CHEMISTRY
A EUROPEAN JOURNAL

Supporting Information

Preparation of Carbohydrate Arrays by using Diels–Alder Reactions with Inverse-Electron-Demand

Henning S. G. Beckmann,[a] Andrea Niederwieser,[a] Manfred Wiessler,[b] and Valentin Wittmann*[a]

chem_201200382_sm_miscellaneous_information.pdf

Contents

General Methods

Technical **solvents** were destilled prior to use. All dry solvents were purchased from *Fluka* and *Sigma-Aldrich*, except for dry CH_2Cl_2 that was freshly distilled after refuxing over calcium hydride. **Reagents** were purchased from *Acros, Fisher Scientific, Fluka, Glycon, Merck* and *Sigma-Aldrich* and used without further purification.

Analytical **thin layer chromatography (TLC)** was carried out on TLC Silica gel 60 F_{254} coated aluminium sheets (*Merck*) with detection by UV light (λ = 254 nm). Additionally, following reagents were used for visualization of spots if applicable: ethanolic sulfuric acid (15 %); aqueous potassium permanganate (1 % w/v); ethanolic ninhydrin solution (3 % w/v). After dipping into one of the described solutions, gentle heating was applied.

Preparative **flash column chromatography (FC)** was performed on silica gel Geduran 60 (40 - 60 µm, *Merck*) with solvent systems specified.

Analytical **reversed-phase high performance liquid chromatography (RP-HPLC)** was conducted on a LC-20A prominence system (pumps LC-20AT, auto sampler SIL-20A, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A and software LC-solution) from *Shimadsu*. A Nucleosil 100-5 C-18 column (4 × 250 mm, flow 0.9 mL min^{-1}) was used as stationary phase. A gradient of water with 0.1 % TFA (eluent A) in MeCN with 0.1 % TFA (eluent B) was used as mobile phase.

Nuclear magnetic resonance (NMR) spectra were recorded at room temperature on instruments Avance III 400 and Avance DRX 600 from *Bruker*. Chemical shifts are reported relative to solvent signals: $CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.0 ppm; DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.5 ppm; CD_3OD: δ_H = 3.31 ppm, δ_C = 49.2 ppm. Signals were assigned by first-order analysis and, when feasible, assignments were supported by two-dimentional ^{1}H, ^{1}H and ^{1}H, ^{13}C correlation spectroscopy (COSY, HSQC and HMBC). $^1J_{H\text{-}C}$ coupling constants were obtained from non-decoupled HSQC NMR spectra.

ESI-IT mass spectra were recorded on a Esquire 3000 plus instrument from *Bruker*. Samples were prepared in MeOH or MeCN (approx. 1 µg mL^{-1}).

High-resolution **ESI-TOF mass spectra** were recorded on a micrOTOF II instrument from *Bruker*.

Elemental analyses were performed on a vario EL instrument from *elementar*.

Synthesis of Tetrazines

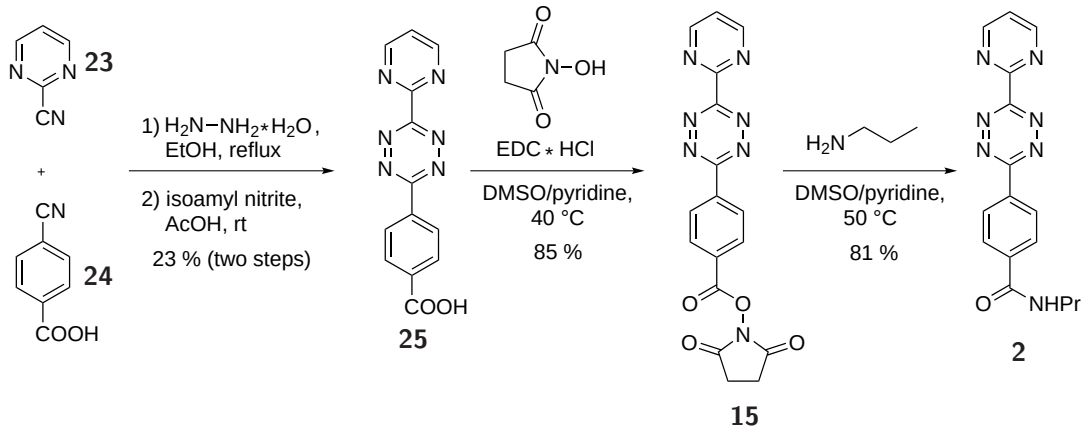
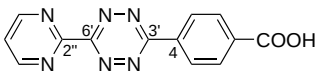


Figure S1: Synthesis of tetrazine derivatives

4-(6-(Pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzoic Acid (25)



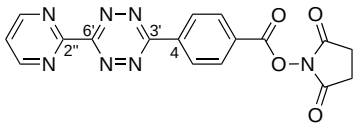
25 $C_{13}H_8N_6O_2$ 280.2 g mol^{-1}

4-Cyanobenzoic acid (**24**) (7.0 g, 48 mmol, 1.0 eq) and pyrimidin-2-carbonitrile (**23**) (5 g, 48 mmol, 1.0 eq) were suspended in dry EtOH (20 mL) under mechanical stirring and hydrazine monohydrate (11.5 mL, 238 mmol, 5.0 eq) was added dropwise. Subsequently, the mixture was stirred at reflux temperature for 9 h. After cooling to rt, the formed orange precipitate was filtered off and washed with small volumes of EtOH. In order to remove the symmetrical byproduct bis(pyrimidin-2-yl)-1,2,4,5-dihydrotetrazine, the solid was stirred in refluxing acetone (30 mL) and filtered off in the heat. This procedure was repeated once. The filtered off orange solid was suspended in acetic acid (115 mL) and oxidized by slow addition of isopentyl nitrite (4.5 mL, 33 mmol, 1.5 eq). After stirring over night, ethyl ether (190 mL) was added in order to precipitate the purple product mixture. After filtration, the crude purple product was recrystallized three times in acetic acid in order to remove the other symmetrical byproduct 4,4'-(1,2,4,5-tetrazine-3,6-diyl)dibenzoic acid. **25**[1] (3.0 g, 10.7 mmol, 23 %) was isolated as purple solid that still contained small amounts of the tetrazinyldibenzoic acid.

TLC: R_f = 0.11 (CH_2Cl_2/MeOH 10:1)
^{1}H NMR (399.8 MHz, DMSO-d_6): δ = 13.35 (br. s, 1 H; COOH), 9.21 (d, J = 4.9 Hz, 2 H; H-4" and H-6"), 8.71 (m, 2 H; H-2 and H-6 or H-3 and H-5), 8.25 (m, 2 H; H-2 and H-6 or H-3 and H-5), 7.84 (t, J = 4.9 Hz, 1 H; H-5") ppm
^{13}C NMR (100.5 MHz, DMSO-d_6): δ = 166.7 (COOH), 163.2, 162.9, 159.0 (each quat. C), 158.5 (C-4" and C-6"), 135.3, 134.5 (each quat. C), 130.2 (C-2 and C-6 or C-3 and C-5), 128.3

(C-2 and C-6 or C-3 and C-5), 127.9 (quat. C), 123.0 (C-5") ppm
ESI-TOF-HRMS (neg. mode): m/z = 279.0645 $[M-H]^-$ (calc. m/z = 279.0645 $[M-H]^-$)

2,5-Dioxopyrrolidin-1-yl 6-(6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzoate (15)



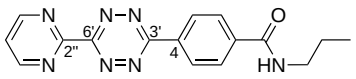
15

$C_{17}H_{11}N_7O_4$
377.31 g mol^{-1}

Tetrazine **25** (605 mg, 2.14 mmol, 1 eq) was suspended in DMSO/pyridine (19:1, 25 mL) and *N*-hydroxysuccinimide (370 mg, 3.21 mmol, 1.5 eq) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (500 mg, 3.22 mmol, 1.50 eq) were added. The mixture was heated to 40 °C and became clear after a few minutes. After 2 h, the solvent was removed under reduced pressure. The residue was redissolved in CH_2Cl_2 and washed once with water. The aqueous layer was extracted once with CH_2Cl_2. The combinded organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was almost completely dissolved in CH_2Cl_2 (40 mL) and precipitated by the addition of diethyl ether (approx. 300 mL). The precipitate was collected by filtration and washed with diethyl ether. After removal of residual solvent in vacuo, (**15**) (689 mg, 1.827 mmol, 85 %) was isolated as a red crystalline solid.

TLC: R_f = 0.63 (CH_2Cl_2/MeOH 10:1)
^{1}H NMR (399.8 MHz, DMSO-d_6): δ = 9.22 (d, J = 4.9 Hz, 2 H; H-4" and H-6"), 8.85 (m, 2 H; H-2 and H-6 or H-3 and H-5), 8.43 (m, 2 H; H-2 and H-6 or H-3 and H-5), 7.86 (t, J = 4.9 Hz, 1 H; H-5"), 2.94 (s, 4 H; CH_2CH_2), ppm
^{13}C NMR (100.5 MHz, DMSO-d_6): δ = 170.2 ($N(C{=}O)_2$), 162.9, 161.3, 159.0 (each quat. C), 158.5 (C-4" and C-6"), 137.7 (quat. C), 131.0 (C-2 and C-6 or C-3 and C-5), 129.0 (C-2 and C-6 or C-3 and C-5), 127.9 (quat. C), 123.1 (C-5"), 25.6 (CH_2CH_2) ppm
ESI-TOF-HRMS (pos. mode): m/z = 378.0918 $[M+H]^+$, 400.0748 $[M+Na]^+$ (calc. m/z = 378.0945 $[M+H]^+$, 400.0765 $[M+Na]^+$)

N-Propyl-4-(6-(pyrimidin-2-yl)-1,2,4,5-tetrazin-3-yl)benzamide (2)



2

$C_{16}H_{15}N_7O$
321.34 g mol^{-1}

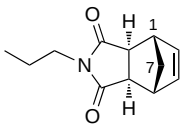
To active ester **15** (230 mg, 0.610 mmol, 1 eq) in dry DMSO/pyridine (18:1, 9.5 mL) propylamine (80 µL, 0.98 mmol, 1.6 eq) was added in portions over 4 h at 50 °C and stirring was continued at rt overnight. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (CH_2Cl_2/MeOH 20:1), **2** (160 mg, 0.499 mmol, 81 %) was isolated

as a purple solid.

TLC: R_f = 0.49 (CH_2Cl_2/MeOH 15:1)
^{1}H NMR (399.8 MHz, $CDCL_3$): δ = 9.13 (d, J = 4.9 Hz, 2 H; H-4" and H-6"), 8.79 (d, J = 8.1 Hz, 2 H; H-2 and H-6 or H-3 and H-5), 8.01 (d, J = 8.1 Hz, 2 H; H-2 and H-6 or H-3 and H-5), 7.59 (t, J = 4.9 Hz, 1 H; H-5"), 6.35 (br. s, 1 H; NH), 3.48 ('q', J = Hz, 2 H; NCH_2), 1.69 (sext., J = 7.3 Hz, 2 H; NCH_2CH_2), 1.02 (t, J = 7.4 Hz, 3 H; CH_3) ppm
^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 166.6, 164.1, 163.3, 159.5 (each quat.), 158.5 (C-4" and C-6"), 139.2, 133.8 (each quat.), 129.0 (C-2 and C-6 or C-3 and C-5), 127.9 (C-2 and C-6 or C-3 and C-5), 122.6 (C-5"), 42.0 (NCH_2), 22.9 (NCH_2CH_2), 11.5 (CH_3) ppm
ESI-TOF-HRMS (pos. mode): m/z = 322.1389 $[M+H]^+$ (calc. m/z = 322.1411 $[M+H]^+$)

DARinv in Solution

N-(Propyl)-exo-norborn-5-en-2,3-dicarboximide (1)



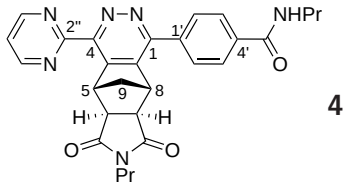
1

$C_{12}H_{15}NO_2$
205.25 g mol^{-1}

5-Norbornene-*exo*-2,3-dicarboxylic anhydride (200 mg, 1.22 mmol, 1 eq) was added to a solution of *n*-propylamine (200 µL, 144 mg, 2 eq) in dry toluene (4 mL). After 30 min, the mixture was heated to reflux temperature for 4.5 h. After cooling to rt, the mixture was diluted with water and EtOAc. The layers were separated and the organic layer was washed two times with water, dried over Na_2SO_4, filtrated and concentrated in vacuo. After FC (petroleum ether/EtOAc 7:1), **1**[2] (220 mg, 1.07 mmol, 88 %) was isolated as a white solid.

TLC: R_f = 0.30 (petroleum ether/EtOAc)
^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 6.27 (t, J = 1.9 Hz, 2 H; H-5 and H-6), 3.42 (m, 2 H; NCH_2), 3.26 ('quin', J = 1.8 Hz, 2 H; H-1 and H-4), 2.66 (d, J = 1.5 Hz, 2 H; H-2 and H-3), 1.58 (m, 2 H; NCH_2CH_2), 1.50 (m, 1 H; H-7a), 1.23 (m, 1 H; H-7b), 0.90 (t, J = 7.5 Hz, 3 H; CH_3) ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 178.1 ($N(C=O)_2$), 137.8 (C-5 and C-6), 47.8 (C-2 and C-3), 45.1 (C-1 and C-4), 42.7 (C-7), 40.3 (NCH_2), 21.1 (NCH_2CH_2), 11.4 (CH_3) ppm
ESI-IT-MS (pos. mode): m/z = 228.1 $[M+Na]^+$ (calc. m/z = 228.1 $[M+Na]^+$)
CHN analysis (in %): C 70.17, H 7.31, N 6.70 (calc.: C 70.22, H 7.37, N 6.82)

N-Propyl-1-(4-(propylcarbamoyl)phenyl)-4-pyrimidin-2-yl-pyridazido[4,5-e]norbornan-exo-6,7-dicarboximid (4)



4

$C_{28}H_{28}N_6O_3$
496.56 g mol^{-1}

Tetrazine **2** (37 mg, 0.12 mmol, 1 eq) and dienophile **1** (29 mg, 0.14 mmol, 1.3 eq) were dissolved in DMSO (2 mL). After 3.5 h, the solvent was removed under reduced pressure. The residue was dissolved in acetic acid (2 mL) and isoamyl nitrite (15 µL, 0.12 mmol, 1 eq) was added. After 15 min, the solvent was removed under reduced pressure. After FC (CH_2Cl_2/MeOH 25:1), **4** (53 mg, 0.11 mmol, 93 %) was isolated as a white solid.

^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 8.92 (d, J = 4.9 Hz, 2 H; H-4" and H-6"), 7.86-7.82 (m, 2 H; H-2' and H-6' or H-3' and H-5'), 7.80-7.77 (m, 2 H; H-2' and H-6' or H-3' and H-5'), 7.36 (t, J = 4.9 Hz, 1 H; H-5"), 6.96 (t, J = 5.6 Hz, 1 H; NH), 4.66 (m, 1 H; H-5 or H-8), 3.95 (m, 1 H; H-5 or H-8), 3.52-3.47 (m, 2 H; NCH_2), 3.47-3.40 (m, 2 H; $NHCH_2$), 3.33 (m, 1 H; H-6 or H-7), 3.15 (m, 1 H; H-6 or H-7), 1.88-1.81 (m, 1 H; H-9a), 1.67 (sext., J = 7.3 Hz, 2 H; $NHCH_2CH_2$), 1.63-1.54 (m, 3 H; H-9b and NCH_2CH_2), 0.99 (t, J = 7.4 Hz, 3 H; $NHCH_2CH_2CH_3$), 0.90 (t, J = 7.4 Hz, 3 H; $NCH_2CH_2CH_3$) ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 176.6, 176.3 (both $N(C{=}O)_2$), 167.2 (NC=O), 162.2 (quat. C), 157.6 (C-4" and C-6"), 153.8, 150.5, 147.4, 145.4, 137.7, 136.0 (each quat. C), 128.7, 127.5 (C-2' and C-6'), 120.7 (5"), 47.1, 46.5 (C-6 and C-7), 45.8, 44.9 (C-5 and C-8), 43.3 (C-9), 41.9 ($NHCH_2$), 40.8 (NCH_2), 22.7 ($NHCH_2CH_2$), 21.1 (NCH_2CH_2), 11.4 ($NHCH_2CH_2CH_3$), 11.3 ($NCH_2CH_2CH_3$) ppm
ESI-TOF-HRMS (pos. mode): m/z = 497.2271 $[M+H]^+$ (calc. m/z = 497.2296 $[M+H]^+$)

Synthesis of Carbohydrate-Dienophile Conjugates

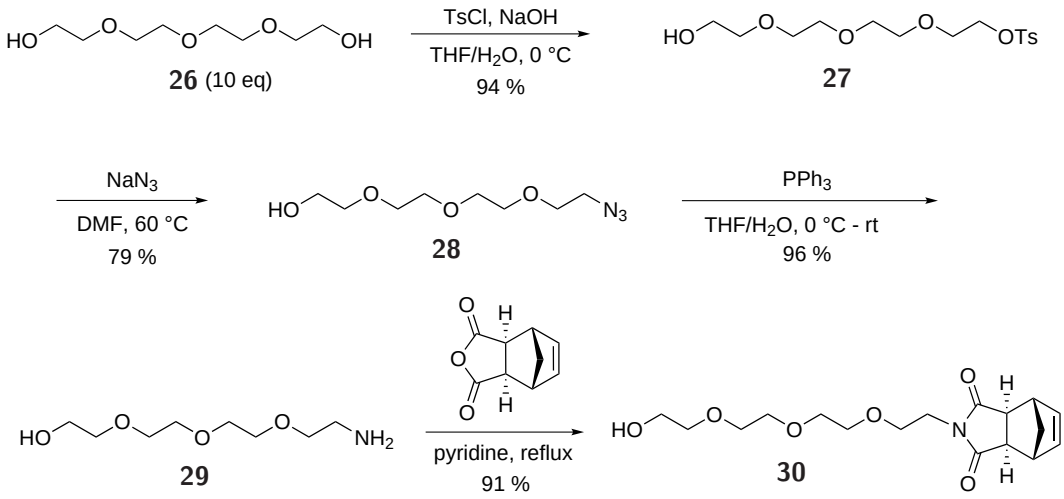
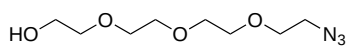


Figure S2: Synthesis of dienophile-spacer conjugate **30**

11-Azido-3,6,9-trioxa-undecan-1-ol (28)

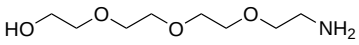


28

$C_8H_{17}N_3O_4$
219.24 g mol^{-1}

Compound **28** was obtained in two steps from tetra(ethylene glycol) (**26**) according to a procedure from Shirude *et al.*:[3] (1) TsCl, NaOH, THF/H_2O, 0 °C, 3 h (76 %); (2) NaN_3, DMF, 60 °C, 1.5 h (79 %).

11-Amino-3,6,9-trioxa-undecan-1-ol (29)

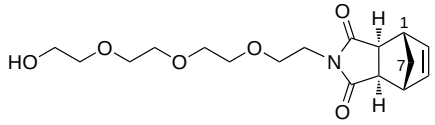


29

$C_8H_{19}NO_4$
193.24 g mol^{-1}

Compound **29** was obtained from **28** according to a procedure from Svedhem *et al.*:[4] PPh_3, THF/H_2O, 0 °C - rt, 19 h (96 %)

N-(3,6,9,12-Tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (30)



30

$C_{17}H_{25}NO_6$
339.38 g mol^{-1}

To a solution of 5-norbornene-*exo*-2,3-dicarboxylic anhydride (3.67 g, 22.4 mmol, 1 eq) in dry pyridine (10 mL) amine **29** (4.75 g, 24.6 mmol, 1.10 eq) dissolved in dry pyridine (15 mL) was added dropwise. Subsequently, the mixture was heated to reflux temperature for 2.5 h. The solvent was evaporated under reduced pressure und the residue was coevaporated three times with toluene. After FC (EtOAc/MeOH 10:1), **30** (6.88 g, 20.3 mmol, 91 %) was isolated as a pale oil.

TLC: R_f = 0.31 (EtOAc/MeOH 10:1)
^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 6.28-6.27 (m, 2 H; H-5 and H-6), 3.74-3.67 (m, 4 H; 2 x CH_2), 3.67-3.63 (m, 4 H; 2 x CH_2), 3.63-3.56 (m, 8 H; 4 x CH_2), 3.28-3.24 (m, 2 H; H-1 and H-4), 2.69-2.66 (m, 2 H; H-2 and H-3), 1.49-1.46 (m, 1 H; H-7a), 1.37-1.33 (m, 1 H; H-7b) ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 178.0 (C=O), 137.8 (C-5 and C-6), 72.5, 70.7, 70.5, 70.4, 69.9, 66.9, 61.8 (each CH_2), 47.8 (C-2 and C-3), 45.2 (C-1 and C-4), 42.7 (C-7), 37.7 (CH_2) ppm
ESI-IT-MS (pos. mode): m/z = 340.1 $[M+H]^+$, 362.1 $[M+Na]^+$, 378.1 $[M+K]^+$ (calc. m/z = 340.2 $[M+H]^+$, 362.2 $[M+Na]^+$, 378.1 $[M+K]^+$)
CHN analysis (in %): C 59.80, H 7.33, N 3.95 (calc.: C 60.16, H 7.42, N 4.13)

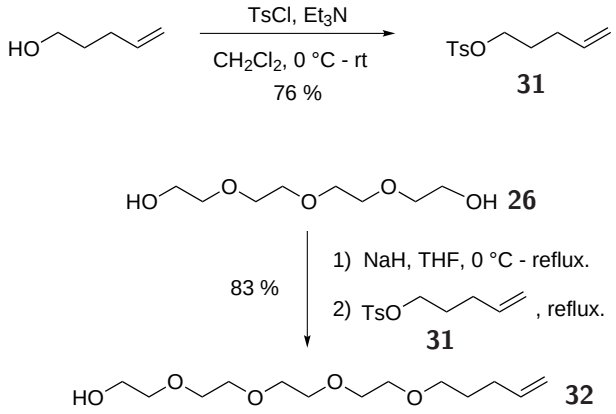
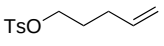


Figure S3: Synthesis of dienophile-spacer conjugate **32**

Pent-4-en-1-yl 4-Methylbenzenesulfonate (31)

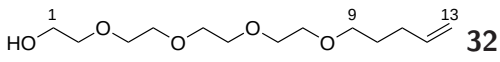


31

$C_{12}H_{16}O_3S$
240.32 g mol^{-1}

Compound **31** was obtained from pent-4-en-1-ol according to a procedure from White *et al.*:[5] TsCl, EtN_3, CH_2Cl_2, 0 °C - rt, 4 h (76 %)

3,6,9,12-Tetraoxa-heptadec-16-en-1-ol (32)



32

$C_{13}H_{26}O5$
262.34 g mol^{-1}

Tetra(ethylene glycol) (**26**) (3.30 g, 17.0 mmol, 5.0 eq) was dissolved in dry THF (15 mL) and NaH (60 % dispersion in mineral oil, 135 mg, 3.38 mmol, 1.1 eq) was added at 0 °C. After stirring at 0 °C for 30 min, the mixture was heated to reflux temperature for 1 h. Tosylate **31** (739 mg, 3.08 mmol, 1 eq) in THF (5 mL) was added and the mixture was heated to reflux temperature for 6 h. Subsequently, the solvent was evaporated under reduced pressure and the residue was dissolved in a mixture of water and EtOAc. The phases were separeted and the aqueous phase was extracted four times with EtOAc. The combined organic phases were washed once with a small volume of brine, dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (EtOAc to EtOAc/MeOH 20:1), pure **32** (667 mg, 2.54 mmol, 82 %) was isolated as pale oil.

TLC: R_f = 0.26 (EtOAc/MeOH 20:1)

^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 5.80 (ddt, J = 16.9, 10.2, 6.6 Hz 1 H; H-12), 5.01 (ddt, J = 17.1, 2.0, 1.6 Hz 1 H; H-13a), 4.94 (ddt, J = 10.2, 2.1, 1.3 Hz 1 H; H-13b), 3.74-3.69 (m, 2 H; CH_2), 3.69-3.55 (m, 14 H; 7 x CH_2), 3.46 (t, J = 6.7 Hz, 2 H; 2 x H-9), 2.13-2.06 (m, 2 H; 2 x H-11), 1.71-1.63 (m, 2 H; 2 x H-8) ppm

^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 138.3 (C-12), 114.7 (C-13), 72.5 (CH_2), 70.7 (C-9), 70.6, 70.6, 70.6, 70.6, 70.3, 70.1, 61.7 (each CH_2), 30.2 (C-11), 28.73 (C-10) ppm

ESI-TOF-HRMS (pos. mode): m/z = 285.1673 $[M+Na]^+$ (calc. m/z = 285.1673 $[M+Na]^+$)

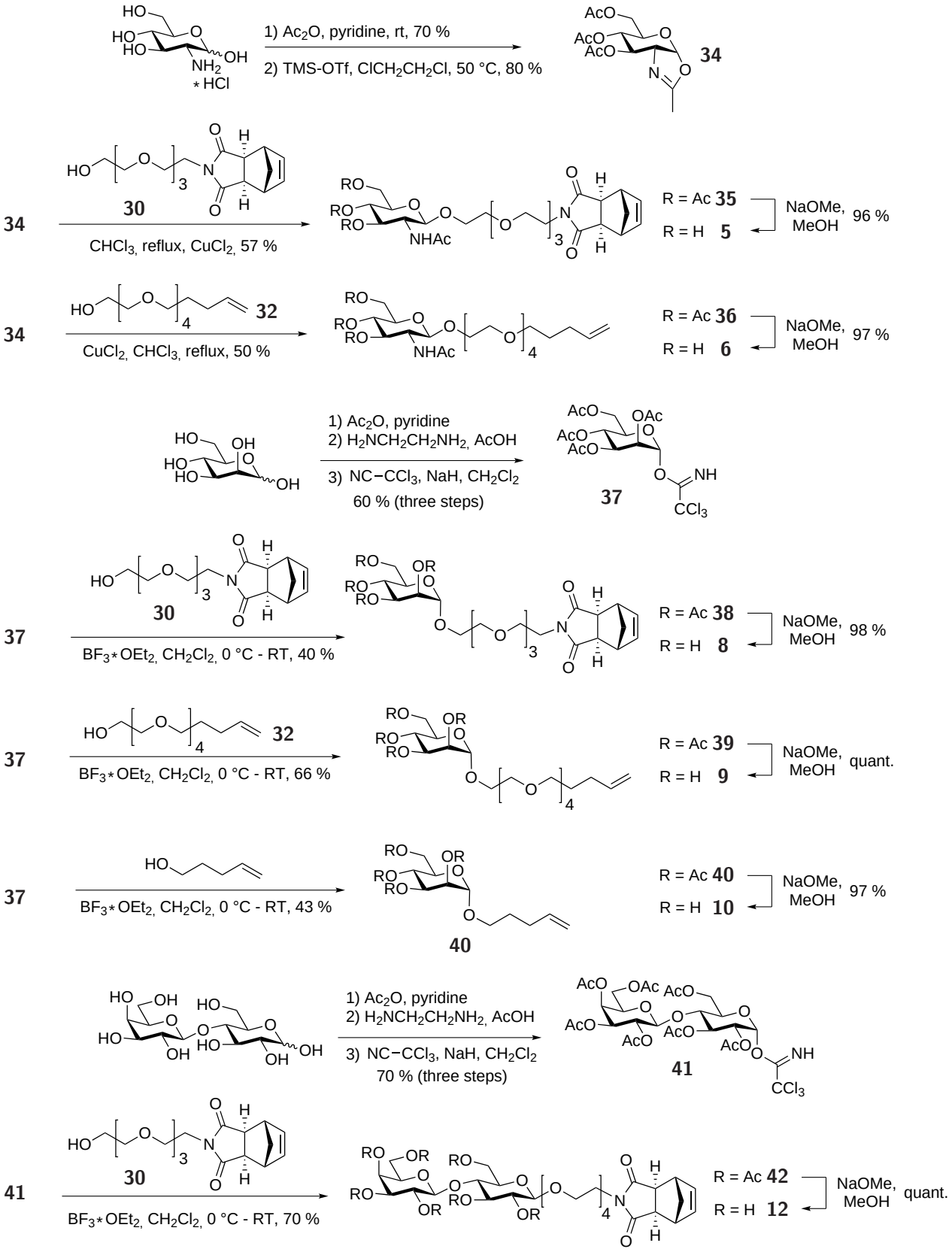
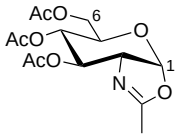


Figure S4: Synthesis of carbohydrate dienophile conjugates

2-Methyl-(3,4,6-tri-O-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-d]-2-oxazoline (34)

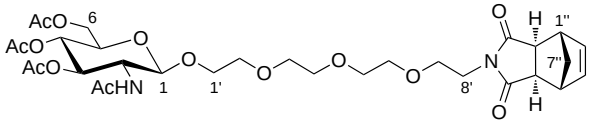


34

$C_{14}H_{19}NO_8$
329.30 g mol^{-1}

Oxazoline **34** was obtained in two steps from glucosamine hydrochloride according to published procedures: (1) Ac_2O, pyridine, 4 d (70 %)[6]; (2) TMS-OTf, $ClCH_2CH_2Cl$, 50 °C, 20 h (80 %).[6]

N-(12-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3,6,9,12-tetraoxadodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (35)



35

$C_{31}H_{44}N_2O_{14}$
668.69 g mol^{-1}

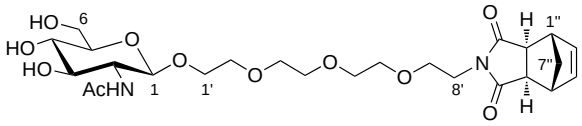
Oxazoline **34** (803 mg, 2.34 mmol, 2.0 eq) was coevaporated twice with toluene. Anhydrous $CuCl_2$[7] (328 mg, 2.44 mmol, 2.0 eq) was added and the mixture was coevaporeted with toluene again. Dienophile-spacer conjugate **30** (414 mg, 1.22 mmol, 1.0 eq) was coevaporated twice with toluene, dissolved in dry $CHCl_3$ (5 mL) and added to the oxazoline. The mixture was heated to reflux temperature for 5.5 h. After cooling to rt, the solvent was removed under reduced pressure, EtOAc was added, and the mixture was washed twice with 1 N HCl, once with sat. $NaHCO_3$ and once with brine. The respective aqueous phases were extracted once with EtOAc and the organic layers were combined before performing the subsequent washing step. Finally, the organic layer was dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (EtOAc/MeOH 30:1 to 15:1), **35** (466 mg, 0.697 mmol, 57 %) was isolated as pale yellow oil. In addition, a fraction of impure **35** (182 mg) was isolated.

TLC: R_f = 0.12 (EtOAc/MeOH 30:1)
RP-HPLC (30-90 % B in 20 min): t_R = 11.11 min
^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 6.59 (d, J = 9.3 Hz, 1 H; NH), 6.26-6.23 (m, 2 H; H-5" and H-6"), 5.09-4.98 (m, 2 H; H-3 and H-4), 4.76 (d, J = 8.5 Hz, 1 H; H-1), 4.24 (dd, J = 12.3, 4.7 Hz, 1 H; H-6a), 4.11-3.97 (m, 2 H; H-2, H-6a), 3.88-3.73 (m, 2 H; CH_2), 3.71-3.48 (m)15H-5 and 7 x CH_2, 3.25-3.18 (m, 2 H; H-1" and H-4"), 2.67-2.62 (m, 2 H; H-2" and H-3"), 2.06 (s, 3 H; C(O)CH_3), 1.99-1.97 (m, 6 H; 2 x C(O)CH_3), 1.94 (s, 3 H; C(O)CH_3), 1.49-1.44 (m, 1 H; H-7a"), 1.35-1.30 (m, 1 H; H-7b") ppm
^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 177.9 (N(C=O)$_2$), 170.7, 170.7, 170.5, 169.3 (each C(O)CH_3), 137.8 (C-5" and C-6"), 101.8 (C-1), 73.4 (3 or 4), 71.6 (CH_2), 71.5 (C-5), 70.8, 70.5, 70.3, 70.0 (each CH_2), 68.6 (C-3 or C-4), 68.6 (CH_2), 66.8 (CH_2), 62.2 (C-6), 53.9 (C-2),

47.8 (C-2" and C-3"), 45.2 (C-1" and C-4"), 42.6 (C-7"), 37.7 (CH_2), 22.9, 20.7, 20.6, 20.6 (each C(O)CH_3) ppm

ESI-TOF-HRMS (pos. mode): m/z = 669.2860 $[M+H]^+$, 691.2682 $[M+Na]^+$ (calc. m/z = 669.2865 $[M+H]^+$, 691.2685 $[M+Na]^+$)

N-(12-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (5)



5

$C_{25}H_{38}N_2O_{11}$
542.58 g mol^{-1}

Peracetylated compound **35** (202 mg, 0.302 mmol, 1 eq) was dissolved in dry MeOH (3 mL) and a 0.5 M solution of NaOMe in MeOH (72 µL, 36 µmol, 0.12 eq) was added. After stirring at rt for 2 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **5** (157 mg, 0.289 mmol, 96 %) was isolated as a colorless oil.

TLC: R_f = 0.13 ($CDCl_3$/MeOH 10:1)

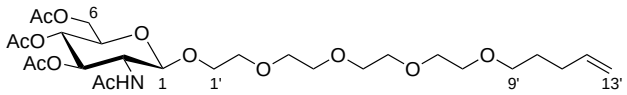
RP-HPLC (5-60 % B in 20 min): t_R = 15.39 min

^{1}H NMR (399.8 MHz, D_3COD): δ = 6.33 ('t', J = 1.9 Hz, 2 H; H-5" and H-6"), 4.49 (d, J = 8.4 Hz, 1 H; H-1), 3.93 (ddd, J = 11.3, 4.9, 3.6 Hz 1 H; H-1a'), 3.87 (dd, J = 11.9, 2.2 Hz, 1 H; H-6a), 3.74-3.54 (m, 17 H; H-2, H-6b, H-1b' and 7 x CH_2), 3.45 (dd, J = 10.3, 8.3 Hz, 1 H; H-3), 3.32 (dd, J = 9.7, 8.3 Hz, 1 H; H-4), 3.27 (ddd, J = 9.6, 5.5, 2.2 Hz 1 H; H-5), 3.20-3.17 (m, 2 H; H-1" and H-4"), 2.72 (d, J = 1.5 Hz, 2 H; H-2" and H-3"), 1.99 (s, 3 H; C(O)CH_3), 1.48-1.44 (m, 1 H; H-7a"), 1.40-1.36 (m, 1 H; H-7b") ppm

^{13}C NMR (100.5 MHz, D_3COD): δ = 180.2 (N(C=O)$_2$), 173.9 (C(O)CH_3), 139.1 (C-5" and C-6"), 102.9 (C-1), 78.1 (C-5), 76.4 (C-3), 72.3 (C-4), 71.8, 71.7, 71.7, 71.6, 71.1 (each CH_3), 70.0 (C-1'), 68.0 (CH_2), 63.0 (C-6), 57.5 (C-2), 49.1 (C-2" and C-3"), 46.6 (C-1" and C-4"), 43.7 (C-7"), 39.1 (C-8'), 23.2 (C(O)CH_3) ppm

ESI-TOF-HRMS (pos. mode): m/z = 543.2539 $[M+H]^+$, 565.2364 $[M+Na]^+$ (calc. m/z = 543.2554 $[M+H]^+$, 565.2373 $[M+Na]^+$)

3,6,9,12-Tetraoxaheptadec-16-en-1-yl 2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (36)



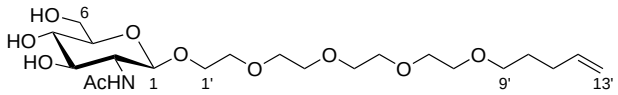
36

$C_{27}H_{45}NO_{13}$
691.65 g mol^{-1}

Oxazoline **34** (833 mg, 2.53 mmol, 2.0 eq) was coevaporated twice with toluene. Anhydrous $CuCl_2$[7] (340 mg, 2.53 mmol, 2.0 eq) was added and the mixture was coevaporeted with toluene again. Dienophile-spacer conjugate **32** (332 mg, 1.26 mmol, 1.0 eq) was coevaporated twice with toluene, dissolved in dry $CHCl_3$ (5 mL) and added to the oxazoline. The mixture was heated to reflux temperature for 10.5 h. After cooling to rt, the solvent was removed under reduced pressure, EtOAc was added, and the mixture was washed once with 0.1 N HCl, once with sat. $NaHCO_3$ and once with brine. The respective aqueous layers were once extracted with EtOAc and the organic layers were combined before performing the subsequent washing step. Finally, the organic layer was dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (EtOAc/MeOH 30:1 to 25:1), **36** (378 mg, 0.639 mmol, 50 %) was isolated as pale yellow oil. In addition, a fraction of impure **36** (193 mg) was isolated.

TLC: R_f = 0.26 (Et_2O/MeOH 10:1)
RP-HPLC (30-90 % B in 20 min): t_R = 13.17 min
^{1}H NMR (399.8 MHz, $CDC3_3$): δ = 6.72 (d, J = 9.3 Hz, 1 H; NH), 5.75 (ddt, J = 17.0, 10.2, 6.6 Hz 1 H; H-12'), 5.07-4.98 (m, 2 H; H-3 and H-4), 4.96 (ddt, J = 17.1, 2.0, 1.6 Hz 1 H; H-13a'), 4.90 (ddt, J = 10.2, 2.0, 1.3 Hz 1 H; H-13b'), 4.74 (d, J = 8.6 Hz, 1 H; H-1), 4.20 (dd, J = 12.2, 4.8 Hz, 1 H; H-6a), 4.06 (dd, J = 12.3, 2.5 Hz, 1 H; H-6b), 4.07-3.99 (m, 1 H; H-2), 3.87-3.48 (m, 17 H; H-5 and 8 x CH_2), 3.41 (t, J = 6.7 Hz, 2 H; 2 x H-9'), 2.09-2.01 (m, 2 H; 2 x H-11'), 2.02 (s, 3 H; C(O)CH_3), 1.95 (s, 3 H; C(O)CH_3), 1.95 (s, 3 H; C(O)CH_3), 1.91 (s, 3 H; C(O)CH_3), 1.62 (m, 2 H; 2 x H-10'), ppm
^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 170.6, 170.6, 170.5, 169.2 (each C(O)CH_3), 138.1 (C-12'), 114.6 (C-12'), 101.8 (C-1), 73.3 (C-3 or C-4), 71.5 (CH_2), 71.4 (C-5), 70.5, 70.5, 70.4, 70.4, 70.2, 70.2, 69.9 (C-9' and 8 x CH_2), 68.6 (C-3 or C-4), 68.6 (CH_2), 62.1 (C-6), 53.7 (C-2), 30.1 (C-11'), 28.6 (C-10'), 22.8, 20.6, 20.6, 20.5 (each C(O)CH$_3$) ppm
ESI-TOF-HRMS (pos. mode): m/z = 592.2956 $[M+H]^+$, 614.2766 $[M+Na]^+$ (calc. m/z = 592.2964 $[M+H]^+$, 614.2783 $[M+Na]^+$)

3,6,9,12-Tetraoxaheptadec-16-en-1-yl 2-Acetamido-2-deoxy-β-D-glucopyranoside (6)



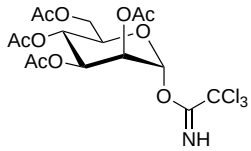
6

$C_{21}H_{39}NO_{10}$
465.26 g mol^{-1}

Peracetylated compound **36** (295 mg, 0.499 mmol, 1 eq) was dissolved in dry MeOH (4 mL) and a 0.5 M solution of NaOMe in MeOH (180 µL, 89.7 µmol, 0.18 eq) was added. After stirring at rt for 2 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **6** (224 mg, 0.481 mmol, 97 %) was isolated as a colorless oil.

TLC: R_f = 0.10 ($CDCl_3$/MeOH 10:1)
RP-HPLC (5-60 % B in 20 min): t_R = 16.75 min
^{1}H NMR (399.8 MHz, D_3COD): δ = 5.83 (ddt, J = 17.1, 10.3, 6.7 Hz 1 H; H-12'), 5.04 (ddt, J = 17.1, 2.1, 1.6 Hz 1 H; H-13a'), 5.02 (ddt, J = 10.2, 2.2, 1.2 Hz 1 H; H-13b'), 4.49 (d, J = 8.4 Hz, 1 H; H-1), 3.94 (ddd, J = 11.3, 4.9, 3.6 Hz 1 H; H-1a'), 3.88 (dd, J = 11.9, 2.3 Hz, 1 H; H-6a), 3.74 (m, 17 H; H-2, H-6b, H-1b' and 7 x CH_2), 3.48 (t, J = 6.6 Hz, 2 H; H-9'), 3.45 (dd, J = 10.3, 8.3 Hz, 1 H; H-3), 3.32 (dd, J = 9.7, 8.3 Hz, 1 H; H-4), 3.27 (ddd, J = 9.7, 5.5, 2.3 Hz 1 H; H-5), 2.15-2.08 (m, 2 H; H-11'), 1.99 (s, 3 H; C(O)CH_3), 1.70-1.61 (m, 2 H; H-10') ppm
^{13}C NMR (100.5 MHz, D_3COD): δ = 173.9 (C(O)CH_3), 139.6 (C-12'), 115.4 (C-13'), 103.0 (C-1), 78.1 (C-5), 76.3 (C-3), 72.3 (C-4), 71.7 (C-9'), 3 x 71.7, 3 x 71.6 and 71.3 (each CH_2), 70.0 (C-1'), 62.9 (C-6), 57.5 (C-2), 31.4 (C-11'), 30.1 (C-10'), 23.2 (C(O)CH$_3$) ppm
ESI-TOF-HRMS (pos. mode): m/z = 466.2634 $[M+H]^+$, 488.2454 $[M+Na]^+$ (calc. m/z = 466.2652 $[M+H]^+$, 488.2472 $[M+Na]^+$)

O-(2,3,4,6-Tetra-O-acetyl-α-D-mannopyranosyl)trichloroacetimidate (37)

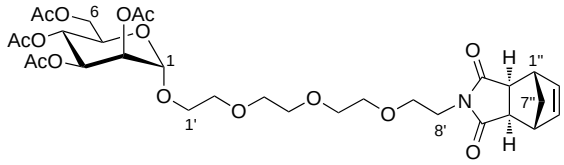


37

$C_{16}H_{20}Cl_3NO_{10}$
492.69 g mol^{-1}

Mannosyl donor **37**[8] was obtained in three steps from D-mannose: 1) Ac_2O, pyridine; 2) $H_2NCH_2CH_2NH_2$, AcOH; 3) NC-CCl_3, NaH, CH_2Cl_2; 60 % over three steps.

N-(12-(2,3,4,6-Tetra-O-acetyl-α-D-mannopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (38)



38

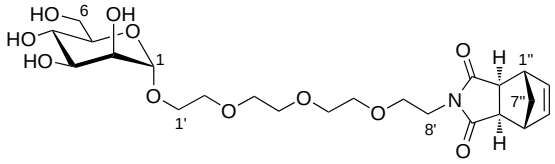
$C_{31}H_{43}NO_{15}$
669.67 g mol^{-1}

Dienophile-spacer conjugate **30** (500 mg, 1.47 mmol, 1.0 eq) and mannosyl donor **37** (1.16 g, 2.36 mmol, 1.6 eq) were dissolved at 0 °C in dry CH_2Cl_2 (7 mL). After addition of BF_3·OEt_2 (111 µL, 0.884 mmol, 0.6 eq), the mixtrure was stirred for 45 min at 0 °C and subsequently for 30 min at rt. After neutralization with Et_3N, water was added to the reaction mixture. The phases were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (toluene/acetone 4:1 to 3:1), pure **38** (398 mg, 0.594 mmol, 40 %) was isolated as pale oil. In addition, a fraction of

impure **38** (351 mg) was isolated.

TLC: R_f = 0.31 (toluene/acetone 4:1)
^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 6.28-6.25 (m, 2 H; H-5"and H-6"), 5.33 (dd, J = 10.0, 3.5 Hz, 1 H; H-3), 5.26 ('t', J = 10.0 Hz, 1 H; H-4), 5.24 (dd, J = 3.5, 1.7 Hz, 1 H; H-2), 4.85 (d, J = 1.7 Hz, 1 H; H-1), 4.27 (dd, J = 12.2, 4.9 Hz, 1 H; H-6a), 4.07 (dd, J = 12.2, 2.5 Hz, 1 H; H-6b), 4.04 (ddd, J = 9.9, 4.9, 2.4 Hz 1 H; H-5), 3.82-3.78 (m, 1 H; H-1a'), 3.70-3.54 (m, 15 H; H-1b' and 7 x CH_2), 3.25-3.23 (m, 2 H; H-1" and H-4"), 2.66-2.64 (m, 2 H; H-2" and H-3"), 2.13 (s, 3 H; C(O)CH_3), 2.08 (s, 3 H; C(O)CH_3), 2.02 (s, 3 H; C(O)CH_3), 1.97 (s, 3 H; C(O)CH_3), 1.47-1.46 (m, 1 H; H-7a"), 1.36-1.33 (m, 1 H; H-7b") ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 177.9 (N(C=O)$_2$), 170.6, 169.9, 169.8, 169.7 (each C(O)CH_3), 137.8 (C-5 and C-6), 97.7 (C-1), 70.6, 70.6, 70.5, 69.9, 69.8 (each CH_2), 69.5 (C-2), 69.0 (C-3), 68.3 (C-5), 67.3 (C-1'), 66.8 (CH_2), 66.1 (C-4), 62.4 (C-6), 47.8 (C-2" and C-3"), 45.2 (C-1" and C-4"), 42.7 (C-7"), 37.7 (C-8'), 20.8, 20.7, 20.7, 20.6 (each C(O)CCH$_3$) ppm
Coupling H-1/C-1 ($CDCl_3$): $^1J_{H\text{-}1,C\text{-}1}$ = 172.3 Hz
ESI-IT-MS (pos. mode): m/z = 692.1 $[M+Na]^+$, 708.1 $[M+K]^+$ (calc. m/z = 692.3 $[M+Na]^+$, 708.2 $[M+K]^+$)
CHN analysis (in %): C 55.56, H 6.46, N 2.07 (calc.: C 55.60, H 6.47, N 2.09)

N-(12-α-D-mannopyranosyl-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (8)



8

$C_{23}H_{35}NO_{11}$
501.52 g mol^{-1}

Peracetylated compound **38** (272 mg, 0.406 mmol, 1 eq) was dissolved in dry MeOH (4 mL) and a 0.5 M solution of NaOMe in MeOH (65 µL, 33 µmol, 0.08 eq) was added. After stirring at rt for 2 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **8** (200 g, 0.399 mmol, 98 %) was isolated as a colorless oil.

TLC: R_f = 0.29 ($CHCl_3$/MeOH 5:1)
^{1}H NMR (600.1 MHz, D_3COD): δ = 6.33 ('t', J = 1.8 Hz, 2 H; H-5" and H-6"), 4.80 (d, J = 1.7 Hz, 1 H; H-1), 3.85-3.81 (m, 3 H; H-2, H-6a, H-1a'), 3.73-3.55 (m, 19 H; H-3, H-4, H-5, H-6b, H-1b', and 7 x CH_2), 3.18 ('quin', 2 H; H-1" and H-4")1.7, 2.71 (d, 2 H; H-2" and H-3")1.3, 1.48-1.45 (m, 1 H; H-7a"), 1.41-1.38 (m, 1 H; H-7b") ppm

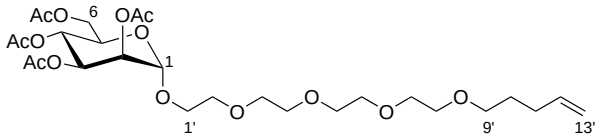
^{13}C NMR (150.9 MHz, D_3COD): δ = 180.2 ($N(C{=}O)_2$), 139.0 (C-5" and C-6"), 101.9 (C-1), 74.7 (C-4), 72.7 (C-3), 72.2 (C-2), 71.7, 71.7, 71.7, 71.5, 71.1 (each CH_2), 68.7 (C-5), 68.0 (CH_2), 67.9 (C-1'), 63.1 (C-6), 49.2 (C-2" and C-3"), 46.6 (C-1" and C-4"), 43.6 (C-7"), 39.1 (C-8') ppm

Coupling H-1/C-1 (D_3COD): $^1J_{H\text{-}1,C\text{-}1}$ = 169.4 Hz

ESI-IT-MS (pos. mode): m/z = 524.0 $[M+Na]^+$, 540.0 $[M+K]^+$ (calc. m/z = 524.2 $[M+Na]^+$, 540.2 $[M+K]^+$)

CHN analysis (in %): C 54.93, H 7.04, N 2.79 (calc.: C 55.08, H 7.03, N 2.79)

3,6,9,12-Tetraoxaheptadec-16-en-1-yl 2,3,4,6-Tetra-O-acetyl-α-D-mannopyranoside (39)



39

$C_{27}H_{44}O_{14}$
592.63 g mol^{-1}

Dienophile-spacer conjugate **32** (100 mg, 0.381 mmol, 1.0 eq) and mannosyl donor **37** (319 mg, 0.648 mmol, 1.7 eq) were dissolved in dry CH_2Cl_2 (5 mL) at 0 °C. After addition of $BF_3{\cdot}OEt_2$ (22 µL, 0.17 mmol, 0.45 eq) the mixture was stirred for 4 h at 0 °C. After neutralization with Et_3N, water was added to the reaction mixture. The phases were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (petroleum ether/EtOAc 1:1 to 1:2), **39** (150 mg, 0.253 mmol, 66 %) was isolated as pale oil.

TLC: R_f = 0.21 (petroleum ether/EtOAc)

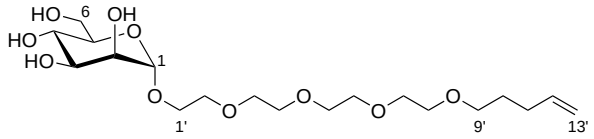
RP-HPLC (30-90 % B in 20 min): t_R = 16.81 min

^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 5.76 (ddt, J = 16.9, 10.1, 6.6 Hz 1 H; H-12'), 5.31 (dd, J = 10.1, 3.5 Hz, 1 H; H-3), 5.24 ('t', J = 10.0 Hz, 1 H; H-4), 5.22 (dd, J = 3.5, 1.8 Hz, 1 H; H-2), 5.00-4.93 (m, 1 H; H-13a'), 4.93-4.88 (m, 1 H; H-13b'), 4.82 (d, J = H-1 Hz, 1 H; 1.7), 4.25 (dd, J = 12.3, 5.1 Hz, 1 H; H-6a), 4.08-3.98 (m, 2 H; H-5, H-6b), 3.81-3.72 (m, 1 H; H-1a'), 3.67-3.56 (m, 13 H; H-1b' and 6 x CH_2), 3.56-3.51 (m, 2 H; CH_2), 3.42 (t, J = 6.7 Hz, 2 H; 2 x H-9'), 2.11 (s, 3 H; $C(O)CH_3$), 2.10-2.02 (m, 5 H; 2 x H-11' and $C(O)CH_3$), 1.99 (s, 3 H; $C(O)CH_3$), 1.94 (s, 3 H; $C(O)CH_3$), 1.63 ('q', 2 H; 2 x H-11') ppm

^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 170.5, 169.9, 169.7, 169.6 (each $C(O)CH_3$), 138.2 (C-12'), 114.6 (C-13'), 97.6 (C-1), 70.6 (C-9'), 70.5, 70.5, 70.5, 70.5, 70.5, 70.0, 69.9 (each CH_2), 69.4 (C-2), 69.0 (C-3), 68.3 (C-5), 67.2 (C-1'), 66.0 (C-4), 62.3 (C-6), 30.1 (C-11'), 28.7 (C-10'), 20.8, 20.6, 20.6, 20.5 (each $C(O)CH_3$) ppm

ESI-TOF-HRMS (pos. mode): m/z = 615.2623 $[M+Na]^+$ (calc. m/z = 615.2623 $[M+Na]^+$)

3,6,9,12-Tetraoxaheptadec-16-en-1-yl α-D-Mannopyranoside (9)



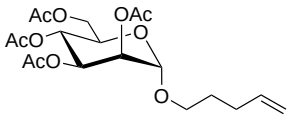
9

$C_{19}H_{36}O_{10}$
424.48 g mol^{-1}

Peracetylated compound **39** (109 mg, 0.184 mmol, 1 eq) was dissolved in dry MeOH (3 mL) and a 0.5 M solution of NaOMe in MeOH (74 µL, 36.7 µmol, 0.2 eq) was added. After stirring at rt for 2.5 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **9** (78 mg, 0.184 mmol, quant.) was isolated as a colorless oil.

^{1}H NMR (399.8 MHz, D_3COD): δ = 5.83 (ddt, J = 17.0, 10.2, 6.8 Hz 1 H; H-12'), 5.02 (ddt, J = 17.1, 2.1, 1.6 Hz 1 H; H-13a'), 4.95 (ddt, J = 10.2, 2.1, 1.2 Hz 1 H; H-13b'), 4.80 (d, J = 1.7 Hz, 1 H; H-1), 3.89-3.78 (m, 3 H; H-2, H-6a, H-1a'), 3.74-3.53 (m, 19 H; H-3, H-4, H-5, H-6b, H-1a' and 7 x CH_2), 3.48 (t, J = 6.5 Hz, 2 H; 2 x H-9'), 2.16-2.09 (m, 2 H; 2 x H-11'), 1.71-1.61 (m, 2 H; 2 x H-10') ppm
^{13}C NMR (100.5 MHz, D_3COD): δ = 139.6 (C-12'), 115.4 (C-13'), 101.9 (C-1), 74.7 (C-4), 72.7 (C-3), 72.3 (C-2), 71.7 (C-9'), 5 x 71.7, 71.5, 71.3 (each CH_2), 68.7 (C-5), 67.9 (C-1'), 63.1 (C-6), 31.5 (C-11'), 30.2 (C-10') ppm
Coupling H-1/C-1 (D_3COD): $^1J_{H\text{-}1,C\text{-}1}$ = 170.1 Hz
ESI-TOF-HRMS (pos. mode): m/z = 447.2201 $[M+Na]^+$ (calc. m/z = 447.2201 $[M+Na]^+$)

Pent-4-enyl 2,3,4,6-Tetra-O-acetyl-α-D-mannopyranoside (40)

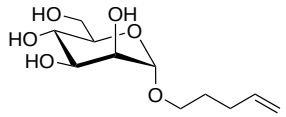


40

$C_{19}H_{28}O_{10}$
416.42 g mol^{-1}

Pent-4-enol (331 µL, 3.21 mmol, 1.5 eq) and mannosyl donor **37** (1.05 g, 2.14 mmol, 1.0 eq) were dissolved in dry CH_2Cl_2 (3 mL). After addition of $BF_3{\cdot}OEt_2$ (27 µL, 0.21 mmol, 0.1 eq), the mixtrure was stirred for 45 min at rt. After neutralization with Et_3N, water was added to the reaction mixture. The phases were separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC (petroleum ether/EtOAc 4:1 to 3:1), pure **40** (383 mg, 0.920 mmol, 43 %) was isolated as pale oil. The recorded spectroskopic data match those reported for title compound.[9]

Pent-4-enyl α-D-Mannopyranoside (10)

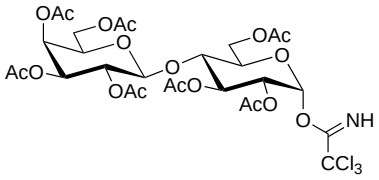


10

$C_{11}H_{20}O_6$
248.27 g mol^{-1}

Peracetylated compound **40** (383 mg, 0.920 mmol, 1 eq) was dissolved in dry MeOH (3 mL) and a 0.5 M solution of NaOMe in MeOH (49 µL, 0.74 mmol, 0.8 eq) was added. After stirring at rt for 70 min, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **10** (222 g, 0.894 mmol, 97 %) was isolated as a colorless oil. The recorded spectroskopic data match those reported for title compound.[10]

O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1$\rightarrow$4)-2,3,6-tri-O-acetyl-β-D-glucopyranosyl)trichloroacetimidate (41)

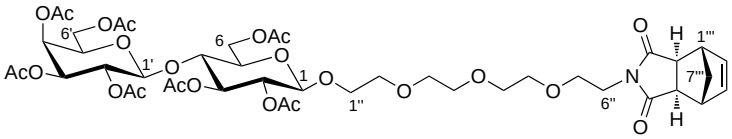


41

$C_{28}H_{36}Cl_3NO_{18}$
780.94 g mol^{-1}

Lactosyl donor **41**[11] was obtained in three steps from lactose: 1) Ac_2O, pyridine; 2) $H_2NCH_2CH_2NH_2$, AcOH; 3) NC-CCl_3, NaH, CH_2Cl_2; 70 % over three steps.

N-(12-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1$\rightarrow$4)-2,3,6-tri-O-acetyl-β-D-glucopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (42)



42

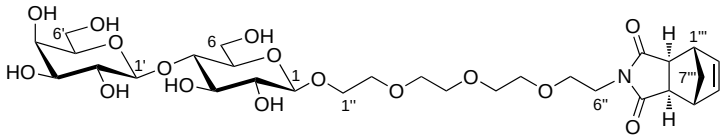
$C_{43}H_{59}NO_{23}$
957.92 g mol^{-1}

Dienophile-spacer conjugate **30** (500 mg, 1.47 mmol, 1 eq) and lactosyl donor **41** (1.97 g, 2.52 mmol, 1.71 eq) were dissolved at 0 °C in dry CH_2Cl_2 (5 mL). After addition of $BF_3{\cdot}OEt_2$ (83.0 µL, 0.663 mmol, 0.45 eq), the mixture was stirred for 30 min at 0 °C and subsequently for 3.5 h at rt. After neutralization with Et_3N, water was added to the reaction mixture. The phases were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4, filtrated and the solvent was evaporated under reduced pressure. After FC

(petroleum ether/EtOAc from 1:3 to 1:5), **42** (986 mg, 1.03 mmol, 70 %) was isolated as white foam.

TLC: R_f = 0.26 (toluene/acetone 3:1)
^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 6.28-6.25 (m, 2 H; H-5"' and H-6"'), 5.32 (dd, J = 3.3, 0.9 Hz, 1 H; H-4'), 5.16 ('t', J = 9.3 Hz, 1 H; H-3), 5.07 (dd, J = 10.4, 8.0 Hz, 1 H; H-2'), 4.93 (dd, J = 10.5, 3.4 Hz, 1 H; H-3'), 4.86 (dd, J = 9.4, 8.0 Hz, 1 H; H-2), 4.54 (d, J = 7.9 Hz, 1 H; H-1), 4.48-4.44 (m, 1 H; H-6a"), 4.46 (d, J = 7,9 Hz, 1 H; H-1'), 4.10 (dd, J = 11.2, 6.3 Hz, 1 H; H-6a'), 4.07 (dd, J = 12.0, 5.2 Hz, 1 H; H-6b), 4.05 (dd, J = 11.1, 7.4 Hz, 1 H; H-6b'), 3.90-3.83 (m, 2 H; H-1a" and H-5'), 3.76 ('t', J = 9.5 Hz, 1 H; H-4), 3.71-3.64 (m, 3 H; H-1b" and 2 x H-8"), 3.64-3.51 (m, 13 H; H-5 and 6 x CH_2), 3.25-3.21 (m, 2 H; H-1"' and H-4"'), 2.67-2.64 (m, 2 H; H-2"' and H-3"'), 2.12 (s, 3 H; $C(O)CH_3$), 2.09 (s, 3 H; $C(O)CH_3$), 2.03 (s, 3 H; $C(O)CH_3$), 2.02 (s, 3 H; $C(O)CH_3$), 2.01 (s, 3 H; $C(O)CH_3$), 2.01 (s, 3 H; $C(O)CH_3$), 1.93 (s, 3 H; $C(O)CH_3$), 1.47-1.44 (m, 1 H; H-7a"'), 1.35-1.32 (m, 1 H; H-7b"') ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 177.9 ($N(C{=}O)_2$), 170.3, 170.3, 170.1, 170.0, 169.7, 169.6, 169.0 (each $C(O)CH_3$), 137.8 (C-5"' and C-6"'), 101.0 (C-1'), 100.6 (C-1), 76.2 (C-4), 72.8 (C-3), 72.5 (C-5), 71.6 (C-2), 70.9 (C-3'), 70.6 (CH_2), 70.6 (CH_2), 70.5 (C-5'), 70.5 (CH_2), 70.2 (CH_2), 69.8 (CH_2), 69.0 (C-1"), 69.0 (C-2'), 66.8 (CH_2), 66.5 (C-4), 62.0 (C-6), 60.7 (C-6'), 47.7 (C-2"' and C-3"'), 45.2 (C-1"' and C-4"'), 42.6 (C-7"'), 37.7 (C-8"), 20.8, 20.7, 20.6, 20.6, 20.6, 20.5, 20.4 (each $C(O)CH_3$) ppm
ESI-IT-MS (pos. mode): m/z = 980.4 $[M+Na]^+$, 996.3 $[M+K]^+$ (calc. m/z = 980.3 $[M+Na]^+$, 996.3 $[M+K]^+$)
CHN analysis (in %): C 53.82, H 6.22, N 1.46 (calc.: C 53.91, H 6.21, N 1.46)

N-(12-(β-D-Galactopyranosyl-(1→4)-β-D-glucopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (12)



12

$C_{29}H_{45}NO_{16}$
663.66 g mol^{-1}

Peracetylated compound **42** (416 mg, 0.434 mmol, 1 eq) was dissolved in dry MeOH (4 mL) and a 0.5 M solution of NaOMe in MeOH (122 µL, 60.8 µmol, 0.14 eq) was added. After stirring at rt for 3 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **12** (294 mg, 0.443 mmol, quant.) was isolated as a colorless oil.

^{1}H NMR (600.1 MHz, D_3COD): δ = 6.33 ('t', J = 1.9 Hz, 2 H; H-5"' and H-6"'), 4.37 (d, J = 7.6 Hz, 1 H; H-1), 4.35 (d, J = 7.8 Hz, 1 H; H-1), 4.03-3.97 (m, 1 H; H-1a"), 3.90 (dd, J = 12.1, 2.5 Hz, 1 H; H-6a), 3.84 (dd, J = 12.2, 4.4 Hz, 1 H; H-6b), 3.83-3.82 (m, 1 H; H-4'), 3.78 (dd,

J = 11.4, 7.5 Hz, 1 H; H-6a'), 3.76-3.52 (m, 20 H; H-3, H-4, H-2', H-5', H-6b', H-1b" and 7 x CH_2), 3.50 (dd, J = 9.8, 3.3 Hz, 1 H; H-3'), 3.42 (ddd, J = 9.4, 4.4, 2.6 Hz 1 H; H-5), 3.27 ('t', J = 8.4 Hz, 1 H; H-2), 3.18 ('quin', J = 1.8 Hz, 2 H; H-1"' and H-4"'), 2.72 (br. d, J = 1.4 Hz, 2 H; H-2"' and H-3"'), 1.47-1.44 (m, 1 H; H-7a"'), 1.40-1.37 (m, 1 H; H-7b"') ppm

^{13}C NMR (150.9 MHz, D_3COD): δ = 180.2 ($N(C{=}O)_2$), 139.1 (C-5"' and C-6"'), 105.2 (C-1'), 104.4 (C-1), 80.8 (C-4), 77.2 (C-5'), 76.6 (C-5), 76.4 (C-3), 74.9 (C-3'), 74.8 (C-2), 72.6 (C-2'), 71.7, 3 x 71.6, 71.1 (CH_2), 70.4 (C-4'), 69.9 (C-1"), 68.0 (CH_2), 62.6 (C-6'), 62.1 (C-6), 49.1 (C-2"' and C-3"'), 46.6 (C-1"' and C-4"'), 43.7 (C-7"'), 39.1 (CH_2) ppm

ESI-IT-MS (pos. mode): m/z = 686.0 $[M+Na]^+$, 702.0 $[M+K]^+$ (calc. m/z = 686.3 $[M+Na]^+$, 702.2 $[M+K]^+$)

CHN analysis (in %): C 52.37, H 6.79, N 2.07 (calc.: C 52.48, H 6.83, N 2.11)

Synthesis of Probes for Negative Controls

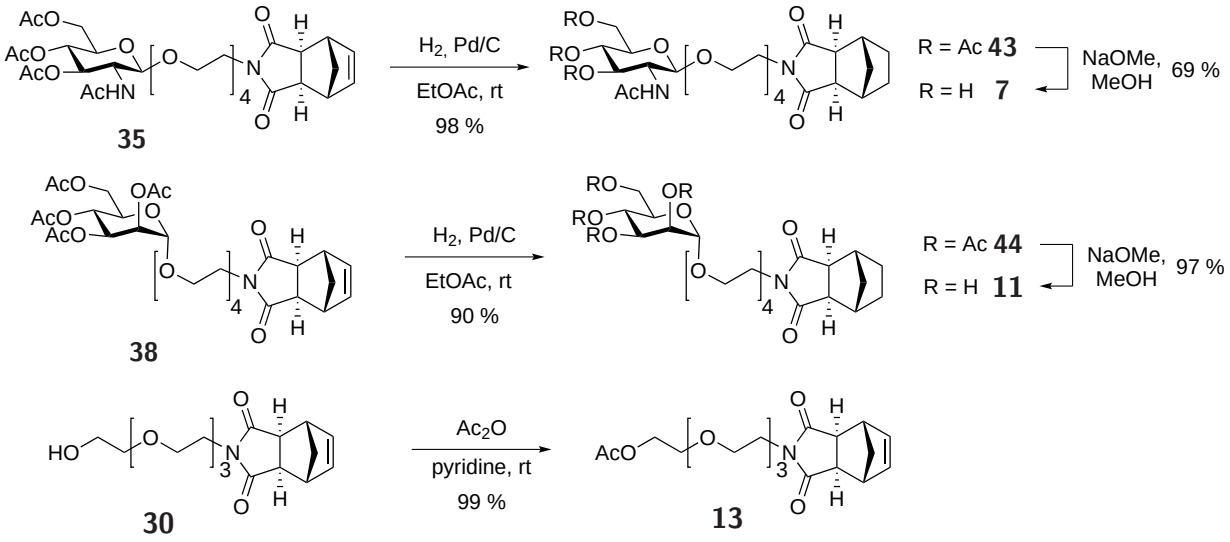
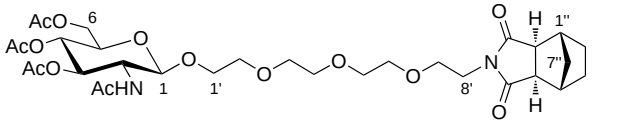


Figure S5: Synthesis of probes for negative controls

N-(12-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3,6,9,12-tetraoxadodecan-1-yl)-exo-norbornan-2,3-dicarboximide (43)



43

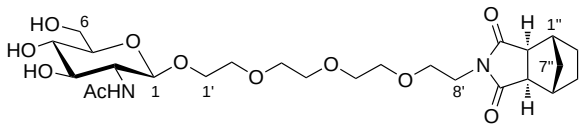
$C_{31}H_{46}N_2O_{14}$
670.70 g mol^{-1}

Conjugate **35** (210 mg, 314 mmol) was dissolved in EtOAc (3 mL) and Pd on carbon (35 mg, 10 wt. % loading) was added. After stirring over night under 1 atm of hydrogen gas, the catalyst was removed by filtration through celite followed by removal of the solvent under reduced pressure. Without

further purification, **43** (207 mg, 309 mmol, 98 %) was obtained as a colourless oil.

TLC: R_f = 0.31 (EtOAc/MeOH 10:1)
RP-HPLC (30-90 % B in 20 min): t_R = 11.46 min
^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 6.60 (d, J = 9.3 Hz, 1 H; NH), 5.10-4.99 (m, 2 H; H-3 and H-4), 4.77 (d, J = 8.6 Hz, 1 H; H-1), 4.22 (dd, J = 12.3, 4.8 Hz, 1 H; H-6a), 4.09 (dd, J = 12.3, 2.4 Hz, 1 H; H-6b), 4.07-4.00 (m, 1 H; H-2), 3.88-3.74 (m, 2 H; CH_2), 3.72-3.50 (m, 15 H; H-5 and 7 x CH_2), 2.66-2.63 (m, 2 H; H-1" and H-4"), 2.58 (br. s, 2 H; H-2" and H-3"), 2.04 (s, 3 H; C(O)CH_3), 1.97 (s, 3 H; C(O)CH_3), 1.96 (s, 3 H; C(O)CH_3), 1.91 (s, 3 H; C(O)CH_3), 1.67-1.60 (m, 2 H; H-5a" and H-6a"), 1.35-1.28 (m, 2 H; H-5b" and H-6b"), 1.20-1.13 (m, 2 H; H-7") ppm
^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 178.78 ($N(C{=}O)_2$), 170.7, 170.6, 170.5, 169.2 (each C(O)CH_3), 101.8 (C-1), 73.3 (C-3), 71.6 (C-5), 71.5, 70.7, 70.5, 70.3, 70.0 (each CH_2), 68.7 (C-4), 68.6 (CH_2), 66.8 (CH_2), 62.2 (C-6), 53.9 (C-2), 48.5 (C-2" and C-3"), 39.7 (C-1" and C-4"), 37.7 (CH_2), 32.9 (C-7"), 28.0 (C-5" and C-6"), 22.9, 20.7, 20.6, 20.5 (each C(O)CH_3) ppm
ESI-TOF-HRMS (pos. mode): m/z = 671.3012 $[M+H]^+$, 693.2822 $[M+Na]^+$ (calc. m/z = 671.3022 $[M+H]^+$, 693.2841 $[M+Na]^+$)

N-(12-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norbornan-2,3-dicarboximide (7)



7

$C_{25}H_{40}N_2O_{11}$
544.59 g mol^{-1}

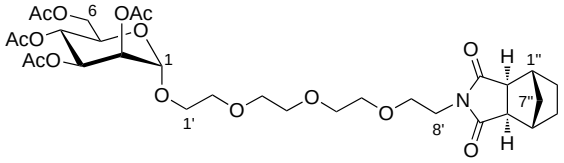
Peracetylated compound **43** (163 mg, 0.243 mmol, 1 eq) was dissolved in dry MeOH (3 mL) and a 0.5 M solution of NaOMe in MeOH (58 µL, 29 µmol, 0.12 eq) was added. After stirring at rt for 2 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **7** (91 mg, 0.167 mmol, 69 %) was isolated as a colorless oil.

RP-HPLC (5-60 % B in 20 min): t_R = 15.72 min
^{1}H NMR (399.8 MHz, D_3COD): δ = 4.50 (d, J = 8.4 Hz, 1 H; H-1), 3.93 (ddd, J = 11.2, 4.8, 3.7 Hz 1 H; H-1'), 3.88 (dd, J = 2.2, , Hz, H-6a H; 12.0) 3.74-3.55 (m, 17 H; H-2, H-6b, H-1b' and 7 x CH_2), 3.44 (dd, J = 10.3, 8.3 Hz, 1 H; H-3), 3.32 (dd, J = 9.7, 8.1 Hz, 1 H; H-4), 3.27 (ddd, J = 9.7, 5.5, 2.2 Hz 1 H; H-5), 2.67 (br. s, 2 H; H-2" and H-3"), 2.61-2.58 (m, 2 H; H-1" and H-4"), 1.99 (s, 3 H; C(O)CH_3), 1.71-1.64 (m, 2 H; H-5a" and H-6a"), 1.42-1.35 (m, 2 H; H-5b" and H-6b"), 1.27-1.18 (m, 2 H; H-7") ppm
^{13}C NMR (100.5 MHz, D_3COD): δ = 181.2 ($N(C{=}O)_2$), 174.0 (C(O)CH_3), 102.9 (C-1), 78.1

(C-5), 76.4 (C-3), 72.3 (C-4), 71.8, 3 x 71.7, 71.1 (each CH_2), 70.0 (C-1'), 68.0 (CH_2), 63.0 (C-6), 57.6 (C-2), 50.0 (C-2" and C-3"), 41.2 (C-1" and C-4"), 39.1 (C-8'), 33.9 (C-7"), 29.1 (C-5" and C-6"), 23.2 (C(O)CH_3) ppm

ESI-TOF-HRMS (pos. mode): m/z = 545.2693 $[M+H]^+$, 567.2526 $[M+Na]^+$ (calc. m/z = 545.2716 $[M+H]^+$, 567.2530 $[M+Na]^+$)

N-(12-(2,3,4,6-Tetra-O-acetyl-α-D-mannopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norbornan-2,3-dicarboximide (44)



44

$C_{31}H_{45}NO_{15}$
671.69 g mol^{-1}

Conjugate **38** (118 mg, 176 mmol) was dissolved in EtOAc (5 mL) and Pd on carbon (35 mg, 10 wt. % loading) was added. After stirring over night under 1 atm of hydrogen gas, the catalyst was removed by filtration through celite followed by removal of the solvent under reduced pressure. Without further purification, **44** (106 mg, 158 mmol, 90 %) was obtained as a colourless oil.

TLC: R_f = 0.36 (EtOAc)

^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 5.31 (dd, J = 10.0, 3.5 Hz, 1 H; H-3), 5.24 ('t', J = 9.9 Hz, 1 H; H-4), 5.22 (dd, J = 3.6, 1.7 Hz, 1 H; H-2), 4.83 (d, J = 1.6 Hz, 1 H; H-1), 4.25 (dd, J = 12.2, 4.9 Hz, 1 H; H-6a), 4.06 (dd, J = 12.2, 2.5 Hz, 1 H; H-6b), 4.03 (ddd, J = 5.0, 2.4, H-5 Hz 1 H; 10.0), 3.81-3.74 (m, 1 H; H-1a'), 3.67-3.52 (m, 15 H; H-1b', 7 x CH_2), 2.65-2.63 (m, 2 H; H-1" and H-4"), 2.56 (br. s, 2 H; H-2" and H-3"), 2.11 (s, 3 H; C(O)CH_3), 2.06 (s, 3 H; C(O)CH_3), 2.00 (s, 3 H; C(O)CH_3), 1.95 (s, 3 H; C(O)CH_3), 1.65-1.60 (m, 2 H; H-5a" and H-6a"), 1.33-1.28 (m, 2 H; H-5b" and H-6b"), 1.20-1.13 (m, 2 H; H-7") ppm

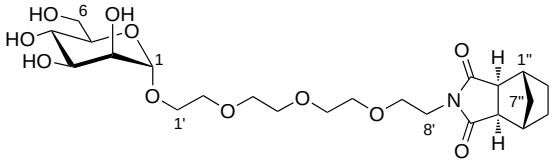
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 178.8 (N(C=O)$_2$), 170.6, 169.9, 169.8, 169.6 (each C(O)CH_3), 97.6 (C-1), 70.6, 70.5, 70.5, 69.9, 69.8 (each CH_2), 69.5 (C-2), 69.0 (C-3), 68.3 (C-5), 67.3 (C-1'), 66.8 (CH_2), 66.1 (C-4), 62.3 (C-6), 48.5 (C-2" and C-3"), 39.7 (C-1" and C-4"), 37.7 (CH_2), 32.9 (C-9"), 28.0 (C-5" and C-6"), 20.8, 20.7, 20.6, 20.6 (each C(O)CH_3) ppm

Coupling H-1/C-1 ($CDCl_3$): $^1J_{H\text{-}1,C\text{-}1}$ = 172.7 Hz

ESI-IT-MS (pos. mode): m/z = 694.2 $[M+Na]^+$, 710.2 $[M+K]^+$ (calc. m/z = 694.3 $[M+Na]^+$, 710.2 $[M+K]^+$)

CHN analysis (in %): C 55.40, H 6.80, N 2.12 (calc.: C 55.43, H 6.75, N 2.09)

N-(12-(α-D-Mannopyranosyl)-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norbornan-2,3-dicarboximide (11)



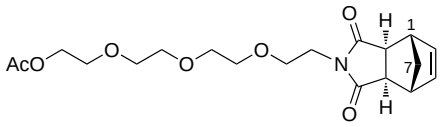
11

$C_{23}H_{37}NO_{11}$
503.54 g mol^{-1}

Peracetylated compound **44** (279 mg, 0.415 mmol, 1 eq) was dissolved in dry MeOH (4 mL) and a 0.5 M solution of NaOMe in MeOH (67 µL, 33.2 µmol, 0.08 eq) was added. After stirring at rt for 2 h, the mixture was neutralized by addition of acidic ion-exchange resin (Dowex 50W-X8, H^+ form) and filtrated. After removal of the solvent under reduced pressure, **11** (204 mg, 0.405 mmol, 97 %) was isolated as a colorless oil.

^{1}H NMR (600.1 MHz, D_3COD): δ = 4.80 (d, J = 1.7 Hz, 1 H; H-1), 3.86-3.81 (m, 3 H; H-2, H-6a and H-1a'), 3.71-3.68 (m, 2 H; H-3, H-6b), 3.68-3.59 (m, 12 H; H-5, H-1b' and 5 x CH_2), 3.59-3.55 (m, 5 H; H-4, 2 x CH_2), 2.67-2.66 (m, 2 H; H-2" and H-3"), 2.60-2.58 (m, 2 H; H-1" and H-4"), 1.70-1.65 (m, 2 H; H-5a" and H-6a"), 1.41-1.36 (m, 2 H; H-5b" and H-6b"), 1.26-1.19 (m, 2 H; H-7") ppm
^{13}C NMR (150.9 MHz, D_3COD): δ = 181.2 ($N(C{=}O)_2$), 101.9 (C-1), 74.7 (C-4), 72.7 (C-3), 72.3 (C-2), 3 x 71.7, 71.5, 71.2 (each CH_2), 68.8 (C-5), 68.0 (CH_2), 97.9 (C-1'), 63.1 (C-6), 50.0 (C-2" and C-3"), 41.2 (C-1" and C-4"), 39.1 (C-8'), 33.9 (C-7"), 29.1 (C-5" and C-6") ppm
Coupling H-1/C-1 (D_3COD): $^1J_{H\text{-}1,C\text{-}1}$ = 170.4 Hz
ESI-IT-MS (pos. mode): m/z = 526.0 $[M+Na]^+$, 542.0 $[M+K]^+$ (calc. m/z = 526.2 $[M+Na]^+$, 542.2 $[M+K]^+$)
CHN analysis (in %): C 54.76, H 7.34, N 2.72 (calc.: C 54.86, H 7.41, N 2.78)

N-(12-O-Acetyl-3,6,9,12-tetraoxa-dodecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (13)



13

$C_{19}H_{27}NO_7$
381.42 g mol^{-1}

Dienophile-spacer conjugate **30** (500 mg, 1.47, 1.0 eq) was dissolved in pyridine (5 mL) and acetic anhydride (280 µL, 2.95 mmol, 2.0 eq) was added. After stirring at rt for 15 h, the solvent was removed under reduced pressure and the residue was coevaporated twice with toluene. **13** (557 mg, 1.46 mmol, 99 %) was isolated as slidly yellow oil without the need for further purification.

^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 6.24 ('t', J = 1.9 Hz, 2 H; H-5 and H-6), 4.17 (m, 2 H; CH_2), 3.67-3.51 (m, 14 H; 7 x CH_2), 3.22 (' quin', J = 1.7 Hz, 2 H; H-1 and H-4), 2.63 (d, J = 1.5 Hz,

2 H; H-2 and H-3), 2.03 (s, 3 H; CH_3), 1.46-1.42 (m, 1 H; H-7a), 1.34-1.30 (m, 1 H; H-7b) ppm
^{13}C NMR (100.5 MHz, $CDCl_3$): δ = 177.8 ($N(C{=}O)_2$), 170.9 ($C(O)CH_3$), 137.7 (C-5 and C-6), 3 x 70.5, 69.8, 69.0, 66.8, 63.5 (each CH_2), 47.7 (C-2 and C-3), 45.2 (C-1 and C-4), 42.6 (C-7), 37.6 (CH_2), 20.8 (CH_3) ppm
ESI-IT-MS (pos. mode): m/z = 382.1 $[M+H]^+$, 404.1 $[M+Na]^+$, 420.0 $[M+K]^+$ (calc. m/z = 382.2 $[M+H]^+$, 404.2 $[M+Na]^+$, 420.1 $[M+K]^+$)
CHN analysis (in %): C 59.73, H 7.12, N 3.71 (calc.: C 59.83, H 7.14, N 3.67)

Preparation of the Bifunctional Linker

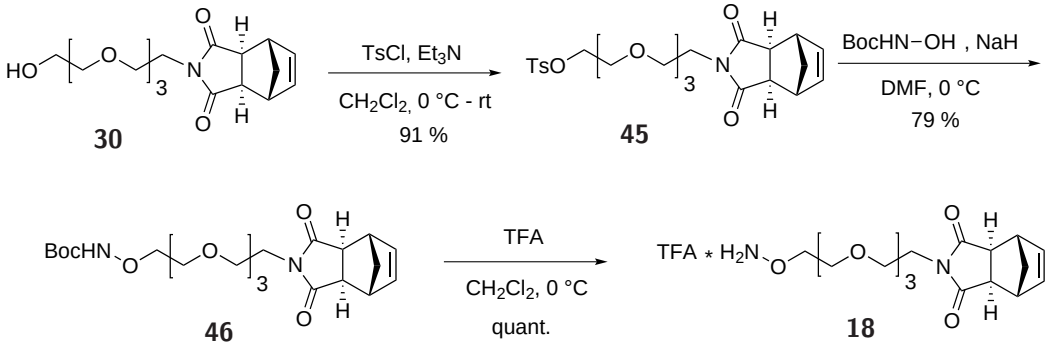
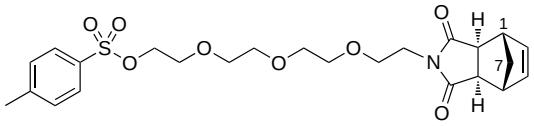


Figure S6: Synthesis of bifunctional linker **18**

N-(11-(Tolylsulfonyloxy)-3,6,9-trioxaundecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (45)



45

$C_{24}H_{31}NO_8S$
493.57 g mol^{-1}

Alcohol **30** (1.54 g, 4.54 mmol, 1.0 eq) was dissoved in dry CH_2Cl_2 (15 mL) and Et_3N (1.15 mL, 8.17 mmol, 1.8 eq) and TsCl (1.30 g, 6.81 mmol, 1.50 eq) were added at 0°C. After stirring at rt for 24 h, the reaction mixture was neutralized with acetic acid and quenched with water. The layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. Combined organic layers were dried over Na_2SO_4, filtrated and the solvent was removed under reduced pressure. After FC (petroleum ether/EtOAc 1:2 to 0:1), **45** (2.06 g, 4.11 mmol, 91 %) was isolated as pale oil.

TLC: R_f = 0.23 (petroleum ether/EtOAc 1:1)
^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 7.80 (m, 2 H; Ar-H), 7.34 (m, 2 H; Ar-H), 6.28 ('t', J = 1.8 Hz, 2 H; H-5 and H-6), 4.16 (m, 2 H; CH_2), 3.70-3.66 (m, 4 H; 2 x CH_2), 3.65-3.62 (m, 2 H; CH_2), 3.58-3.53 (m, 8 H; 4 x CH_2), 3.26 ('quin', J = 1.7 Hz, 2 H; H-1 and H-4), 2.67 (d, J =

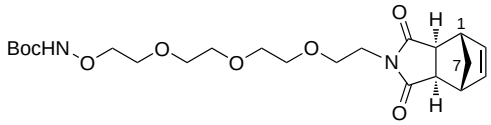
1.5 Hz, 2 H; H-2 and H-3), 2.45 (s, 3 H; CH_3), 1.49-1.46 (m, 1 H; H-7a), 1.37-1.34 (m, 1 H; H-7b) ppm

^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 178.0 ($N(C{=}O)_2$), 144.8 (quat. C), 137.8 (C-5 and C-6), 133.1 (quat. C), 129.8, 128.0 (both Ar), 70.7, 70.6, 70.6, 69.9, 69.2, 68.7, 66.9 (each CH_2), 47.8 (C-2 and C-3), 45.3 (C-1 and C-4), 42.7 (C-7), 37.7 (CH_2), 21.6 (CH_3) ppm

ESI-IT-MS (pos. mode): m/z = 494.3 $[M+H]^+$, 516.3 $[M+Na]^+$, 532.2 $[M+K]^+$ (calc. m/z = 494.2 $[M+H]^+$, 516.2 $[M+Na]^+$, 532.1 $[M+K]^+$)

CHN analysis (in %): C 58.30, H 6.49, N 2.79 (calc.: C 58.40, H 6.33, N 2.84)

N-(11-(N-(tert-Butyloxycarbonyl)aminooxy)-3,6,9-trioxaundecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide (46)



46

$C_{22}H_{34}N_2O_8$
454.51 g mol^{-1}

N-Boc-hydroxyl amine (265 mg, 1.99 mmol, 2.0 eq) was dissoved in dry DMF (5 mL) and NaH (60 % (w/w) in mineral oil, 119 mg, 2.98 mmol, 3.0 eq) was added at 0 °C. After 10 min, tosylate **45** (500 mg, 1.01 mmol, 1 eq) in 3 mL dry DMF was added and the mixture was stirred at 0 °C for 2 h. After neutalization with acetic acid, the solvent was removed under reduced pressure. The residue was redissolved in a mixture of water and EtOAc. the layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtrated and the solvent was removed under reduced pressure. After FC (petroleum ether/EtOAc 1:3), **46** (357 mg, 0.786 mmol, 79 %) was isolated as a pale oil.

TLC: R_f = 0.31 (EtOAc)

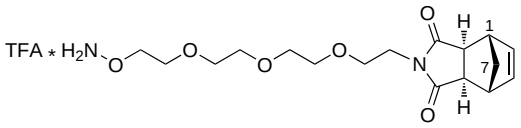
^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 7.71 (br. s, 1 H; NH), 6.27 ('t', J = 1.9 Hz, 2 H; H-5 and H-6), 4.01 (m, 2 H; CH_2), 3.73-3.55 (m, 14 H; 7 x CH_2), 3.26 ('quin', J = 1.7 Hz, 2 H; H-1 and H-4), 2.68 (d, J = 1.4 Hz, 2 H; H-2 and H-3), 1.49-1.44 (m, 10 H; $C(CH_3)_3$ and H-7a), 1.36-1.31 (m, 1 H; H-7b) ppm

^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 178.0 ($N(C{=}O)_2$), 156.7 (NC(O)O), 137.8 (C-5 and C-6), 81.4 ($C(CH_3)_3$), 75.3, 3 x 70.5, 69.9, 69.1, 66.9 (each CH_2), 47.8 (C-2 and C-3), 45.2 (C-1 and C-4), 42.7 (C-7), 37.7 (CH_2), 28.2 ($C(CH_3)_3$) ppm

ESI-IT-MS (pos. mode): m/z = 477.0 $[M+Na]^+$, 493.0 $[M+K]^+$ (calc. m/z = 477.2 $[M+Na]^+$, 493.2 $[M+K]^+$)

CHN analysis (in %): C 57.92, H 7.51, N 6.18 (calc.: C 58.14, H 7.54, N 6.16)

N-(11-Aminooxy-3,6,9-trioxaundecan-1-yl)-exo-norborn-5-en-2,3-dicarboximide, TFA salt (18)



18

$C_{17}H_{26}N_2O_6$
354.40 g mol^{-1}

Boc-protected oxyamine **46** (345 mg, 0.759 mmol, 1.0 eq) was dissolved in CH_2Cl_2 (5 mL) and TFA (2.5 mL) was added at 0 °C. After stirring at 0 °C for 1 h, the solvent was removed in a stream of nitrogen. The residue was dissolved in a small amount of water and lyophilised. This procedure was repeated twice, in order to remove excess TFA. **18** (364 mg, 0.78 mmol, quant.) was isolated as a pale oil.

TLC: R_f = 0.09 (EE/MeOH 20:1)
RP-HPLC (20-40 % B in 20 min): t_R = 9.71 min
^{1}H NMR (399.8 MHz, $CDCl_3$): δ = 6.29 ('t', J = H-5 and H-6 Hz, 2 H; 1.8), 4.29 (m, 2 H; CH_2), 3.90 (m, 2 H; CH_2), 3.75-3.70 (m, 4 H; 2 x CH_2), 3.62-3.57 (m, 4 H; 2 x CH_2), 3.55 (m, 4 H; 2 x CH_2), 3.27 ('quin', J = 1.8 Hz, 2 H; H-1 and H-4), 2.73 (d, J = 1.4 Hz, 2 H; H-2 and H-3), 1.52-1.47 (m, 1 H; H-7a), 1.29-1.25 (m, 1 H; H-7b) ppm
^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 179.1 ($N(C{=}O)_2$), 137.8 (C-5 and C-6), 72.5, 71.1, 70.0, 69.7, 69.6, 69.5, 68.0 (each CH_2), 47.8 (C-2 and C-3), 45.3 (C-1 and C-4), 42.5 (C-7), 38.6 (CH_2) ppm
CHN analysis (in %): C 49.06, H 5.98, N 6.37 (calc.: C 48.72, H 5.81, N 5.98)
ESI-TOF-HRMS (pos. mode): m/z = 355.1858 $[M+H]^+$ (calc. m/z = 355.1864 $[M+H]^+$)

References

[1] M. Wiessler, E. Mueller, P. Lorenz, C. Kliem, H. Fleischhacker, *PCT Int. Appl.* **2007**, WO 2007/144200 A1.

[2] C. Du, G. Zhang, Z. Wang, L. Li, J. Tang, L. Wang, *Chin. Sci. Bull.* **2009**, *54,* 382-386.

[3] P. S. Shirude, V. A. Kumar, K. N. Ganesh, *Eur. J. Org. Chem* **2005**, 5207-5215.

[4] S. Svedhem, C.-A. Hollander, J. Shi, P. Konradsson, B. Liedberg, S. C. T. Svensson, *J. Org. Chem.* **2001**, *66,* 4494-4503.

[5] J. D. White, P. Hrnciar, *J. Org. Chem.* **2000**, *65,* 9129-9142.

[6] S. Nakabayashi, C. D. Warren, R. W. Jeanloz, *Carbohydr. Res.* **1986**, *150,* c7-c10.

[7] V. Wittmann, D. Lennartz, *Eur. J. Org. Chem* **2002**, 1363-1367.

[8] M. Mori, Y. Ito, T. Ogawa, *Carbohydr. Res.* **1990**, *195,* 199-224.

[9] C.-C. Lin, Y.-C. Yeh, C.-Y. Yang, C.-L. Chen, G.-F. Chen, C.-C. Chen, Y.-C. Wu, *J. Am. Chem. Soc.* **2002**, *124,* 3508-3509.

[10] I. Cumpstey, T. D. Butters, R. J. Tennant-Eyles, A. J. Fairbanks, R. R. France, M. R. Wormald, *Carbohydr. Res.* **2003**, *338,* 1937-1949.

[11] F. G. Núñez, M. T. C. Valdes, E. Aruca, R. R. Schmidt, V. V. Bencomo, *J. Carbohydr. Chem.* **2003**, *22,* 395 - 406.

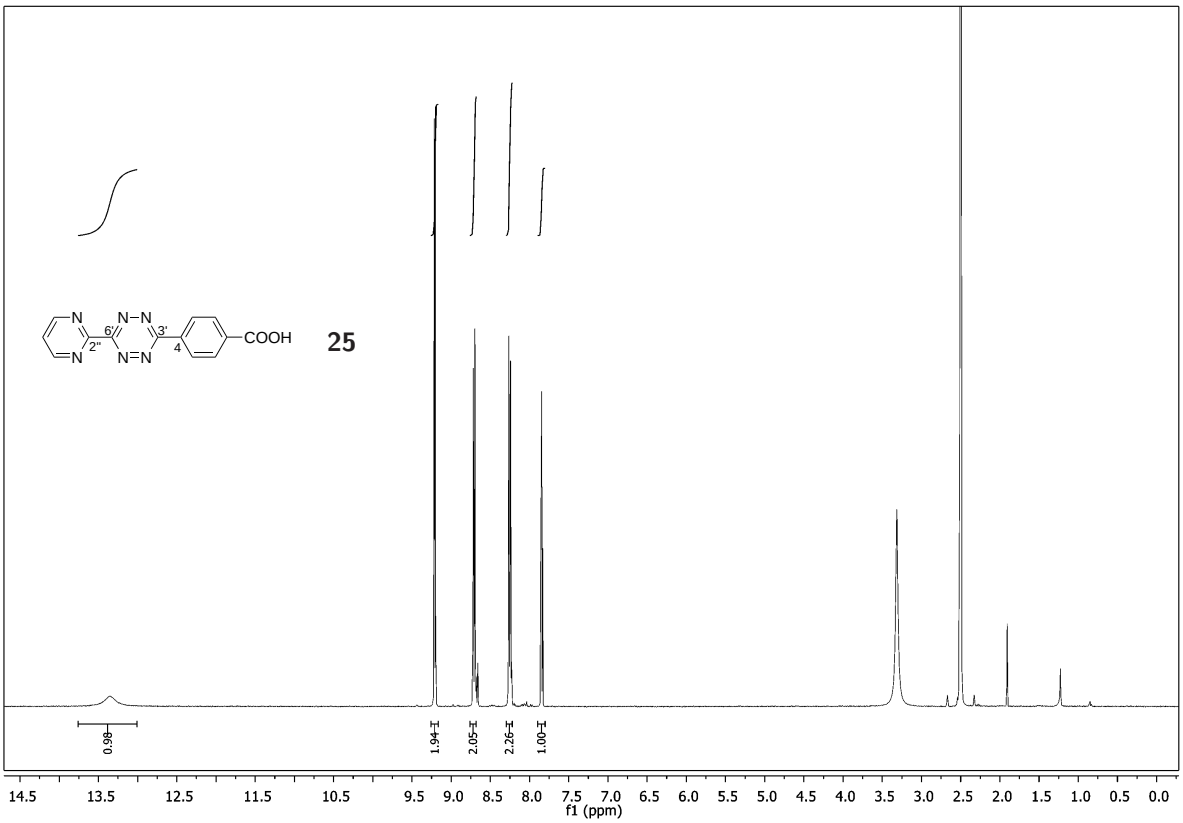


Figure S7: ^{1}H NMR (DMSO-d_6, 399.8 MHz) of compound **25**

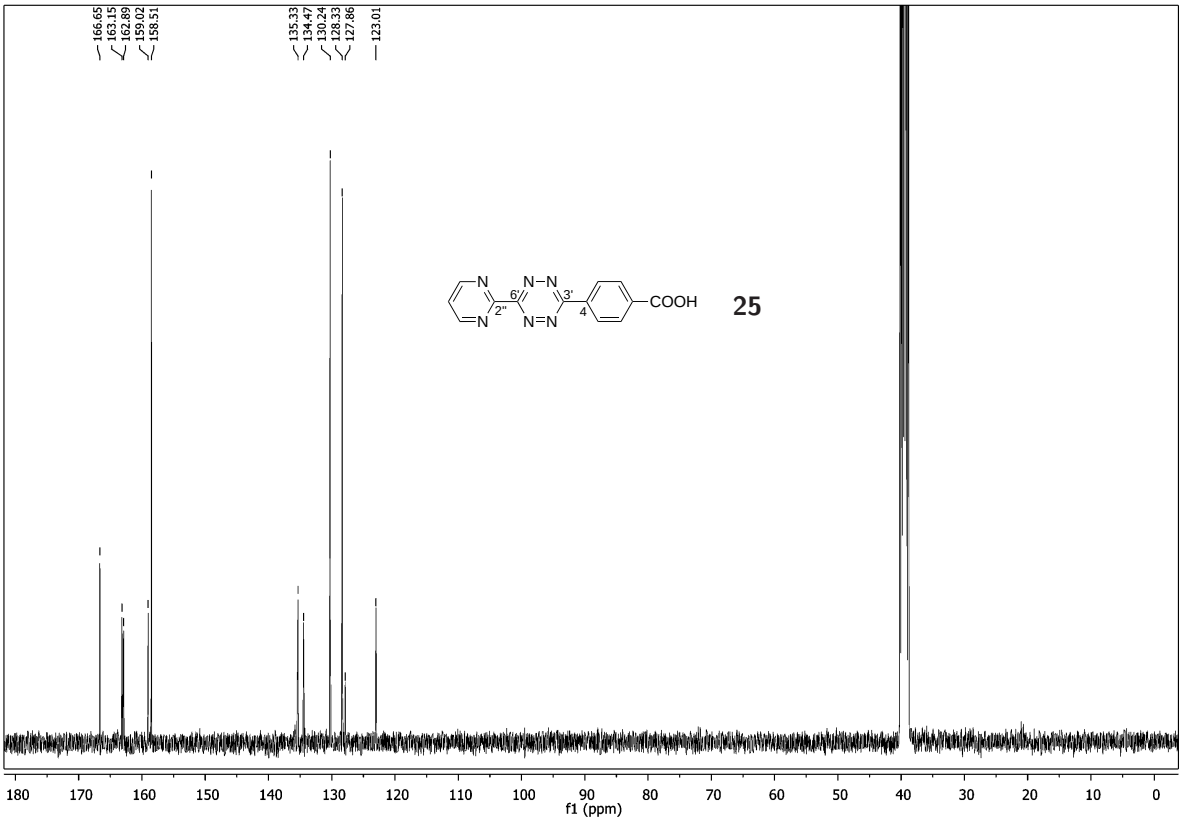


Figure S8: ^{13}C NMR (DMSO-d_6, 100.5 MHz) of compound **25**

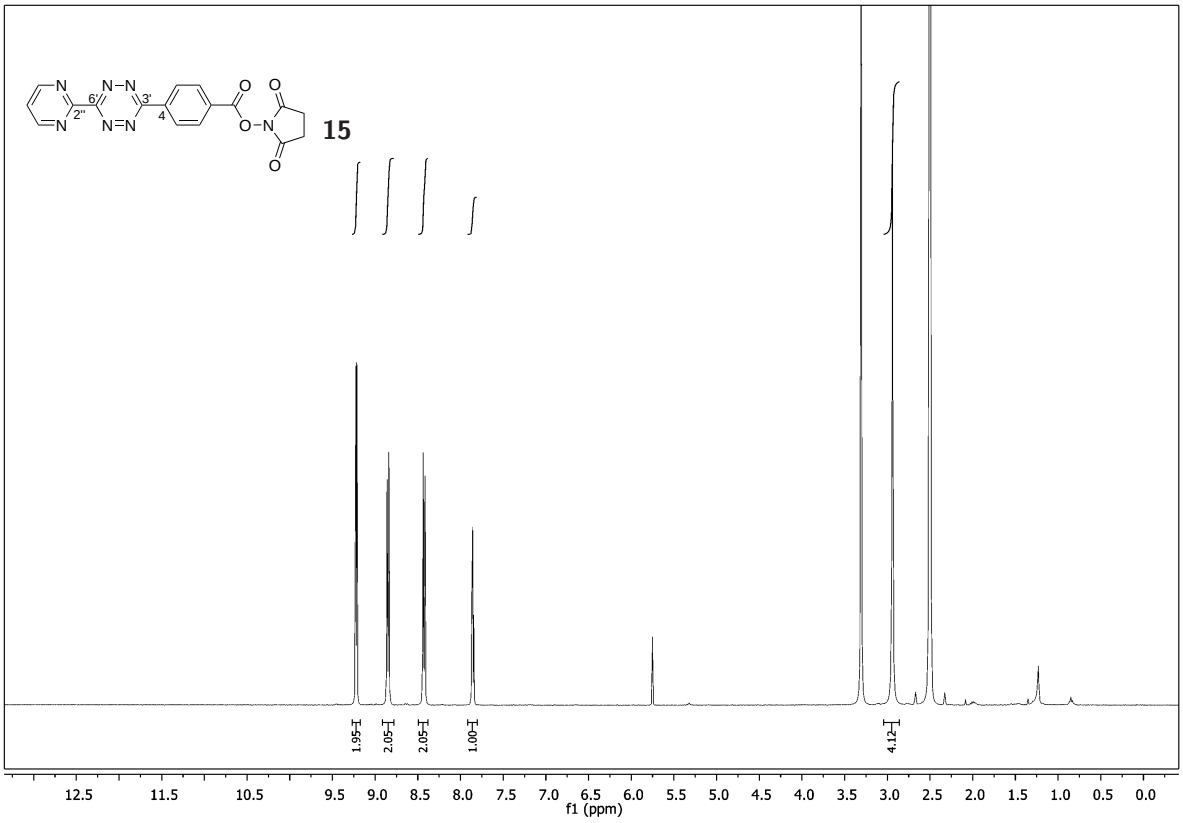


Figure S9: ^{1}H NMR (DMSO-d_6, 399.8 MHz) of compound **15**

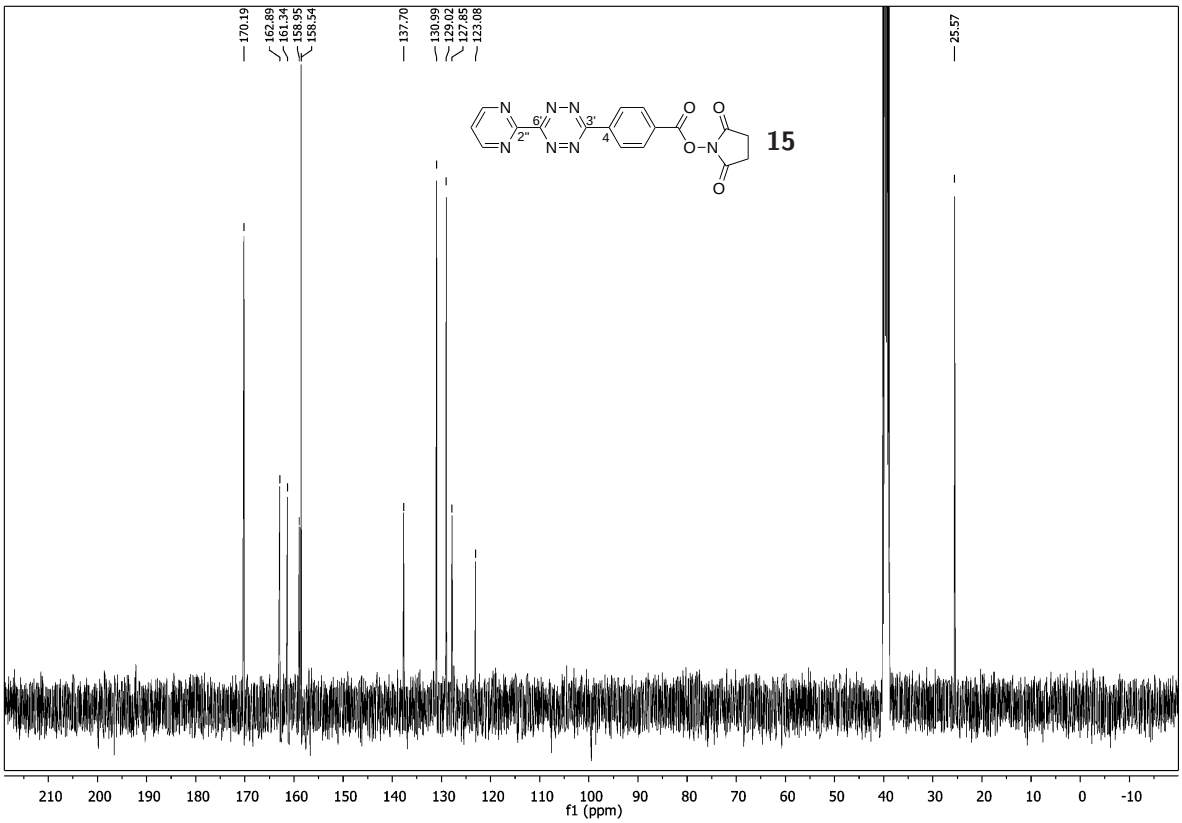


Figure S10: ^{13}C NMR (DMSO-d_6, 100.5 MHz) of compound **15**

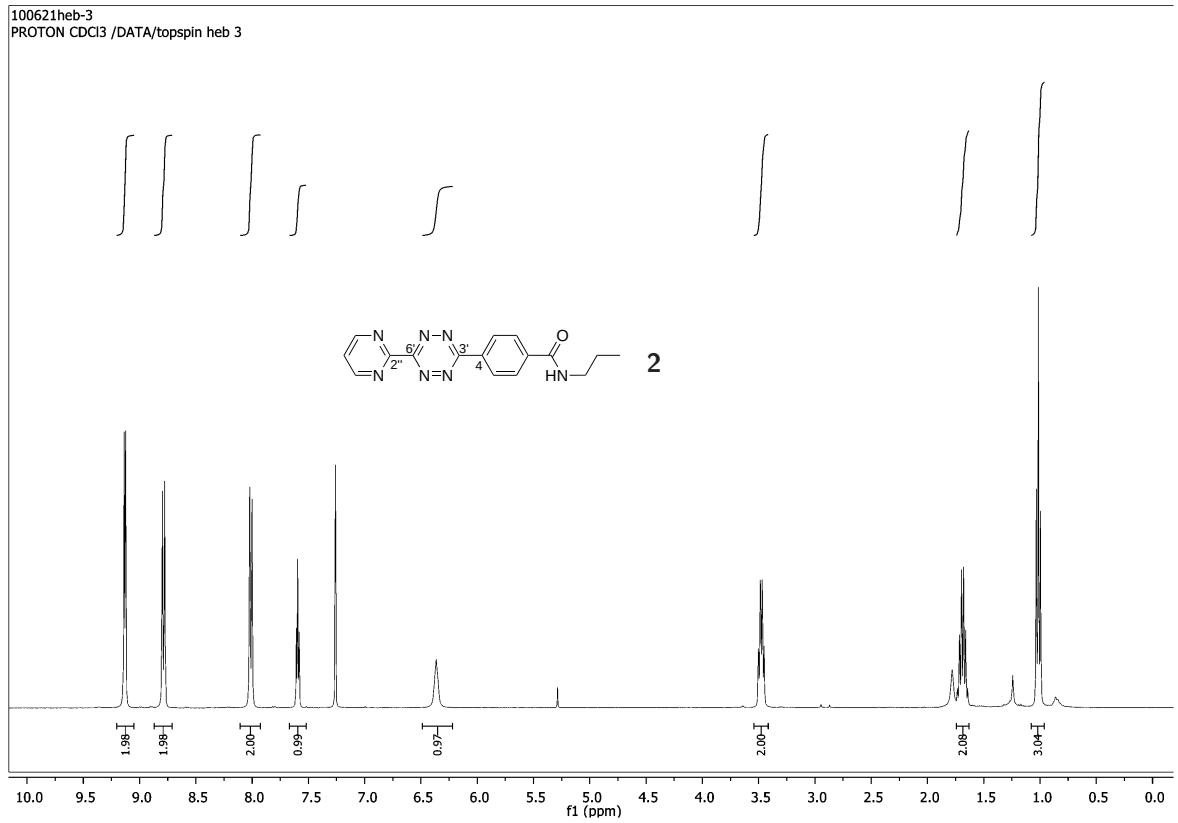


Figure S11: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **2**

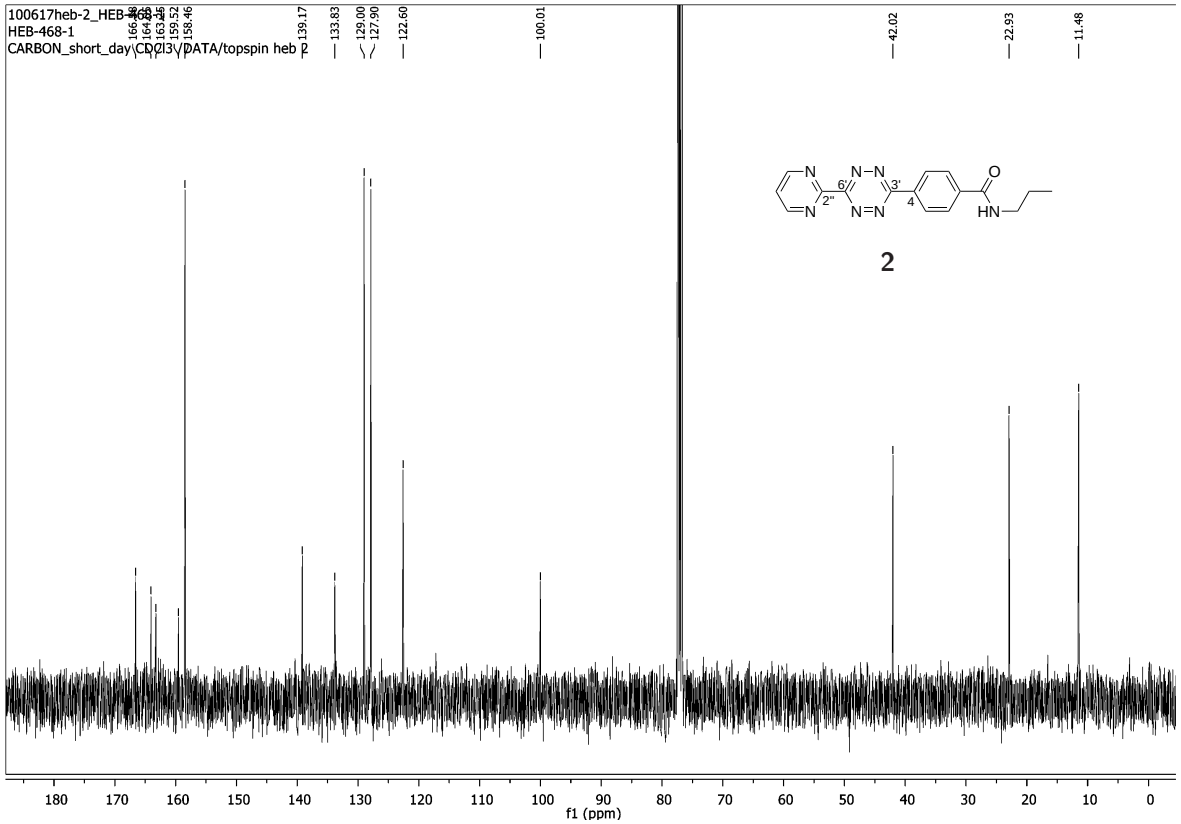


Figure S12: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **2**

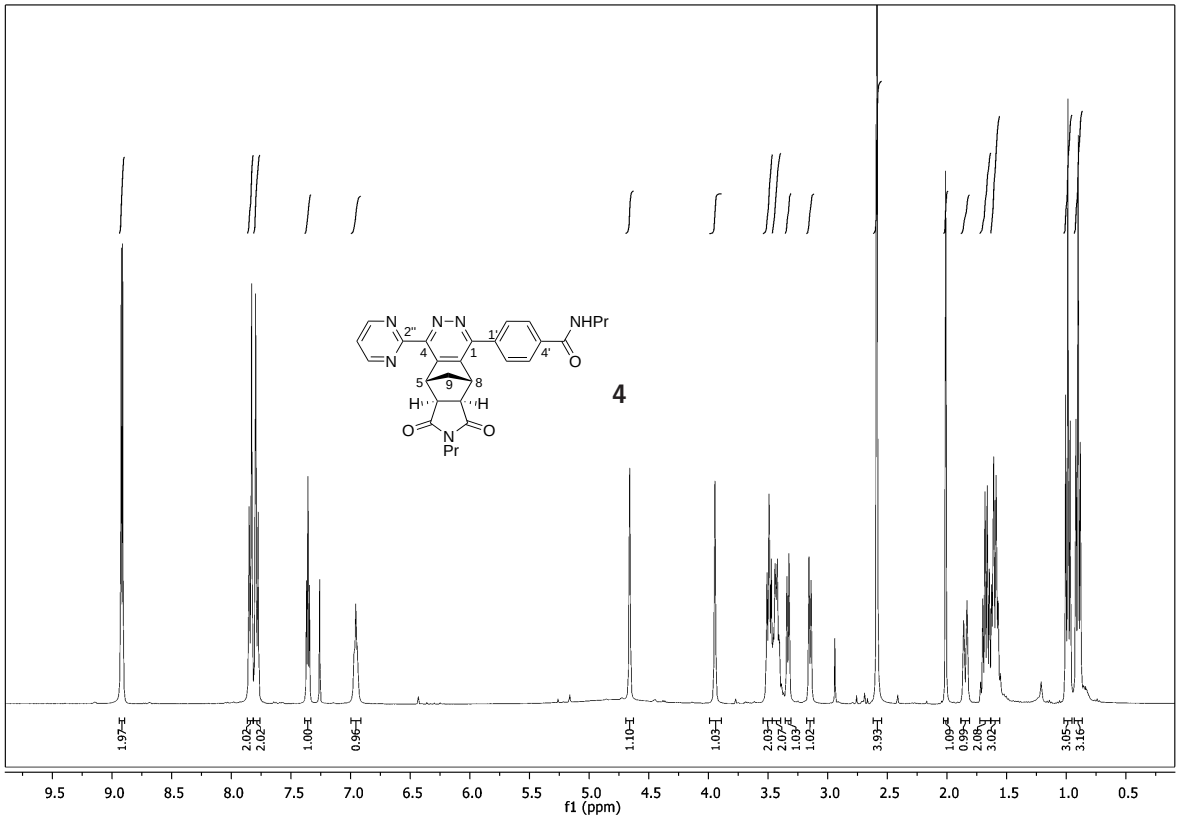


Figure S13: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **4**

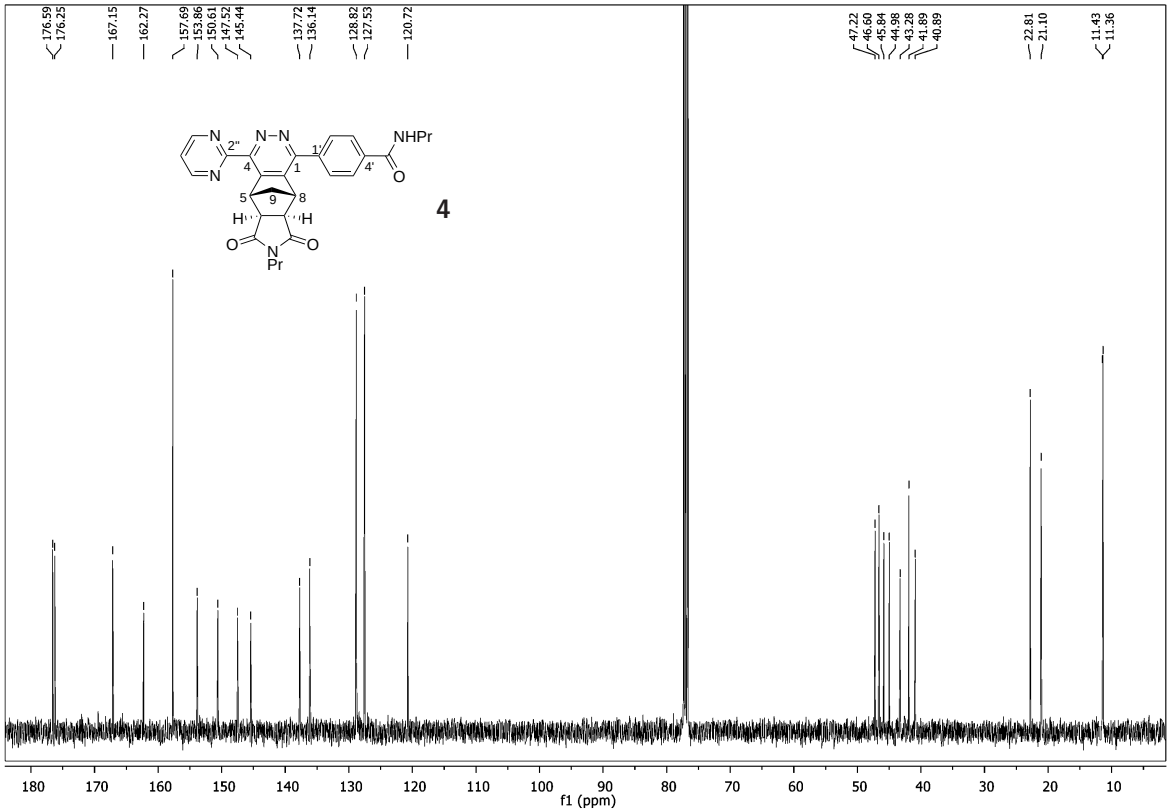


Figure S14: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **4**

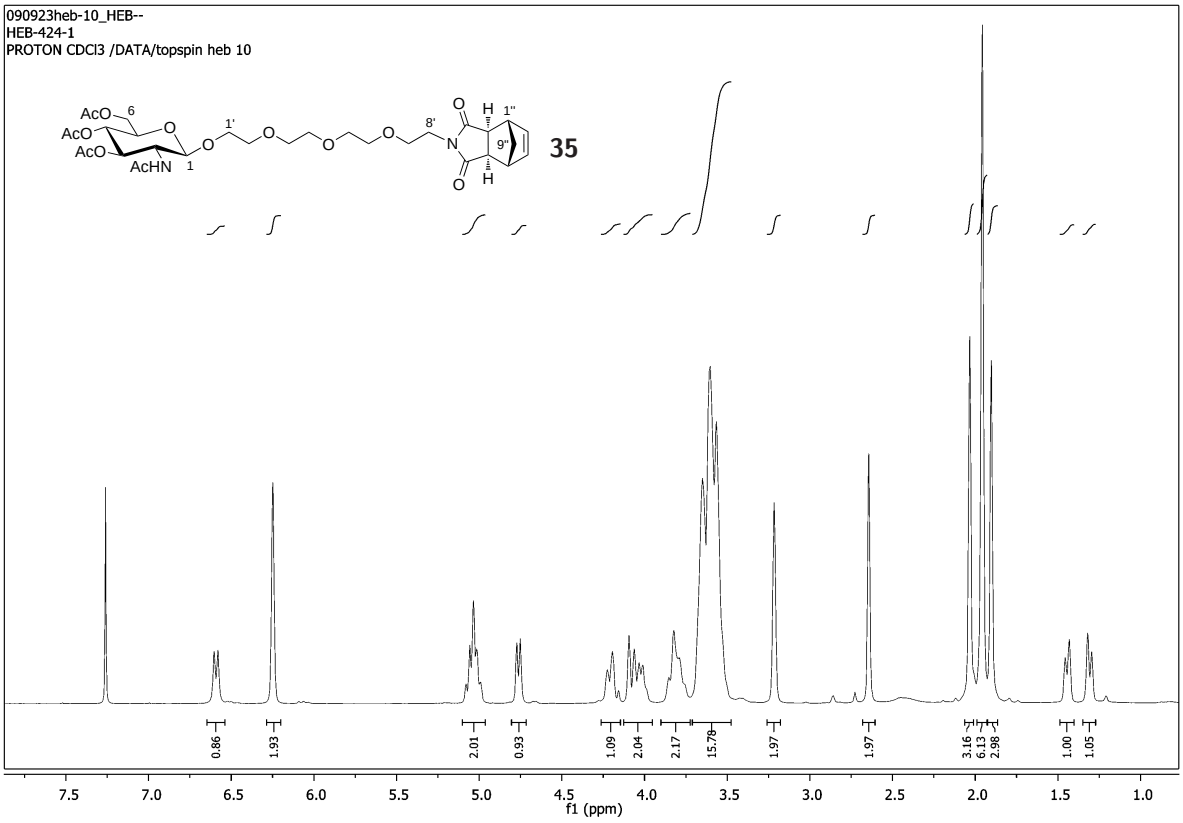


Figure S15: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **35**

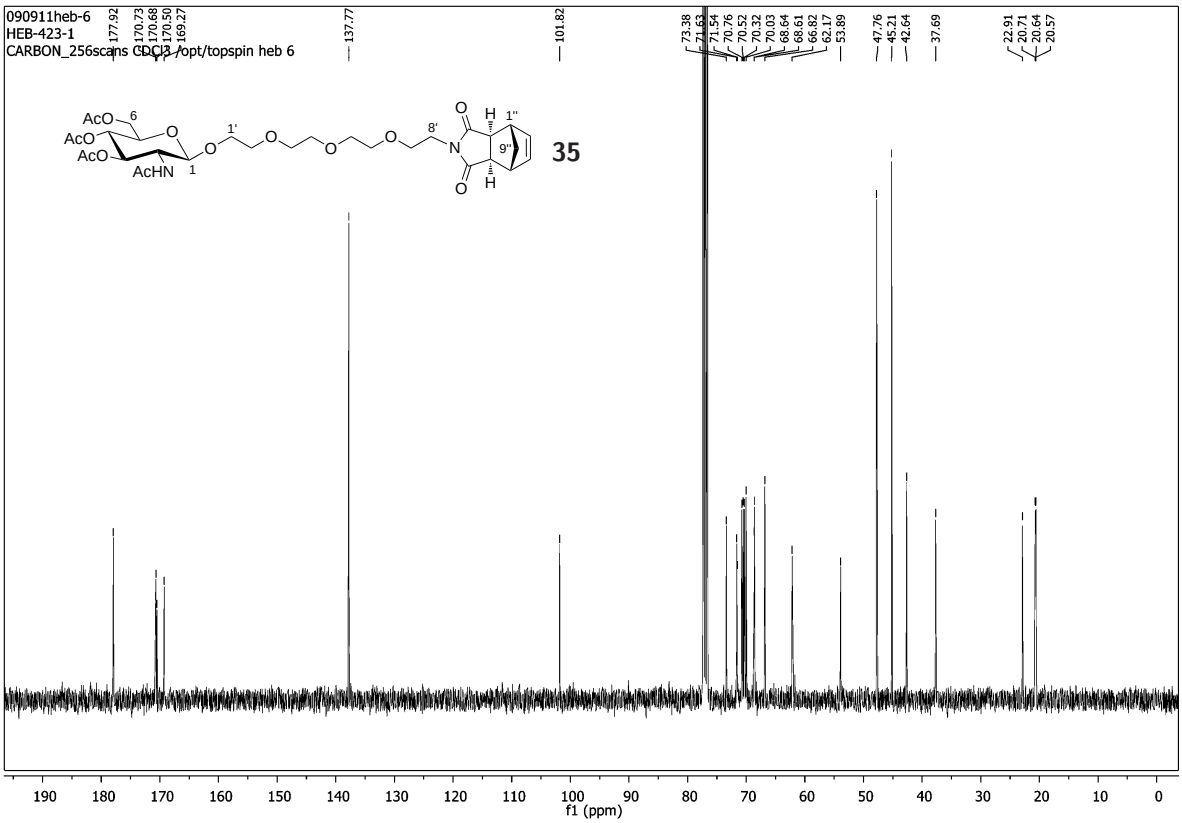


Figure S16: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **35**

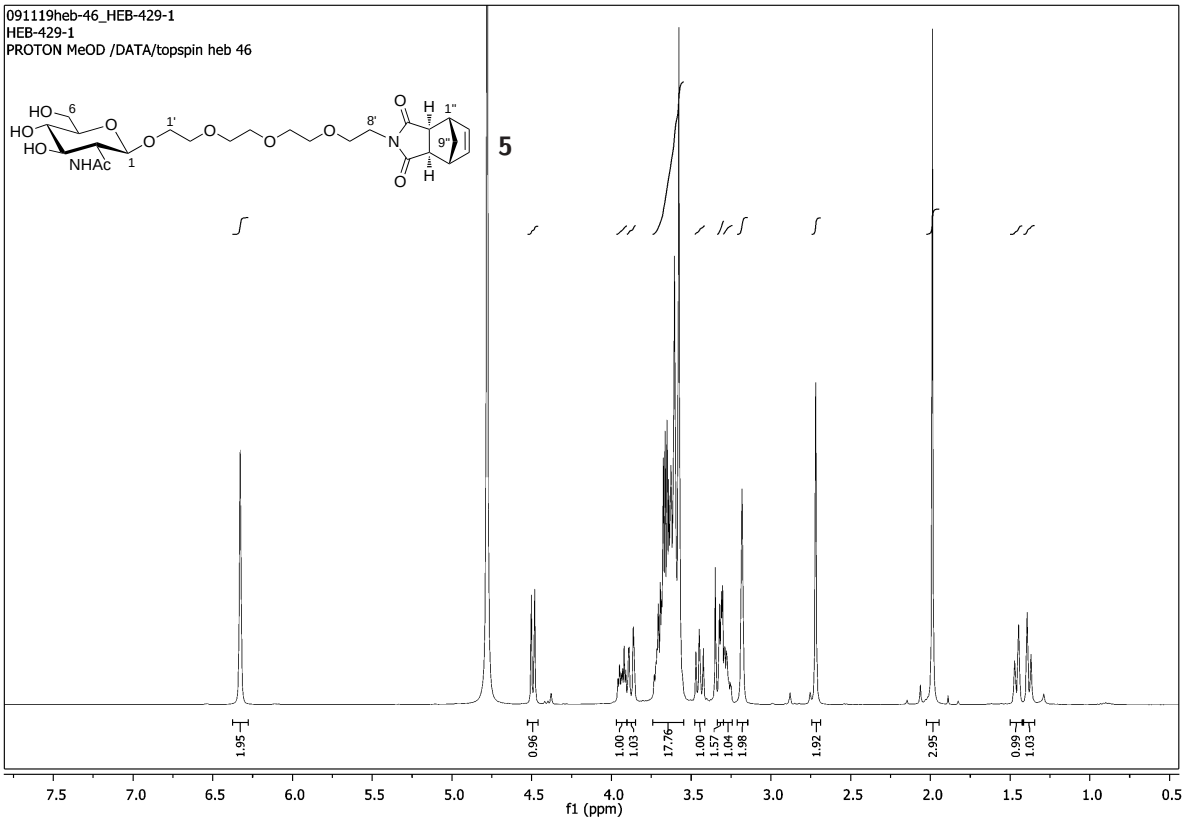


Figure S17: ^{1}H NMR (D_3COD, 399.8 MHz) of compound **5**

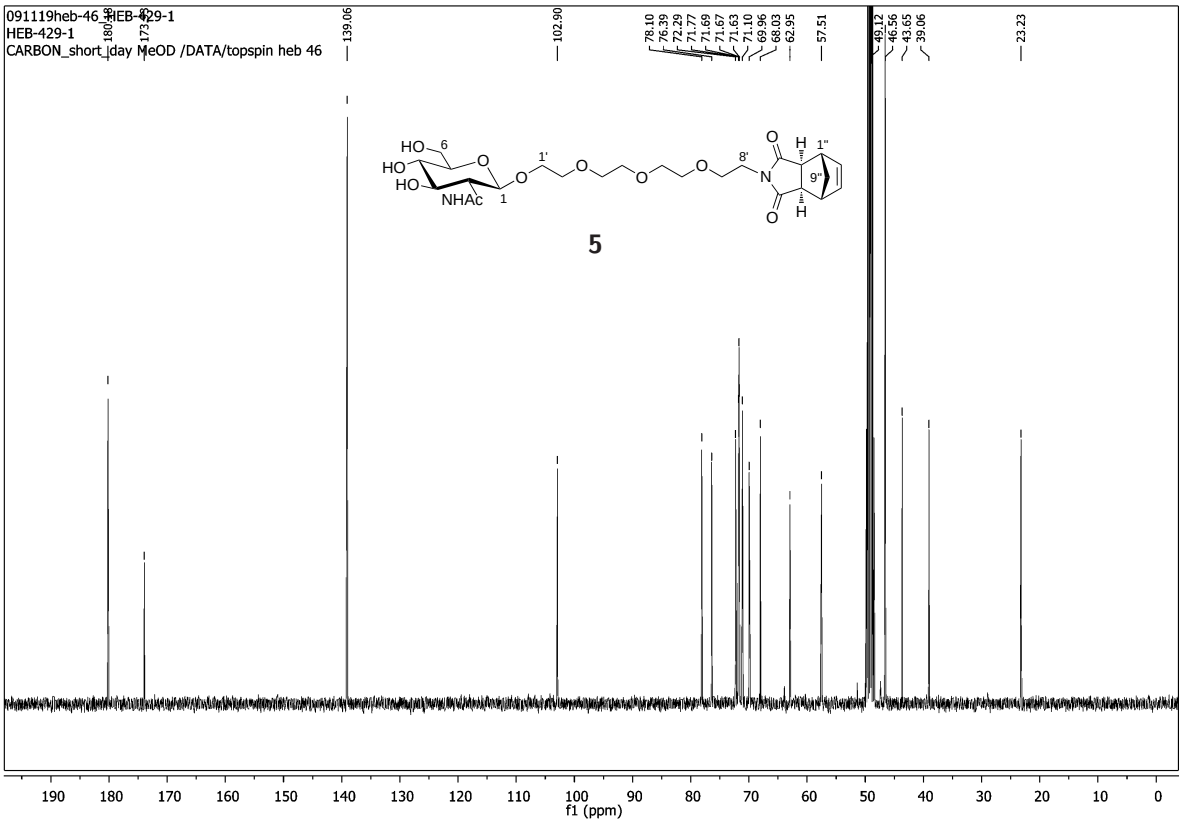


Figure S18: ^{13}C NMR (D_3COD, 100.5 MHz) of compound **5**

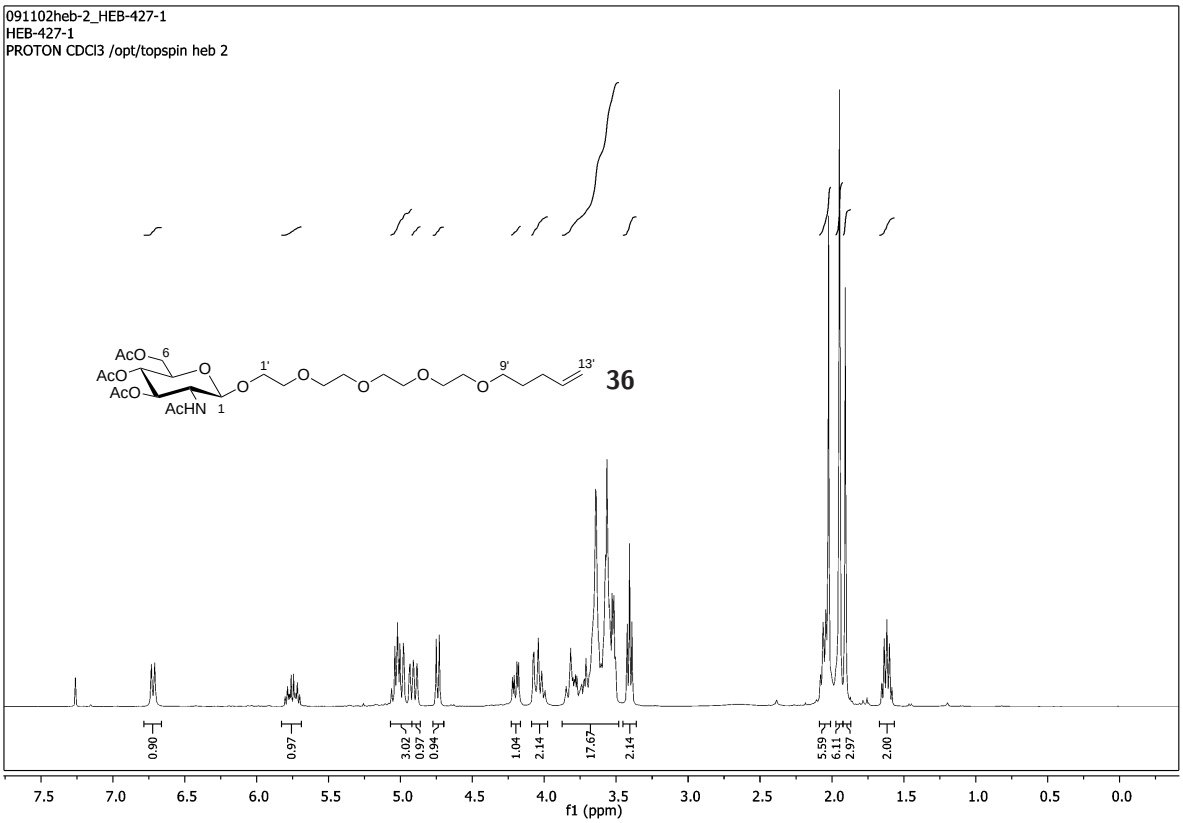


Figure S19: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **36**

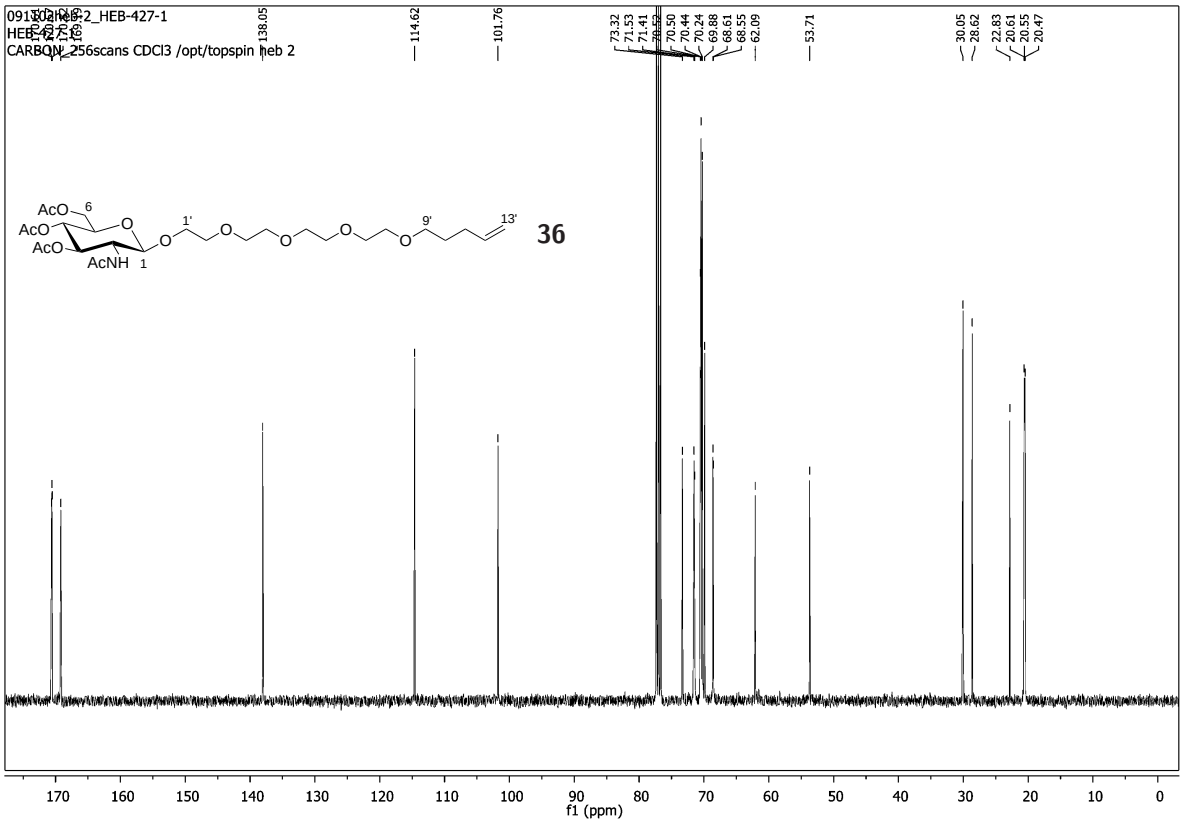


Figure S20: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **36**

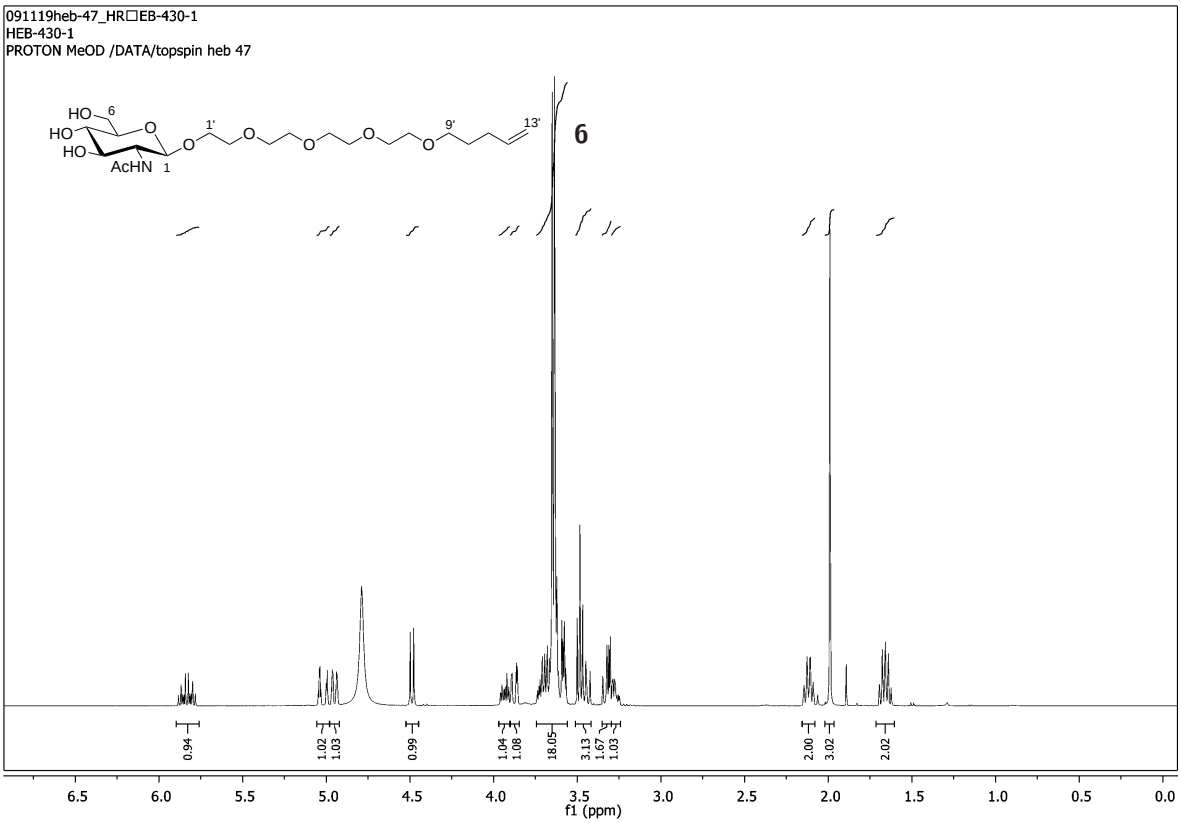


Figure S21: ^{1}H NMR (D_3COD, 399.8 MHz) of compound **6**

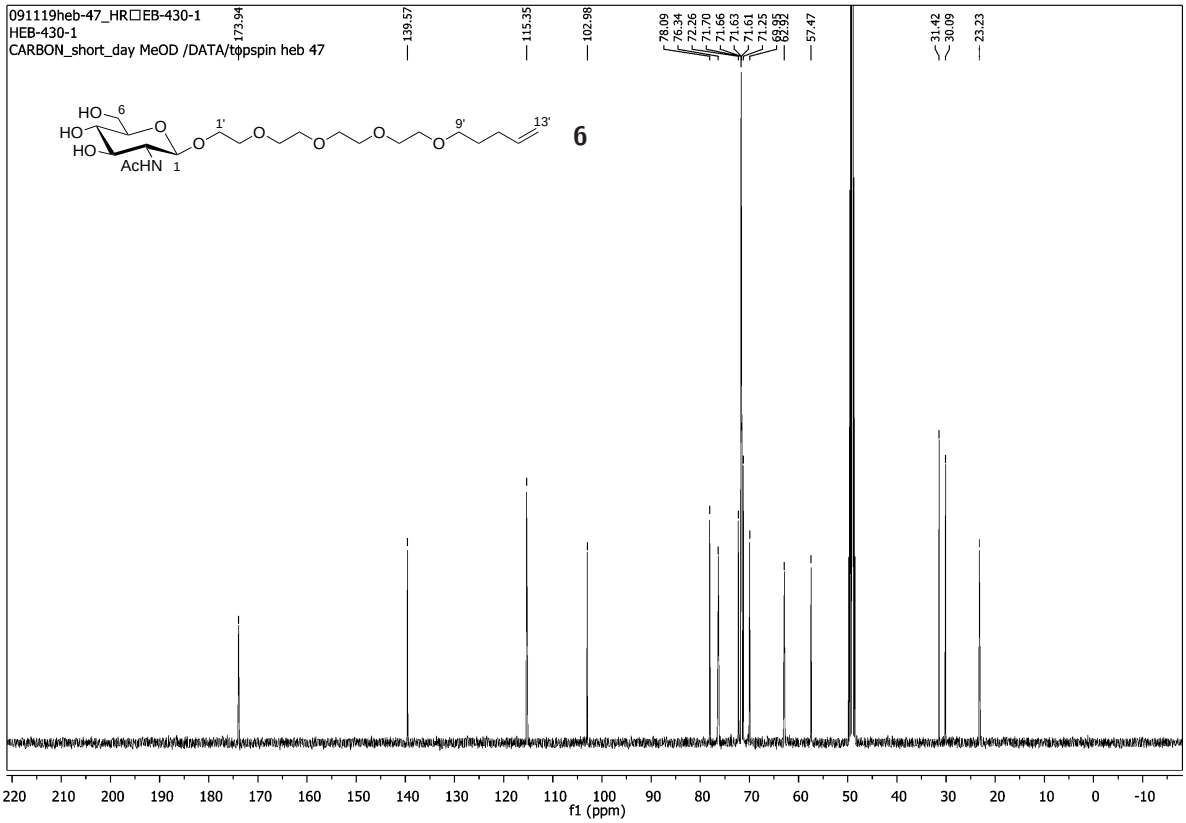


Figure S22: ^{13}C NMR (D_3COD, 100.5 MHz) of compound **6**

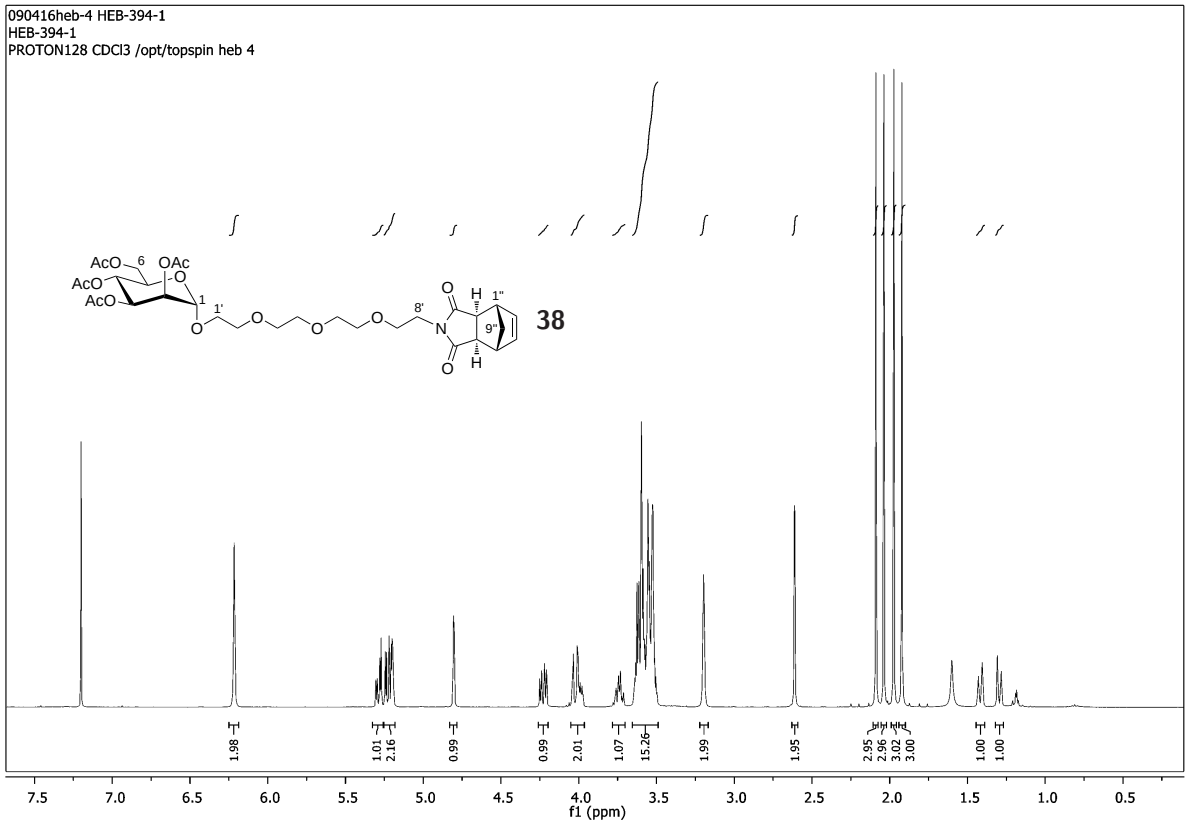


Figure S23: ^{1}H NMR ($CDCl_3$, 600.1 MHz) of compound **38**

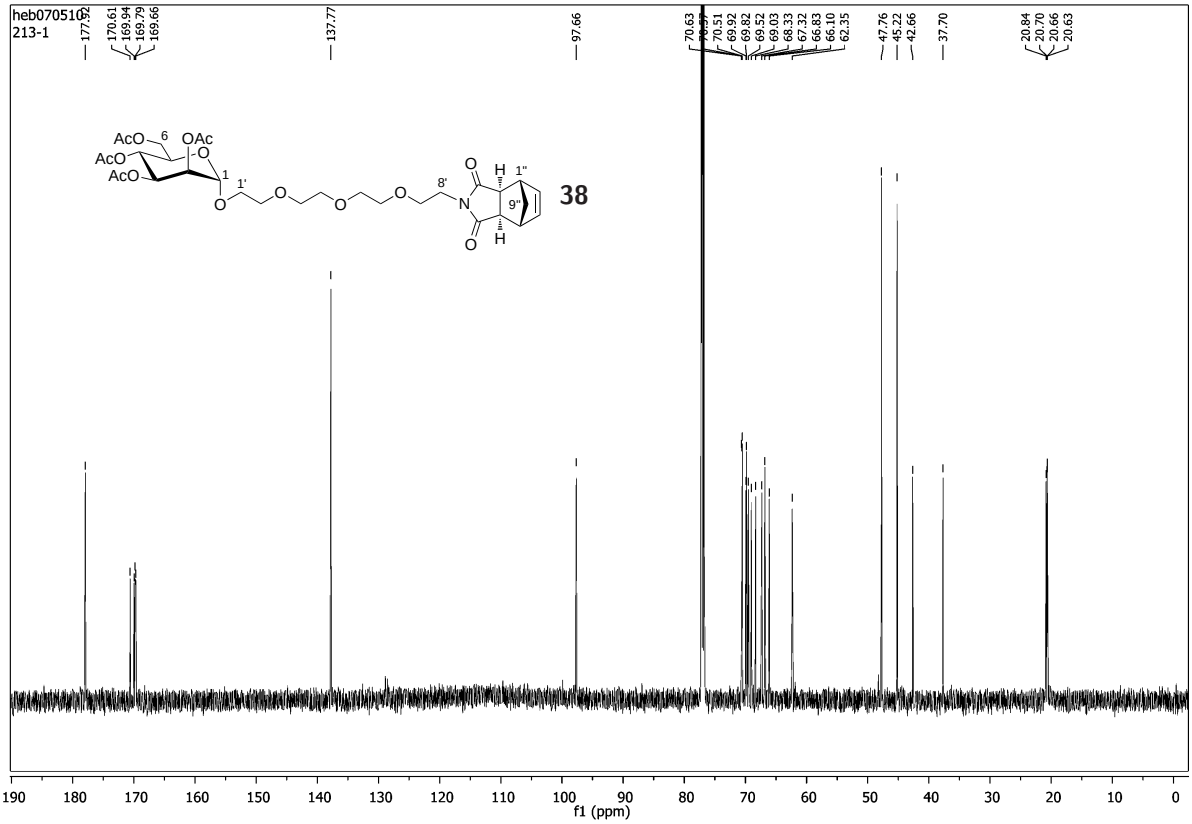


Figure S24: ^{13}C NMR ($CDCl_3$, 150.9 MHz) of compound **38**

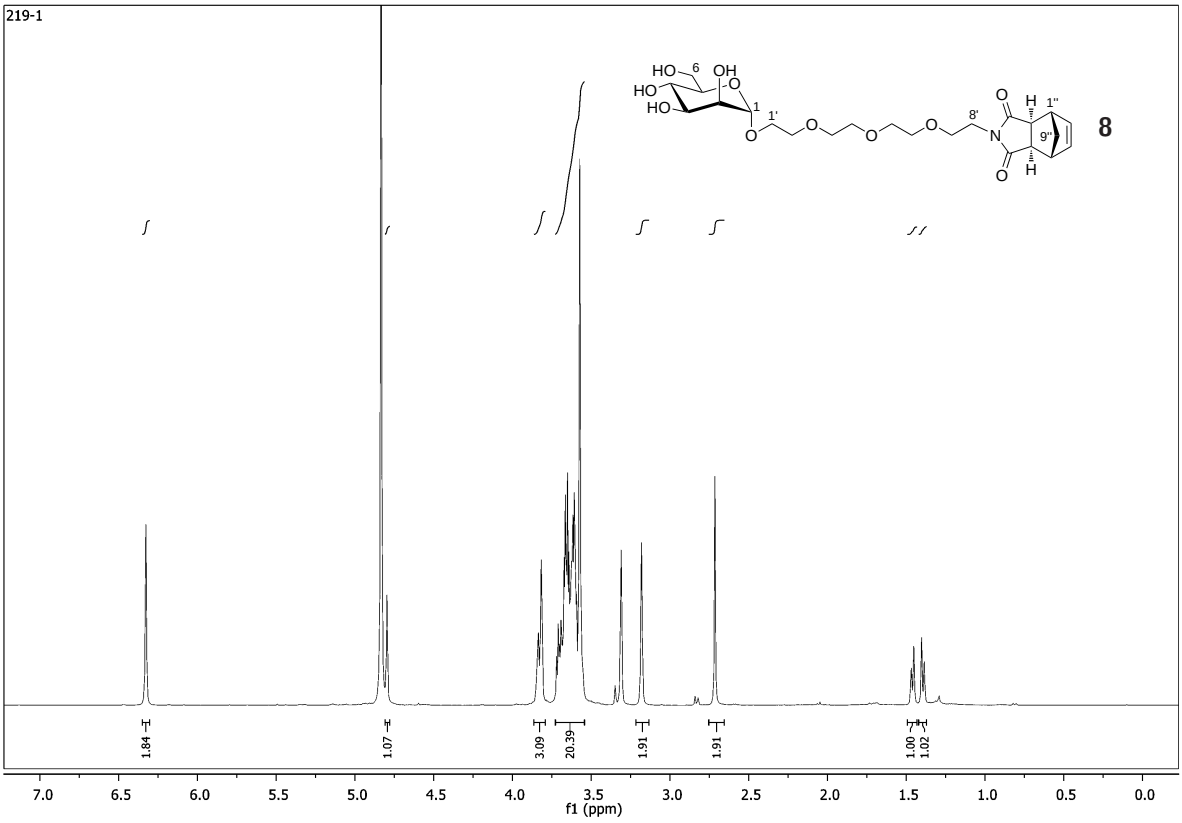


Figure S25: ^{1}H NMR (D_3COD, 600.1 MHz) of compound **8**

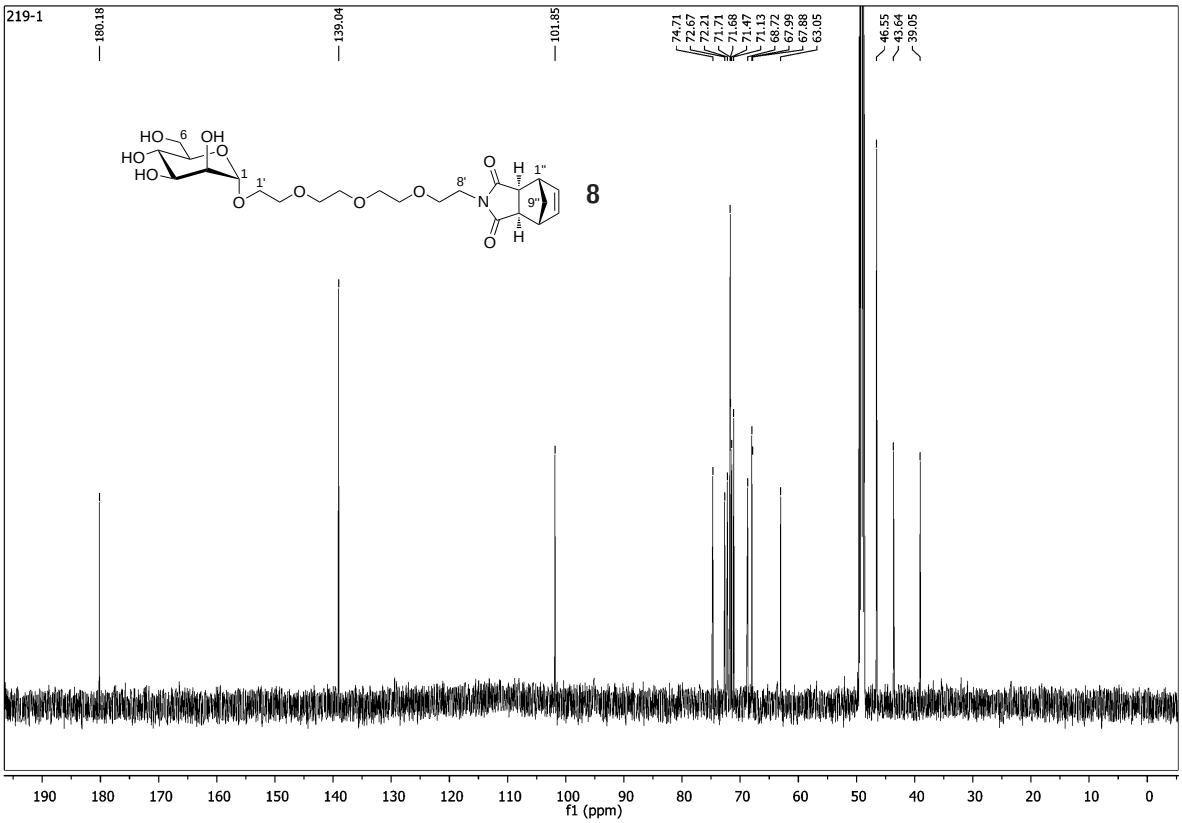


Figure S26: ^{13}C NMR (D_3COD, 150.9 MHz) of compound **8**

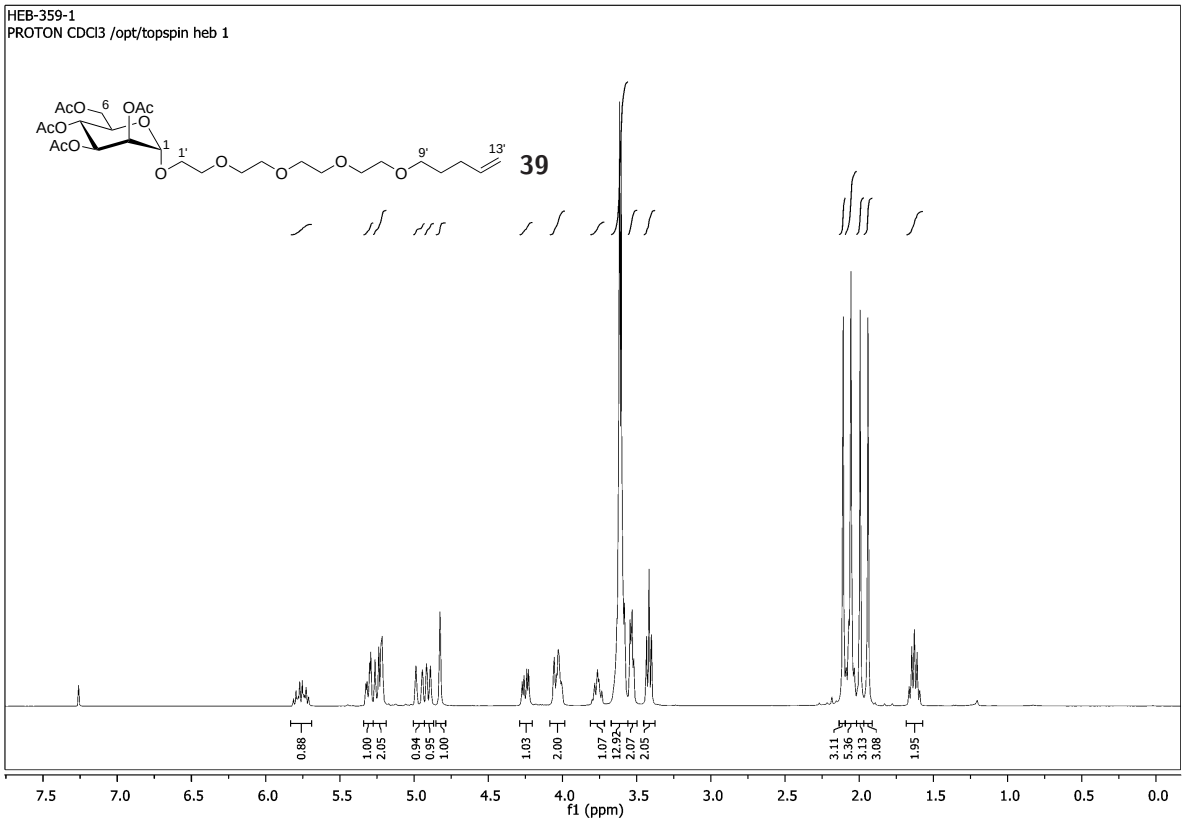


Figure S27: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **39**

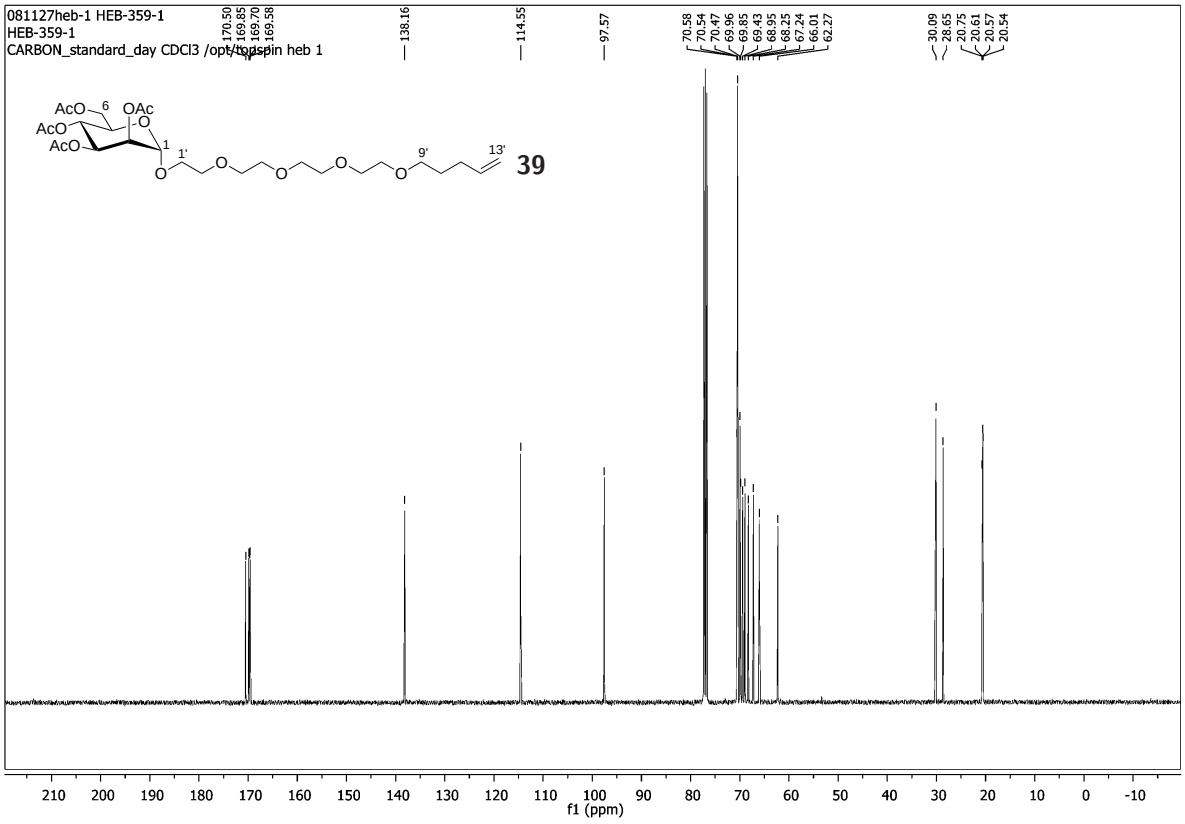


Figure S28: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **39**

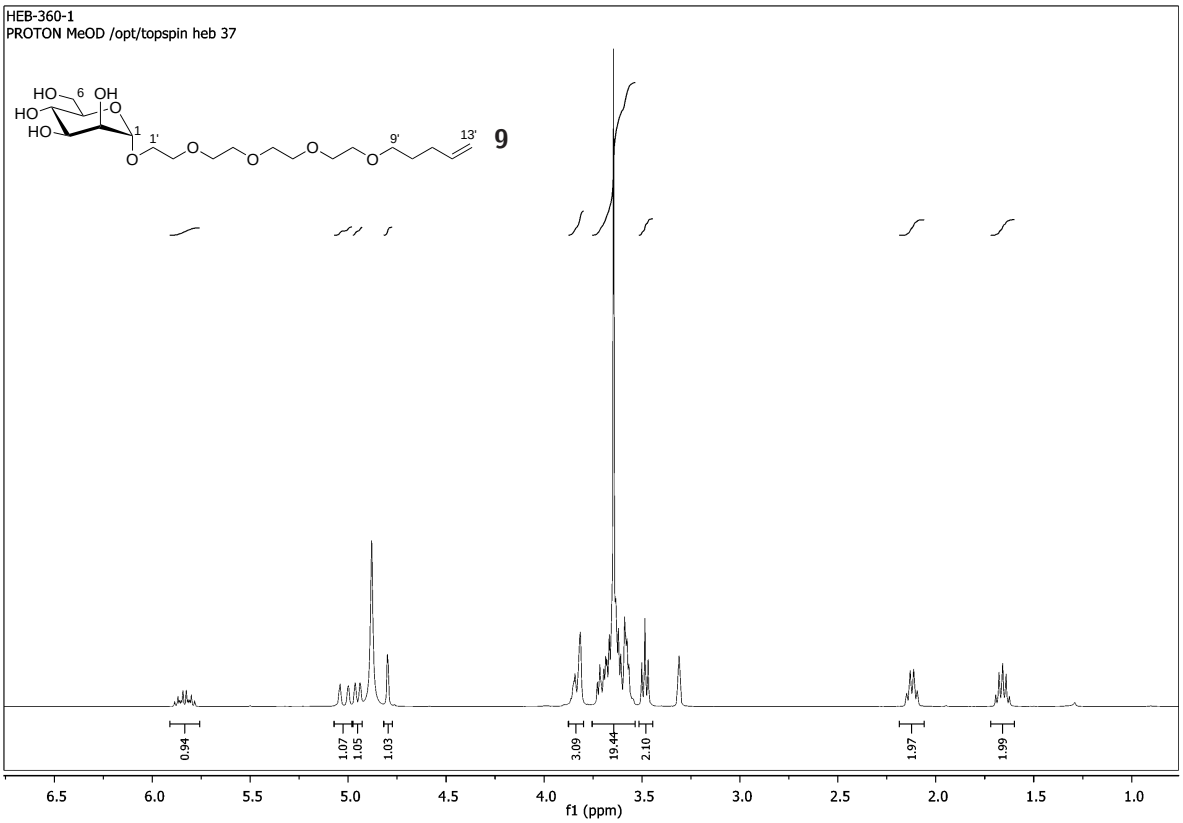


Figure S29: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **9**

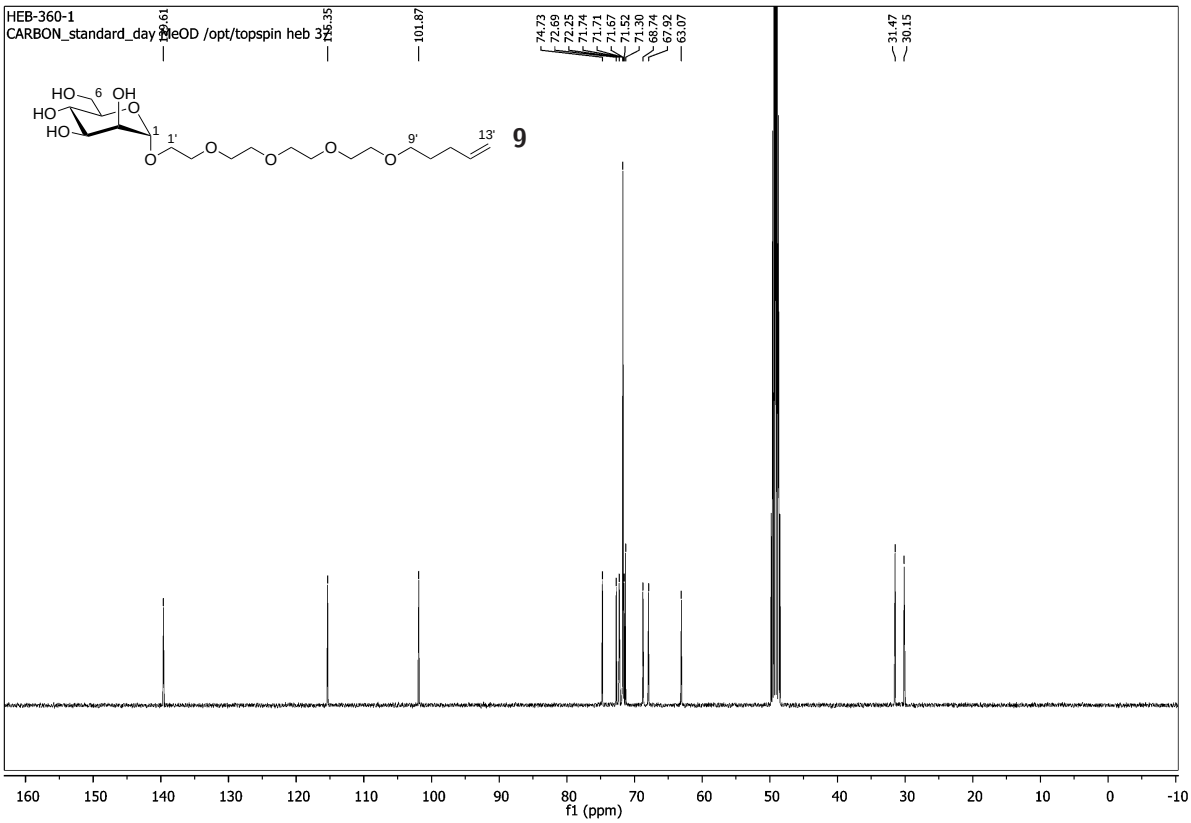


Figure S30: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **9**

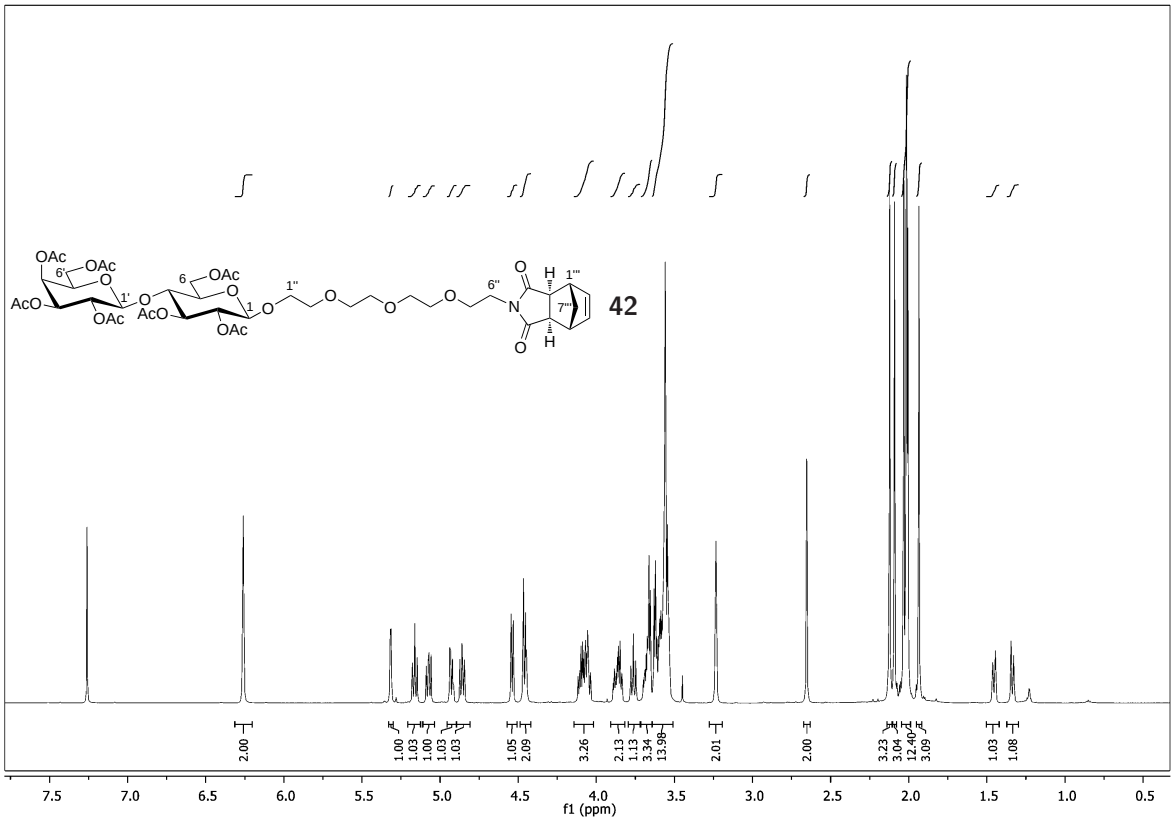


Figure S31: ^{1}H NMR ($CDCl_3$, 600.1 MHz) of compound **42**

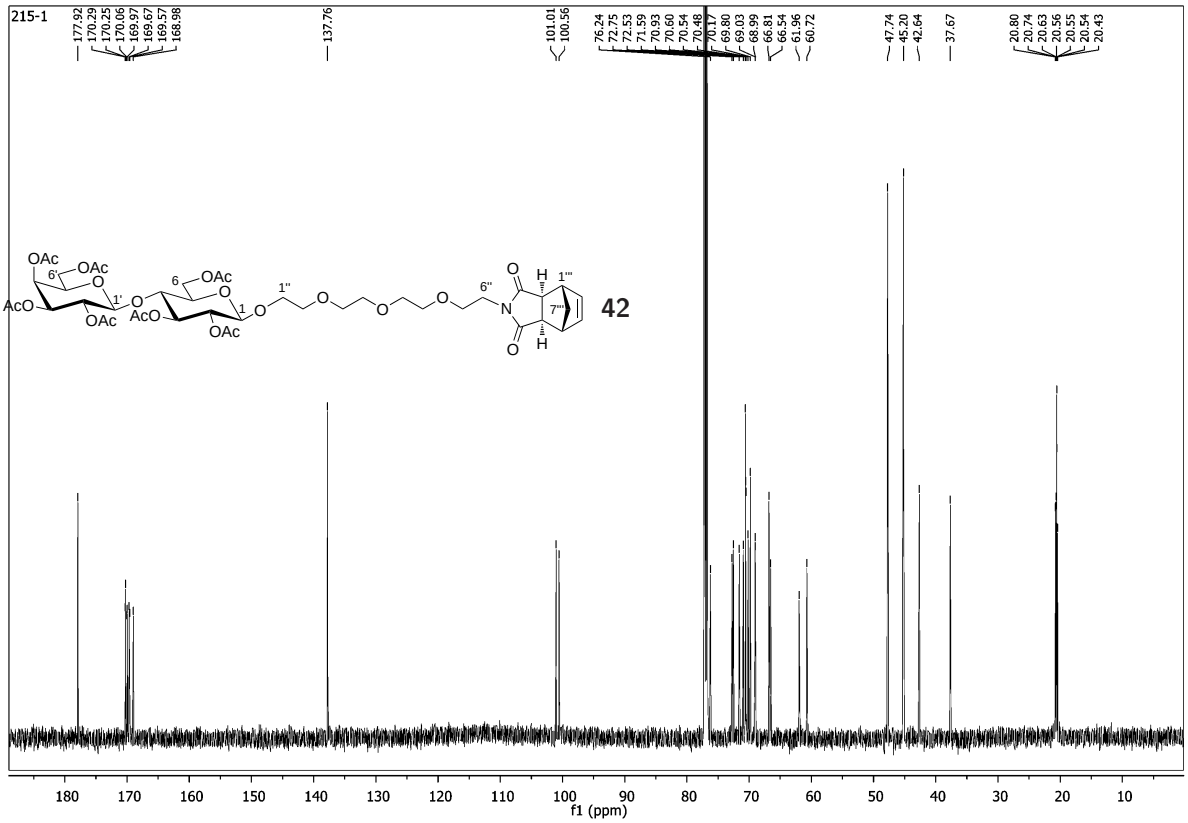


Figure S32: ^{13}C NMR ($CDCl_3$, 150.9 MHz) of compound **42**

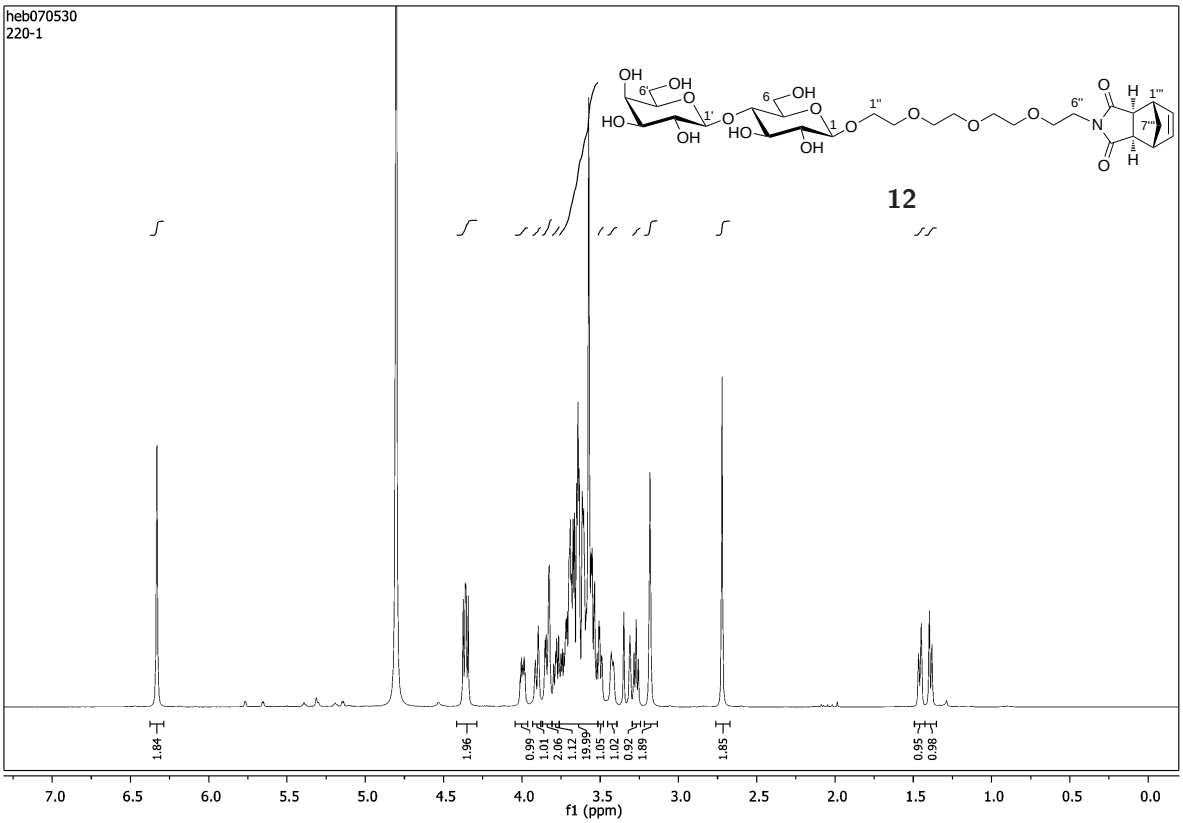


Figure S33: ^{1}H NMR (D_3COD, 600.1 MHz) of compound **12**

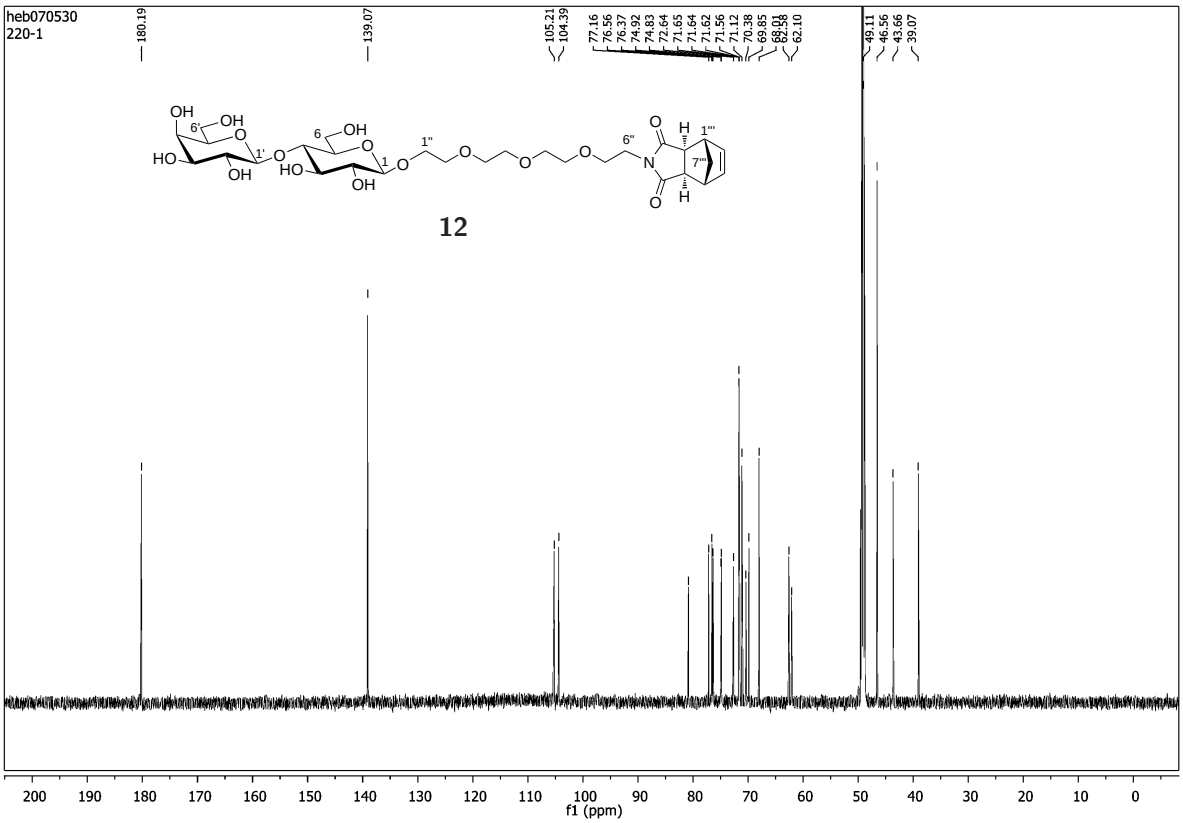


Figure S34: ^{13}C NMR (D_3COD, 150.9 MHz) of compound **12**

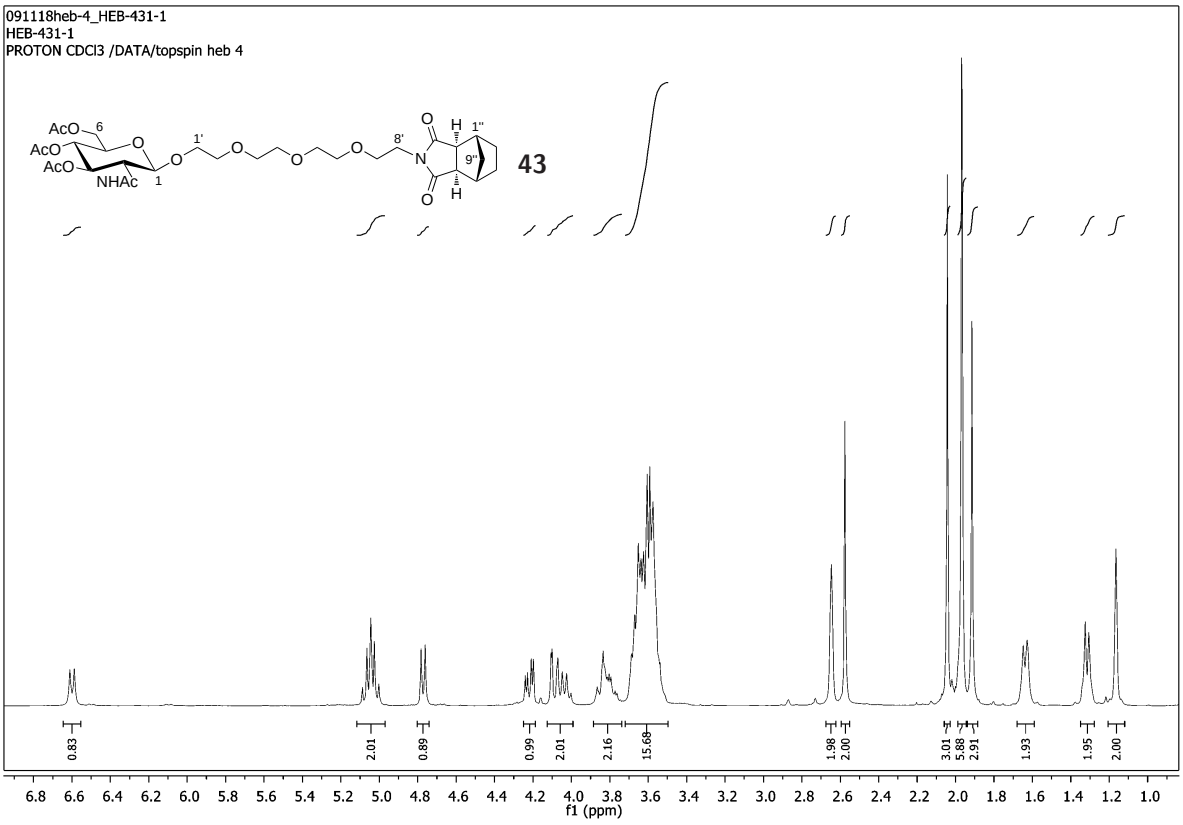


Figure S35: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **43**

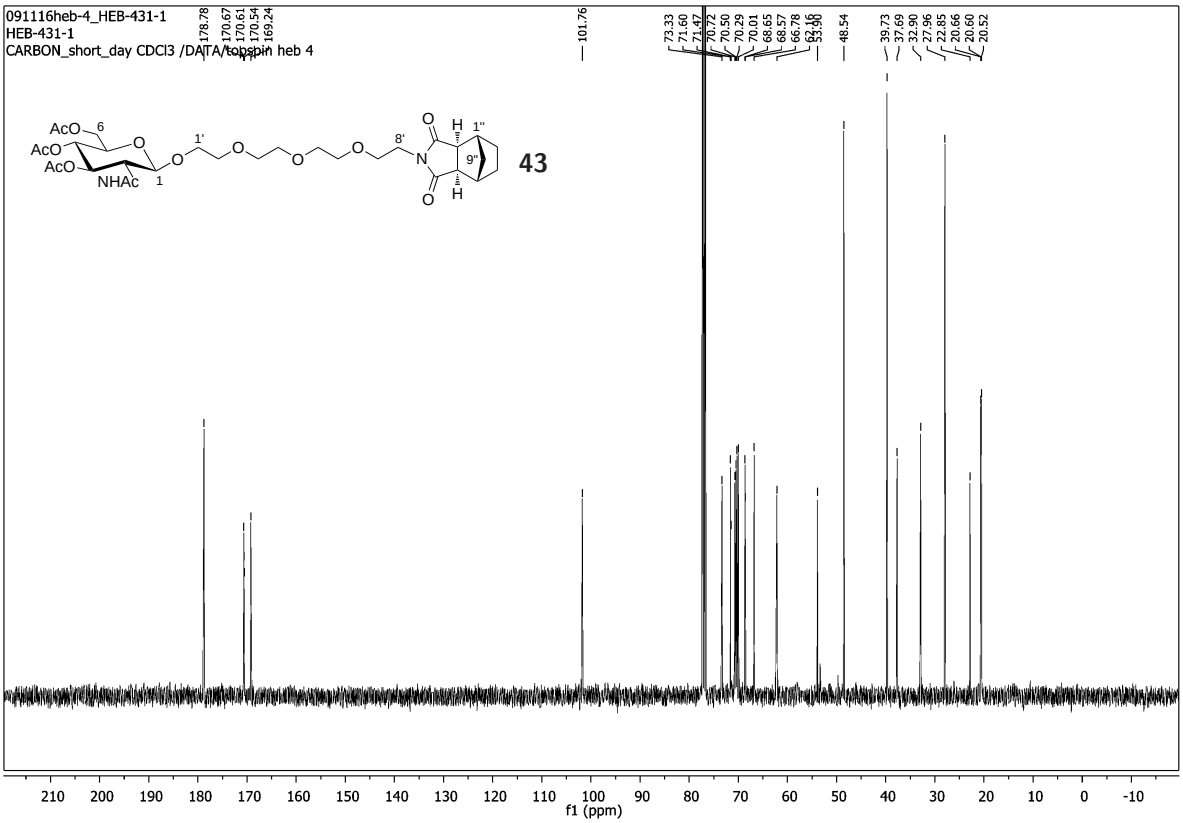


Figure S36: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **43**

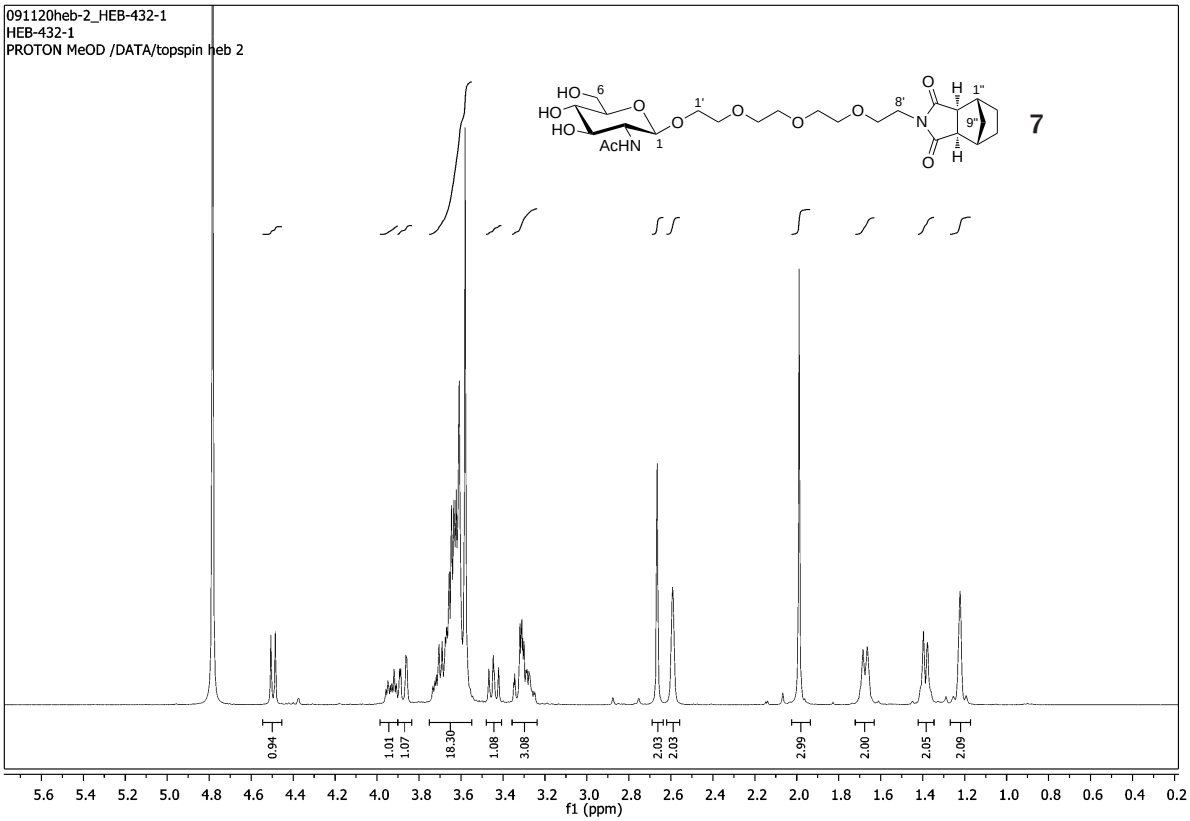


Figure S37: ^{1}H NMR (D_3COD, 399.8 MHz) of compound **7**

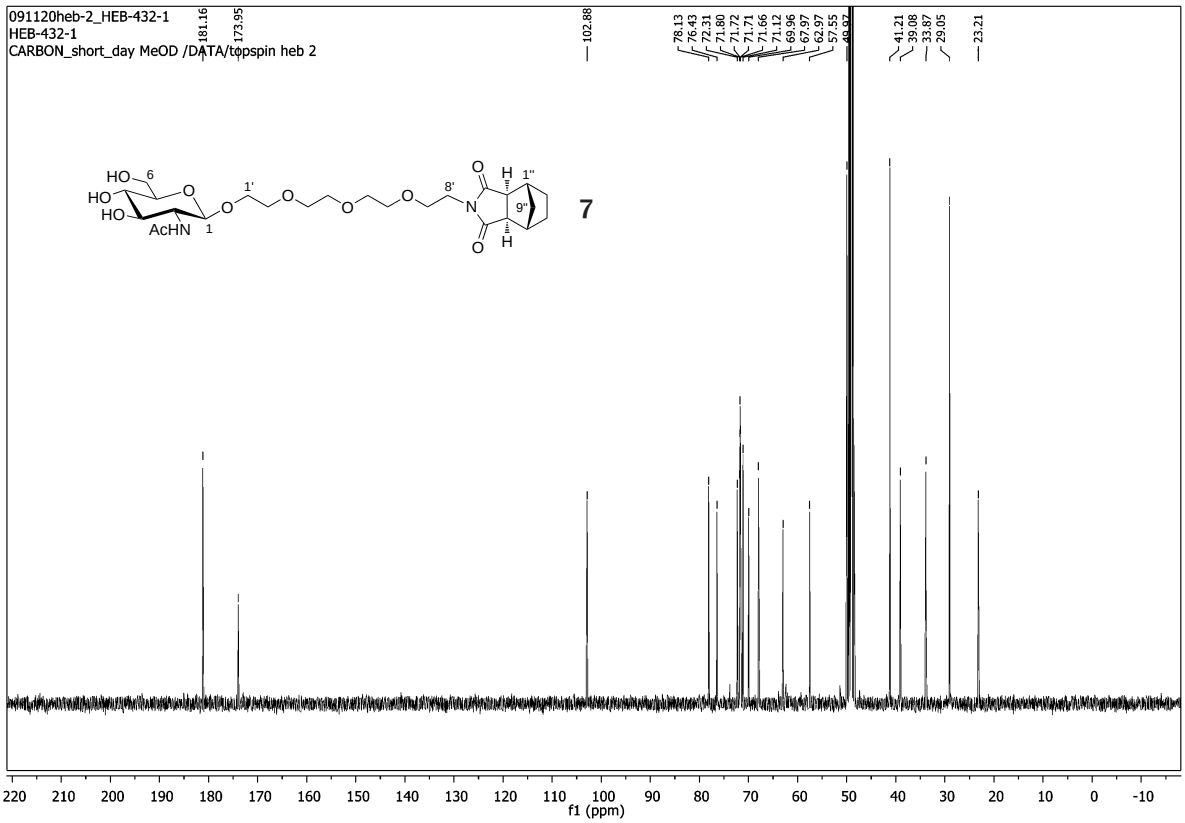


Figure S38: ^{13}C NMR (D_3COD, 100.5 MHz) of compound **7**

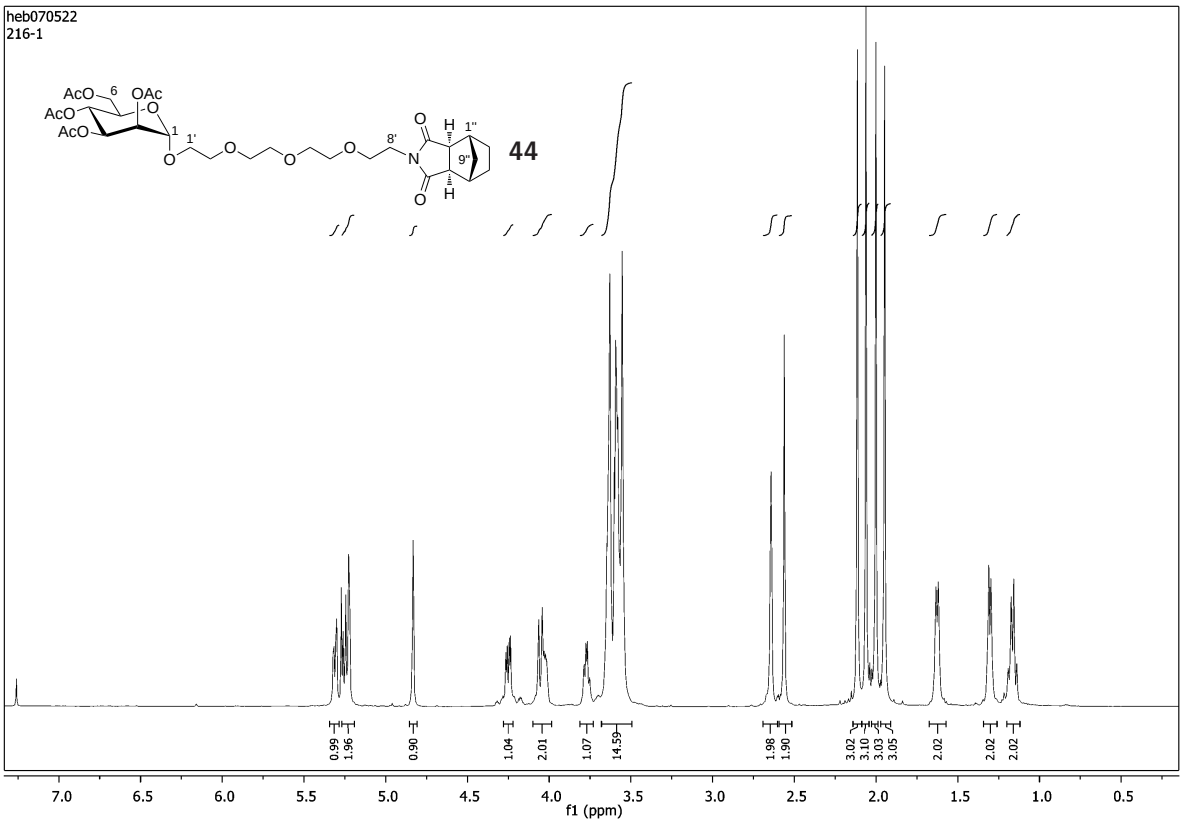


Figure S39: ^{1}H NMR ($CDCl_3$, 600.1 MHz) of compound **44**

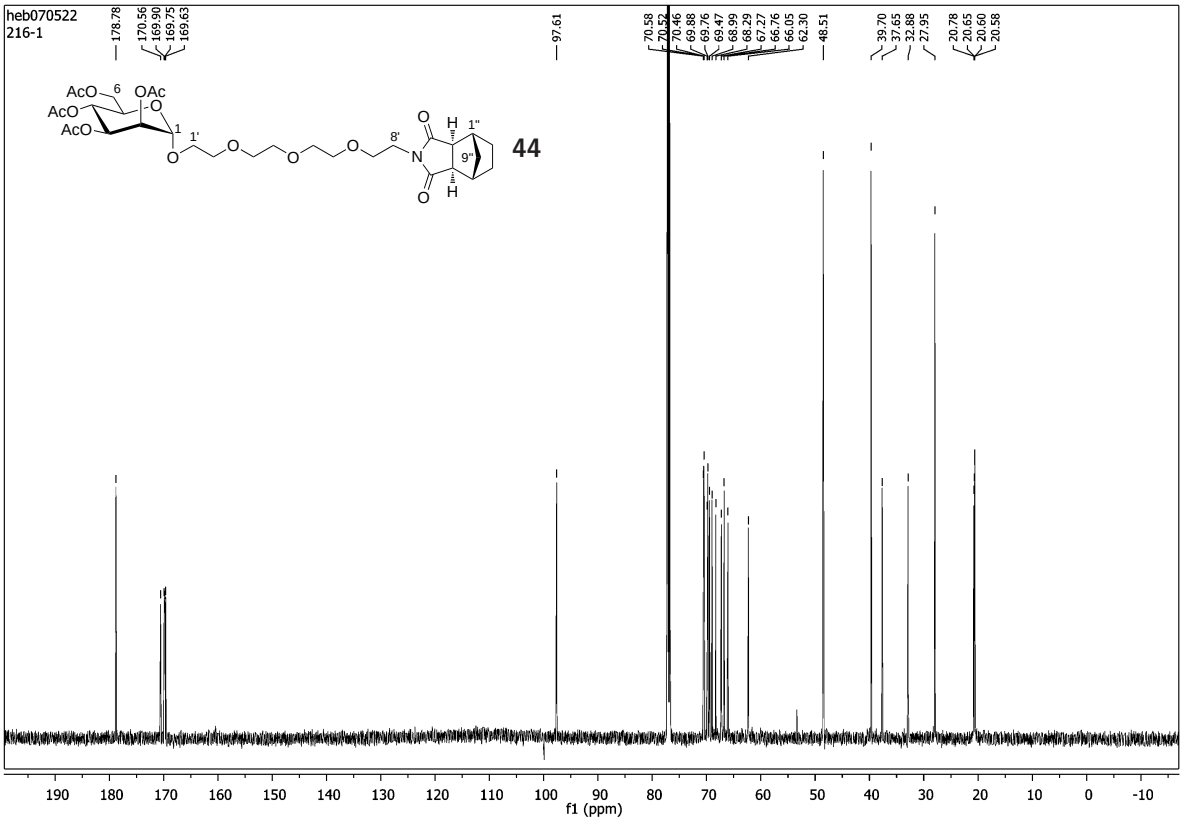


Figure S40: ^{13}C NMR ($CDCl_3$, 150.9 MHz) of compound **44**

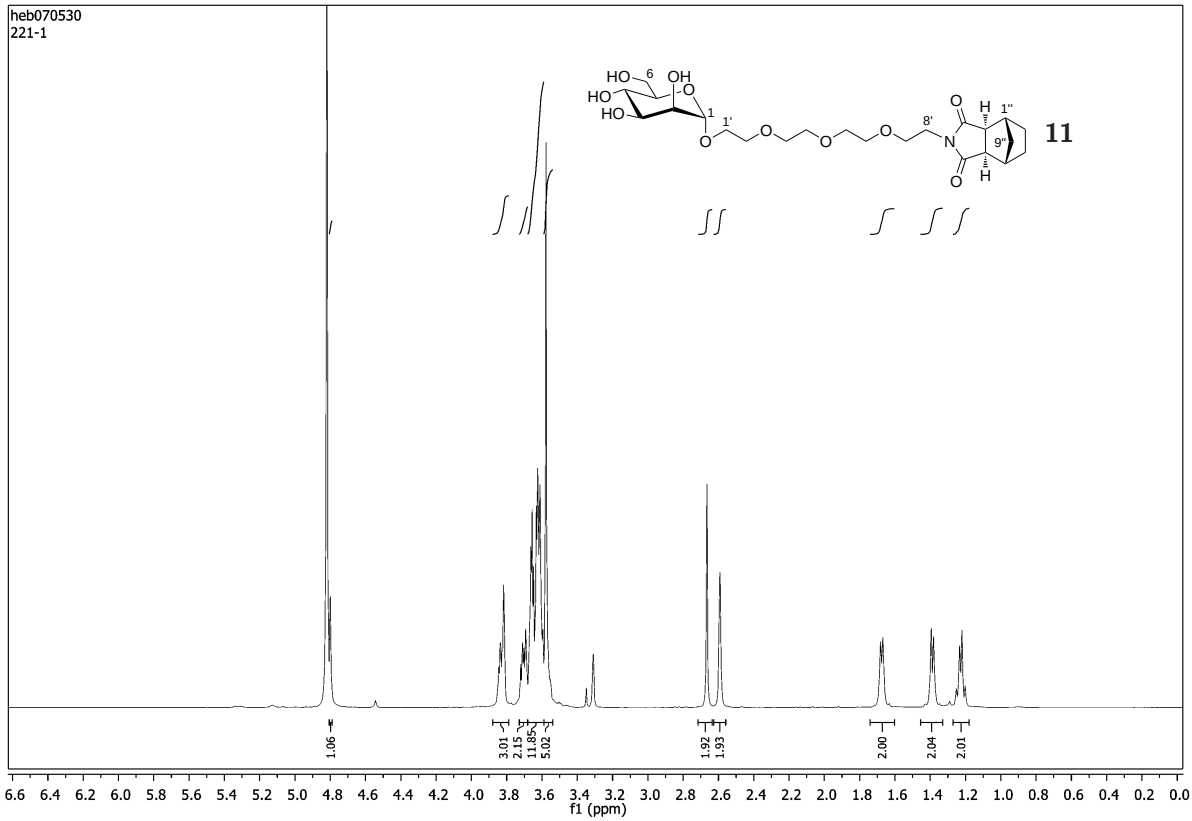


Figure S41: ^{1}H NMR (D_3COD, 600.1 MHz) of compound **11**

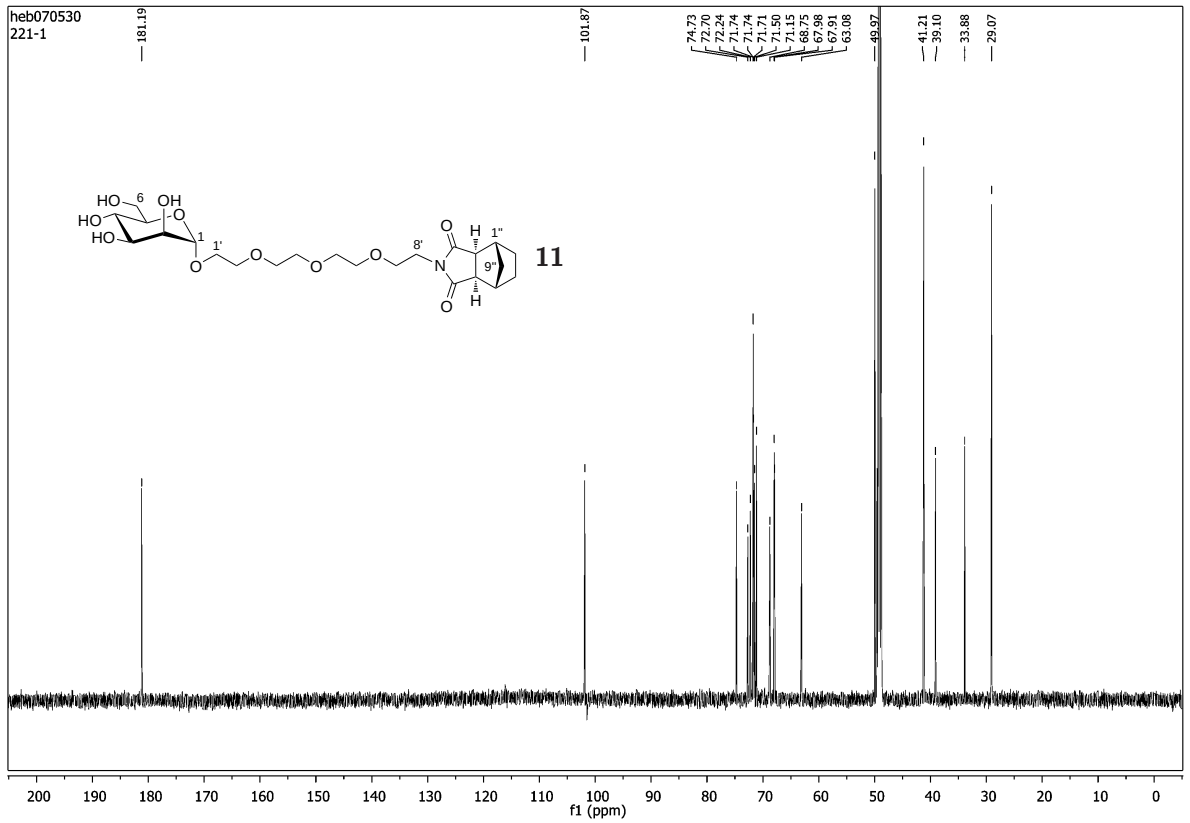


Figure S42: ^{13}C NMR (D_3COD, 150.9 MHz) of compound **11**

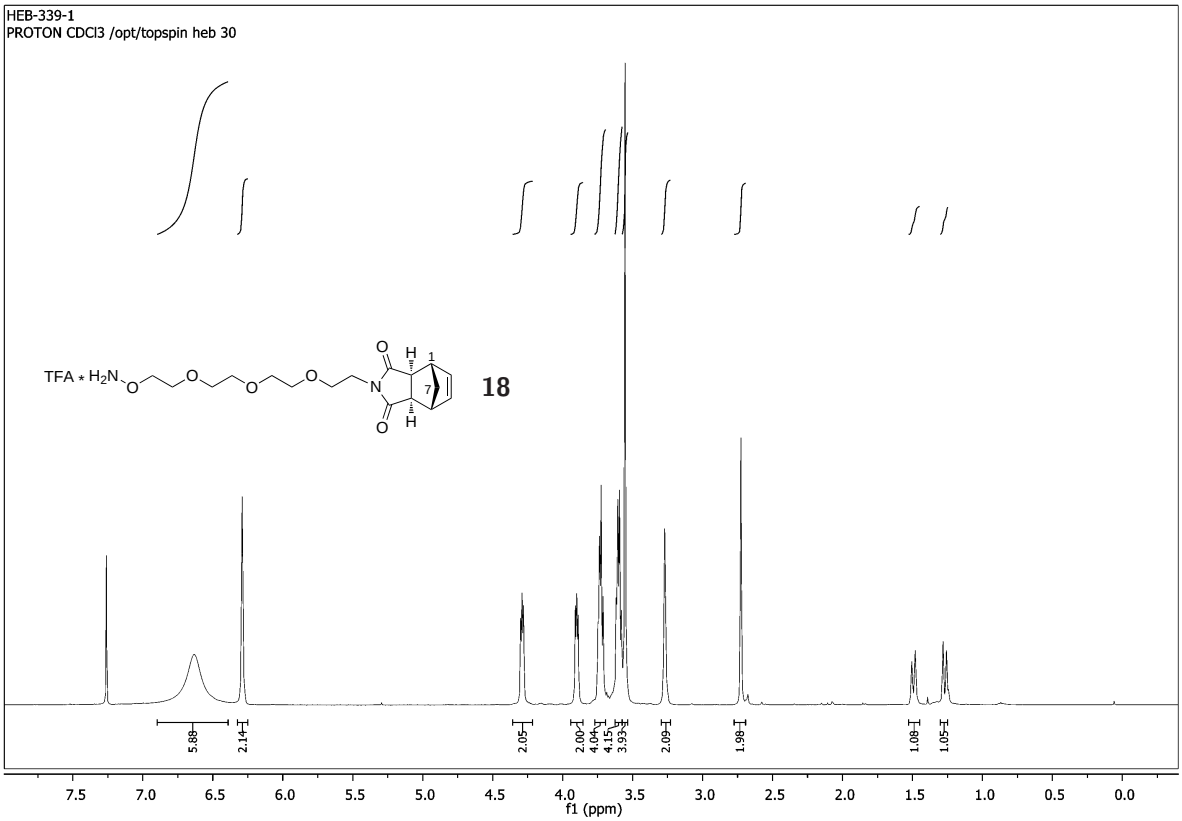


Figure S43: ^{1}H NMR ($CDCl_3$, 399.8 MHz) of compound **18**

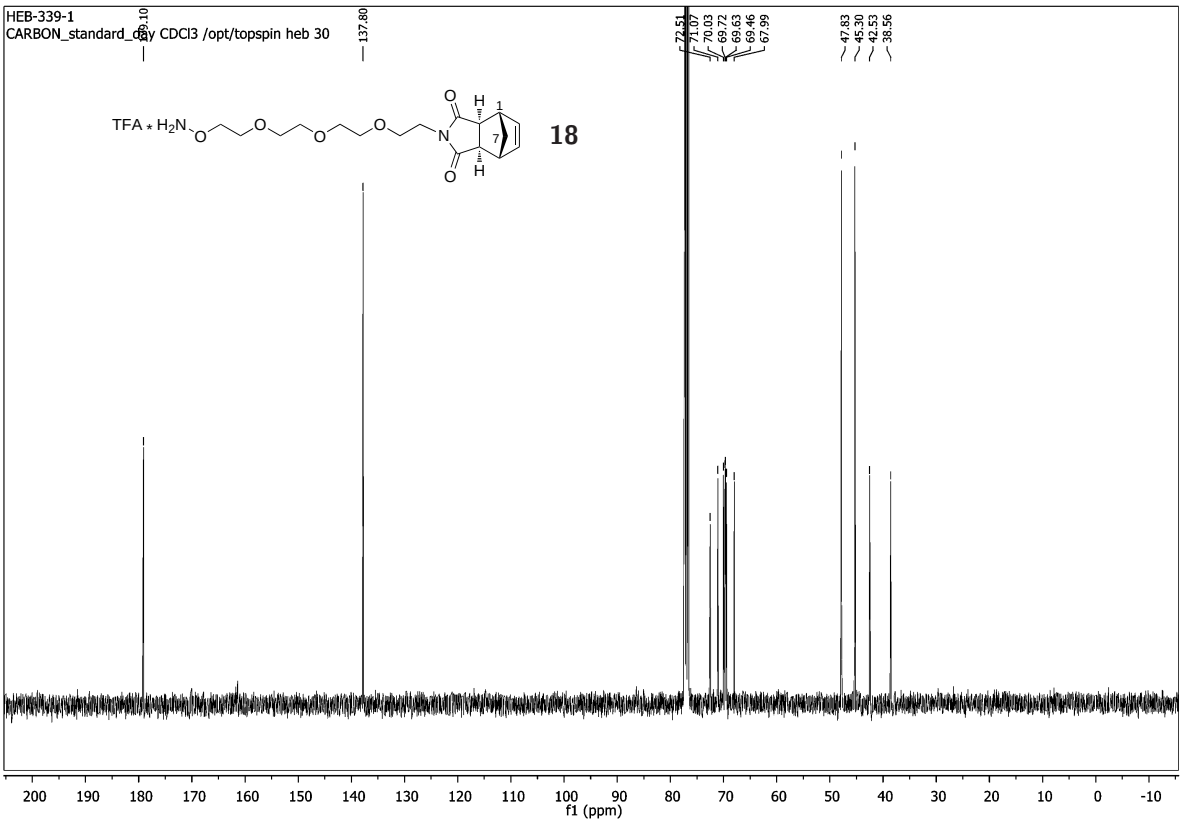


Figure S44: ^{13}C NMR ($CDCl_3$, 100.5 MHz) of compound **18**