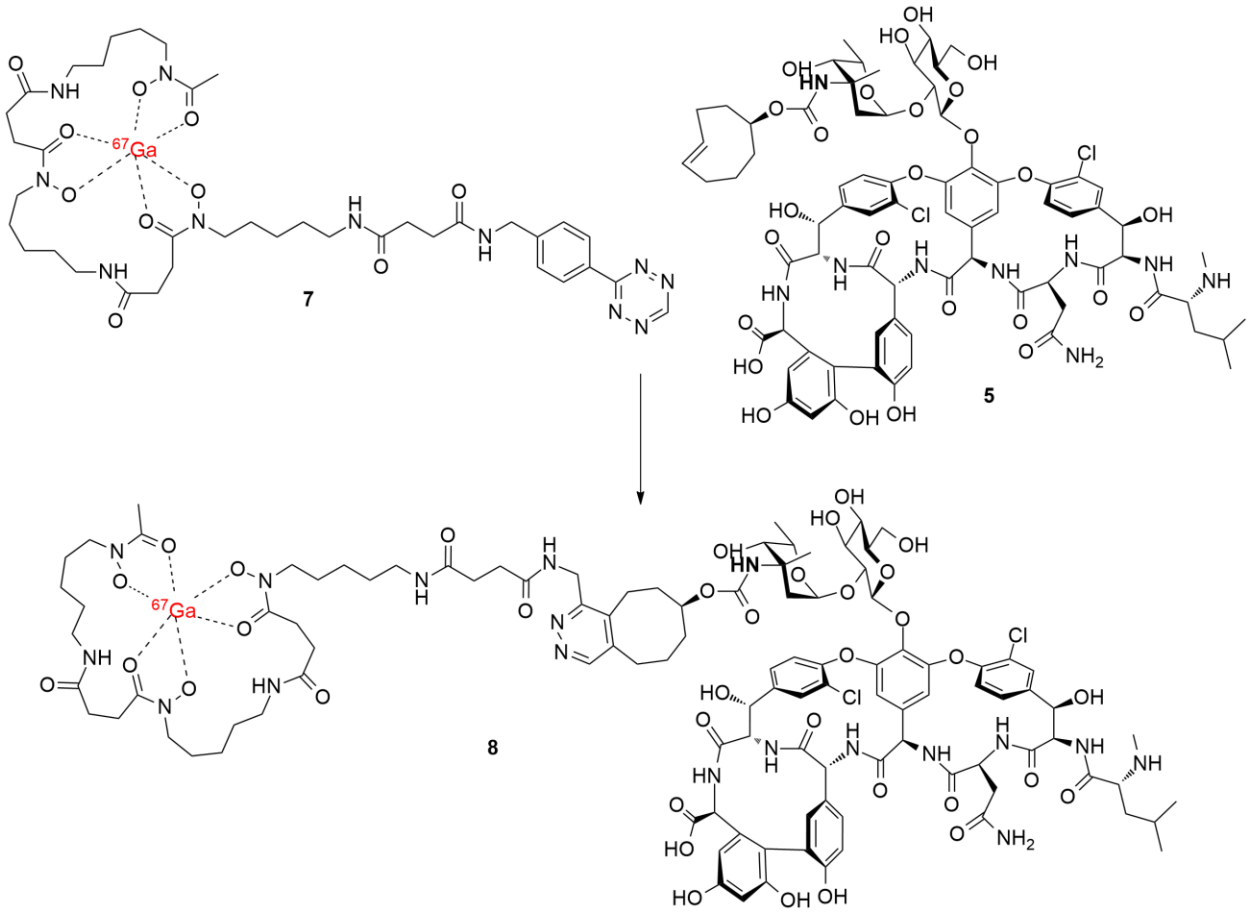


Figure S 3.1 HPLC chromatogram (Method B) of **5**.

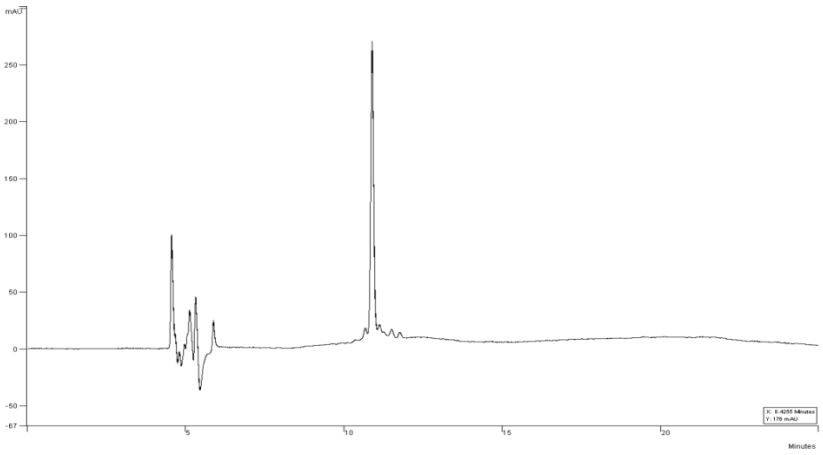


Figure S 3.2 ESI HRMS of **5** between m/z 900 to 4000.

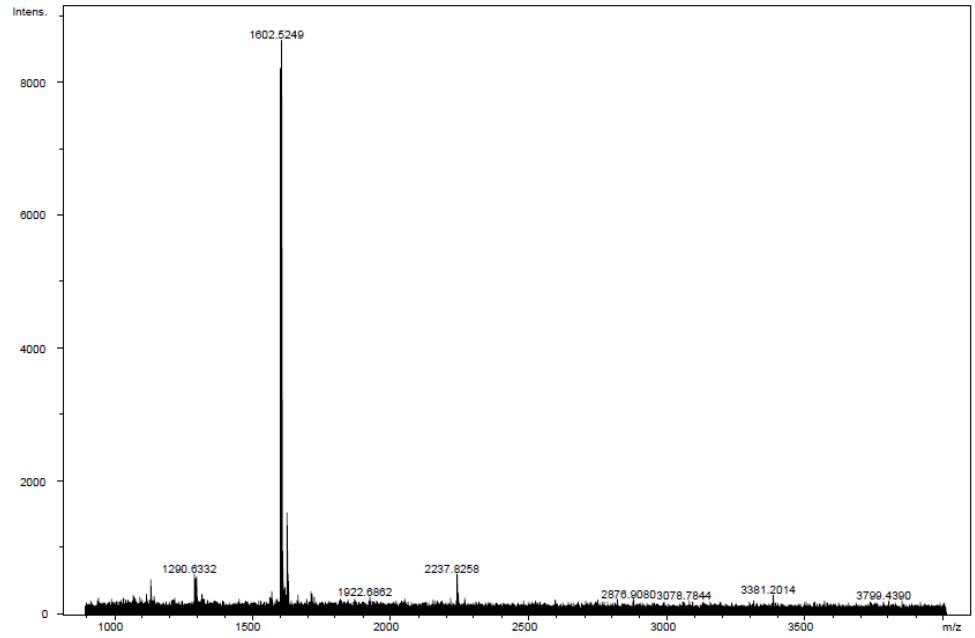


Figure S 3.3 Expansion of HRMS shown in Figure S2.

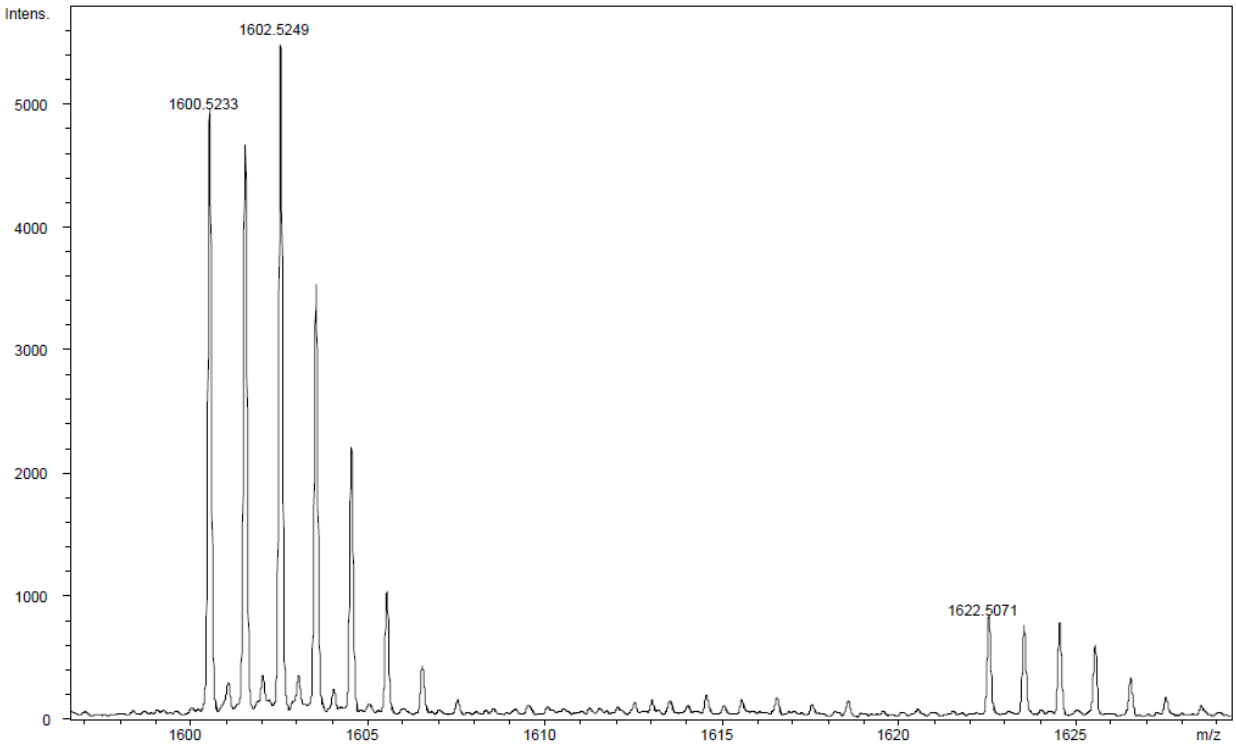


Figure S 3.4 HPLC chromatogram (Method B) of 6.

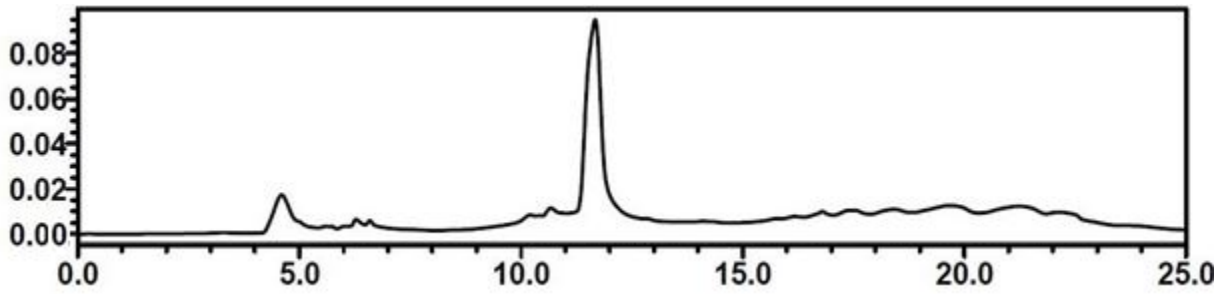
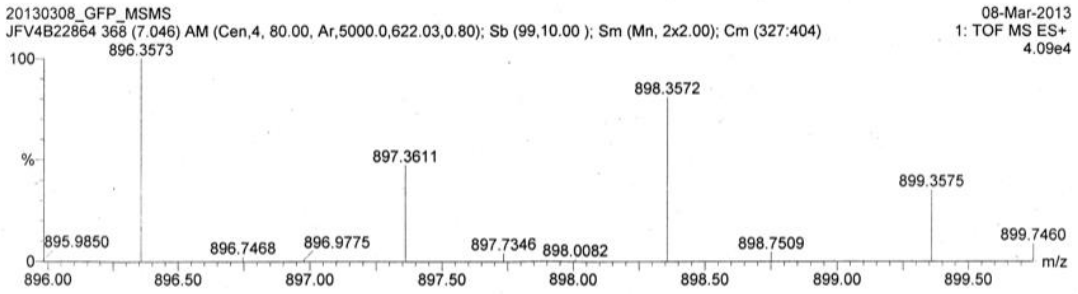


Figure S 3.5 High-resolution mass spectrum of 6.

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
41 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)



Minimum:				-1.5		
Maximum:		20.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
896.3573	896.3586	-1.3	-1.4	20.5	3	C43 H57 N9 O8 Ga
	896.3599	-2.6	-2.9	20.0	4	C45 H59 N6 O9 Ga
	896.3546	2.7	3.0	16.5	2	C38 H57 N11 O10 Ga ✓
	896.3532	4.1	4.5	17.0	1	C36 H55 N14 O9 Ga

Figure S 3.6 IR spectrum of **6** (KBr pellet).

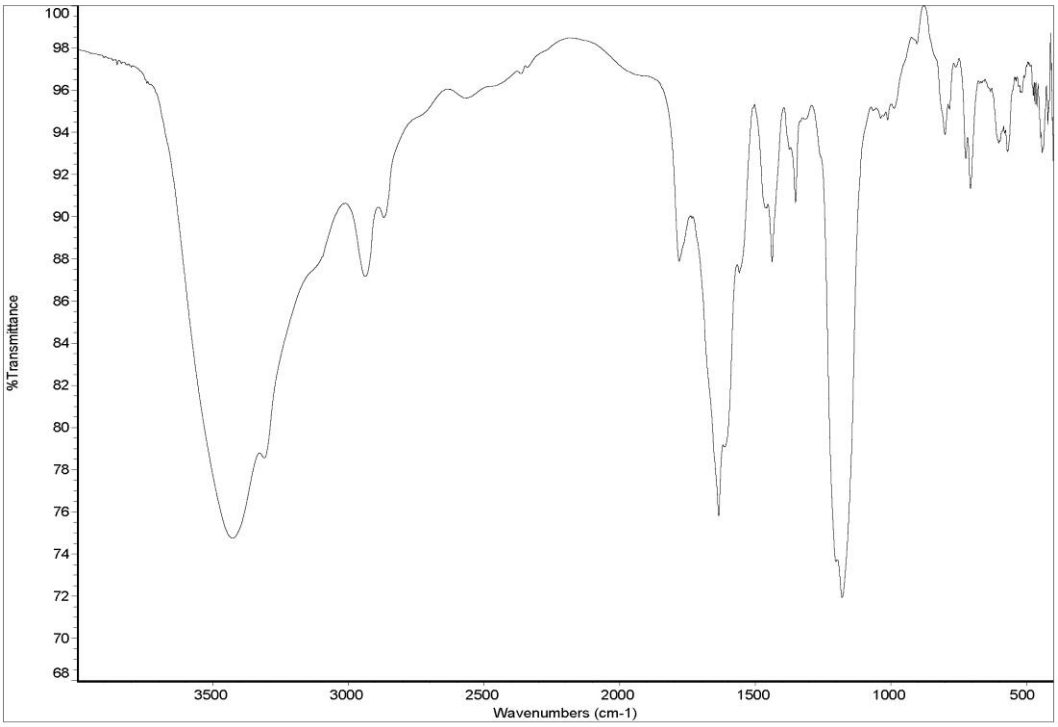


Figure S 3.7 ^{1}H NMR spectrum of 6 in DMSO-d_6 at 300 K.

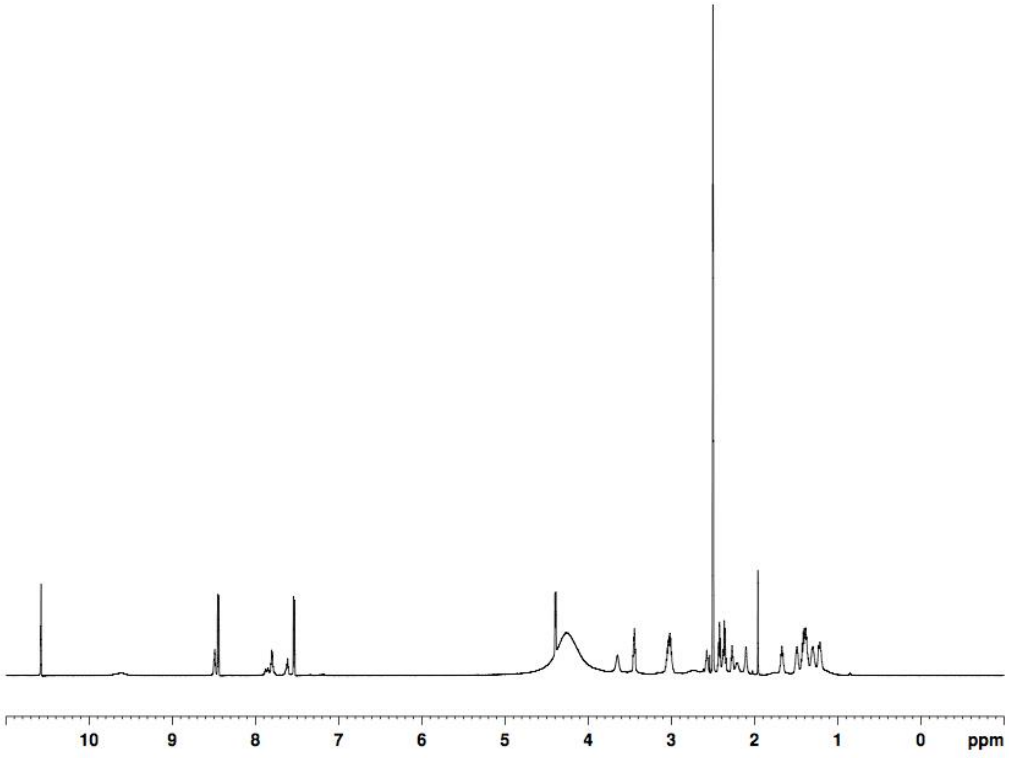


Figure S 3.8 HPLC chromatogram (Method D) of **6**, UV peak at λ = 240 nm

(Note: Injection volume contains DMSO).

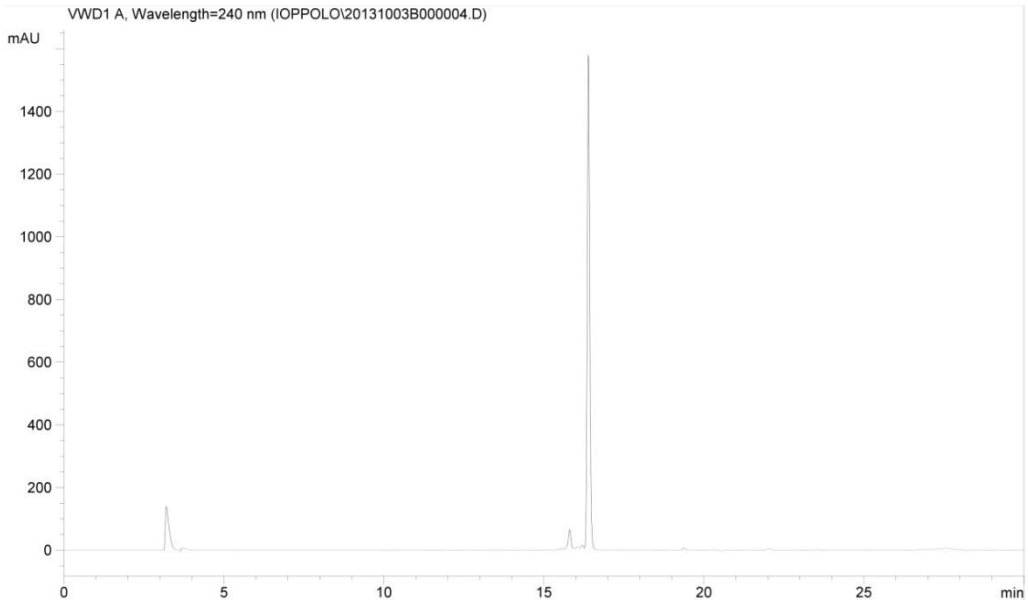


Figure S 3.9 HPLC chromatograms (Method D) of **7** co-injected with **6**.

Radio-HPLC peak (top), UV peak at λ = 240 nm (bottom).

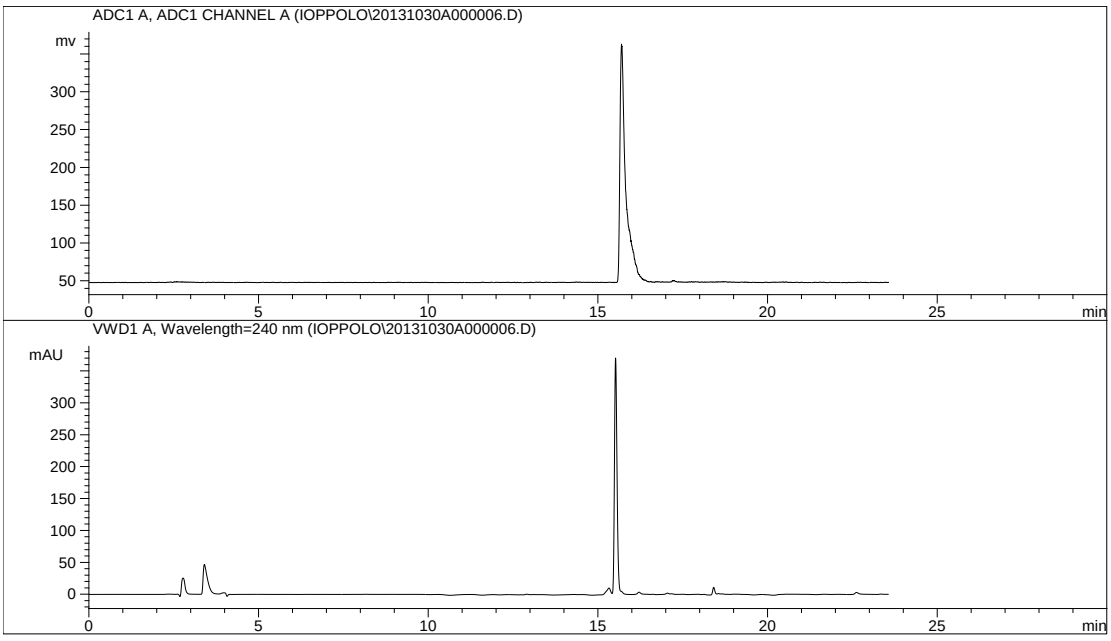


Figure S 3.10 Analytical HPLC chromatogram (Method B) of 7

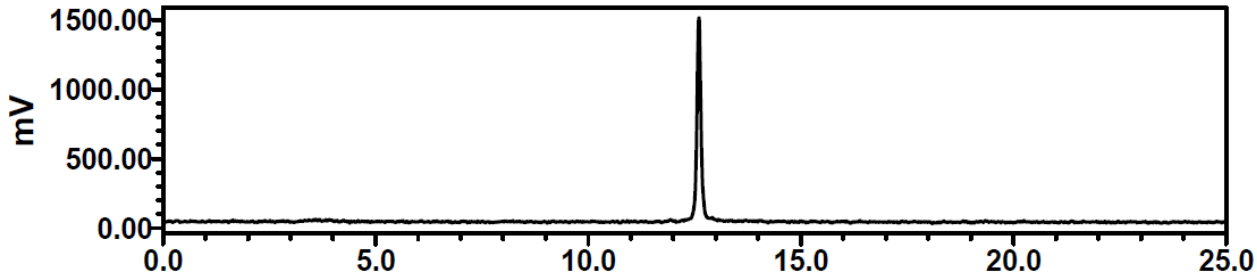


Figure S 3.11 Analytical HPLC chromatogram (Method B) of **8**

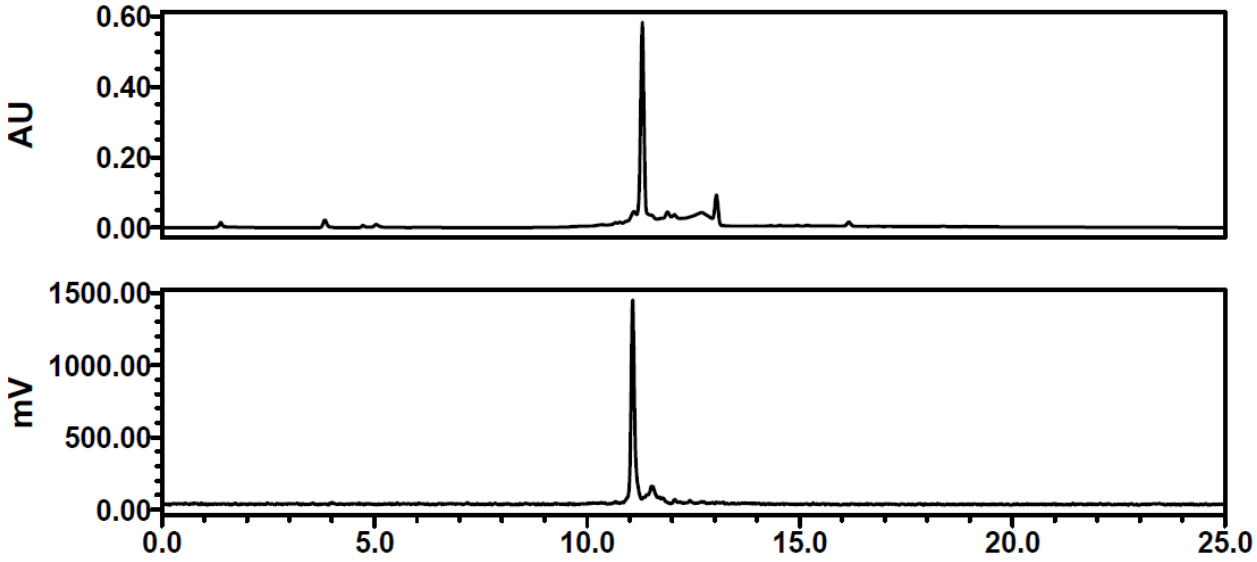


Figure S 3.12 HPLC chromatograms (Method B) of **8** over 3 days.

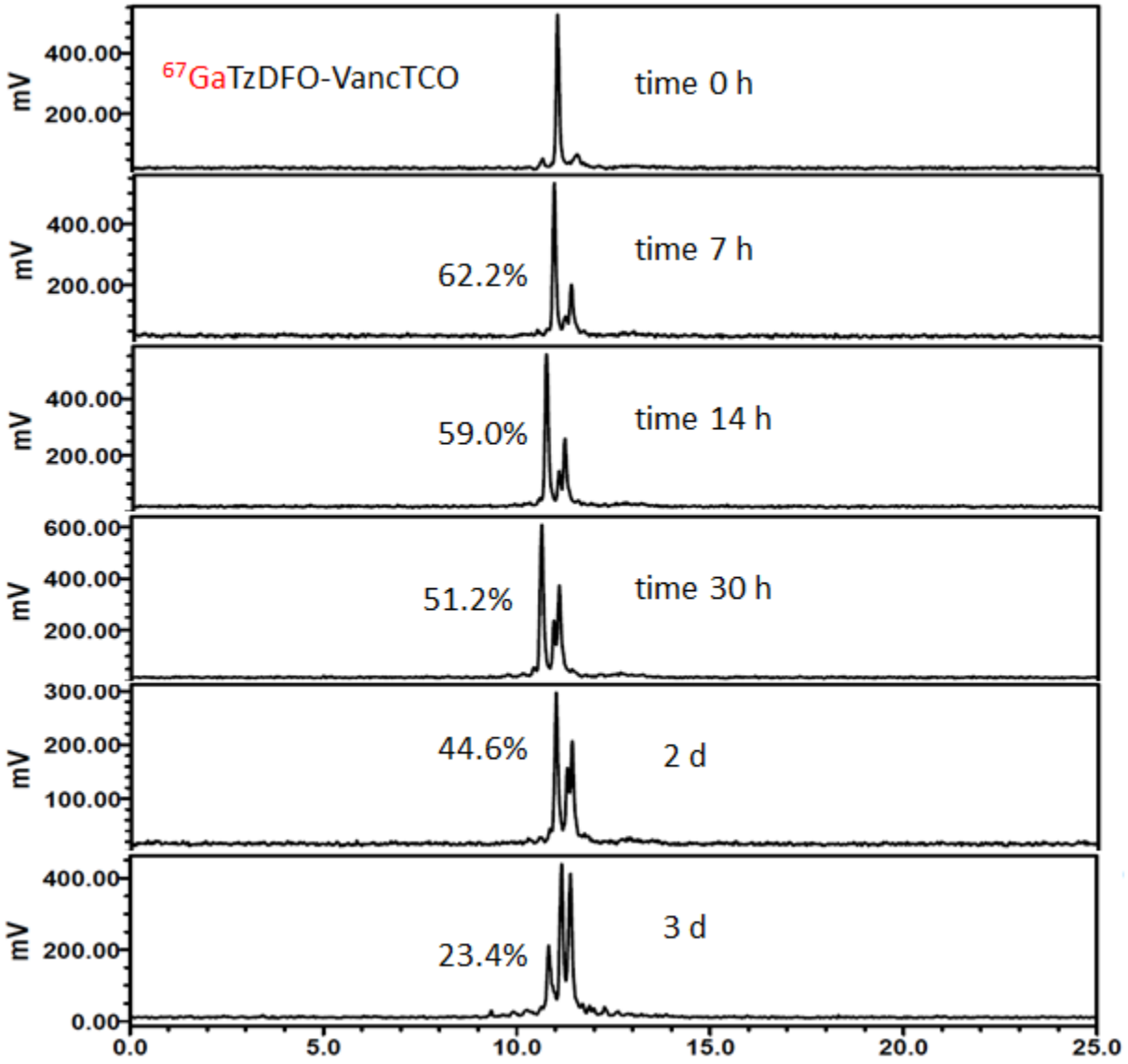


Figure S 3.13 HPLC Peak integration of **8** over 3 days

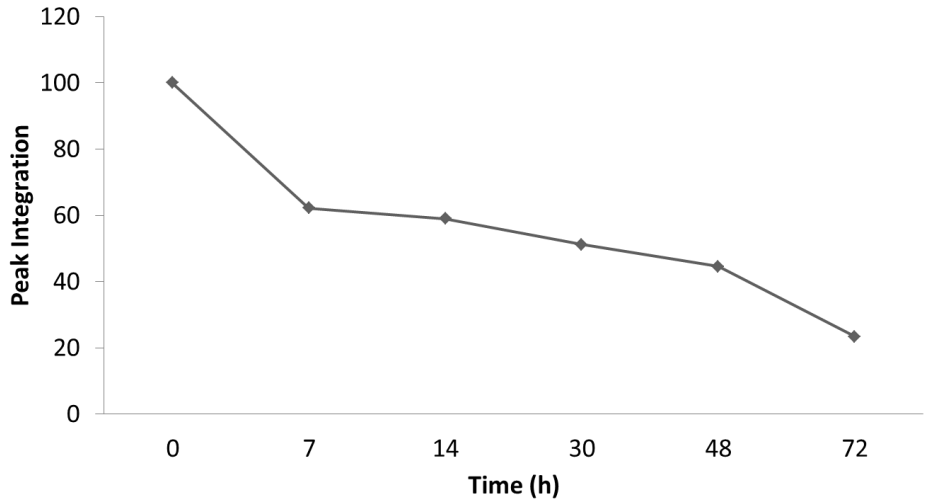


Figure S 3.14 *In vitro* uptake of ^{67}GaDFO-Tz and GaDFO-Tz (control) by *S. aureus* over time. Note that time zero represents samples processed immediately following the addition of the radioactive material. All experiments were performed in duplicate.

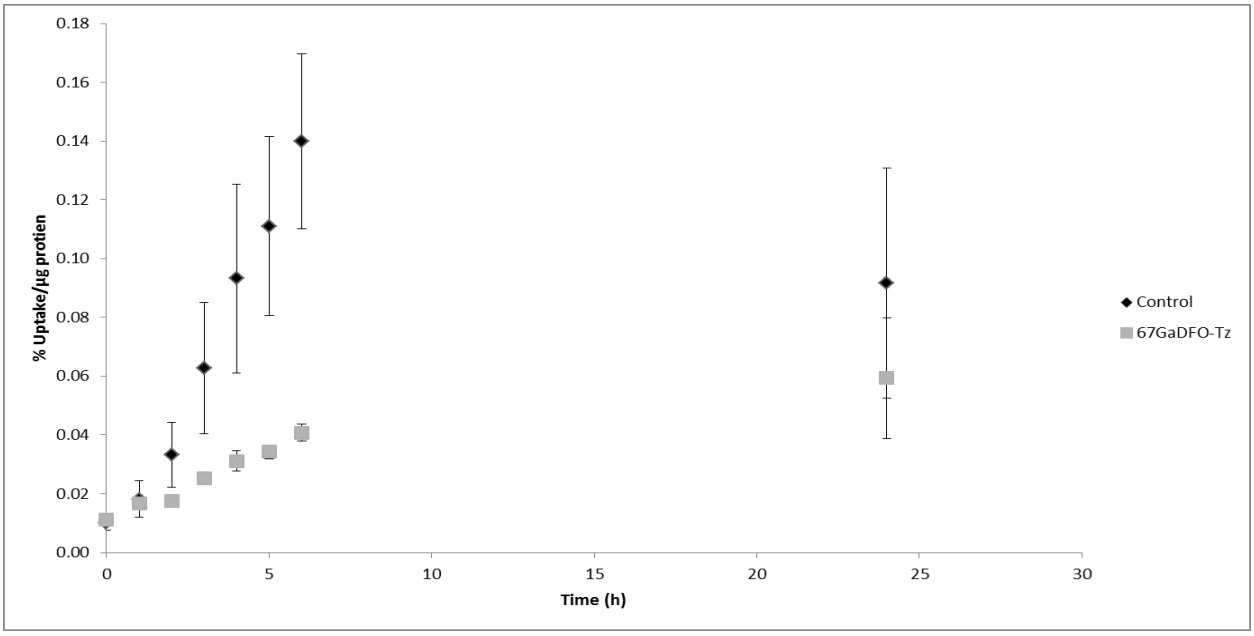


Figure S 3.15 Plot of the percentage of vanco-TCO conjugate 8 binding to *S. aureus* at 0, 5, 15,30,45, 60, 120 minutes and 6 hours.

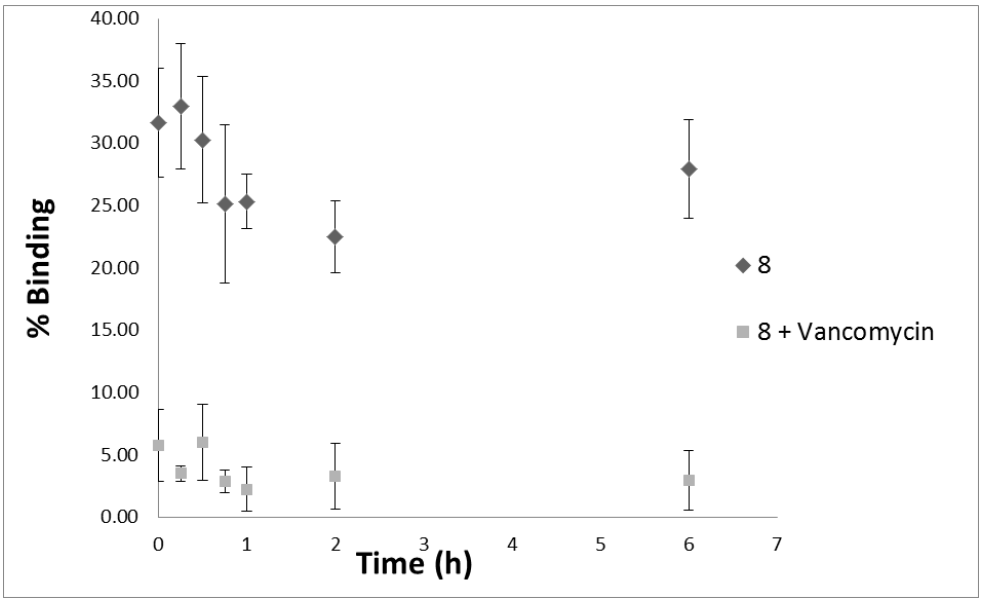


Figure S 3.16 Plot of the percentage of ^{67}GaDFO-Tz 7 bioorthogonally binding to *S. aureus* at 1and 6 hours.

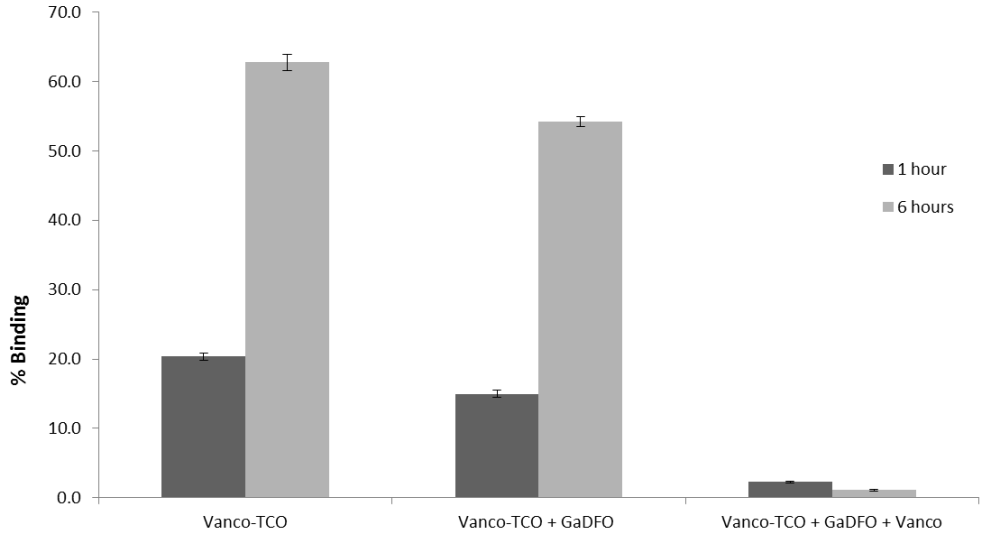


Figure S 3.17 SPECT/CT sagittal (left) and transverse (right) of Mouse 1 after 1 h p.i.

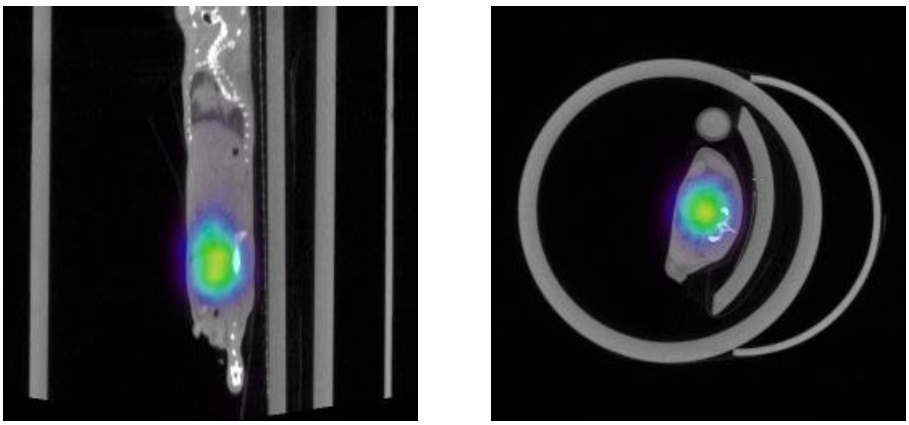


Figure S 3.18 SPECT/CT sagittal (left) and transverse (right) of Mouse 1 after 24 h p.i.

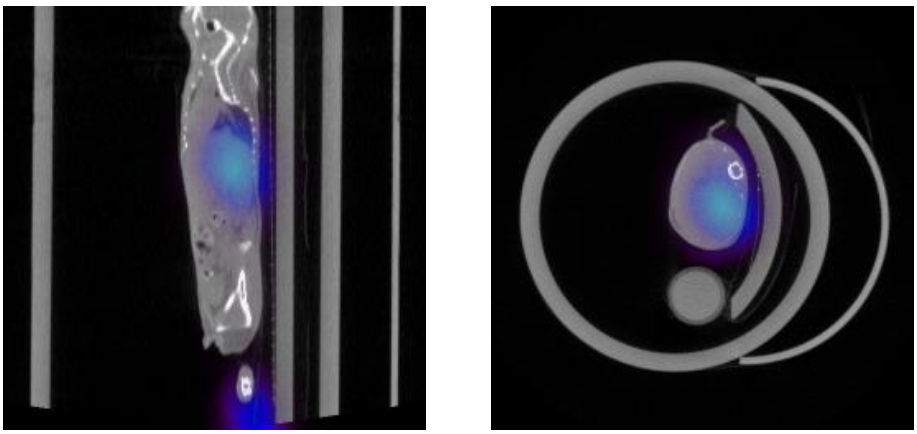


Figure S 3.19 SPECT/CT sagittal (left) and transverse (right) of Mouse 2 after 1 h p.i.

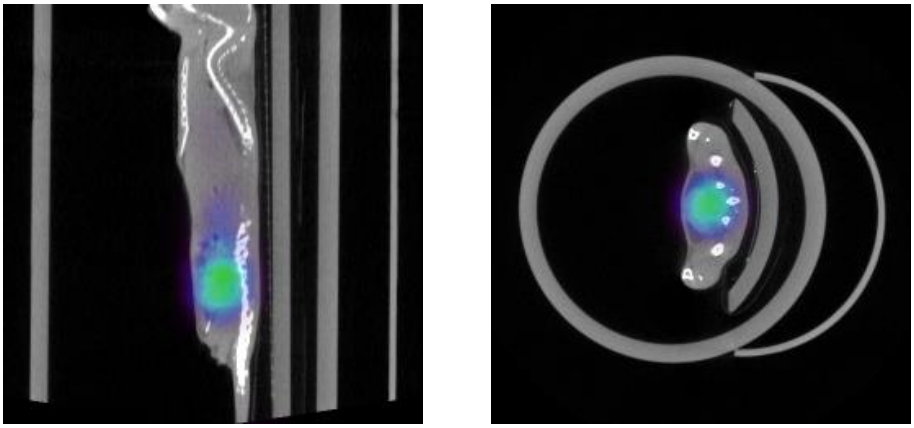


Figure S 3.20 SPECT/CT sagittal (left) and transverse (right) of Mouse 2 after 1 h p.i.

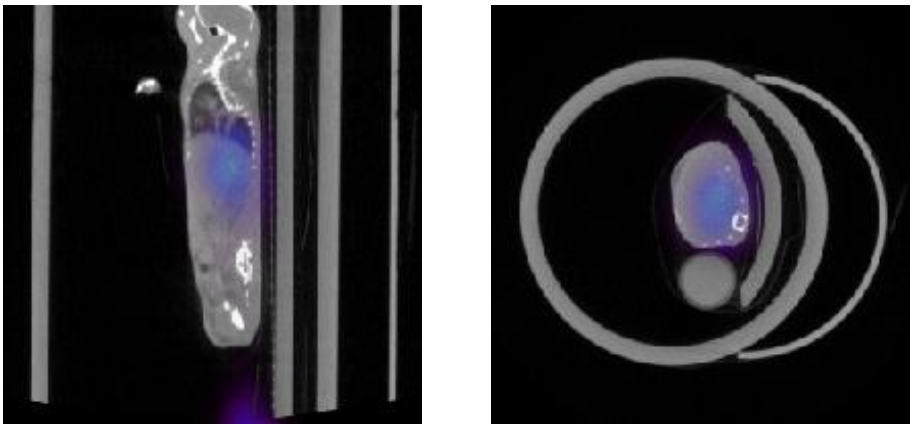


Figure S 3.21 SPECT/CT sagittal (left) and transverse (right) of Mouse 3 after 24 h p.i.

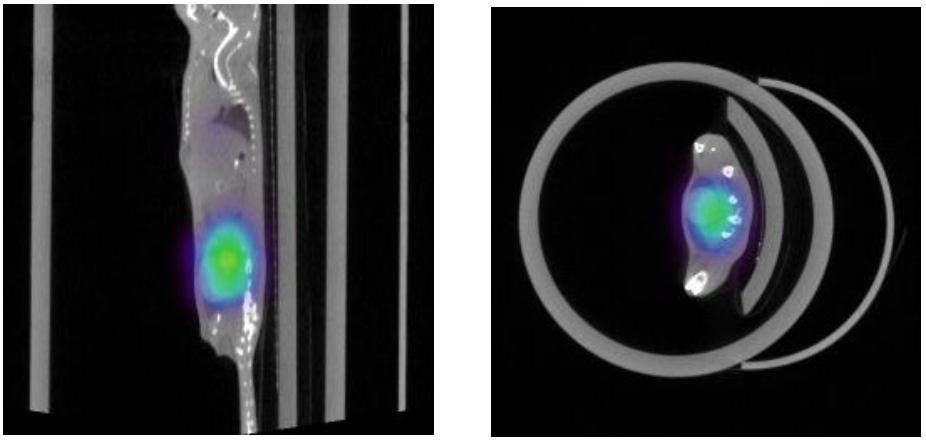


Figure S 3.22 SPECT/CT sagittal (left) and transverse (right) of Mouse 3 after 24 h p.i.

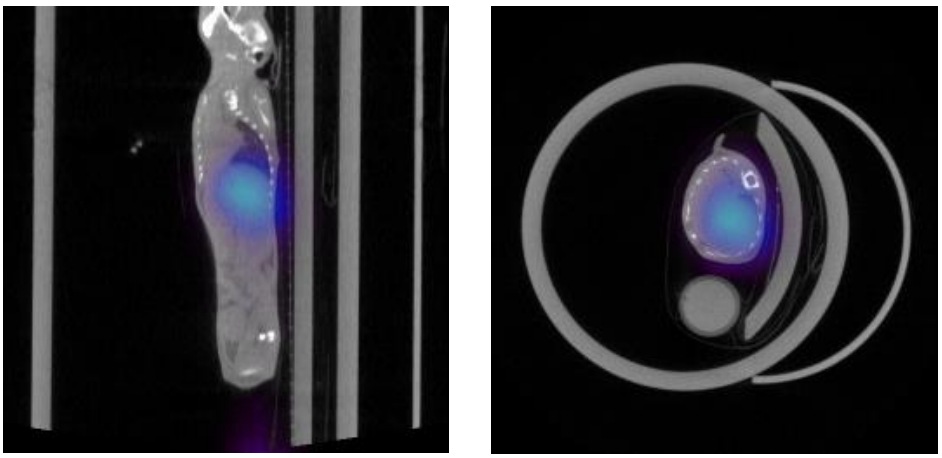


Figure S 3.23 SPECT/CT sagittal (left) and transverse (right) of Mouse 4 after 1 h p.i.

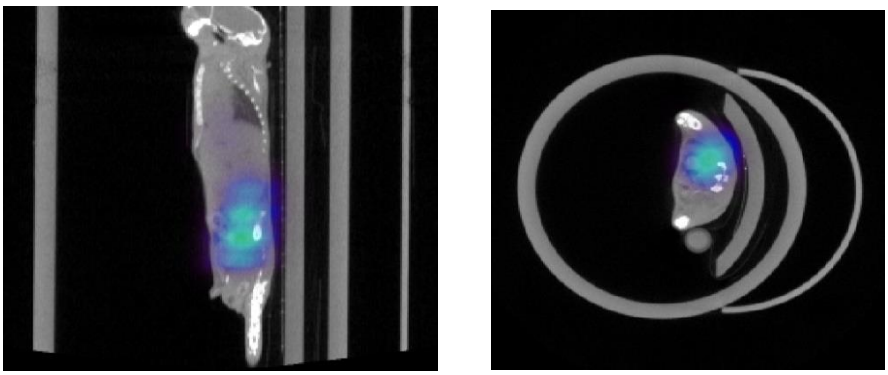


Figure S3.24. SPECT/CT sagittal (left) and transverse (right) of Mouse 4 after 24 h p.i.

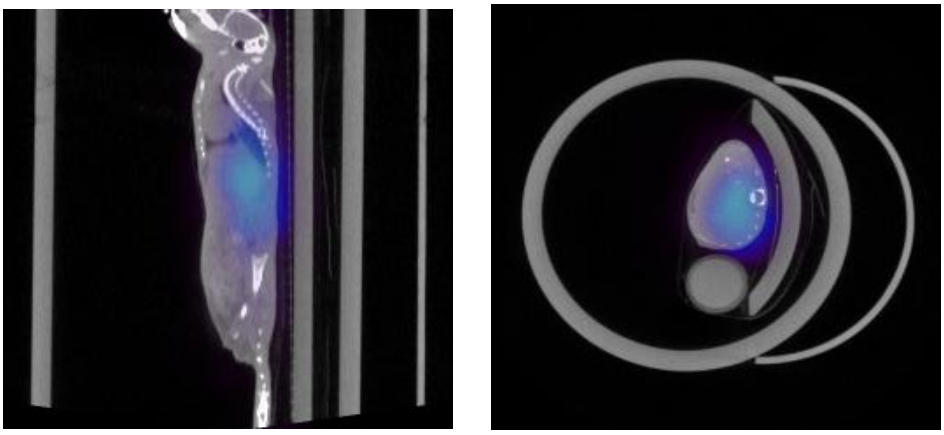


Figure S 3.24 SPECT/CT coronal image of Mouse 4 after 24 h p.i.

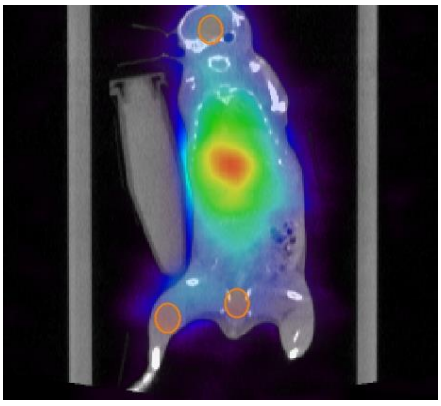


Figure S 3.25 Percent injected dose per gram (%ID/g) for select tissues and fluids obtained from the biodistribution of [^{67}Ga]-**1** and **7** in *S. aureus* murine models at 1 h p.i.

Data are expressed as mean ± SEM (n=3).

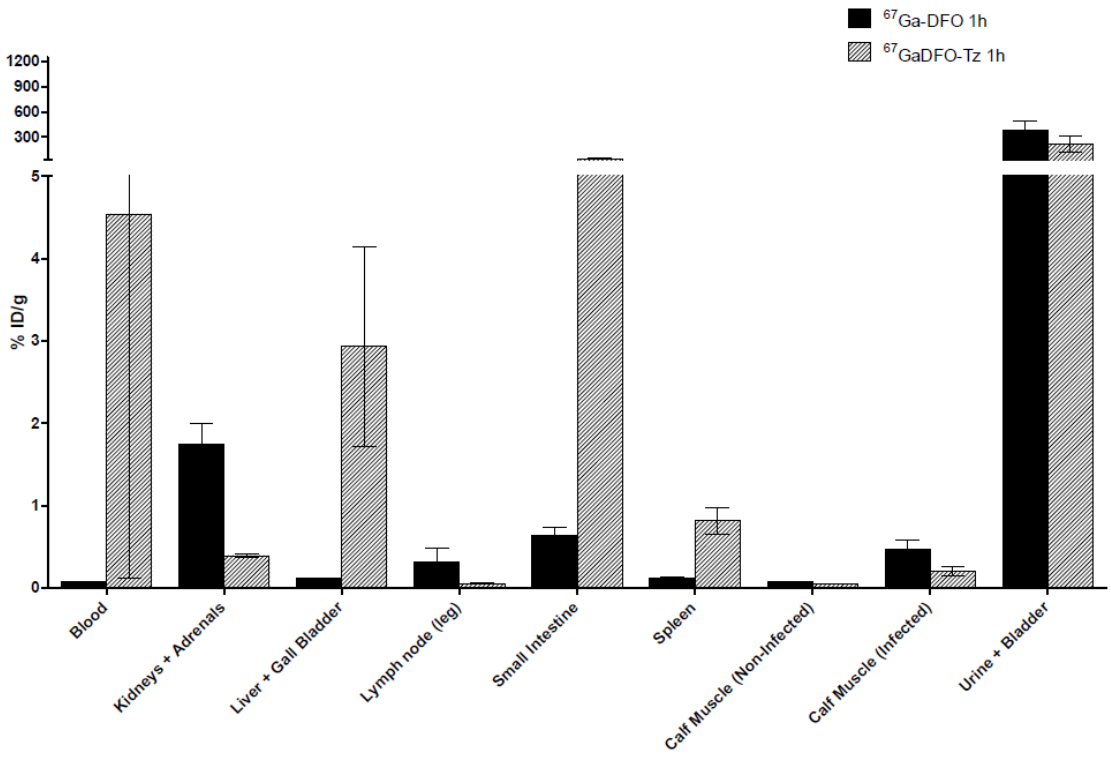


Figure S 3.26 Infected and non-infected calf muscle %ID/g of [^{67}Ga]-1 and 7 in *S. aureus* murine infected models at 1 h p.i.

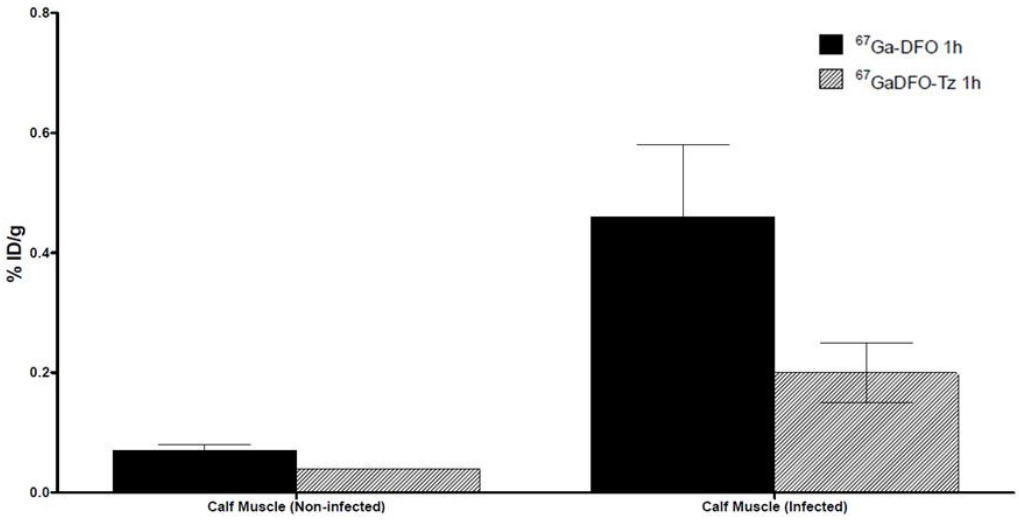


Figure S 3.27 Plot of infected calf muscle to other tissues. %ID/g of [^{67}Ga]-**1** and **7** in *S. aureus* murine infected models at 1 h p.i.

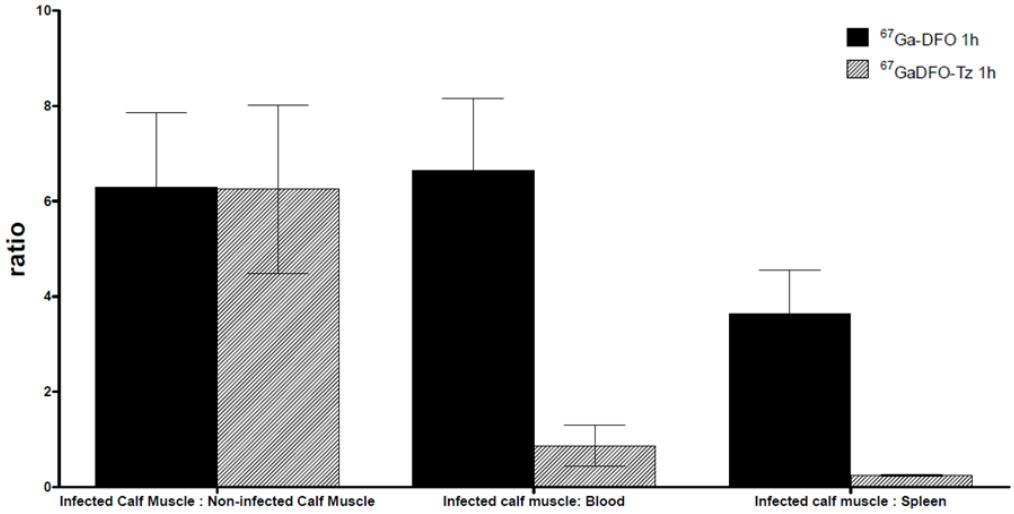


Table S 3-1 Tissue distribution of 1 and 7 in *Staphylococcus aureus* mouse infection model at 1 h p.i.

Data are expressed as ratios of %ID/g, expressed as the mean ± SEM (n=3).

Organs	**1**	**7**
Blood	0.07 ± 0.01	4.54 ± 4.42
Kidneys + Adrenals	1.75 ± 0.25	0.39 ± 0.02
Liver + Gall Bladder	0.11 ± 0.01	2.93 ± 1.21
Lymph Nodes	0.32 ± 0.16	0.05 ± 0.01
Small Intestine	0.63 ± 0.11	37.77 ± 5.73
Spleen	0.12 ± 0.01	0.81 ± 0.16
Calf Muscle (Left)	0.07 ± 0.01	0.04 ± 0.00
Calf Muscle (Right)	0.46 ± 0.12	0.20 ± 0.05
Urine + Bladder	381.75 ± 107.15	214.09 ± 100.96

Chapter 4

Synthesis of 9-oxabiclo[6.1.0]nonane

Cis-cyclooctene (1 g, 9.1 mmol; Sigma-Aldrich, Milwaukee, USA) was added to a solution of acetic acid (1.71 mL, 29.9 mmol; Sigma-Aldrich) and sodium perborate tetrahydrate (1.75 g, 11.3 mmol; Sigma-Aldrich, Oakville, Canada) in 10 mL dichloromethane. The reaction was stirred for one week in room temperature. The product was isolated by extraction. The crude reaction mixture was combined with water and extracted three times with dichloromethane. The dichloromethane layers were combined and dried by rotary evaporator and high vacuum. The yield was determined to be 0.70 g, 63.6%. ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.9 (d, 1H), 2.1 (d, 1H), 1.6-1.3 (m, 12H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 55.6, 26.5, 26.3, 25.6 LRMS-ESI (m/z): $[M+H]^+$ calcd for $C_8H_{14}O$: 127, obsd 127.

Synthesis of (*Z*)-cyclooct-2-enol

9-oxabiclo[6.1.0]nonane (70.0 mg, 5.5 mmol) was dissolved in DMSO. KOH powder (0.94 g, 16.7 mmol; Sigma-Aldrich) was added to the solution and heated to 95 °C and stirred for 2 nights yielding yellow oil as expected. LRMS-ESI (m/z): $[M+H]^+$ calcd for $C_8H_{14}O$: 127, obsd 127. The product has not yet been isolated.

Synthesis of Vancomycin-succinic acid

Vancomycin hydrochloride hydrate (50 mg, 33.7μmol; Sigma-Aldrich, Oakville, Canada) was added to a solution of succinic anhydride (7.4 mg, 74.0 μmol; Sigma-Aldrich) in 7 mL DMSO and stirred overnight. LRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{70}H_{79}Cl_2N_9O_{27}$: 1547, obsd 1547.