Supporting Information

Diversity-Oriented Synthesis and Cytotoxic Activity Evaluation of Biaryl-Containing Macrocycles

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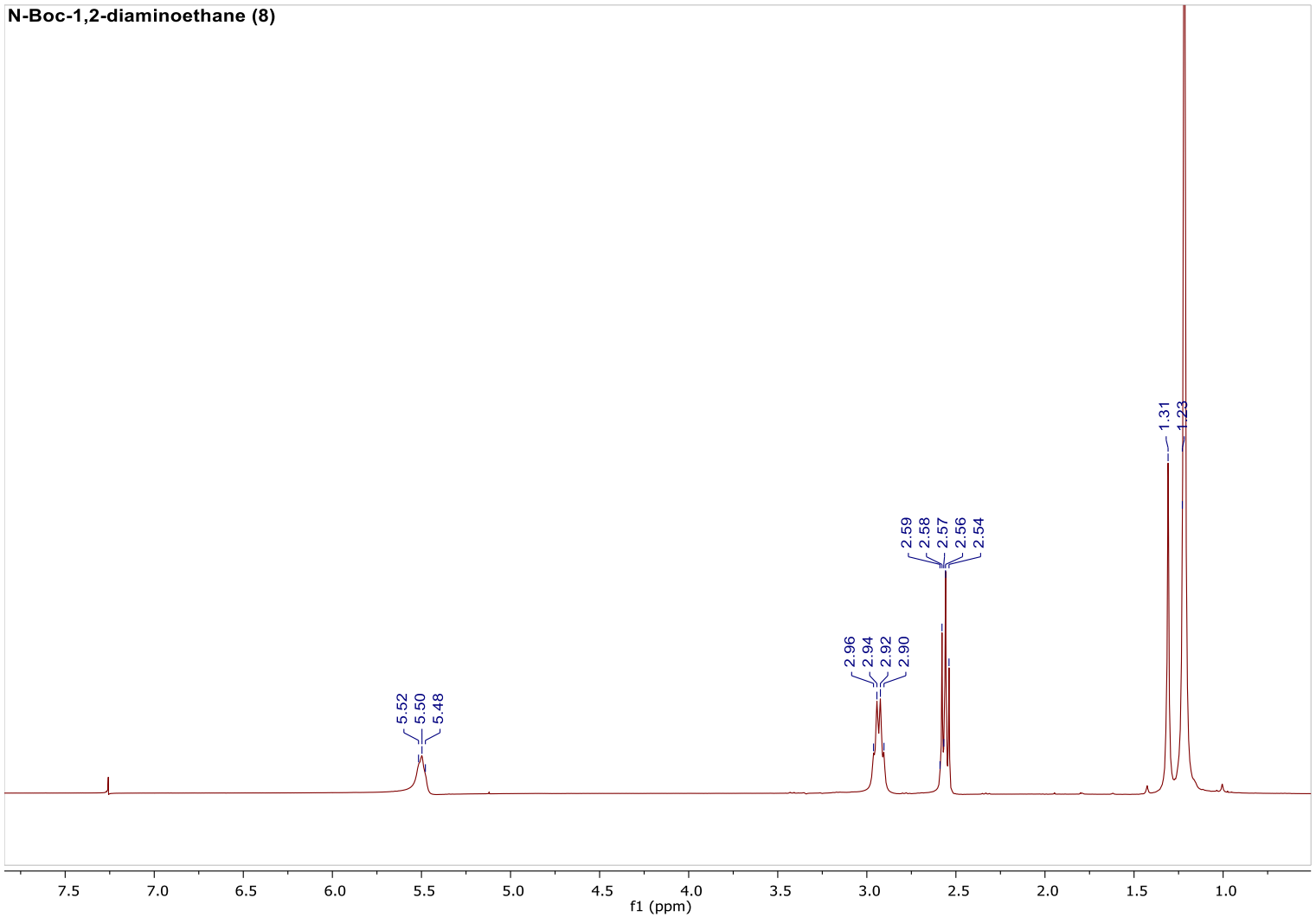


Figure 1. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of compound **8**

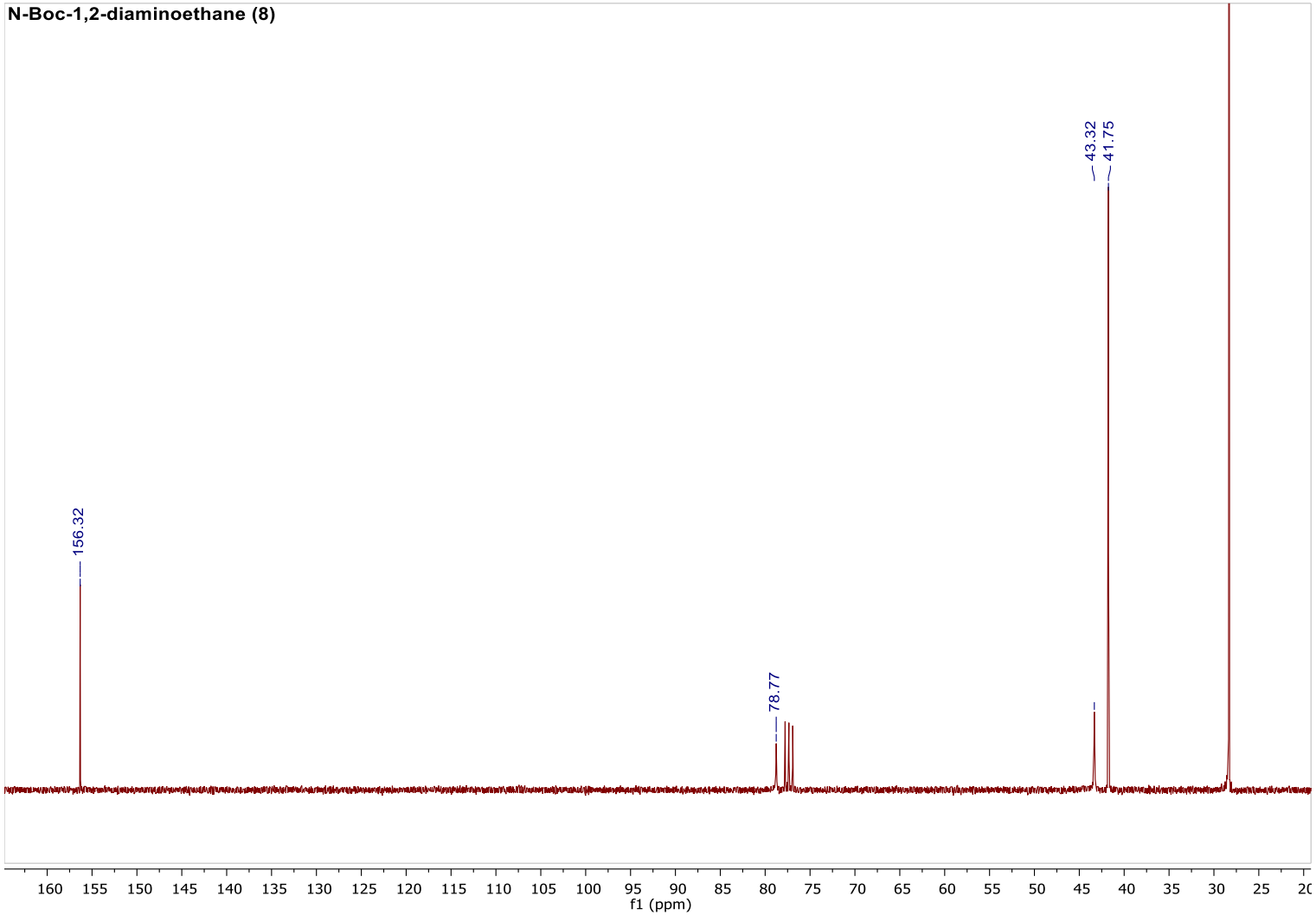


Figure 2. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of compound **8**

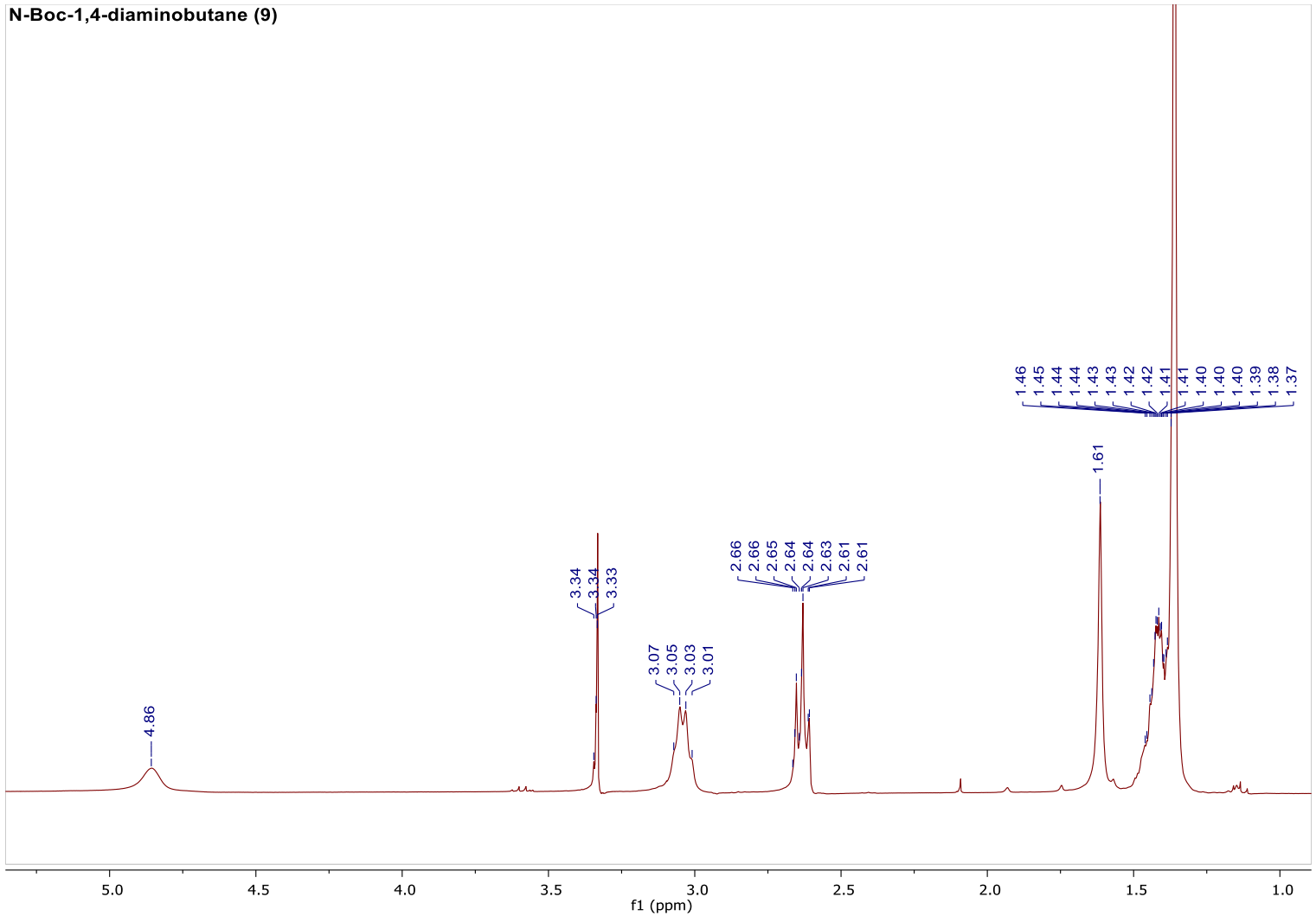


Figure 3. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of compound **9**

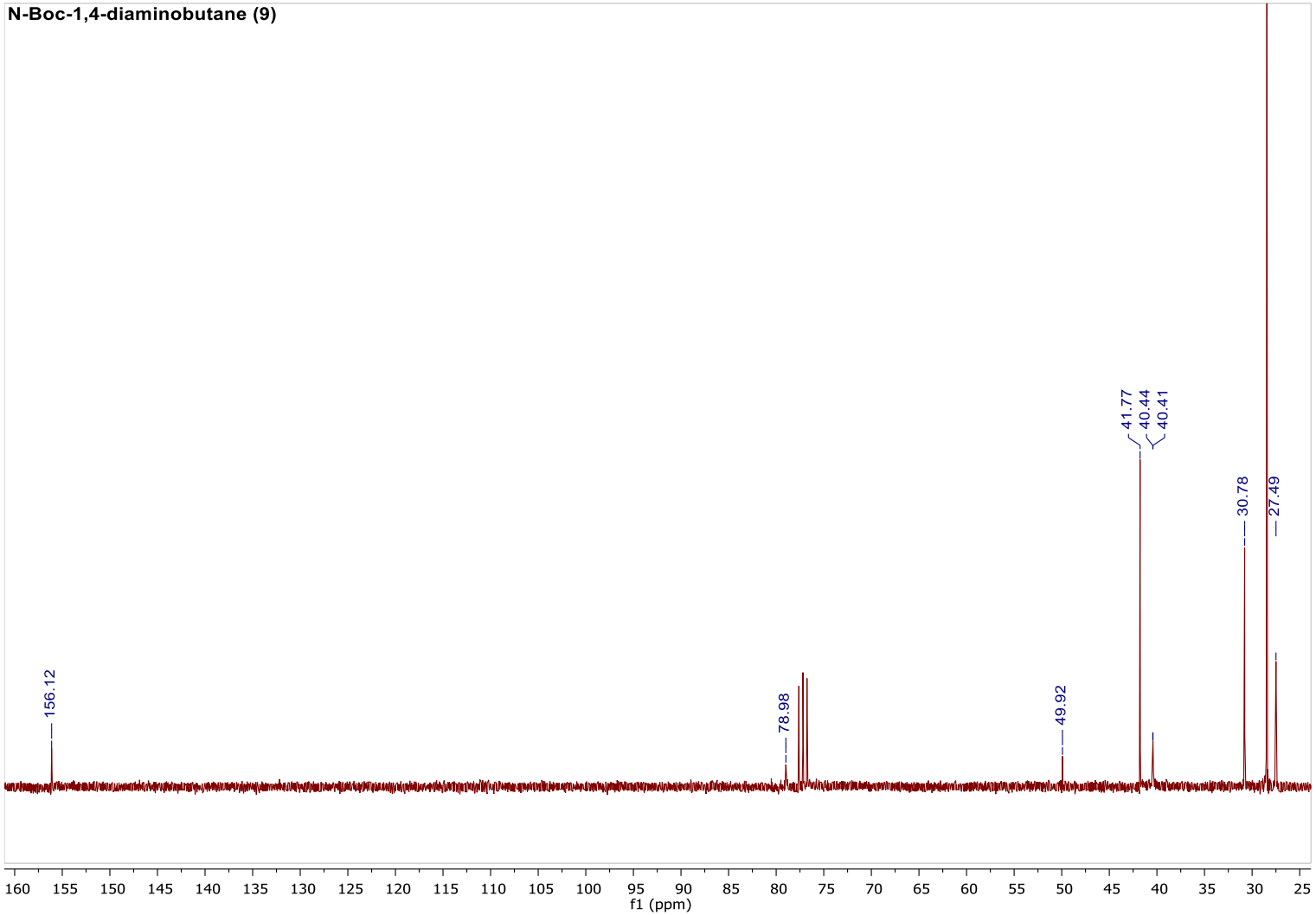


Figure 4. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of compound **9**

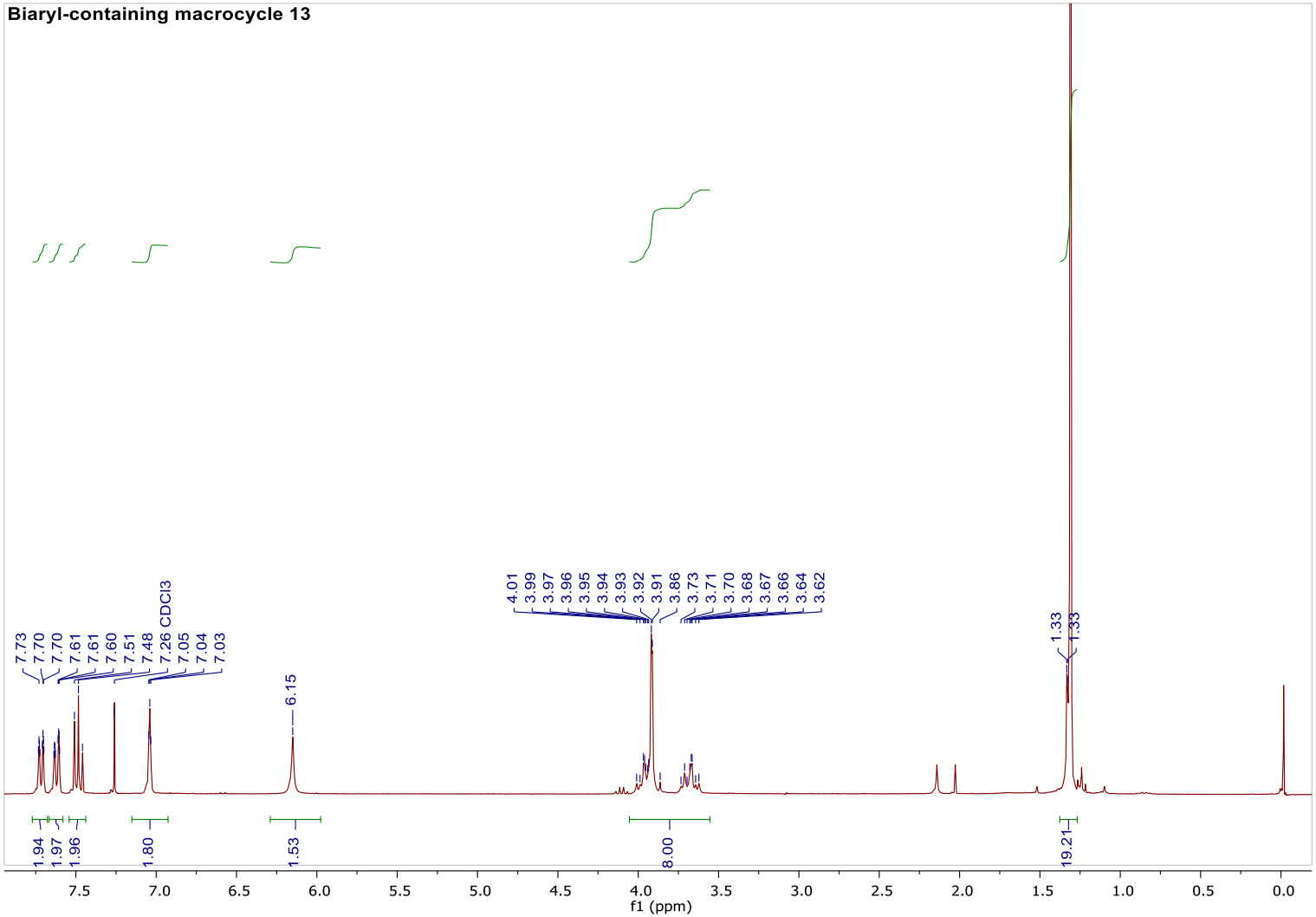


Figure 5. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **13**

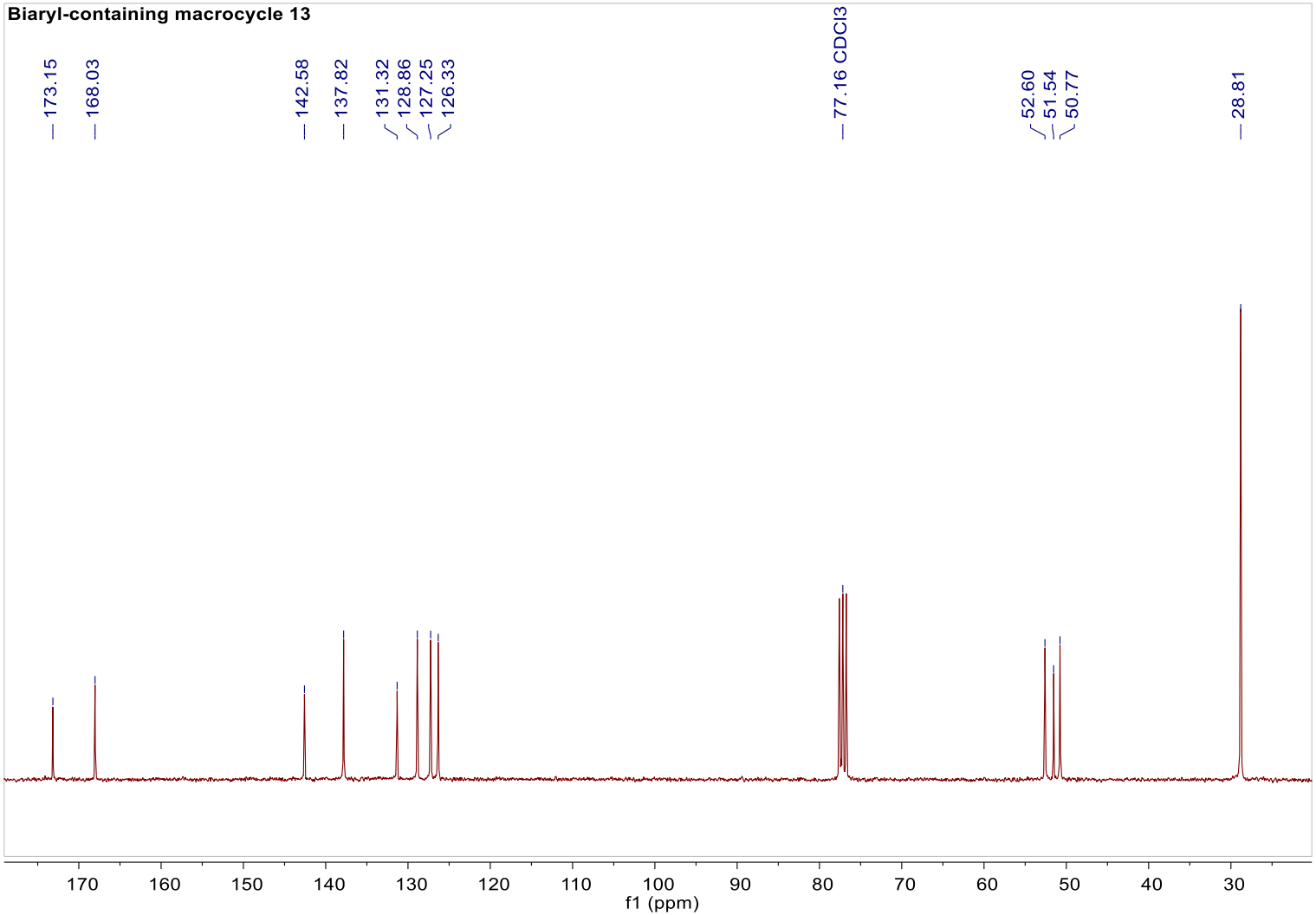
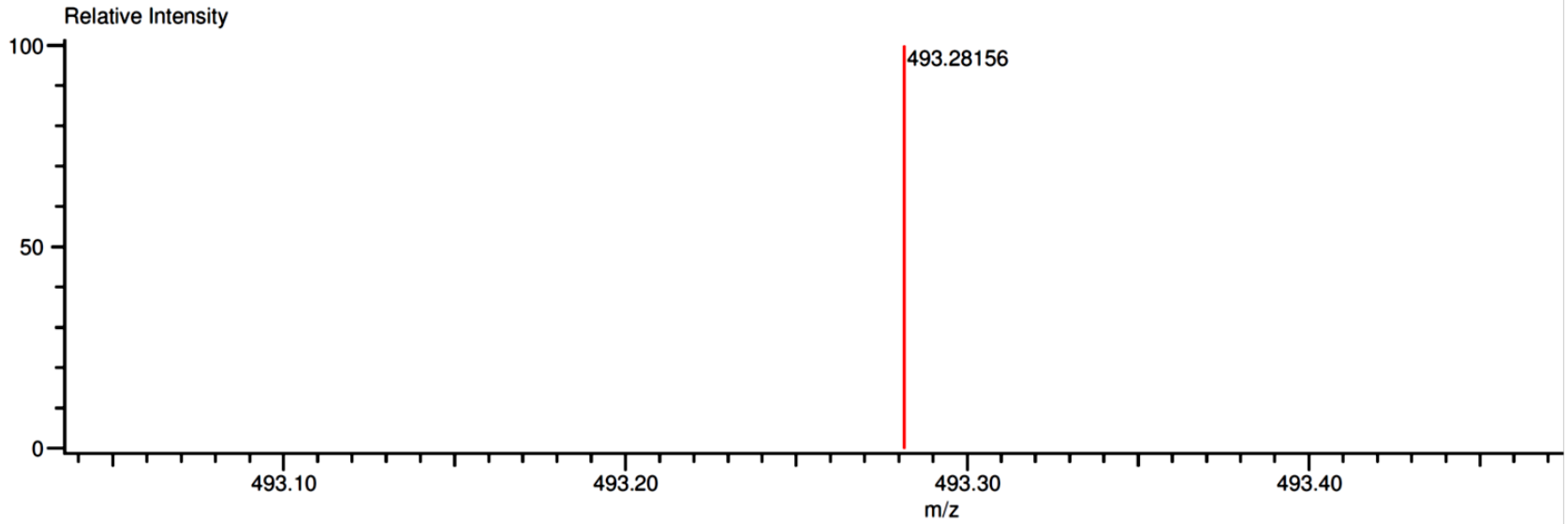


Figure 6. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **13**

Data:2484 MCM-032
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 0.7...

Acquired:9/26/2014 12:23:58
Operator:AccuTOF
Mass Calibration data:Cal_Pe
Created:10/9/2014 12:42:43 F
Created by:AccuTOF

Charge number:1
Tolerance:3.00(mmu)
Unsaturation Number:0.0 .. 20
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:0 .. 5, ^{16}O:0 .. 5



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
493.28156	1911985.04	493.28148	0.08	$^{12}C_{28}{}^{1}H_{37}{}^{14}N_{4}{}^{16}O_{4}$	12.5

Figure 7. HRMS (DART+) spectra of macrocycle **13**

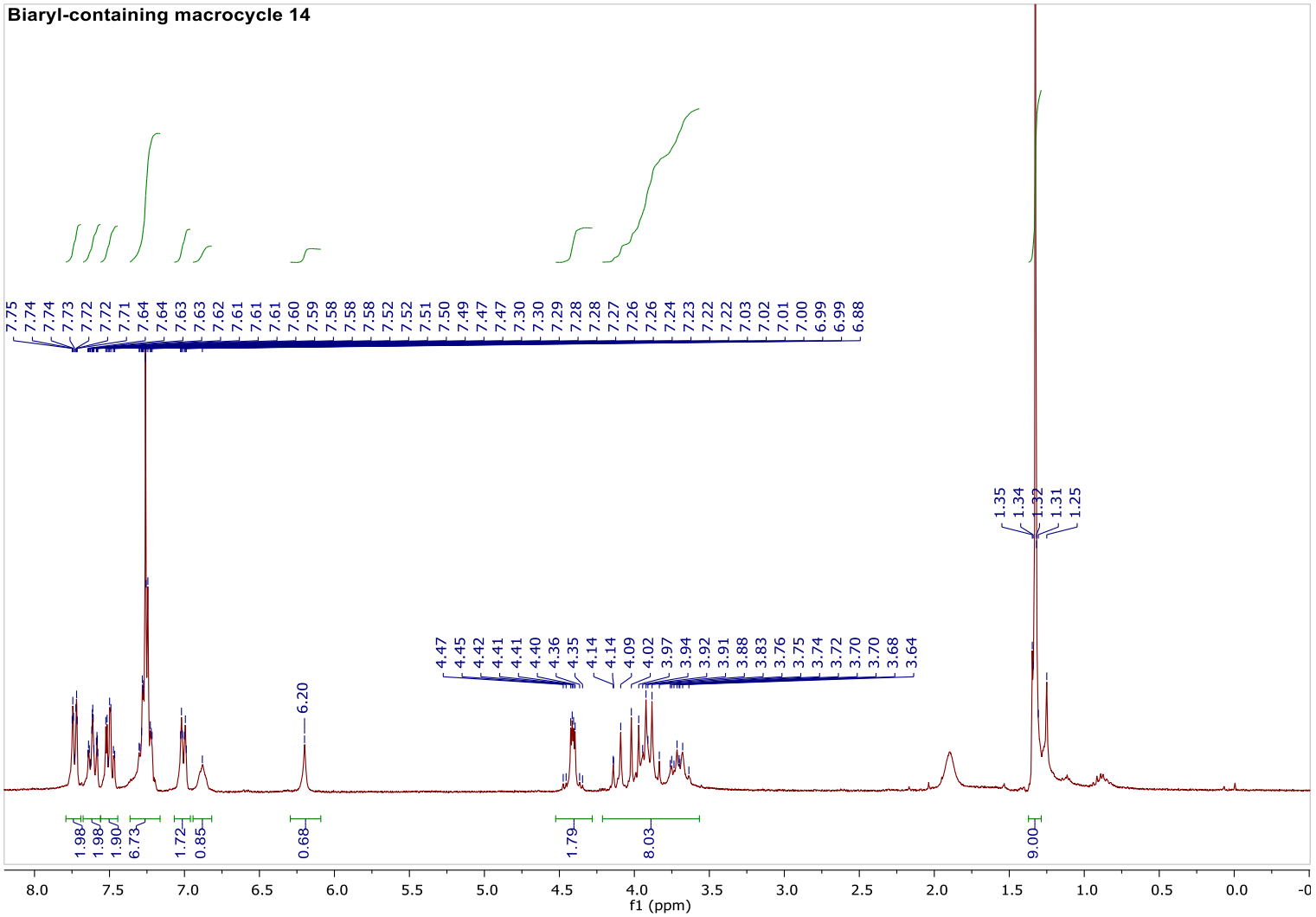


Figure 8. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **14**

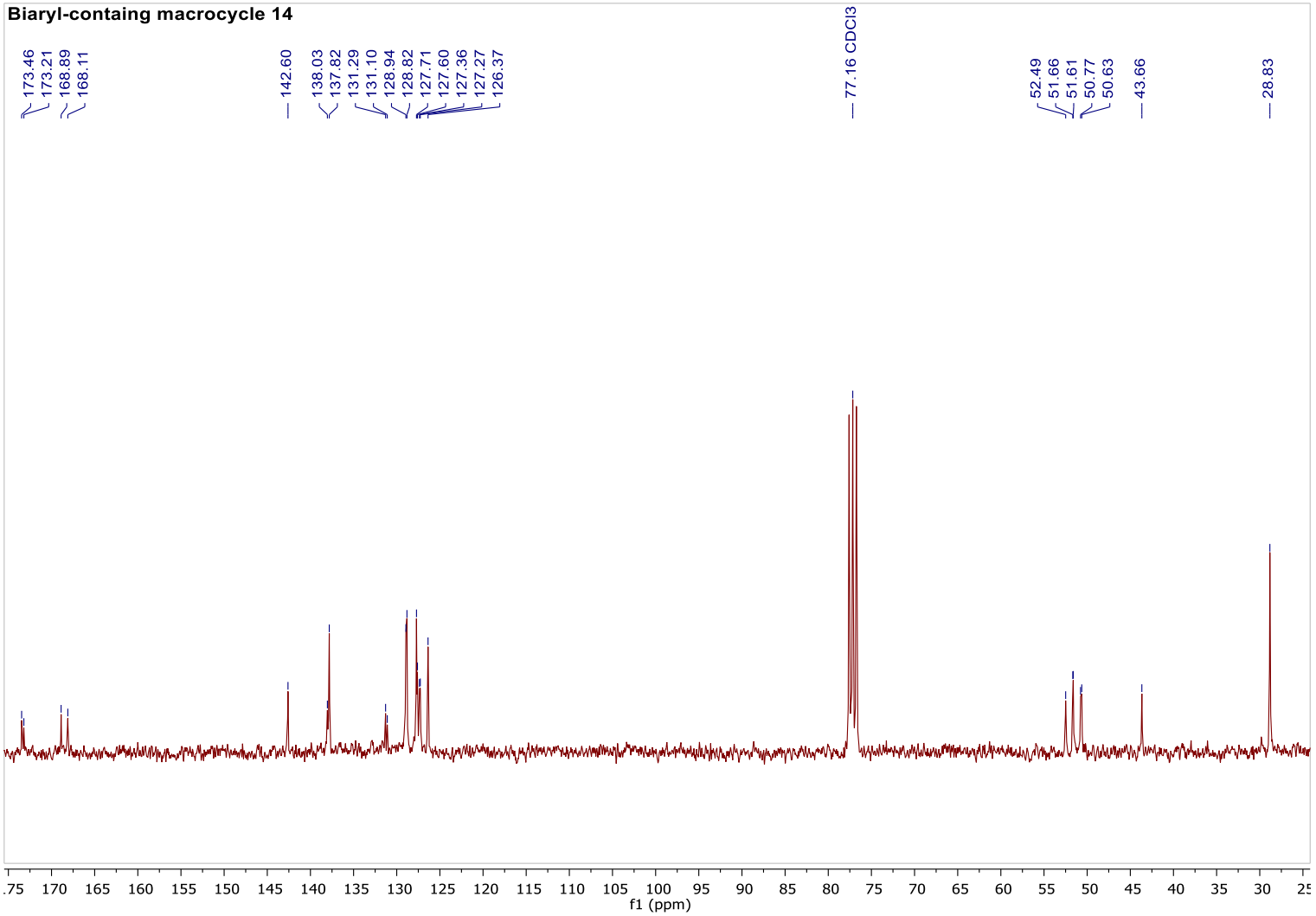
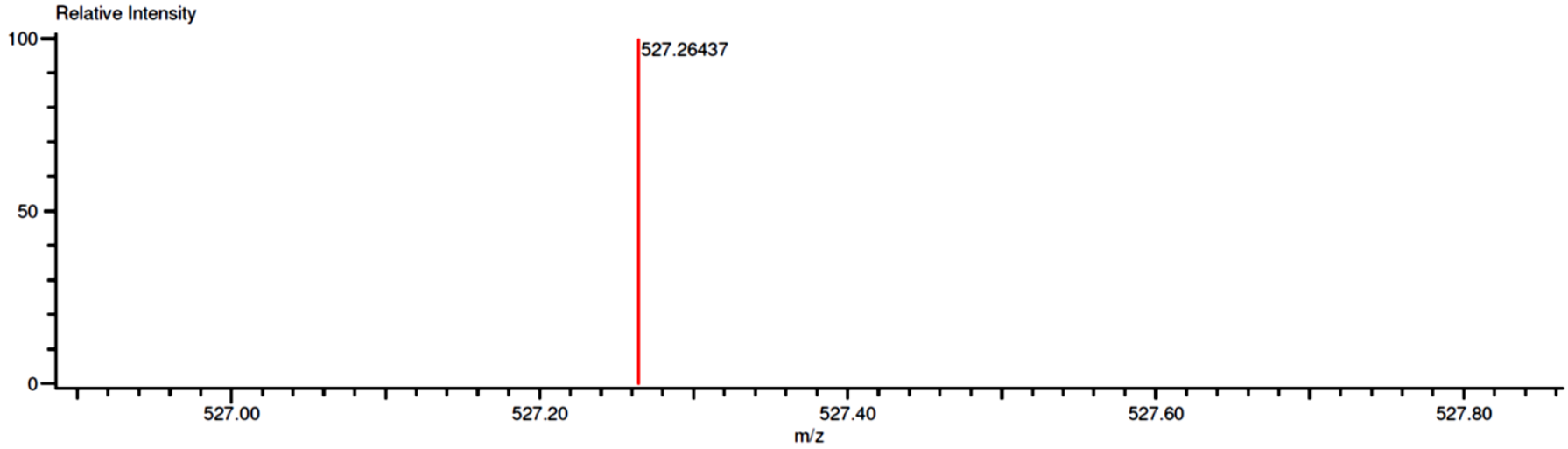


Figure 9. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **14**

Data:2604 MCM-034
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 0.3...

Acquired:10/7/2014 6:52:16 PM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:10/15/2014 1:10:24 PM
Created by:AccuTOF

Charge number:1
Tolerance:3.00(mmu)
Unsaturation Number:0.0 .. 18.0 (Fraction:.5)
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:0 .. 4, ^{16}O:0 .. 5



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
527.26437	323866.88	527.26583	-1.45	$^{12}C_{31}{}^{1}H_{35}{}^{14}N_4{}^{16}O_4$	16.5

Figure 10. HRMS (DART+) spectra of macrocycle **14**

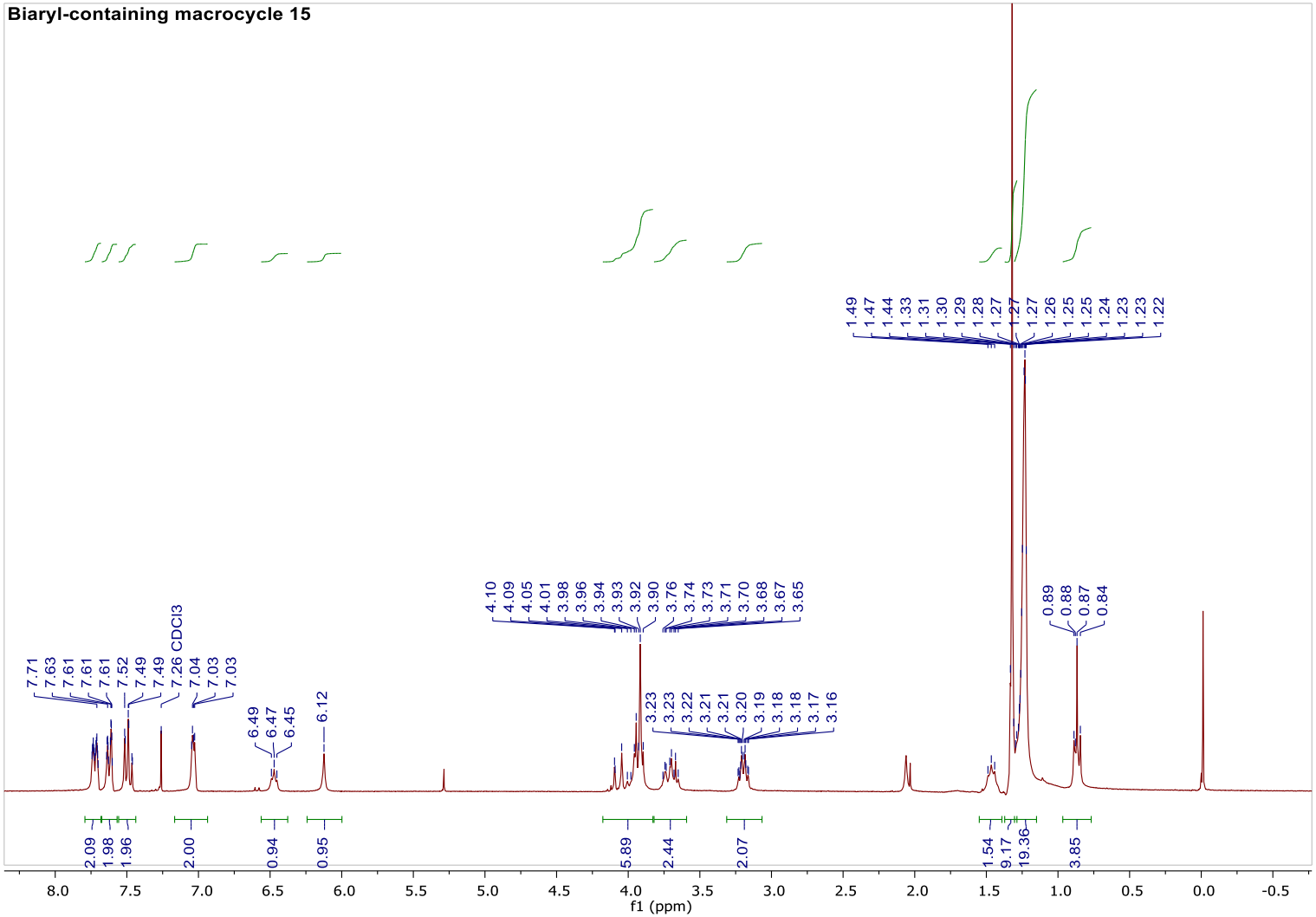


Figure 11. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **15**

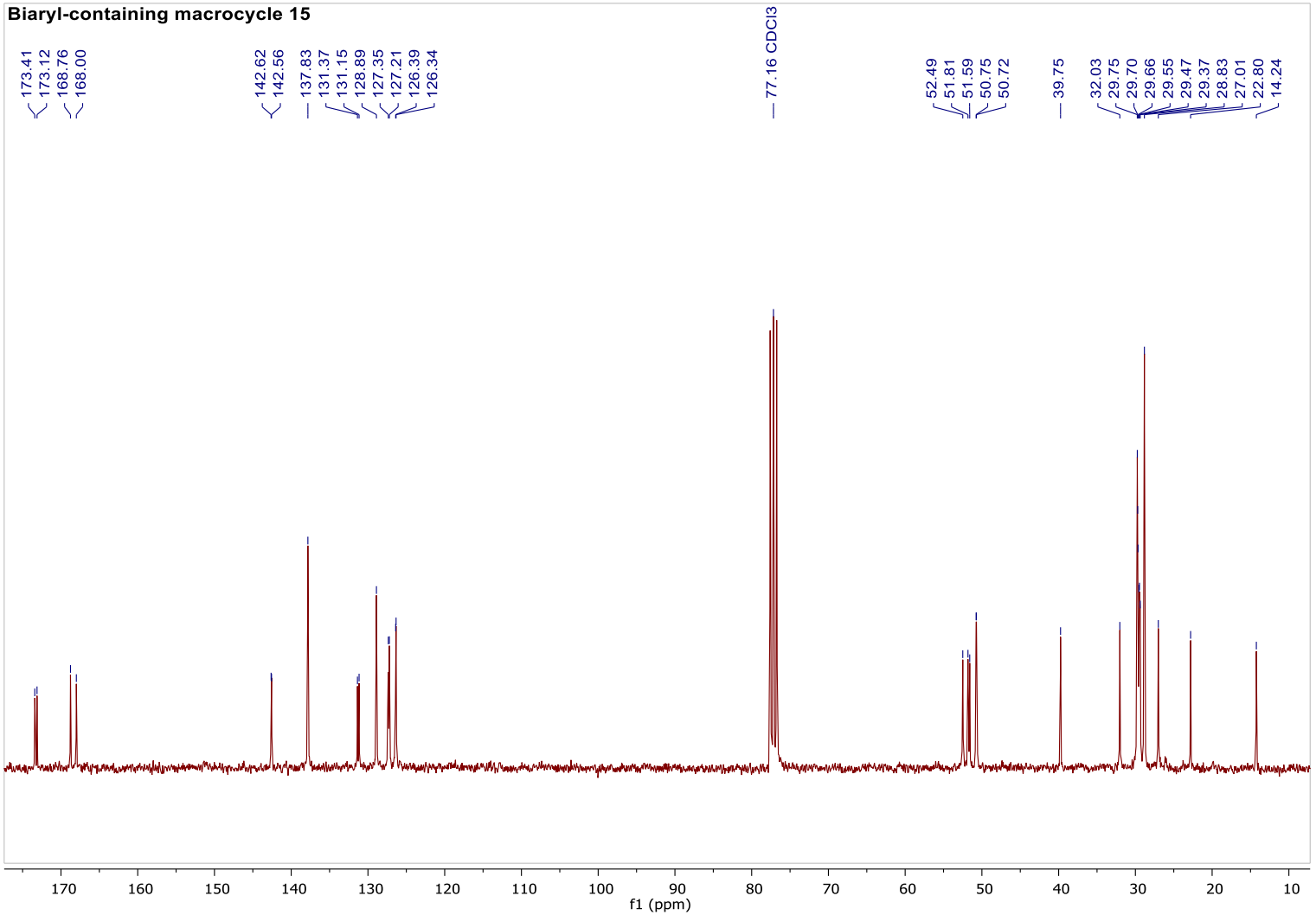


Figure 12. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **15.**

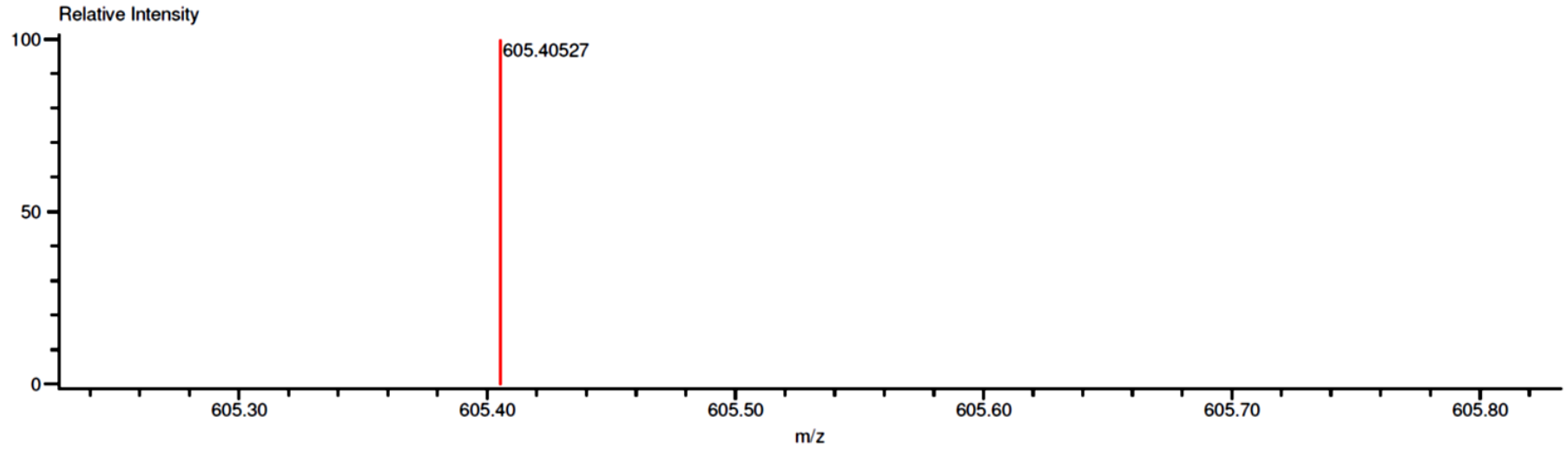
Data:3332 MCM-081
Sample Name:Dr Miranda Luis III
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1.1...

Acquired:11/25/2014 5:10:24 PM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:12/5/2014 2:13:19 PM
Created by:AccuTOF

Charge number:1
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:3 .. 6, ^{16}O:2 .. 5

Tolerance:3.00(mmu)

Unsaturation Number:0.0 .. 200.0 (Fraction:Both)



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
605.40527	409949.75	605.40668	-1.41	$^{12}C_{36}{}^{1}H_{53}{}^{14}N_{4}{}^{16}O_{4}$	12.5

Figure 13. HRMS (DART+) spectra of macrocycle **15**

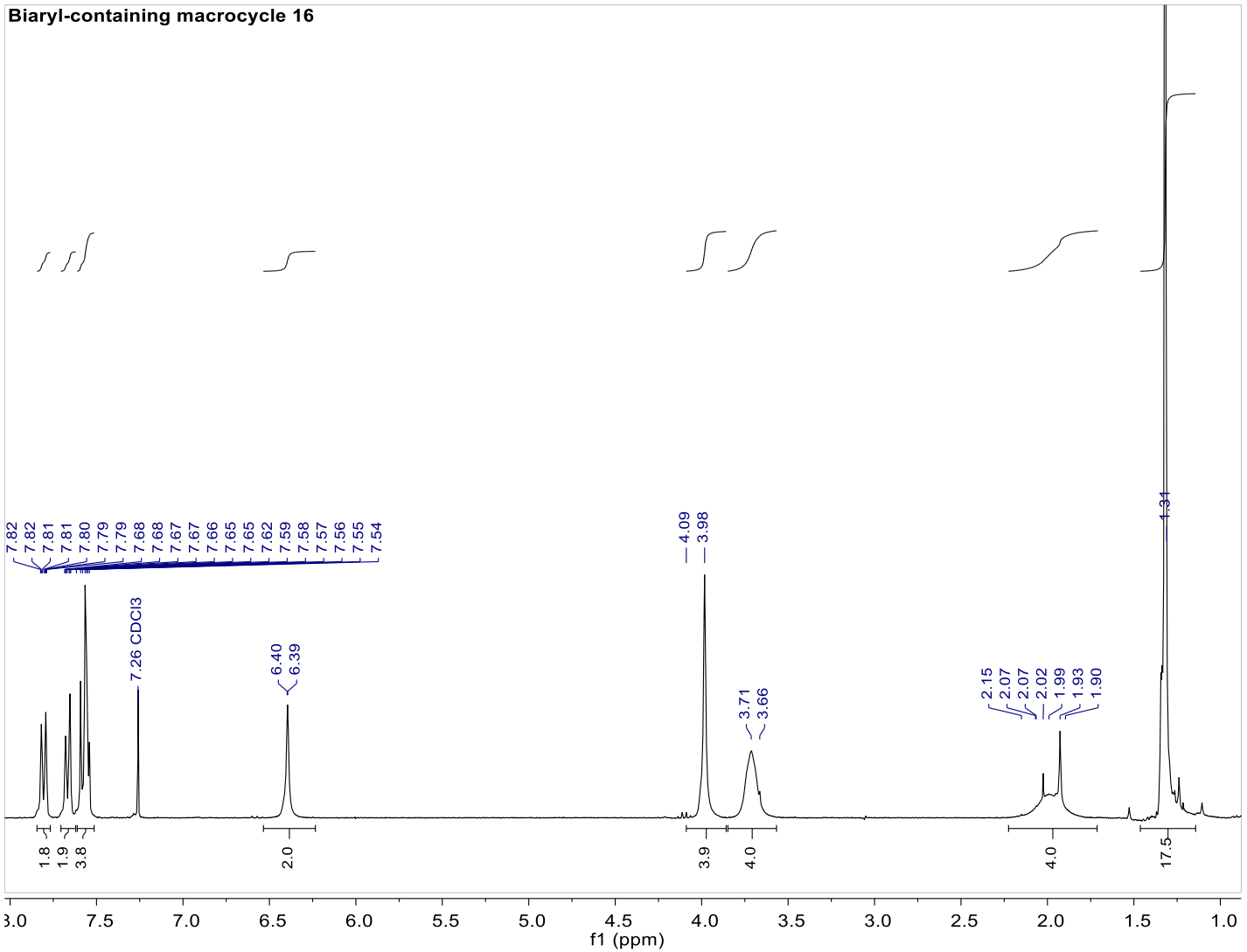


Figure 14. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **16**

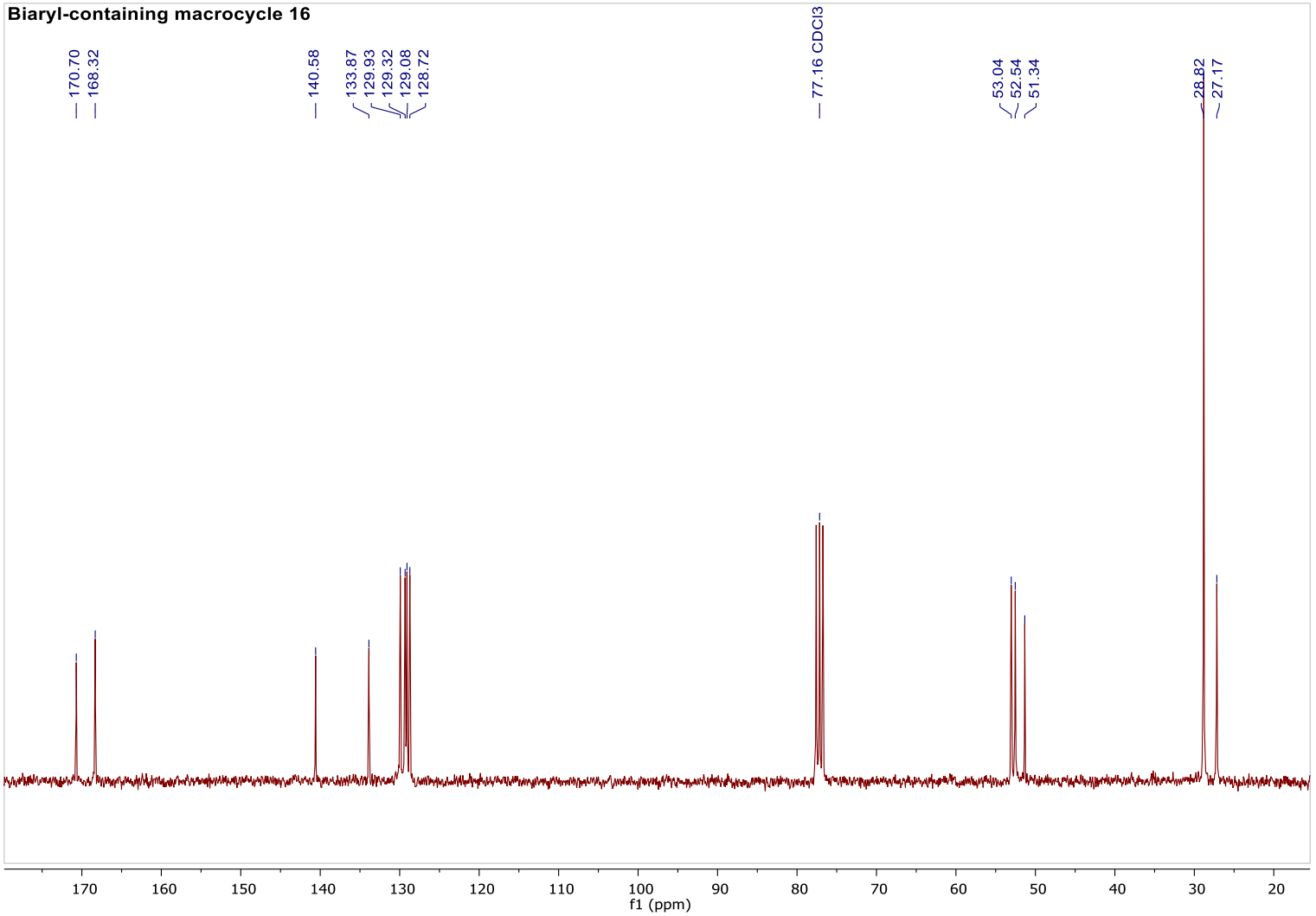
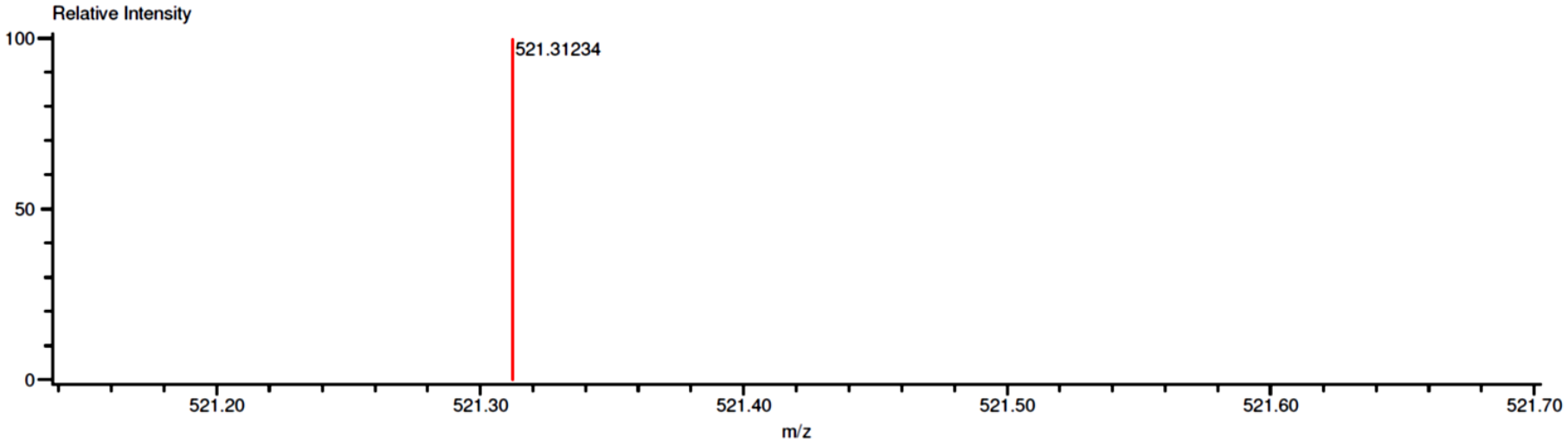


Figure 15. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **16**

Data:3359 MCM-068A
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 0.9...

Acquired:11/25/2014 5:50:24 PM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:1/6/2015 4:13:44 PM
Created by:AccuTOF

Charge number:1
Tolerance:3.00(mmu)
Unsaturation Number:0.0 .. 15.0 (Fraction:.5)
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:0 .. 5, ^{16}O:0 .. 5



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
521.31234	384596.50	521.31278	-0.44	$^{12}C_{30}{}^{1}H_{41}{}^{14}N_{4}{}^{16}O_{4}$	12.5

Figure 16. HRMS (DART+) spectra of macrocycle **16**

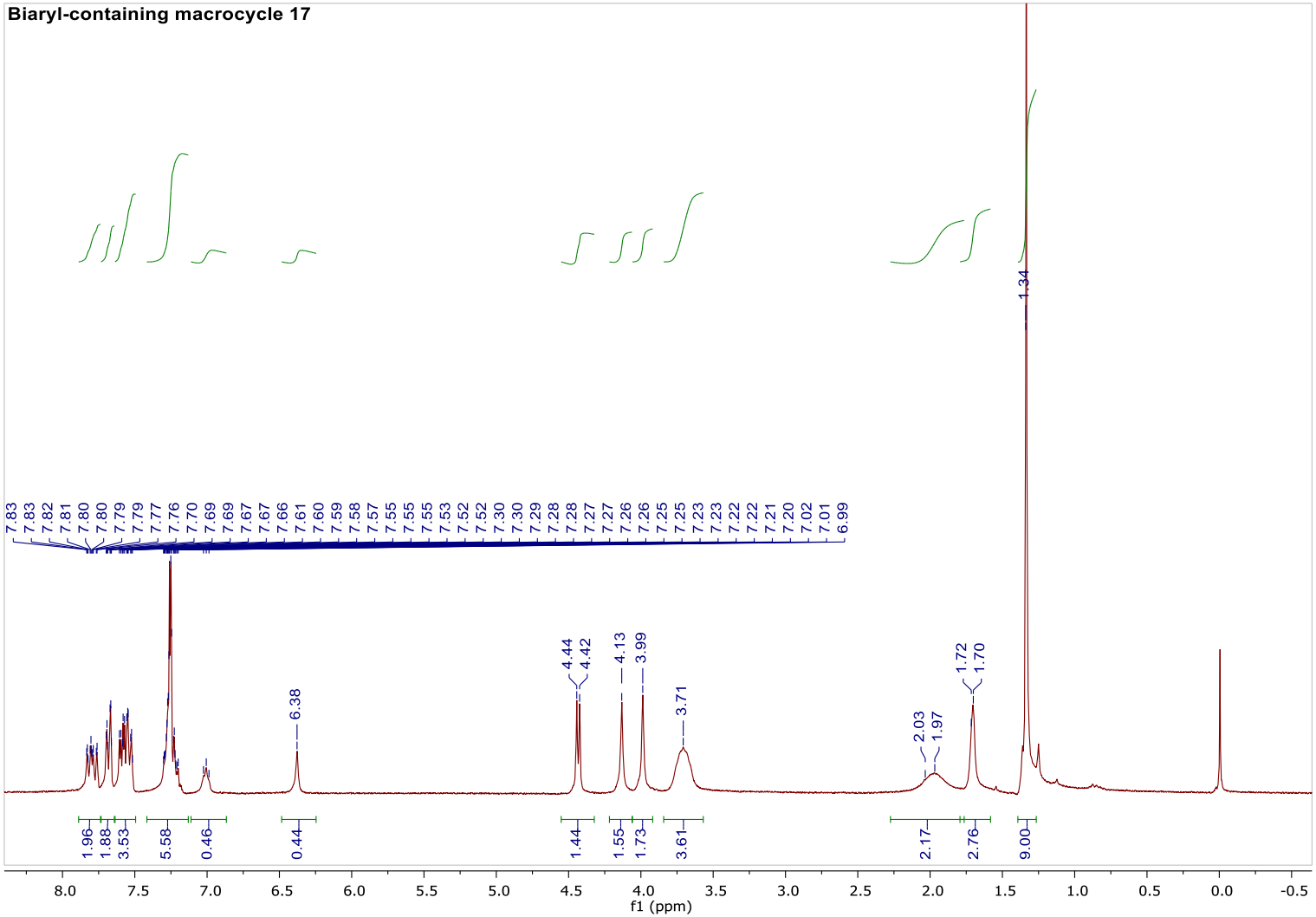


Figure 17. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **17**

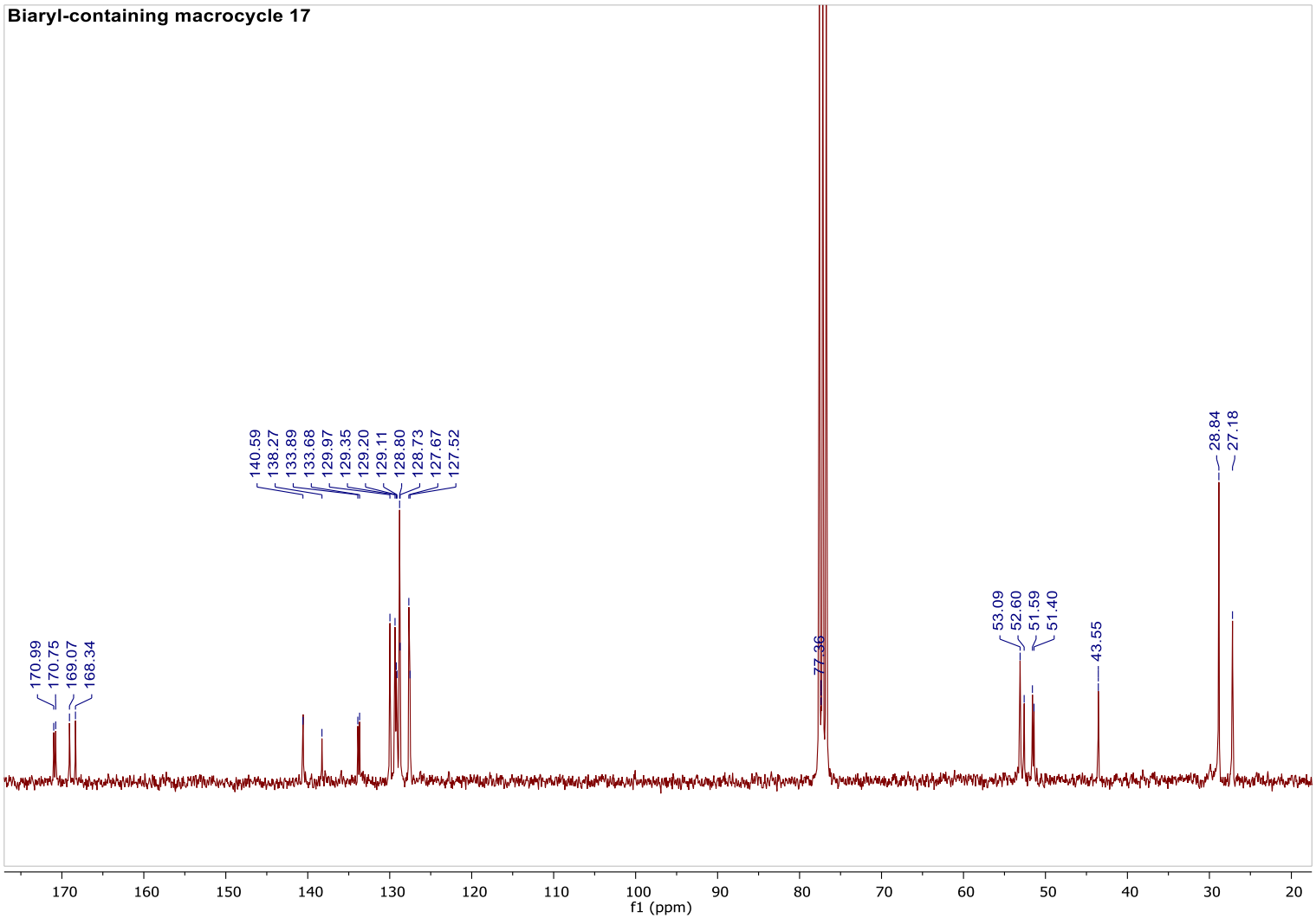
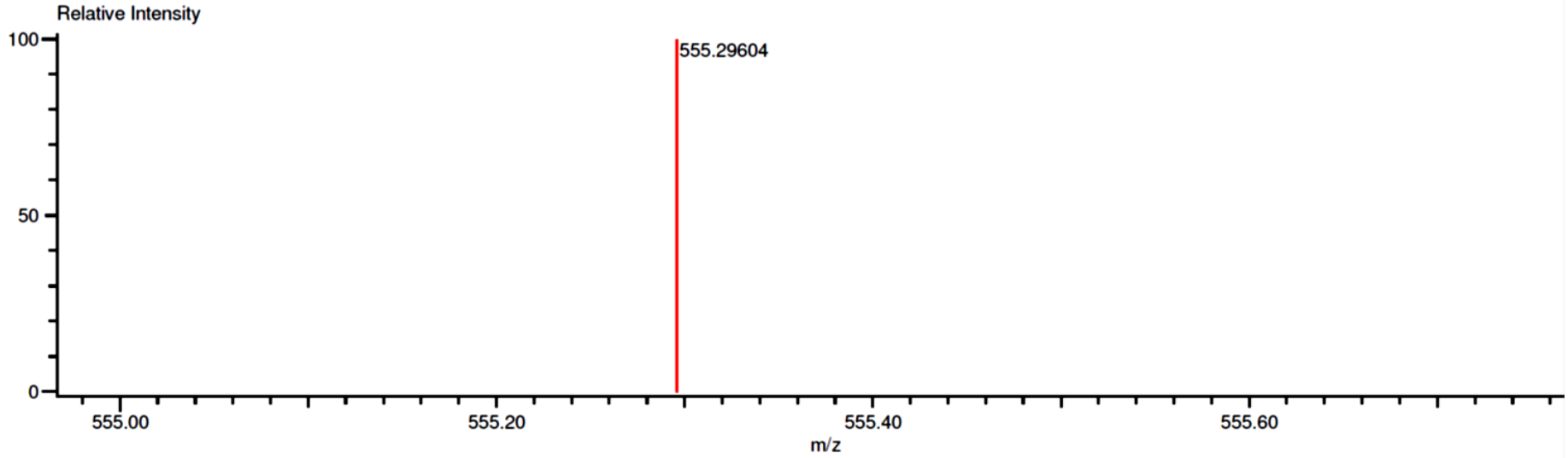


Figure 18. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **17**

Data:3375 MCM-075
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1.1...

Acquired:11/27/2014 6:40:03 PM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:12/5/2014 2:14:46 PM
Created by:AccuTOF

Charge number:1
Tolerance:3.00(mmu)
Unsaturation Number:0.0 .. 200.0 (Fraction:Both)
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:3 .. 6, ^{16}O:2 .. 5



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
555.29604	170540.33	555.29713	-1.09	$^{12}C_{33}{}^{1}H_{39}{}^{14}N_{4}{}^{16}O_{4}$	16.5

Figure 19. HRMS (DART+) spectra of macrocycle **17**

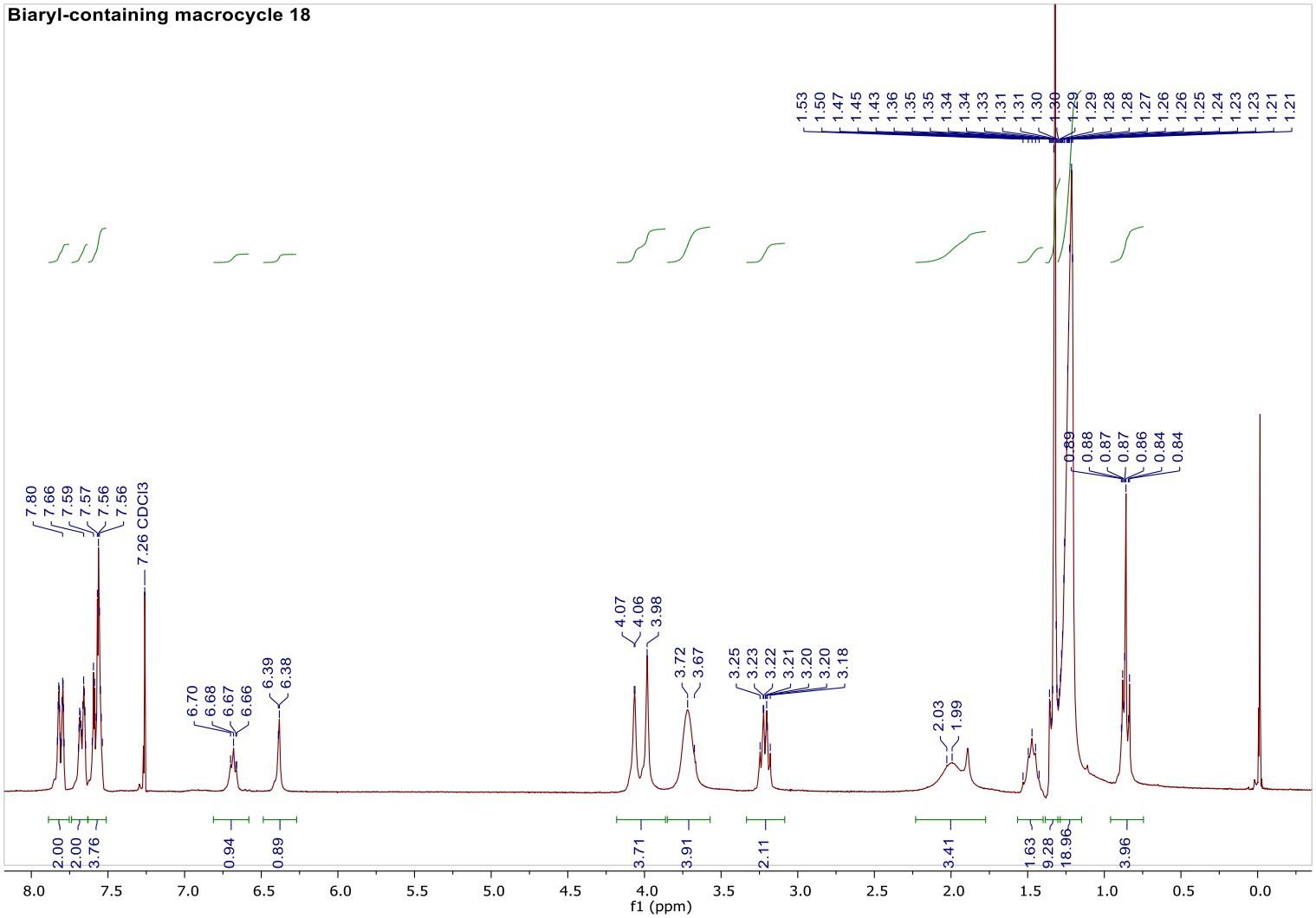


Figure 20. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **18**

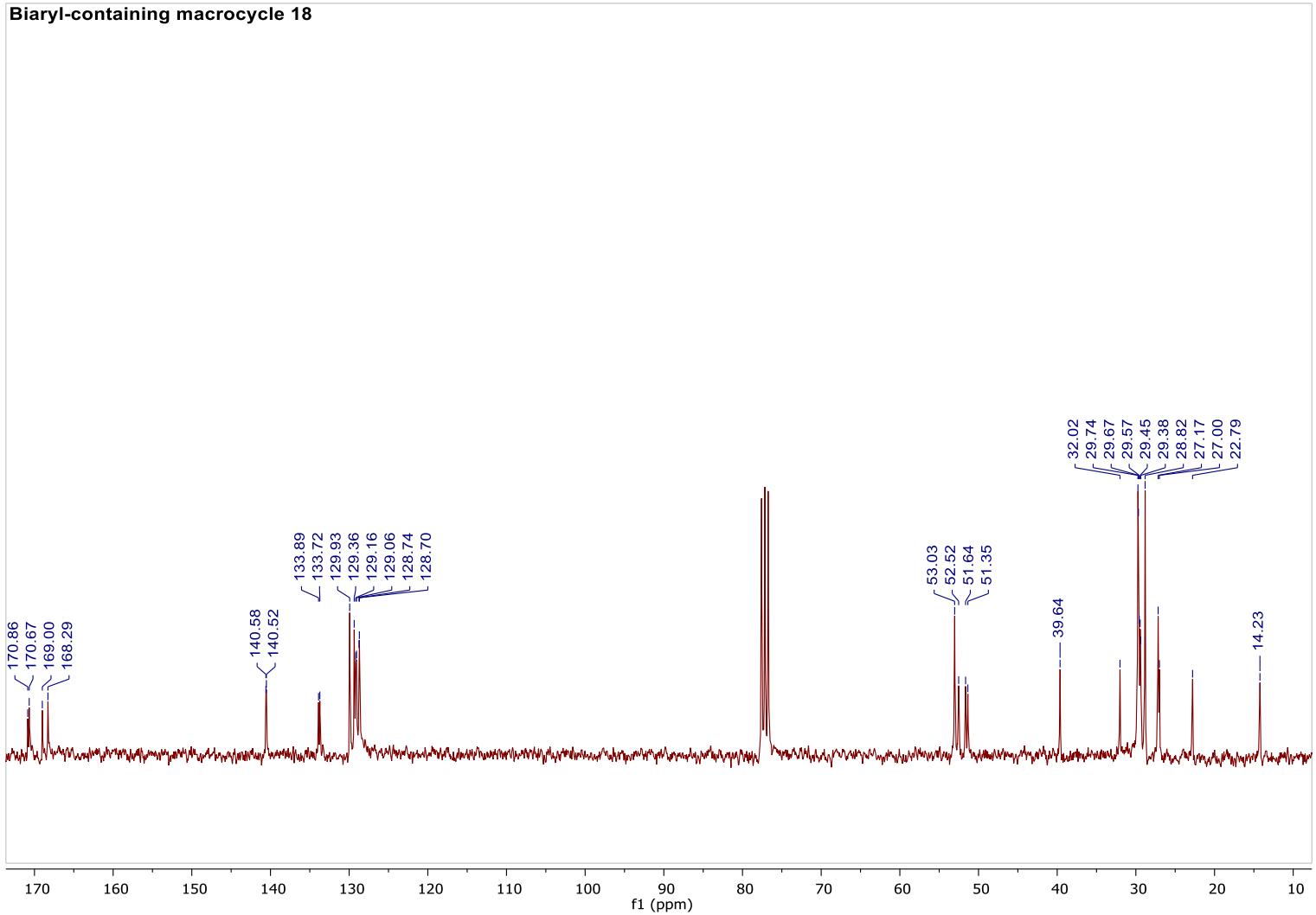
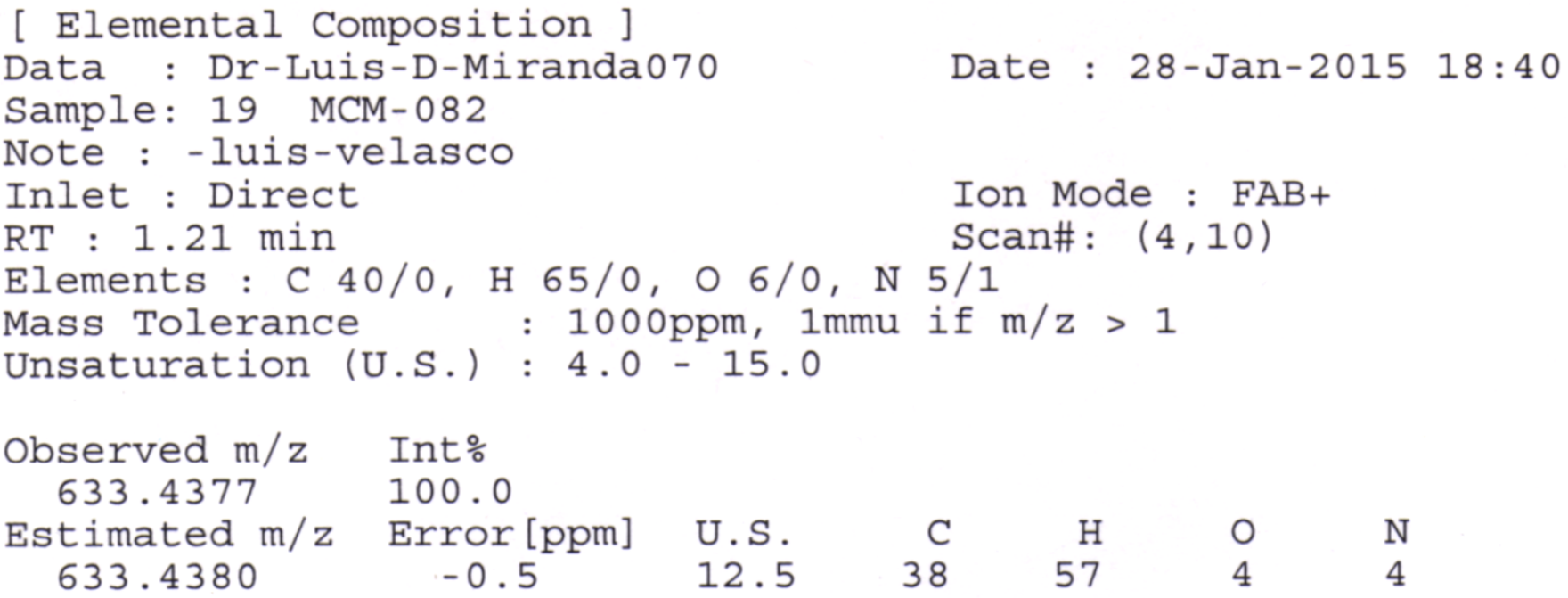


Figure 21. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **18**



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[ Elemental Composition ]
Data  : Dr-Luis-D-Miranda070          Date : 28-Jan-2015 18:40
Sample: 19  MCM-082
Note : -luis-velasco
Inlet : Direct                        Ion Mode : FAB+
RT : 1.21 min                         Scan#: (4,10)
Elements : C 40/0, H 65/0, O 6/0, N 5/1
Mass Tolerance       : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z   Int%
  633.4377     100.0
Estimated m/z  Error[ppm]  U.S.     C     H     O     N
  633.4380       -0.5      12.5    38    57     4     4
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Figure 22. HRMS (FAB+) spectra of macrocycle **18**

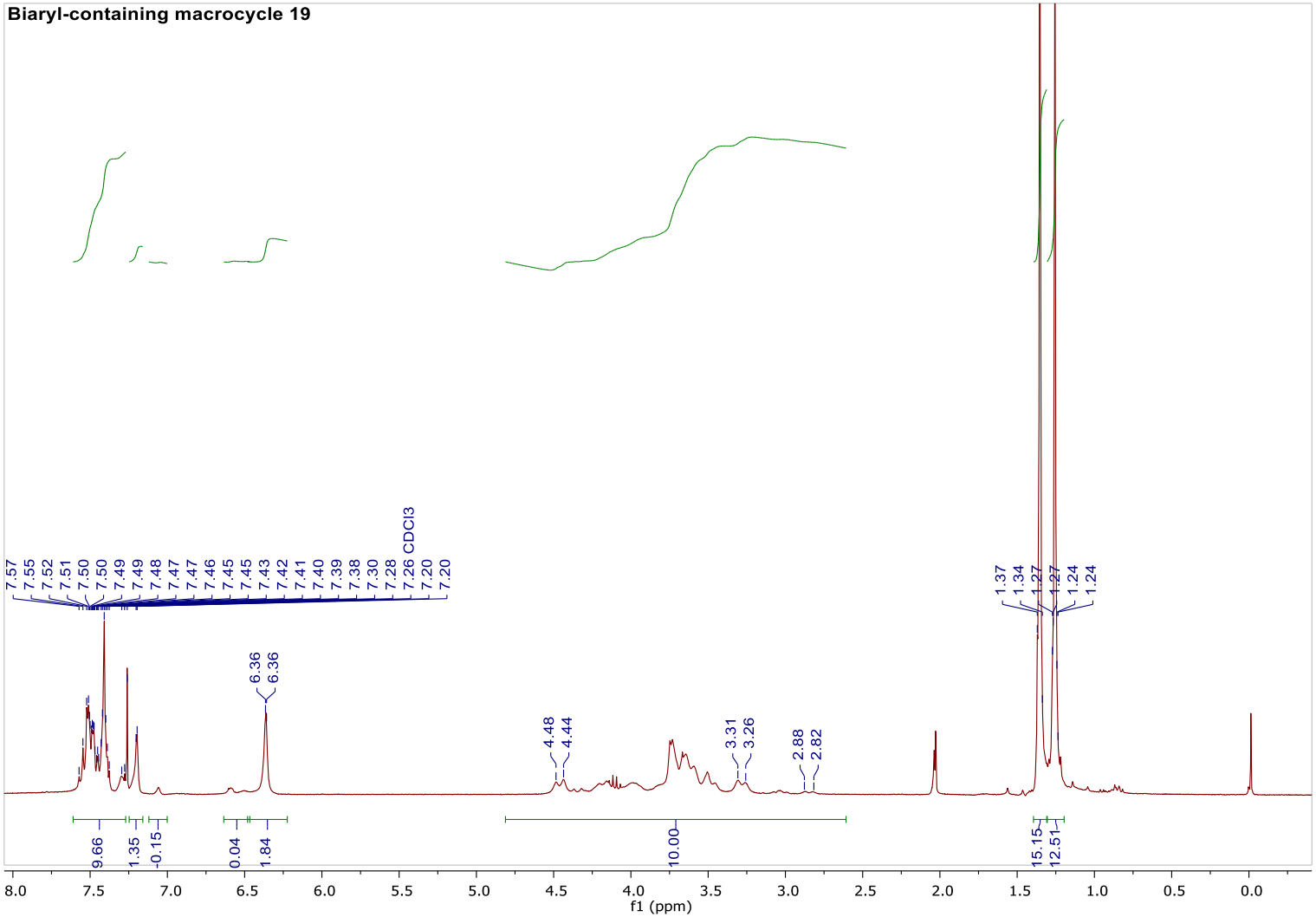


Figure 23. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **19**

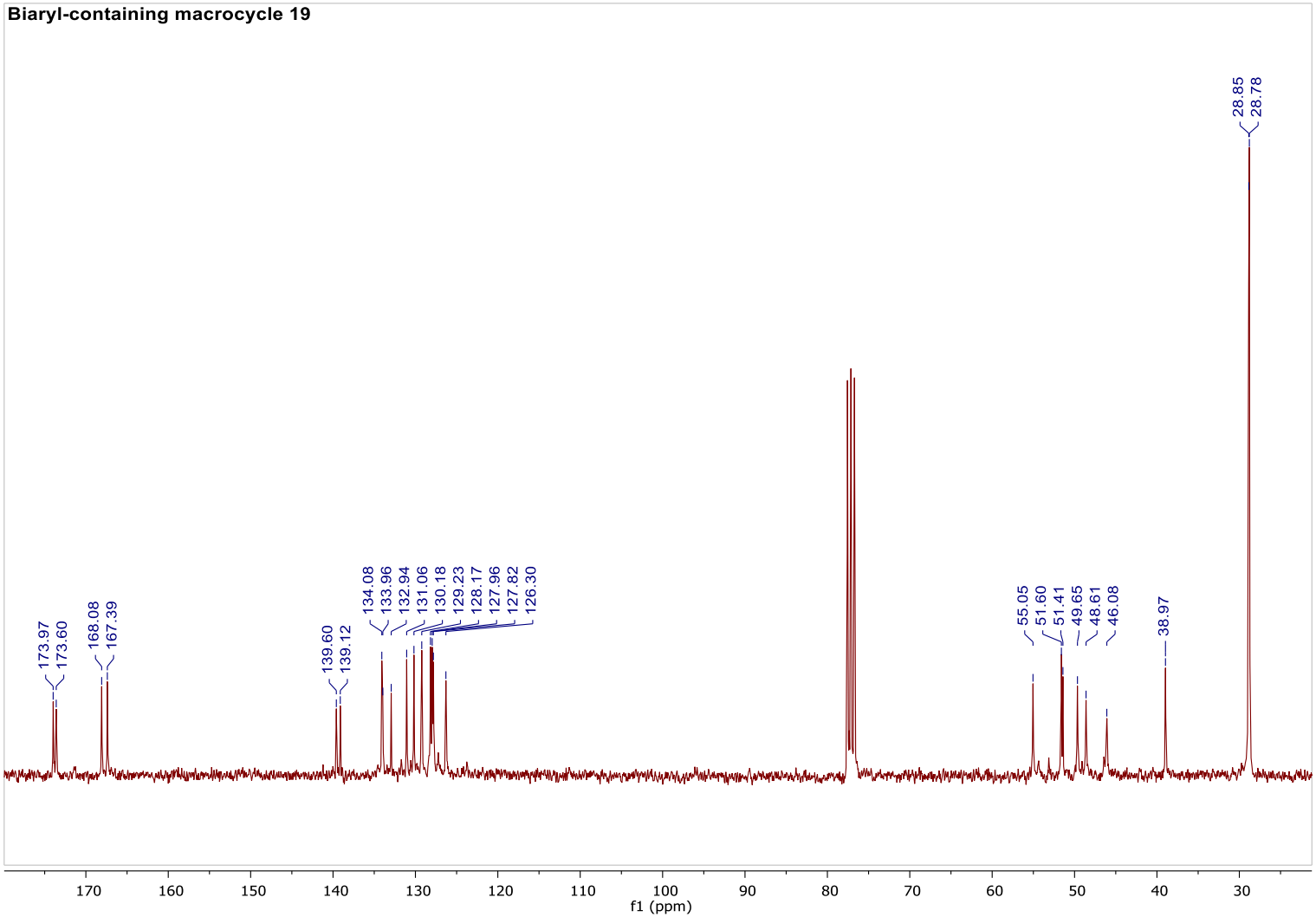
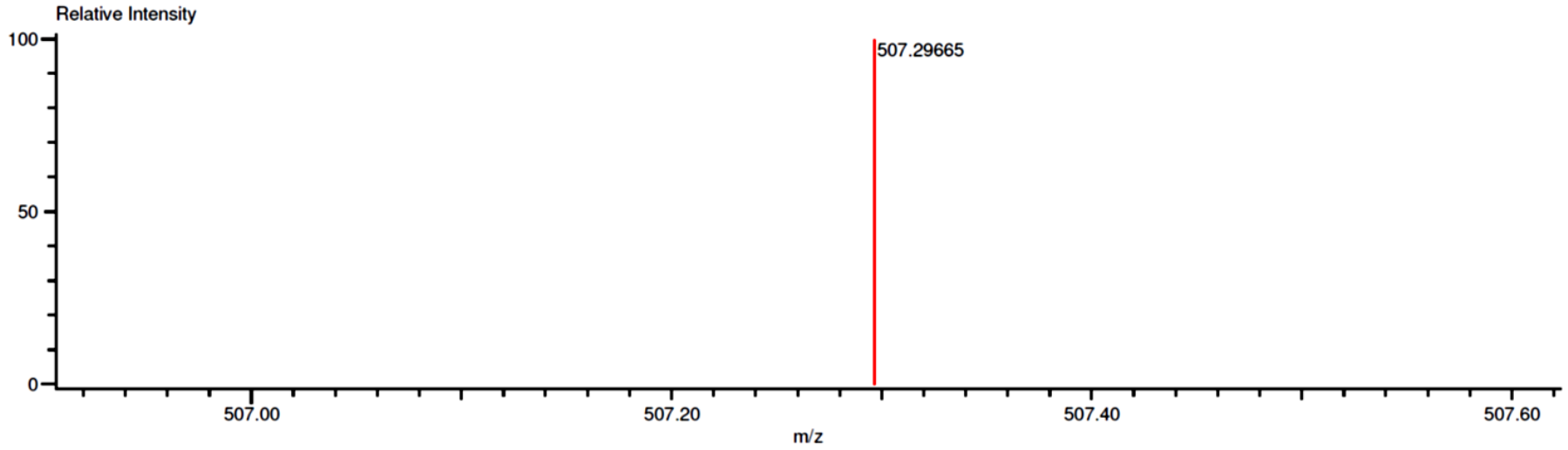


Figure 24. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **19**

Data:2424 MCM-029
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1.2...

Acquired:9/23/2014 4:47:52 PM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:9/30/2014 1:28:52 PM
Created by:AccuTOF

Charge number:1
Tolerance:3.50(mmu)
Unsaturation Number:0.0 .. 16.0 (Fraction:Both)
Element:^{12}C:0 .. 50, ^{1}H:0 .. 120, ^{14}N:0 .. 4, ^{16}O:0 .. 4



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
507.29665	1304971.09	507.29713	-0.48	$^{12}C_{29}{}^{1}H_{39}{}^{14}N_{4}{}^{16}O_{4}$	12.5

Figure 25. HRMS (DART+) spectra of macrocycle **19**

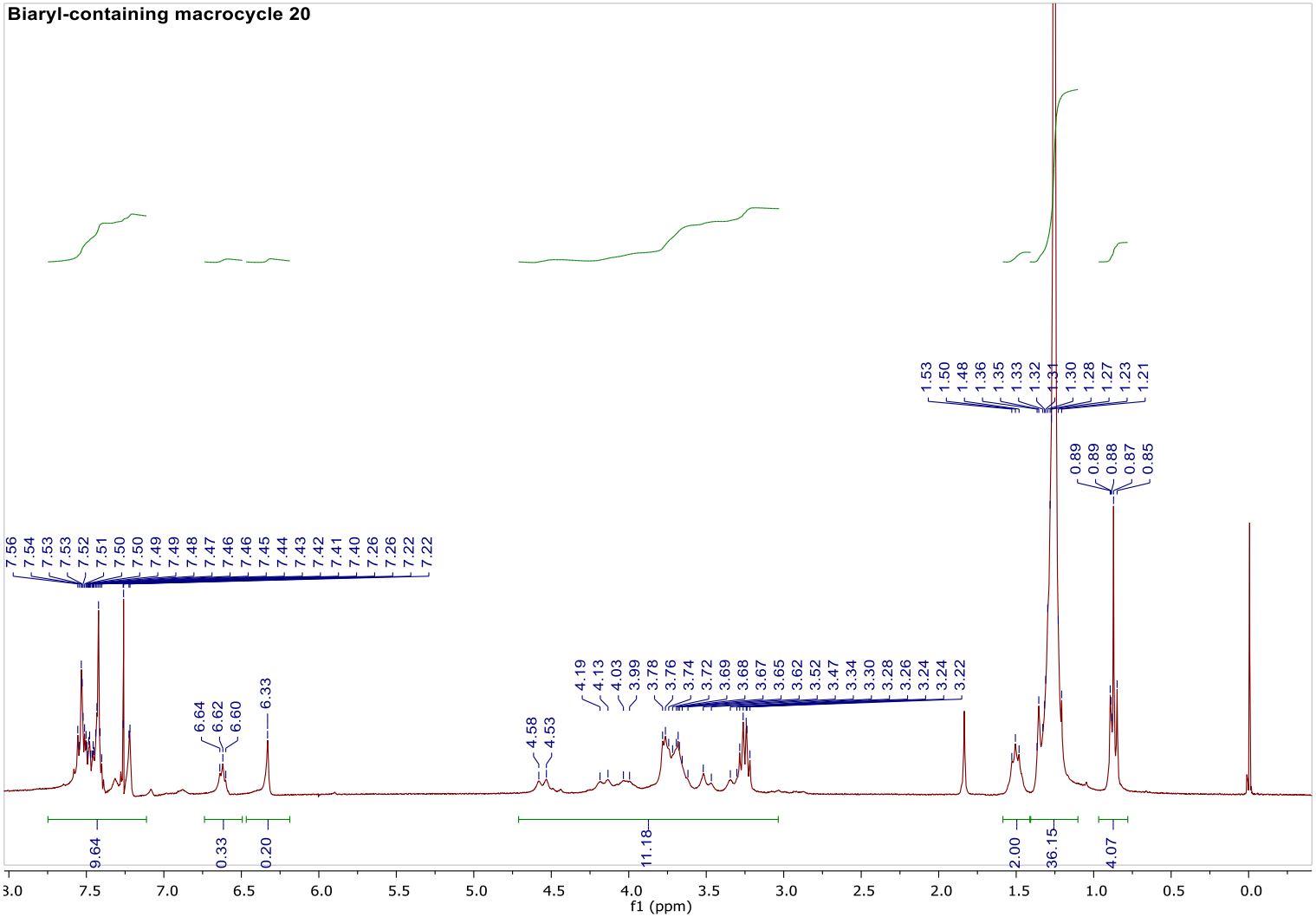


Figure 26. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **20**

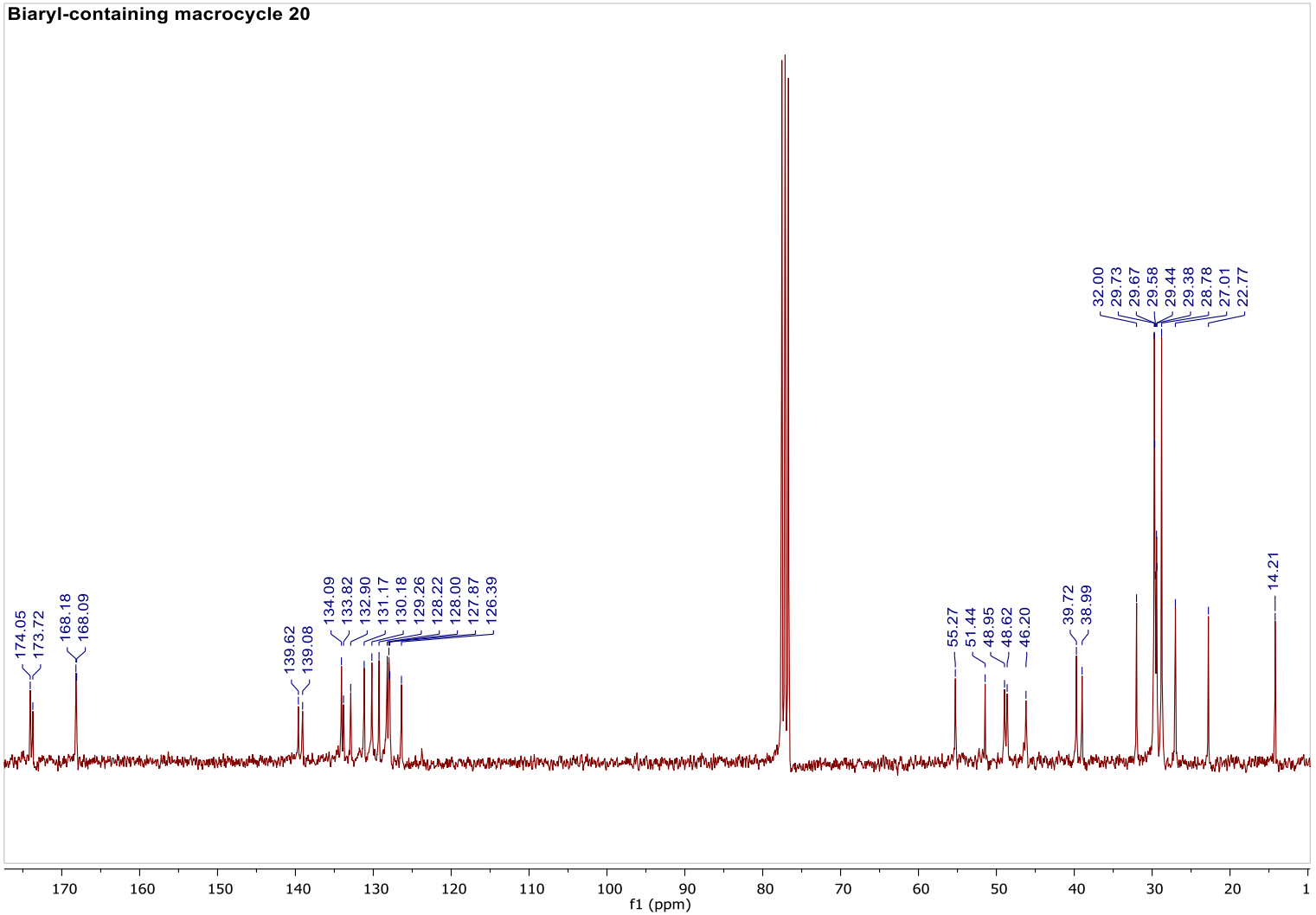


Figure 27. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **20**

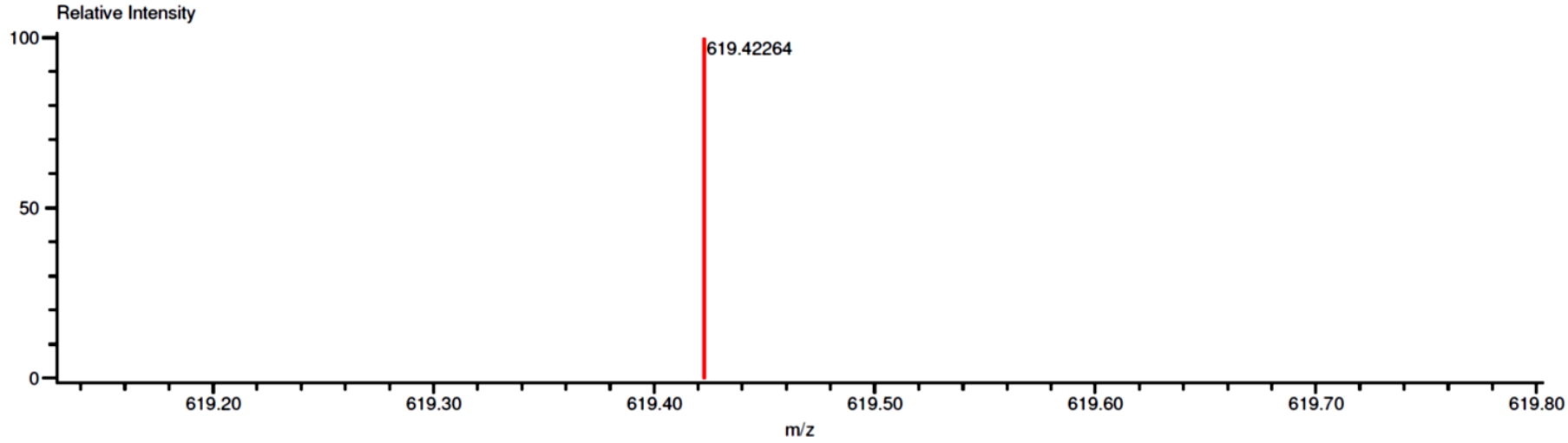
Data:69 MCM-085
Sample Name:Dr Miranda Luis
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1.1...

Acquired:1/14/2015 11:20:56 AM
Operator:AccuTOF
Mass Calibration data:Cal_Peg_600
Created:4/13/2015 10:26:54 AM
Created by:AccuTOF

Charge number:1
Element:^{12}C:0 .. 57, ^{1}H:0 .. 120, ^{14}N:0 .. 5, ^{16}O:0 .. 5

Tolerance:3.00(mmu)

Unsaturation Number:0.0 .. 20.0 (Fraction:.5)



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Possible Formula	Unsaturation Number
619.42264	184423.25	619.42233	0.31	$^{12}C_{37}{}^{1}H_{55}{}^{14}N_{4}{}^{16}O_{4}$	12.5

Figure 28. HRMS (DART+) spectra of macrocycle **20**

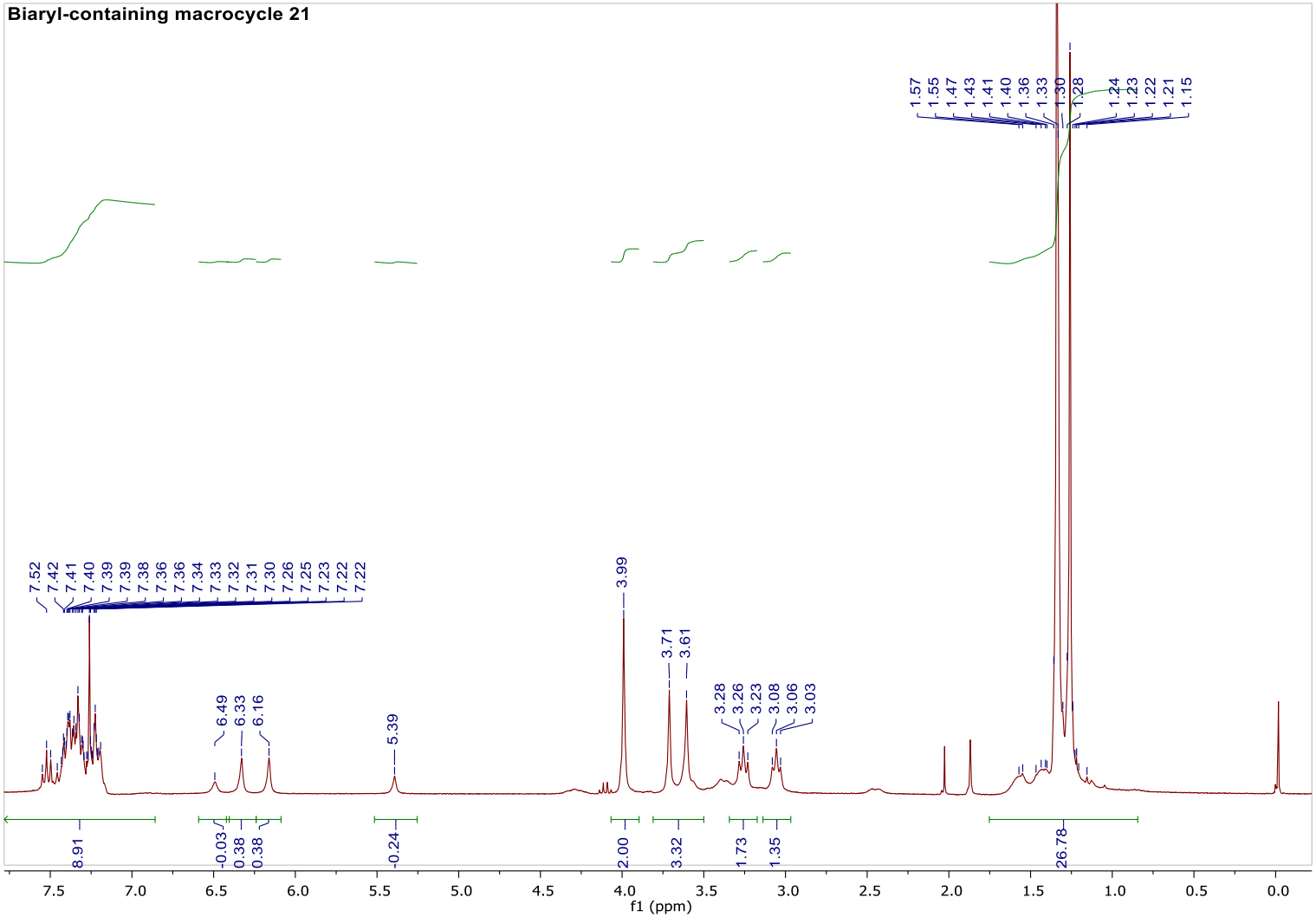


Figure 29. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **21**

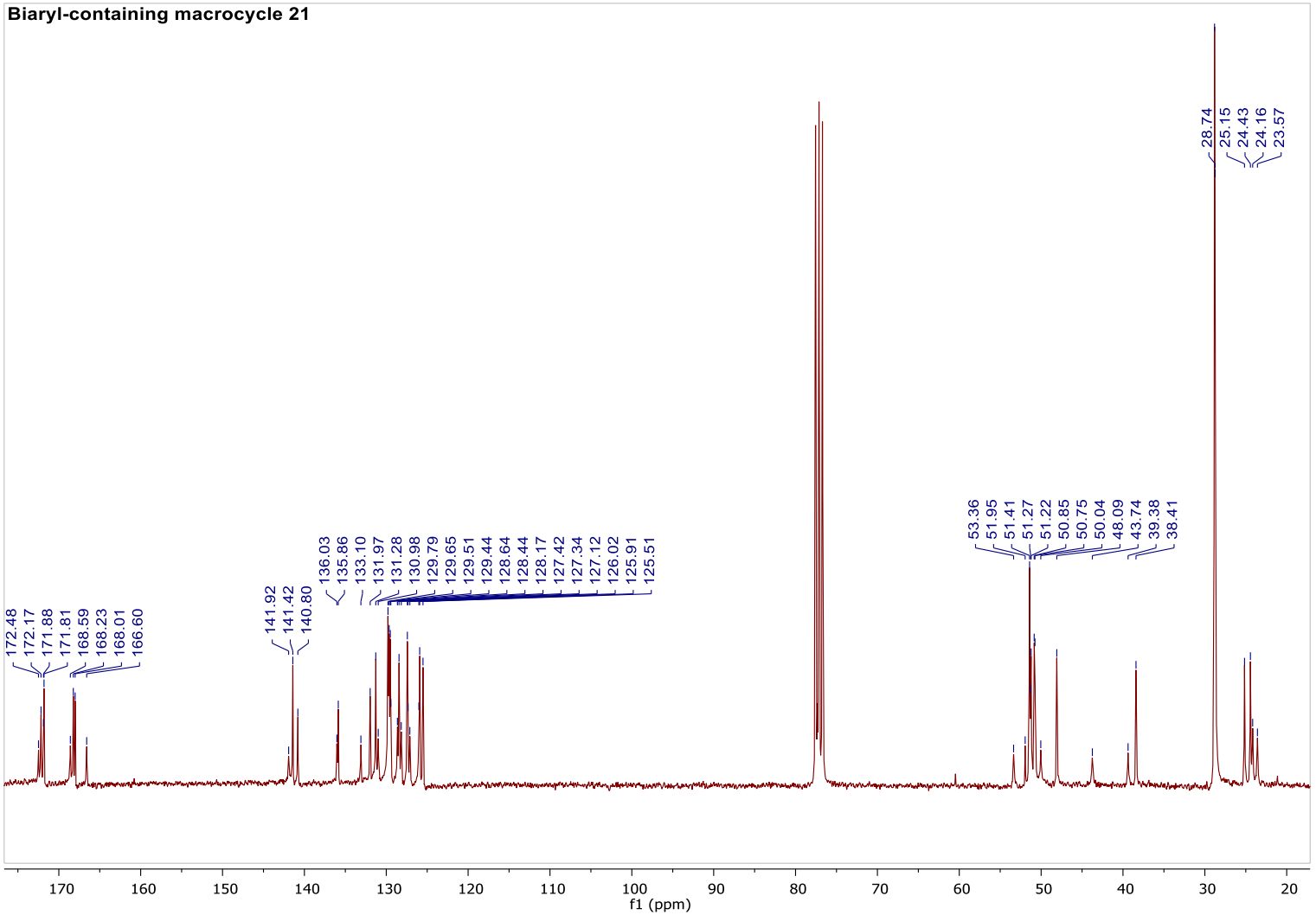
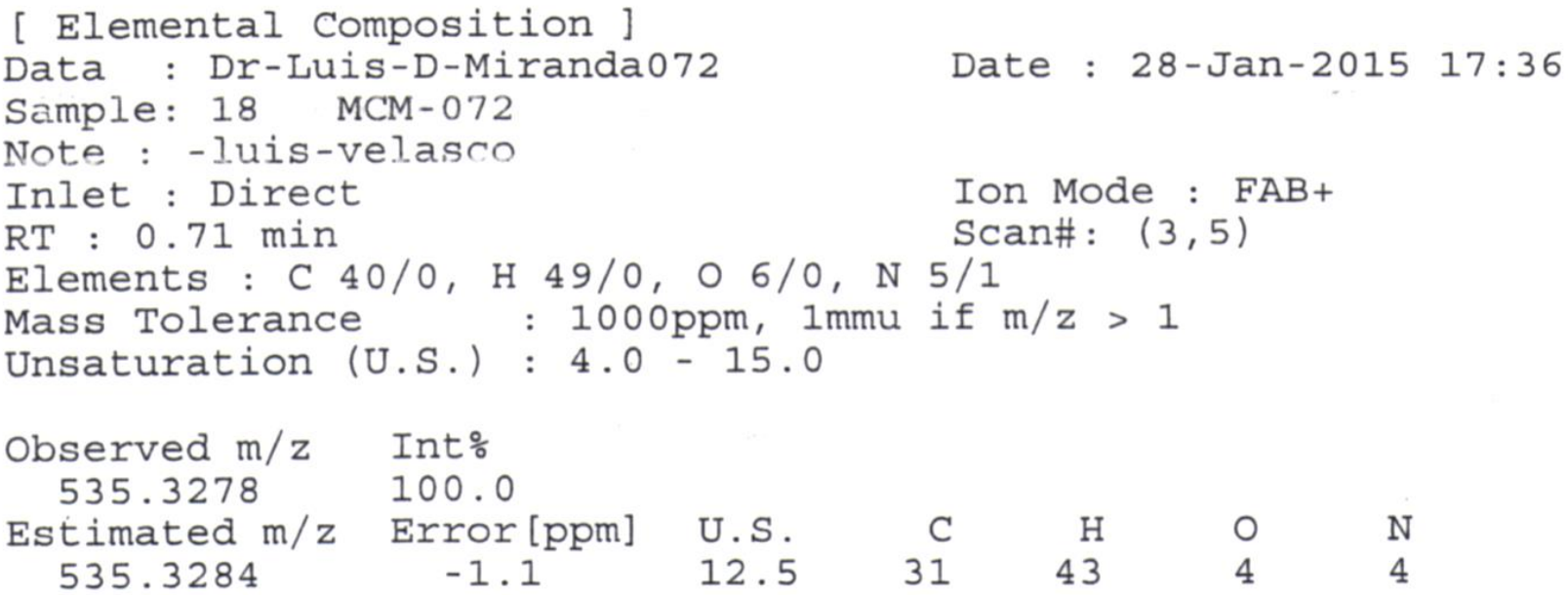


Figure 30. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **21**



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Data  : Dr-Luis-D-Miranda072          Date : 28-Jan-2015 17:36
Sample: 18   MCM-072
Note : -luis-velasco
Inlet : Direct                        Ion Mode : FAB+
RT : 0.71 min                         Scan#: (3,5)
Elements : C 40/0, H 49/0, O 6/0, N 5/1
Mass Tolerance       : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z   Int%
  535.3278     100.0
Estimated m/z  Error[ppm]  U.S.     C     H     O     N
  535.3284       -1.1      12.5    31    43     4     4
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Figure 31. HRMS (FAB+) spectra of macrocycle **21**

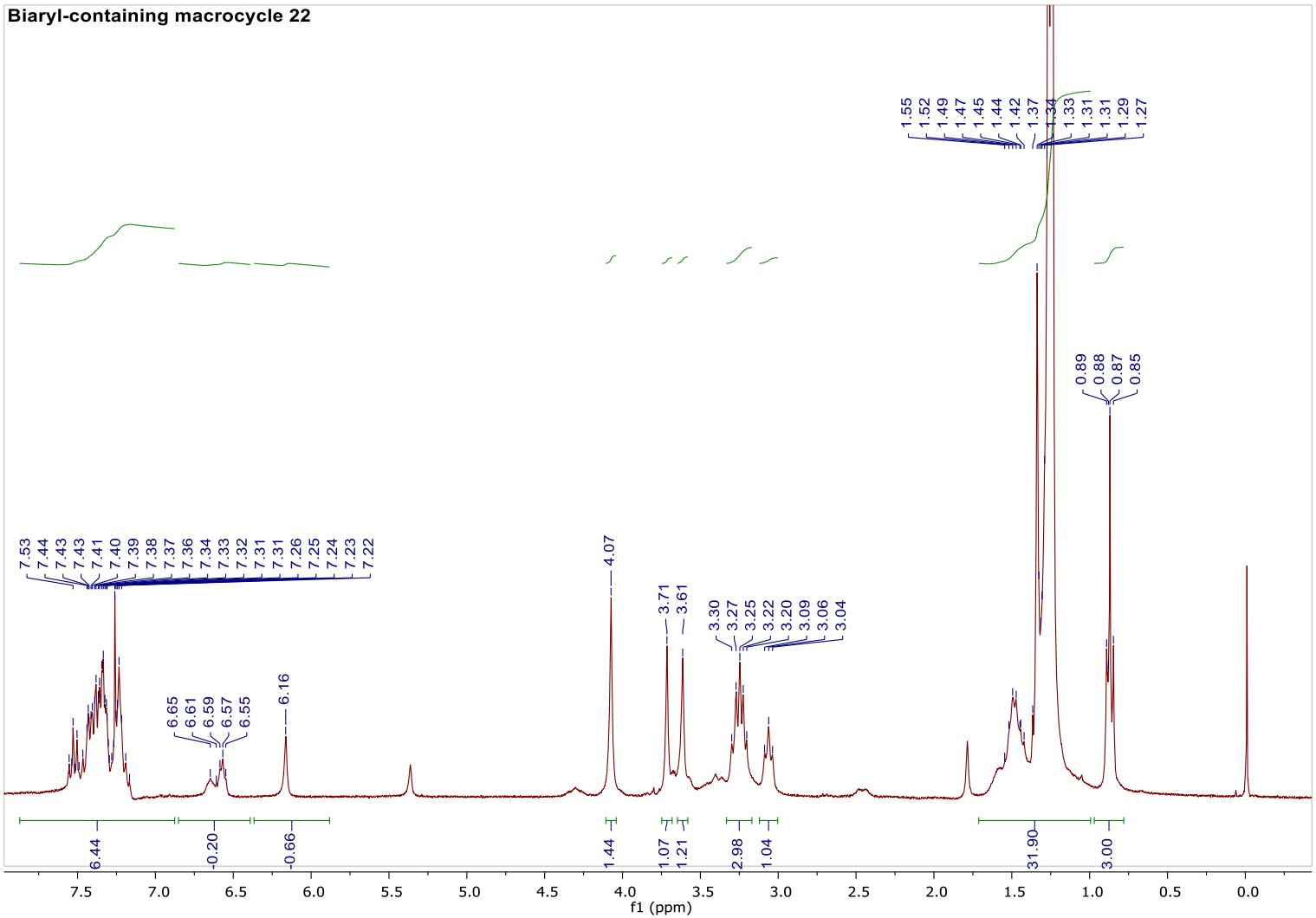


Figure 32. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **22**

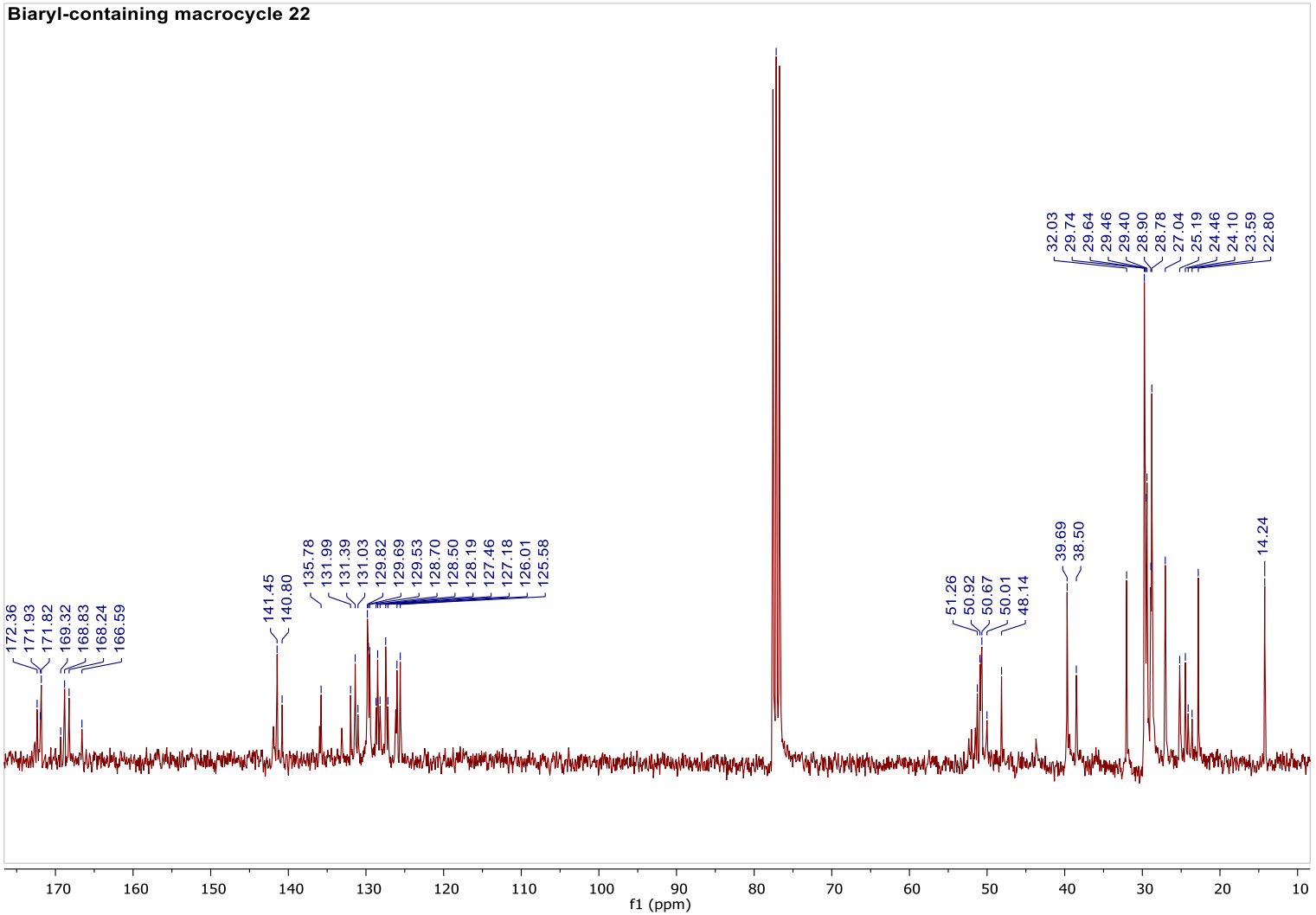
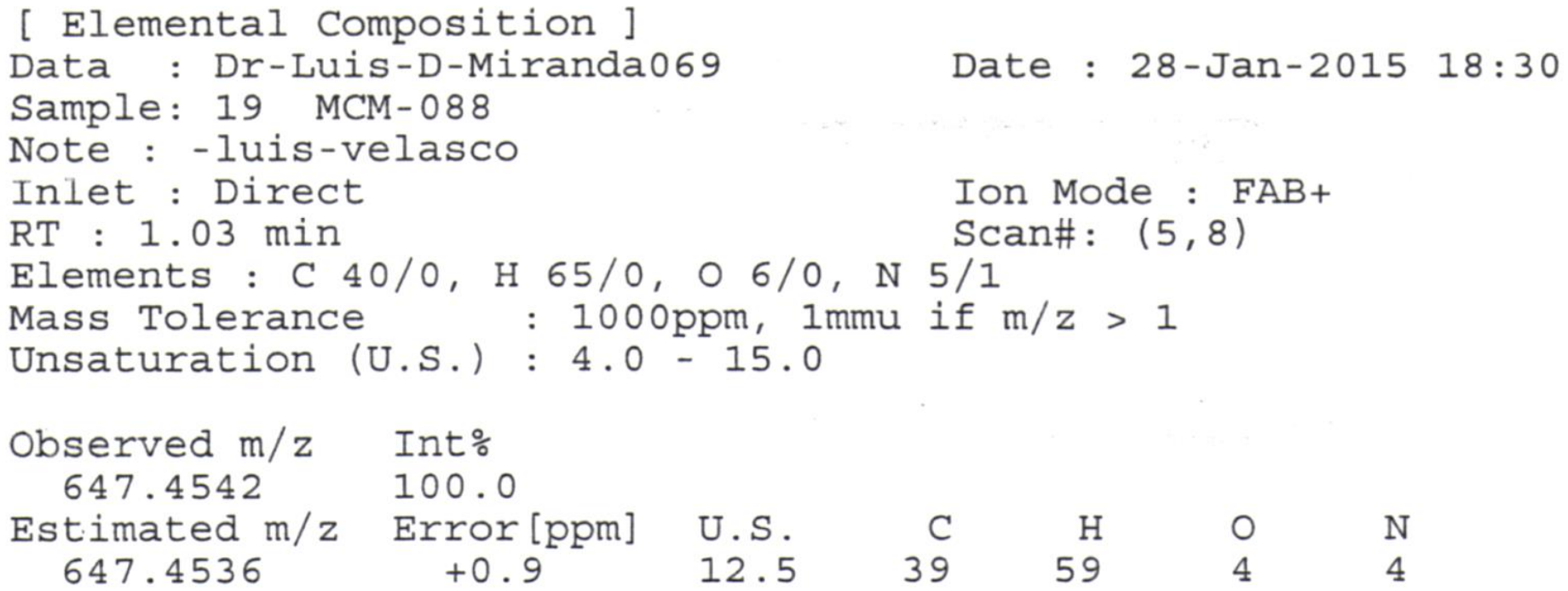


Figure 33. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **22**



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[ Elemental Composition ]
Data  : Dr-Luis-D-Miranda069          Date : 28-Jan-2015 18:30
Sample: 19  MCM-088
Note : -luis-velasco
Inlet : Direct                        Ion Mode : FAB+
RT : 1.03 min                         Scan#: (5,8)
Elements : C 40/0, H 65/0, O 6/0, N 5/1
Mass Tolerance       : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z   Int%
  647.4542     100.0
Estimated m/z  Error[ppm]  U.S.     C     H     O     N
  647.4536       +0.9      12.5    39    59     4     4
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Figure 34. HRMS (FAB+) spectra of macrocycle **22**

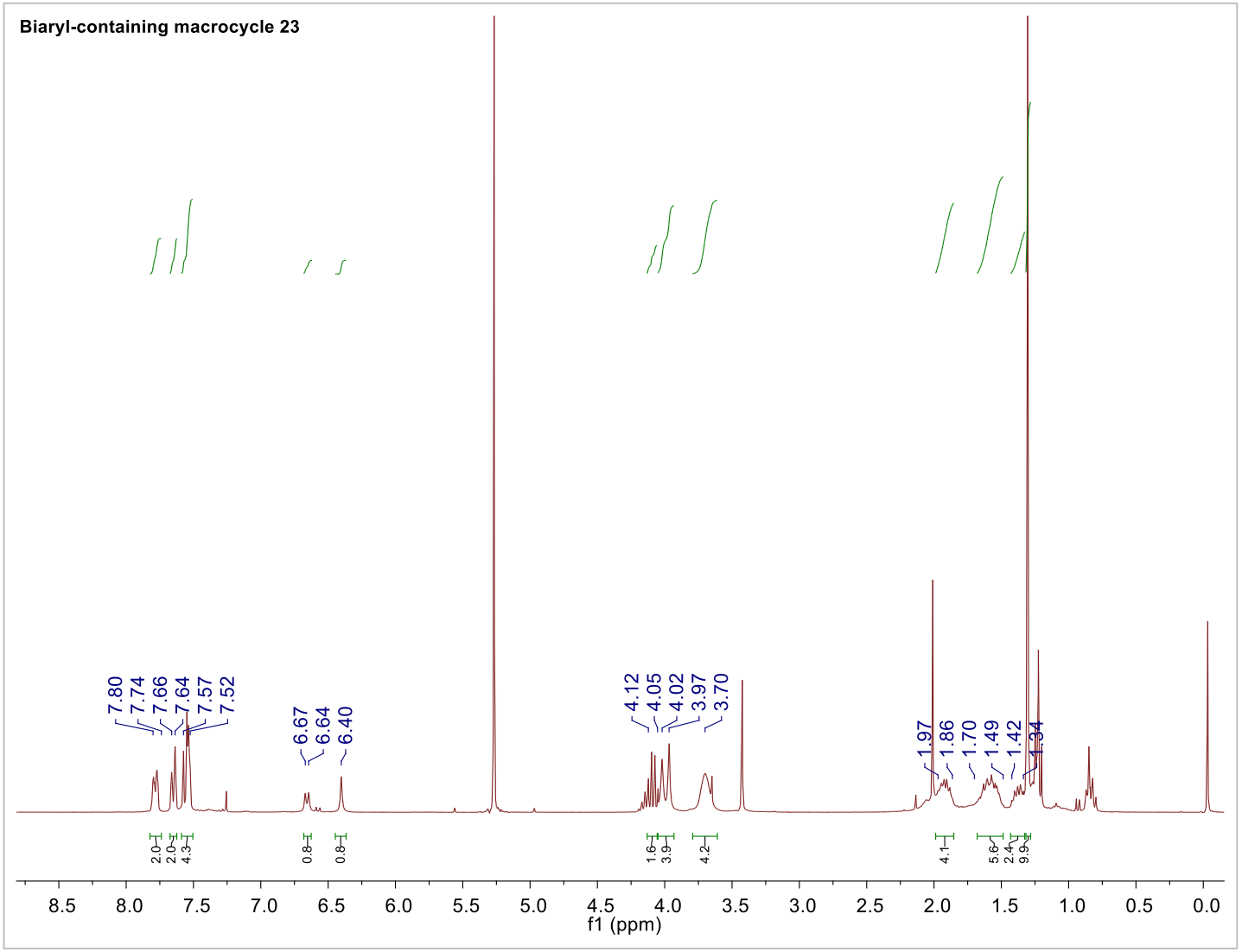


Figure 35. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **23**

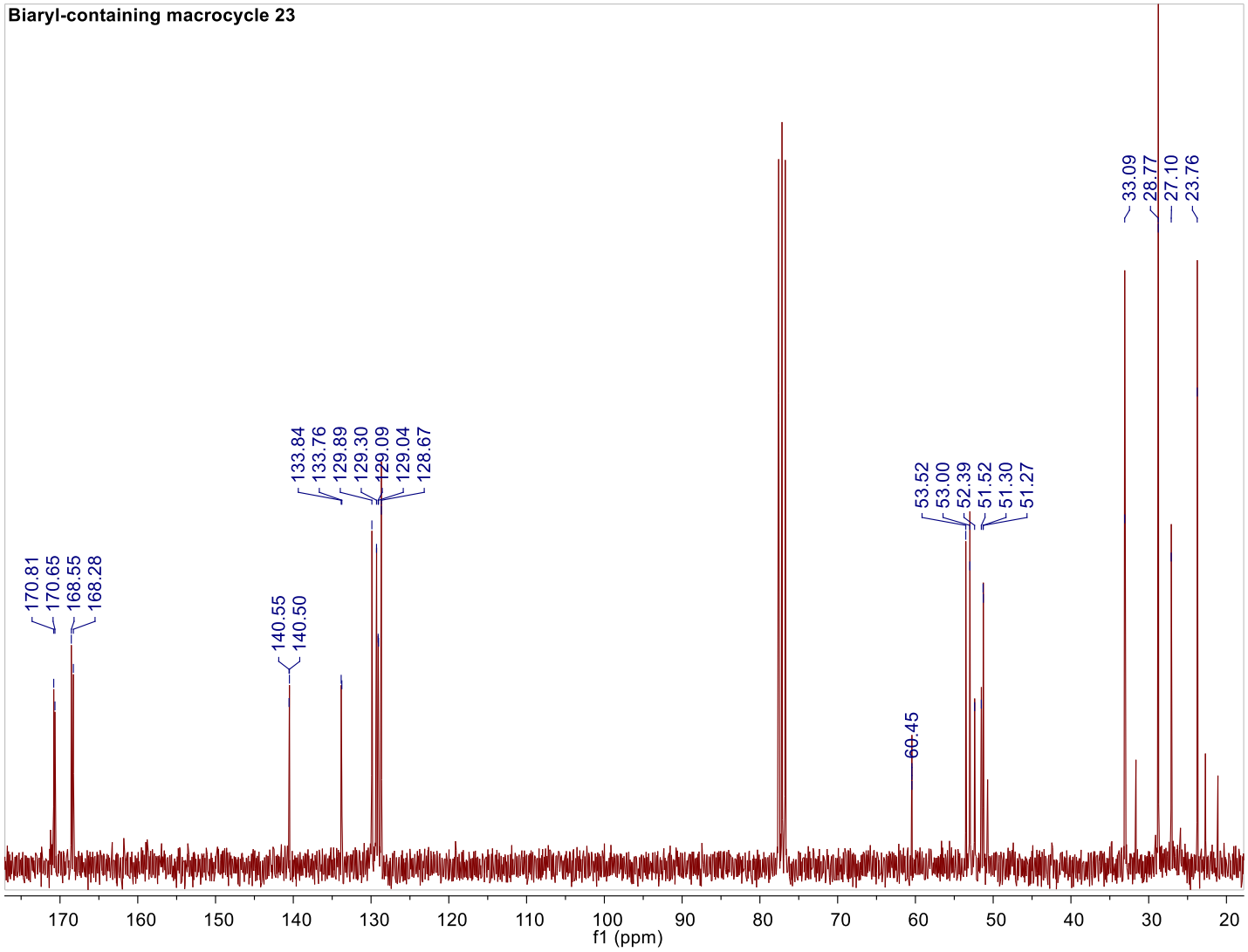
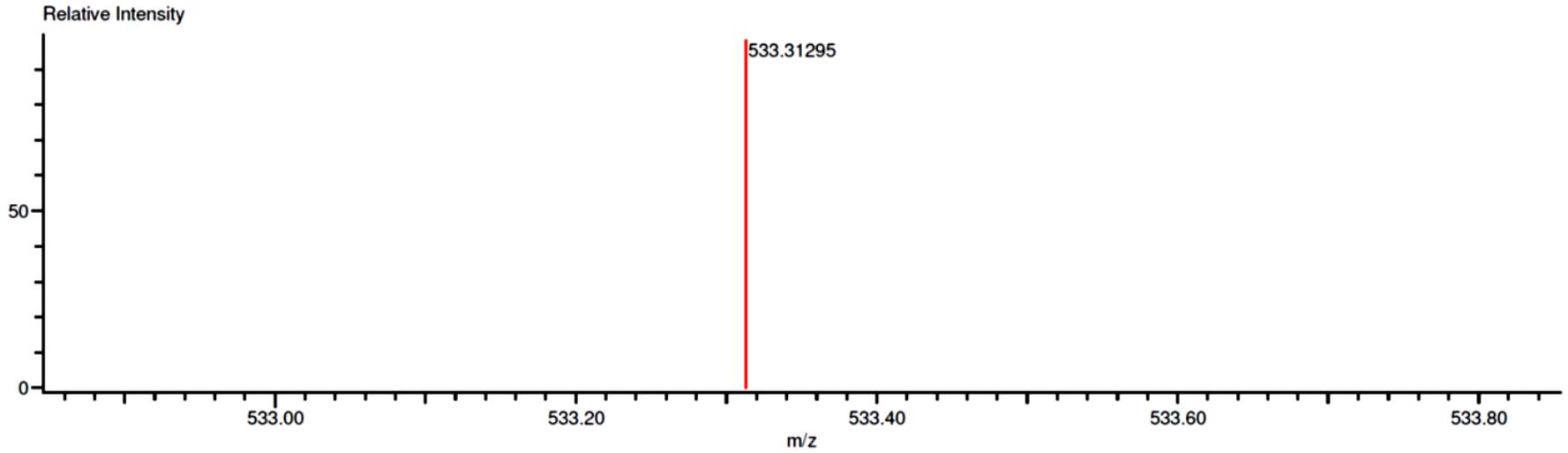


Figure 36. 75 MHz ^{13}C NMR spectra in $CDCl_3$ of macrocycle **23**

Data:ACR-1-60
Sample Name:Operador:Eduardo Hdz
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,50,Area];Correct Base[50.0%]];Correct Base[5.0%];Average(MS[1] 0....

Acquired:12:00:00 AM
Operator:AccuTOF
Mass Calibration data:Cal PEG 600
Created:12/6/2016 10:36:41 AM
Created by:AccuTOF

Charge number:1
Tolerance:10.00(mmu)
Unsaturation Number:0.0 .. 50.0 (Fraction:Both)
Element:^{12}C:0 .. 50, ^{1}H:0 .. 100, ^{14}N:4 .. 4, ^{16}O:4 .. 4



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Mass Difference (ppm)	Possible Formula	Unsaturation Number
533.31295	97510.94	533.31278	0.17	0.31	$^{12}C_{31}{}^{1}H_{41}{}^{14}N_{4}{}^{16}O_{4}$	13.5

Figure 37. HRMS (DART+) spectra of macrocycle **23**

Biaryl-containing macrocycle 24

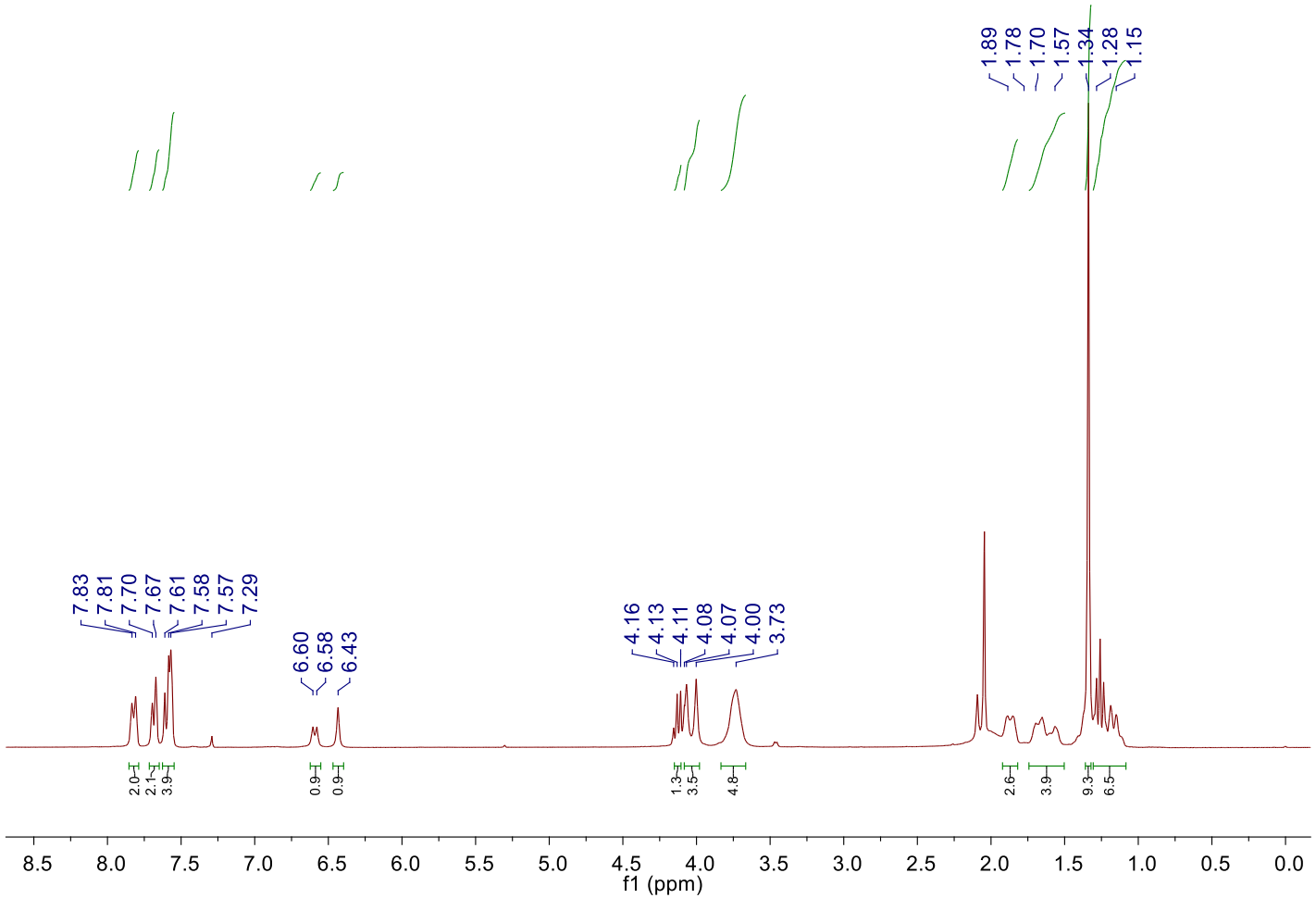


Figure 38. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **24**

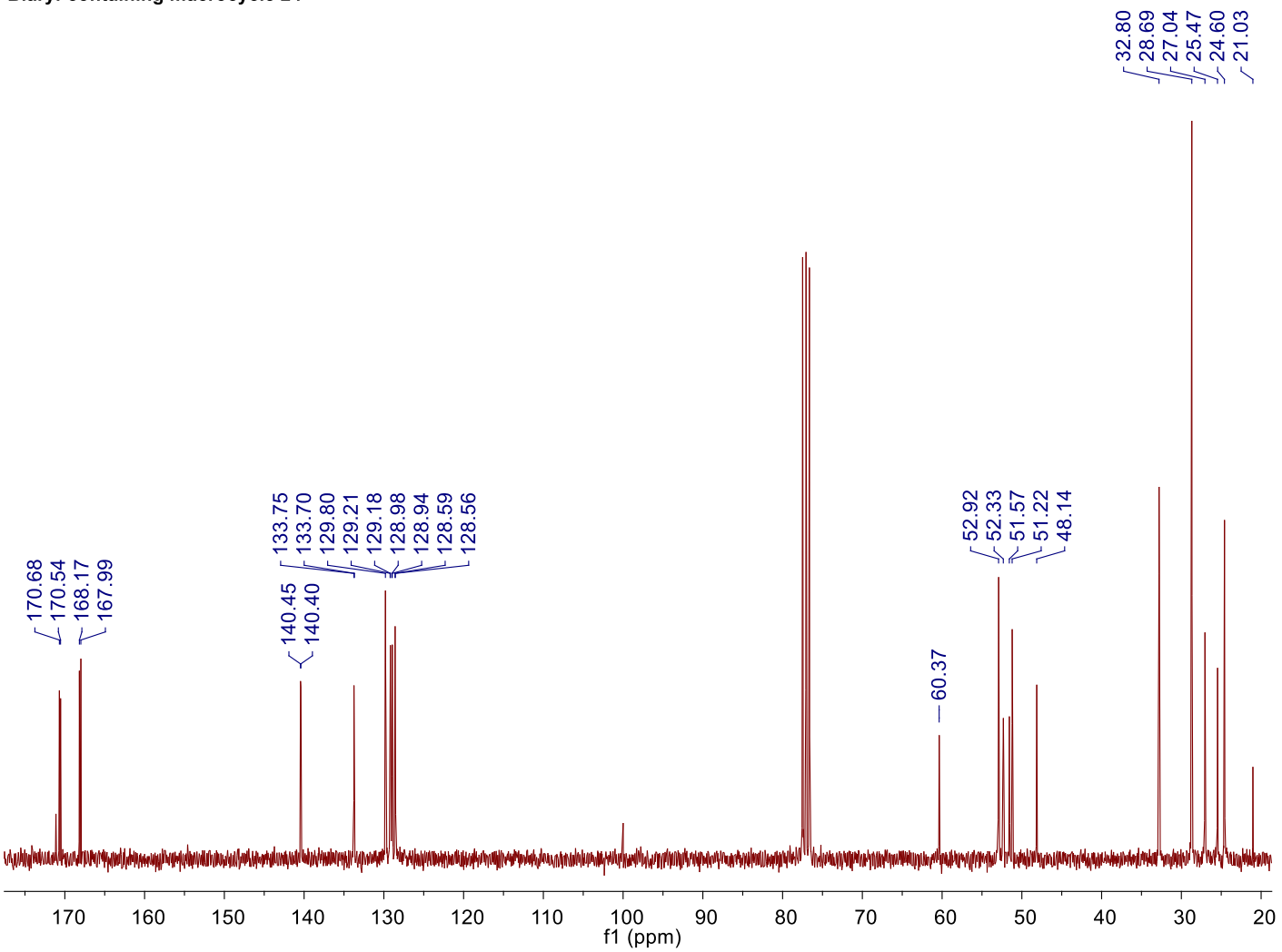
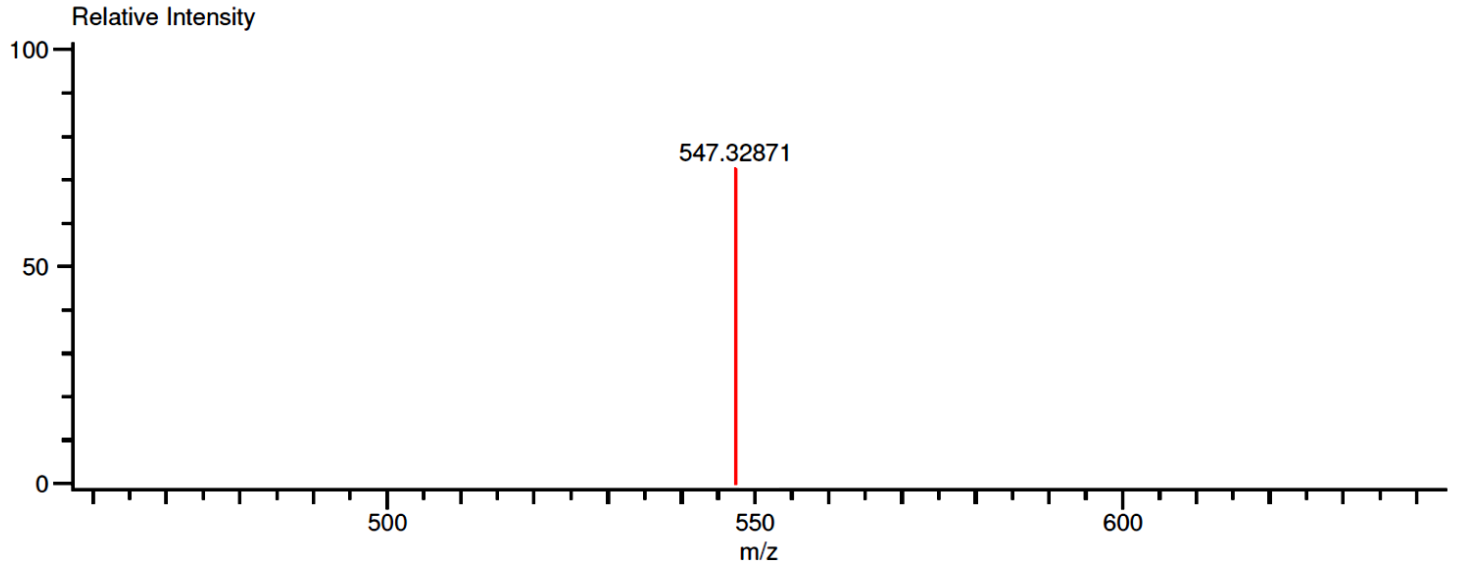


Figure 39. 300 MHz ^{1}H NMR spectra in $CDCl_3$ of macrocycle **24**

Data:U-319 ACR-1-56
Sample Name:Dr. Luis Miranda-Abigail Balderas
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,50,Area];Correct Base[50.0%]];Corre...

Acquired:11/28/2016 11:10:13 AM
Operator:AccuTOF
Mass Calibration data:Cal PEG 600
Created:11/28/2016 11:30:09 AM
Created by:AccuTOF

Charge number:1 Tolerance:20.00(mmu) Unsaturation Number:0.0 .. 30.0 (Fracti
Element:^{12}C:0 .. 32, ^{1}H:0 .. 60, ^{14}N:0 .. 4, ^{16}O:4 .. 5

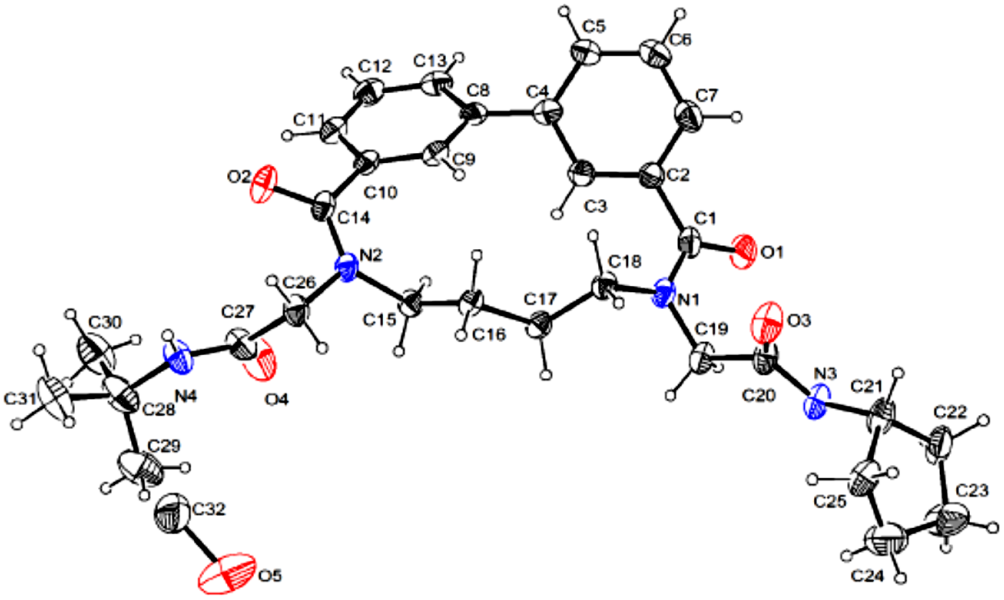


Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Mass Difference (ppm)	Possible Formula
547.32871	15370.25	547.32843	0.28	0.52	$^{12}C_{32}{}^{1}H_{43}{}^{14}N_{4}{}^{16}O_{4}$

Figure 40. HRMS (DART+) spectra of macrocycle 24

Crystal data and structure refinement for **23** (CCDC number 1530930)

Empirical formula	C63 H80 N8 O9	
Formula weight	1093.35	
Temperature	298(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 7.5086(2) Å	α= 90°.
	b = 20.5310(5) Å	β= 97.9726(15)°.
	c = 20.0462(5) Å	γ = 90°.
Volume	3060.43(13) $Å^3$	
Z	2	
Density (calculated)	1.186 Mg/m^3	
Absorption coefficient	0.643 mm^{-1}	
F(000)	1172	
Crystal size	0.294 x 0.260 x 0.142 mm^3	
Theta range for data collection	3.096 to 68.396°.	
Index ranges	-8<=h<=6, -24<=k<=24, -24<=l<=23	
Reflections collected	13187	
Independent reflections	5417 [R(int) = 0.0342]	
Completeness to theta = 67.679°	96.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7531 and 0.6386	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5417 / 93 / 410	
Goodness-of-fit on F^2	1.197	
Final R indices [I>2sigma(I)]	R1 = 0.1513, wR2 = 0.3364	
R indices (all data)	R1 = 0.1764, wR2 = 0.3543	
Largest diff. peak and hole	0.715 and -0.405 $e.Å^{-3}$	


C5
C6
C12
C13
C8
C4
C7
C11
C9
C2
O2
C10
C3
C14
C1
O1
N2
C18
C26
C27
C15
C16
C17
N1
O3
C19
C30
C31
N4
C28
O4
C20
N3
C21
C22
C29
C25
C23
C32
O5
C24