Molecular wipes: application to epidemic keratoconjuctivitis

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6,19-diaza-22-(9H-fluoren-9-yl)-10,13,16,21-tetraoxa-7,20-dioxo-dokosanyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (2a). **1** (151 mg, 0.189 mmol) was dissolved in dry DMF (5 mL) and then piperidine (706 μL, 7.14 mmol) was added to the solution. The reaction mixture was stirred for 2h after which the solvent and remaining piperidine were evaporated under reduced pressure to give a crude intermediate. This crude intermediate (36.3 mg, 0.063 mmol) and Fmoc-NH-CH_2CH_2O-$(PEG)_2$-CH_2CH_2-COOH were dissolved in DCM (1 mL) and the solution was cooled to 0 °C. EDC•HCl (18.2 mg, 0.095 mmol) was added to the solution and the reaction mixture was stirred for 18 h. The crude was subjected to flash column chromatography (DCM/MeOH 25:1) to give **2a** (45.0 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28-1.57 (m), 1.87 (s, 3H), 1.90-1.96 (m), 2.01 (s, 3H), 2.02 (s, 3H), 2.13 (s, 3H), 2.13 (s, 3H), 2.42 (t, 2H), 2.53-2.58 (m, 1H), 3.17-3.27 (m, 3H), 3.38-3.40 (m), 3.55-3.62 (m), 3.68-3.78 (m), 4.02-4.10 (m, 3H) 4.21 (t, 1H), 4.29-4.33 (m, 1H), 4.40 (d, 2H), 4.79-4.86 (m, 1H), 5.19-5.22 (m, 1H), 5.29-5.32 (m, 1H), 5.37-5.44 (m, 2H), 6.37 (t, 1H), 7.28-7.32 (m, 2H), 7.39 (t, 2H), 7.60 (d, 2H), 7.76 (d, 2H). HRMS calcd. for $C_{49}H_{67}N_3O_{19}$ $(M+Na)^+$ 1024.4266, found 1024.4921.

6,25-diaza-28-(9H-fluoren-9-yl)-10,13,16,19,22,28-hexaoxa-7,26-dioxo-oktaeikosanyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (2b). The following compound was synthesized in an analogous method to compound **2a**, using Fmoc-NH-CH_2CH_2O-$(PEG)_4$-CH_2CH_2-COOH instead of Fmoc-NH-CH_2CH_2O-$(PEG)_2$-CH_2CH_2-COOH. Yield 83.4 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27-1.57 (m), 1.86-2.04 (m), 2.13 (s, 6H), 2.43 (t, 2H), 2.53-2.58 (m, 1H), 3.17-3.24 (m, 3H), 3.36-3.40 (m), 3.55-3.62 (m), 3.68-3.77 (m), 4.02-4.11 (m, 3H), 4.21 (t, 1H), 4.29-4.32 (m, 1H), 4.39 (d,

2H), 4.79-4.85 (m, 1H), 5.23-5.25 (m, 1H), 5.29-5.32 (m, 1H), 5.36-5.40 (m, 1H), 5.48 (t, 1H), 6.47 (t, 1H), 7.28-7.32 (m, 2H), 7.37-7.41 (m, 2H), 7.60 (d, 2H), 7.75 (d, 2H). HRMS calcd. for $C_{53}H_{75}N_3O_{21}$ $(M+Na)^+$ 1112.4791, found 1112.5548.

6,46-diaza-49-(9H-fluoren-9-yl)-10,13,16,19,22,25,28,31,34,37,40,43,48-tridekaoxa-7,47-dioxo-nonatetrakontanyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (2c). The following compound was synthesized in an analogous method to compound **2a**, using Fmoc-NH-CH_2CH_2O-$(PEG)_{11}$-CH_2CH_2-COOH instead of Fmoc-NH-CH_2CH_2O-$(PEG)_2$-CH_2CH_2-COOH. Yield 45.8 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23-1.57 (m), 1.86 (s, 3H), 1.88-1.98 (m), 2.01 (s, 3H), 2.02 (s, 3H), 2.12 (s, 6H), 2.43 (t, 2H), 2.53-2.57 (m, 1H), 3.16-3.27 (m, 3H), 3.37-3.43 (m, 2H), 3.54-3.62 (m), 3.69-3.75 (m), 3.75-3.77 (m), 4.01-4.10 (m), 4.20 (t, 1H), 4.28-4.32 (m, 1H), 4.34-4.39 (m, 2H), 4.78-4.85 (m, 1H), 5.24-5.31 (m, 2H), 5.35-5.39 (m, 1H), 5.43 (t, 1H), 6.50 (t, 1H), 7.27-7.31 (m, 2H), 7.36-7.40 (m, 2H), 7.58-7.63 (m, 2H), 7.74 (d, 2H). HRMS calcd. for $C_{67}H_{103}N_3O_{28}$ $(M+Na)^+$ 1420.6626, found 1420.7222.

6,25-diaza-10,13,16,19,22-pentaoxa-7,26-dioxo-tritetrakontanyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (3). **2b** (26.7 mg, 0.024 mmol) was dissolved in DMF (1.5 mL) and then piperidine (92 μL, 0.93 mmol) was added. The reaction mixture was stirred for 3 h. The solvent was evaporated to give a crude intermediate. The crude intermediate was dissolved in DCM (1.5 mL) and then stearic acid (10.2 mg, 0.036 mmol) was added to the solution and the reaction was cooled to 0 °C. EDC•HCl (6.9 mg, 0.036 mmol) was added to the solution. The reaction mixture was stirred for 17 h. The reaction mixture was washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was subjected to flash column

chromatography (DCM/MeOH 25:1) to give **3** (14.2 mg, 52% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t), 1.25-1-42 (m), 1.46-1.67 (m), 1.79-1.83 (m), 1.88 (s, 3H), 1.91-1.97 (m), 2.03, (s, 3H), 2.04 (s, 3H), 2.10-2.19 (m), 2.44-2.47 (t, 2H), 2.54-2.60 (m), 3.18-3.33 (m), 3.42-3.46 (m, 2H), 3.54-3.56 (m, 2H), 3.61-3.65 (m), 3.71-3.77 (m), 3.79 (s, 3H), 4.02-4.11 (m, 3H), 4.30-4.33 (m, 1H), 4.80-4.87 (m, 1H), 5.15.5.17 (m, 1H), 5.30-5.33 (m, 1H), 5.37-5.41 (m, 1H), 6.18 (t, 1H), 6.51 (t, 1H). HRMS calcd. for $C_{56}H_{99}N_3O_{20}$ $(M+Na)^+$ 1156.6720, found 1156.7217.

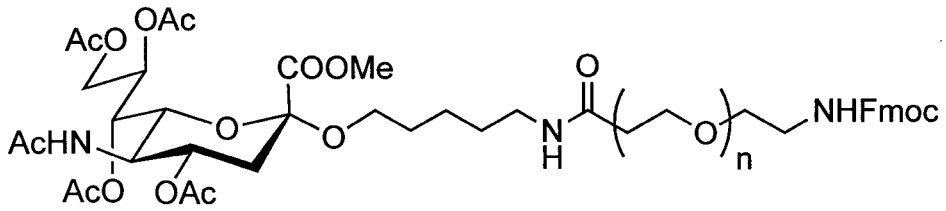
6,25-diaza-10,13,16,19,22-pentaoxa-7,26-dioxo-nonatetrakontanyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (4). Compound **4** was synthesized in an analogous method to compound **3**, using **2b** and tetracosanoic acid. Yield 18.3 mg (63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H), 1.24-1.40 (m), 1.46-1.62 (m), 1.87 (s, 3H), 1.90-1.96 (m), 2.02 (s, 3H), 2.03 (s, 3H), 2.10-2.18 (m), 2.43-2.46 (t, 2H), 2.54-2.59 (m), 3.17-3.30 (m), 3.41-3.45 (m, 2H), 3.53-3.56 (m, 2H), 3.60-3.64 (m), 3.70-3.76 (m), 3.78 (s, 3H), 4.02-4.11 (m), 4.29-4.33 (m, 1H), 4.79-4.86 (m, 1H), 5.22-5.24 (m, 1H), 5.29-5.32 (m, 1H), 5.36-5.40 (m, 1H), 6.15 (t, 1H), 6.51 (t, 1H). HRMS calcd. for $C_{62}H_{111}N_3O_{20}$ $(M+H)^+$ 1218.7839, found 1218.7875.

6,19-diaza-10,13,16-trioxa-7,20-dioxo-29,31-tetratetrakonta-diynyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (5a). Compound **5a** was synthesized in an analogous method to compound **3**, using **2a** and 10,12-pentacosadiynoic acid. Yield 36.3 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H), 1.23-1.41 (m), 1.42-1.61 (m), 1.86 (s, 3H), 1.89-1.97 (m), 2.01 (s, 3H), 2.02 (s, 3H), 2.08-2.18 (m), 2.20-2.23 (m), 2.43 (t, 2H), 2.53-2.59 (m, 1H), 3.18-3.31 (m), 3.4-3.44 (m, 2H), 3.52-3.55 (m, 2H), 3.59-3.62 (m), 3.69-3.75 (m), 3.77 (s, 3H), 4.01-4.10 (m), 4.28-4.32 (m, 1H), 4.78-4.85 (m, 1H),

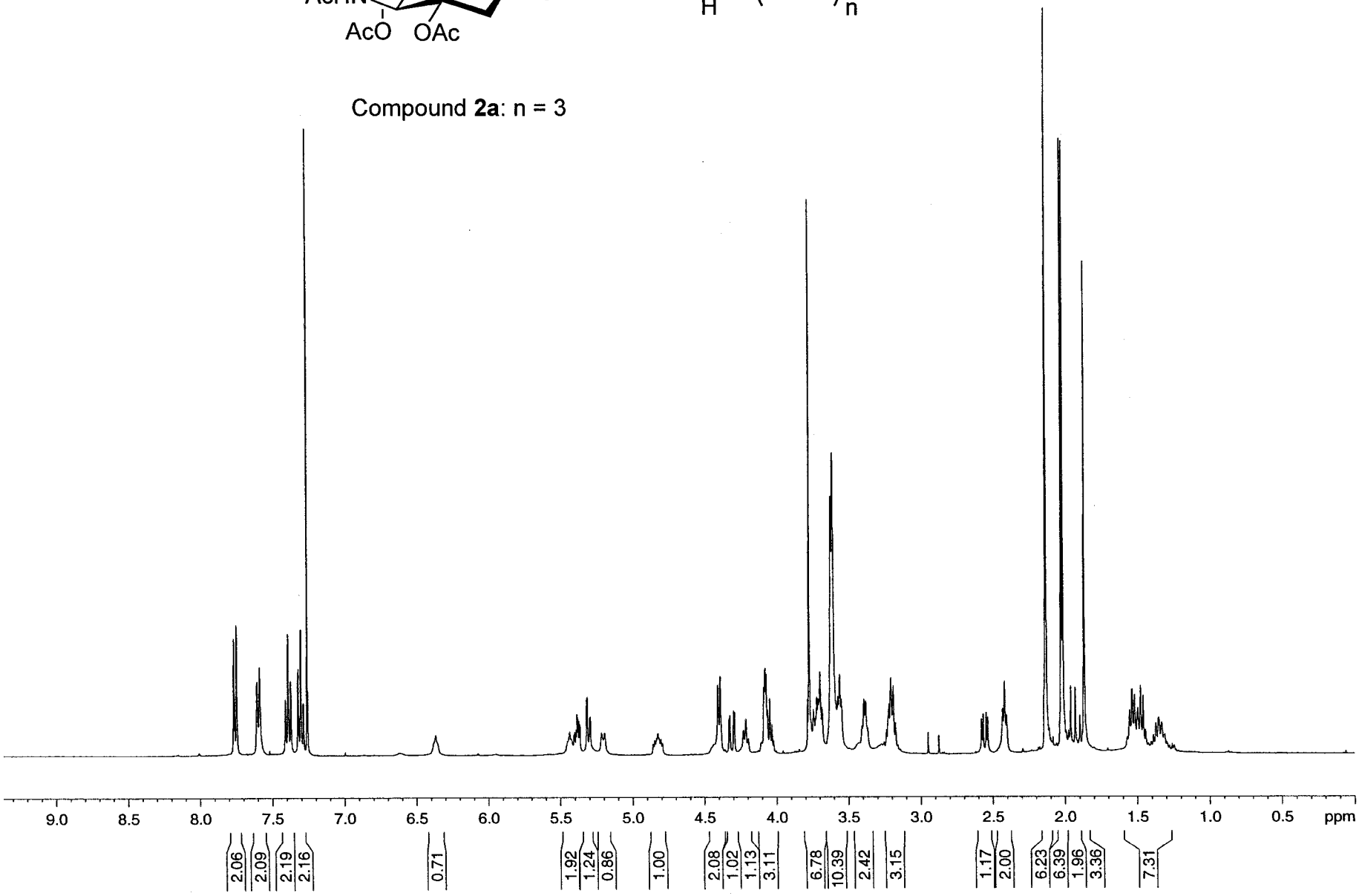
5.28-5.39 (m, 3H), 6.11 (t, 1H), 6.43 (t, 1H). HRMS calcd. for $C_{59}H_{97}N_3O_{18}$ $(M+Na)^+$ 1158.6665, found 1158.6655.

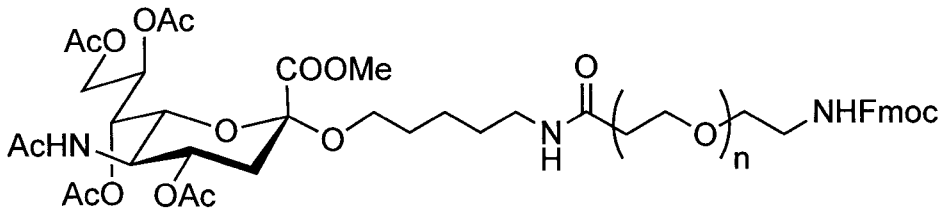
6,25-diaza-10,13,16,19,22-pentaoxa-7,26-dioxo-35,37-pentakontadiynyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (5b). Compound **5b** was synthesized in an analogous method to compound **3**, using **2b** and 10,12-pentacosadiynoic acid. Yield 21.9 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H), 1.24-1.39 (m), 1.45-1.62 (m), 1.86 (s, 3H), 1.92-1.95 (m), 2.01 (s, 3H), 2.02 (s, 3H), 2.10-2.17 (m), 2.20-2.24 (m), 2.45 (t, 2H), 2.53-2.59 (m), 3.17-3.31 (m), 3.41-3.45 (m, 2H), 3.53-3.55 (m, 2H), 3.61-3.64 (m), 3.70-3.76 (m), 3.78 (s, 3H), 4.01-4.10 (m), 4.28-4.35 (m, 1H), 4.78-4.85 (m, 1H), 5.26-5.31 (m, 2H), 5.35-5.40 (m, 1H), 6.19 (t, 1H), 6.52 (t, 1H). HRMS calcd. for $C_{63}H_{105}N_3O_{20}$ $(M+Na)^+$ 1246.7189, found 1246.7118.

6,46-diaza-10,13,16,19,22,25,28,31,34,37,40,43,46-dodekaoxa-7,47-dioxo-56,58-henheptakonta-diynyl methyl(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonylopyranosyl)onate (5c). Compound **5c** was synthesized in an analogous method to compound **3**, using **2c** and 10,12-pentacosadiynoic acid. Yield 25.2 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H), 1.24-1.41 (m), 1.46-1.62 (m), 1.87 (s, 3H), 1.90-2.02 (m), 2.03 (s, 3H), 2.05 (s, 3H), 2.13-2.18 (m), 2.21-2.24 (m), 2.46 (t, 2H), 2.54-2.58 (m, 1H), 3.17-3.26 (m), 3.42-3.49 (m), 3.54-3.56 (m), 3.62-3.65 (m), 3.70-3.75 (m), 3.79 (s, 3H), 4.02-4.11 (m), 4.29-4.32 (m, 1H), 4.79-4.86 (m, 1H), 5.17-5.20 (m, 1H), 5.29-5.32 (m, 1H), 5.36-5.40 (m, 1H), 6.17 (s, 1H), 6.58 (s, 1H). HRMS calcd. for $C_{77}H_{133}N_3O_{27}$ $(M+Na)^+$ 1554.9024, found 1554.9325.



Compound **2a**: n = 3





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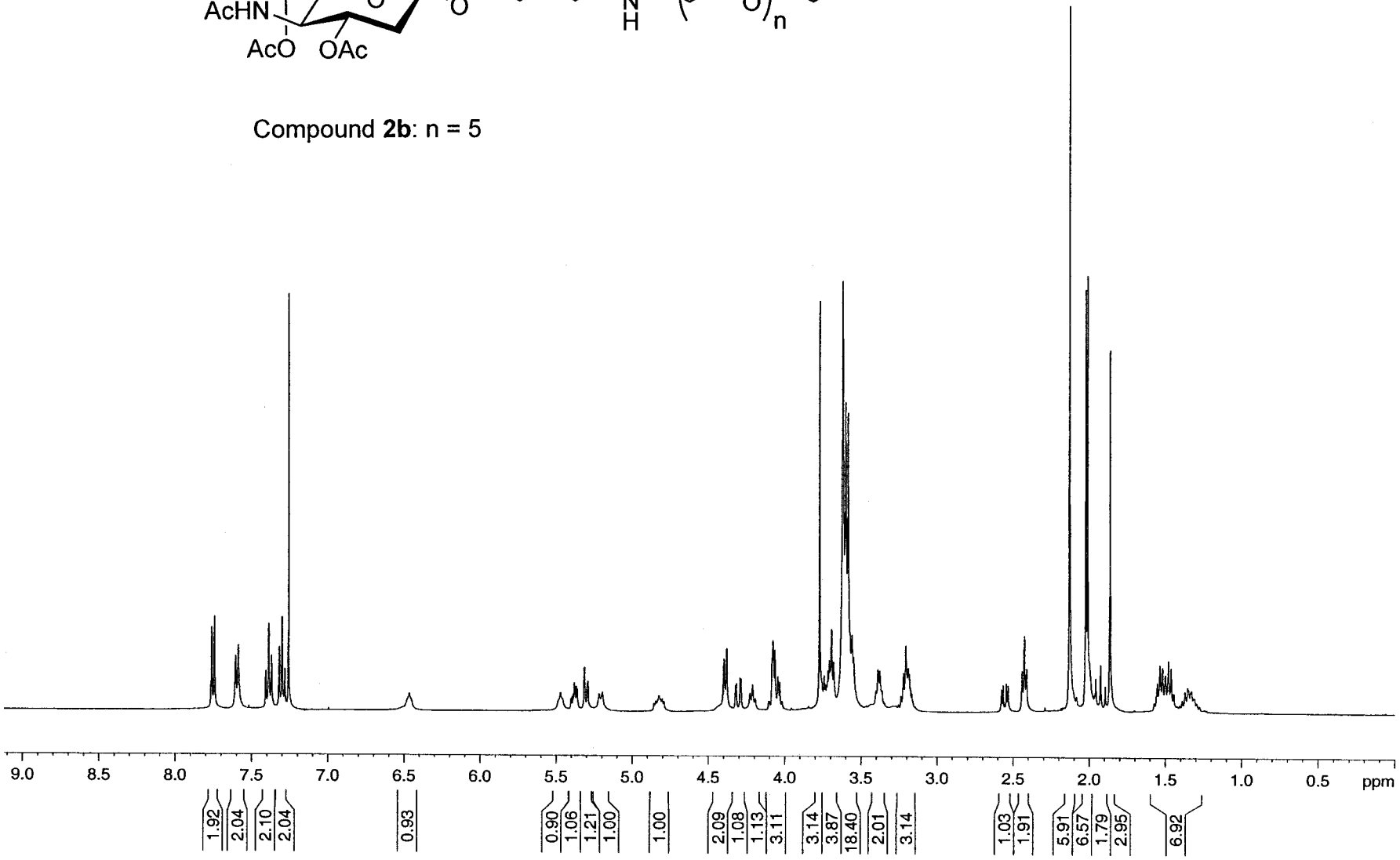
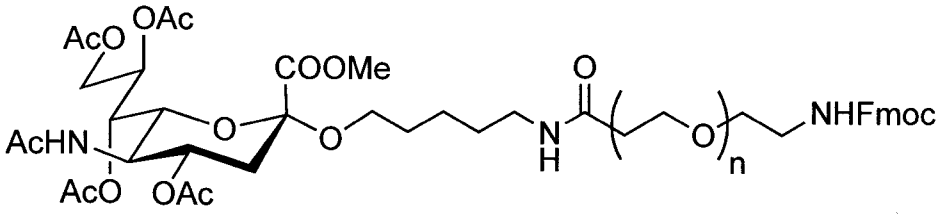
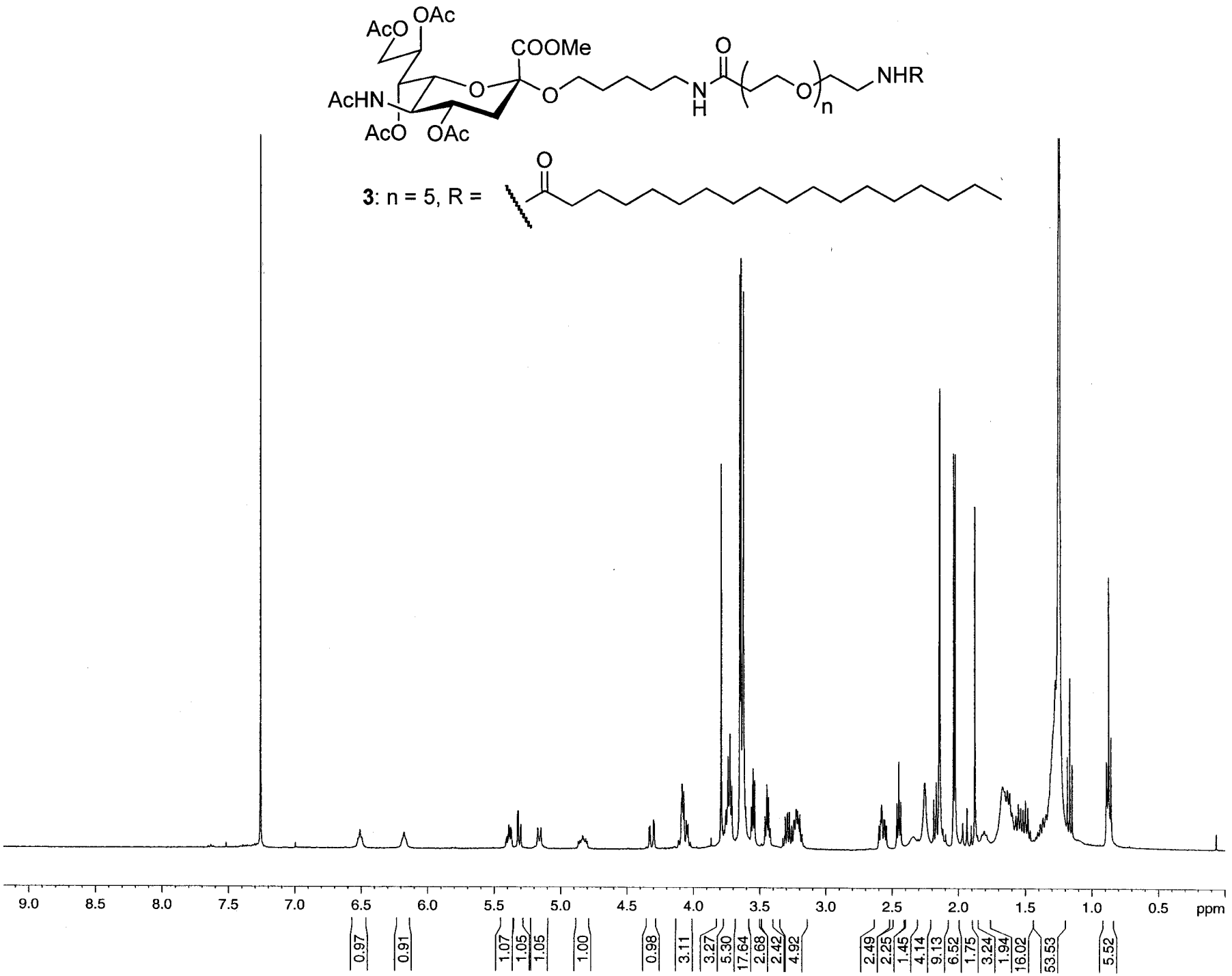




Compound **2c**: n = 11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OAc
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O
O
N
H
O
n
NHR
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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ppm
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0.91
1.07
1.05
1.05
1.00
0.98
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3.27
5.30
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4.92
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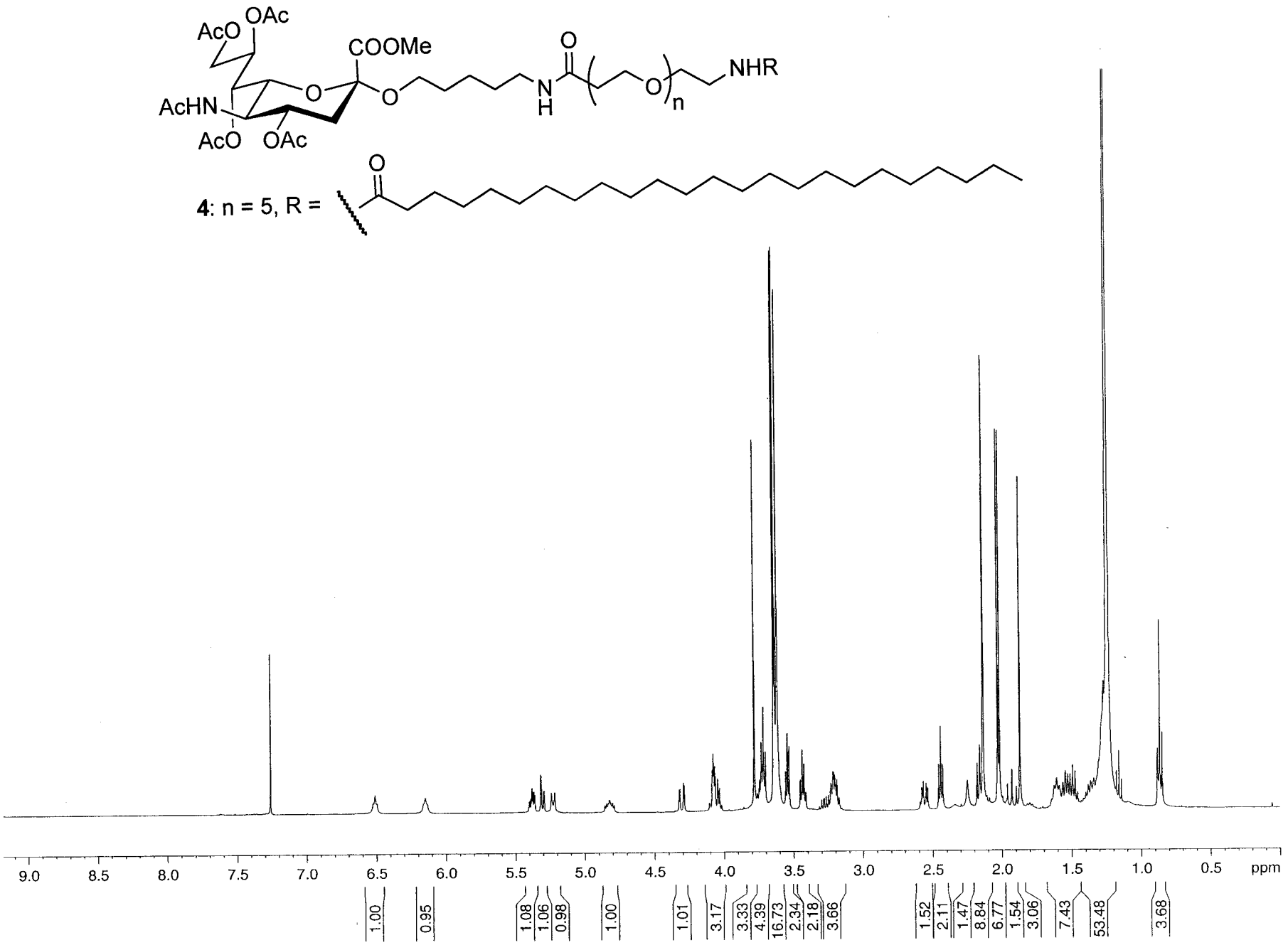
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H
O
n
NHR
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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2.0
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0.5
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4.39
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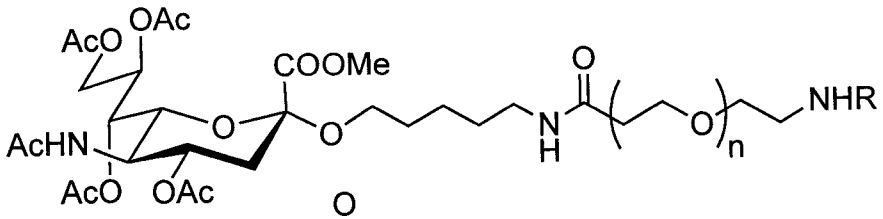
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N
H
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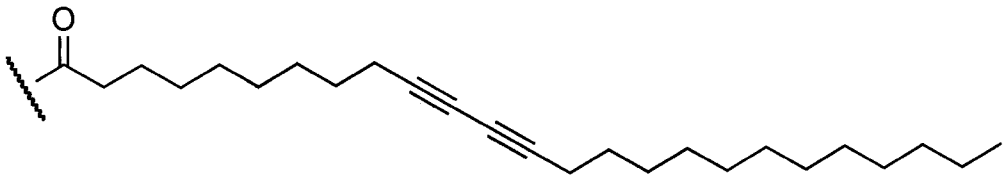
NHR
AcO
OAc

5a: n = 3, R =


O

9.0
8.5
8.0
7.5
7.0
6.5
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5.0
4.5
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2.5
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1.06
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3.03
3.75
7.51
1.97
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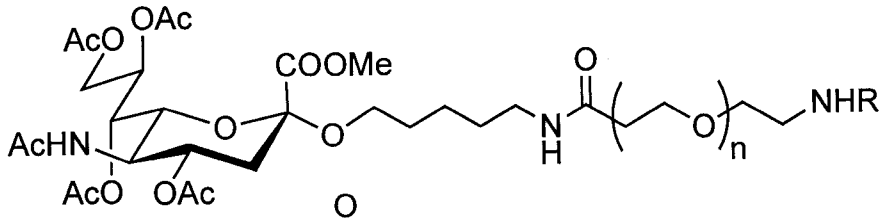
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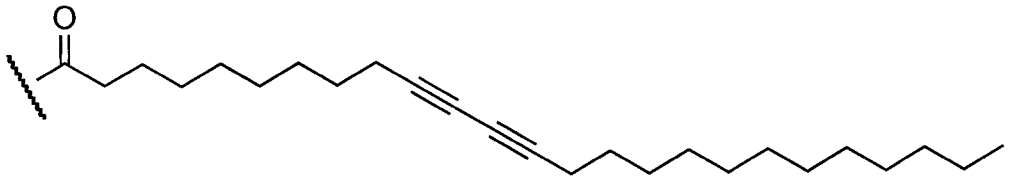
OAc

5b: n = 5, R =


O

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3.5
3.0
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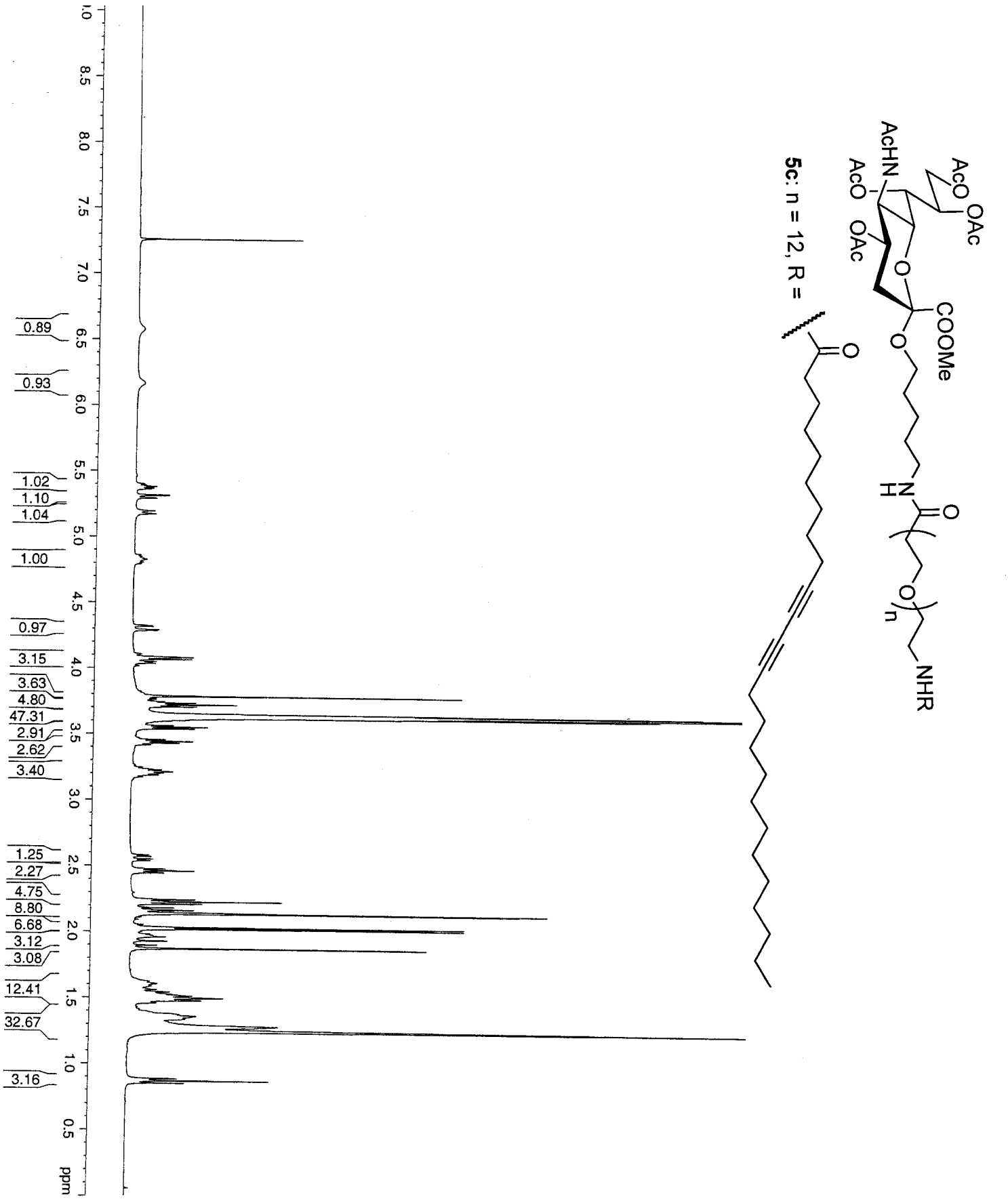
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COOMe
O
N
H
O
O
n
NHR
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0.93
1.02
1.10
1.04
1.00
0.97
3.15
3.63
4.80
47.31
2.91
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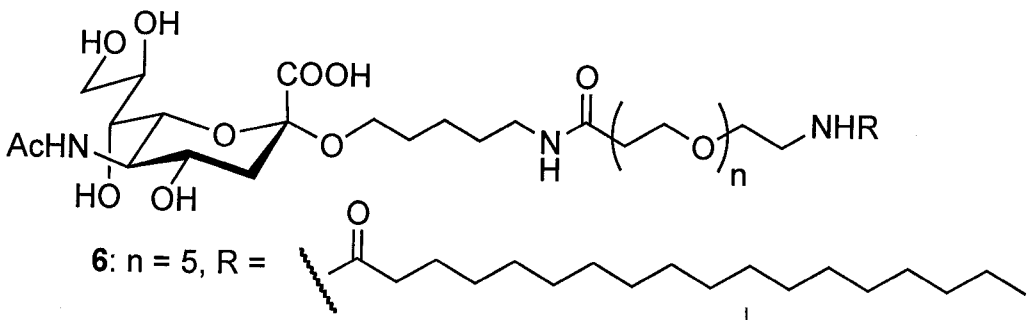
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OH
COOH
AcHN
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O
N
H
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O
n
NHR
HO
OH
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O

9.0
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8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
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3.0
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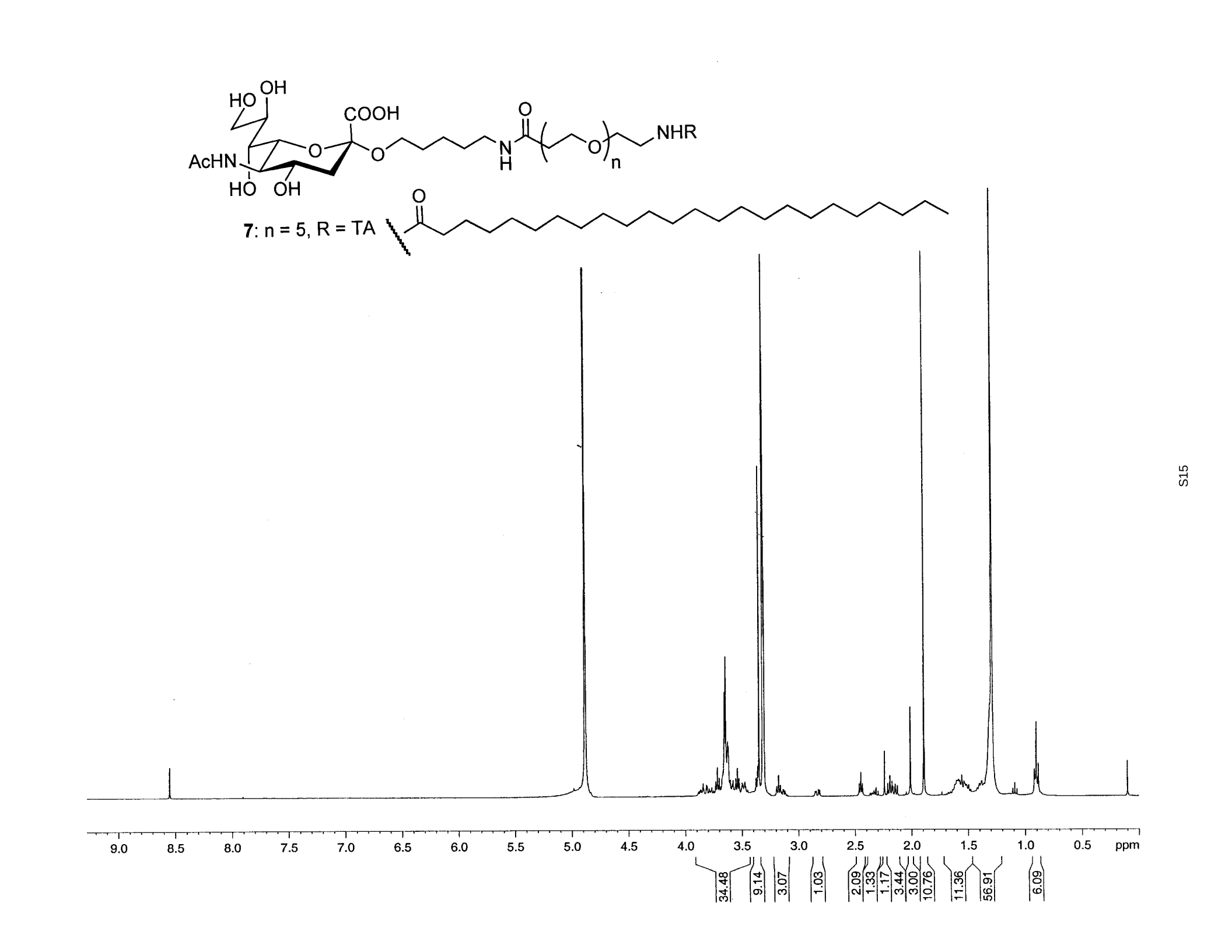
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AcHN
HO OH
O
O
N
H
O
O
n
NHR
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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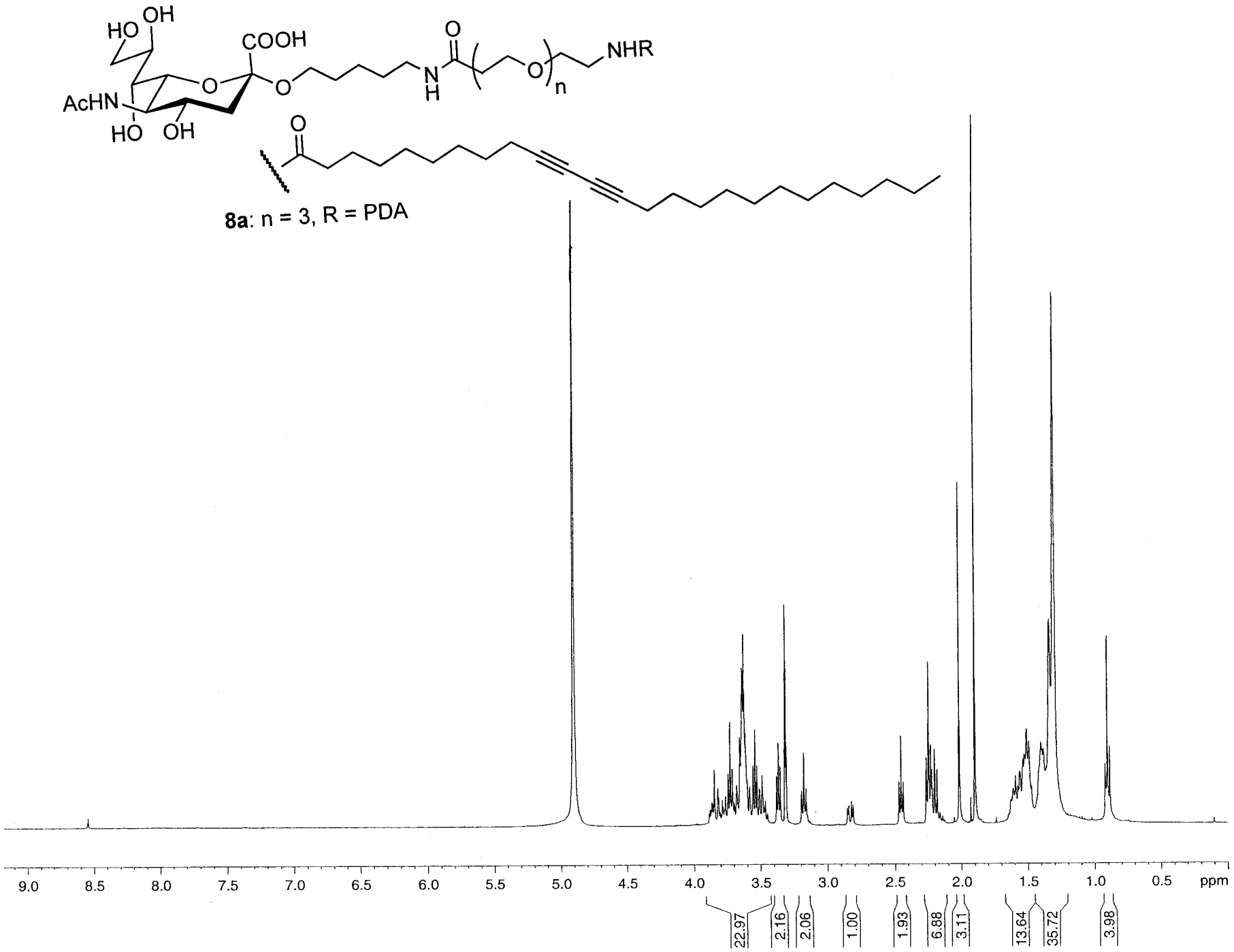
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OH
COOH
O
NHR
AcHN
N
H
O
n
HO
OH
O
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8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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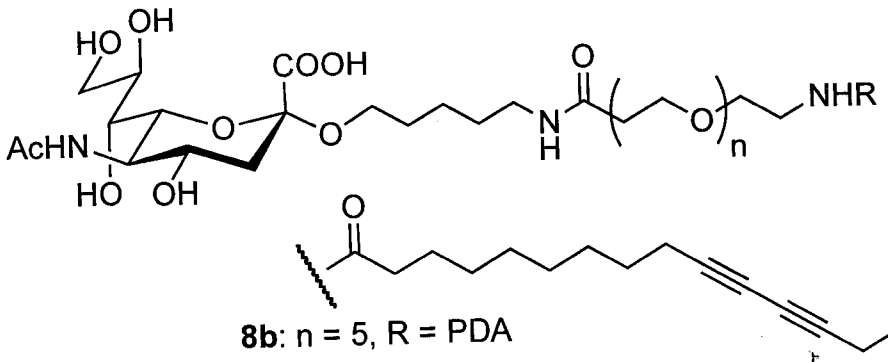
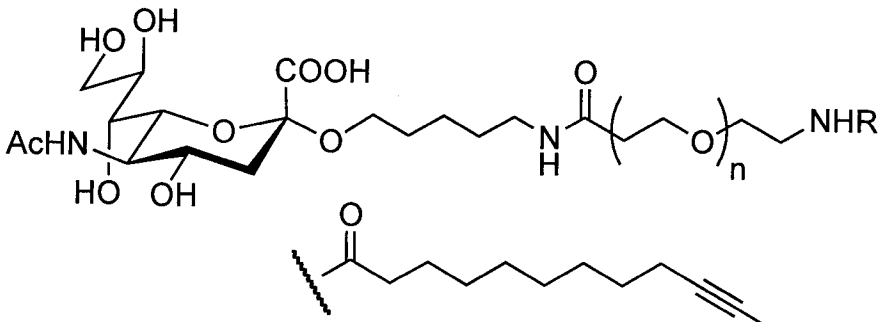
2.06
1.00
1.93
6.88
3.11
13.64
35.72
3.98

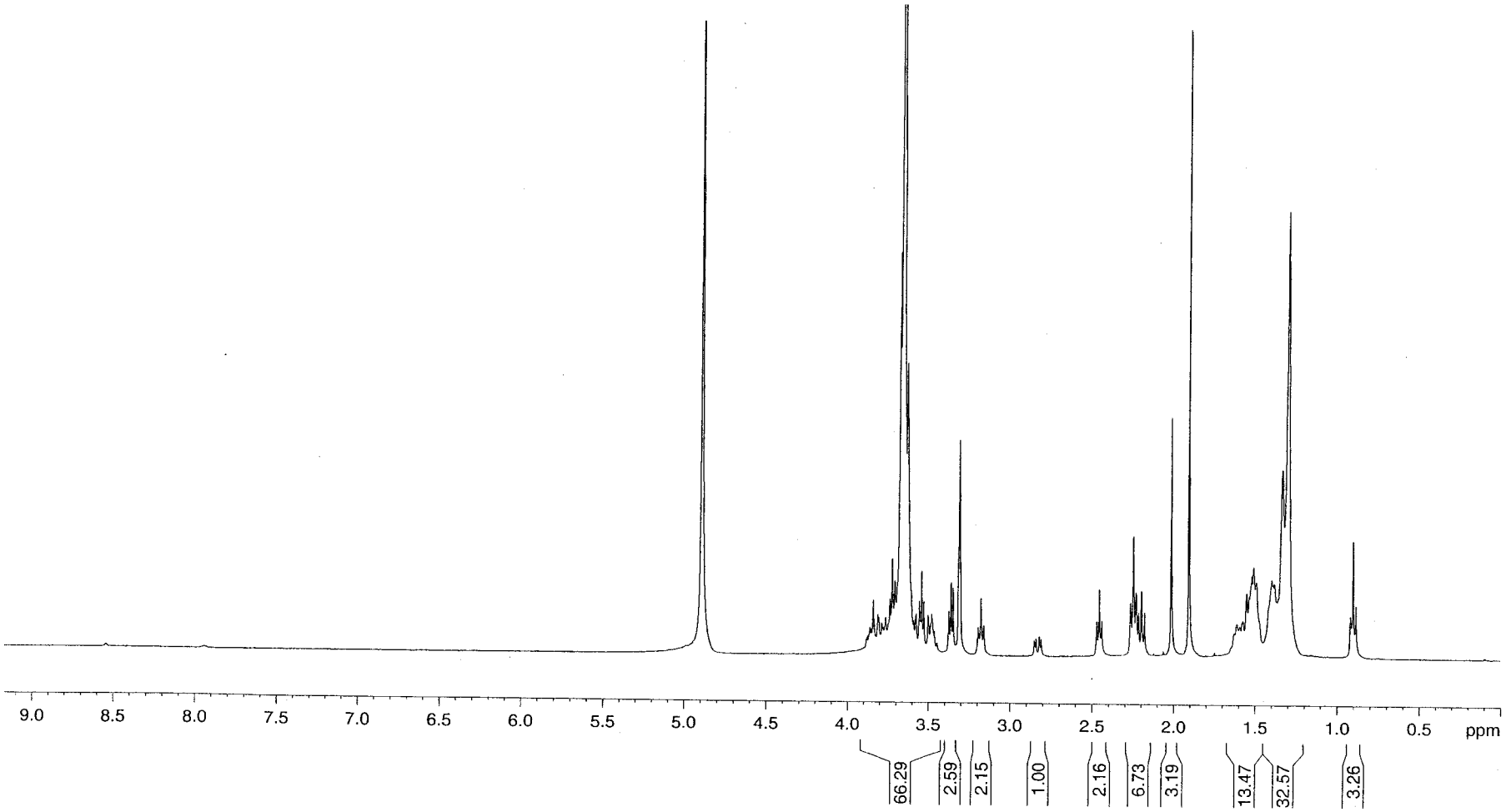

HO
OH
COOH
O
NHR
AcHN
O
N
H
O
n
HO
OH
O

8b: n = 5, R = PDA

9.0
8.5
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
1.0
0.5
ppm
27.30
2.16
2.41
0.84
0.15
1.65
1.13
6.23
3.00
8.97
12.37
31.99
3.28


HO
OH
COOH
O
AcHN
O
O
N
H
O
n
NHR
HO
OH
O

8c: n = 12, R = PDA


9.0
8.5
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
1.0
0.5
ppm
66.29
2.59
2.15
1.00
2.16
6.73
3.19
13.47
32.57
3.26