Eur. J. Org. Chem. **2007** · © WILEY-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2007 · ISSN 1434–193X

SUPPORTING INFORMATION

Title: Direct Preparation of N-Glycosidic Bond-Linked Nonionic Carbohydrate-Based Surfactant (NICBS) via Ritter Reaction

Author(s): Zerong Daniel Wang,* Samia O. Sheikh, Shannon Cox, Yulu Zhang, Keegan Massey

Ref. No.: O200700079

1. General

The high-speed shaker used in this study was a Wrist Action^{TM} Shaker (Model 75) purchased from Burrell Scientific (Pittsburg, PA, USA). High resolution mass spectra (HRMS) were recorded in MALDI mode on a Voyager-DE STR 4160, using α-cyano-4-hydroxycinnamic acid as matrix, at the Department of Chemistry, University of Houston. ^{1}H- and ^{13}C-NMR were recorded in $CDCl_3$ with a Bruker Avance 600 MHz NMR spectrometer (at 600 Mz for ^{1}H and 150 MHz for ^{13}C, respectively, TMS as internal standard) at the Keck/IMD NMR center founded by the W. M. Keck Foundation and the University of Houston. The unacylated surfactant molecules were purified on silica gel using EtOAc/MeOH (5:1 to 3:1) as eluent, whereas the acetylated products were purified by silica gel column chromatography using hexane/EtOAc (5:1 to 3:2) as eluent. Thin-layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck) and detected by heating with 1.5% H_2SO_4 in EtOH.

2. Direct preparation of 1-*N*-lauroyl-2,3,4,6-tetraacetyl-β-*D*-glucopyranosylamine from β-*D*-glucose pentaacetate

To an 18 mL of scintillation vial were added 0.2169 g of β-*D*-glucose pentaacetate (0.56 mmol), 1.0 mL of undecyl cyanide (d = 0.827 g/mL, 4.56 mmol), 0.1048 g of $AgClO_4$ (0.5 mmol), and 0.5 mL of TMSOTf (d = 1.228 g/mL, 2.76 mmol). The vial was capped and mounted to the high-speed shaker. After 24 hours, the reaction was quenched by 0.5 mL of Et_3N and 0.1663 g of 1-*N*-lauroyl-2,3,4,6-tetraacetyl-β-*D*-glucopyranosylamine was isolated by column chromatography, in yield of 56%.

3. The reaction between glucose and 4-methylbenzyl cyanide

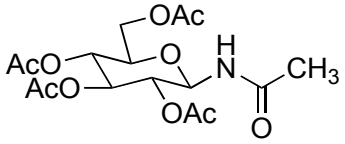
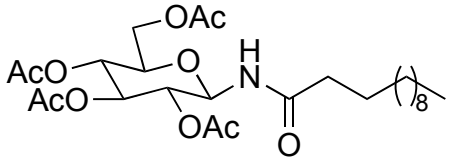
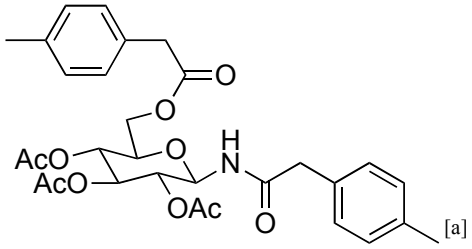
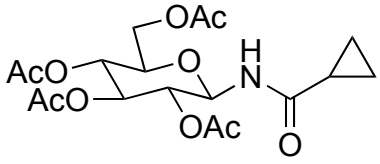
To an 18 mL of scintillation vial were added 0.2418 g of *D*-glucose (1.34 mmol), 1.5 mL of 4-methylbenzyl cyanide (d = 0.992 g/mL, 11.3 mmol), 0.1244 g of $AgClO_4$ (0.6 mmol), and 0.5 mL of TMSOTf (2.76 mmol). The vial was capped and mounted to the high-speed shaker. After 24 hours, the reaction was quenched by 0.5 mL of Et_3N and the mixture was directly loaded to a 10 cm silica gel column and washed with hexane/EtOAc (2:1 to 1:1) to remove unreacted cyanide and Et_3N, and 0.1218 g of colorless oil was obtained, when the column was eluted with EtOAc/MeOH (5:1) (R_f = 0.80 for EtOAc/MeOH = 3:1), which was further acetylated with Ac_2O in pyridine. The reaction mixture was diluted with 50 mL of EtOAc, and washed with 1*N* HCl (3 × 20 mL), saturated $NaHCO_3$ aqueous solution (2 × 20 mL) and brine (20 mL), and dried over $CaCl_2$. After removal of solvent, the residue was purified by silica gel column chromatography using hexane/EtOAc (3:1) to afford 75 % of 1-*N*,6-di(4-methylphenyl)-acetyl-2,3,4-triacetyl-β-*D*-glucopyranosylamine, as evidenced from the following NMR characterization, as well as high resolution Mass spectroscopy.

4. The reaction between glucose and cyclopropyl cyanide

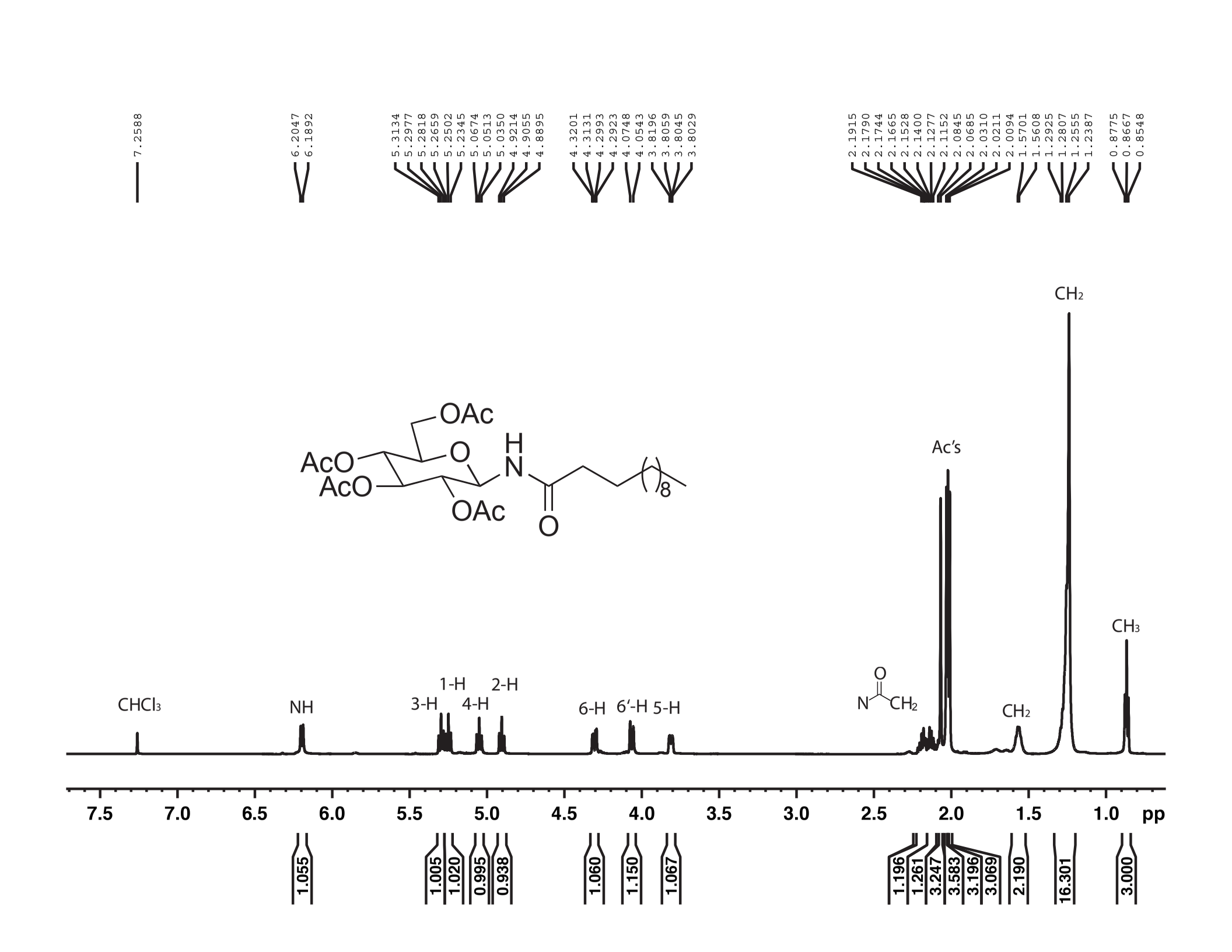
To an 18 mL of scintillation vial were added 0.225 g of *D*-glucose (1.25 mmol), 1.5 mL of cyclopropyl cyanide (d = 0.911 g/mL, 20.4 mmol), 0.135 g of $AgClO_4$ (0.65 mmol), and 0.5 mL of TMSOTf (2.76 mmol). The vial was capped and mounted to the high-speed shaker. After shaking for 3 hours, most of the solid sugar disappeared, and after 24 hours, the reaction was quenched by 0.5 mL of Et_3N and the mixture was directly loaded to a 10 cm silica gel column and washed with hexane/EtOAc (2:1 to 1:1) to remove unreacted cyanide and Et_3N, and 0.223 g of very viscous oil (68.8%) was obtained when

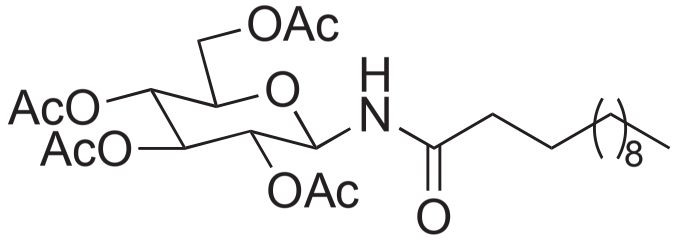
the column was further eluted with EtOAc/MeOH (5:1) (R_f = 0.41 for EtOAc/MeOH = 3:1), which was then acetylated with Ac_2O in pyridine. The reaction mixture was diluted with 50 mL of EtOAc, and washed with 1*N* HCl (3 × 20 mL), saturated $NaHCO_3$ aqueous solution (2 × 20 mL) and brine (20 mL), and dried over $CaCl_2$. After removal of solvent, the residue was purified by silica gel column chromatography using hexane/EtOAc (3:1) to afford 0.1671 g of 1-*N*-(cyclopropyl)formyl-2,3,4,6-tetracetyl-*β*-*D*-glucopyranosylamine (47.7%), as evidenced from the following NMR characterization, as well as high resolution Mass spectroscopy.

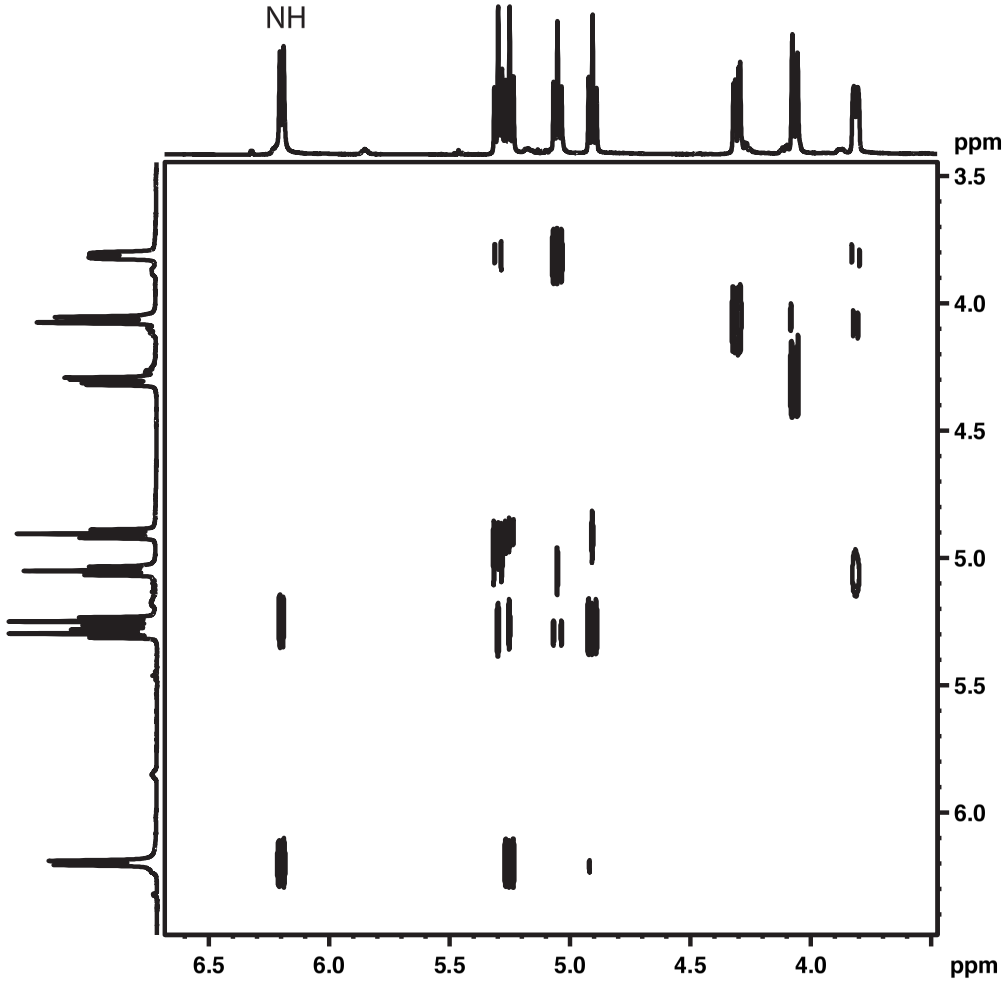
5. Summary of high resolution MS of prepared surfactant molecules from *D*-glucose

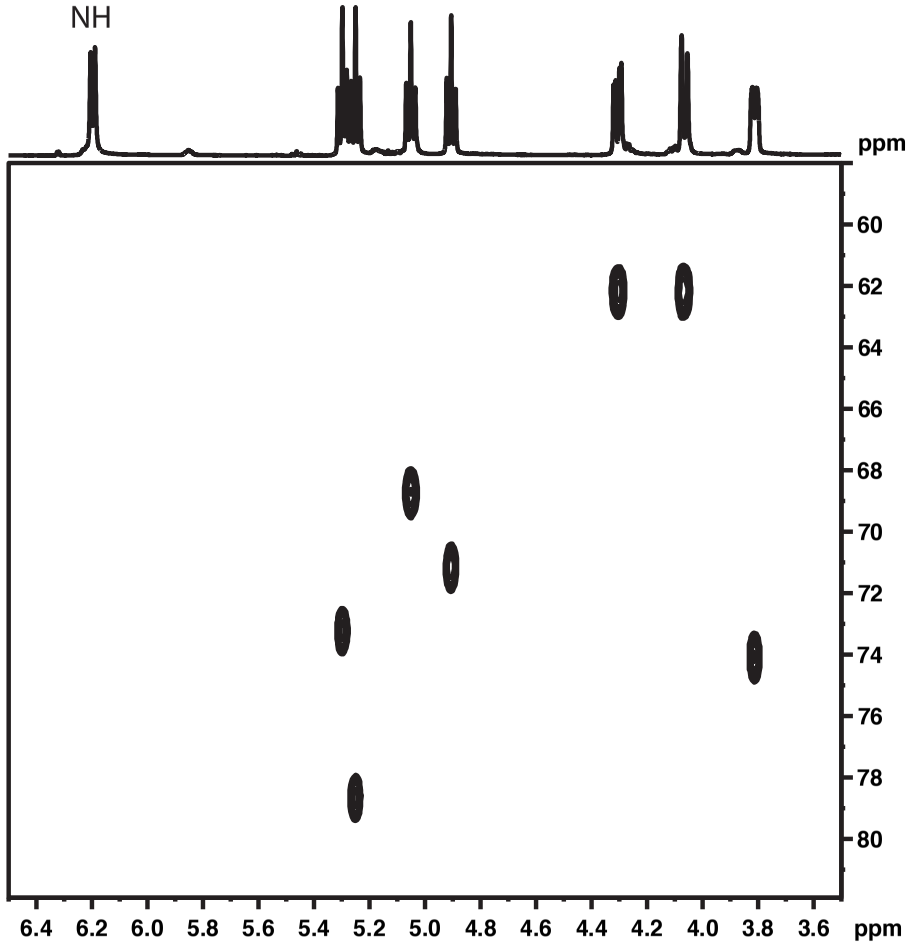
Nitrile	Structure	Formula	Calc. MS	Found MS
CH_3CN		$C_{16}H_{23}NO_{10}Na$	412.1220	412.1219
n-$C_{11}H_{23}CN$		$C_{26}H_{43}NO_{10}Na$	552.2785	552.2790
4-$CH_3C_6H_4CH_2CN$		$C_{30}H_{35}NO_{10}Na$	592.2159	592.2152
c-C_3H_5-CN		$C_{18}H_{25}NO_{10}Na$	438.1376	438.1355

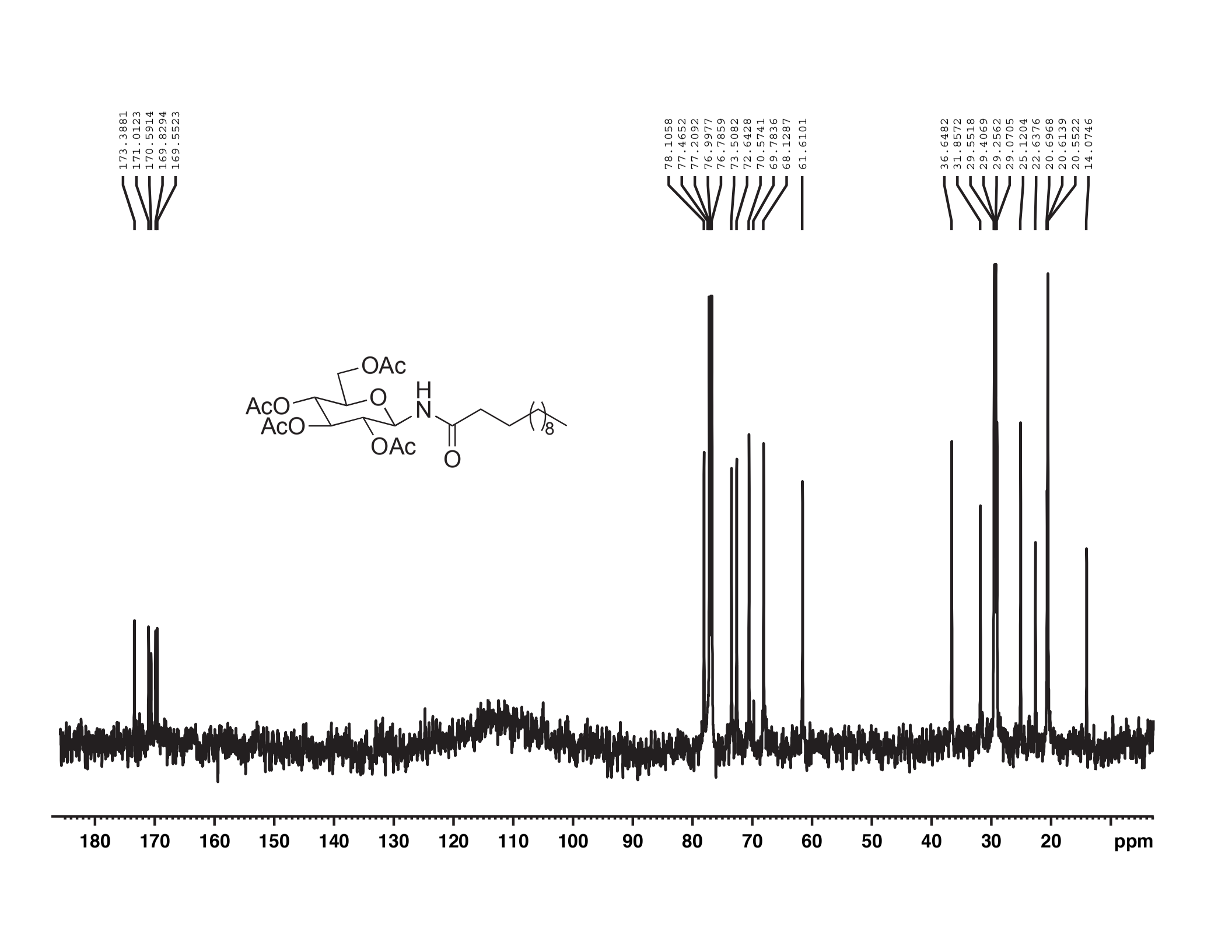
[a] the second (4-methylphenyl)acetyl group is assigned to position 6, for the nucleophilic attack of OH on cyano group to form ester, because among the rest OHs, the 6-OH is primary OH, and has less steric hindrance than 2-OH, 3-OH and 4-OH.

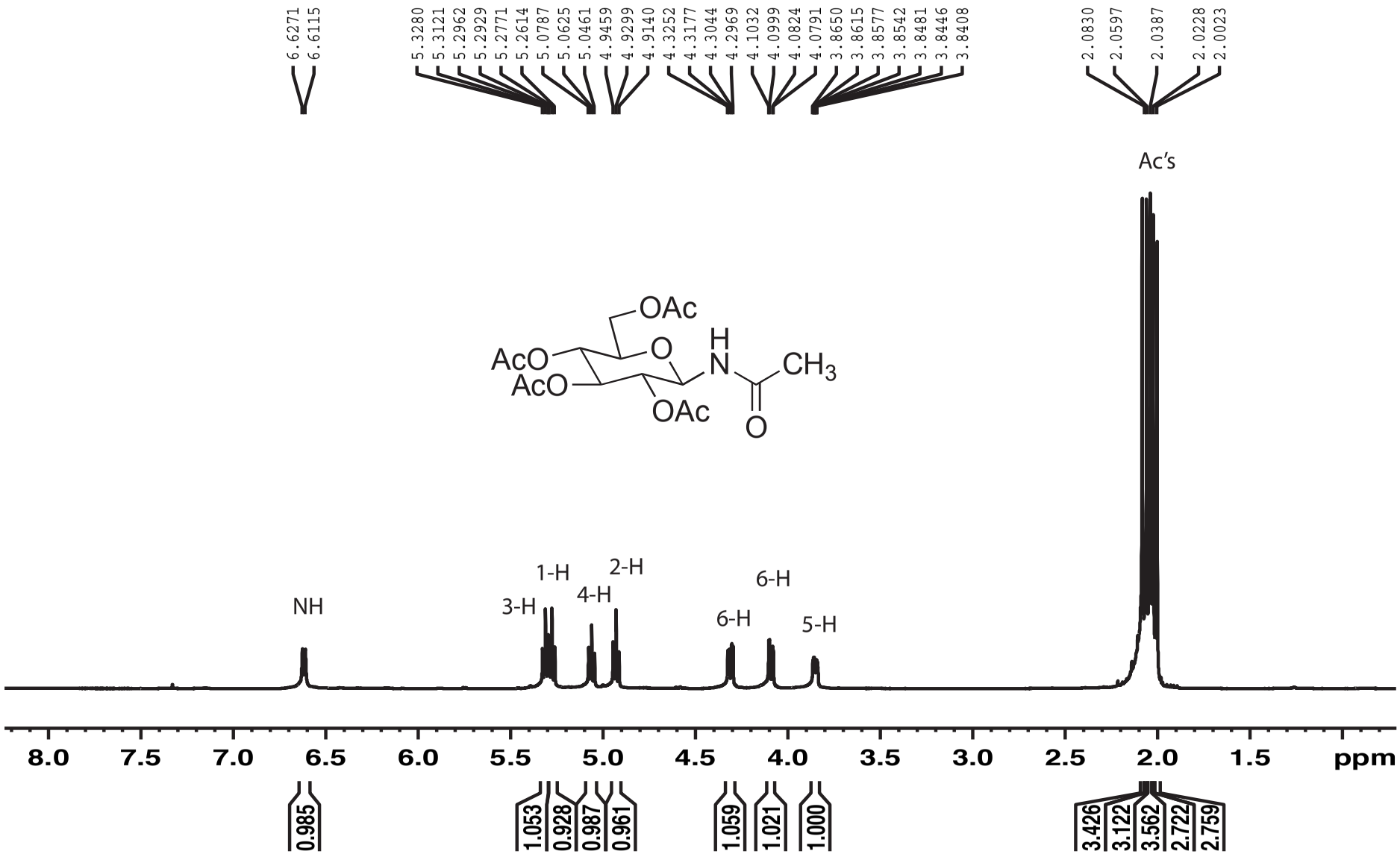

7.2588
6.2047
6.1892
5.3134
5.2977
5.2818
5.2659
5.2502
5.2345
5.0674
5.0513
5.0350
4.9214
4.9055
4.8895
4.3201
4.3131
4.2993
4.2923
4.0748
4.0543
3.8196
3.8059
3.8045
3.8029
2.1915
2.1790
2.1744
2.1665
2.1528
2.1400
2.1277
2.1152
2.0845
2.0685
2.0310
2.0211
2.0094
1.5701
1.5608
1.2925
1.2807
1.2555
1.2387
0.8775
0.8667
0.8548
OAc
AcO
AcO
O
H
N
OAc
8
O
CHCl3
NH
3-H
1-H
4-H
2-H
6-H
6'-H
5-H
Ac's
CH2
CH2
CH3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
pp
1.055
1.005
1.020
0.995
0.938
1.060
1.150
1.067
1.196
1.261
3.247
3.583
3.196
3.069
2.190
16.301
3.000

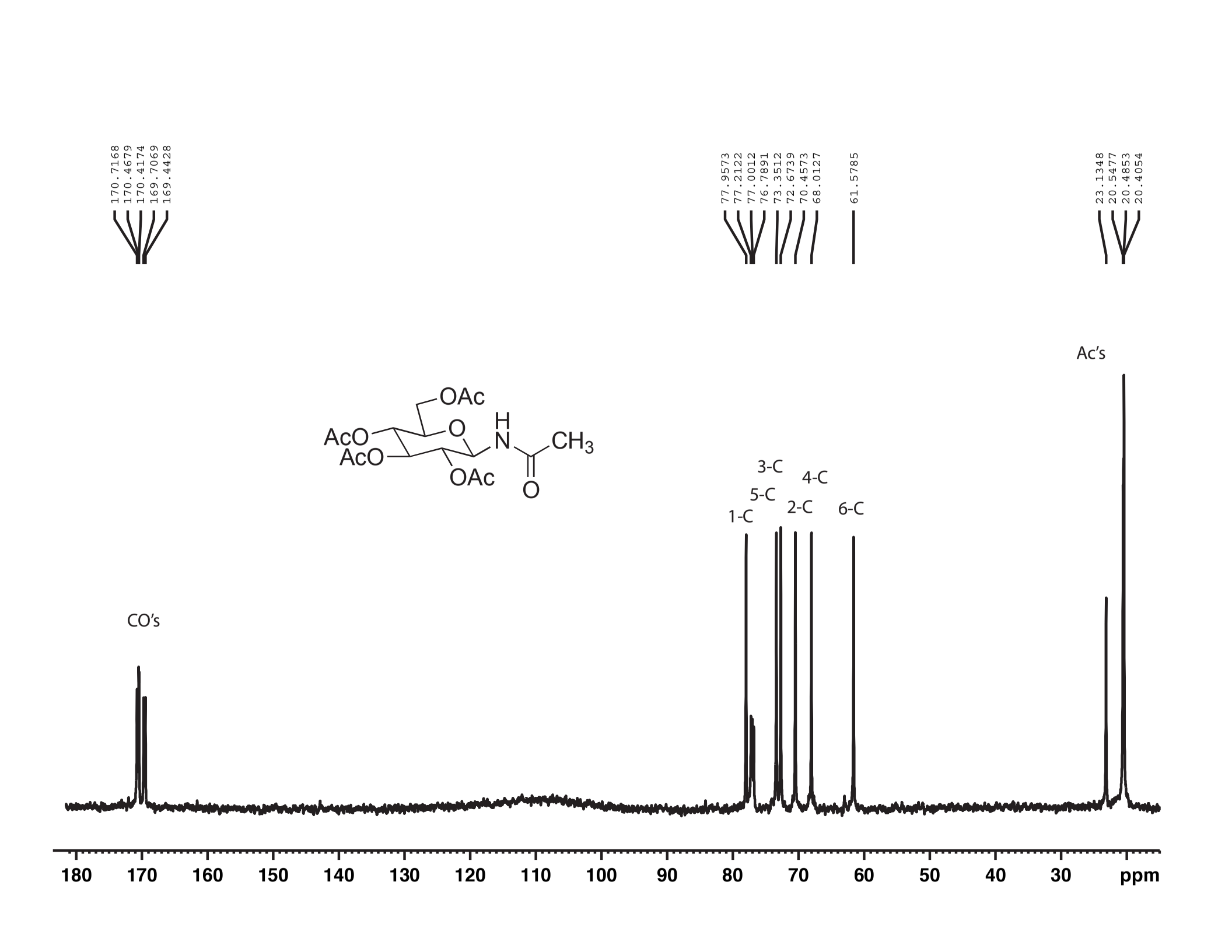

OAc
AcO
O
H
N
AcO
OAc
8
O

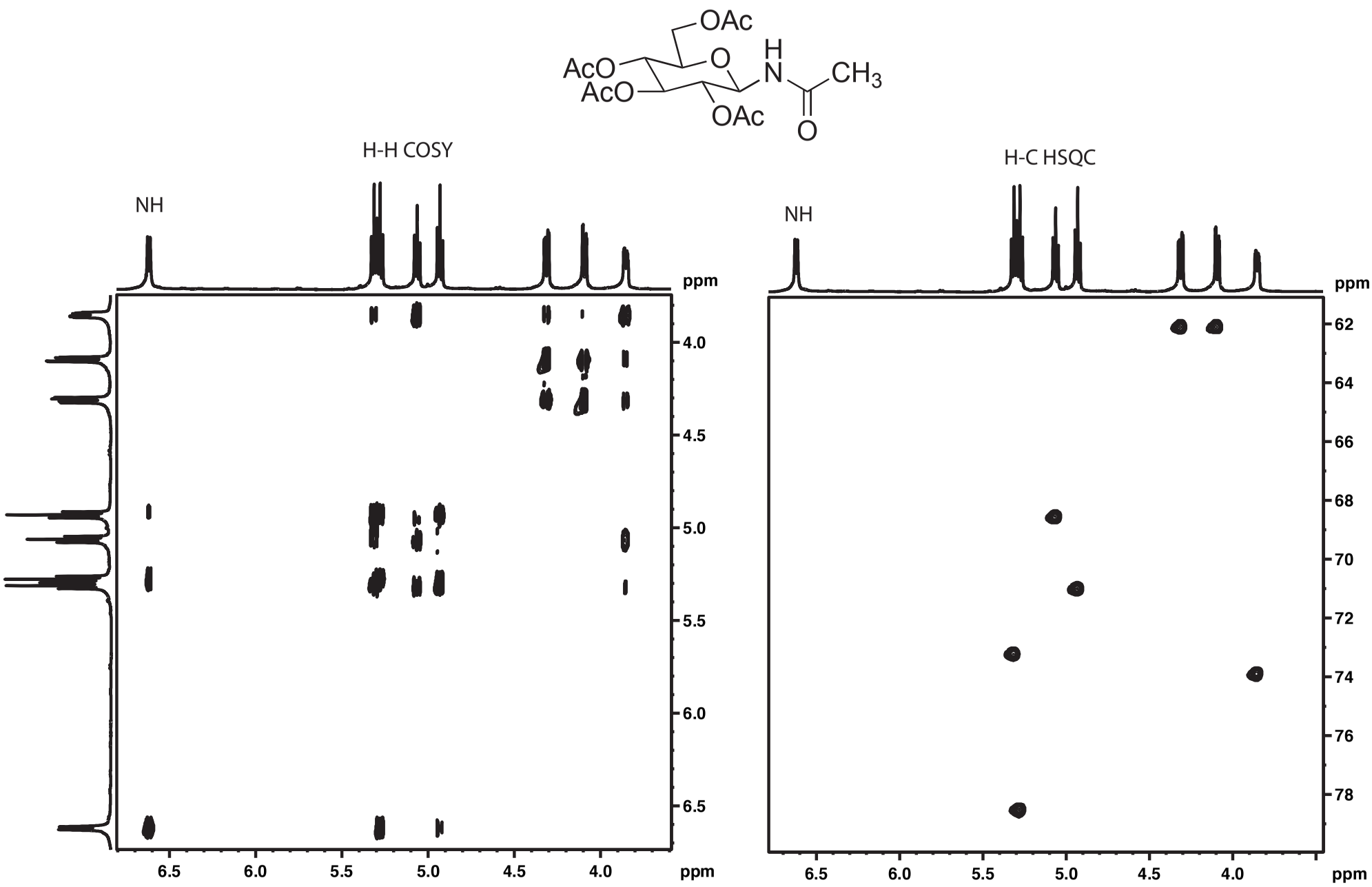

NH
ppm
3.5
4.0
4.5
5.0
5.5
6.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm

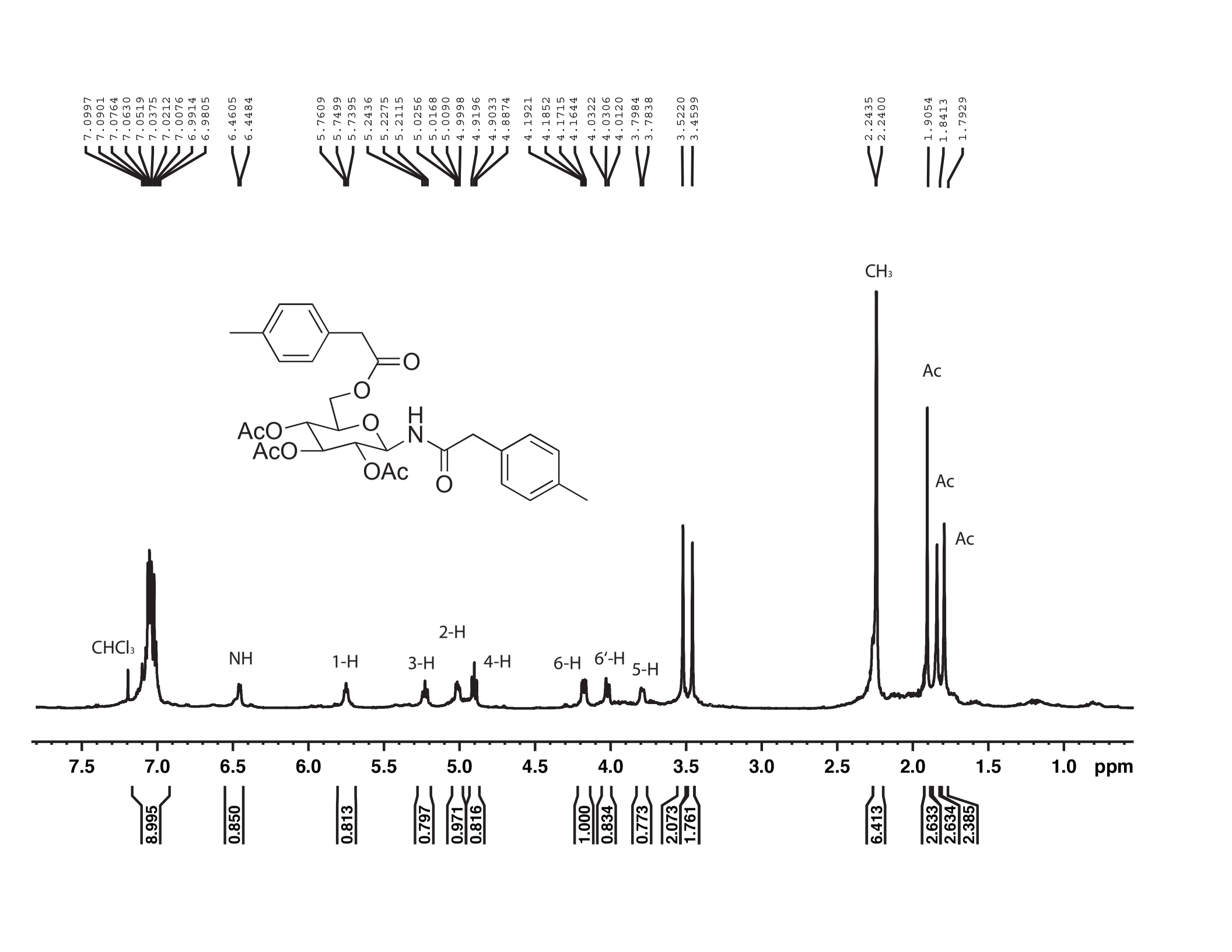

NH
ppm
60
62
64
66
68
70
72
74
76
78
80
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
ppm

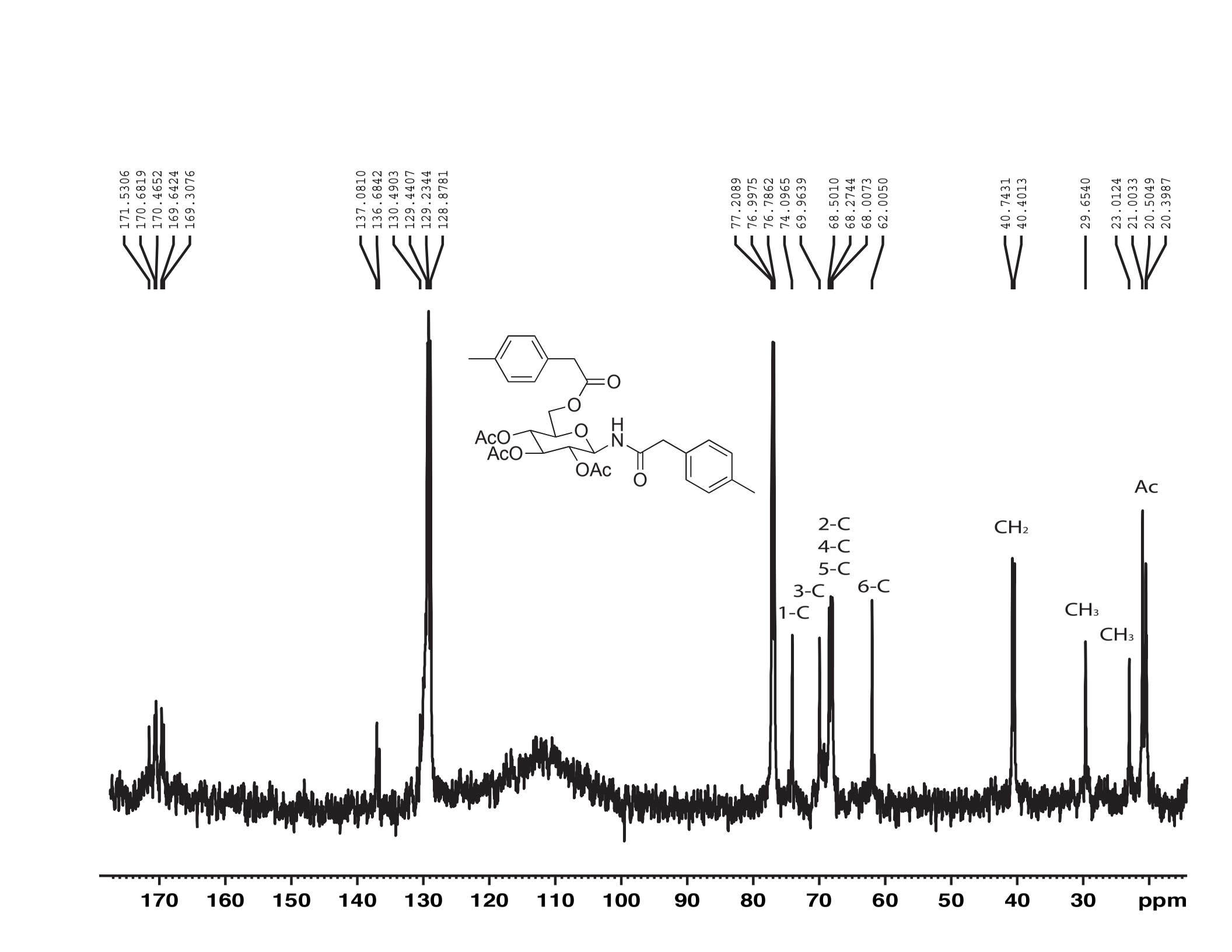

173.3881
171.0123
170.5914
169.8294
169.5523
78.1058
77.4652
77.2092
76.9977
76.7859
73.5082
72.6428
70.5741
69.7836
68.1287
61.6101
36.6482
31.8572
29.5518
29.4069
29.2562
29.0705
25.1204
22.6376
20.6968
20.6139
20.5522
14.0746
OAc
AcO
AcO
OAc
O
H
N
O
8
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

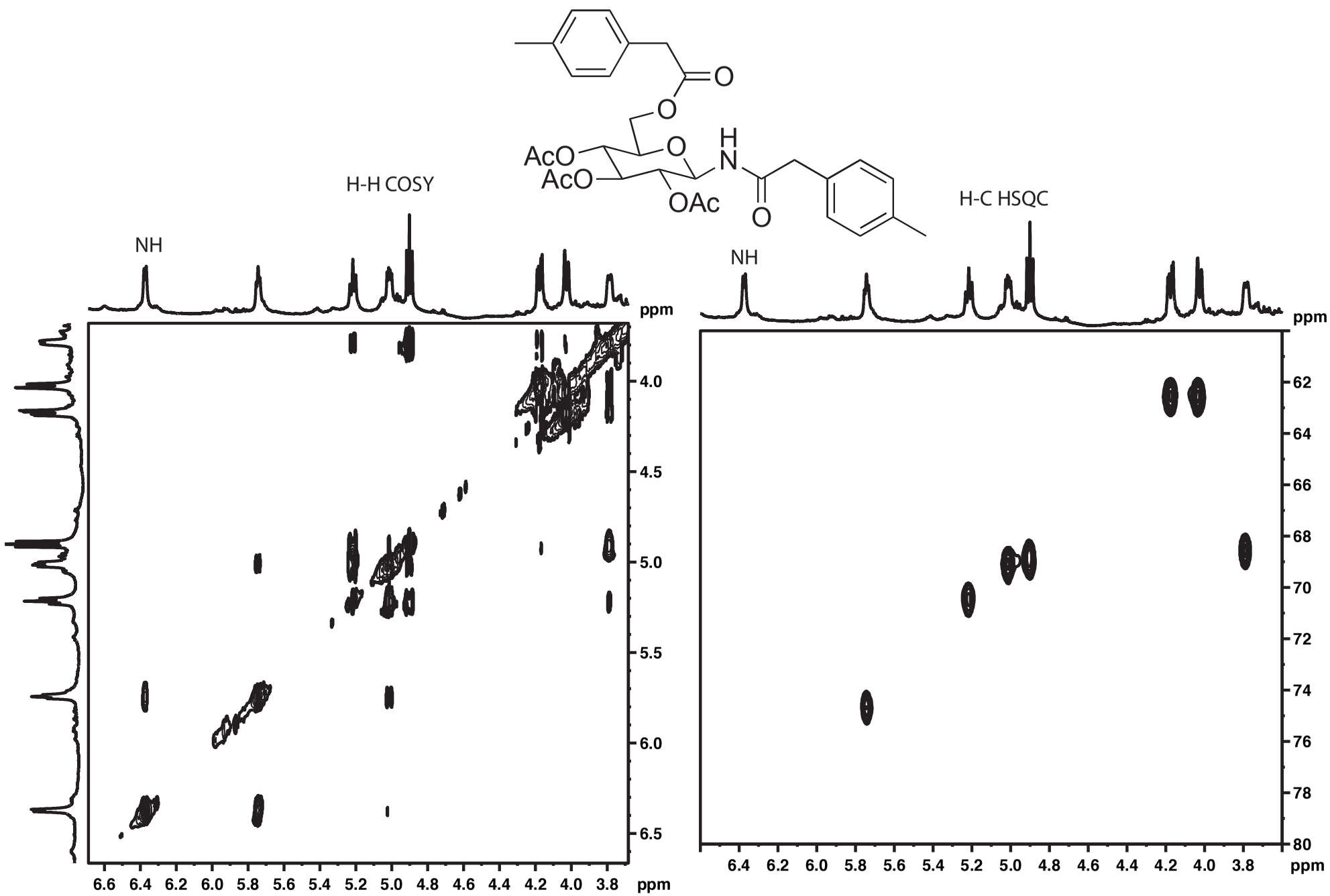

6.6271
6.6115
5.3280
5.3121
5.2962
5.2929
5.2771
5.2614
5.0787
5.0625
5.0461
4.9459
4.9299
4.9140
4.3252
4.3177
4.3044
4.2969
4.1032
4.0999
4.0824
4.0791
3.8650
3.8615
3.8577
3.8542
3.8481
3.8446
3.8408
2.0830
2.0597
2.0387
2.0228
2.0023
Ac's
OAc
AcO
AcO
OAc
O
H
N
CH3
O
NH
3-H
1-H
4-H
2-H
6-H
6-H
5-H
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.985
1.053
0.928
0.987
0.961
1.059
1.021
1.000
3.426
3.122
3.562
2.722
2.759

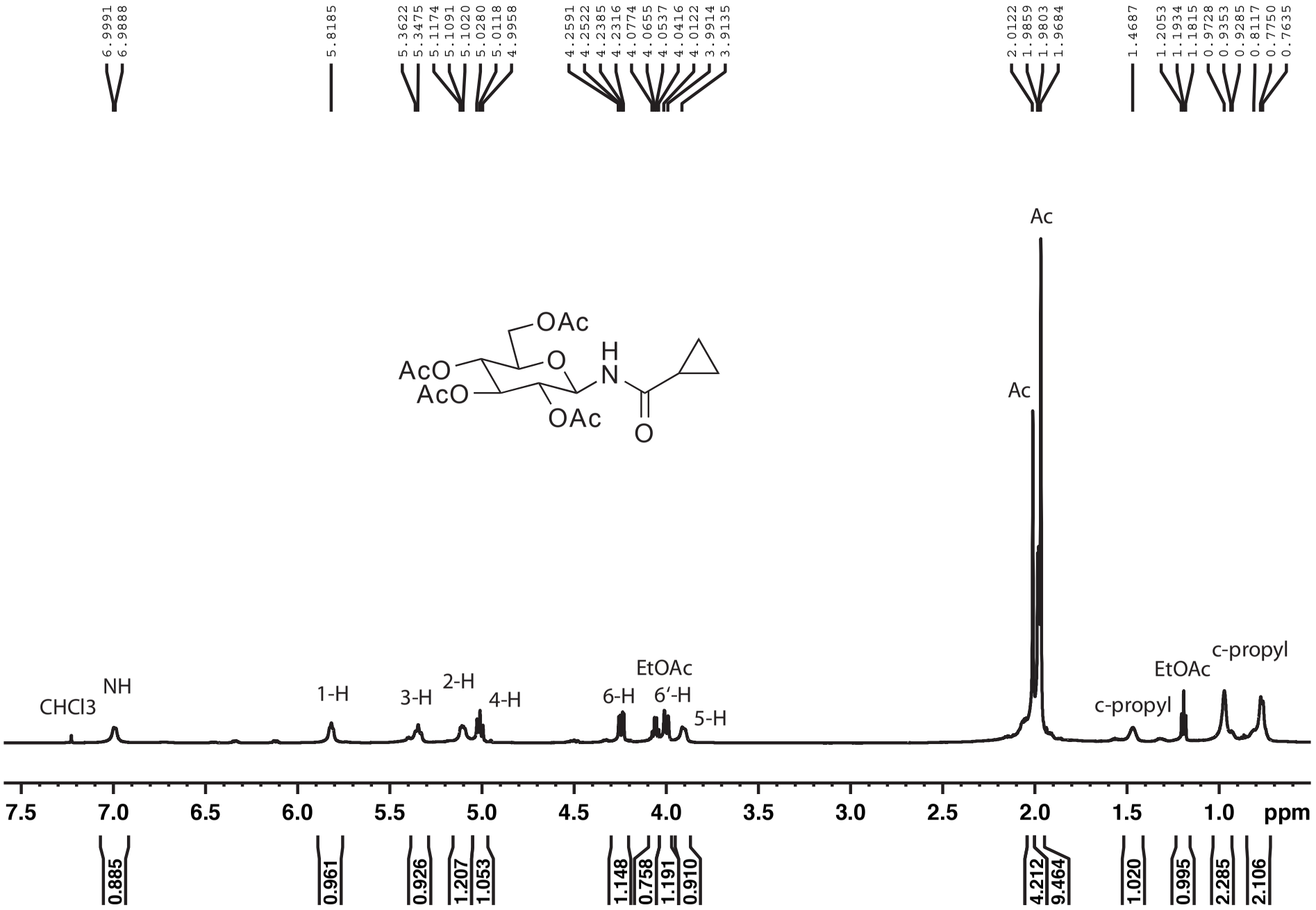

170.7168
170.4679
170.4174
169.7069
169.4428
77.9573
77.2122
77.0012
76.7891
73.3512
72.6739
70.4573
68.0127
61.5785
23.1348
20.5477
20.4853
20.4054
OAc
AcO
AcO
OAc
O
H
N
CH3
O
Ac's
CO's
1-C
5-C
3-C
2-C
4-C
6-C
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

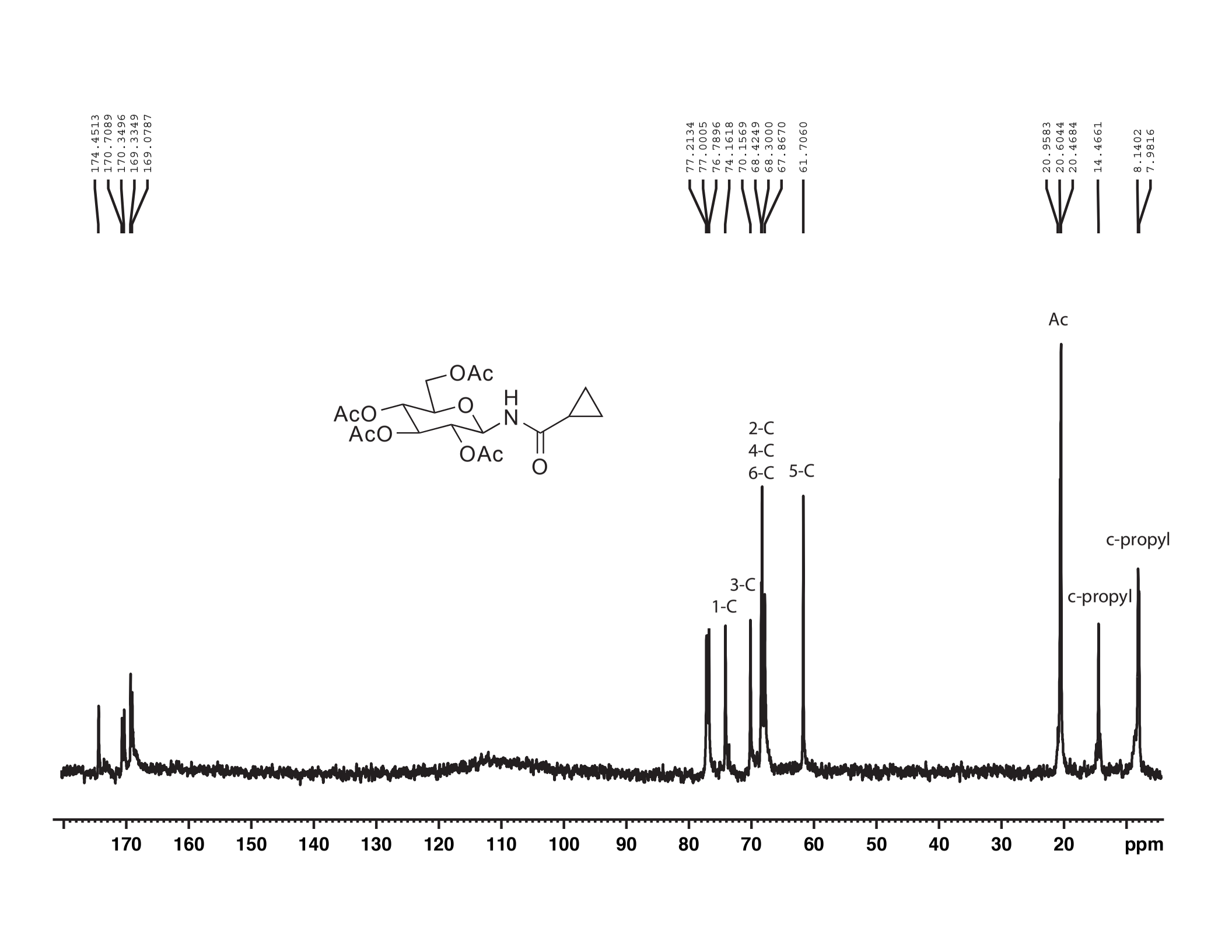

OAc
AcO
O
H
N
CH3
AcO
OAc
O
H-H COSY
NH
ppm
4.0
4.5
5.0
5.5
6.0
6.5
6.5
6.0
5.5
5.0
4.5
4.0
ppm
H-C HSQC
NH
ppm
62
64
66
68
70
72
74
76
78
6.5
6.0
5.5
5.0
4.5
4.0
ppm

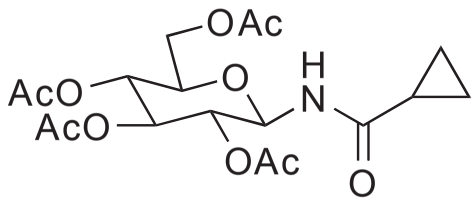

7.0997
7.0901
7.0764
7.0630
7.0519
7.0375
7.0212
7.0076
6.9914
6.9805
6.4605
6.4484
5.7609
5.7499
5.7395
5.2436
5.2275
5.2115
5.0256
5.0168
5.0090
4.9998
4.9196
4.9033
4.8874
4.1921
4.1852
4.1715
4.1644
4.0322
4.0306
4.0120
3.7984
3.7838
3.5220
3.4599
2.2435
2.2400
1.9054
1.8413
1.7929
AcO
AcO
OAc
O
O
O
H
N
O
CH₃
Ac
Ac
Ac
CHCl₃
NH
1-H
2-H
3-H
4-H
6-H
6′-H
5-H
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
8.995
0.850
0.813
0.797
0.971
0.816
1.000
0.834
0.773
2.073
1.761
6.413
2.633
2.634
2.385


171.5306
170.6819
170.4652
169.6424
169.3076
137.0810
136.6842
130.4903
129.4407
129.2344
128.8781
77.2089
76.9975
76.7862
74.0965
69.9639
68.5010
68.2744
68.0073
62.0050
40.7431
40.4013
29.6540
23.0124
21.0033
20.5049
20.3987
AcO
AcO
OAc
O
O
O
H
N
O
1-C
3-C
2-C
4-C
5-C
6-C
CH₂
CH₃
CH₃
Ac
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

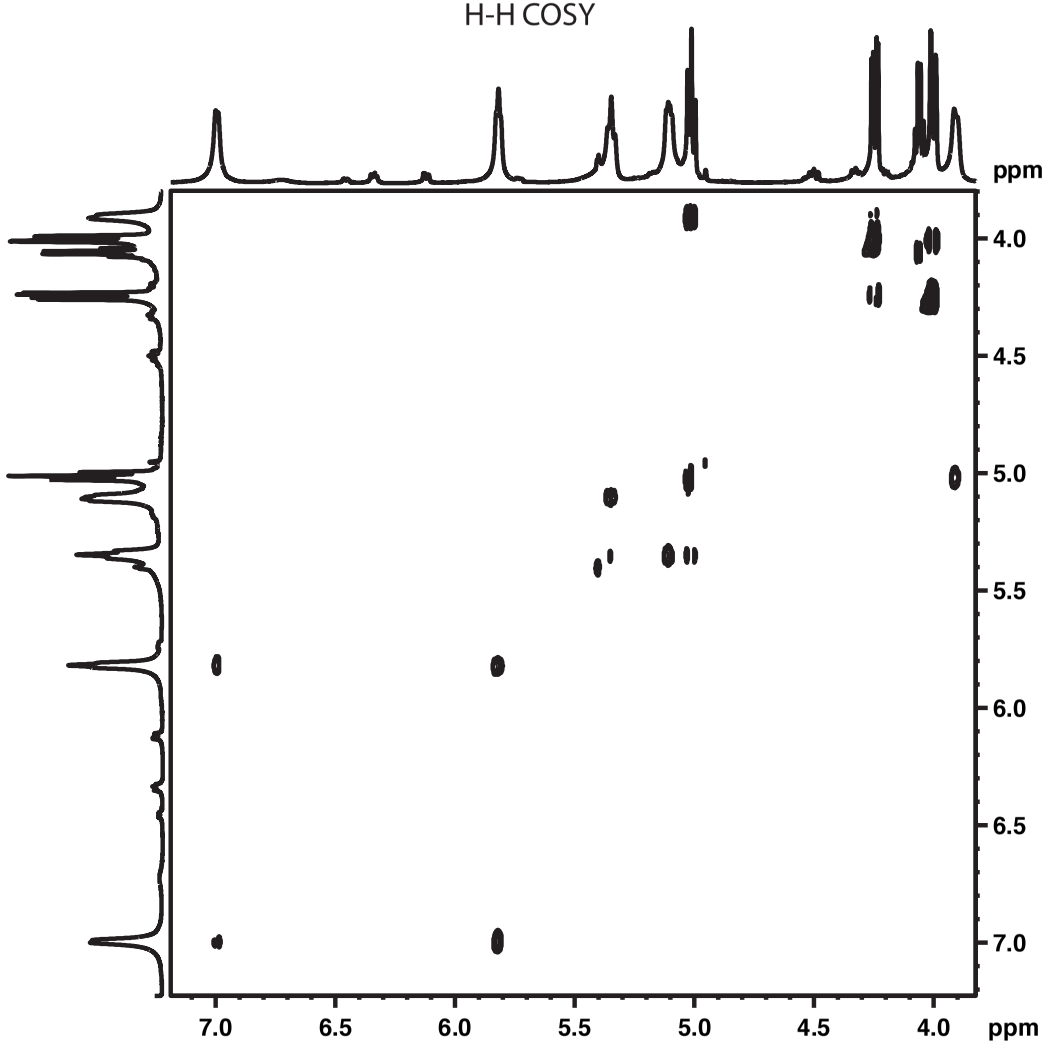

H-H COSY
H-C HSQC
NH
NH
AcO
AcO
OAc
O
O
O
O
H
N
ppm
ppm
ppm
ppm
6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8
4.0 4.5 5.0 5.5 6.0 6.5
6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8
62 64 66 68 70 72 74 76 78 80


6.9991
6.9888
5.8185
5.3622
5.3475
5.1174
5.1091
5.1020
5.0280
5.0118
4.9958
4.2591
4.2522
4.2385
4.2316
4.0774
4.0655
4.0537
4.0416
4.0122
3.9914
3.9135
2.0122
1.9859
1.9803
1.9684
1.4687
1.2053
1.1934
1.1815
0.9728
0.9353
0.9285
0.8117
0.7750
0.7635
OAc
AcO
AcO
O
H
N
OAc
O
Ac
Ac
CHCl3
NH
1-H
3-H
2-H
4-H
6-H
EtOAc
6′-H
5-H
c-propyl
EtOAc
c-propyl
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.885
0.961
0.926
1.207
1.053
1.148
0.758
1.191
0.910
4.212
9.464
1.020
0.995
2.285
2.106


174.4513
170.7089
170.3496
169.3349
169.0787
77.2134
77.0005
76.7896
74.1618
70.1569
68.4249
68.3000
67.8670
61.7060
20.9583
20.6044
20.4684
14.4661
8.1402
7.9816
OAc
AcO
AcO
OAc
O
H
N
O
Ac
2-C
4-C
6-C
5-C
c-propyl
3-C
1-C
c-propyl
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



H-H COSY



H-C HSQC