Angewandte Chemie
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Supporting Information

69451 Weinheim, Germany

Extensions of the Icosahedral Closomer Structure by Using Azide–Alkyne Click Reactions**

*Lalit N. Goswami, Shatadru Chakravarty, Mark W. Lee, Satish S. Jalisatgi, and M. Frederick Hawthorne**

anie_201101066_sm_miscellaneous_information.pdf

Supporting information

Contents:

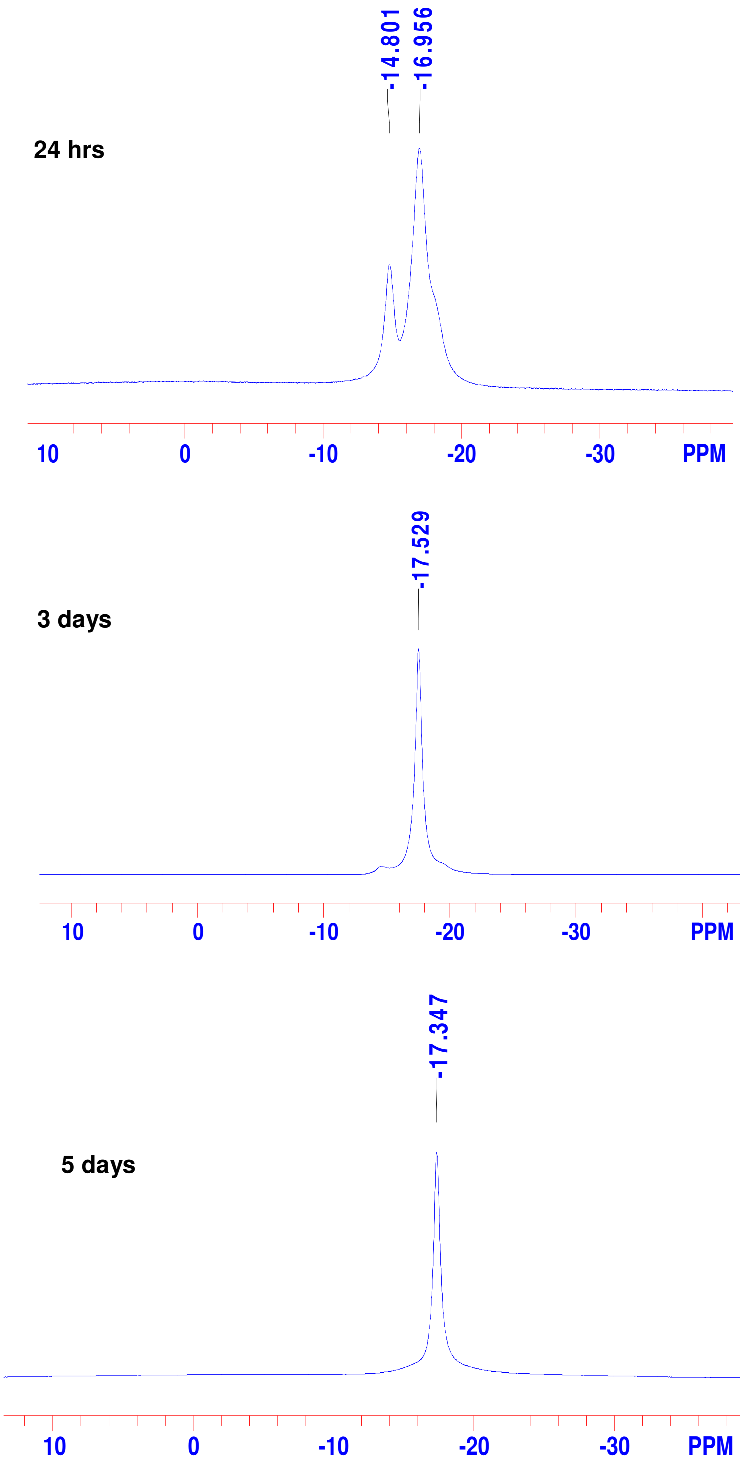


Fig. SI-1: ^{11}B NMR spectra of reaction mixture showing progress of twelve fold esterification reaction using chloroacetic anhydride (Compound **2**).

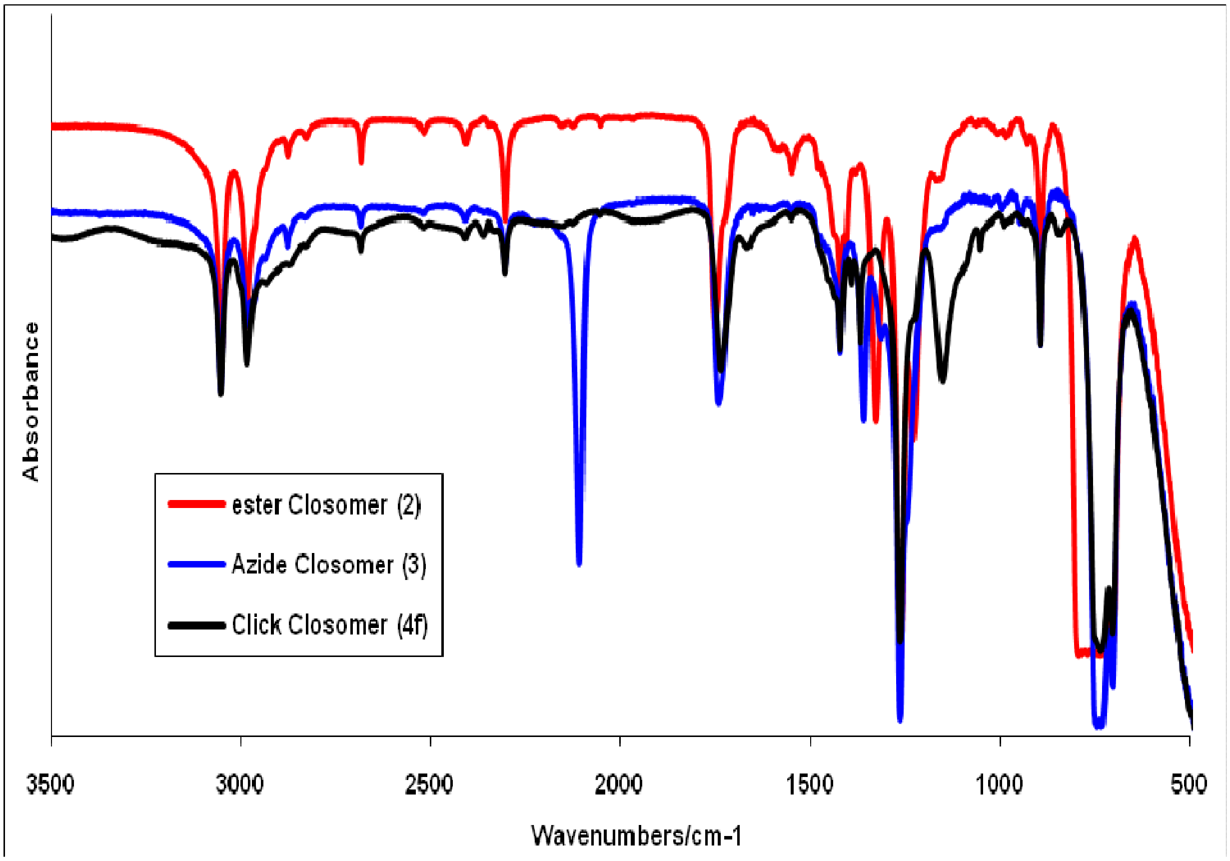


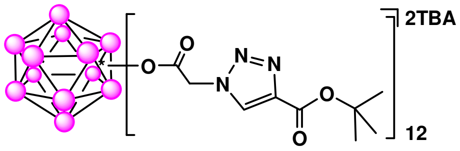
Fig. SI-2: IR spectras of compounds **2, 3** and **4f** in dichloromethane.

Experimental procedures and characterization

General information:

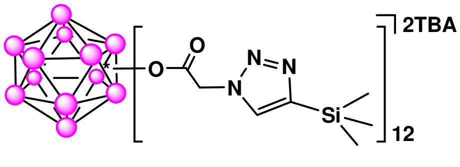
All reactions were carried out in oven-dry glassware under an atmosphere of argon. Thin-layer chromatography (TLC) was carried out on precoated silica gel XHL TLC glass plates w/UV254 and aluminum oxide TLC glass plates w/UV254 (Sorbent Technologies). Column chromatography was performed over Silica Gel (40-63 μm particles size) obtained from Sorbent Technologies or on neutral Alumina (Brockmann grade III, 200 μm), obtained from Acros Organics. Size exclusion chromatography was performed using Lipophilic Sephadex® LH-20 obtained from GE Healthcare. THF was distilled over sodium benzophenone ketyl and DCM was distilled over P_2O_5. Anhydrous DMF, anhydrous triethylamine, anhydrous pyridine and other solvents were obtained from commercial suppliers (J.T. Baker®, EMD® and Aldrich®) and used without any further purification. NMR spectra were recorded on Bruker DRX 300, 400 and 500MHz spectrometers. All chemical shifts are reported in parts per million (δ). All NMR spectra were recorded at room temperature in CD_3CN, $CDCl_3$ or CD_3OD solutions. ^{1}H NMR spectra was referenced to residual $CHCl_3$ (7.26 ppm) and the ^{13}C spectra was referenced to $CDCl_3$ (77.2 ppm). The high-resolution mass spectrometry analyses were performed using Applied Biosystems Mariner ESI-TOF. IR spectra were recorded on Thermo Nicolet-AEM spectrophotometer using DCM as solvent.

Compound 4b:



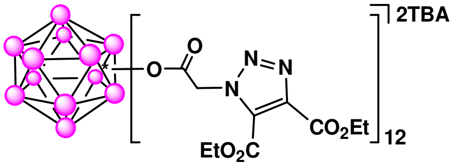
4b was synthesized from the azide functionalized closomer **3** (100 mg, 0.055 mmol), tert-butyl propiolate (416 mg, 3.30 mmol), copper (I) iodide (126 mg, 0.660 mmol) and diisopropylethylamine (853 mg, 6.60 mmol) using the general method for click reaction on closomers described in the article. Yield: 135 mg (74%). ^{1}H NMR (500 MHz, CD_3CN): δ 8.30 (s, 12H), 4.98 (m, 24H), 3.11 (m, 16H), 1.60 (m, 16H), 1.50 (s, 108H), 1.27 (m, 16H), 0.99 (t, 24H, J = 7.5 Hz). ^{13}C NMR (125 MHz, CD_3CN): δ 164.90, 160.00, 81.50, 58.00, 51.92, 27.30, 23.19, 19.20 and 12.69. ^{11}B NMR (160 MHz, CD_3CN): δ -17.18. HRMS (m/z): Calcd. for $C_{108}H_{144}B_{12}N_{36}O_{48}$ (M^{2-}) 1421.3627. Found: 1421.5554.

Compound 4c:



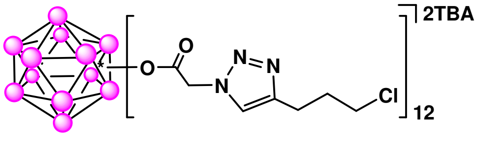
4c was synthesized from the azide functionalized closomer **3** (100 mg, 0.055 mmol), ethynyltrimethylsilane (324 mg, 3.30 mmol), copper (I) iodide (126 mg, 0.660 mmol) and diisopropylethylamine (853 mg, 6.60 mmol) using the general method for click reaction on closomers described in the article. Yield: 115 mg (70%). ^{1}H NMR (500 MHz, CD_3CN): δ 7.56 (s, 12H), 4.89 (s, 24H), 3.11 (t, 16H, *J* = 8.5Hz), 1.63 (m, 16H), 1.34 (m, 16H), 0.99 (t, 24H, *J* = 7.5 Hz), 0.30 (s, 108H). ^{11}B NMR (96 MHz, CD_3CN): δ -16.94. HRMS (m/z): Calcd. for $C_{84}H_{144}B_{12}N_{36}O_{24}Si_{12}$ (M^{2-}) 1254.5135. Found: 1254.7012.

Compound 4d:



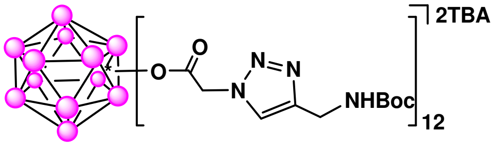
4d was synthesized from the azide functionalized closomer **3** (100 mg, 0.055 mmol), 5-diethyl acetylenedicarboxylate (561 mg, 3.30 mmol), copper (I) iodide (126 mg, 0.660 mmol) and diisopropylethylamine (853 mg, 6.60 mmol) using the general method for click reaction on closomers described in the article. Yield: 125 mg (59%). ^{1}H NMR (400 MHz, CD_3CN): δ 5.26 (m, 24H), 4.37 (m, 24H), 4.22 (m, 24H), 3.12 (t, 16H, *J* = 8.4Hz), 1.62 (m, 16H), 1.34 (m, 52H), 1.22 (m, 36H), 0.97 (t, 24H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, CD_3CN): δ 163.55, 160.16, 157.53, 139.49, 130.49, 62.51, 61.27, 58.06, 51.88, 23.03, 19.03, 13.17, 13.03, and 12.53. ^{11}B NMR (128 MHz, CD_3CN): δ -17.62. HRMS (m/z): Calcd. for $C_{120}H_{180}B_{12}N_{48}O_{48}$ (M^{2-}) 1685.9968. Found: 1685.9170 (11-fold and 10-fold substitution were also seen in mass spectrum).

Compound 4e:



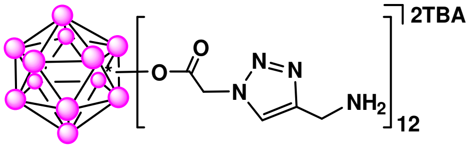
4e was synthesized from the azide functionalized closomer **3** (100 mg, 0.055 mmol), 5-chloro-1-pentyne (337 mg, 3.30 mmol), copper (I) iodide (126 mg, 0.660 mmol) and diisopropylethylamine (853 mg, 6.60 mmol) using the general method for click reaction on closomer described in the article. Yield: 130 mg (78%). ^{1}H NMR (400 MHz, CD_3CN): δ 7.44 (s, 12H), 4.90 (s, 24H), 3.64 (t, 24H, *J* = 6.8Hz), 3.11 (t, 16H, *J* = 8.4Hz), 2.83 (t, 24H, *J* = 7.2Hz), 2.10 (m, 24H), 1.62 (m, 16H), 1.36 (m, 16H), 0.98 (t, 24H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, CD_3CN): δ 165.43, 145.74, 122.53, 57.83, 51.31, 44.03, 31.60, 22.79, 22.04, 18.82 and 12.30. ^{11}B NMR (128 MHz, CD_3CN): δ -17.48. HRMS (m/z): Calcd. for $C_{84}H_{108}B_{12}C_{112}N_{36}O_{24}$ (M^{2-}) 1278.2858. Found: 1278.3260.

Compound 4f:



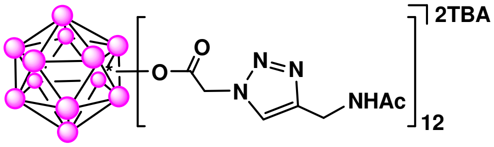
4f was synthesized from the azide functionalized closomer **3** (100 mg, 0.055 mmol), 5-N-Boc-propargylamine (512 mg, 3.30 mmol), copper (I) iodide (126 mg, 0.660 mmol) and Diisopropylethylamine (853 mg, 6.60 mmol) using the general method for click reaction on closomers described in the article. Yield: 160 mg (79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (s, 12H), 6.36 (broad s, 12H), 4.93 (s, 24H), 4.37 (d, 24H, *J* = 6Hz), 3.19 (t, 16H, *J* = 8.5Hz), 1.63 (m, 16H), 1.39 (s, 108H), 1.26 (m, 16H), 0.98 (t, 24H, *J* = 7.2 Hz). ^{13}C NMR (125 MHz, CD_3CN): δ 165.61, 155.81, 145.90, 123.72, 78.49, 58.23, 51.80, 35.7, 27.58, 23.21, 19.24 and 12.73. ^{11}B NMR (96 MHz, CD_3CN): δ -16.34. HRMS (m/z): Calcd. for $C_{120}H_{144}B_{12}N_{36}O_{72}$ (M^{2-}) 1596.2171. Found: 1596.1645.

Compound 4g:

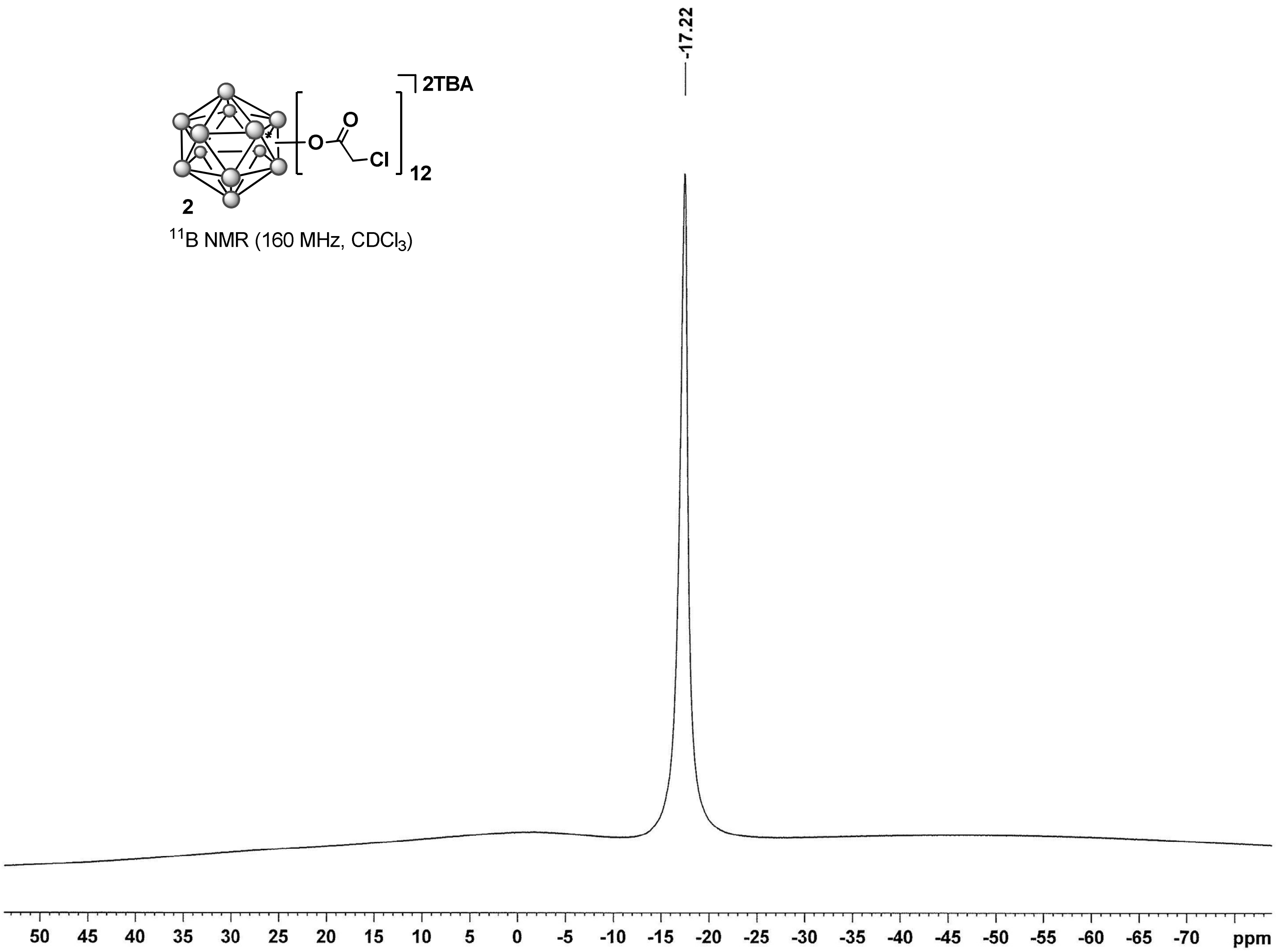


Closomer **4f** (80 mg, 0.020 mmol) was taken in an 100 mL round bottom flask and 20% trifluoroacetic acid/dichloromethane (10 mL) was added to it. The reaction mixture was stirred at 0°C for 1.5 hrs under an ensuing argon atmosphere. The reaction mixture so obtained was concentrated under high vacuum using a liquid N_2 trap. The crude product thus obtained was triturated with ether and used directly in the next step without any further purification. Crude yield: 80 mg. ^{1}H NMR (500 MHz, CD_3OD): δ 7.93 (s, 12H), 5.1 (s, 24H), 4.42 (s, 24H), (undesired peaks at 5.19, 3.3 and 1.58 ppm are attributed to methanol and water; undesired peaks at 3.74, 3.23 and 1.37 ppm are attributed to diisopropylamine). ^{13}C NMR (400 MHz, CD_3OD): δ 166.02, 126.72, 87.50, 54.30, 51.71, 42.50, 34.07, 26.18, 17.17, 15.73 and 11.57(undesired additional peaks are attributed to methanol, water and diisopropylamine). ^{11}B NMR (96 MHz, CD_3OD): δ -17.21. HRMS (m/z): Calcd. for $C_{60}H_{84}B_{12}N_{48}O_{24}$ $(M+4H)^{+2}$ 997.4165. Found: 997.4799 and 664.60056 $(M+5H)^{+3}$.

Compound 4h:



Crude N-Boc-deprotected closomer **4g** (crude from previous step, ~0.020 mmol) was taken in a dry 50 mL round bottom flask and 10 mL dry pyridine was added to it. To this mixture, acetic anhydride (266 mg, 2.60 mmol) was added at 0°C and the reaction mixture was slowly allowed to warm up to room temperature under continuous stirring. After stirring for 2 days under an ensuing argon atmosphere, the reaction mixture was concentrated to dryness and the crude mixture so obtained was purified on a size-exclusion column (Lipophilic Sephadex® LH-20) using acetonitrile as the eluent. Yield: 40 mg (62% over two steps). ^{1}H NMR (500 MHz, CD_3OD): δ 7.76 (s, 12H), 5.06 (s, 24H), 4.50 (s, 24H) and 1.94 (s, 36H). ^{11}B NMR (96 MHz, CD_3OD): δ -17.11. HRMS (m/z): Calcd. for $C_{84}H_{108}B_{12}N_{48}O_{36}$ $(M)^{-2}$ 1247.89415. Found: 1247.7986.



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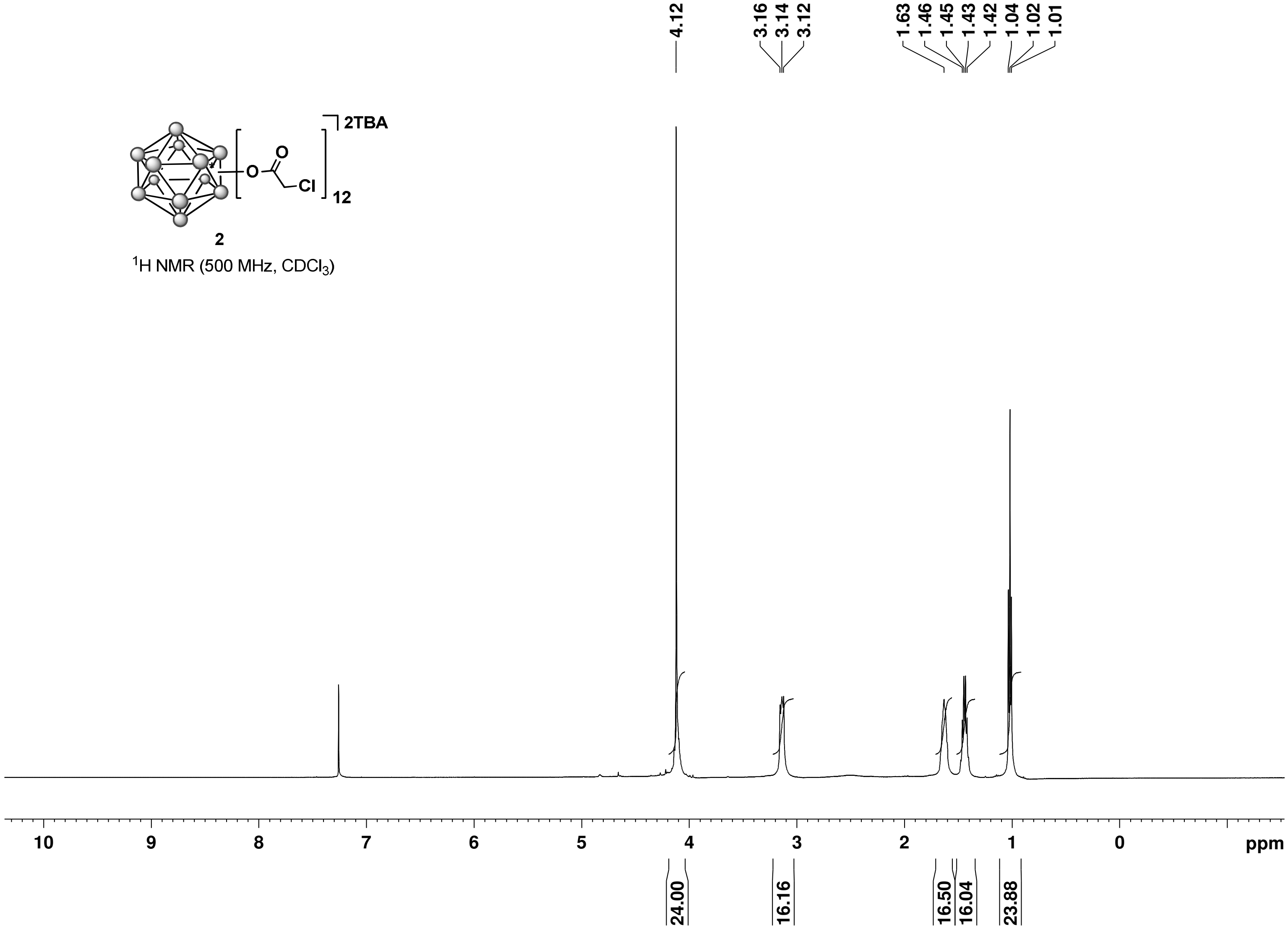
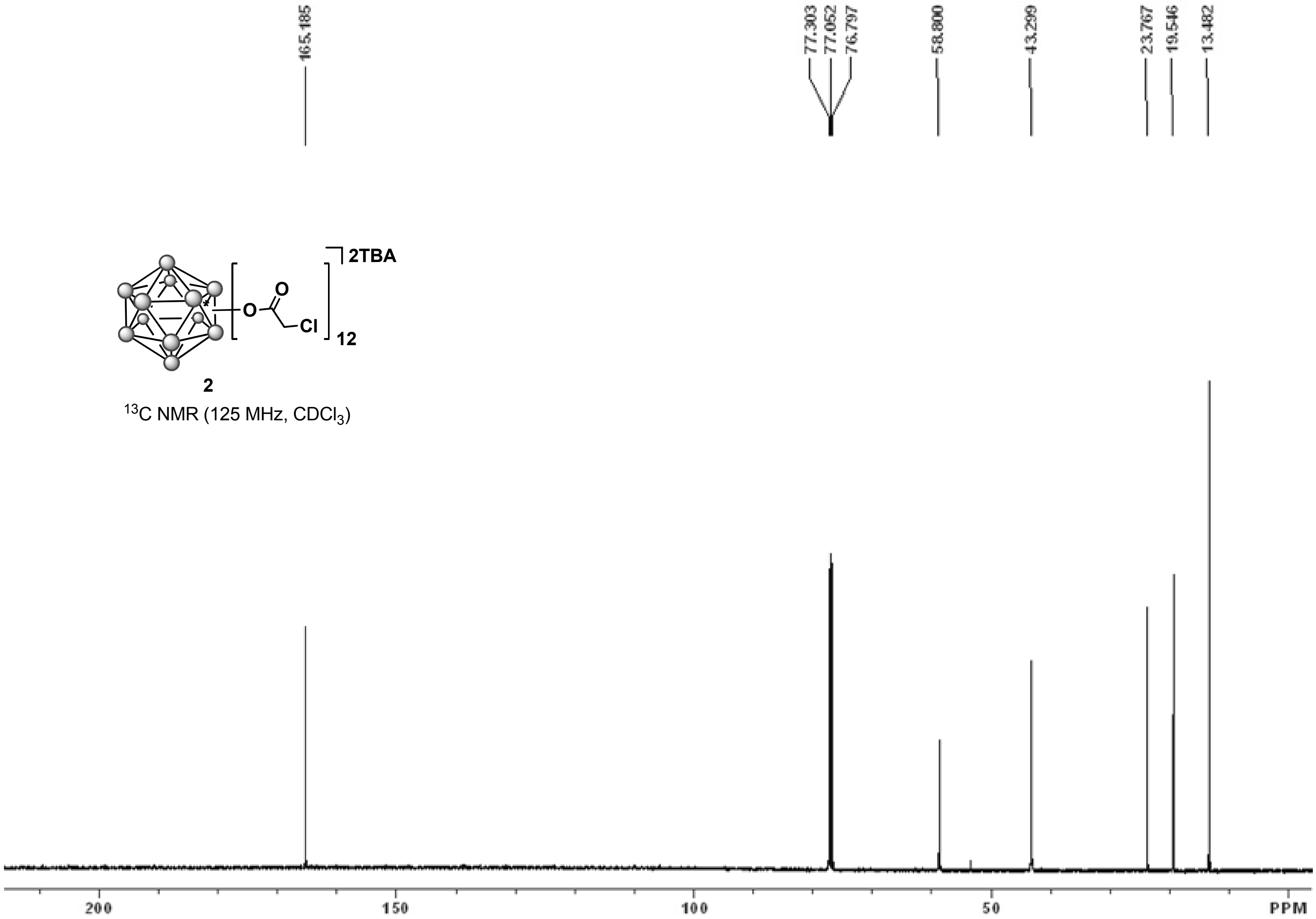
^{11}B NMR (160 MHz, $CDCl_3$)



2

^{1}H NMR (500 MHz, $CDCl_3$)



2

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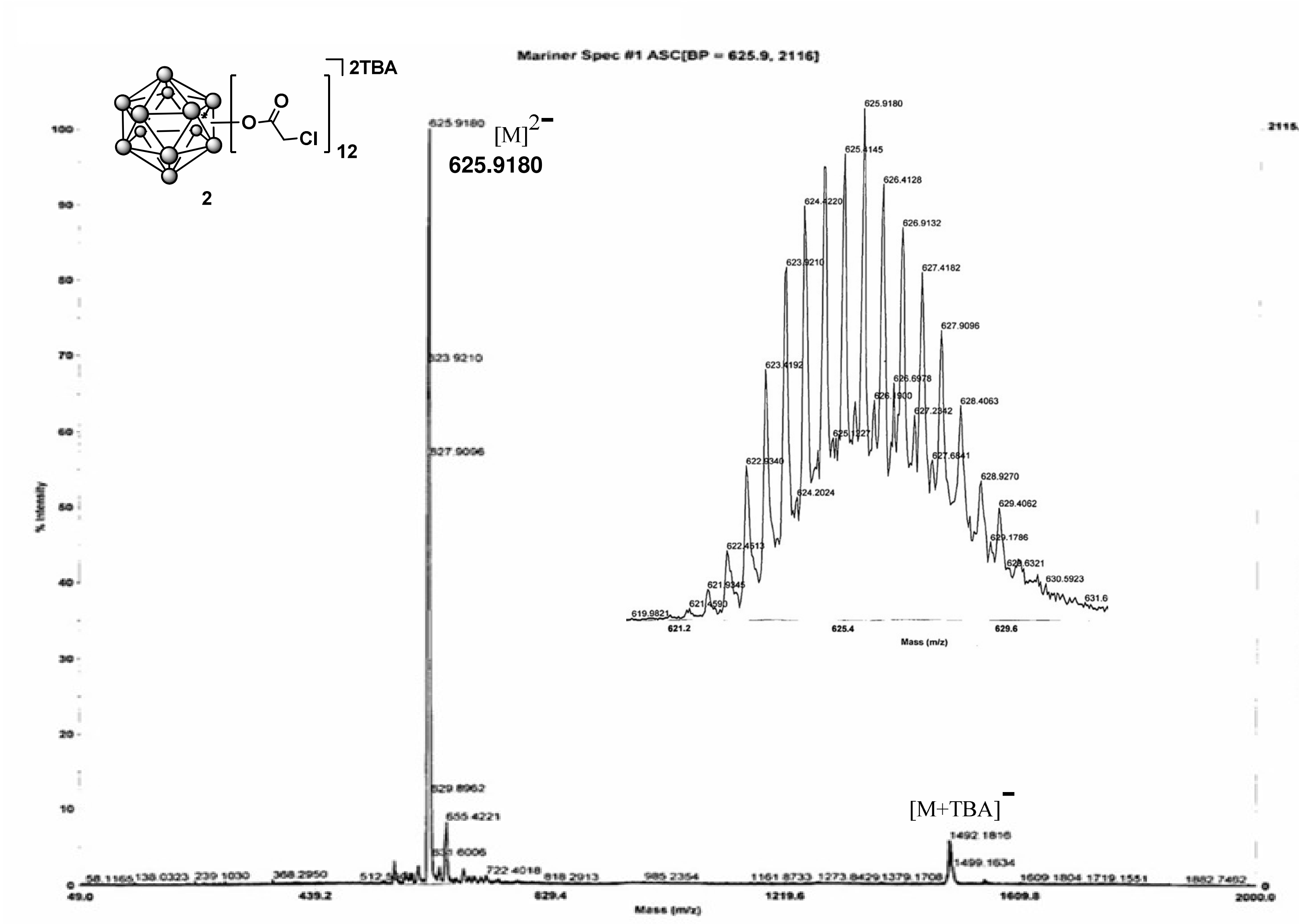
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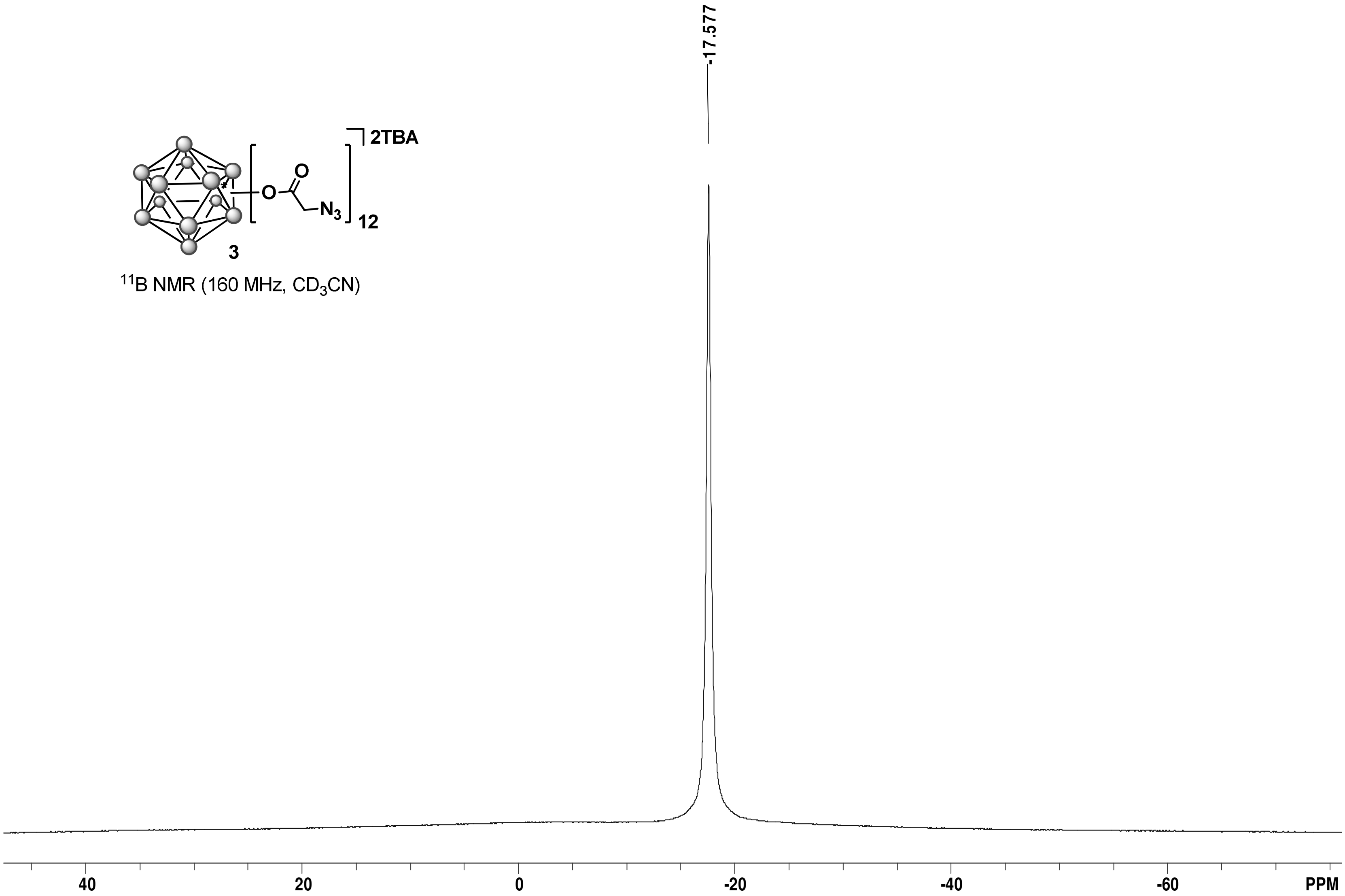

3

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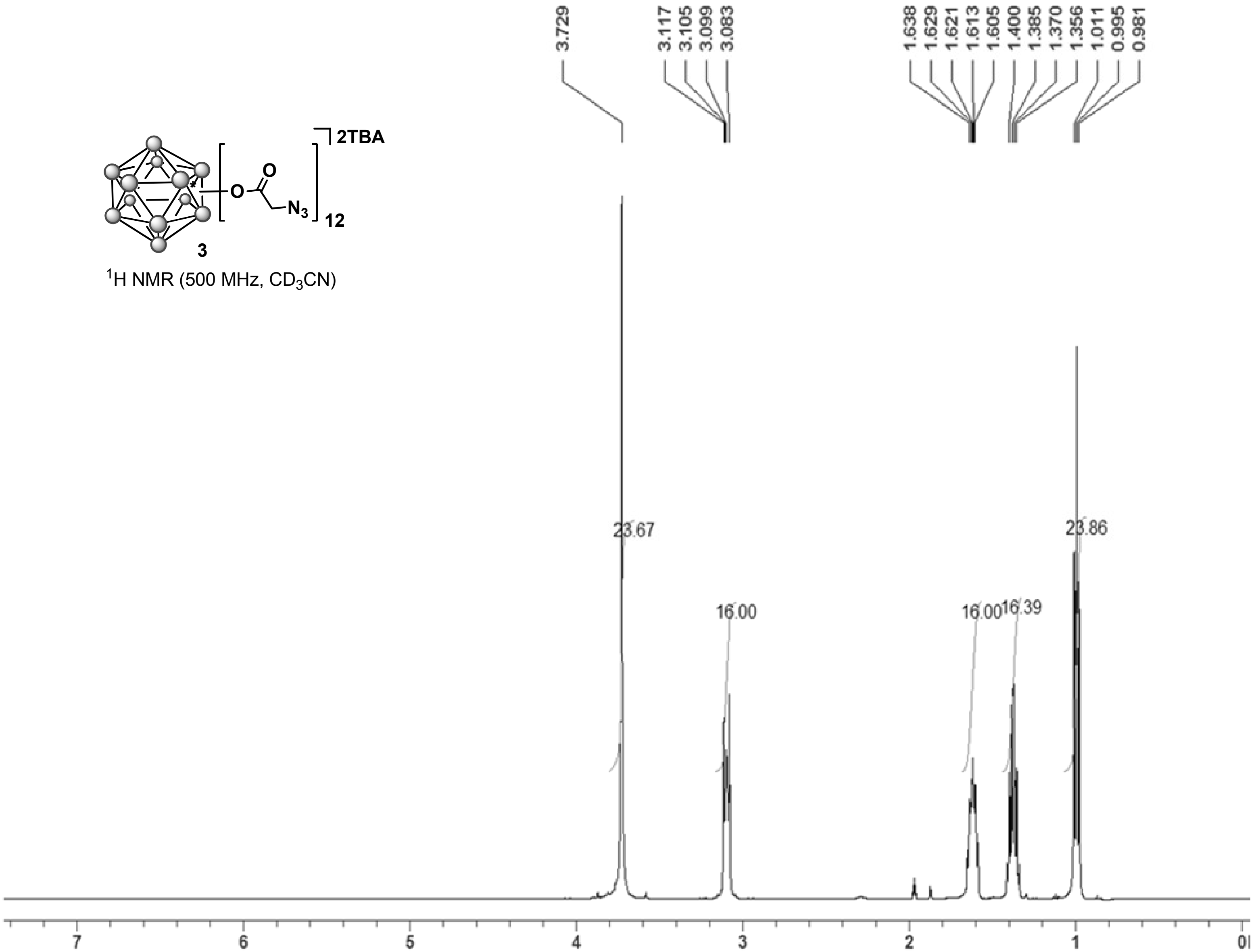
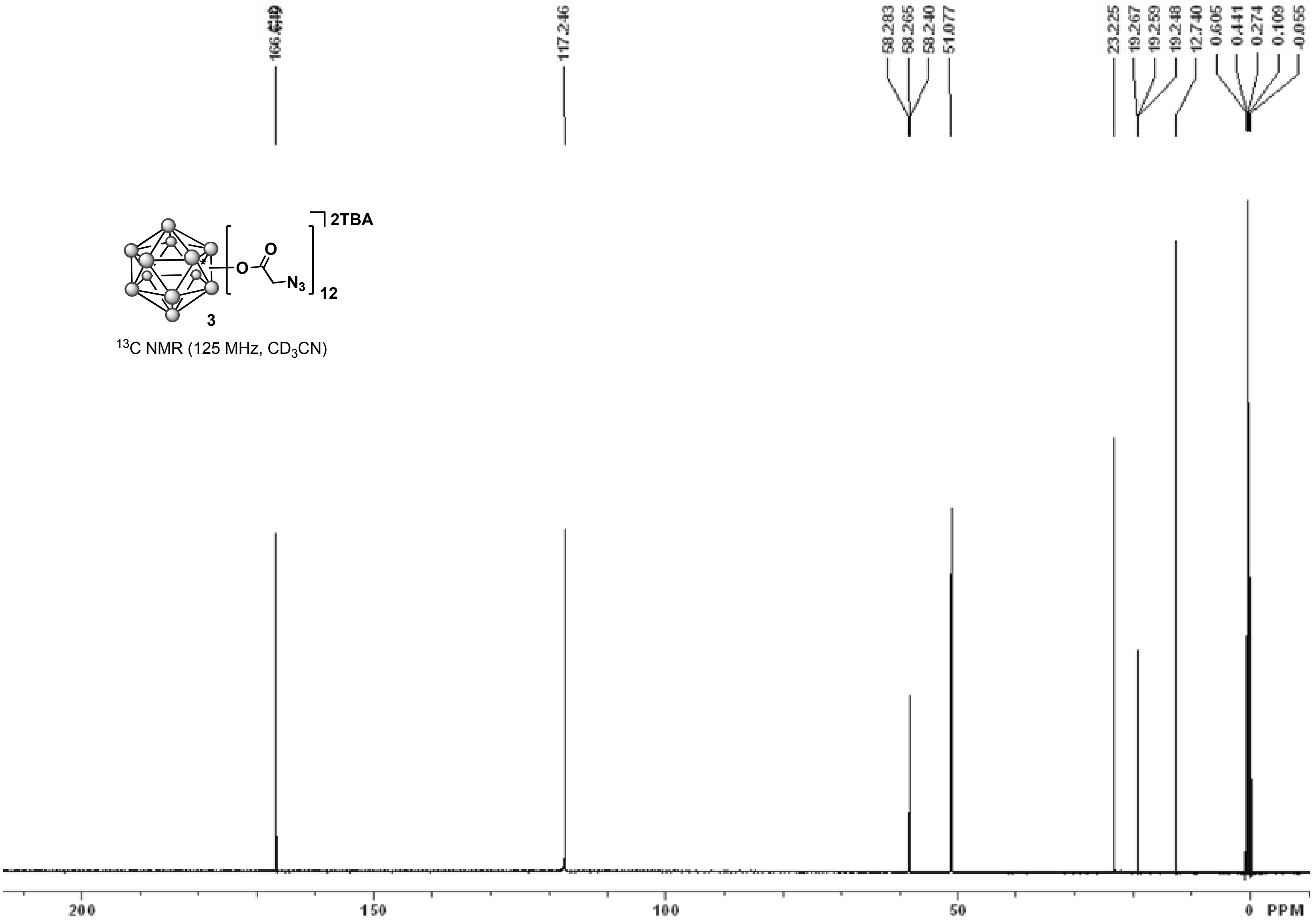


3

^{1}H NMR (500 MHz, CD_3CN)



3

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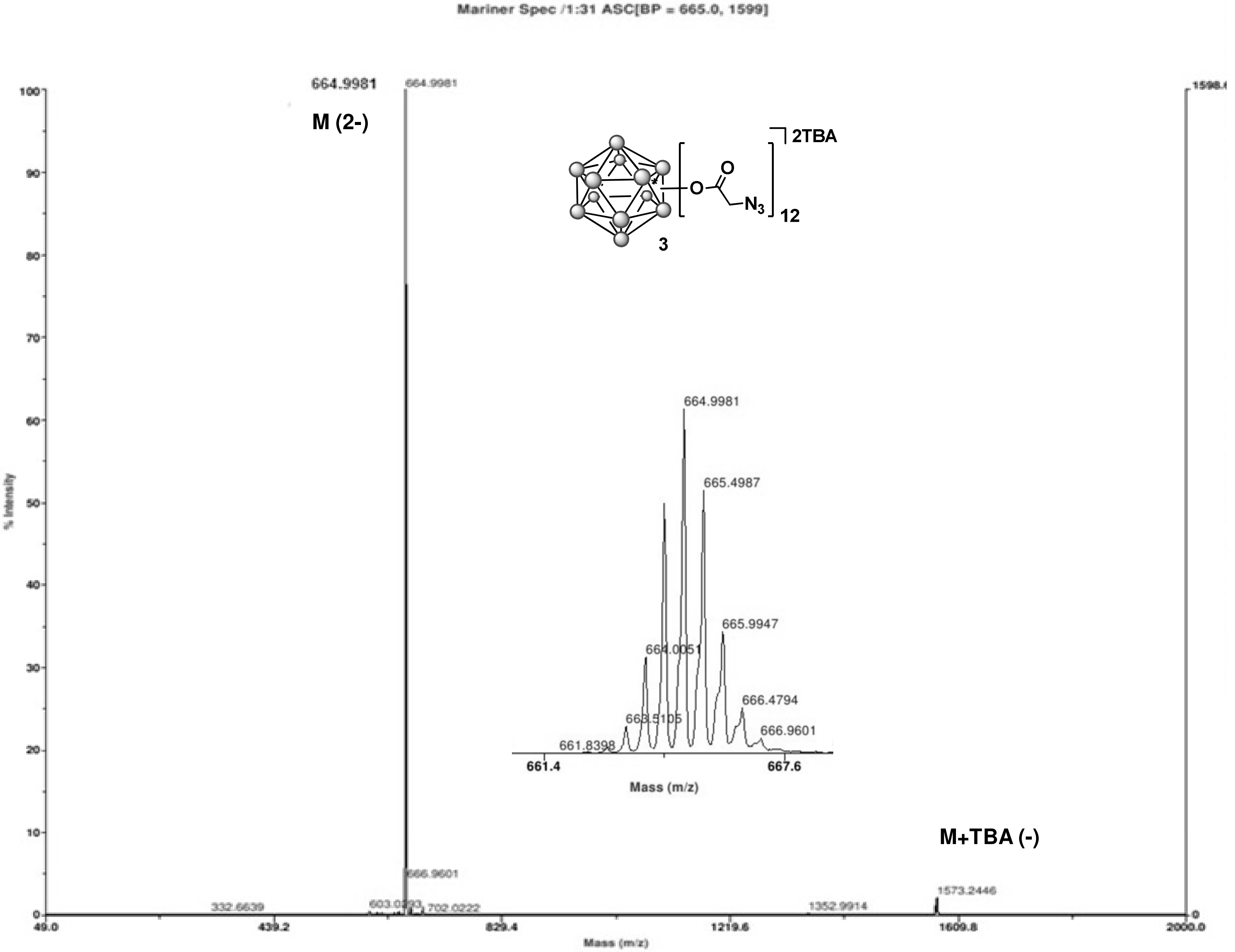
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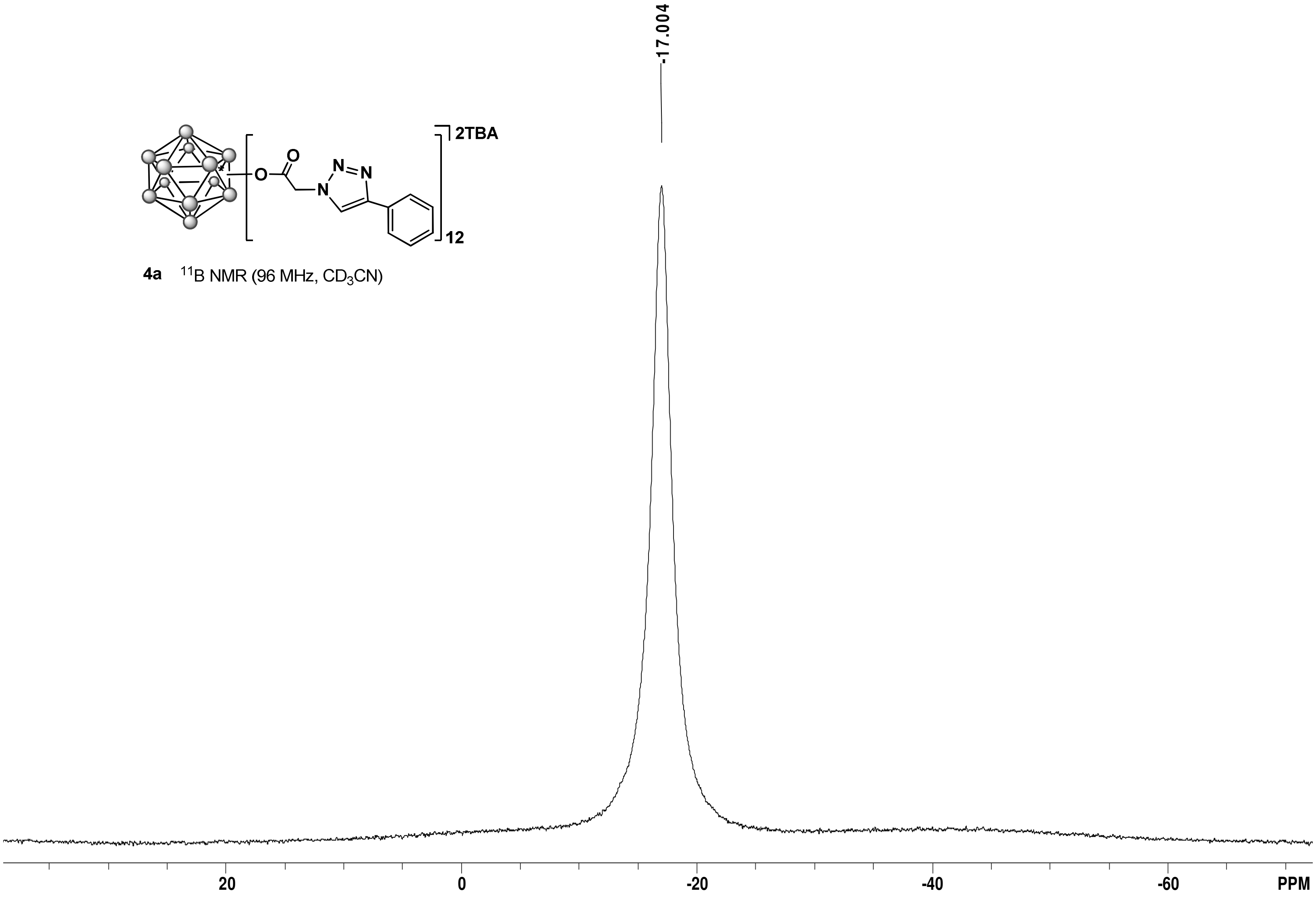

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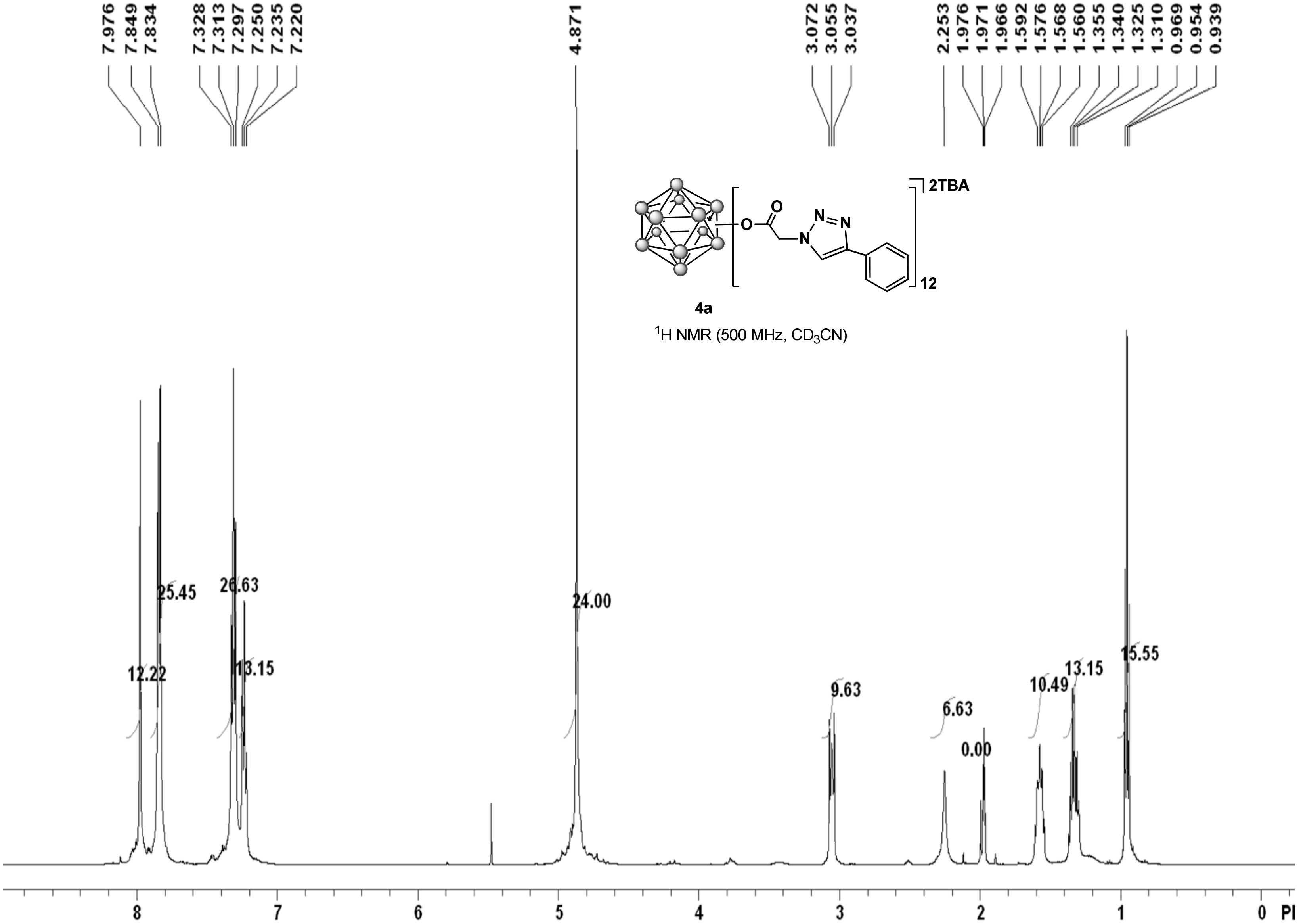
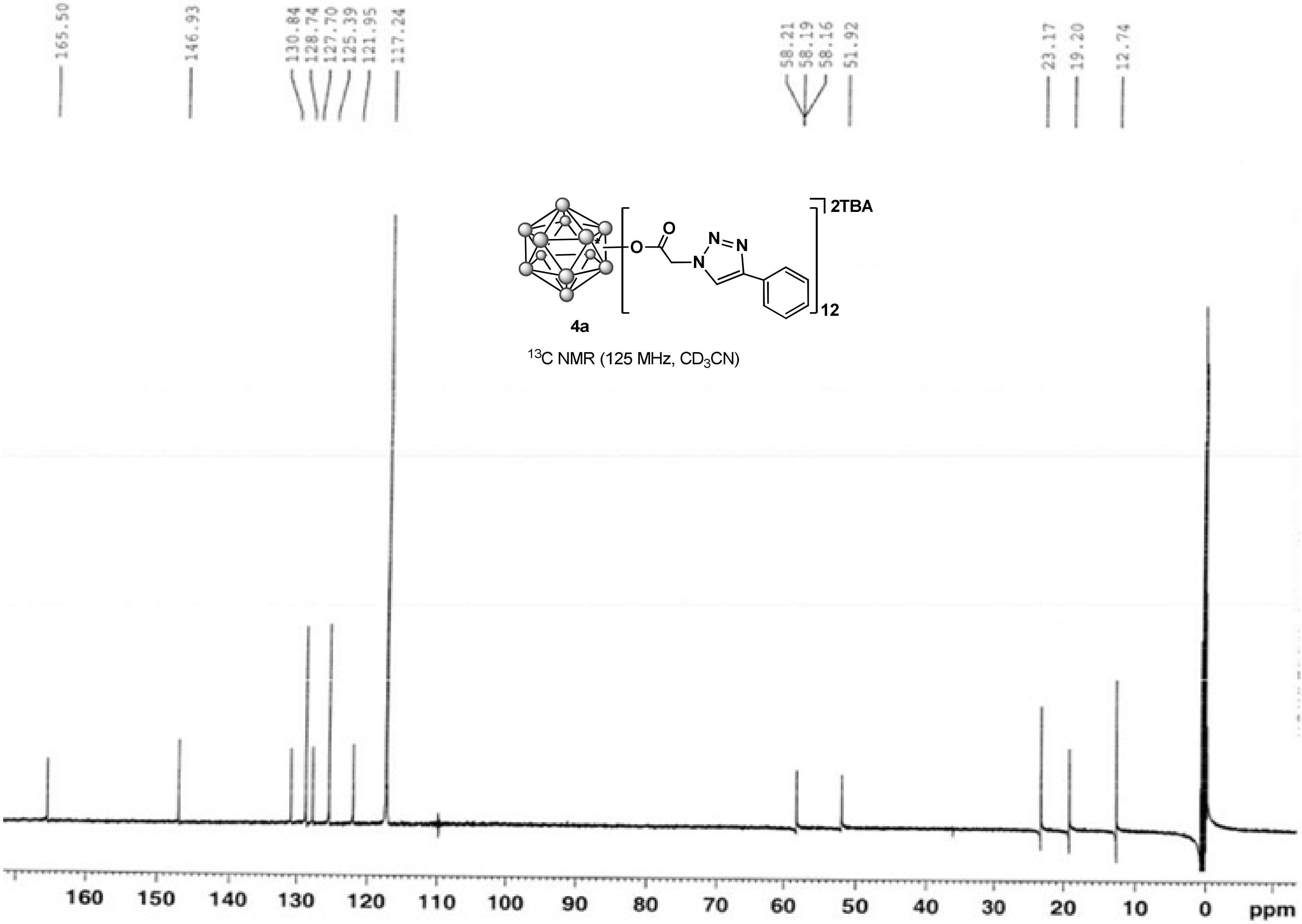


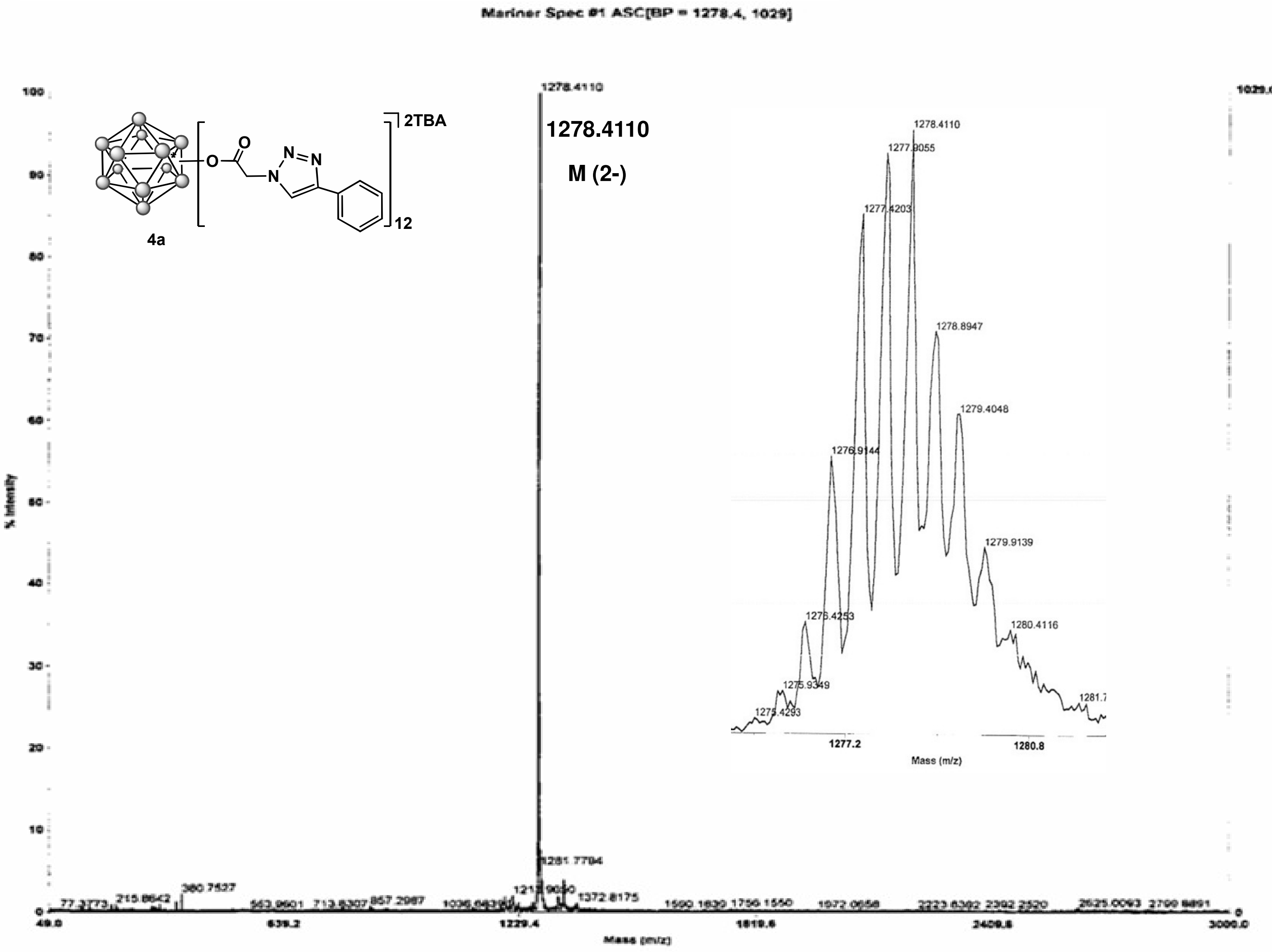
4a

^{1}H NMR (500 MHz, CD_3CN)



4a

^{13}C NMR (125 MHz, CD$_3$CN)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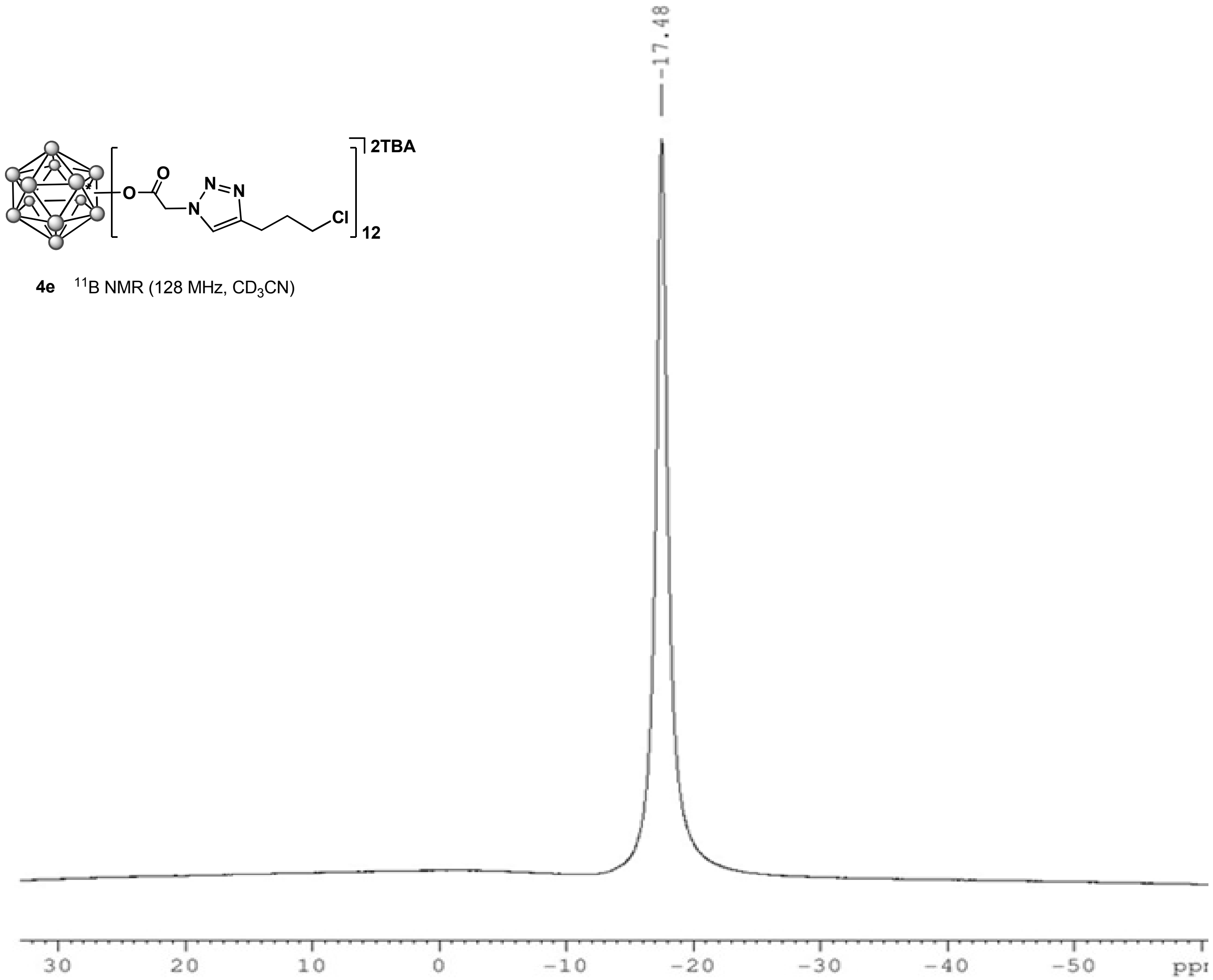
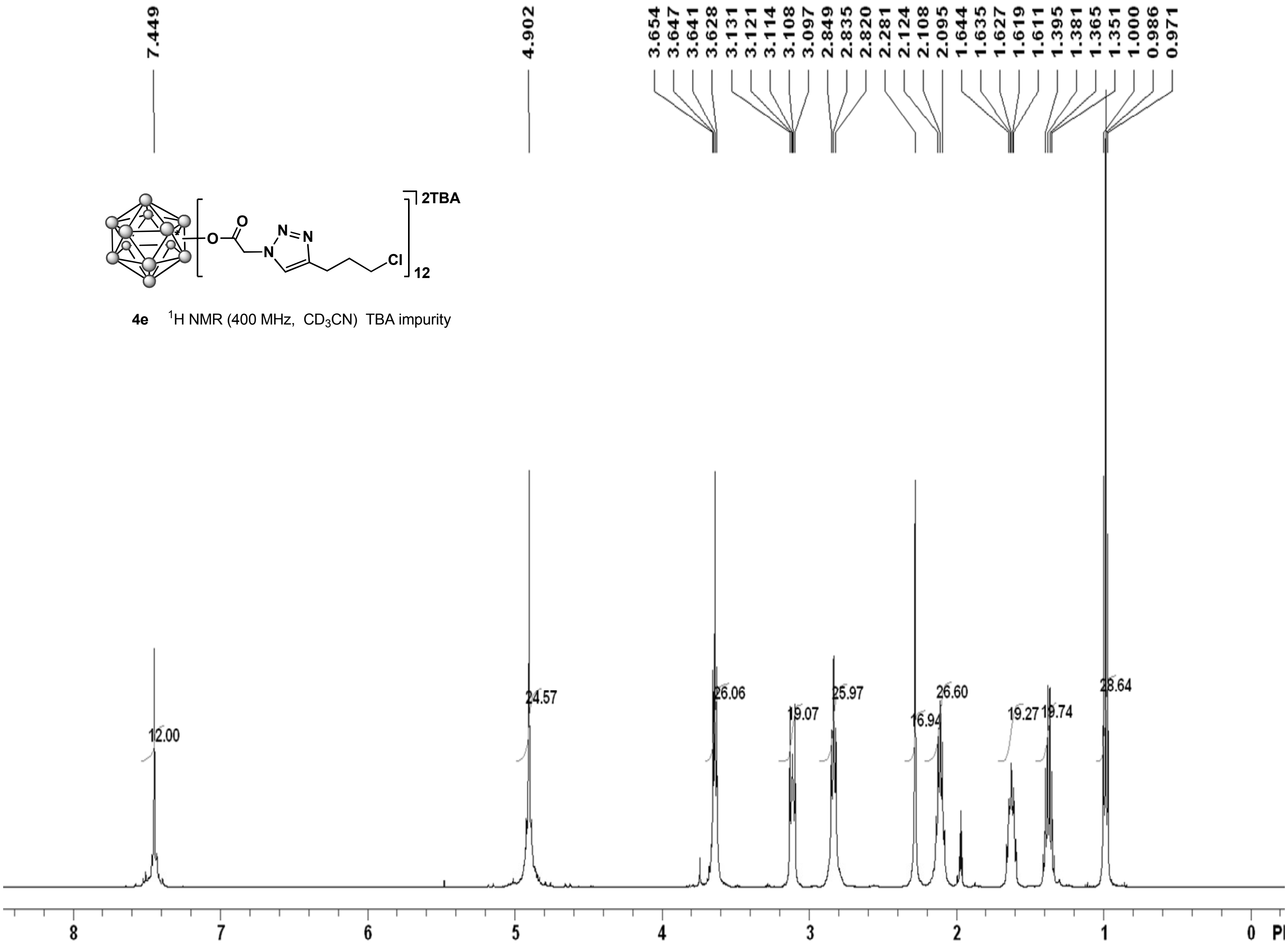
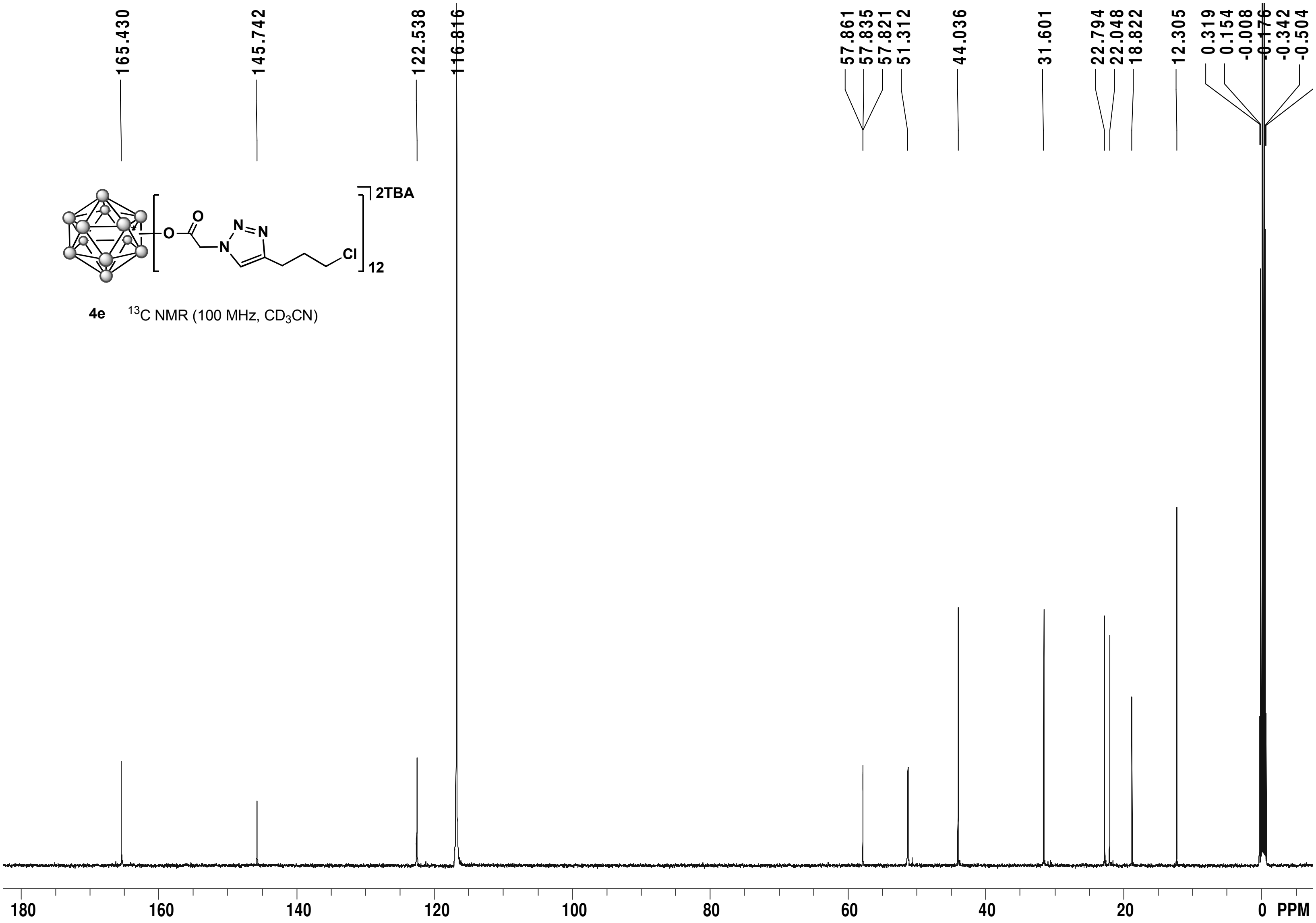


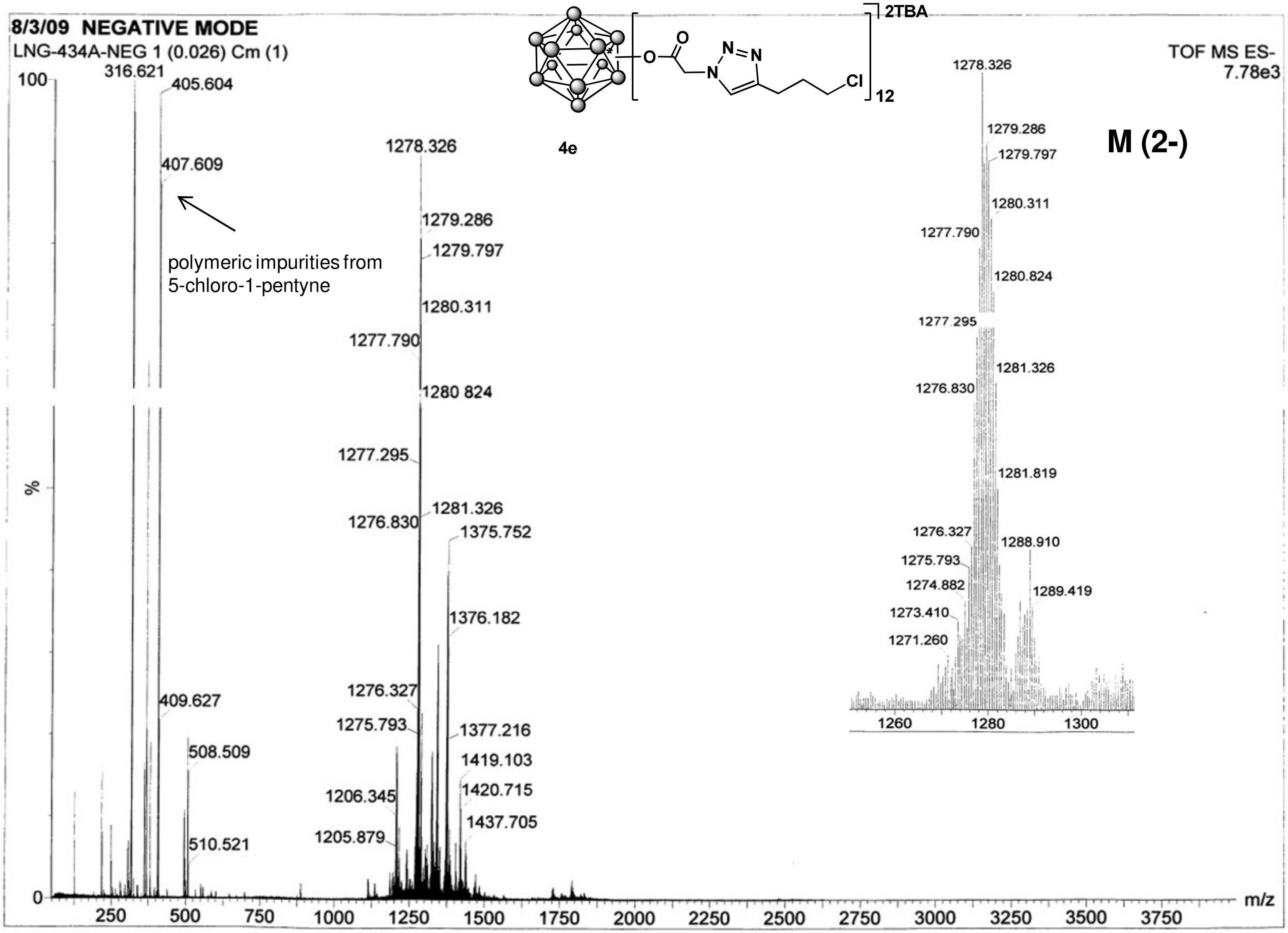
4e ^{11}B NMR (128 MHz, CD_3CN)



4e ^{1}H NMR (400 MHz, CD_3CN) TBA impurity



4e ^{13}C NMR (100 MHz, CD_3CN)



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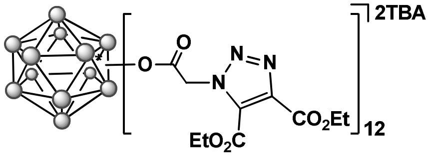
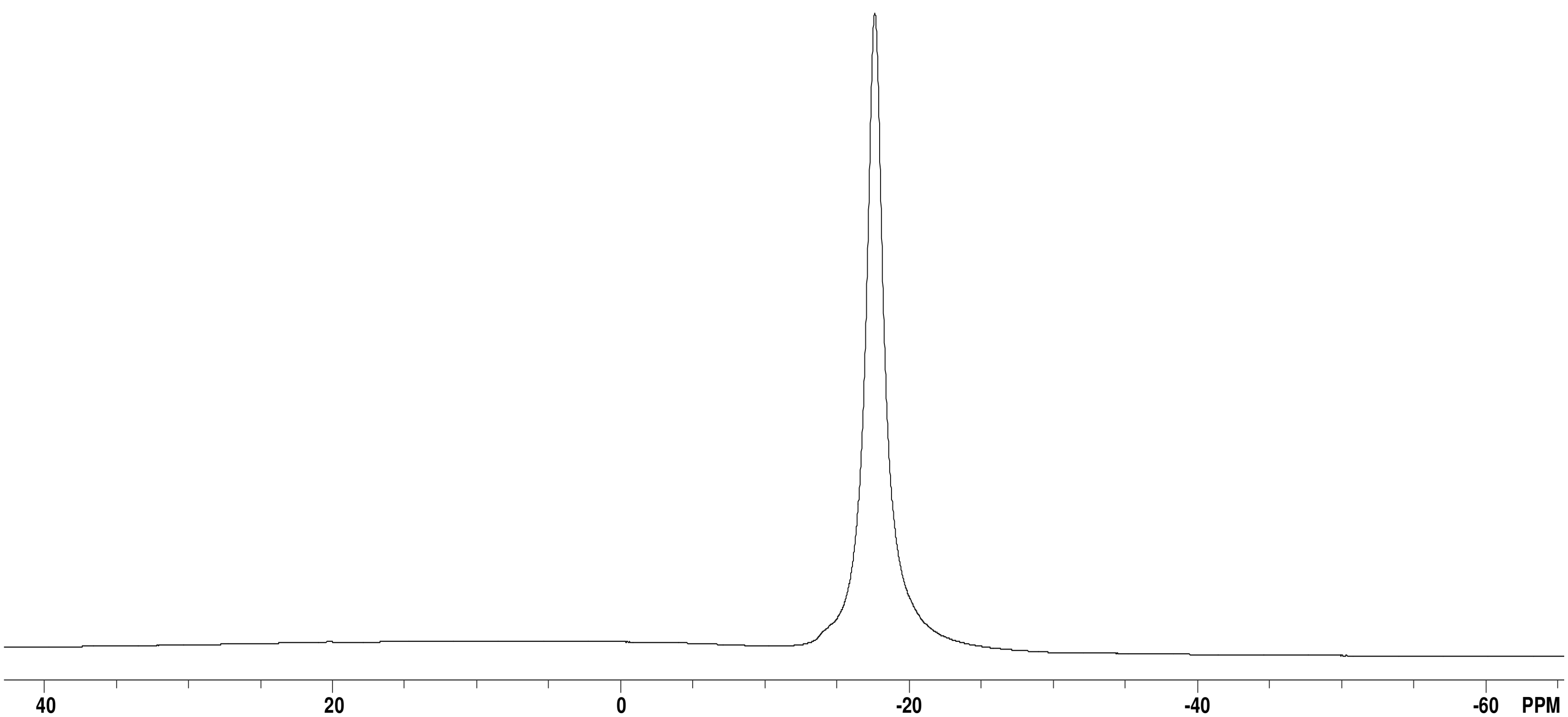
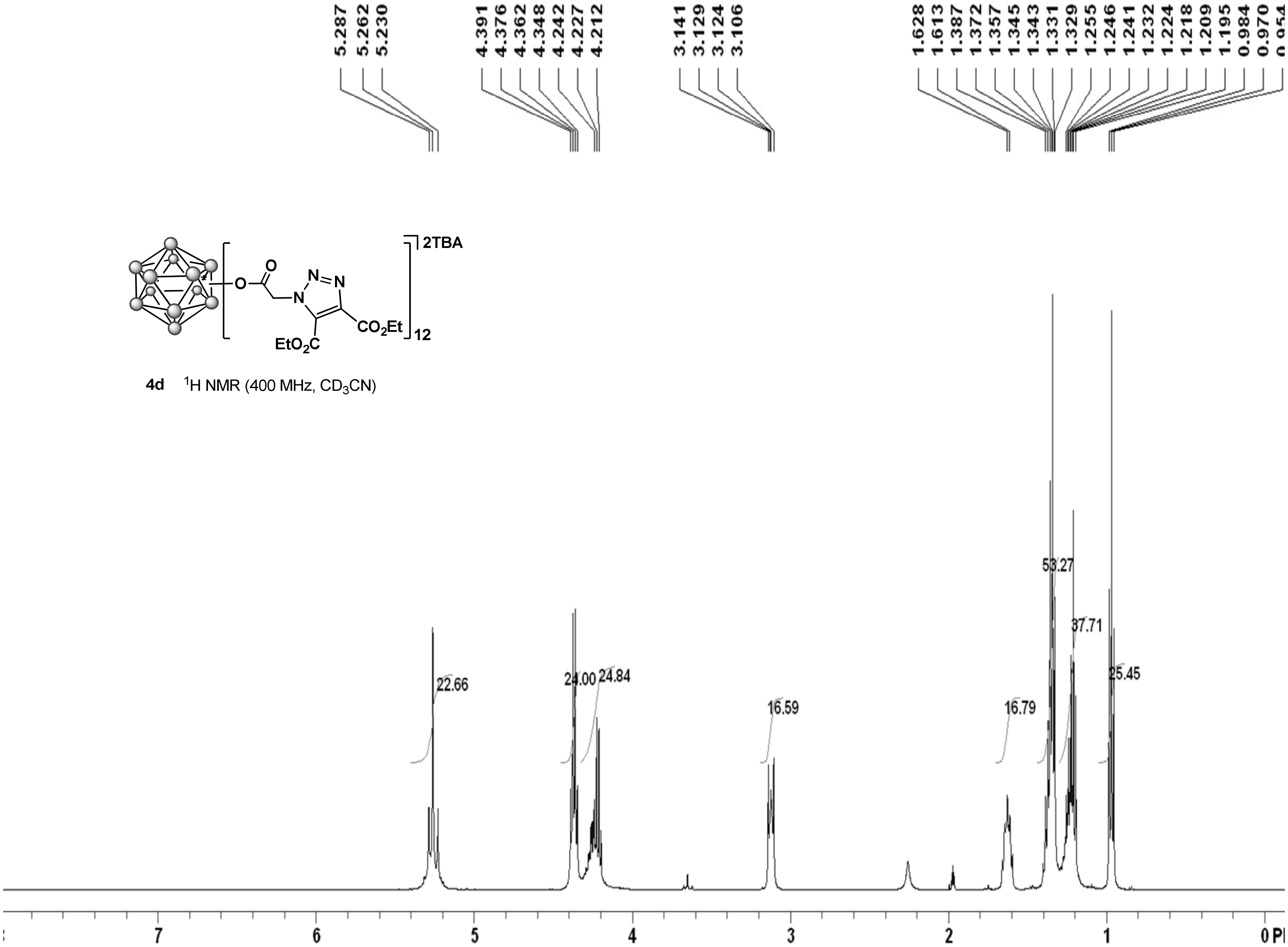


4d ^{11}B NMR (128 MHz, CD_3CN)





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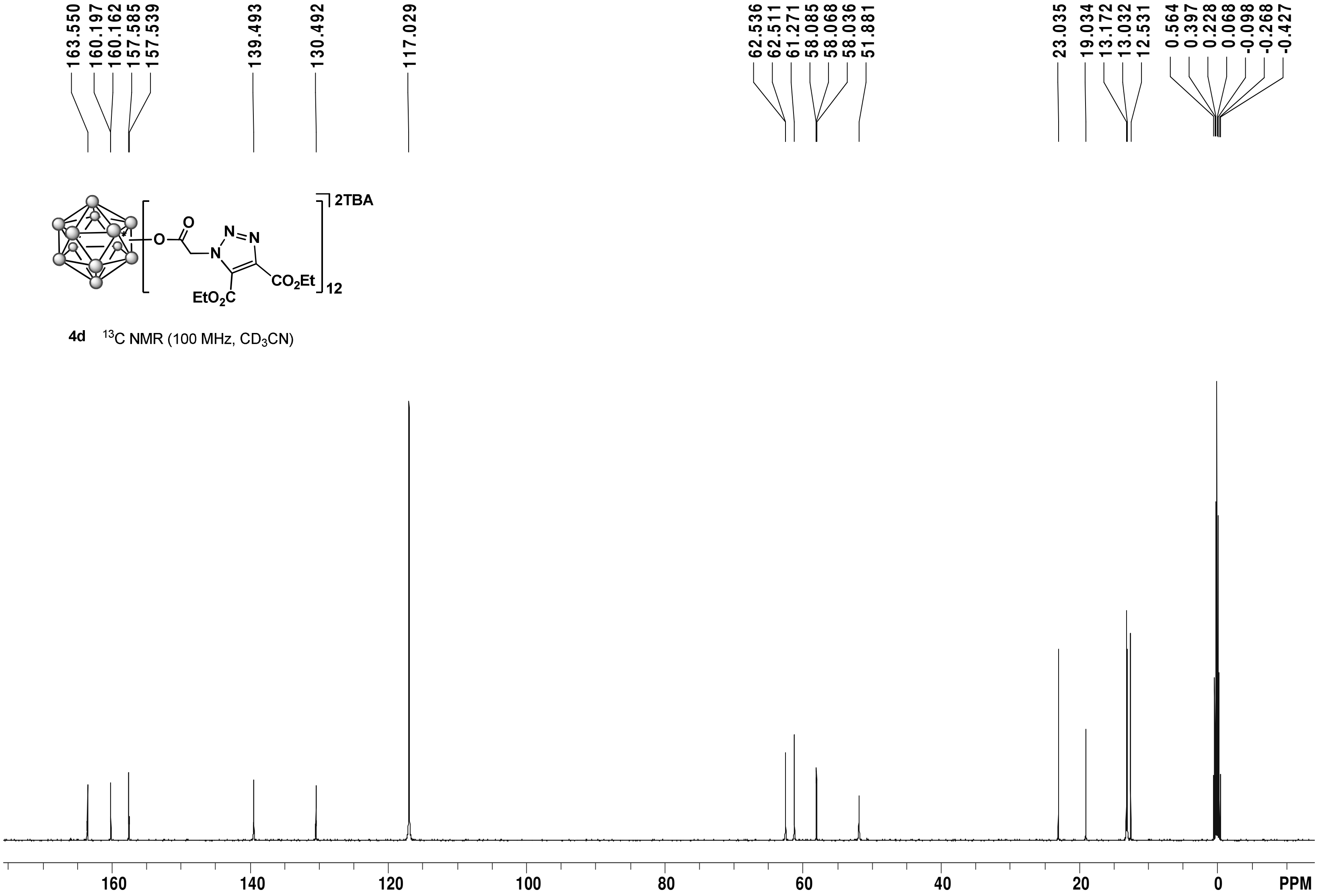

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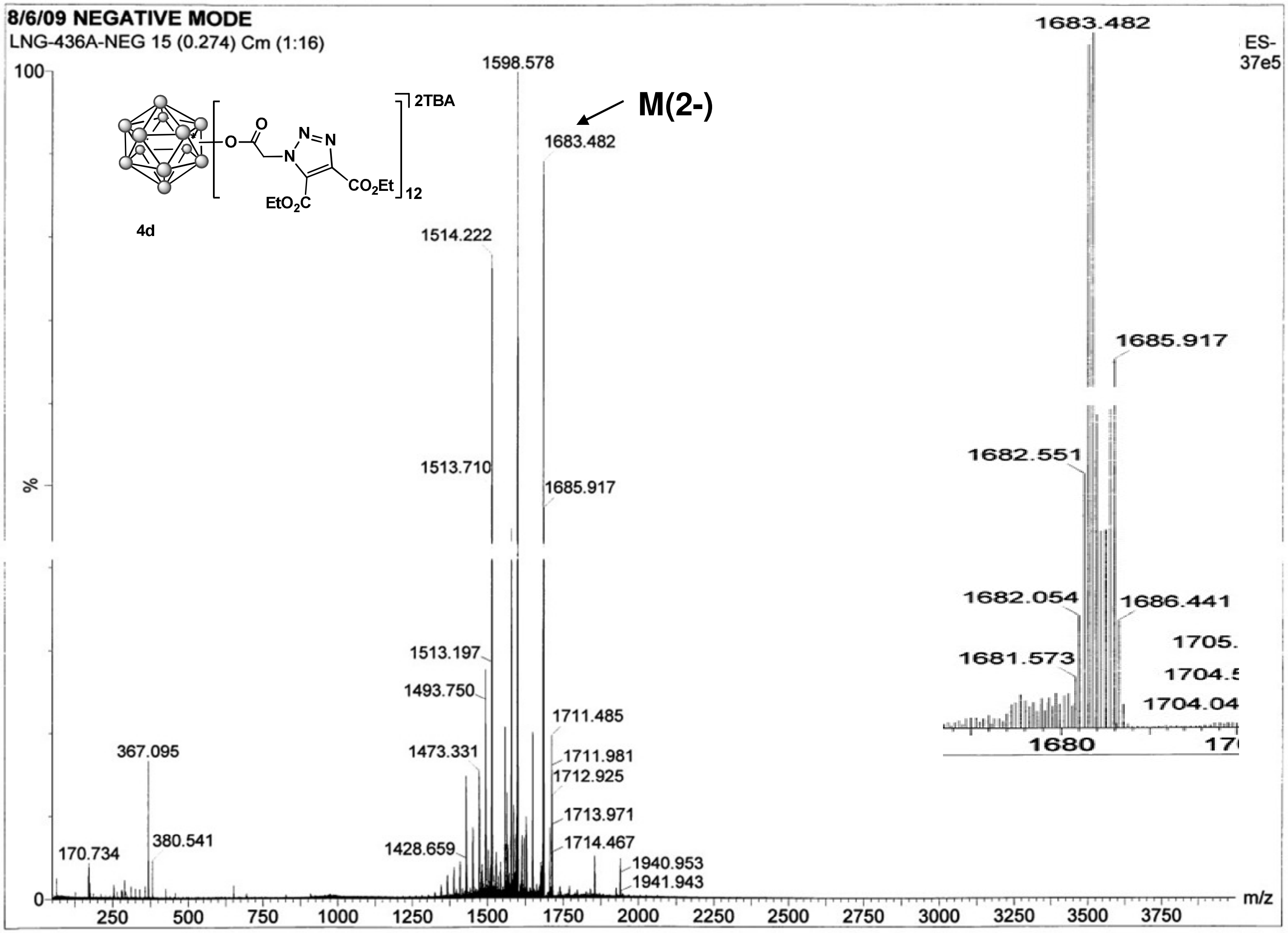
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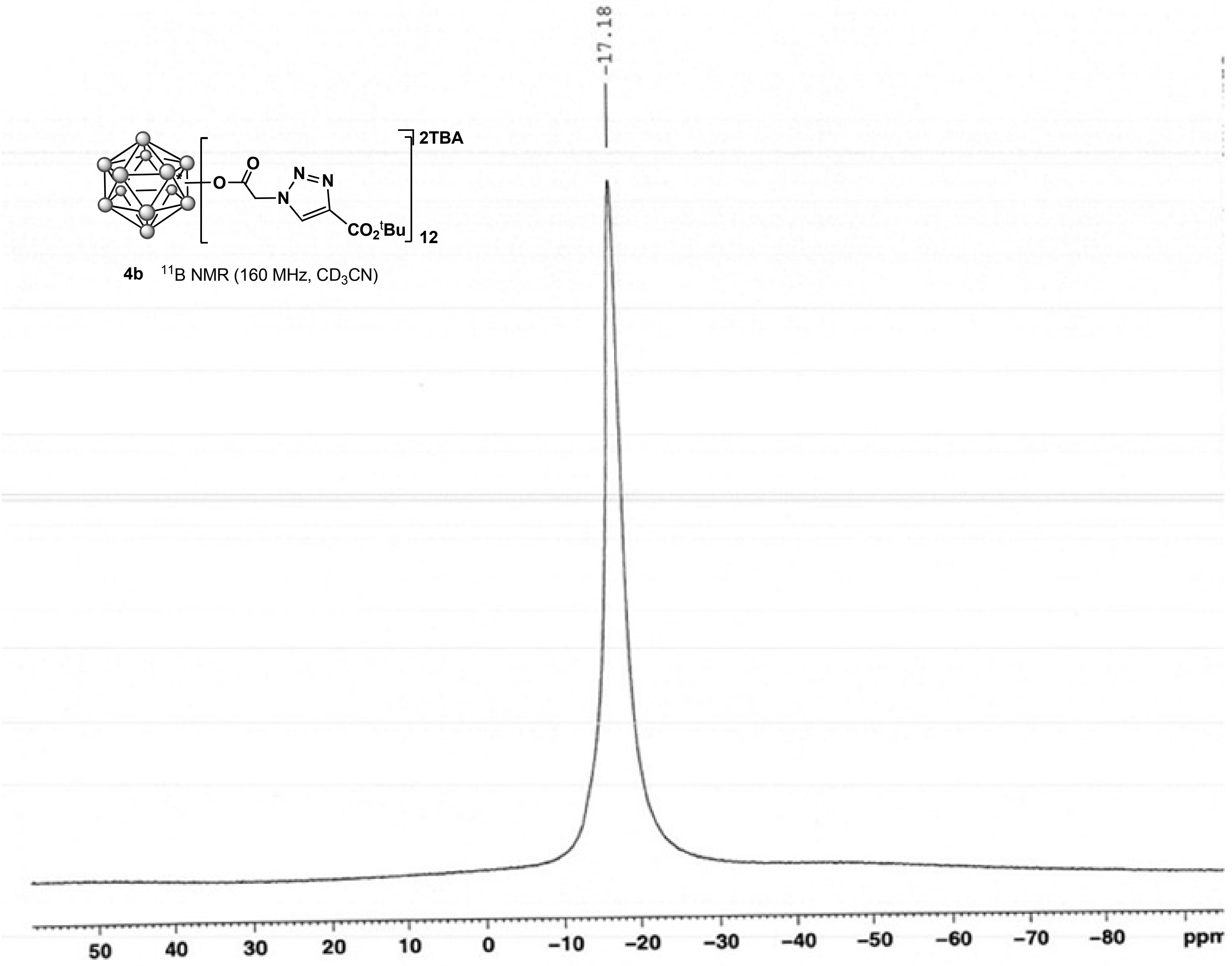
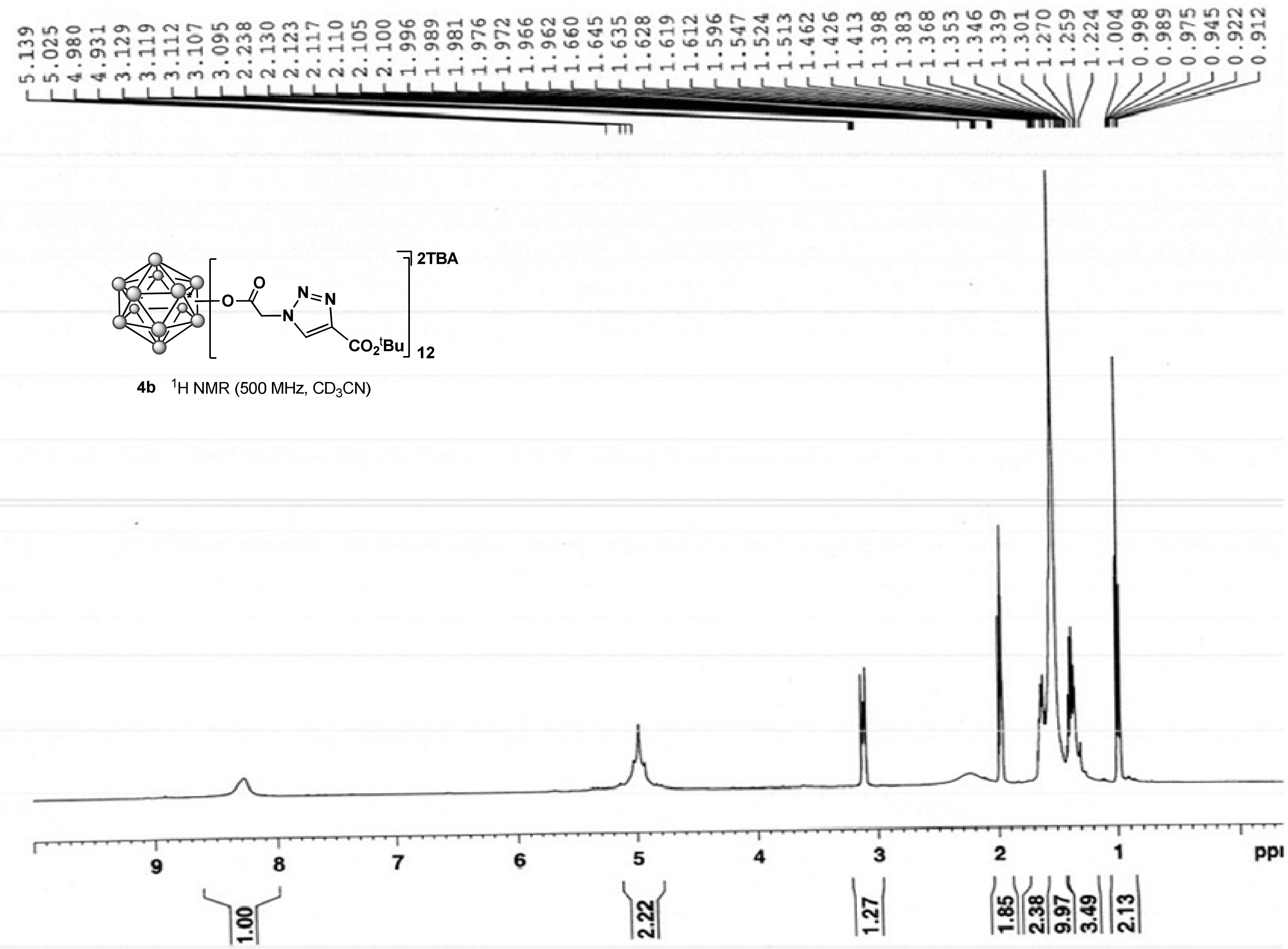
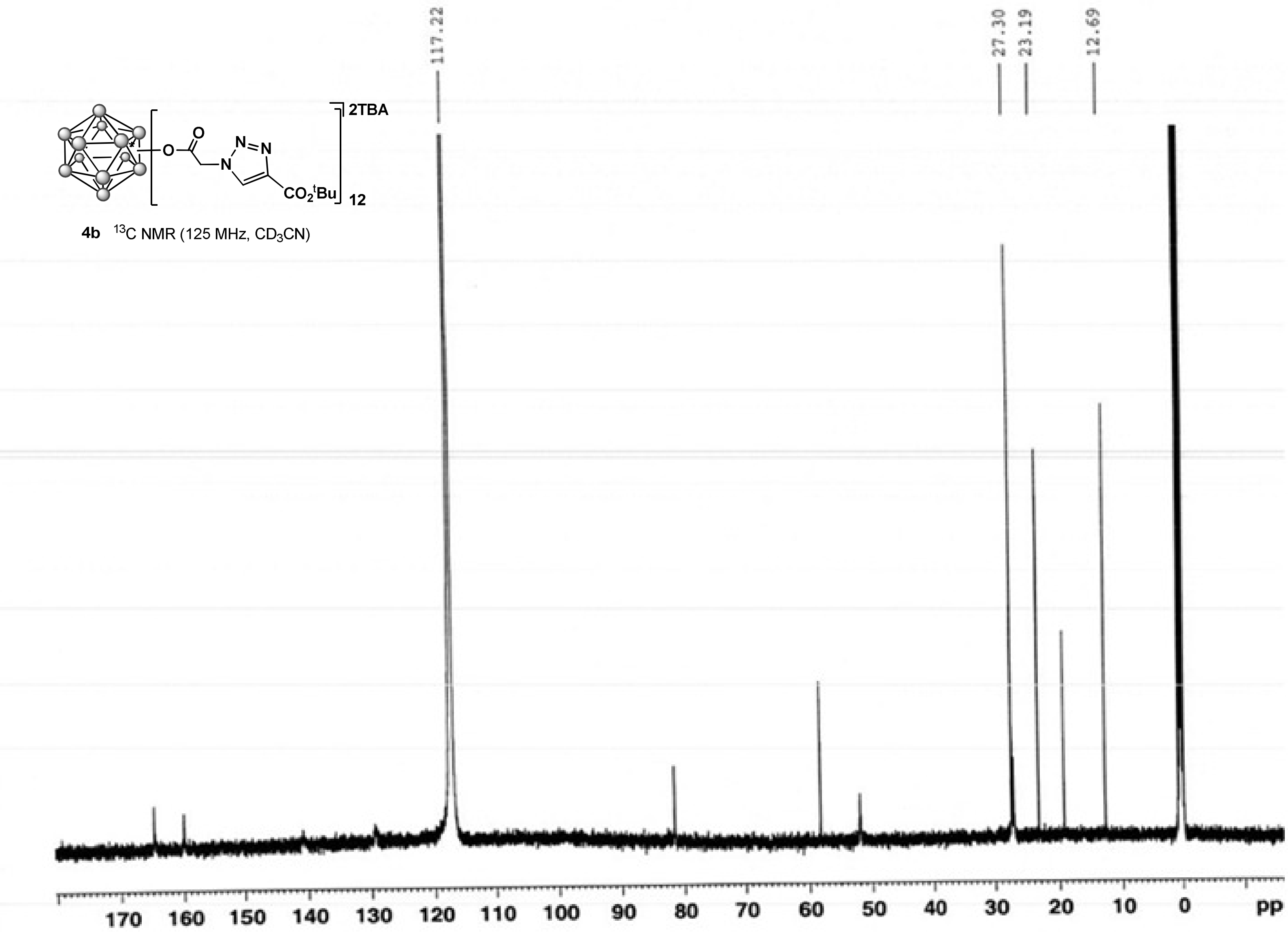
1705.
1681.573
1704.5
1704.04
1680
17



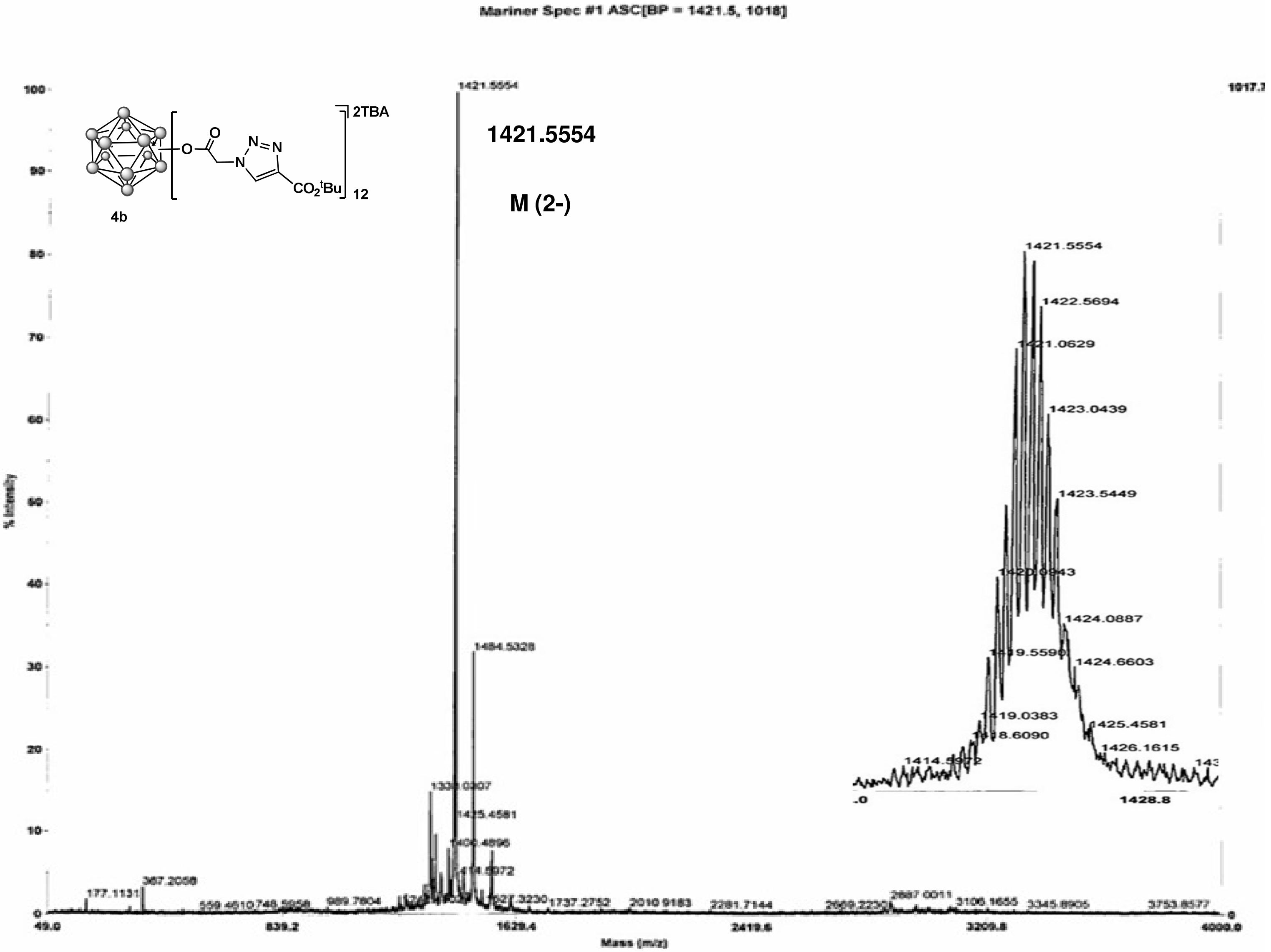
4b ^{11}B NMR (160 MHz, CD_3CN)

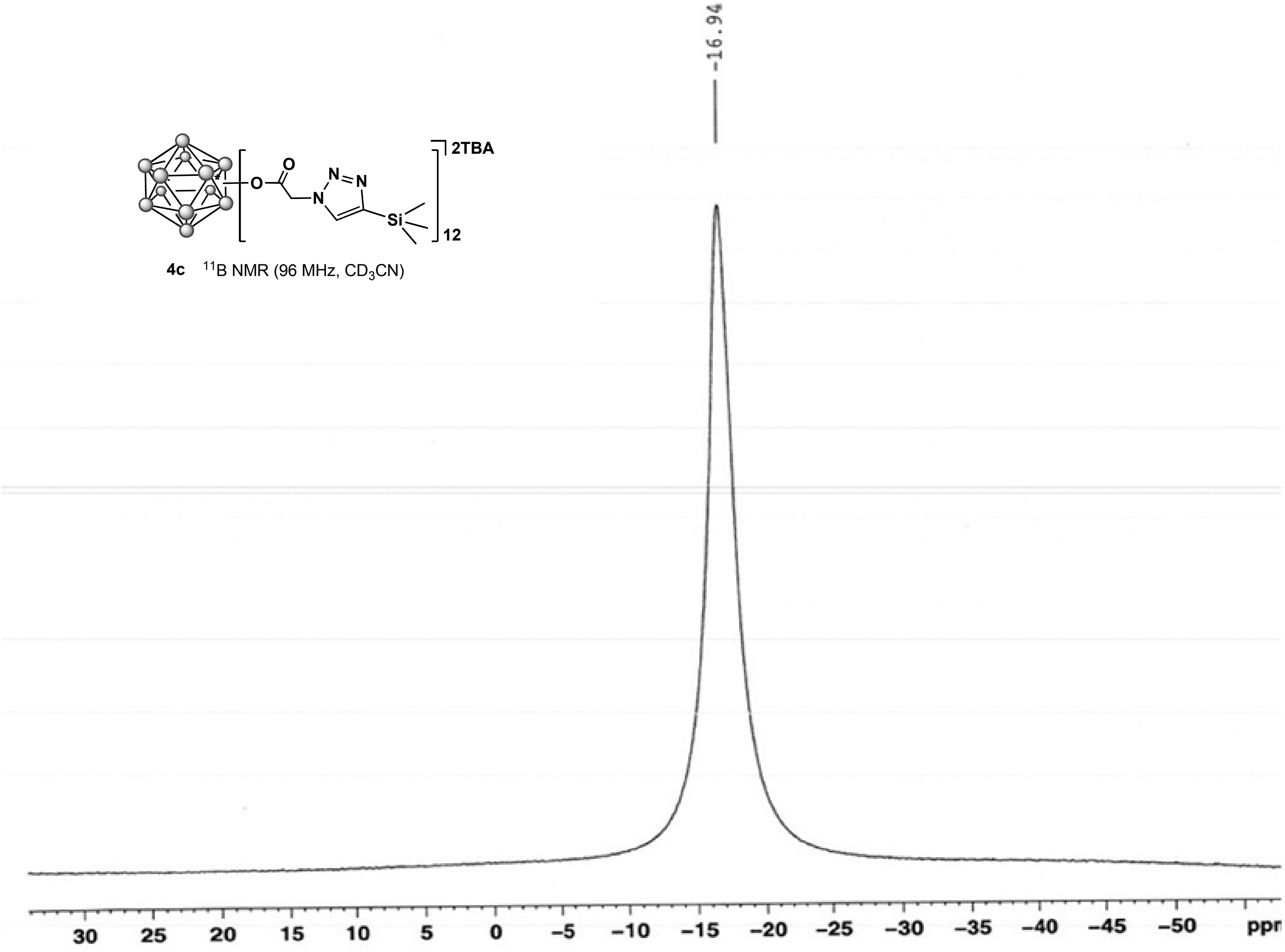


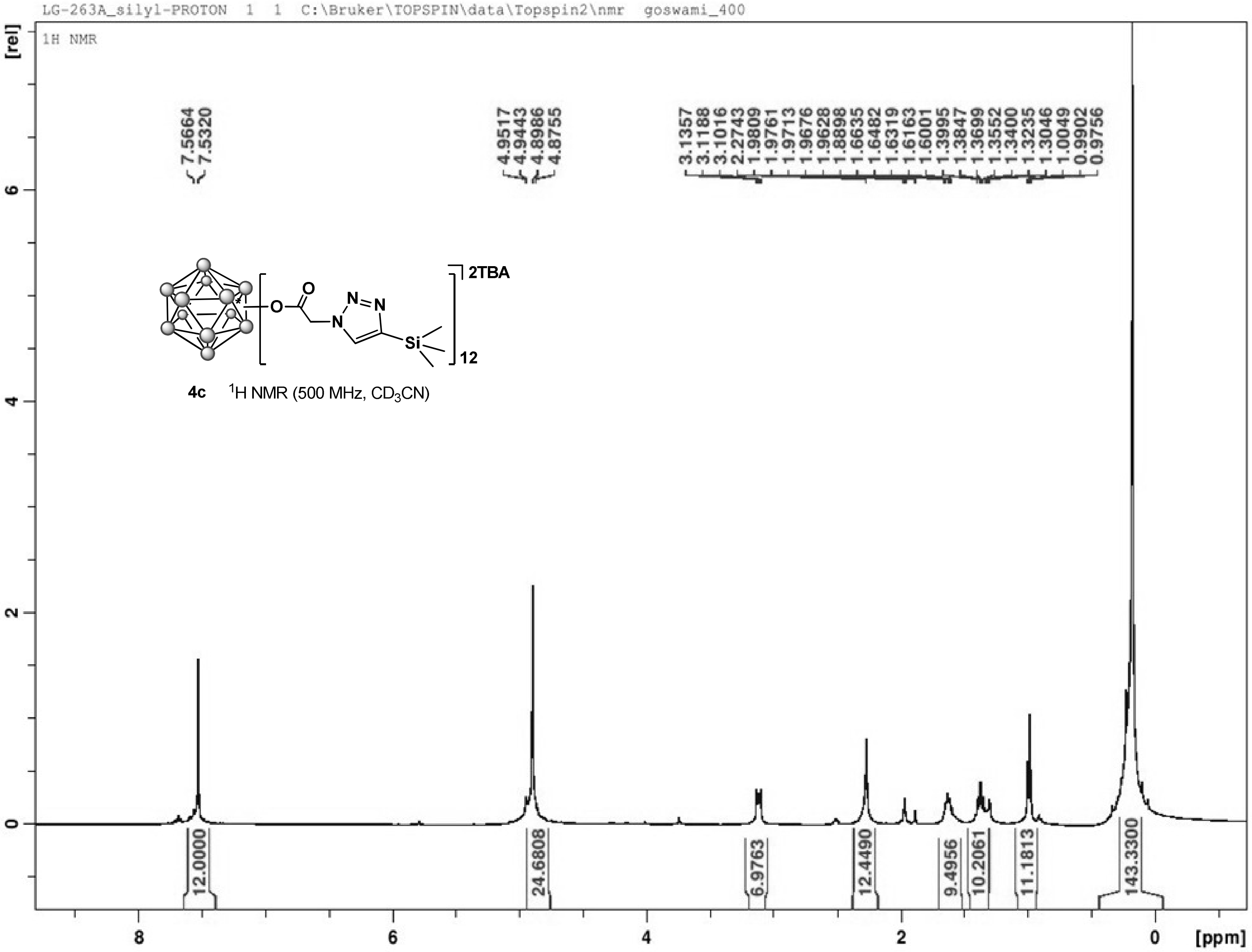
4b ^{1}H NMR (500 MHz, CD_3CN)



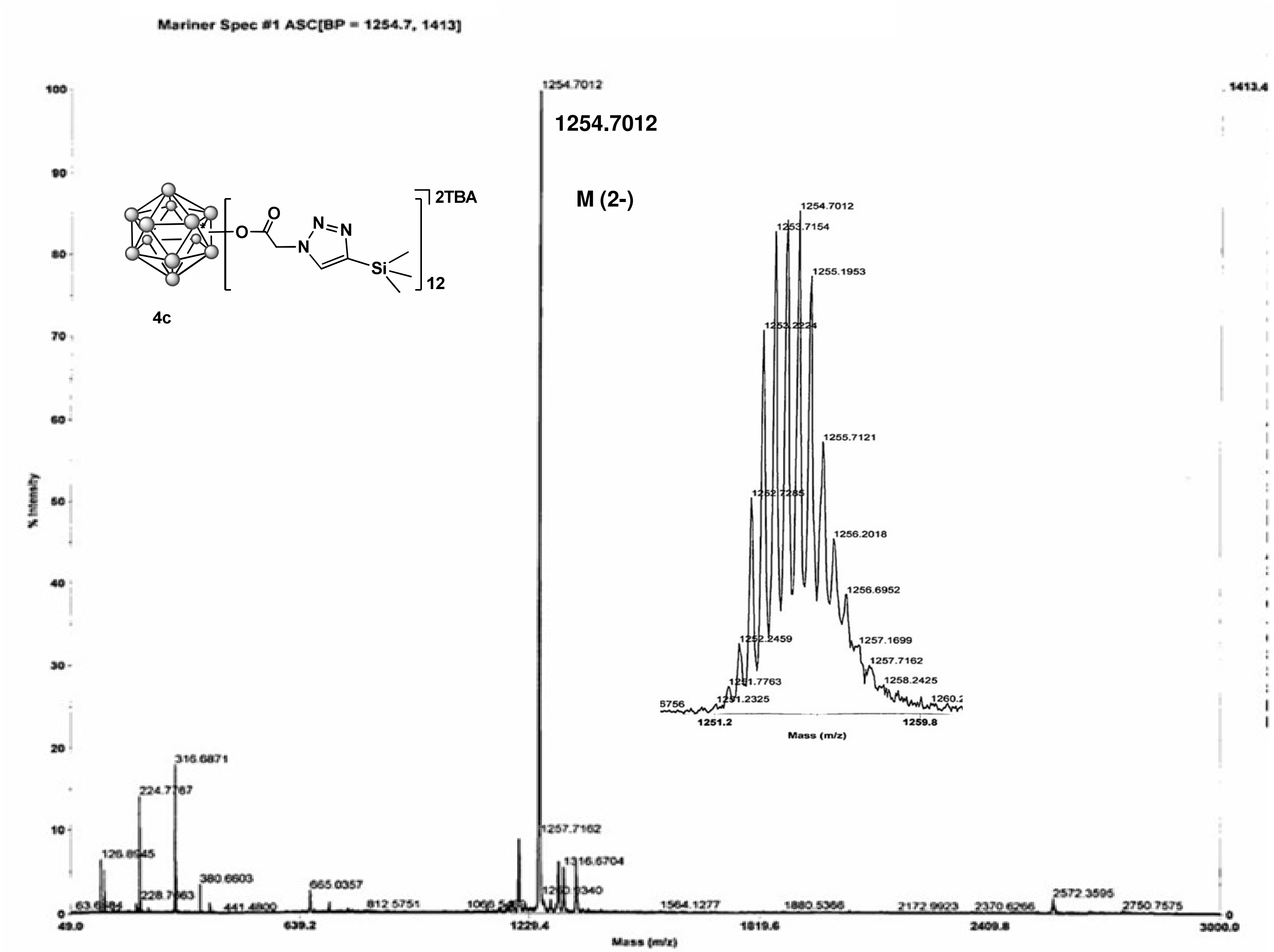
4b ^{13}C NMR (125 MHz, CD$_3$CN)

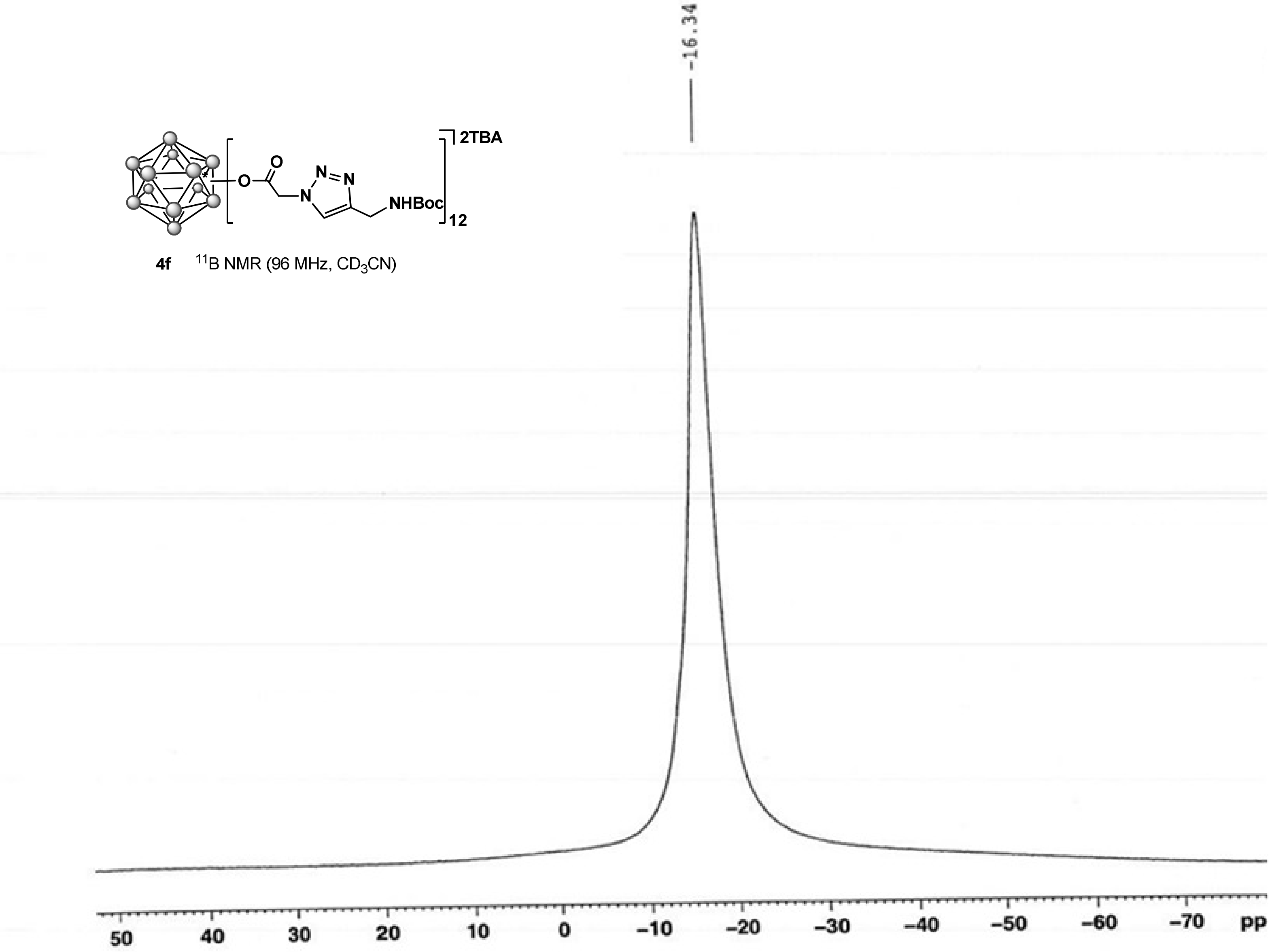

Mariner Spec #1 ASC[BP = 1421.5, 1018]
2TBA
O
N
N
N
CO2tBu
12
4b
1421.5554
M (2-)
1421.5554
1484.5328
1338.0307
1425.4581
1400.4896
1414.5972
177.1131
367.2058
559.4510
748.5958
989.7804
1627.3230
1737.2752
2010.9183
2281.7144
2669.2230
2887.0011
3106.1655
3345.8905
3753.8577
1421.5554
1422.5694
1421.0629
1423.0439
1423.5449
1420.0943
1424.0887
1419.5590
1424.6603
1419.0383
1418.6090
1425.4581
1426.1615
1414.5972
1428.8
% Intensity
Mass (m/z)
49.0
839.2
1629.4
2419.6
3209.8
4000.0
0
10
20
30
40
50
60
70
80
90
100
1017.7


4c ^{11}B NMR (96 MHz, CD_3CN)

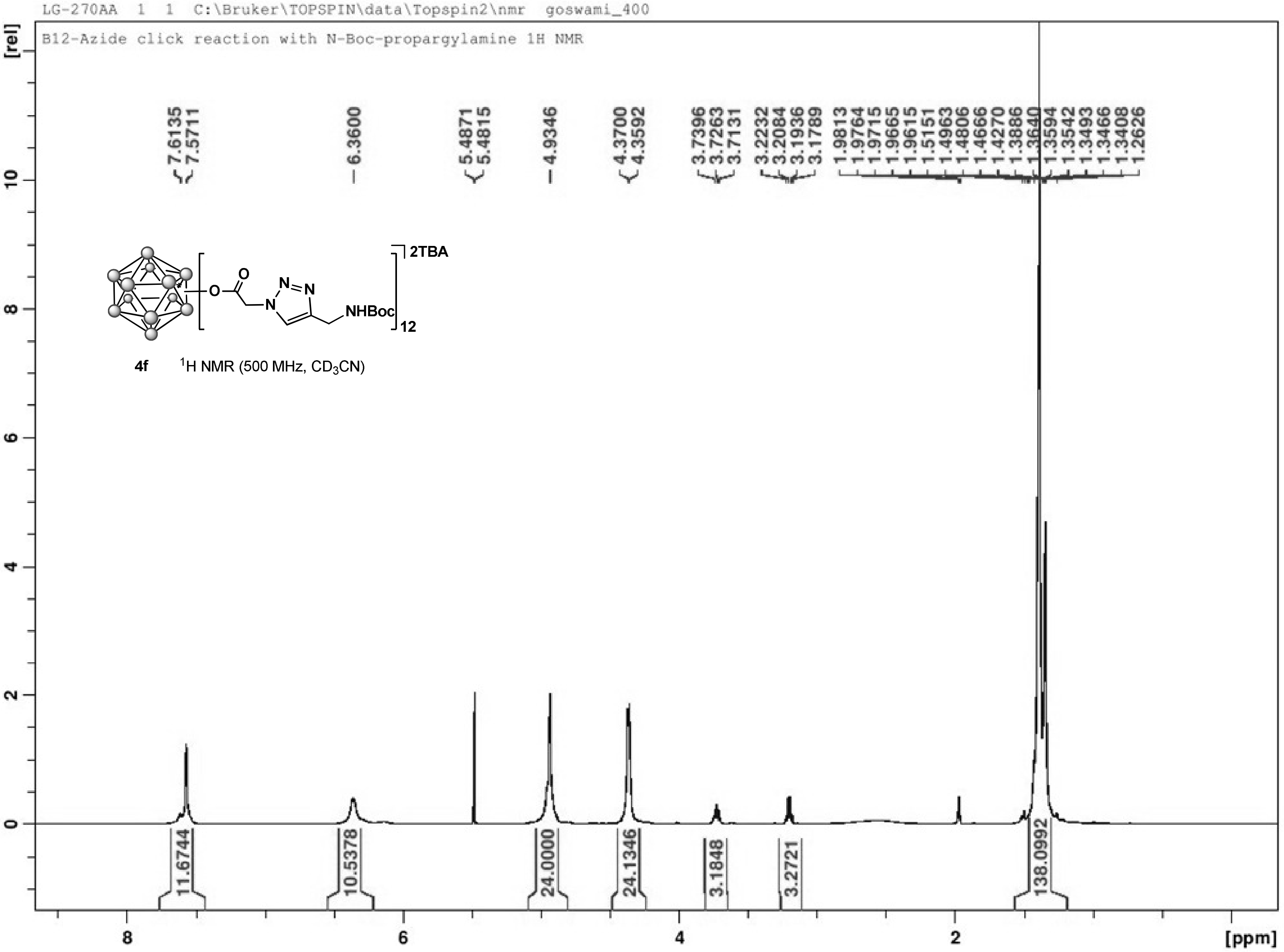


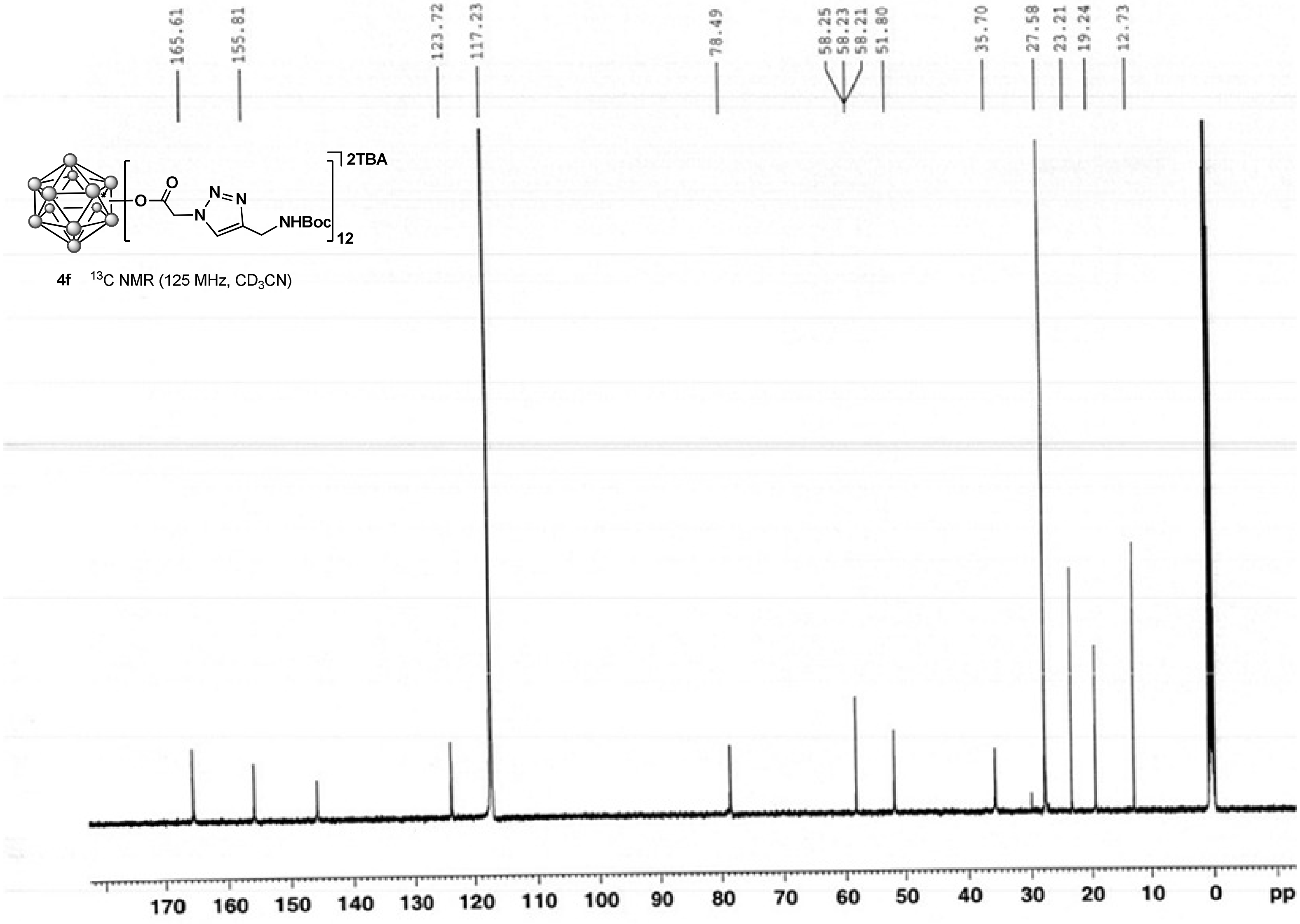
4c ^{1}H NMR (500 MHz, CD_3CN)


Mariner Spec #1 ASC[BP = 1254.7, 1413]
1254.7012
1254.7012
M (2-)
2TBA
O
O
N
N
N
N
Si
12
4c
% Intensity
Mass (m/z)
316.6871
224.7767
126.8945
380.6603
228.7063
63.6984
441.4800
665.0357
812.5751
1066.5
1257.7162
1316.6704
1290.5340
1564.1277
1880.5366
2172.9923
2370.6266
2572.3595
2750.7575
49.0
639.2
1229.4
1819.6
2409.8
3000.0
1413.4
0
10
20
30
40
50
60
70
80
90
100
1254.7012
1253.7154
1255.1953
1253.2224
1255.7121
1252.7285
1256.2018
1256.6952
1252.2459
1257.1699
1257.7162
1251.7763
1258.2425
1251.2325
1260.2
5756
1251.2
1259.8
Mass (m/z)

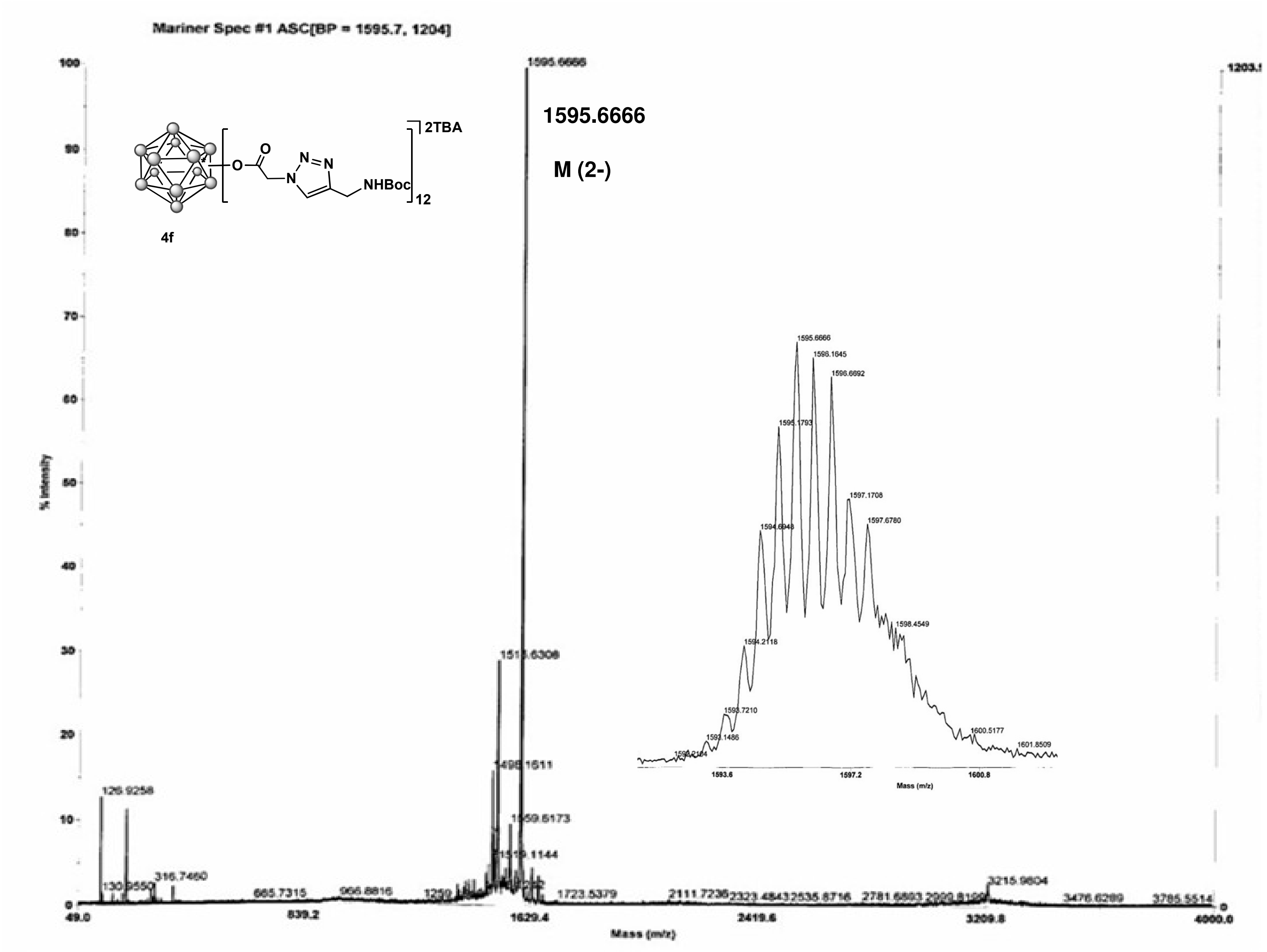


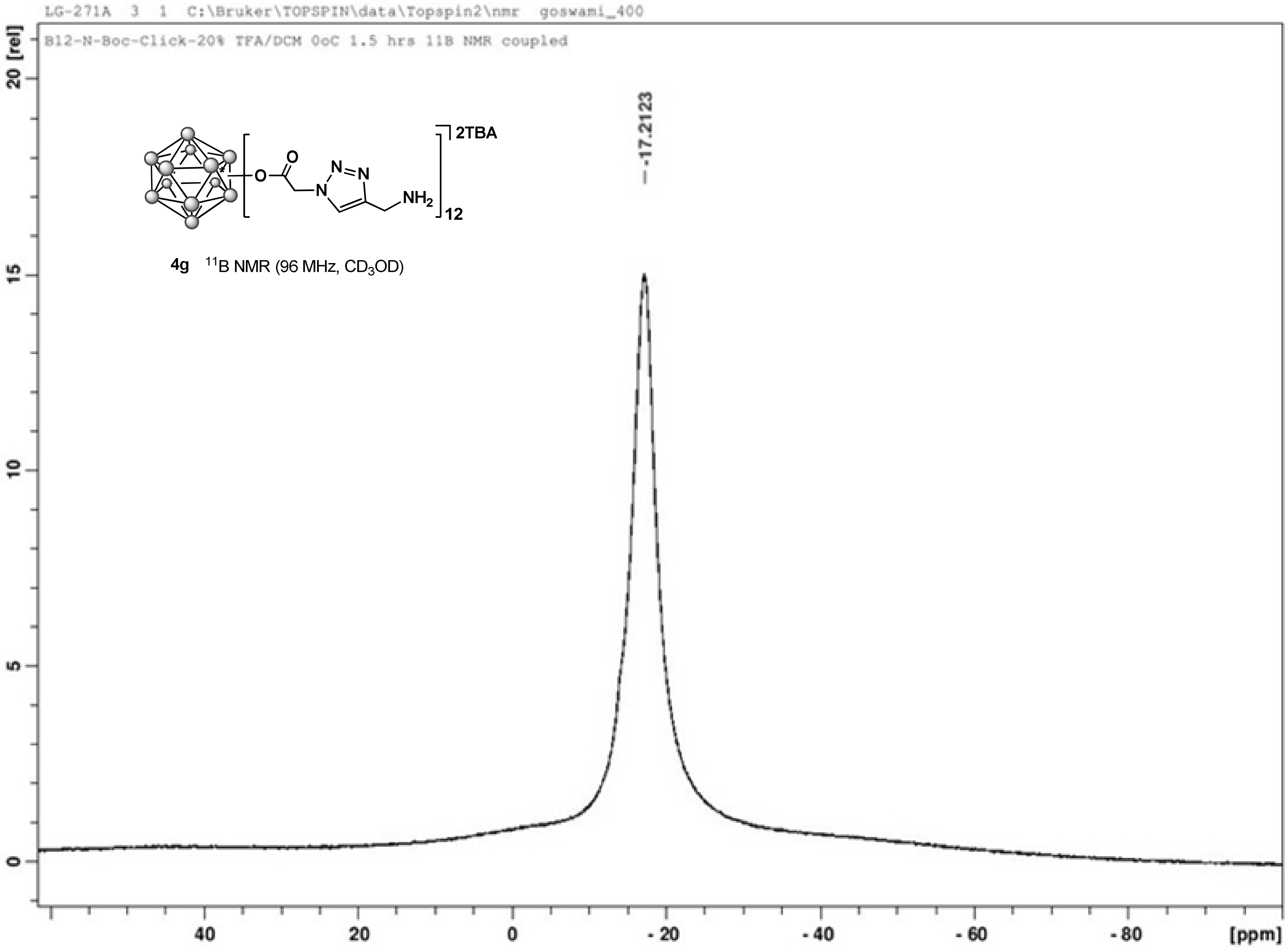
4f ^{11}B NMR (96 MHz, CD$_3$CN)

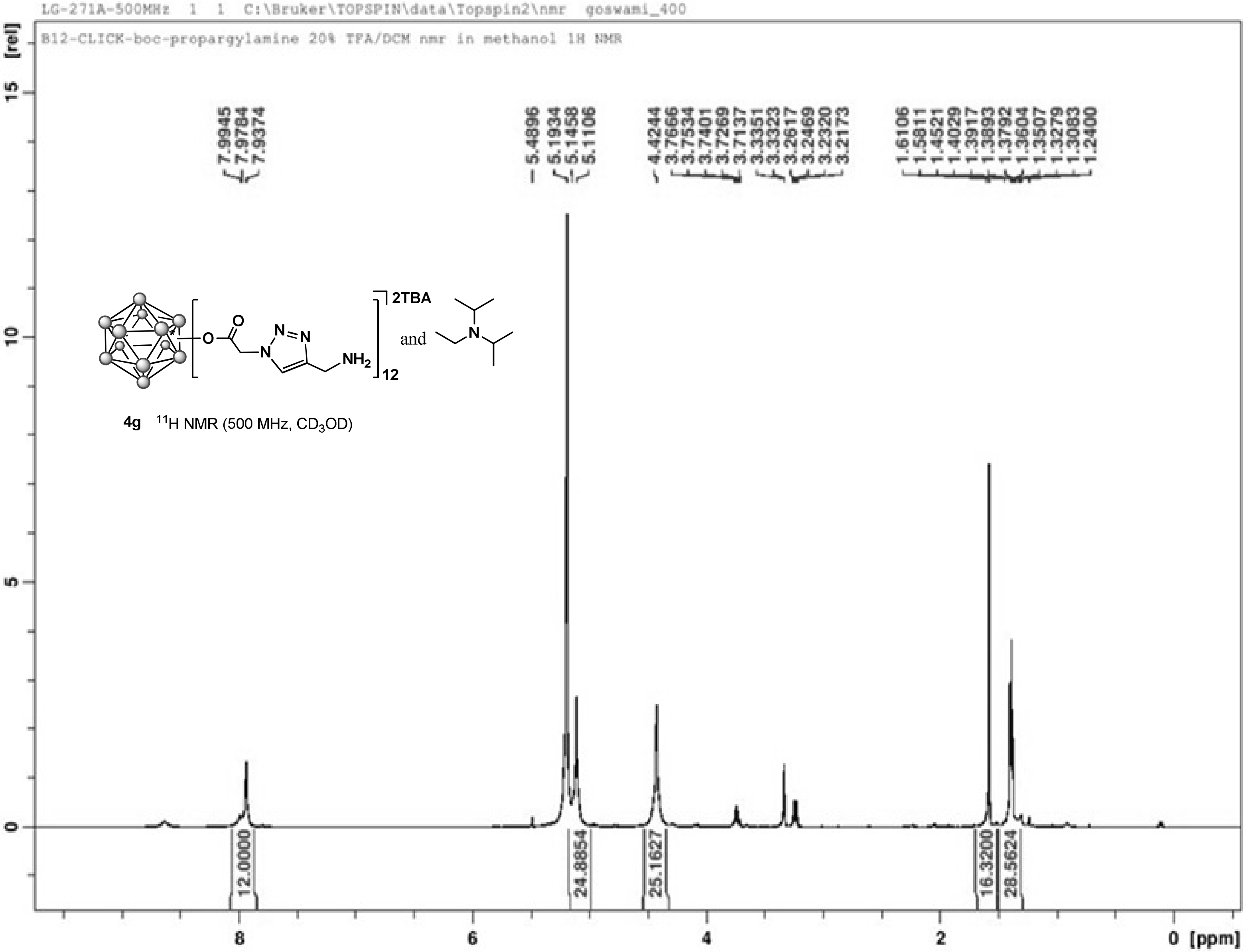

LG-270AA 1 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr goswami_400
B12-Azide click reaction with N-Boc-propargylamine 1H NMR
[rel]
7.6135
7.5711
6.3600
5.4871
5.4815
4.9346
4.3700
4.3592
3.7396
3.7263
3.7131
3.2232
3.2084
3.1936
3.1789
1.9813
1.9764
1.9715
1.9665
1.9615
1.5151
1.4963
1.4806
1.4666
1.4270
1.3886
1.3640
1.3594
1.3542
1.3493
1.3466
1.3408
1.2626
O
O
N
N
N
NHBoc
12
2TBA
4f
^{1}H NMR (500 MHz, CD_3CN)
11.6744
10.5378
24.0000
24.1346
3.1848
3.2721
138.0992
10
8
6
4
2
0
8
6
4
2
[ppm]



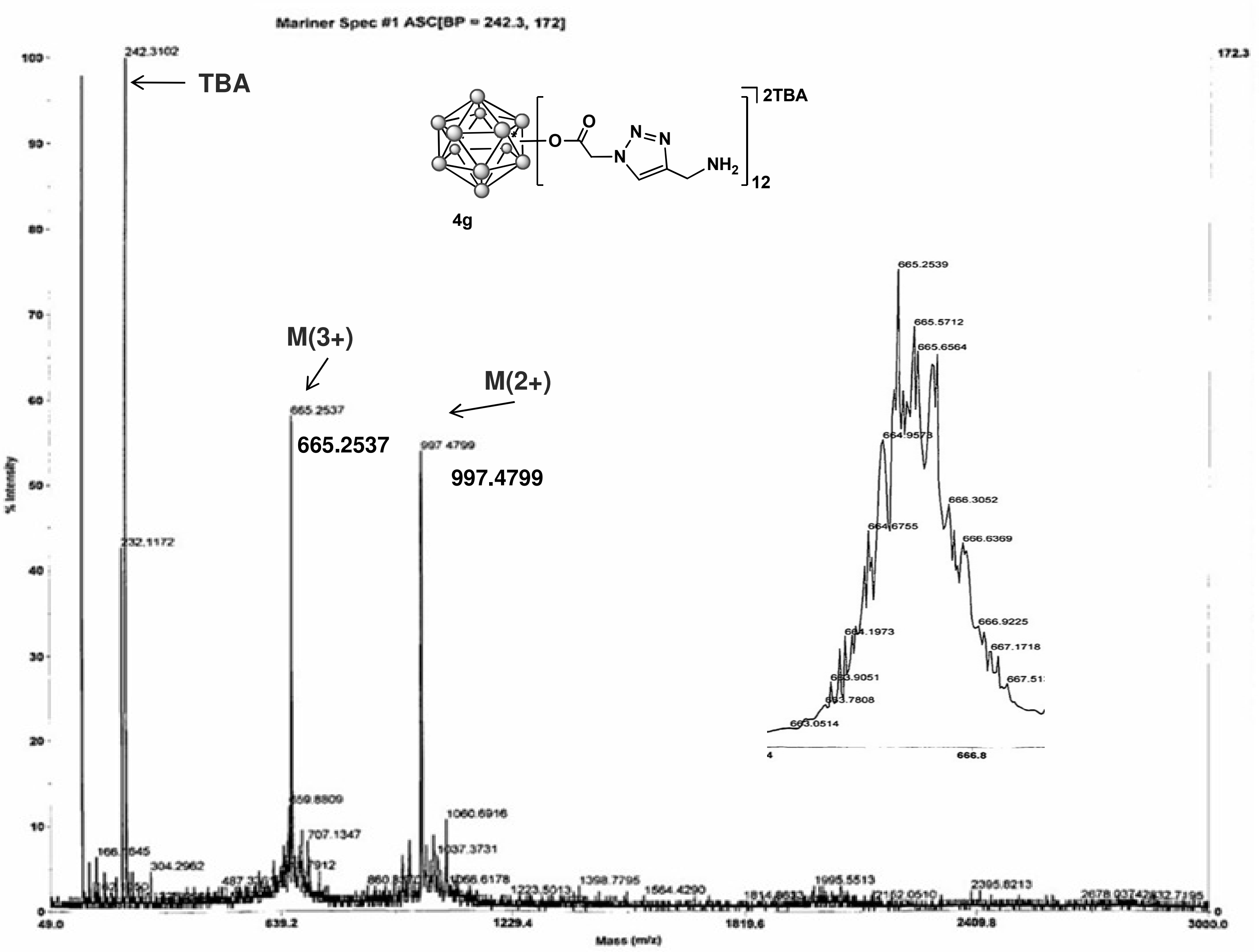
4f ^{13}C NMR (125 MHz, CD_3CN)

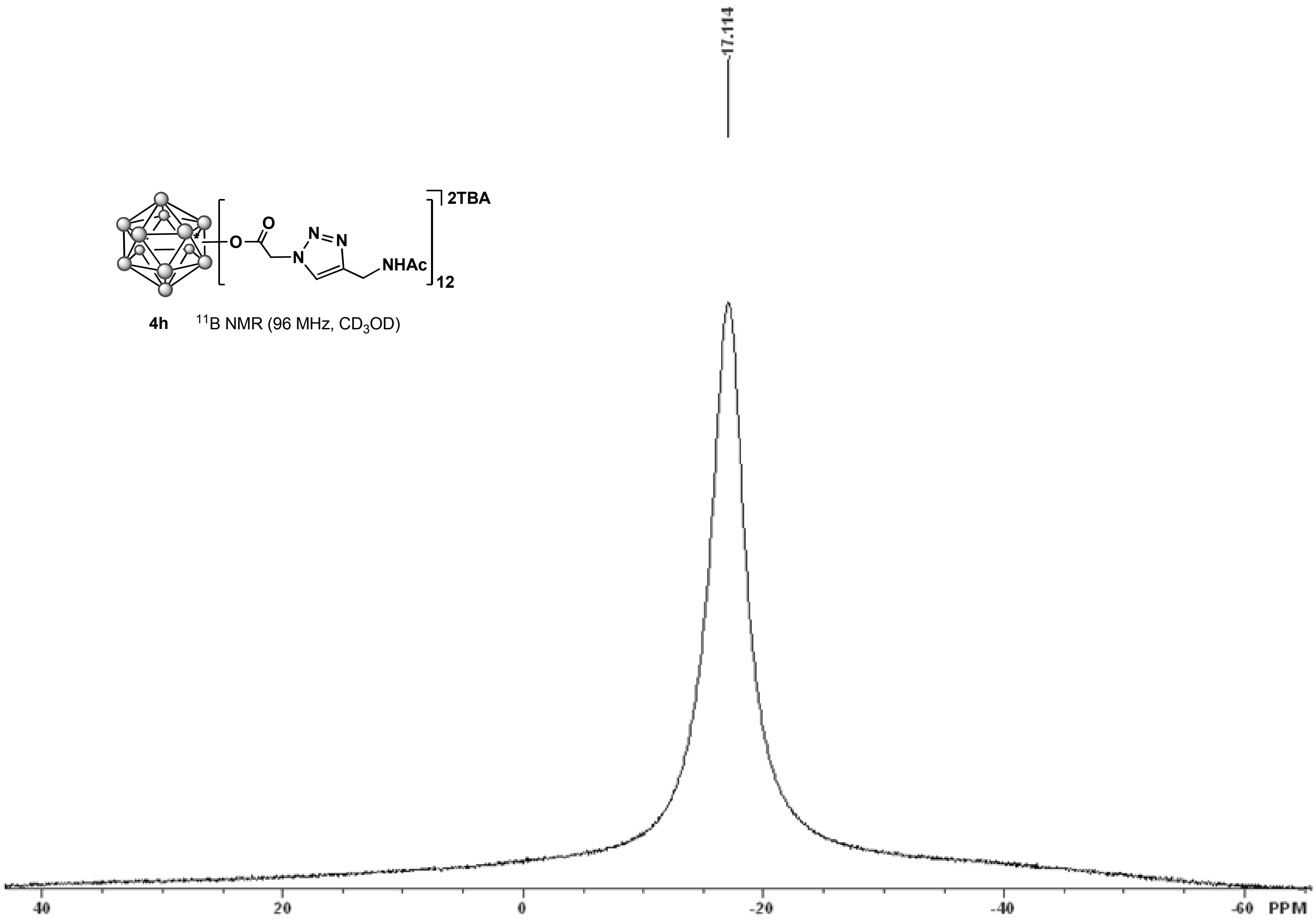

Mariner Spec #1 ASC[BP = 1595.7, 1204]
% Intensity
Mass (m/z)
1595.6666
M (2-)
2TBA
O
O
N
N
N
NHBoc
12
4f
1595.6666
1515.6308
1498.1611
1559.5173
1519.1144
126.9258
130.9550
316.7460
665.7315
966.8816
1259
1723.5379
2111.7236
2323.4843
2535.8716
2781.6803
2990.8199
3215.9604
3476.6289
3785.5514
49.0
839.2
1629.4
2419.6
3209.8
4000.0
0
10
20
30
40
50
60
70
80
90
100
1203.
1596.1645
1596.6692
1595.1793
1597.1708
1597.6780
1594.6948
1594.2118
1598.4549
1593.7210
1593.1486
1592.2164
1600.5177
1601.8509
1593.6
1597.2
1600.8


LG-271A 3 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr goswami_400
B12-N-Boc-Click-20% TFA/DCM 0oC 1.5 hrs 11B NMR coupled
2TBA
O
N
N=N
NH2
12
4g
11B NMR (96 MHz, CD3OD)
-17.2123
20 [rel]
15
10
5
0
40
20
0
-20
-40
-60
-80
[ppm]

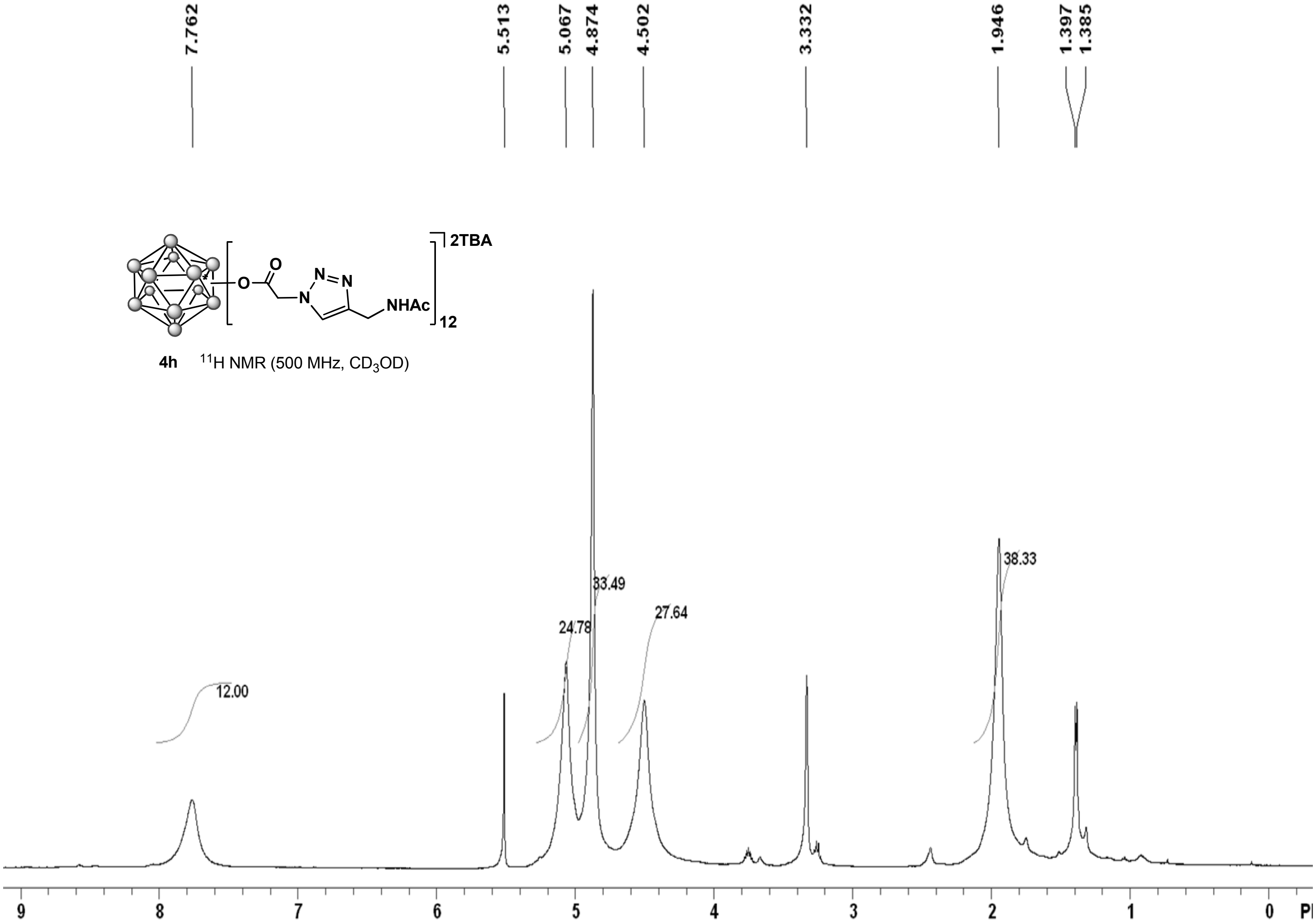


4g ^{11}H NMR (500 MHz, CD$_3$OD)

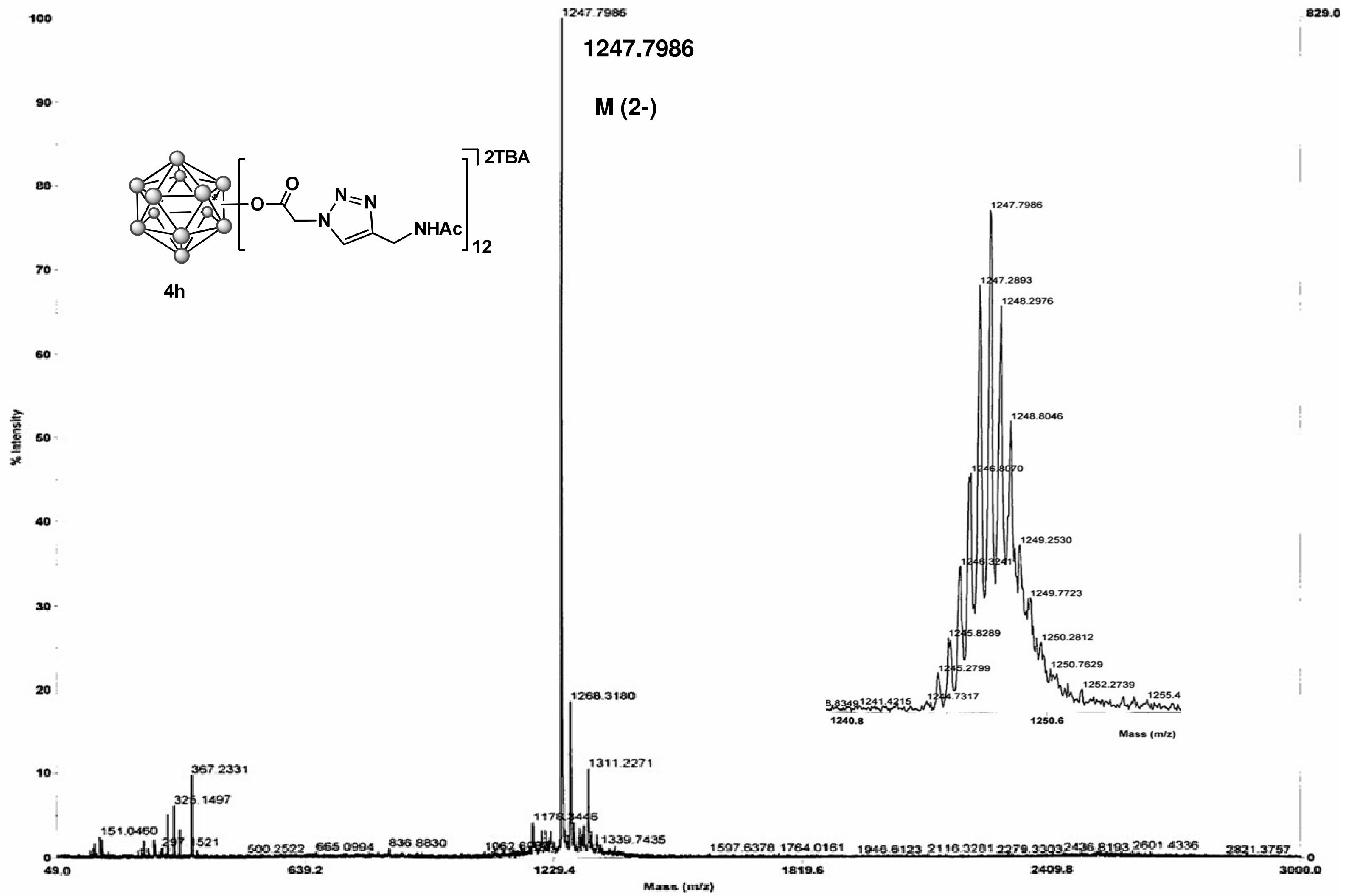

Mariner Spec #1 ASC[BP = 242.3, 172]
242.3102
TBA
2TBA
O
N
N
N
N
O
NH2
12
4g
232.1172
M(3+)
665.2537
665.2537
M(2+)
997.4799
997.4799
659.8809
707.1347
1060.6916
1037.3731
166.1545
304.2962
1066.6178
1223.5013
1398.7795
1564.4290
1814.8633
1995.5513
2152.0510
2395.8213
2678.0374
2832.7195
665.2539
665.5712
665.6564
664.9573
666.3052
664.6755
666.6369
664.1973
666.9225
667.1718
663.9051
667.51
663.7808
663.0514
666.8
% Intensity
Mass (m/z)
100
90
80
70
60
50
40
30
20
10
0
49.0
639.2
1229.4
1819.6
2409.8
3000.0
172.3
0



4h ^{11}B NMR (96 MHz, CD_3OD)



4h ^{11}H NMR (500 MHz, CD$_3$OD)



4h

Acquired: Oct 14 16:16:00 2008
Mariner Mass Spectrum
C:\Mariner\Data\2008\Oct\14Tues\LNG-275001.dat