Supporting Information

Synthesis of amino acid N-Carboxyanhydrides

Synthesis of γ-Benzyl-L-glutamate- N-carboxyanhydride (**3c**) :To a solution of γ-Benzyl-L-glutamate amino acid (1 g, 4.21 mmol) in freshly distilled out tetrahydrofuran (10 ml) was added a solution of triphosgene (625mg, 2.11 mmol) in anhydrous tetrahydrofuran (4 ml) under argon and the reaction mixture was heated to 50°-55° C. Then α-pienene (1.0 ml, 6.32 mmol) was added and the reaction mixture was allowed to stir for 2 hrs. The reaction mixture was then cooled to room temperature and thereafter poured into dry hexane (400 ml) to afford a white precipitate. The white precipitate of N-carboxyanhydrides was filtered off by vacuum quickly and crystallized two more times by using ethyl acetate/petroleum ether mixtures. Finally the precipitate of γ-Benzyl-L-glutamate- N-carboxyanhydride was dried under vacuum and transferred into glove box. Final yield 900 mg (81%).

Compound **3c**: ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 2.33-2.58(m, 2H), 2.85(t, 2H, *J* = 7.0 Hz), 4.66(t, 1H, *J* = 6.0 Hz), 5.40(s, 2H), 7.25(bs, 1H), 7.61-7.65(m, 5H); ^{13}C NMR (100.61MHz, $CDCl_3$): δ = 26.7, 29.5, 56.7, 67.0, 128.2-128.7, 135.2, 152.2, 169.9, 172.3.

Synthesis of ε-N-carbobenzoxy-L-lysine-N-carboxyanhydride (**3d**) :To a solution of ε,α-di-N-carbobenzoxy-L-lysine (1 g, 2.41 mmol) in freshly distilled out diethyl ether (10 ml) was added phosphorous pentachloride (603 mg, 2.90mmol) under argon at 0°-5° C and the reaction mixture was allowed to stir for 30 min. As soon as the reaction mixture turned homogeneous, the solvent was removed slowly under reduced pressure and the residue redissolved in dry ethyl acetate. The mixture was filtered to remove undissolved solid particles and the filtrate was poured into dry hexane (400 ml) to afford white precipitate. The white precipitate of N-carboxyanhydride was filtered off by vacuum quickly and crystallized two more times by using ethyl acetate/petroleum ether mixtures. Finally precipitate of ε- N-carbobenzoxy-L-lysine-carboxyanhydride was dried under vacuum and transferred into glove box. Final yield 500 mg(67%).

Compound **3d**: ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 1.32-1.56(m, 4H), 1.70-1.91(m, 2H), 3.12(dd, 2H, *J* = 6.5, 12.8 Hz), 4.33(t, 1H, *J* = 6.0 Hz), 5.07(s, 2H), 5.70(bs, 1H), 6.96(bs, 1H), 7.31-7.42(m, 5H); ^{13}C NMR (100.61MHz, $CDCl_3$): δ = 22.6, 29.9, 31.7, 41.0, 58.3, 66.7, 128.5-129.4, 138.4, 152.9, 157.4, 172.1.

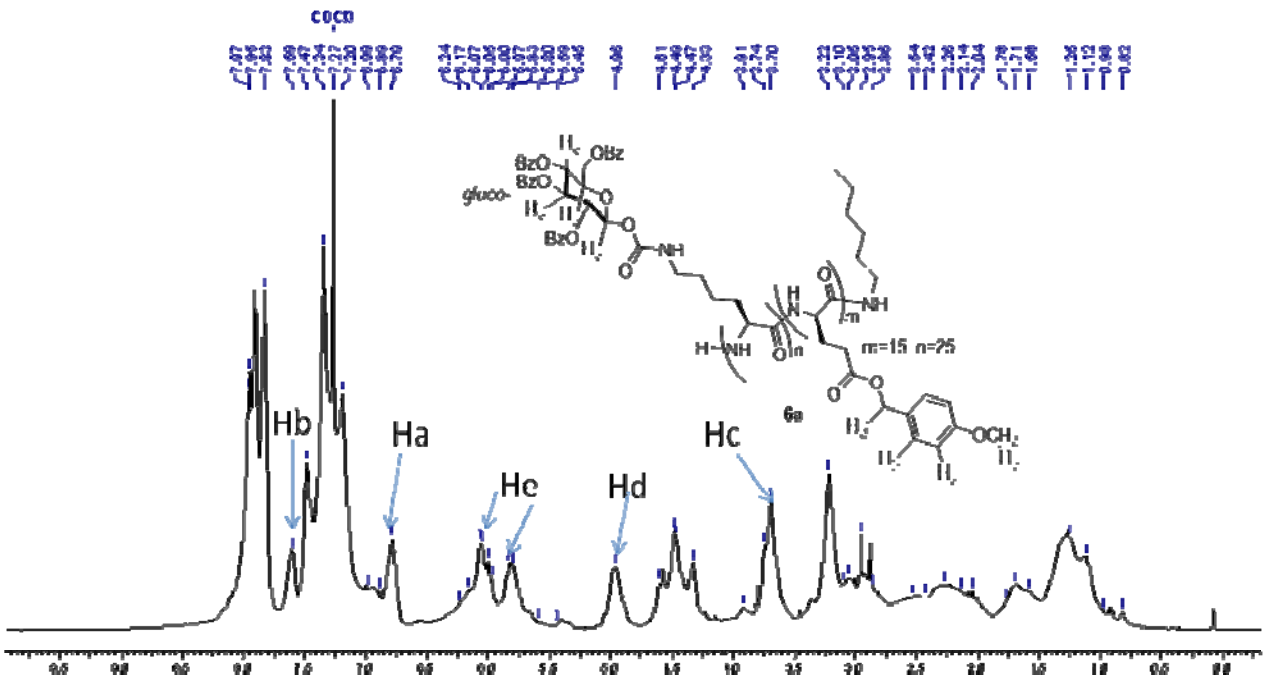
Synthesis of γ-p-OMe-benzyl-L-glutamate-N-carboxyanhydride (**3e**) :To a solution of γ-p-OMe-benzyl-L-glutamate amino acid (1 g, 3.74 mmol) in freshly distilled out tetrahydrofuran (10 ml) was added a solution of triphosgene (555 mg, 1.87 mmol) in anhydrous tetrahydrofuran (4 ml) under argon and the reaction mixture was heated to 50°-55° C. Then α-pienene (0.89 ml, 5.6 mmol) was added and the reaction mixture was allowed to stir for 2

hrs. The reaction mixture was then cooled to room temperature, thereafter poured into dry hexane (400 ml) and then kept in the refrigerator for 4-5 hrs at -20° C under argon to afford a white precipitate. The white precipitate of N-carboxyanhydride was filtered off by vacuum quickly and crystallized two more times by using ethyl acetate/petroleum ether mixture. Finally the white precipitate of γ-p-OMe-benzyl-L-glutamate-N-carboxyanhydride was dried under vacuum and transferred into the glove box. Final yield 800 mg (80%).

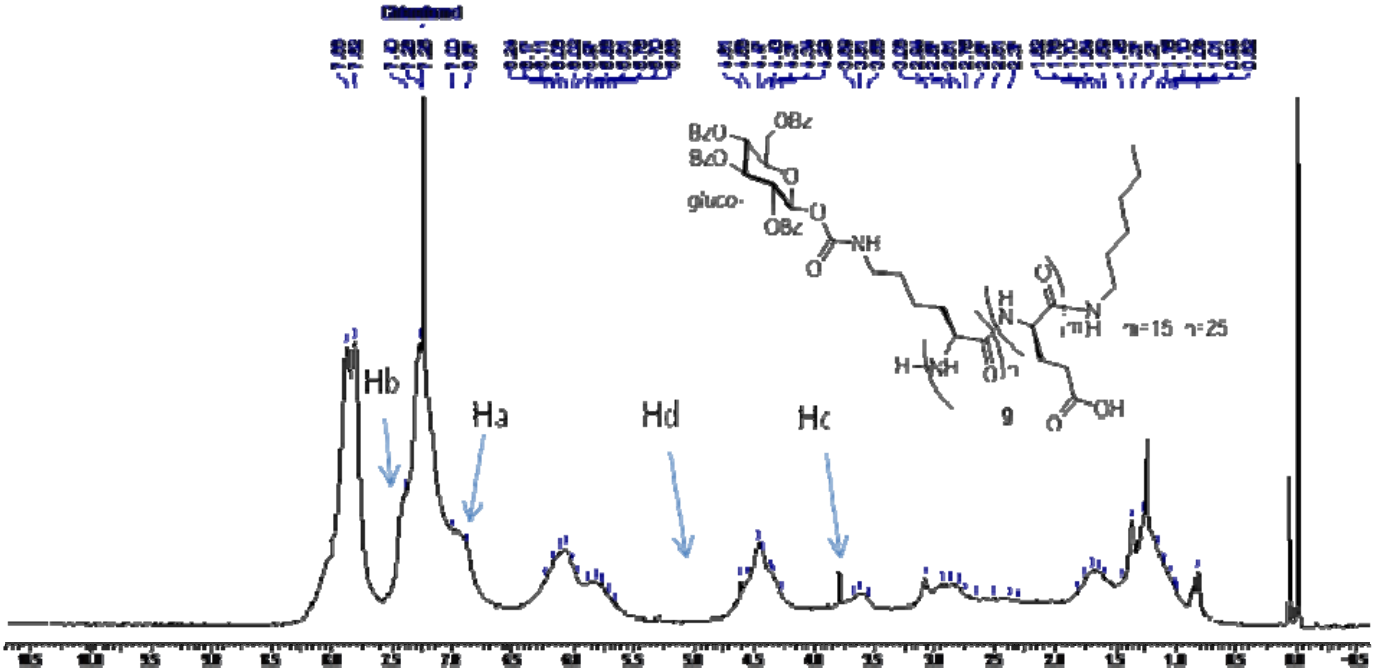
Compound **3e**: ^{1}H NMR (400.13 MHz, CD_3CN): δ = 1.98-2.23(m, 2H), 2.49(dt, 2H, *J* = 3.3, 7.4 Hz), 3.80(s, 3H), 4.41(t, 1H, *J* = 6.6 Hz), 5.05(s, 2H), 6.86(bs, 1H), 6.93(m, 2H), 7.32(m, 2H); ^{13}C NMR (100.61MHz, CD_3CN): δ = 27.4, 30.1, 55.8, 57.4, 66.9, 114.8(2C), 129.1, 130.9(2C), 152.7, 166.6, 171.7, 172.2.

Synthesis of poly-L-glutamate-*b*-poly-per-*O*-benzoylated-D-glucose-L-Lysine (9)

To a solution of Poly-PMBnLG-*b*-poly-per-*O*-benzoylated-D-glucose-L-lysine (**6a**) polymer in dichloromethane was added 10% TFA in dichloromethane (2.5 equivalent) and the reaction mixture was stirred for 30 min at room temperature. The reaction was then quenched by the addition of triethylamine (3 equivalent) and the volume of the reaction mixture was reduced to half. The polymer was precipitated out by addition of diethyl ether and resultant white precipitate (**9**) was collected by centrifugation. The complete deprotection of the p-methoxybenzylester was confirmed by ^{1}H (S1 and S2) and ^{13}C NMR (page 18) as shown below. Yield 90%.



S1. ^{1}H NMR of **6a**

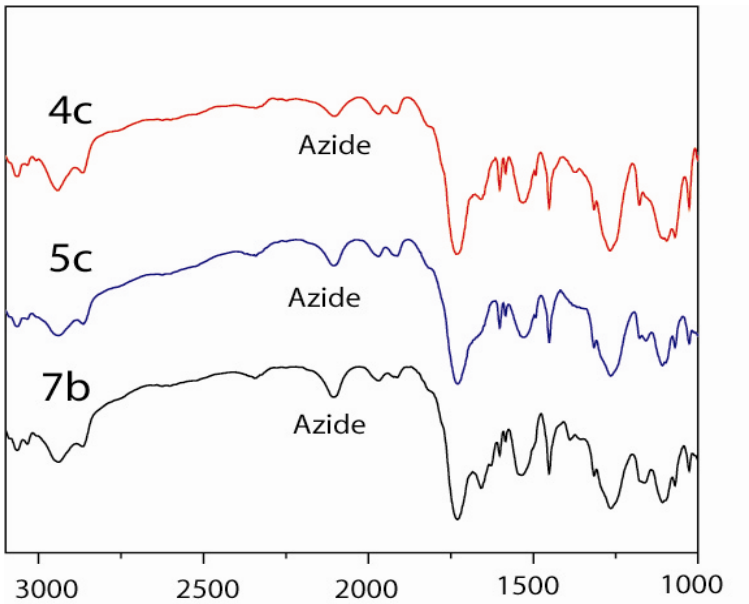


S2. ^{1}H NMR of polymer **9**.

Estimation of the monomer ratio in poly-PMBnLG-*b*-poly-per-*O*-benzoylated-D-glucose-L-lysine (6a)

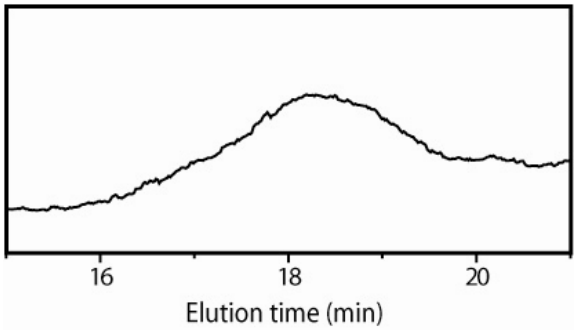
The ratio of PMBn-glu and β-gluco-O-lys in polymer **6a** was estimated using ^{1}H NMR. The ratios of the number of protons H_d to H_e, that are characteristic of both the monomers, were used for calculation. The ratio was found out to be 1:1.5 (expected 1:1.7).

FT-IR of the azide end functionalized glycopolypeptides 4c, 5c and 7b



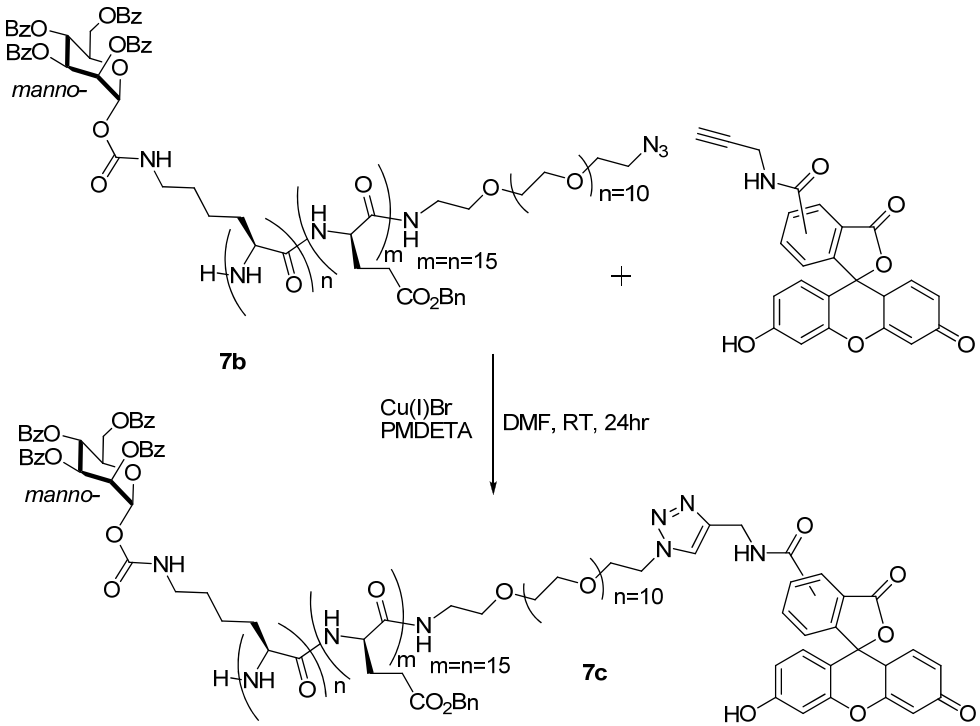
S3. FT-IR of end-functionalized polymers **4c**, **5c**, and **7b**.

Size exclusion chromatogram of glycopolypeptide 4a (Run 1, Table 1)



S4. Size exclusion chromatogram of polymer **4a** synthesized in acetonitrile

Quantitaive estimation of amount of azide-PEG in polymer 7b

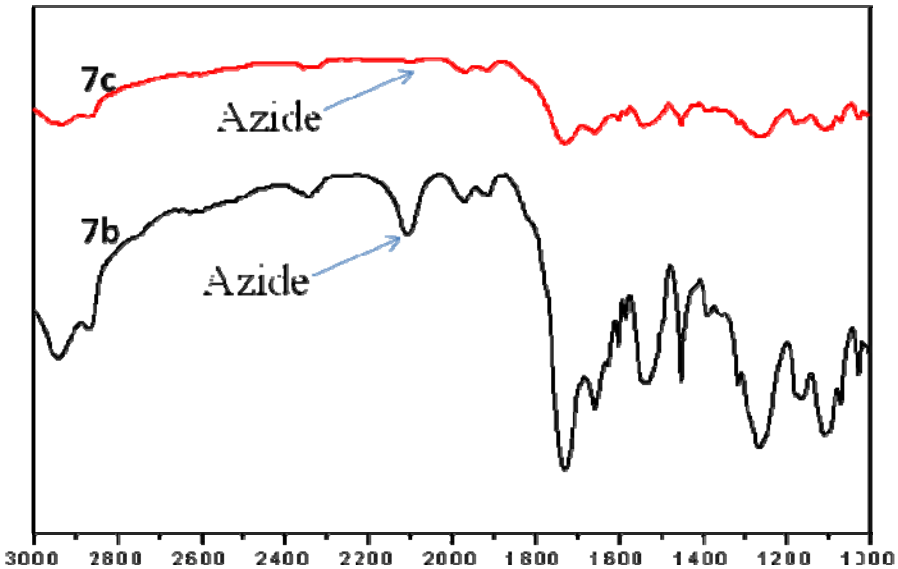


Scheme 4. Click reaction of Azido labeled block copolymer **7b** with fluorescein-alkyne

*Synthesis of fluorescein labelled block polypeptide **7c***

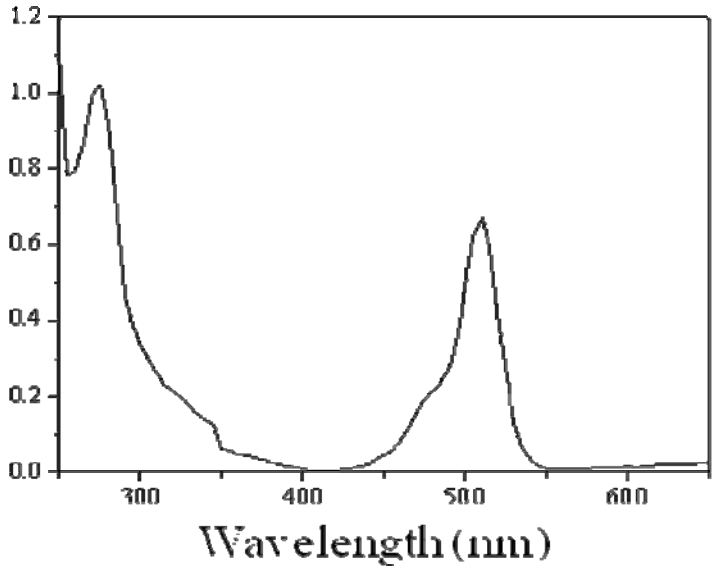
The alkyne labelled fluorescein was synthesized according to published procedures (Bioconjugate Chem. **2005**, *16*, 1536). To a solution of 22 mg azide functionalized blockcopolymer (**7b**) in DMF was added alkyl fluorecein (1mg, 3 eq), Cu(I)Br (0.1 mg, 0.50 eq) and PMDETA (0.5 eq) under nitrogen and o the reaction mixture was stirred for 24 hrs. The completion of the reaction was observed by the near dissaperance (more than 90-95%) of the azide stretching by FT-IR. Then, the solvent was removed under reduced pressure and the reaction mixture was dissolved in dichloromethane. It was then washed multiple times using dil aqueous ammonia solution to remove copper(I) salt and excess fluorecein alkyne. Finally the dichloromethane was removed and the resultant polymer **7c** reprecipitated three times by addition of methanol to the solution of **7c** in dichloromethane. Polymer **7c** was thoroughly dried and its absorption spectra taken in UV-VIS spectrophotometer. Yield: 8 mg

FT-IR spectra



S5. FT-IR spectra for azide functionalized polymer **7b** and the crude reaction mixture upon completion of the click reaction (**7c**)

UV-VIS Spectra of **7c**

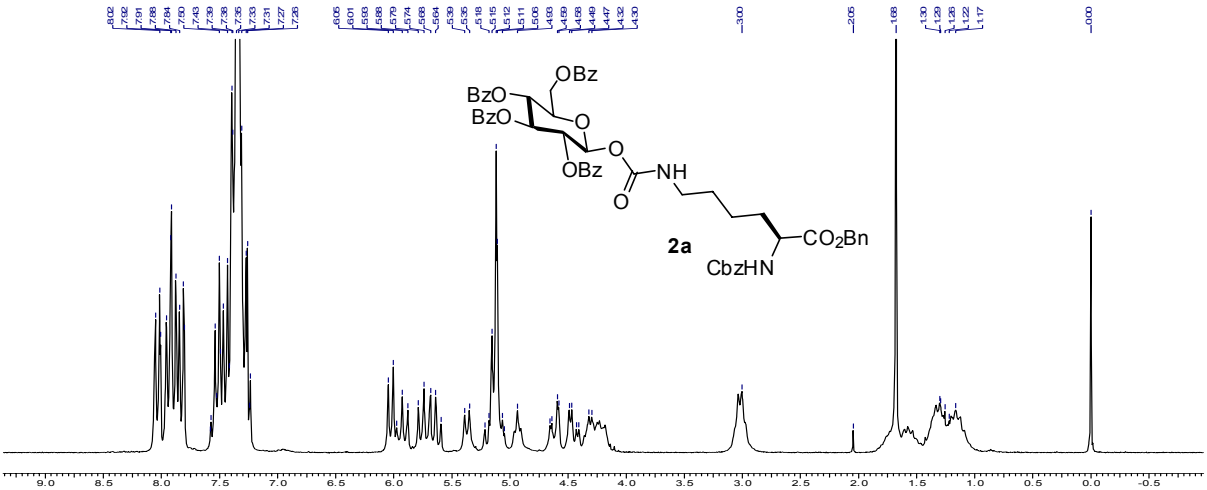


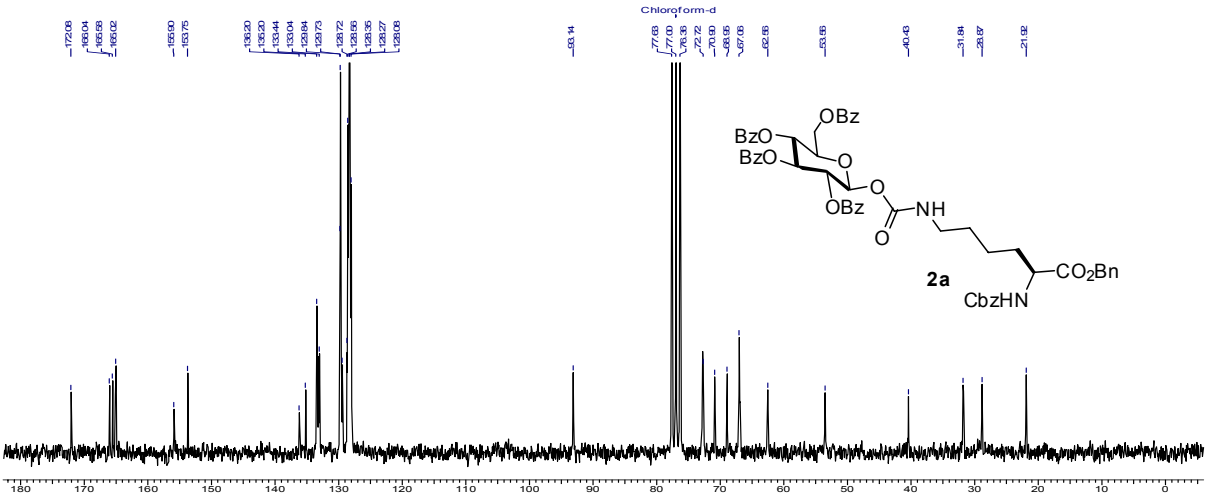
S6. UV-VIS spectra of the fluorescein labelled polymer **7c** solution (10 μM) in DMF/pH7 100 mM phosphate buffer mixture.

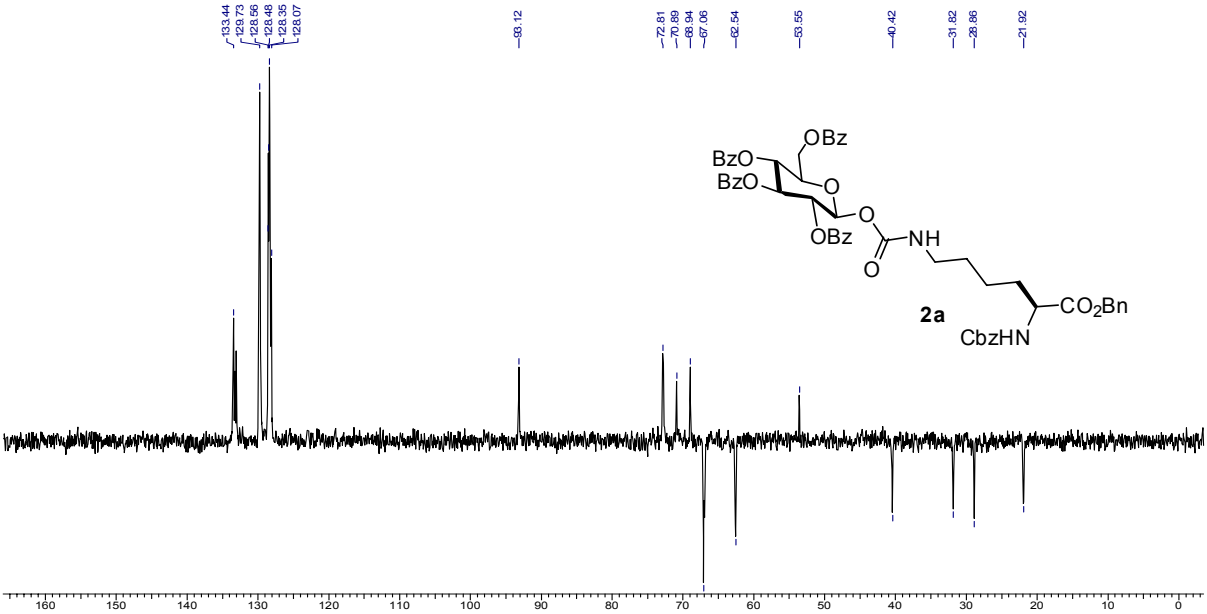
*Method for estimation of azide incorporation into block copolypeptide **7b***

The block copolypeptide **7b** was converted to **7c** using click chemistry. The theoretical concentration of the fluorescein labelled polymer **7c** was calculated using the M_n value of 19,000 kDa that was obtained from GPC. Since only one fluorescein moiety will be conjugated to the polymer if all the polymer chains have one azide group attached to its end, the concentration of fluorescein in solution would be equal to the concentration of the polymer. The concentration of fluorescein in solutions of **7c** was estimated from its absorption spectra (λ_{max}=510 nm, ε=90,000 $M^{-1}cm^{-1}$) in DMF/pH7 phosphate buffer mixtures. (Ref: Spectroscopic Letters, **1994**, *27*, 1049) The percentage of azide group incorporated was estimated from the ratio of the experimentally calculated concentration from absorption spectra of fluorescein to the theoretical concentration calculated from M_n values of **7b**.

^{1}H and ^{13}C Spectra of monomers and polymers



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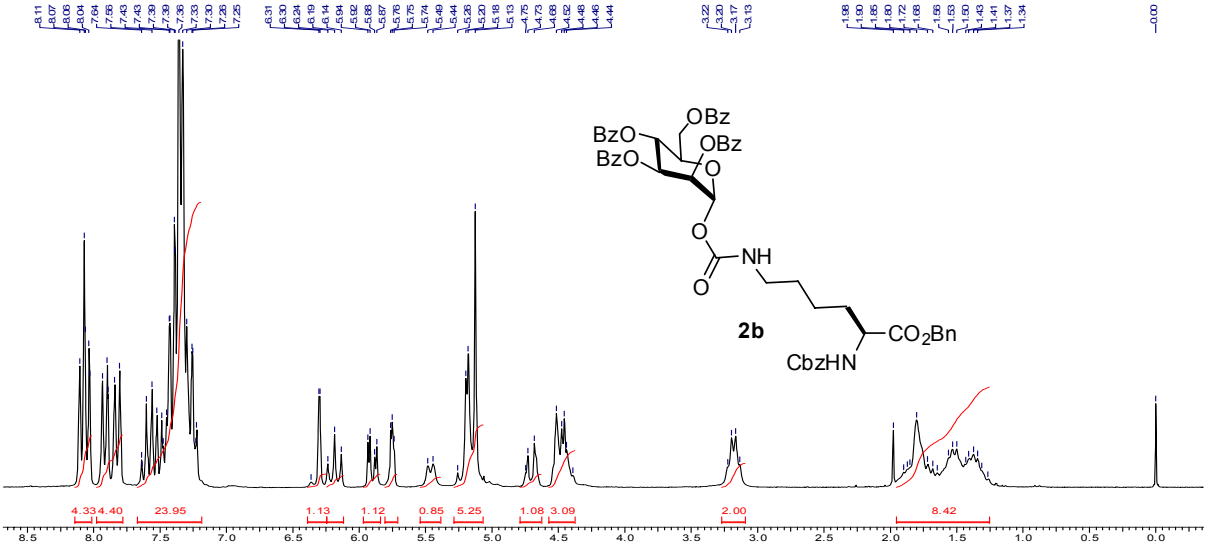
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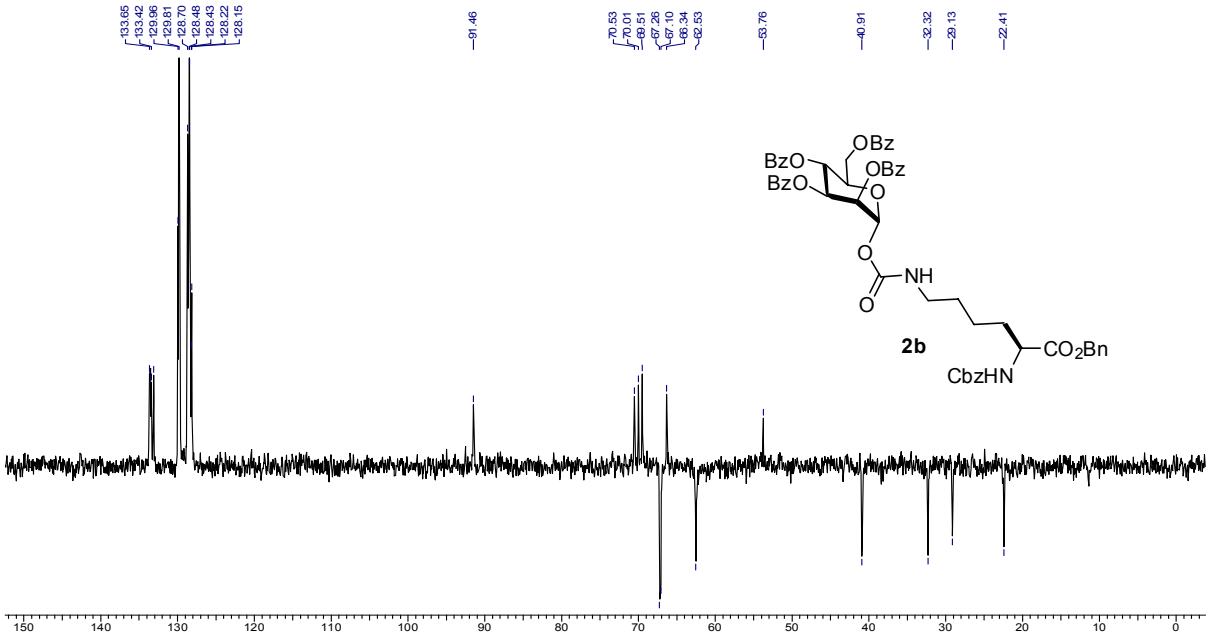
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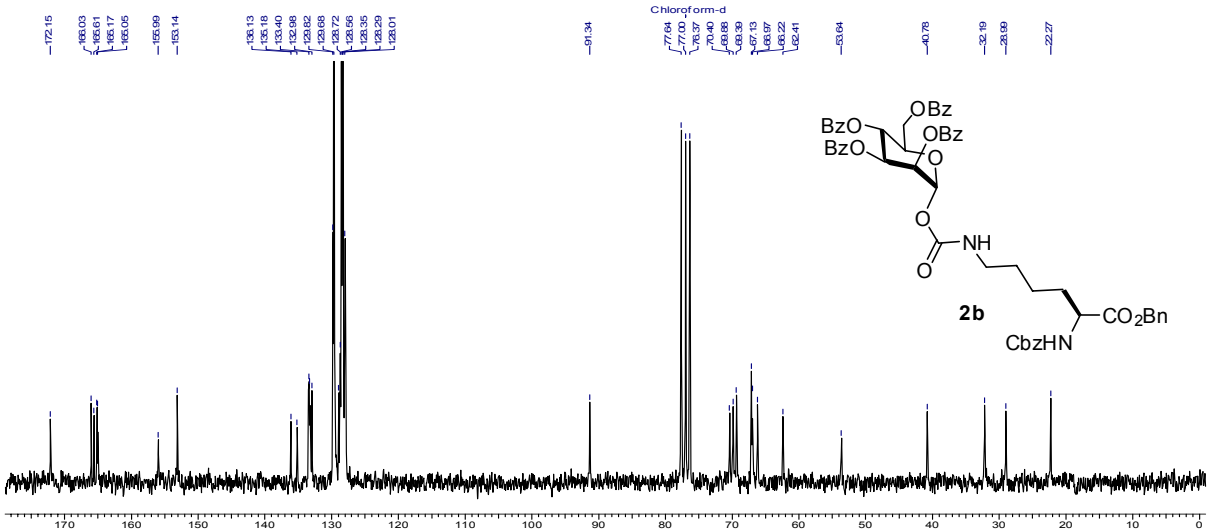
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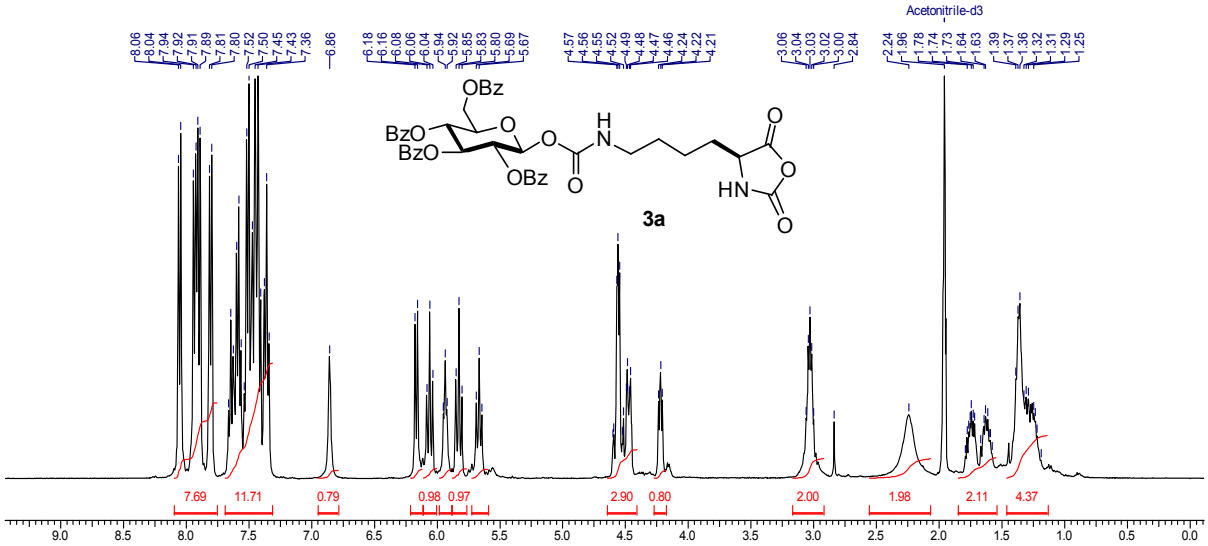
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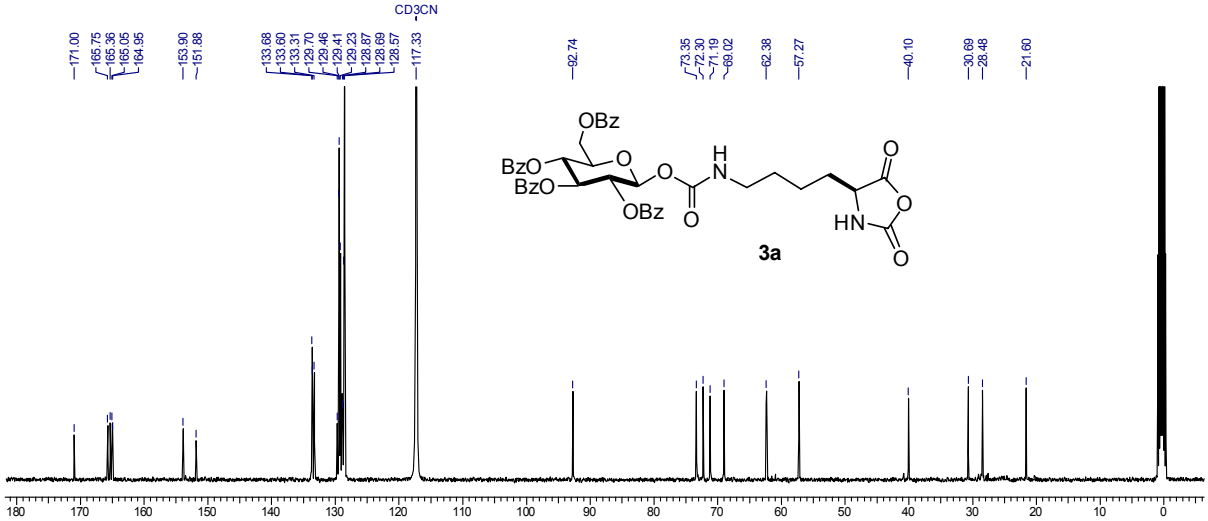
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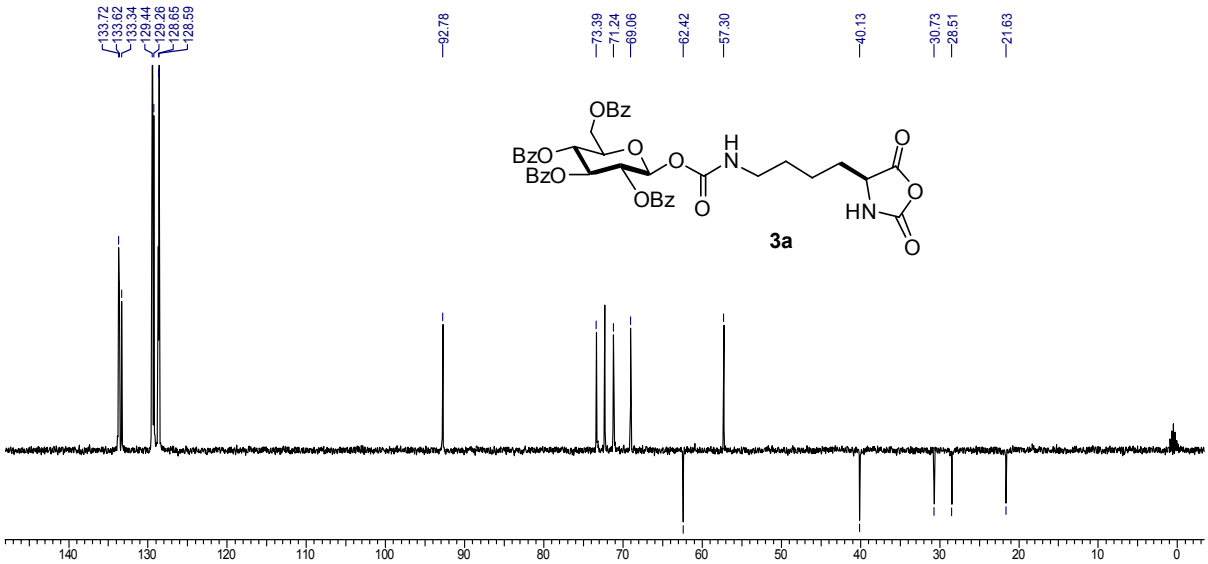
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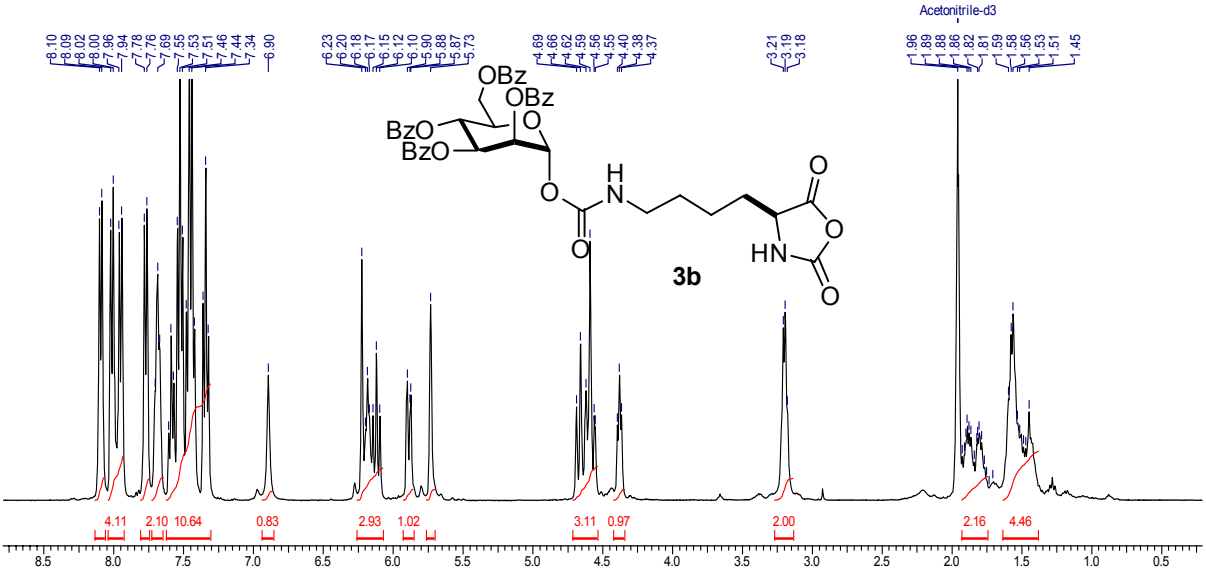
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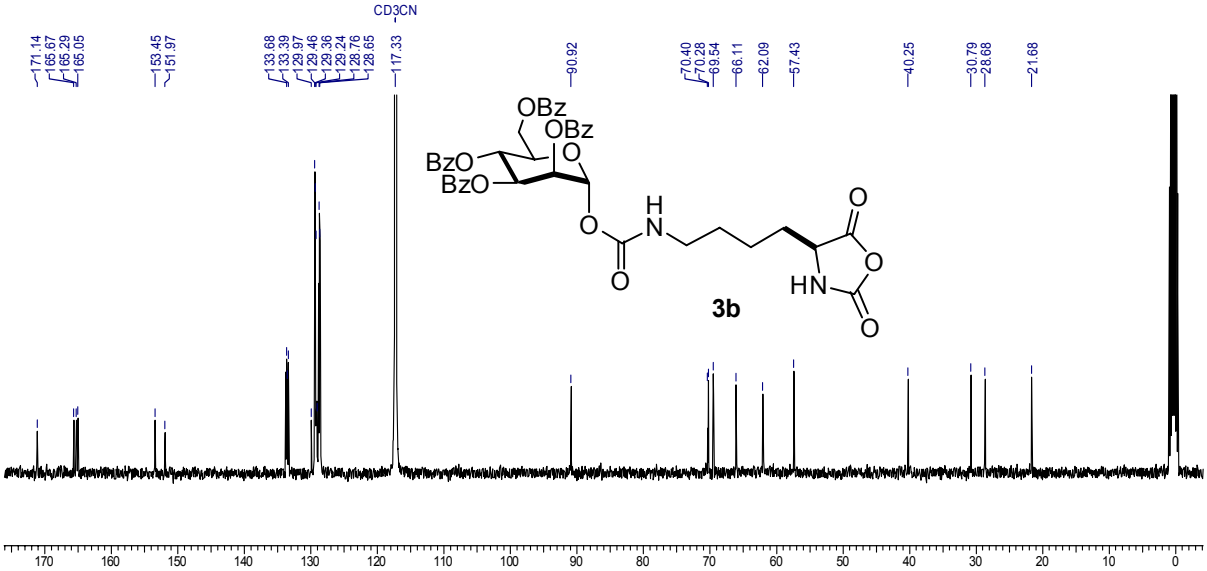
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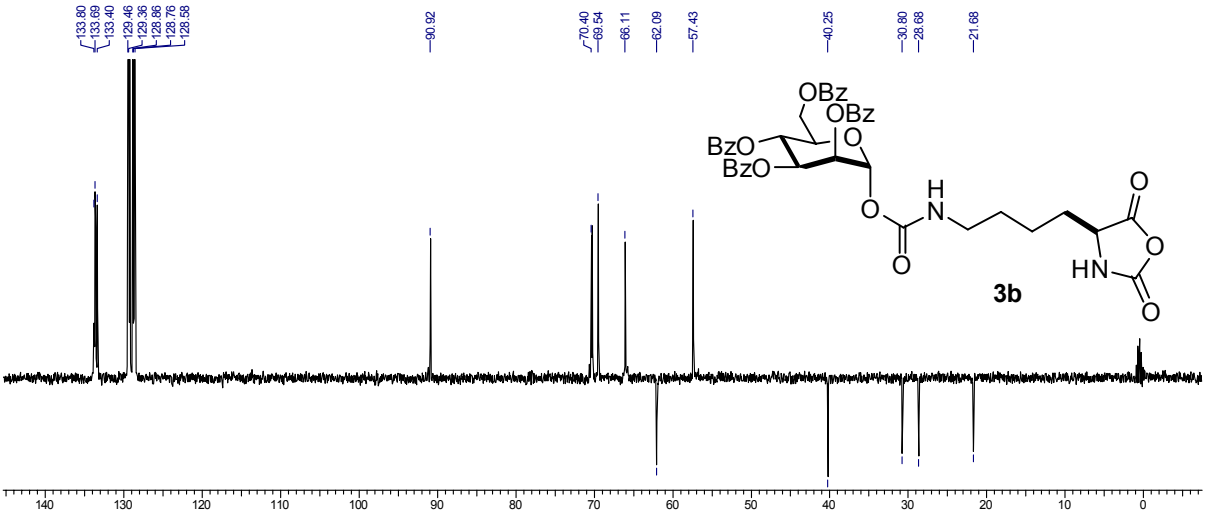
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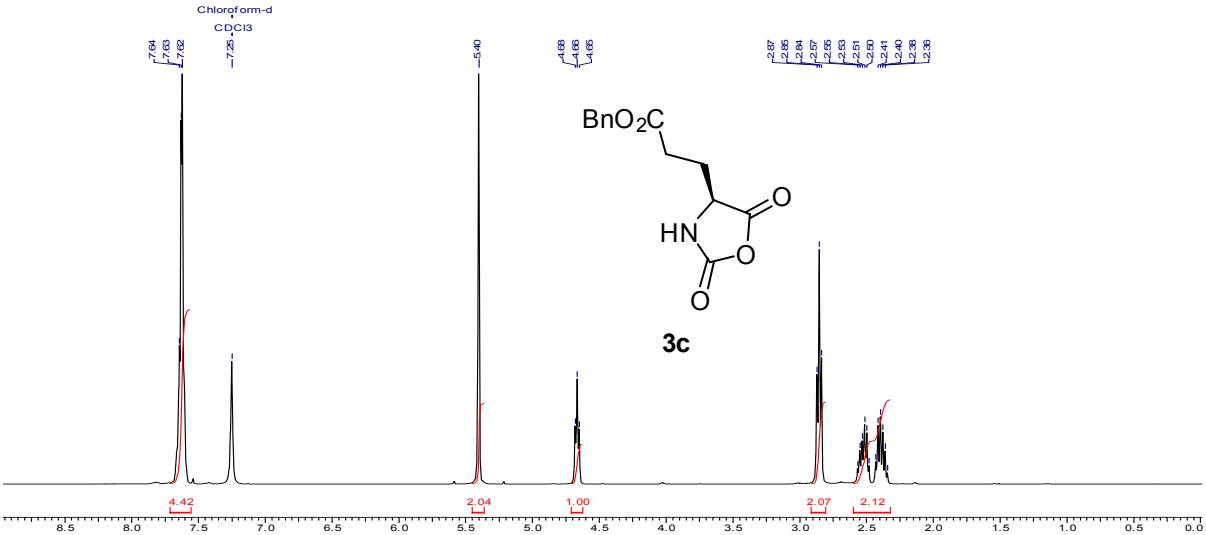
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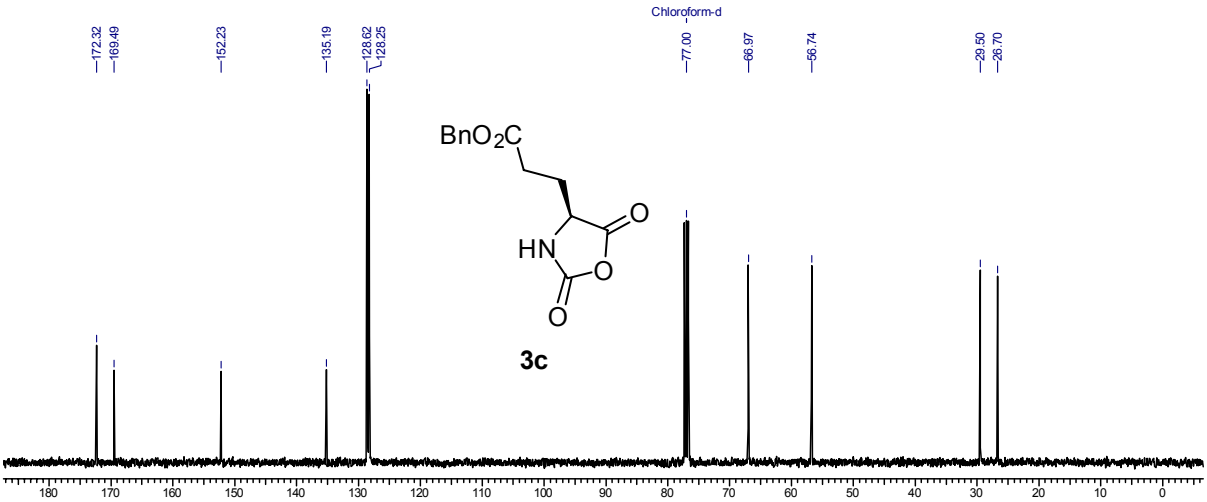
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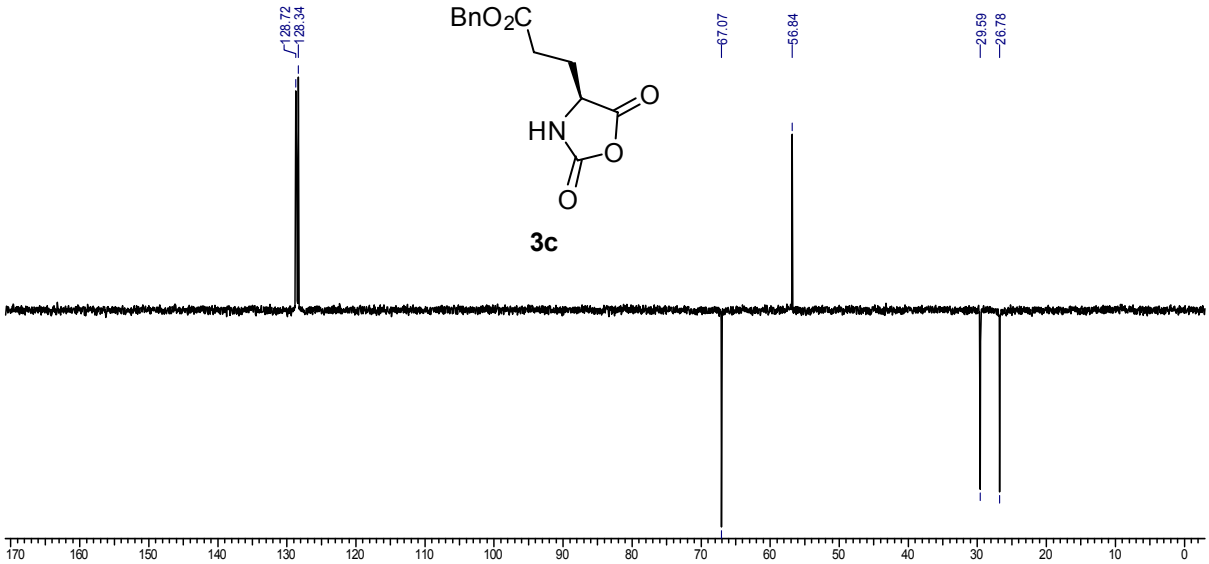
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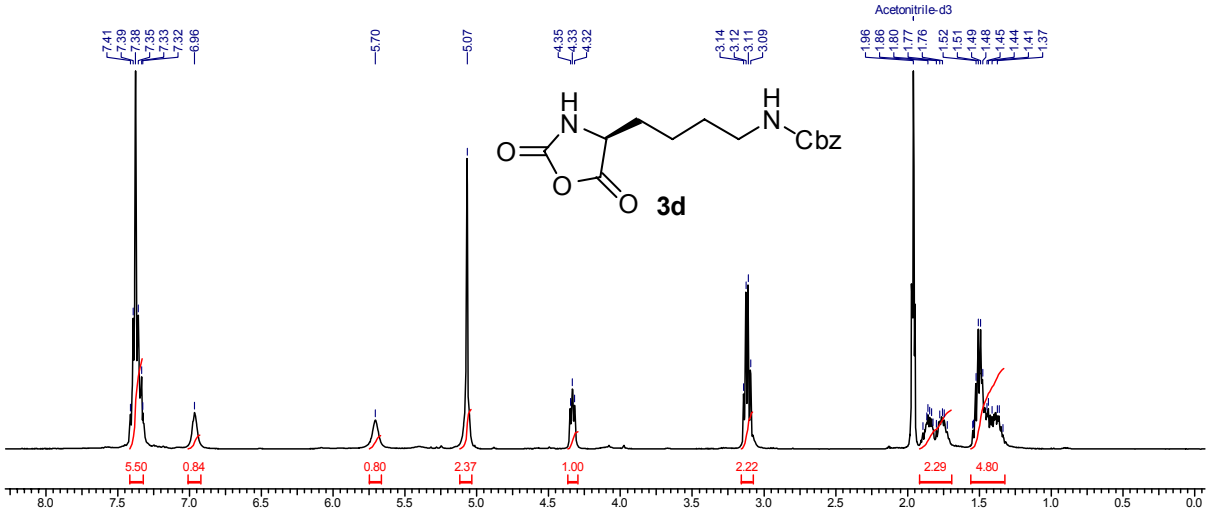
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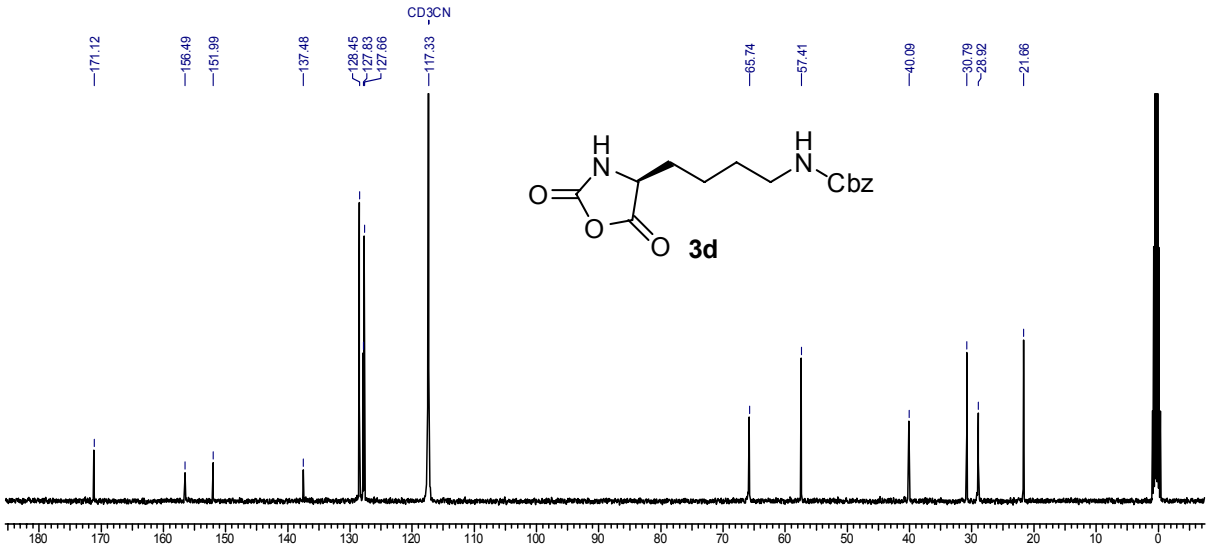
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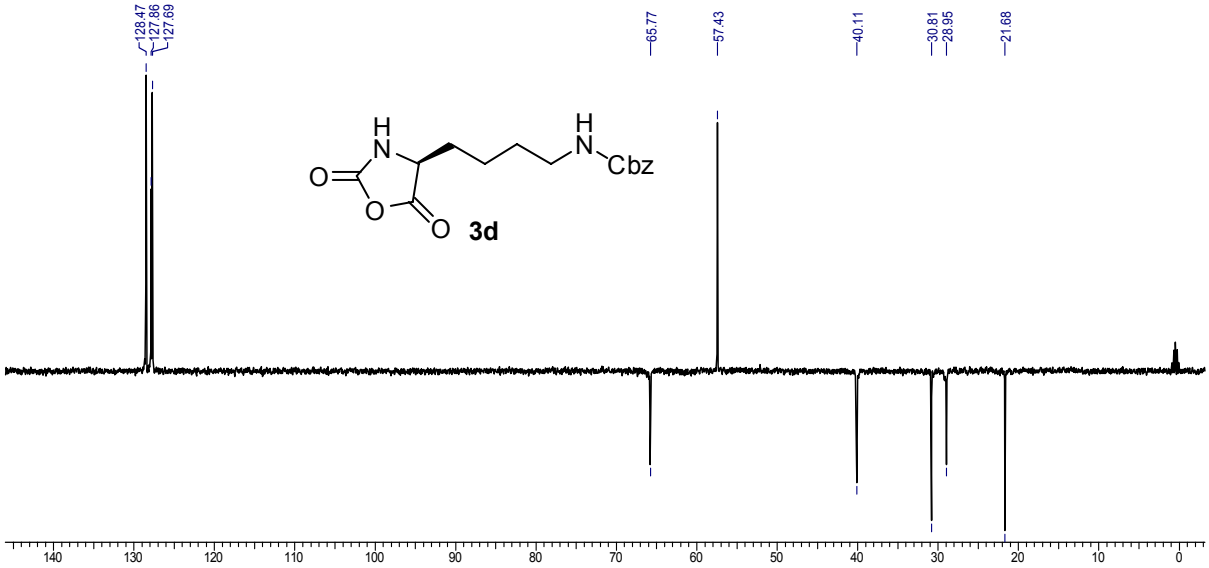
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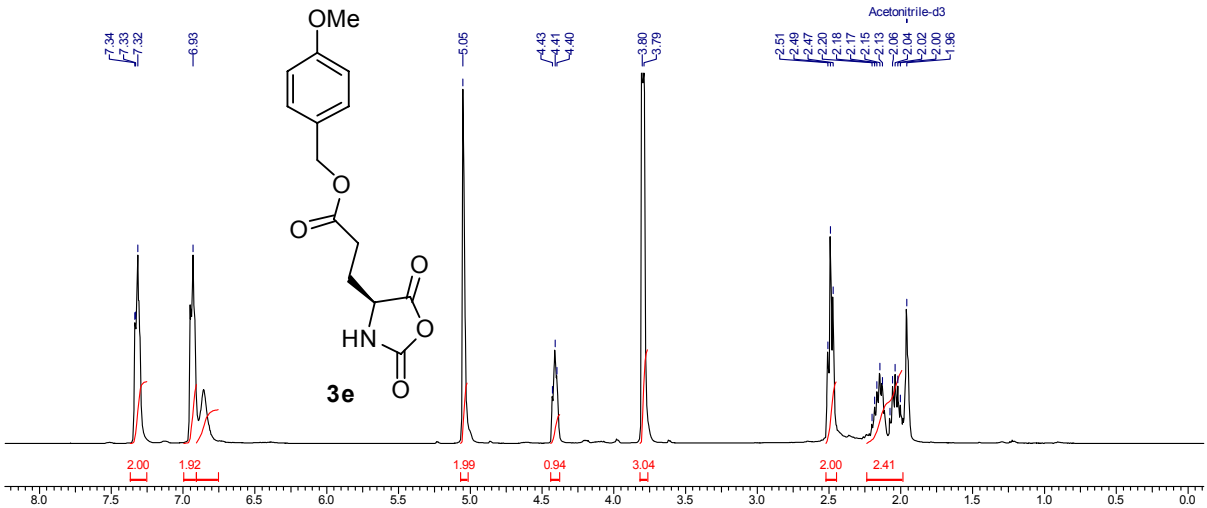
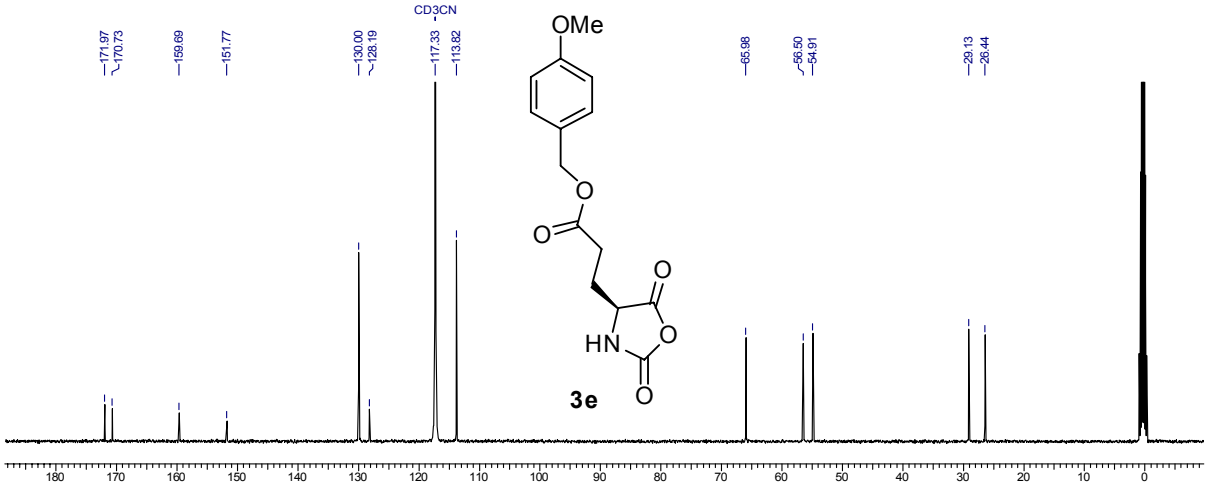
3d


OMe
7.34
7.33
7.32
6.93
5.05
4.43
4.41
4.40
3.80
3.79
Acetonitrile-d3
2.51
2.49
2.47
2.20
2.18
2.17
2.15
2.13
2.06
2.04
2.02
2.00
1.96
3e
2.00
1.92
1.99
0.94
3.04
2.00
2.41


CD3CN
171.97
170.73
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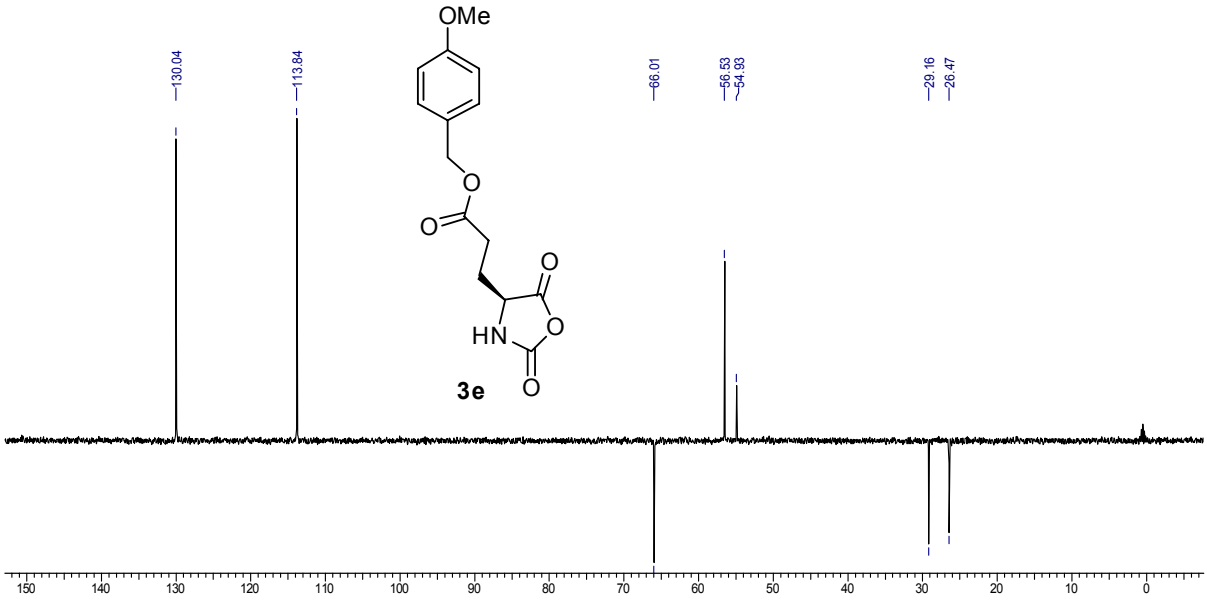
128.19
117.33
113.82
OMe
65.98
56.50
54.91
29.13
26.44
3e


OMe
130.04
113.84
66.01
56.53
54.93
29.16
26.47
O
O
O
O
HN
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3e
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140
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70
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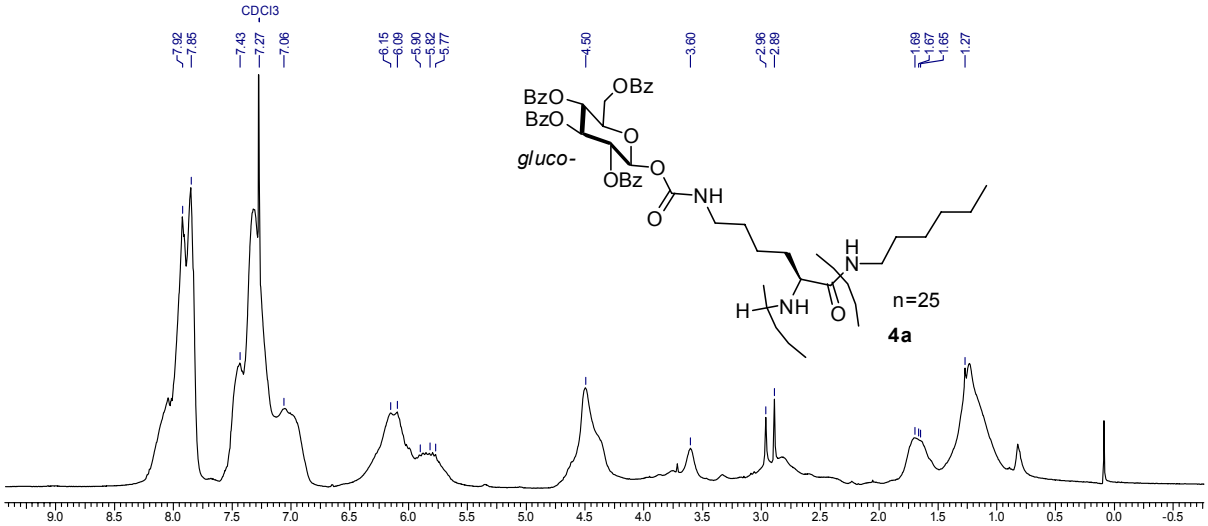
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7.92
7.85
7.43
7.27
7.06
6.15
6.09
5.90
5.82
5.77
4.50
3.60
2.96
2.89
1.69
1.67
1.65
1.27
BzO
BzO
OBz
O
gluco-
OBz
O
NH
O
H
N
H
NH
O
n=25
4a
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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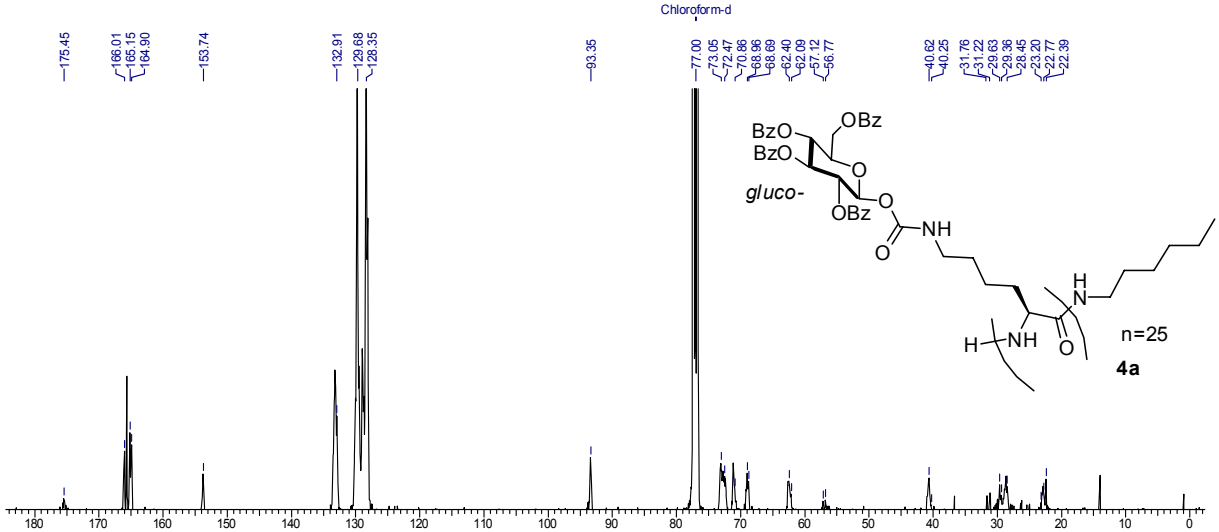
0.0
-0.5


Chloroform-d
175.45
166.01
165.15
164.90
153.74
132.91
129.68
128.35
93.35
77.00
73.05
72.47
70.86
68.96
68.69
62.40
62.09
57.12
56.77
40.62
40.25
31.76
31.22
29.63
29.36
28.45
23.20
22.77
22.39
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BzO
OBz
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gluco-
OBz
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NH
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H
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NH
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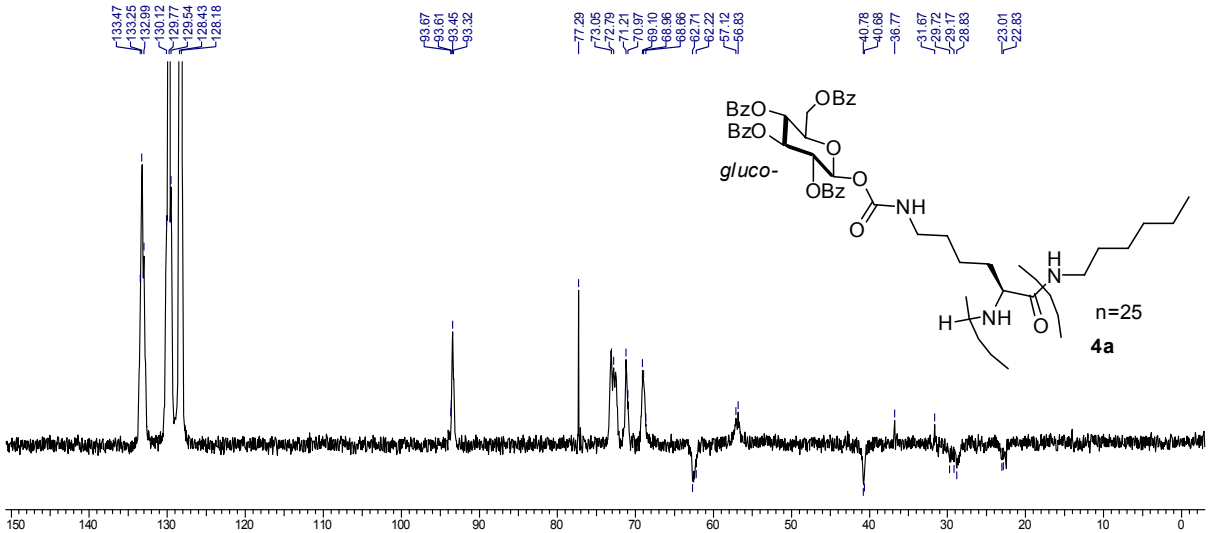
n=25
4a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128.43
128.18
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93.45
93.32
77.29
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70.97
69.10
68.96
68.66
62.71
62.22
57.12
56.83
40.78
40.68
36.77
31.67
29.72
29.17
28.83
23.01
22.83
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OBz
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OBz
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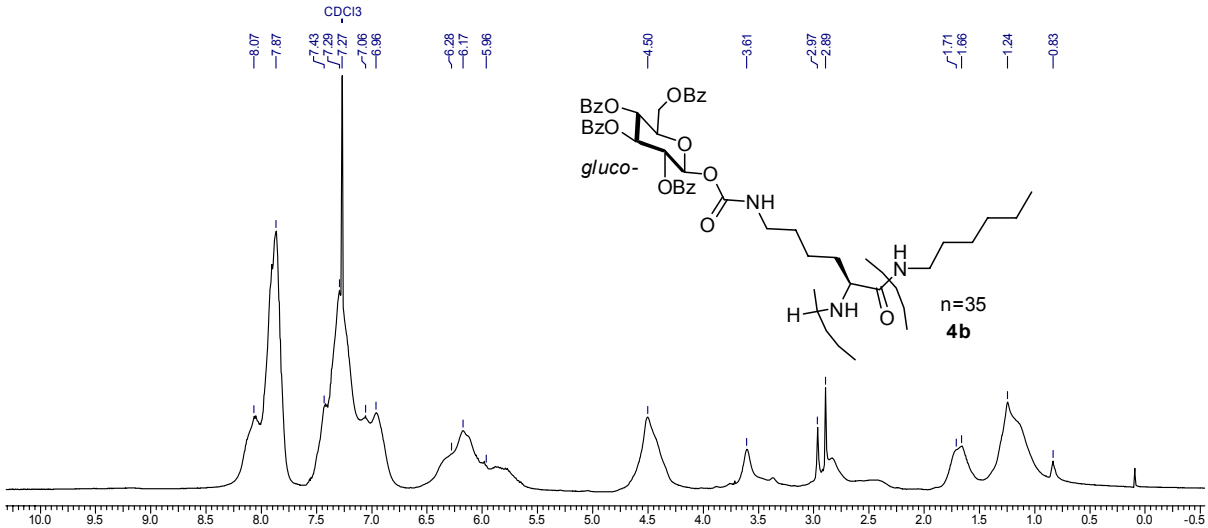
4a


CDCl3
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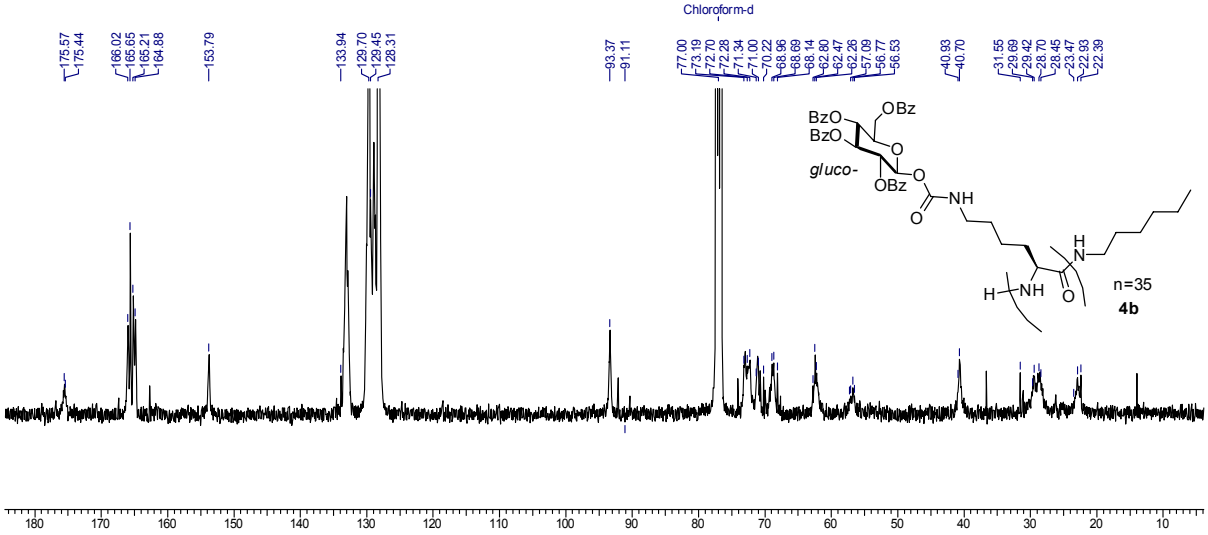
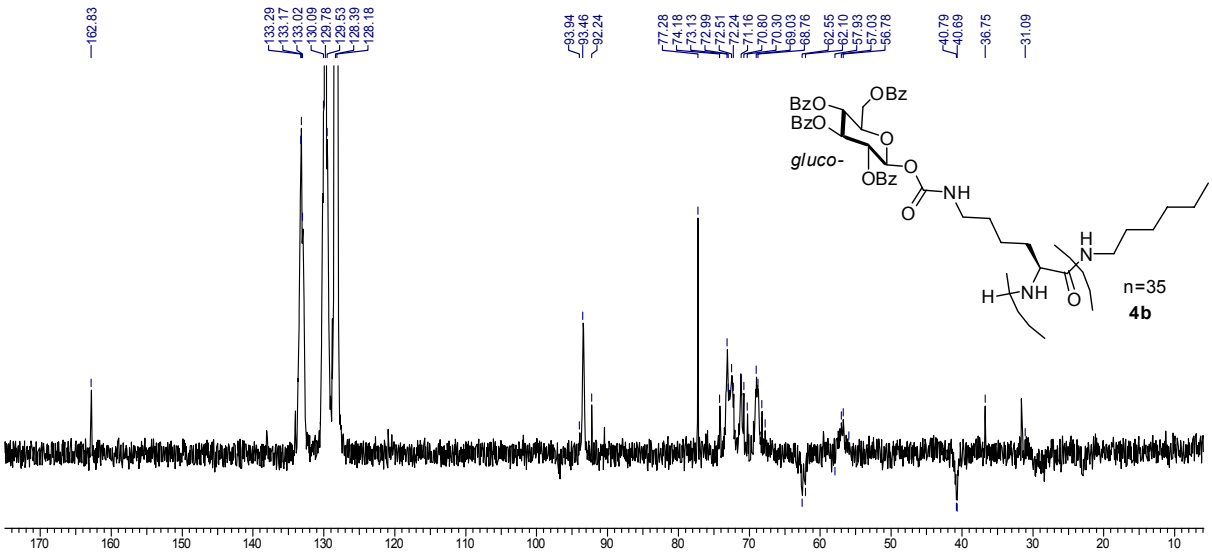
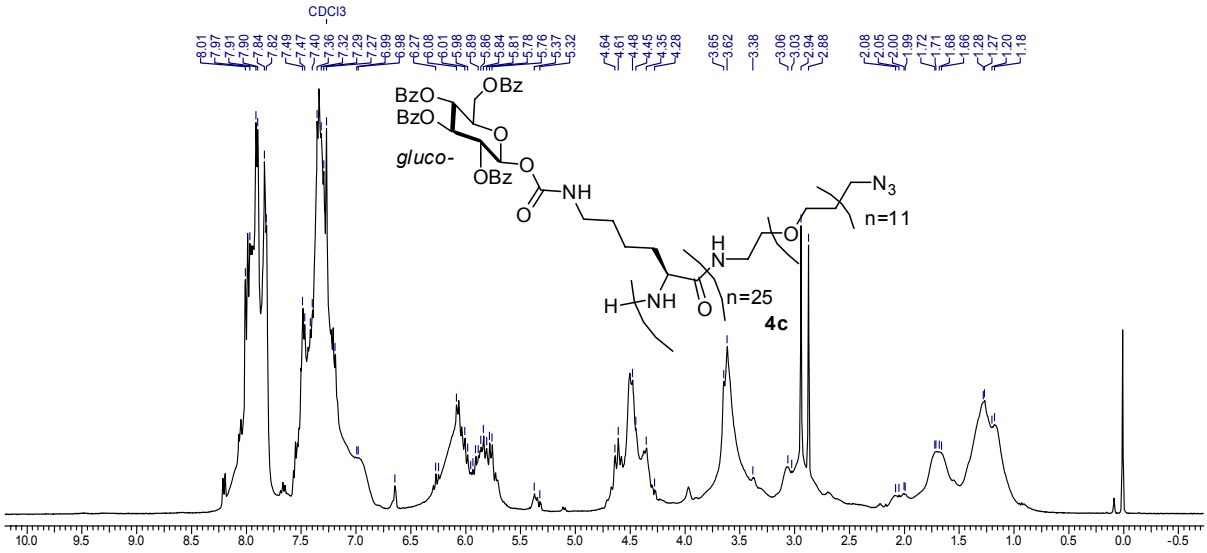
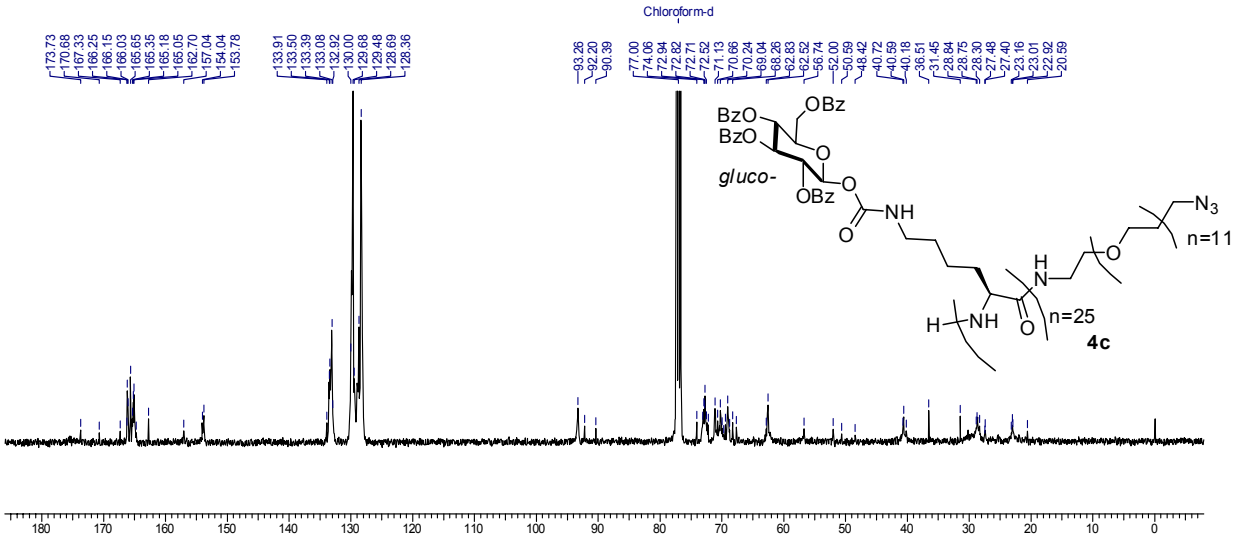
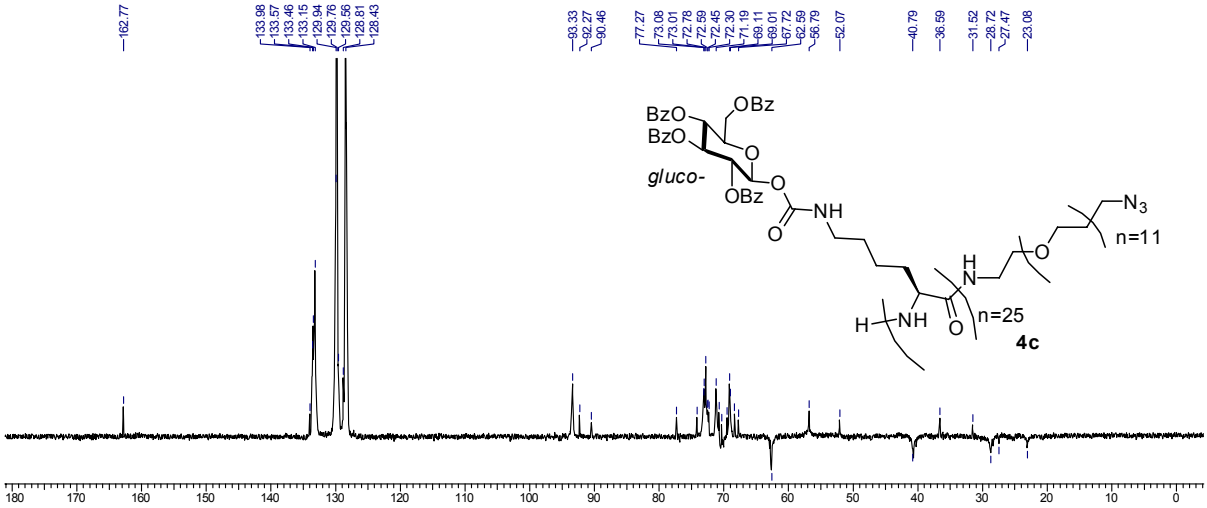
7.87
7.43
7.29
7.27
7.06
6.96
6.28
6.17
5.96
4.50
3.61
2.97
2.89
1.71
1.66
1.24
0.83
BzO
BzO
OBz
O
gluco-
OBz
O
NH
O
H
N
H
NH
O
n=35
4b

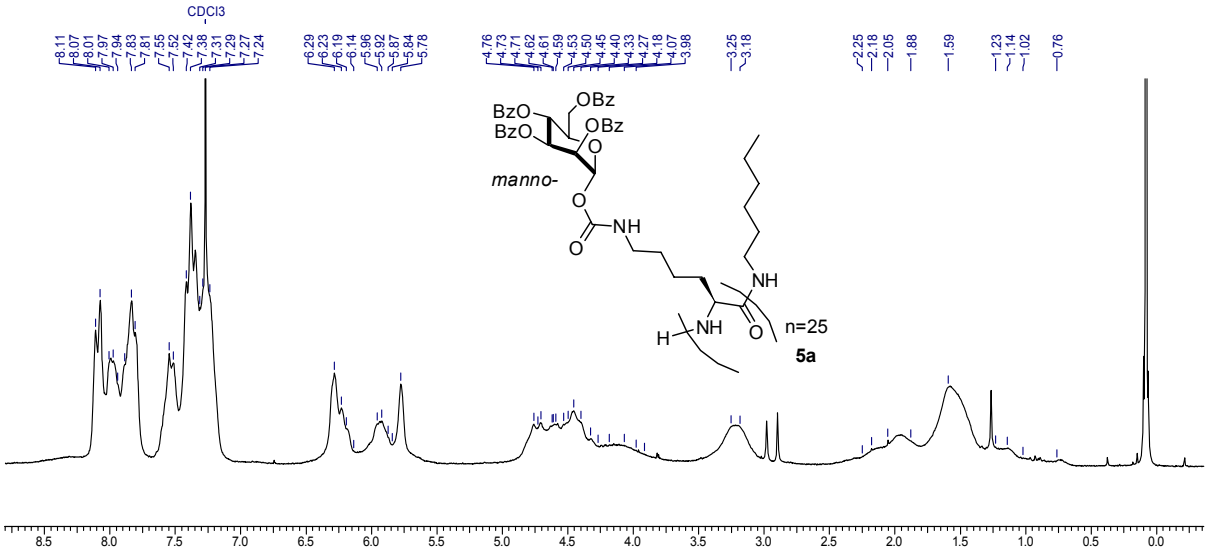

Chloroform-d
BzO
BzO
OBz
O
gluco-
OBz
O
NH
O
H
N
H
NH
O
n=35
4b

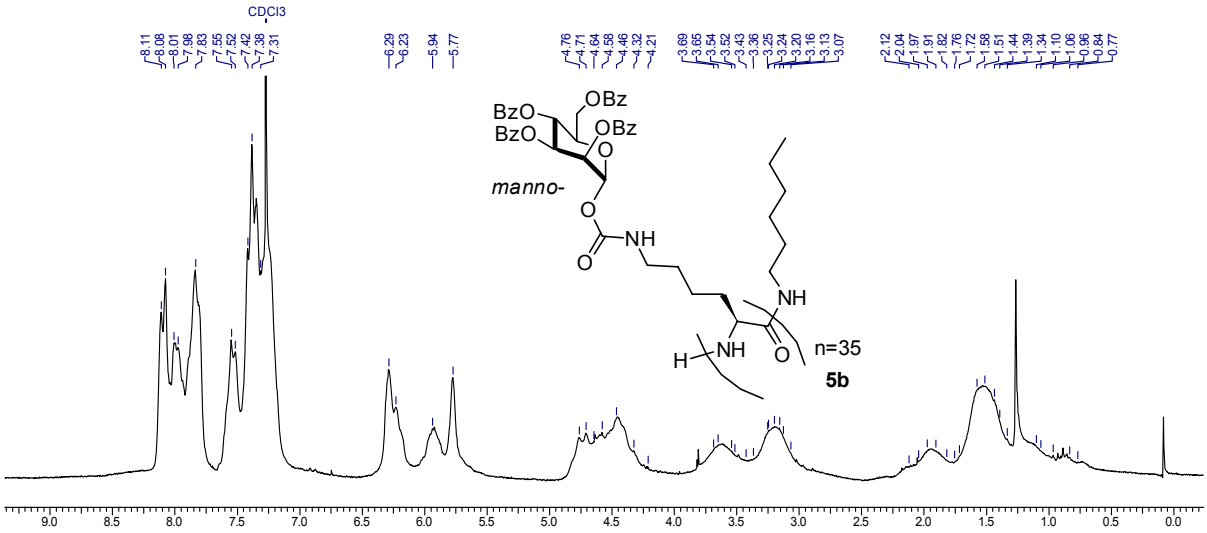

BzO
BzO
OBz
O
gluco-
OBz
O
NH
O
H
N
H
NH
O
n=35
4b


CDCl3
BzO
BzO
OBz
O
gluco-
OBz
O
NH
O
N3
n=11
O
H
N
H
NH
O
n=25
4c


Chloroform-d
BzO
BzO
OBz
OBz
gluco-
NH
N3
n=11
n=25
4c


BzO
BzO
OBz
OBz
gluco-
NH
N3
n=11
n=25
4c


CDCl3
BzO
BzO
OBz
OBz
manno-
NH
n=25
5a


CDCl3
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6.29 6.23
5.94
5.77
4.76 4.71 4.64 4.58 4.46 4.32 4.21
3.69 3.65 3.54 3.52 3.43 3.36 3.25 3.24 3.20 3.16 3.13 3.07
2.12 2.04 1.97 1.91 1.82 1.76 1.72 1.58 1.51 1.44 1.39 1.34 1.10 1.06 0.96 0.84 0.77
BzO
BzO
OBz
OBz
O
manno-
O
NH
O
NH
H
NH
O
n=35
5b
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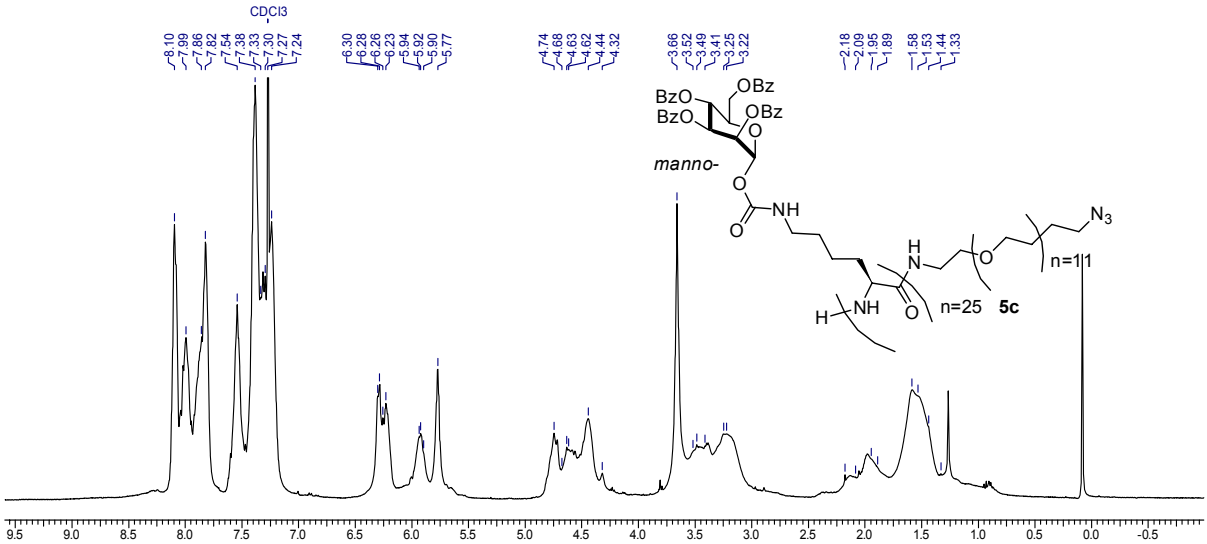
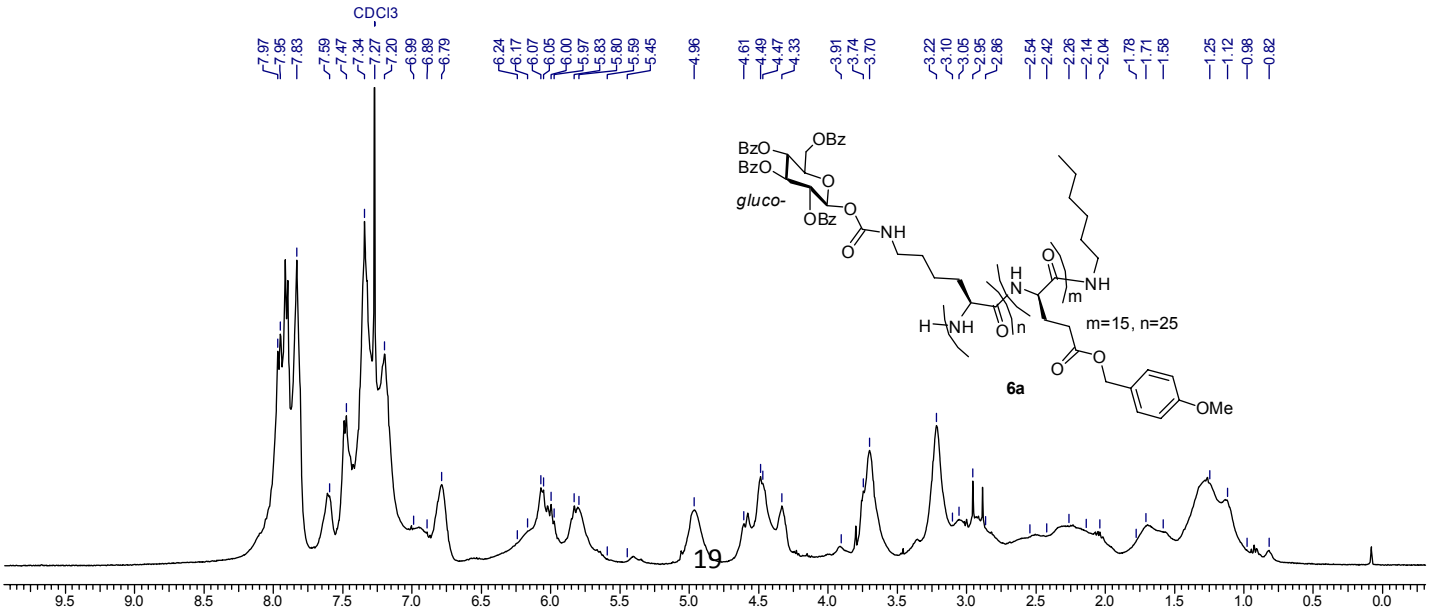

CDCl3
8.10 7.99 7.86 7.82 7.54 7.38 7.33 7.30 7.27 7.24
6.30 6.28 6.26 6.23
5.94 5.92 5.90 5.77
4.74 4.68 4.63 4.62 4.44 4.32
3.66 3.52 3.49 3.41 3.25 3.22
2.18 2.09 1.95 1.89
1.58 1.53 1.44 1.33
BzO
BzO
OBz
OBz
O
manno-
O
NH
O
H
N
O
N3
n=11
H
NH
O
n=25
5c
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


CDCl3
7.97 7.95 7.83
7.59 7.47 7.34 7.27 7.20
6.99 6.89 6.79
6.24 6.17 6.07 6.05 6.00 5.97 5.83 5.80 5.59 5.45
4.96
4.61 4.49 4.47 4.33
3.91 3.74 3.70
3.22 3.10 3.05 2.95 2.86
2.54 2.42
2.26 2.14 2.04
1.78 1.71 1.58
1.25 1.12 0.98 0.82
BzO
BzO
OBz
OBz
O
gluco-
O
NH
O
H
N
O
m
NH
H
NH
O
n
m=15, n=25
O
O
6a
OMe
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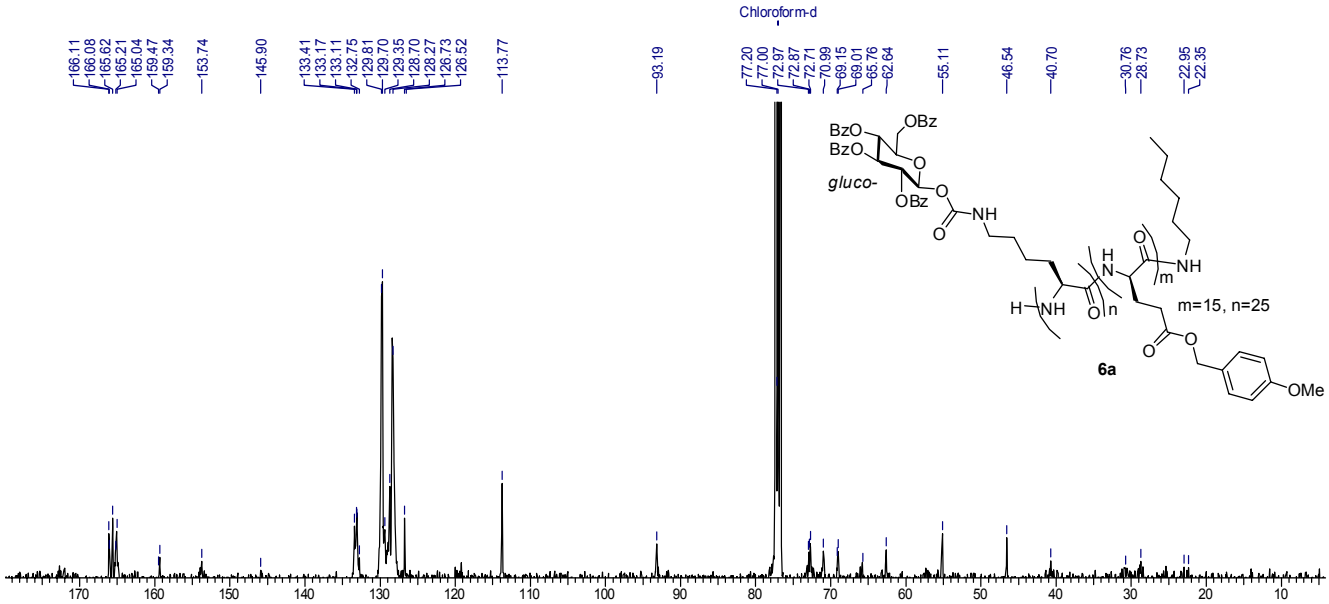
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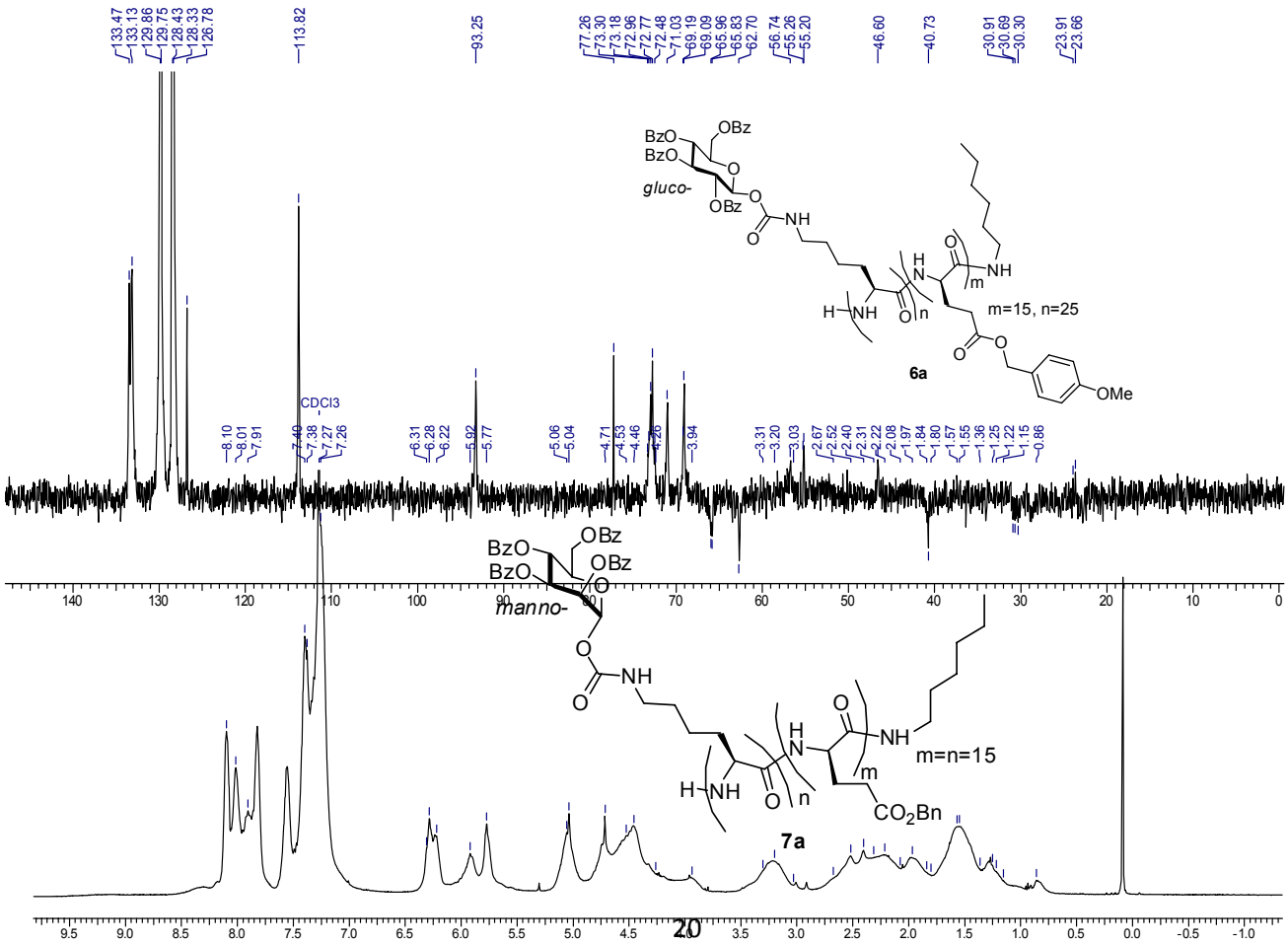
m=15, n=25
6a


CDCl3
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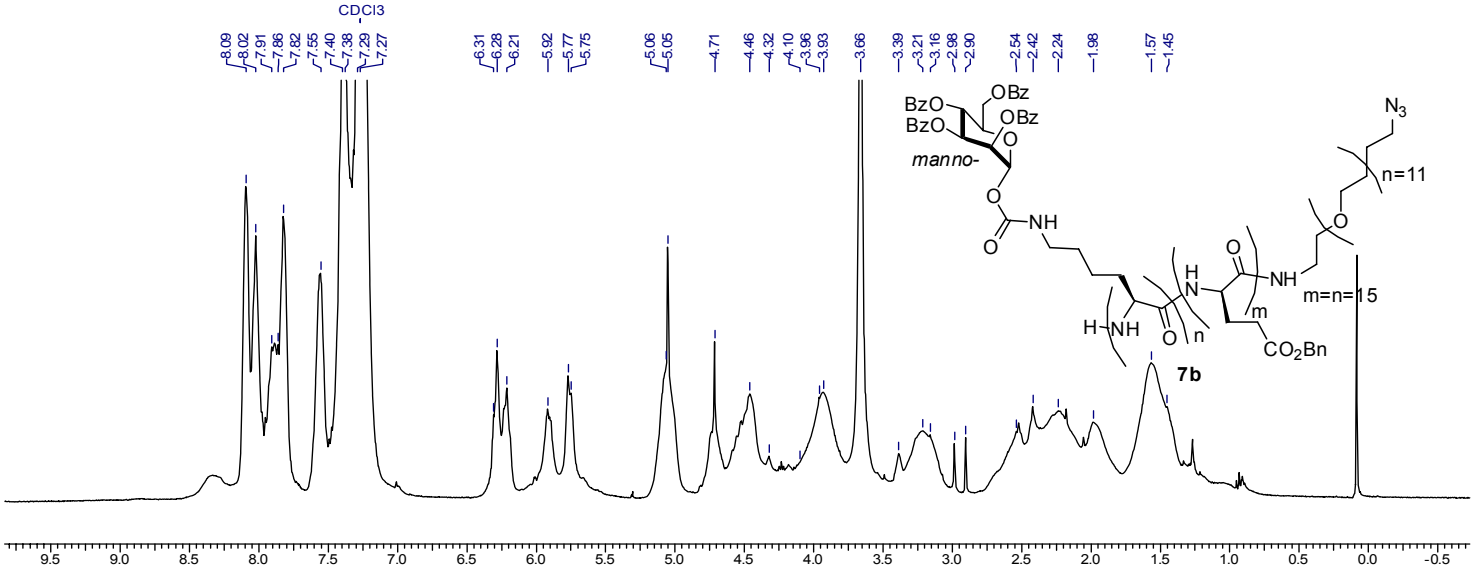
m=15, n=25
6a
manno-
m=n=15
7a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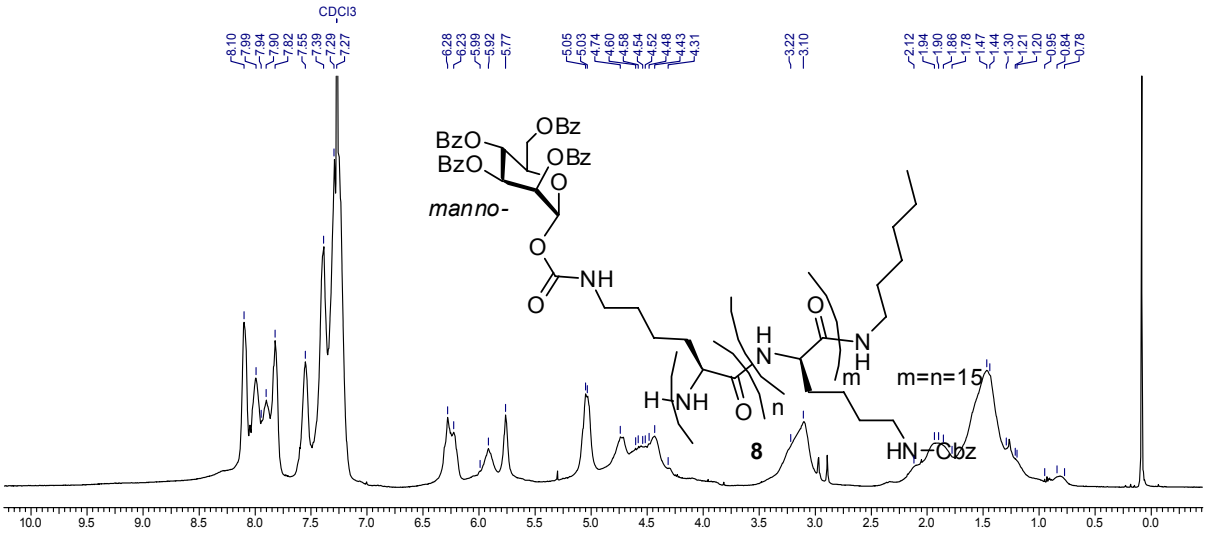
manno-
n=11
m=n=15
7b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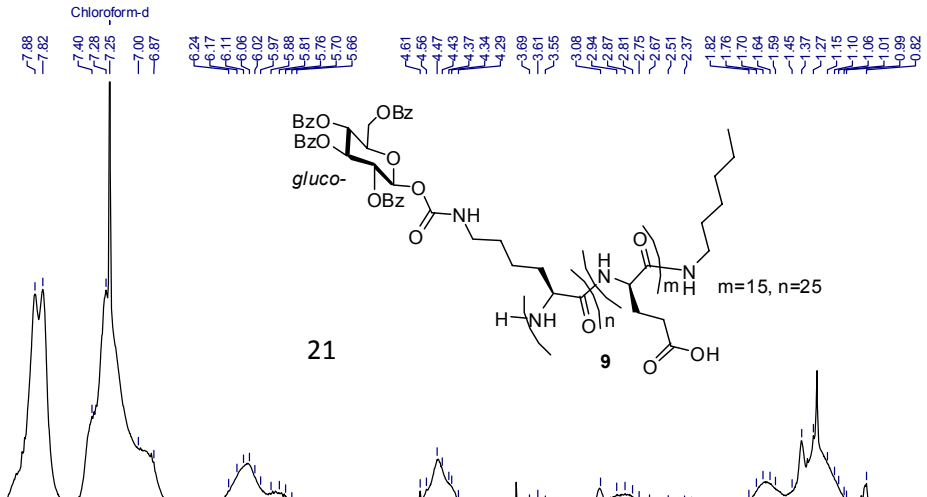
Chloroform-d
gluco-
m=15, n=25
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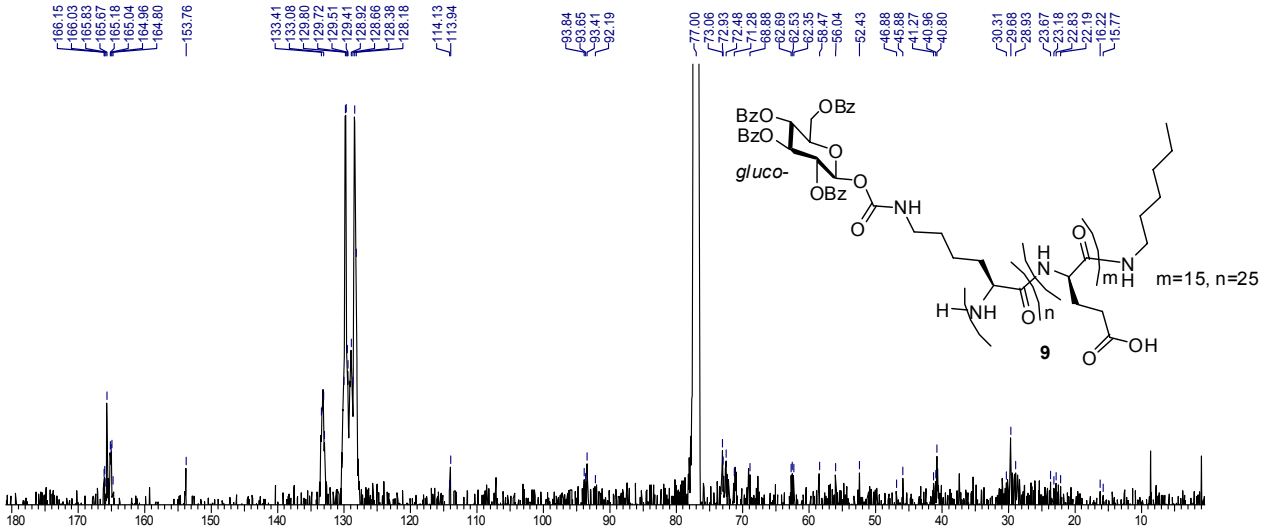
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129.51
129.41
128.92
128.66
128.38
128.18
114.13
113.94
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93.65
93.41
92.19
77.00
73.06
72.93
72.48
71.28
68.88
62.69
62.53
62.35
58.47
56.04
52.43
46.88
45.88
41.27
40.96
40.80
30.31
29.68
28.93
23.67
23.18
22.83
22.19
16.22
15.77
BzO
BzO
OBz
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gluco-
OBz
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O
N
m
H
m=15, n=25
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NH
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n
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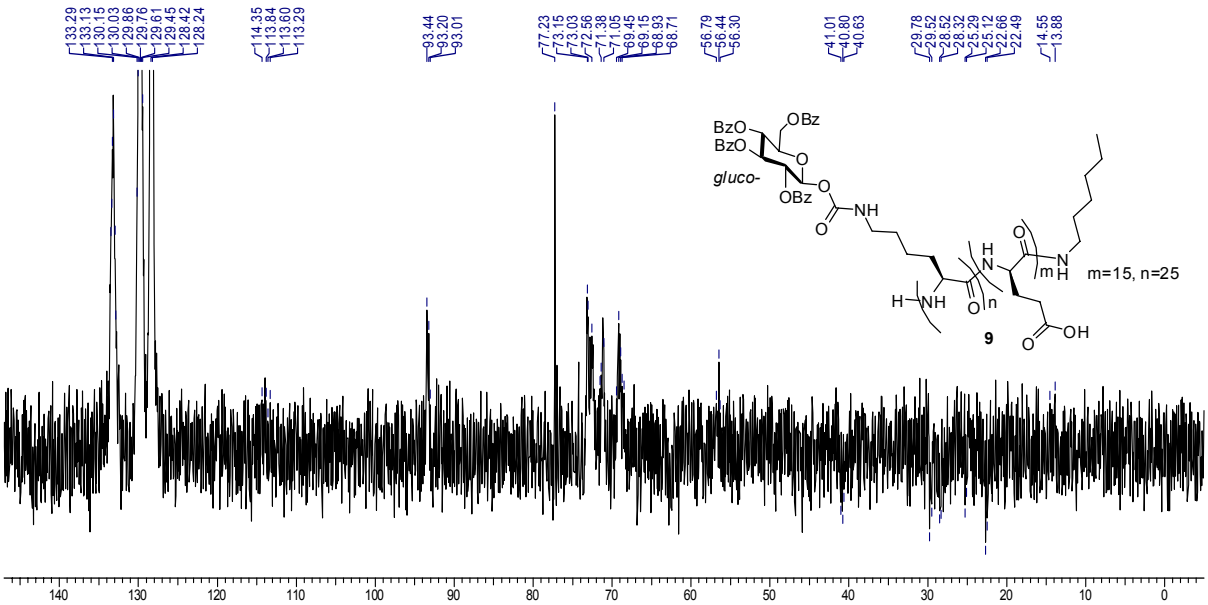
10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113.60
113.29
93.44
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93.01
77.23
73.15
73.03
72.56
71.38
71.05
69.45
69.15
68.93
68.71
56.79
56.44
56.30
41.01
40.80
40.63
29.78
29.52
28.52
28.32
25.29
25.12
22.66
22.49
14.55
13.88
BzO
BzO
OBz
O
gluco-
OBz
O
NH
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H
N
O
N
m
H
m=15, n=25
H
NH
O
n
9
OH
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130
120
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100
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80
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30
20
10
0