Analogues of desferrioxamine B designed to attenuate iron-mediated neurodegeneration: Synthesis, characterisation and activity in the MPTP-mouse model of Parkinson's disease

Michael P. Gotsbacher, Thomas J. Telfer, Paul K. Witting, Kay L. Double, David I. Finkelstein, and Rachel Codd*

Supporting Information

List of Figures

Figure 1: Antiradical activity of **1**–**9** and standards as determined by the $ABTS^{\bullet+}$ assay	2
Figure 2: Complete time for **1**, **2** or **9** in the Pole test	3
Figure 3: ^{1}H-NMR spectrum for compound **2**	4
Figure 4: ^{13}C-NMR spectrum for compound **2**	4
Figure 5: ^{1}H-NMR spectrum for compound **5**	5
Figure 6: ^{13}C-NMR spectrum for compound **5**	5
Figure 7: ^{1}H-NMR spectrum for compound **6**	6
Figure 8: ^{13}C-NMR spectrum for compound **6**	6
Figure 9: ^{1}H-NMR spectrum for compound **7**	7
Figure 10: ^{13}C-NMR spectrum for compound **7**	7
Figure 11: Numbered structure and ^{1}H-NMR spectrum for compound **8**	8
Figure 12: ^{13}C-NMR spectrum for compound **8**	8
Figure 13: ^{1}H-NMR spectrum for compound **9**	9
Figure 14: ^{13}C-NMR spectrum for compound **9**	9
Figure 15: High resolution mass spectrometry (ESI+) for compound **2**	10
Figure 16: High resolution mass spectrometry (ESI+) for compound **3**	10
Figure 17: High resolution mass spectrometry (ESI+) for compound **4**	11
Figure 18: High resolution mass spectrometry (ESI+) for compound **5**	11
Figure 19: High resolution mass spectrometry (ESI+) for compound **6**	12
Figure 20: High resolution mass spectrometry (ESI+) for compound **7**	12
Figure 21: High resolution mass spectrometry (ESI+) for compound **8**	13
Figure 22: High resolution mass spectrometry (ESI+) for compound **9**	13

Data for antioxidant ABTS$^{\bullet+}$ assay

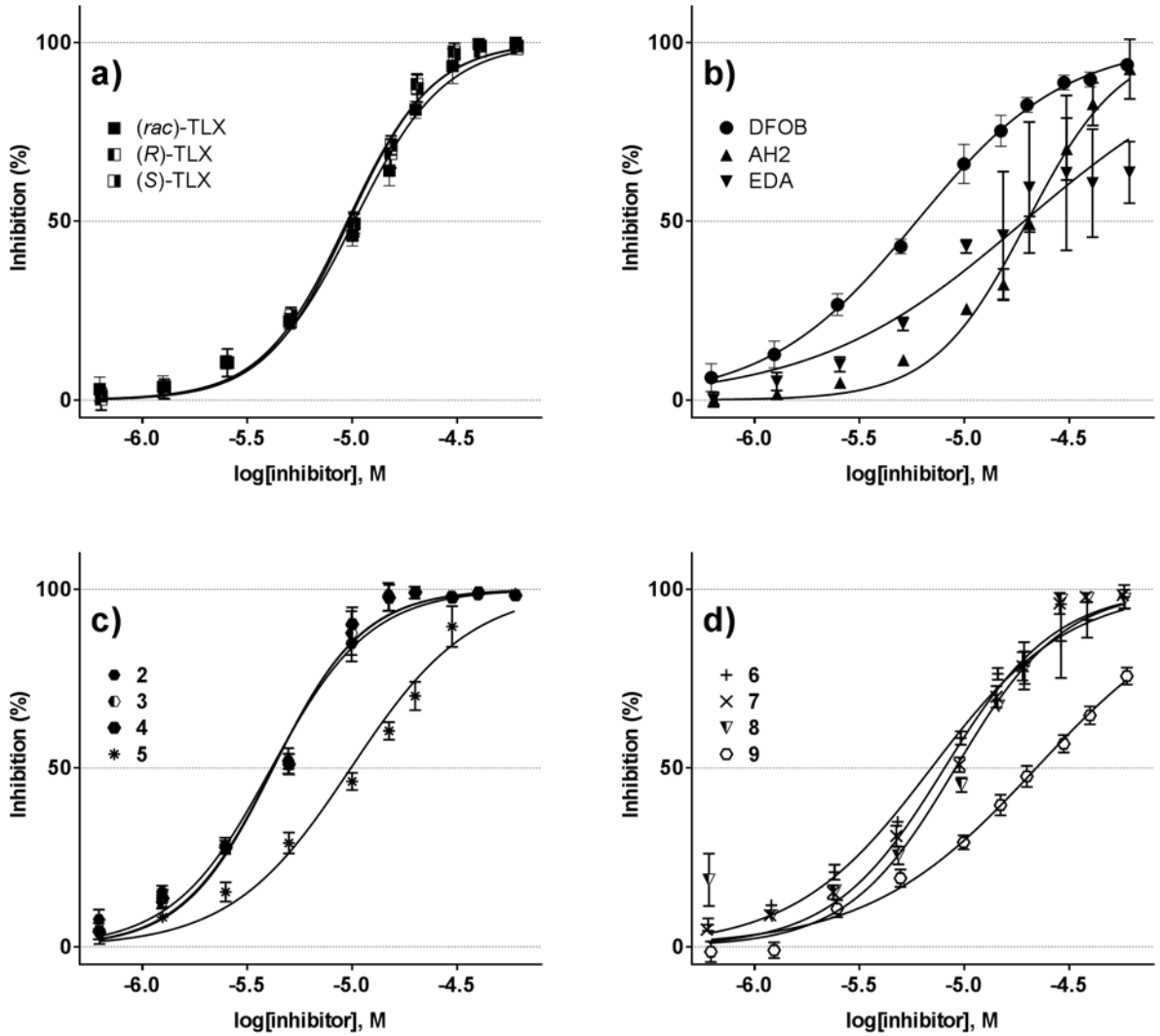

Figure 1: Antiradical activity as determined by the ABTS$^{\bullet+}$ assay. Panel a) (*rac*)-TLX (full square), (*R*)-TLX (left semi-filled square), (*S*)-TLX (right semi-filled square); panel b) DFOB (full circle), AH_2 (closed upwards triangle), EDA (closed downwards triangle); panel c) conjugates **2**–**5** (respective numbers); panel d) conjugates **6**–**9** (respective numbers).

MPTP$^+$ Parkinson's disease mouse model

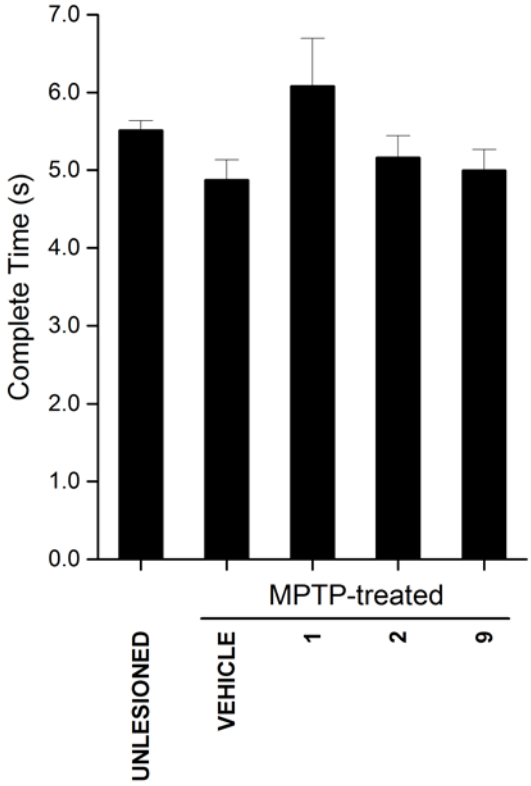

Figure 2: Treatment with **2** or **9** did not significantly improve complete time in the pole test following MPTP-intoxication. Data is presented as average time ± SEM and *t*-test with Welch correction.

NMR (^{1}H, ^{13}C) spectra for compounds 2 and 5–9

NMR (^{1}H, ^{13}C) spectra were recorded in 5 mm Pyrex tubes, using a Varian 400-MR NMR spectrometer at a frequency of 399.73 MHz (^{1}H) or 100.52 MHz (^{13}C) at 24 °C operated with VnmrJ 3.1 software. The spectral data are reported in ppm (δ) and referenced to residual solvent (DMSO-d_6 2.50/39.52 ppm).

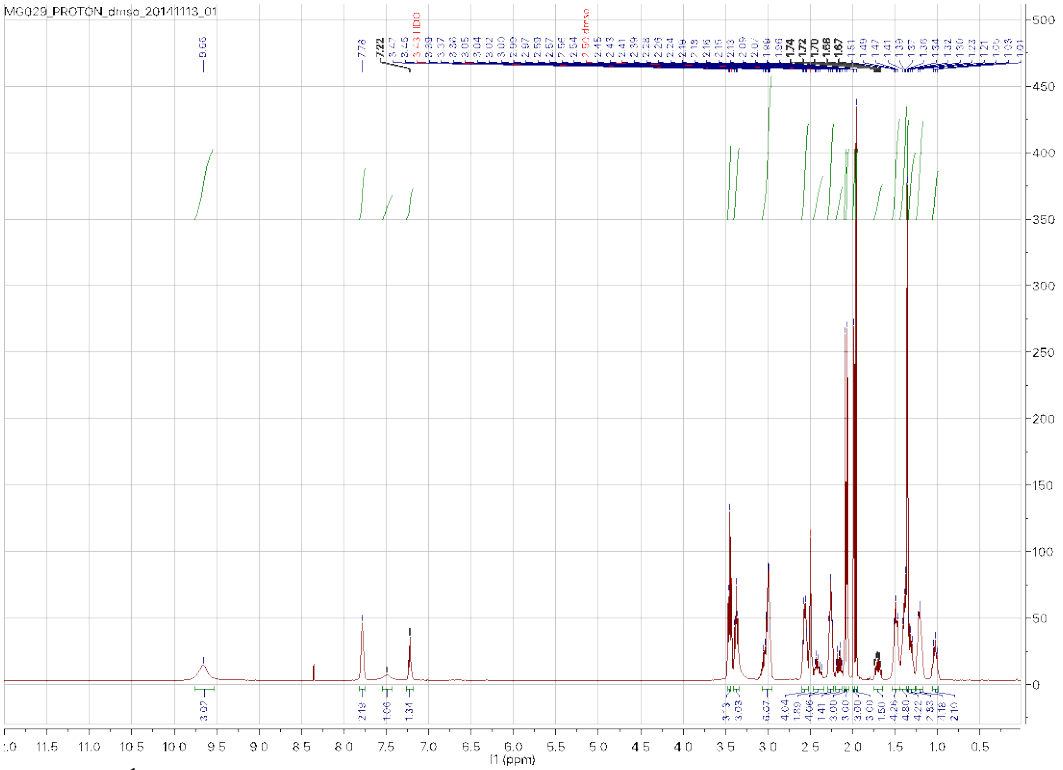

Figure 3: ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **2**

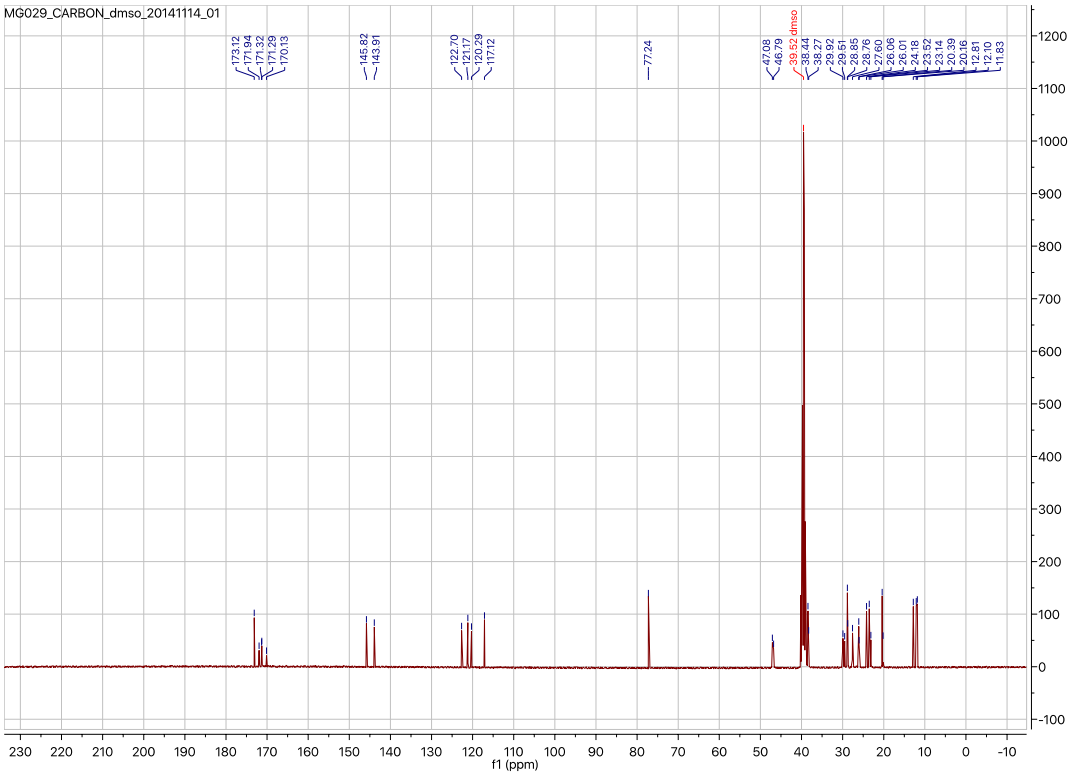

Figure 4: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **2**

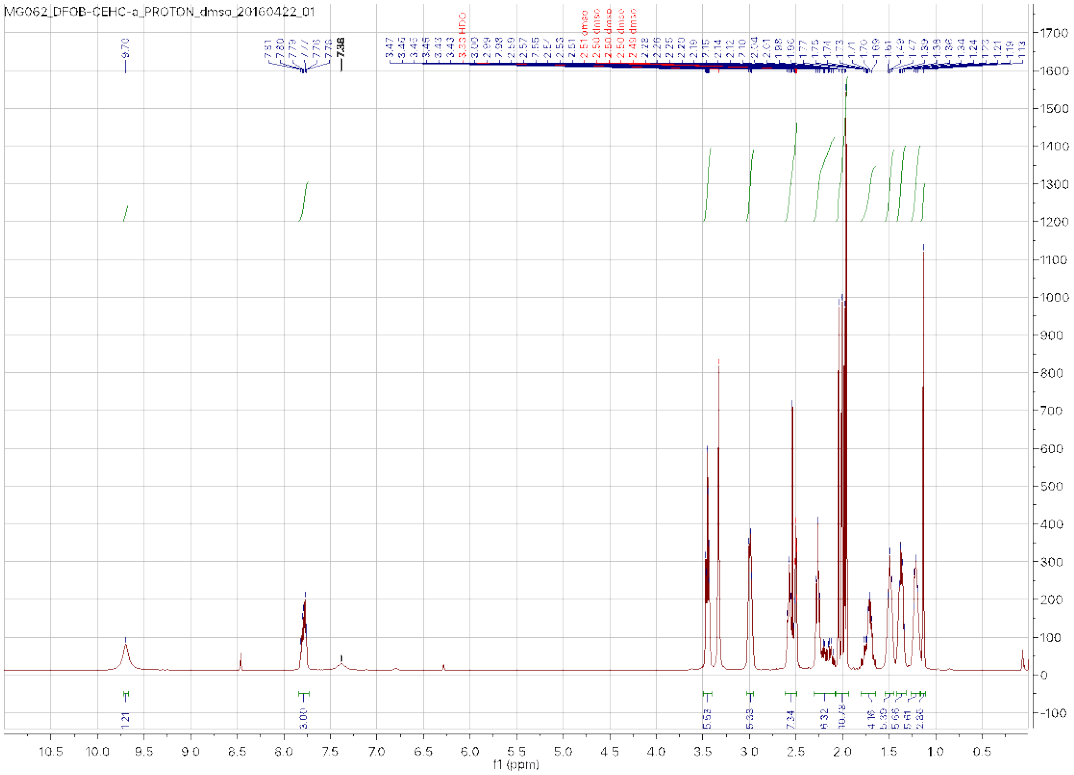

Figure 5: ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **5**

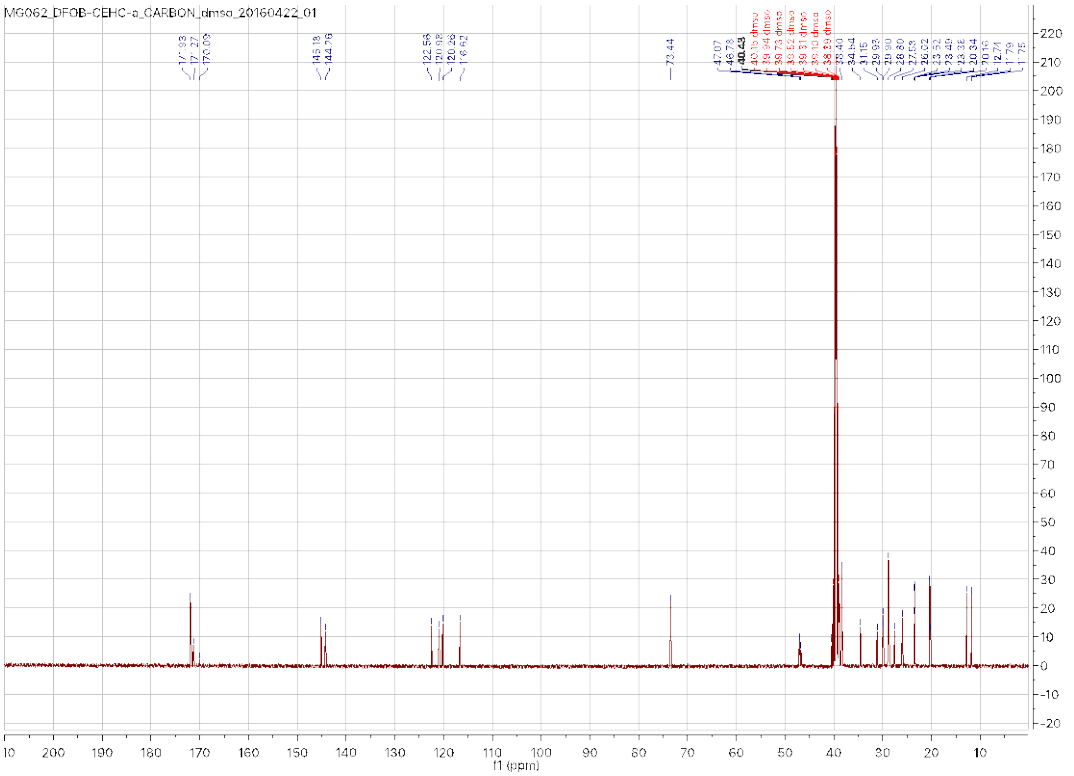

Figure 6: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **5**

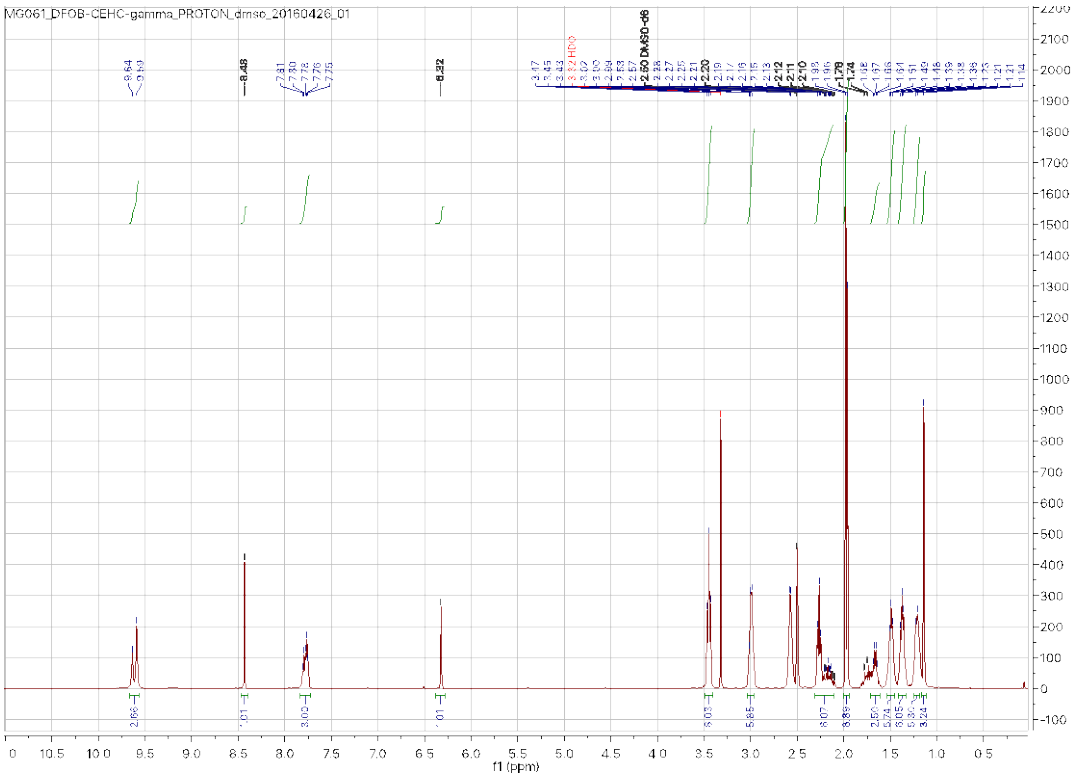

Figure 7: ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **6**

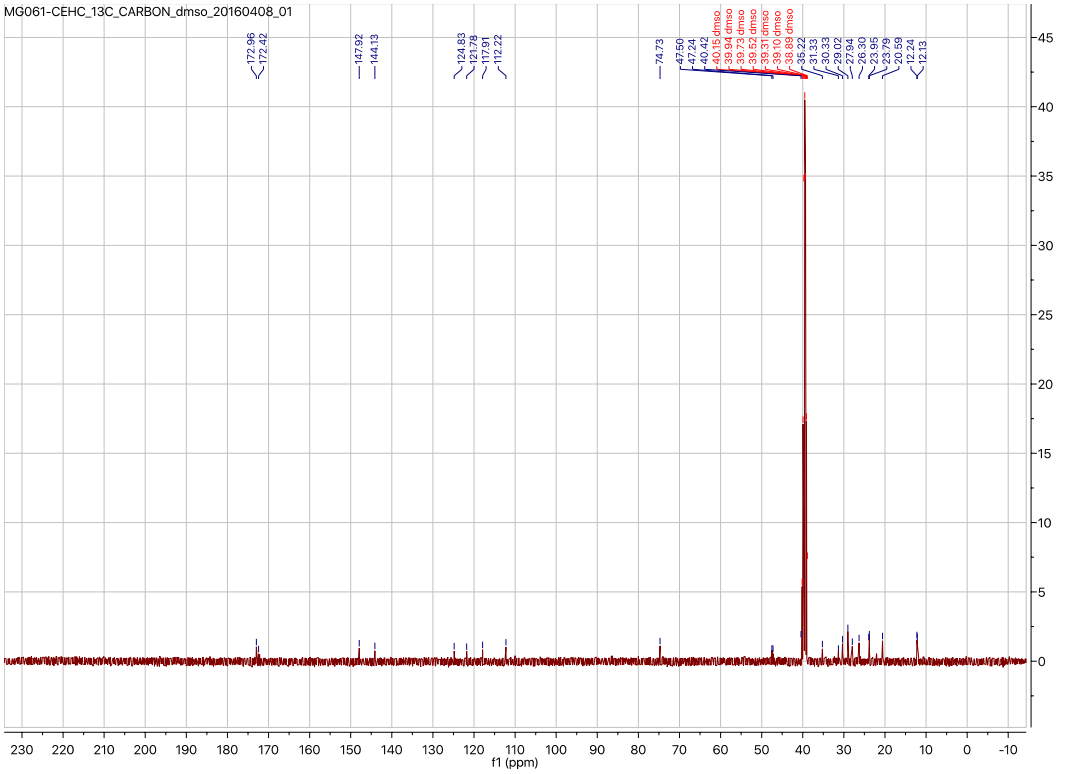

Figure 8: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **6**

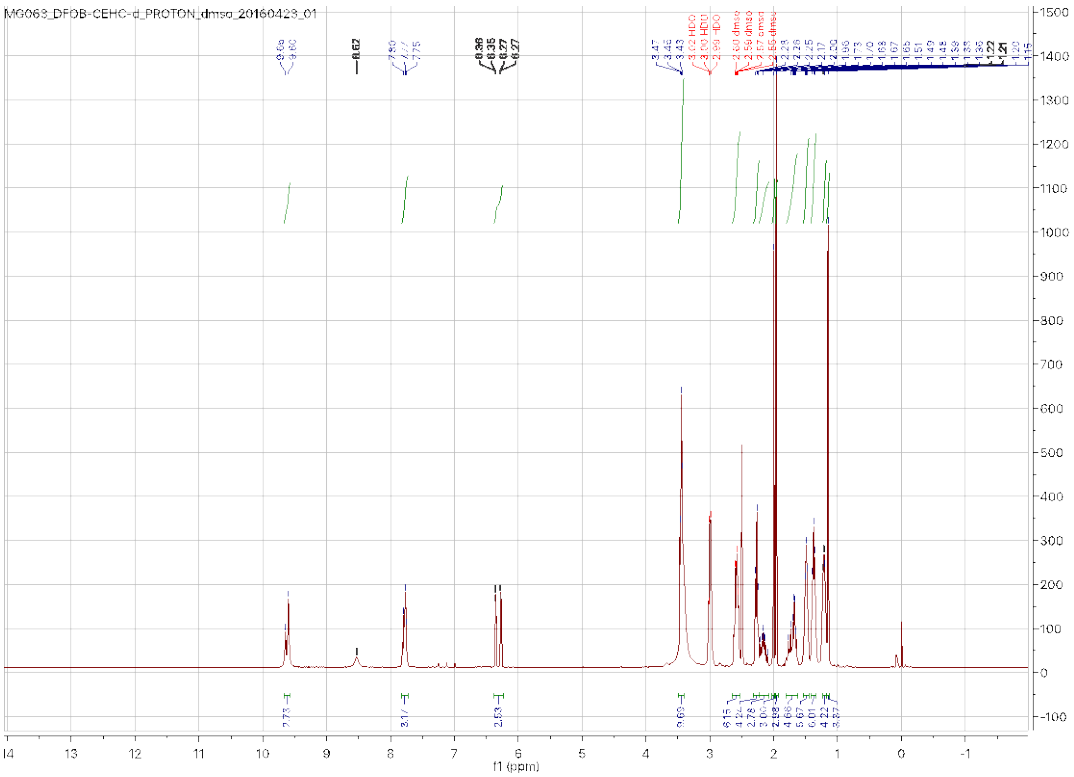

Figure 9: ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **7**

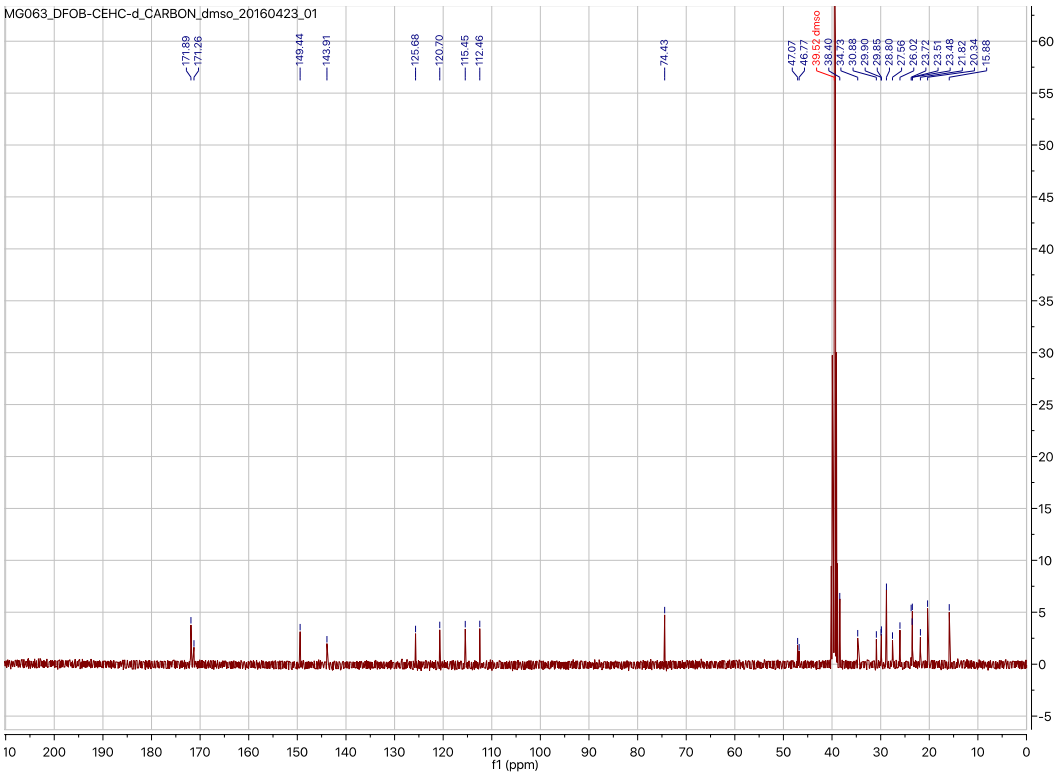

Figure 10: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **7**

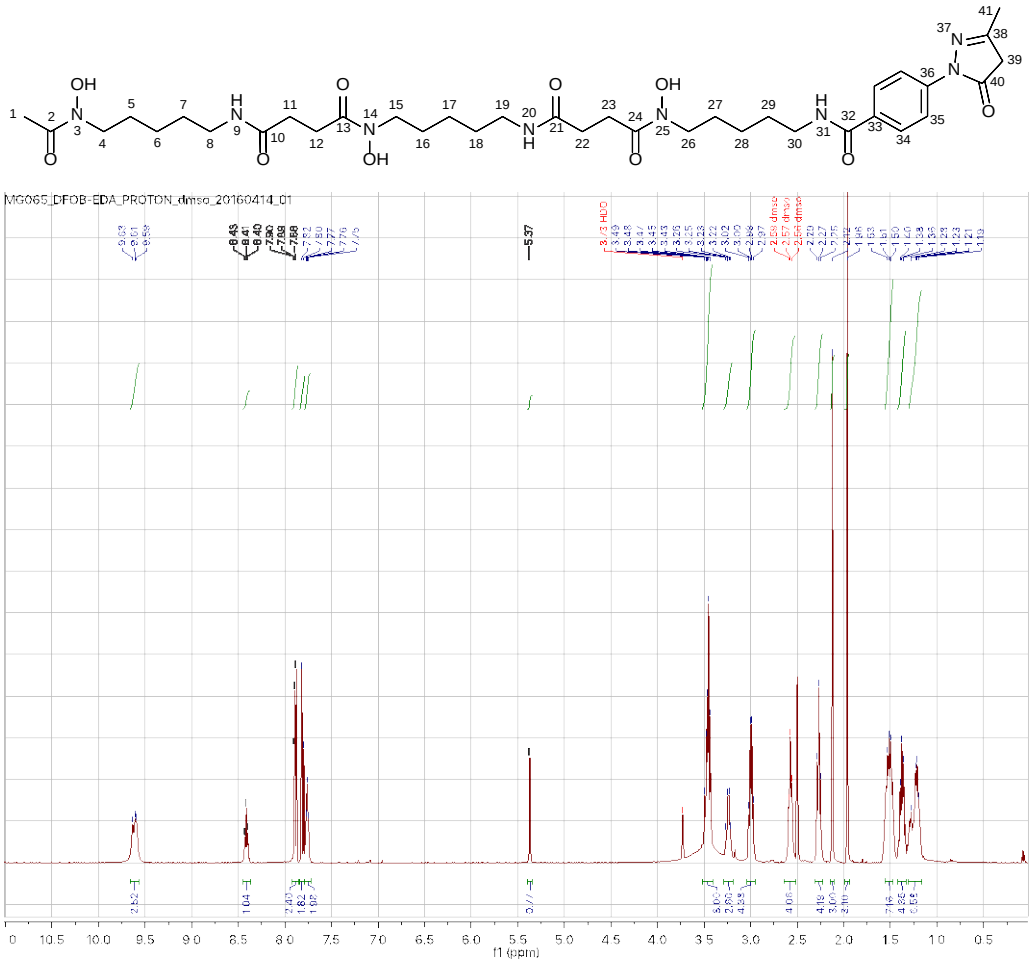

Figure 11: Numbered structure and ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **8**

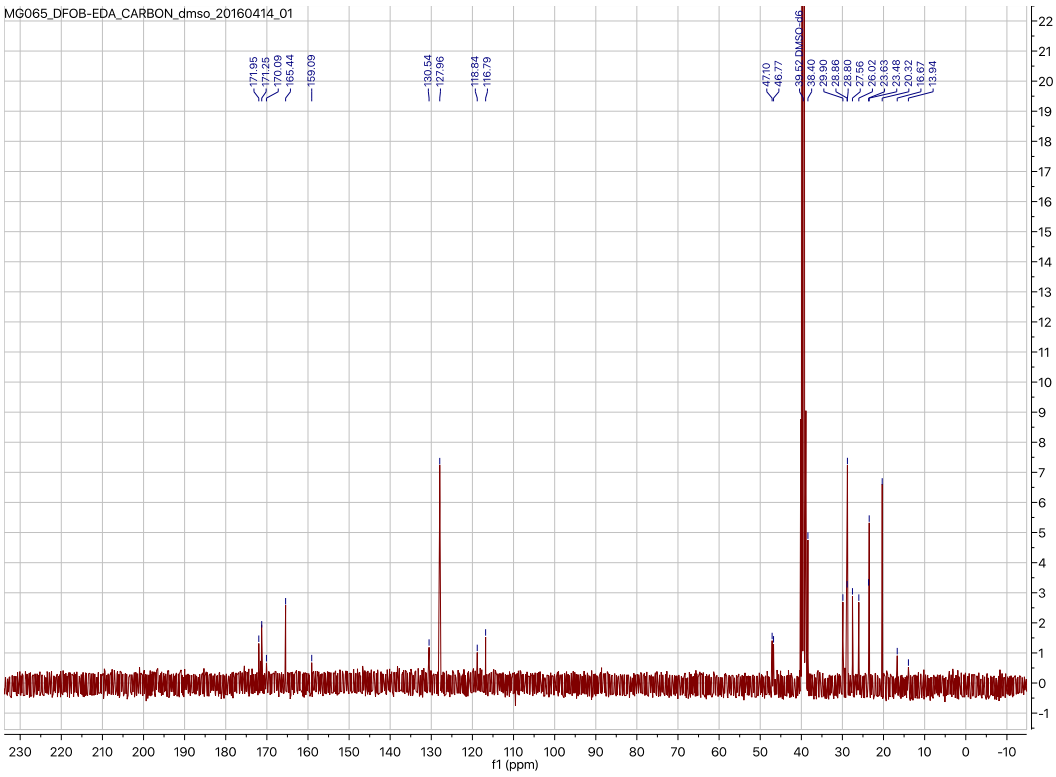

Figure 12: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **8**

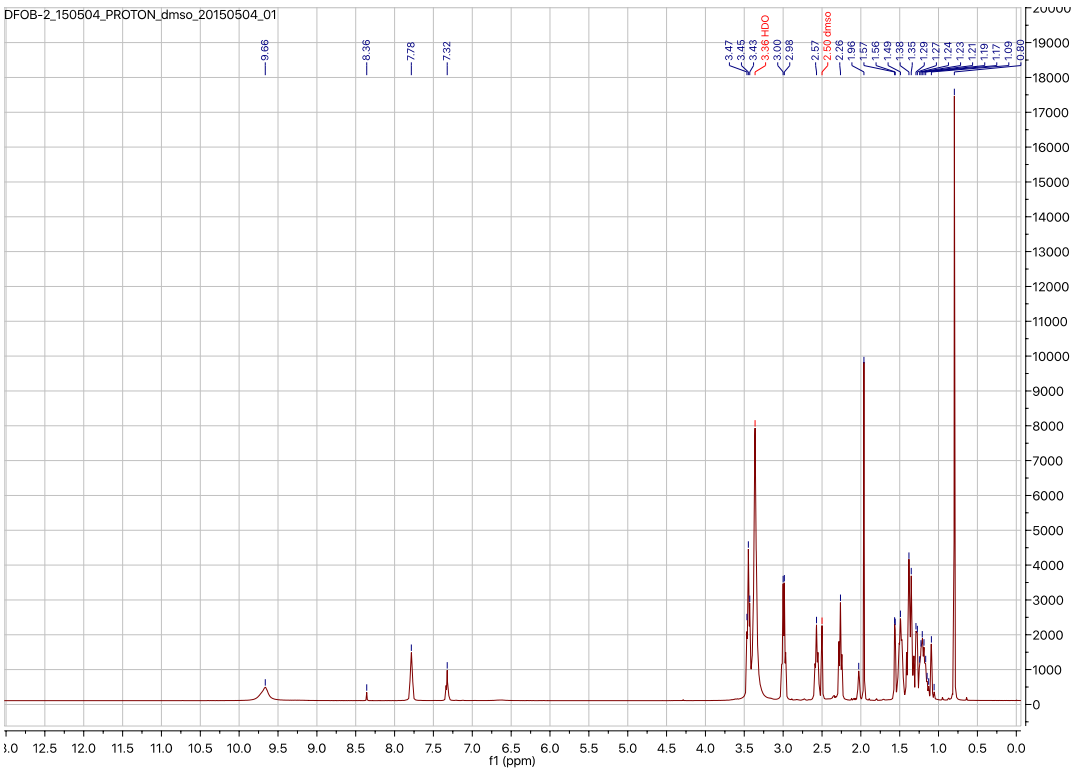

Figure 13: ^{1}H-NMR spectrum (DMSO-d_6, 400 MHz) for compound **9**

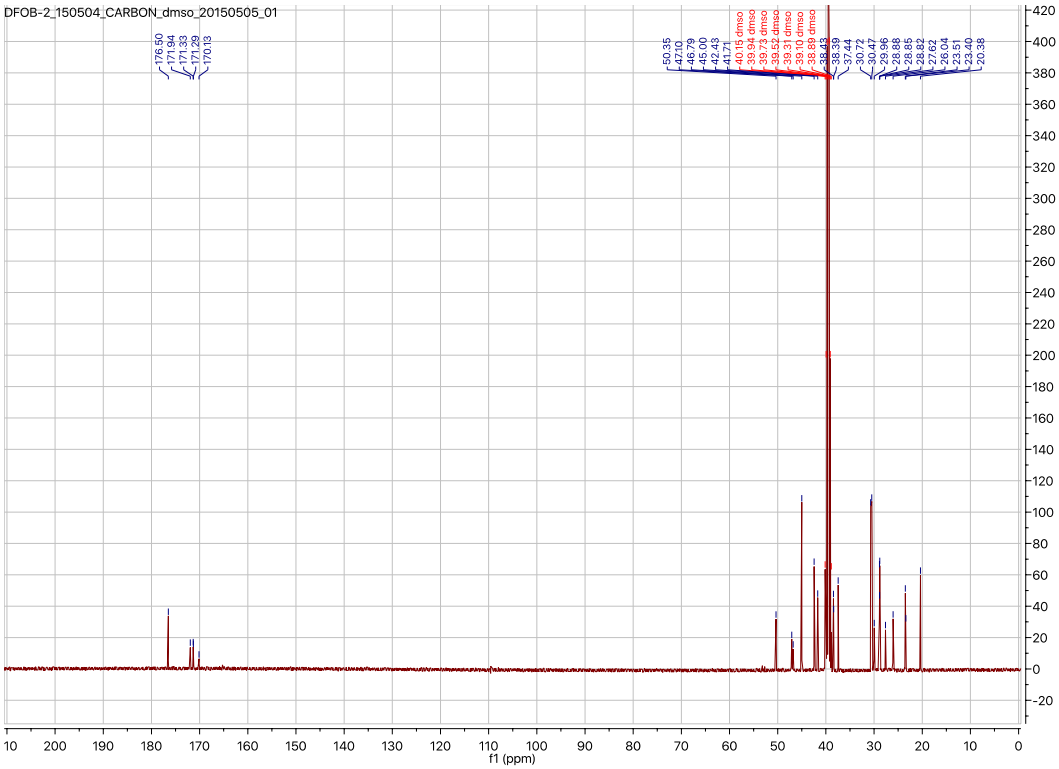

Figure 14: ^{13}C-NMR spectrum (DMSO-d_6, 100 MHz) for compound **9**

High resolution mass spectrometry spectra for compounds 2–9

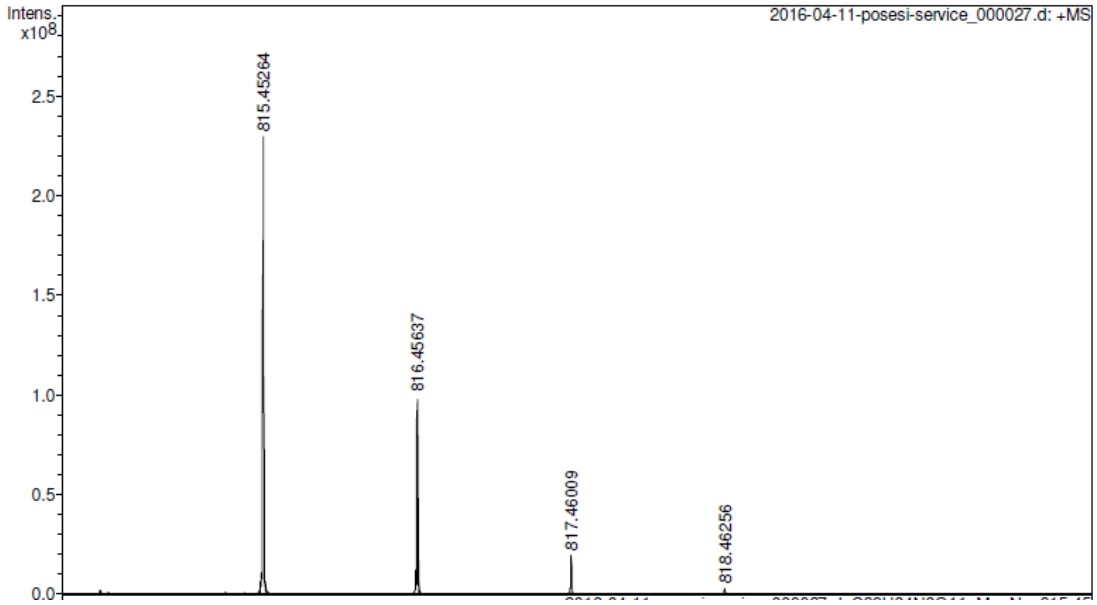

Figure 15: High resolution mass spectrometry (ESI+) for compound **2** found *m/z* 815.45264 ($[M+Na]^+$], $C_{39}H_{64}N_6O_{11}Na$ requires 815.45308.

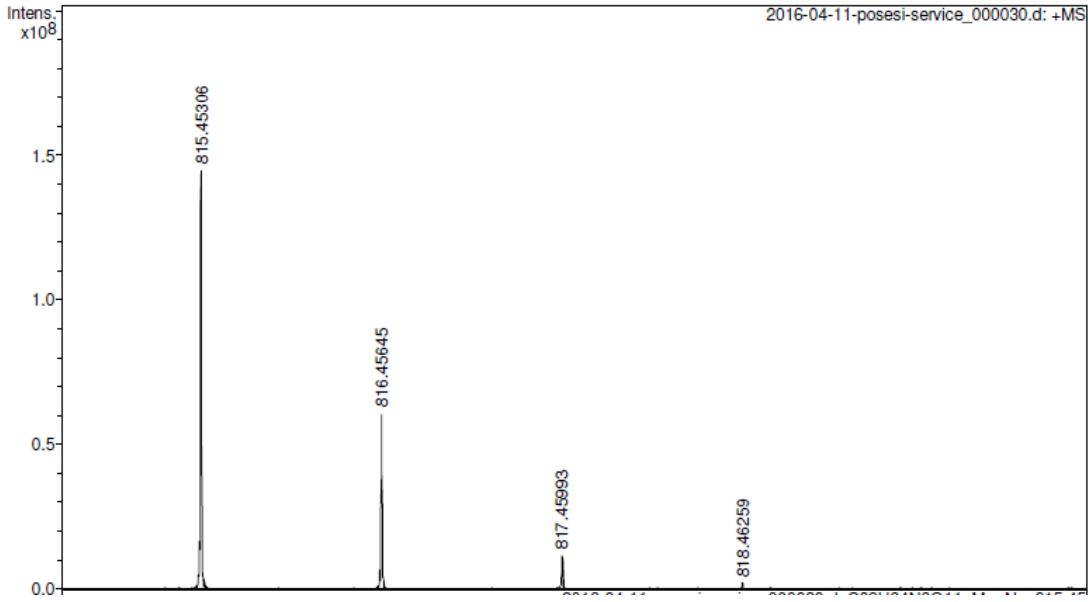

Figure 16: High resolution mass spectrometry (ESI+) for compound **3** found *m/z* 815.45306 ($[M+Na]^+$], $C_{39}H_{64}N_6O_{11}Na$ requires 815.45308.

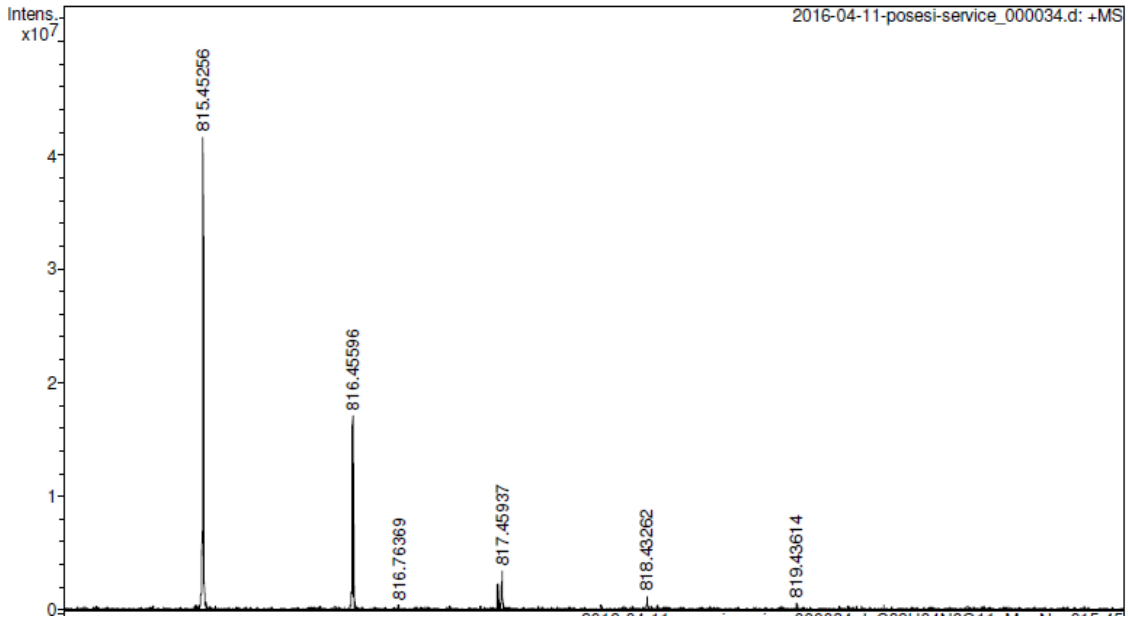

Figure 17: High resolution mass spectrometry (ESI+) for compound **4** found *m/z* 815.45256 ($[M+Na]^+$], $C_{39}H_{64}N_6O_{11}Na$ requires 815.45308.

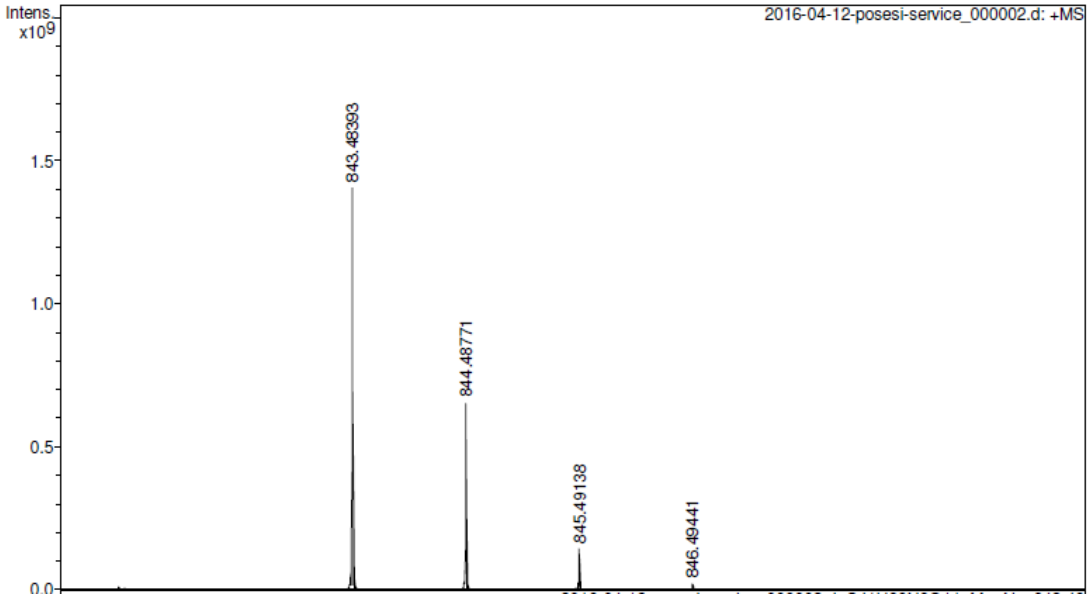

Figure 18: High resolution mass spectrometry (ESI+) for compound **5** found *m/z* 843.48393 ($[M+Na]^+$], $C_{41}H_{68}N_6O_{11}Na$ requires 843.48438.

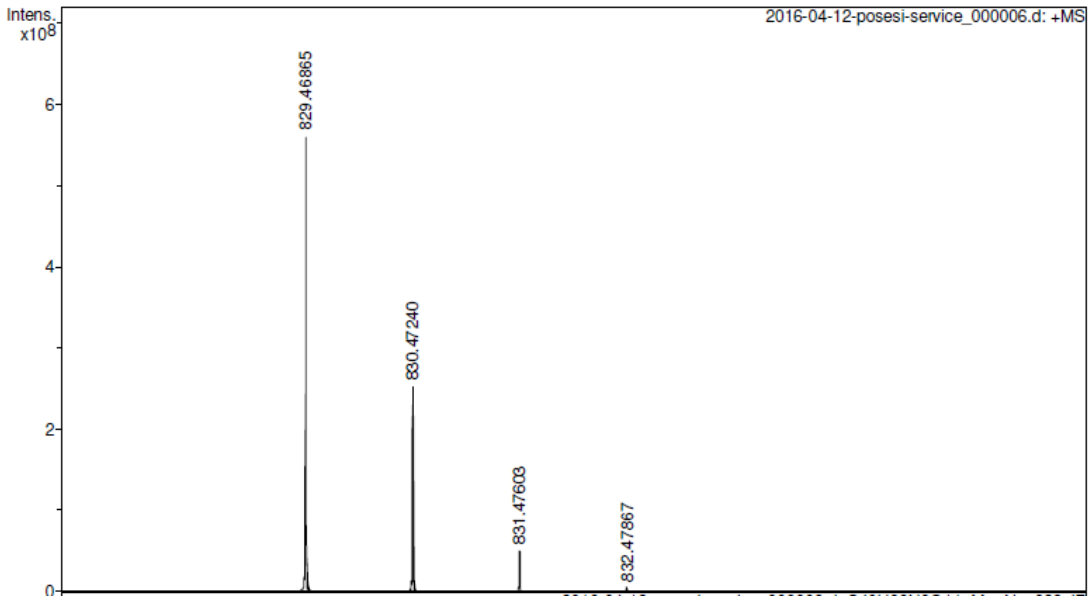

Figure 19: High resolution mass spectrometry (ESI+) for compound **6** found *m/z* 829.46865 ($[M+Na]^+$], $C_{40}H_{66}N_6O_{11}Na$ requires 829.46873.

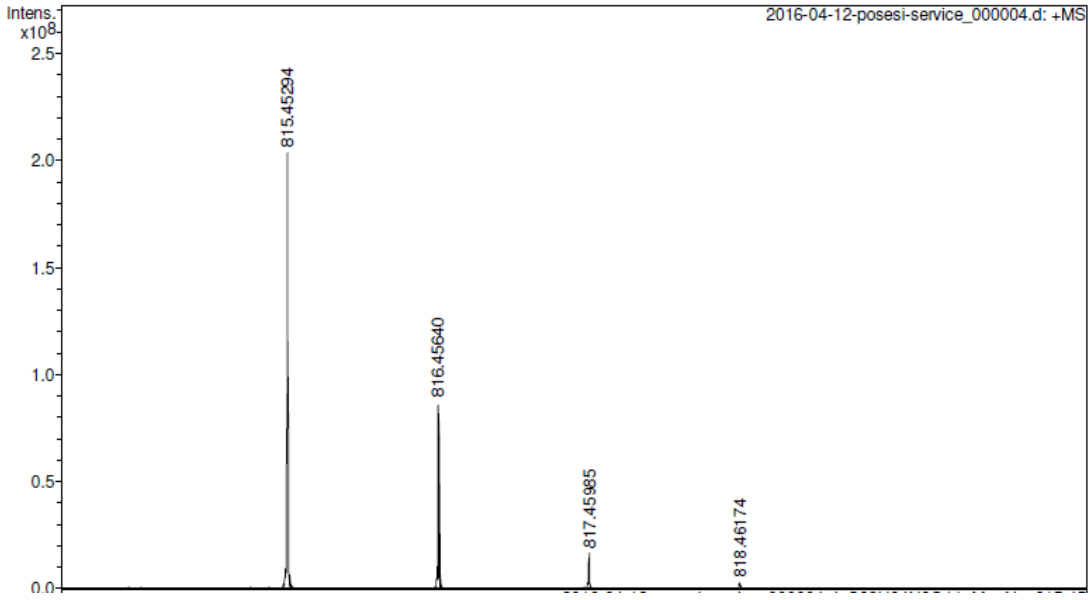

Figure 20: High resolution mass spectrometry (ESI+) for compound **7** found *m/z* 815.45294 ($[M+Na]^+$], $C_{39}H_{64}N_6O_{11}Na$ requires 815.45308.

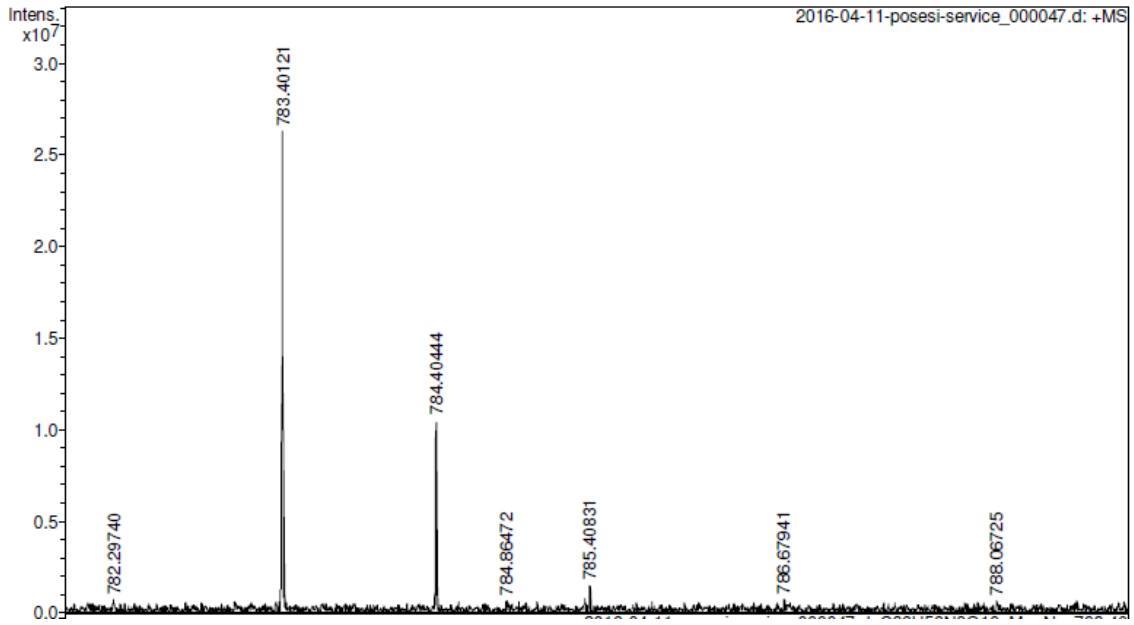

Figure 21: High resolution mass spectrometry (ESI+) for compound **8** found *m/z* 783.40121 ($[M+Na]^+$], $C_{36}H_{56}N_8O_{10}Na$ requires 783.40171.

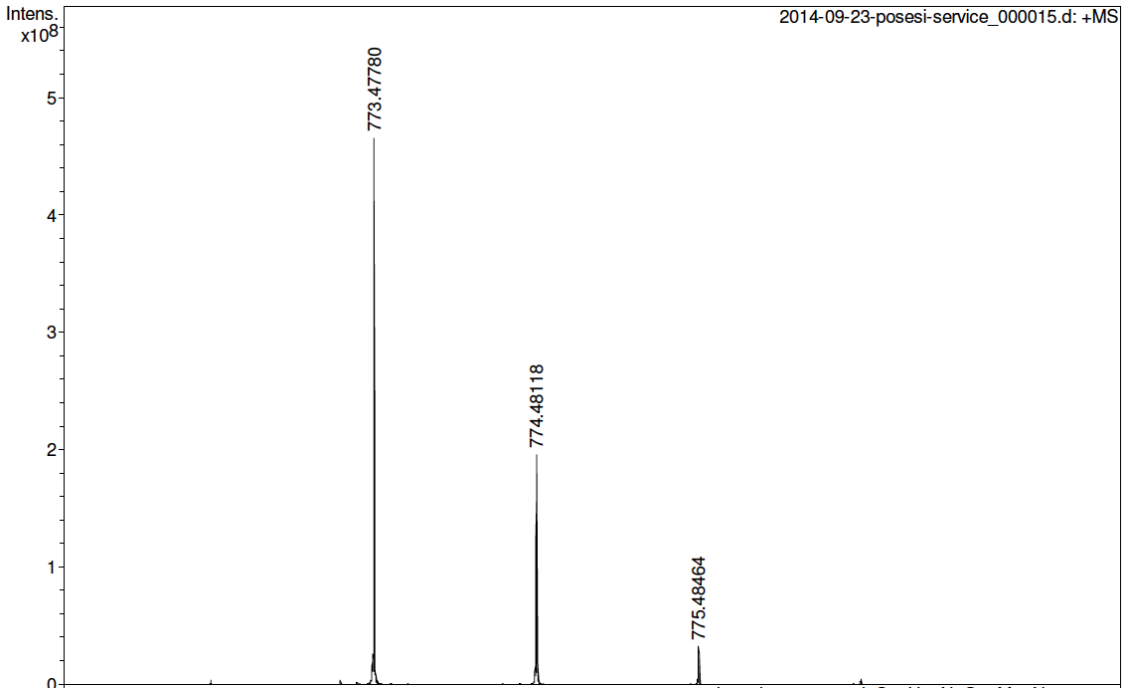

Figure 22: High resolution mass spectrometry (ESI+) for compound **9** found *m/z* 773.47780 ($[M+Na]^+$], $C_{38}H_{66}N_6O_9Na$ requires 773.4789.