Electronic Supporting Information

Strategy for catch and release of azide-tagged biomolecules utilizing a photolabile strained alkyne construct

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1. General methods

All chemicals were used as received unless noted otherwise. Dry solvents were prepared according to standard methods (DMF: P_2O_5; DIPEA: CaH_2; THF: sodium/benzophenone; MeOH: Mg), distilled and stored over molecular sieves 3 Å under an atmosphere of nitrogen until used.

NMR-spectra were recorded on either a Bruker Avance 400 or a Bruker ACX 250 spectrometer and calibrated for TMS (0.0 ppm) or the solvent-signal (^{1}H-$CDCl_3$: 7.26 ppm; ^{13}C-$CDCl_3$: 77.16 ppm; ^{1}H-MeOH-d_4: 3.31 ppm; ^{13}C-MeOH-d_4: 49.00 ppm, ^{1}H-DMSO-d_6: 2.50 ppm; ^{13}C-DMSO-d_6: 39.52 ppm; ^{1}H-benzene-d_6: 7.16 ppm; ^{13}C-benzene-d_6: 128.39 ppm).

FT-ICR-MS spectra were recorded on a Bruker Apex II FT-ICR-MS (FAB) spectrometer and FAB-spectra on a Finnigan model TSQ 70. Optical rotations were measured with a Perkin-Elmer Model 341 polarimeter. Melting points were determined with a Büchi Melting Point M-560 and are uncorrected. Elemental analysis was performed on a HEKAtech Euro EA Analyzer. IR-spectra were recorded on a Bruker Tensor 27. HPLC analysis was performed with either a Thermo Betasil C8 column or a ZORBAX Eclipse XDB-C8 column with a flow rate of 1.5 ml/min. of methanol/KH_2PO_3 pH 2.3 buffer. TLC-analysis was performed with Polygram SIL G/UV pre-coated polyester sheets (Macherey-Nagel). UV-spectra for photometry were recorded on a Perkin-Elmer Lambda 25 UV-Vis spectrometer using 1 cm quartz cuvettes. Absorbance was measured at 266.8 nm.

Dibenzocyclooctynol **2**[17] and the corresponding *p*NP-carbonate **8**,[11b] nitroaromatic **4**,[9] ethylene glycol linker **6**[20] were prepared following the published procedures.

For irradiation of the photolabile samples a 150 W medium pressure mercury lamp from UV-Consulting Peschl Model TQ 150 was used. For elimination of UV light <350 nm a filter solution composed of 2 M aq. KNO_3 containing 0.02 *w*% 5,7-dimethyl-3,6-dihydro-2H-1,4-diazepinium perchlorate was placed between light source and sample.[21] The filter solutions layer thickness was adjusted to ~2 cm and the samples placed perpendicular and as close as possible to the light bulb. The filter solution was replaced with a freshly prepared one every 12 h of irradiation.

*Immobilization of **3** on TOYOPEARL-AF-650-amino*: 1 ml of a TOYOPEARL-AF-650-amino suspension in aq. EtOH was transferred to a 5 ml PP-syringe with inserted PE-frit (35 µm pore size) and washed successively 3 times with H_2O and 5 times with dry MeCN. After re-suspending the beads in 3 ml dry MeCN, 21.4 mg of *p*NP-ester **3a** (25 µmol) and 13.1 µl DIPEA (75 µmol) were added and the mixture shaken at 1500 rpm and rt for 72 h. Subsequently 94.5 µl Ac_2O (1 mmol, 10 eq.) and 172.3 µl DIPEA (1 mmol, 10 eq.) were added and the mixture shaken as described for additional 12 h at RT. Then the beads were washed successively 3 times each with DMSO and water. For storage at 4°C the alkyne functionalized beads were suspended in 20 % aqueous ethanol.

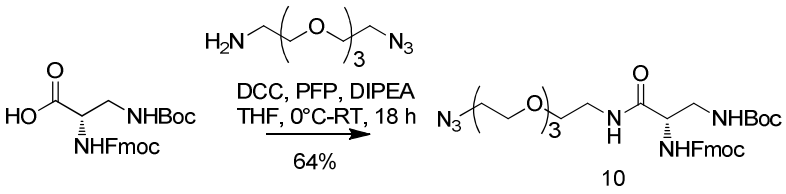
*Capture of azide **10** onto the alkyne functionalized solid support:* The alkyne functionalized beads from above were washed 3 times with dioxane/PBS 2:3 *v*/*v* and then re-suspended in 3 ml of the named solvent mixture containing 31,3 mg of azide **10** (50 µmol, 2 eq.). The resulting suspension was shaken at RT or 0°C and 1500 rpm for 3 h and the reaction progress tracked photometrically. After 30 min. no more progression of the reaction was observed.

Afterwards the beads were washed 5 times with dioxane/PBS 2:3 *v*/*v*, 3-times with water, re-suspended in 20 % aqueous ethanol and stored at 4°C until used further. Quantitative analysis of the UV-spectra and subtraction of a relative amount of **10** non-specifically bound to the beads (see below) indicated an effective loading of the beads with 12.5 µmol of the corresponding triazole (uncorrected 14.7 µmol).

*Non-specific binding of azide **10** on 2-azidoethanol-blocked alkyne functionalized solid support:* The alkyne functionalized beads from above were washed 3 times with dioxane/PBS 2:3 *v*/*v* and then re-suspended in 3 ml of the named solvent mixture containing 100 mg of 2-azidoethanol (1.15 mmol, 46 eq. based on **3a**). The resulting suspension was shaken at rt and 1500 rpm for 12 h. Afterwards the beads were washed 5 times with dioxane/PBS 2:3 *v*/*v*, 3-times with water. Then the beads were re-suspended in 3 ml dioxane/PBS 2:3 *v*/*v* containing 31,3 mg of azide **10** (50 µmol, 2 eq.). The resulting suspension was shaken at RT and 1500 rpm for 90 min. and the reaction progress tracked photometrically. Quantitative analysis revealed approx. 2.2 µmol non-specific binding to the blocked beads. The assumption was confirmed by subjecting the beads to the cleavage conditions described below. No **11** could be detected in the supernatant as indicated by HPLC-analysis, precluding that **10** was immobilized due to reaction with residual non-blocked **3b**.

*UV light induced liberation of the immobilized model compound **11***: The triazole-loaded beads from above were washed 5-times either with dioxane/PBS 2:3 *v*/*v* or dioxane/Na-phosphate pH 6.3 buffer 3:2 *v*/*v* containing 10 mM DTT. Then the beads were re-suspended in 10 ml of one of the named solvent mixtures, transferred to a transparent 20 ml PP-tube and subjected to irradiation >350 nm for 4 h at RT while being shaken at 1500 rpm. The reaction was monitored photometrically and after 120 min. and 40 min. no more progression of the cleavage reaction could be observed, respectively. Quantitative analysis of the supernatant indicated 85% recovery of triazole **11** in an HPLC-purity of 98.2 %.

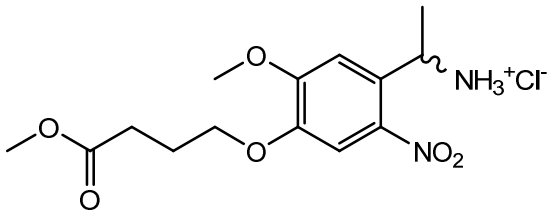
2. Synthesis and characterization of the compounds **5**, **7**, **9**, **3** and **10**, **11**



Scheme 5: Synthesis of model compound **10**.

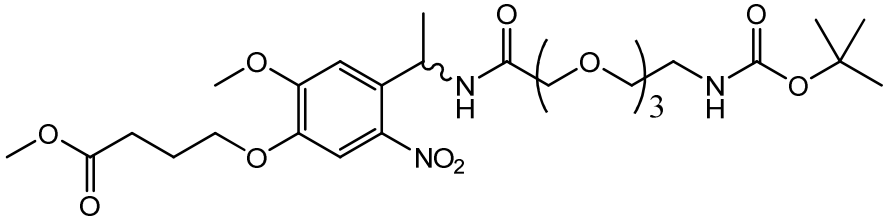
General Procedure for HBTU-mediated amide coupling **A**: In a round bottom flask equipped with a gas inlet and a stirring bar the corresponding free base or ammonium derivative was dissolved in dry DMF at a concentration of 0.18 M under an atmosphere of nitrogen. After cooling the solution to 0°C HOBt (1.5 eq.), DIPEA (1.5 eq. for free bases; 3 eq. for ammonium derivatives), the free carboxylic acid (1 eq.) and subsequently HBTU (1.5 eq.) were added. Stirring was continued for 2 h at 0°C and at rt for 14 h. Then, the solution was diluted with ethyl acetate, transferred to a separatory funnel, the organic layer separated and washed twice each with 1 M $NaHSO_4$-soln. and sat. $NaHCO_3$-soln. and once with brine. After drying the organic layer with Na_2SO_4 the solvent was removed under reduced pressure and

the residue subjected to column chromatography, eluting with the solvent mixtures indicated below.



5

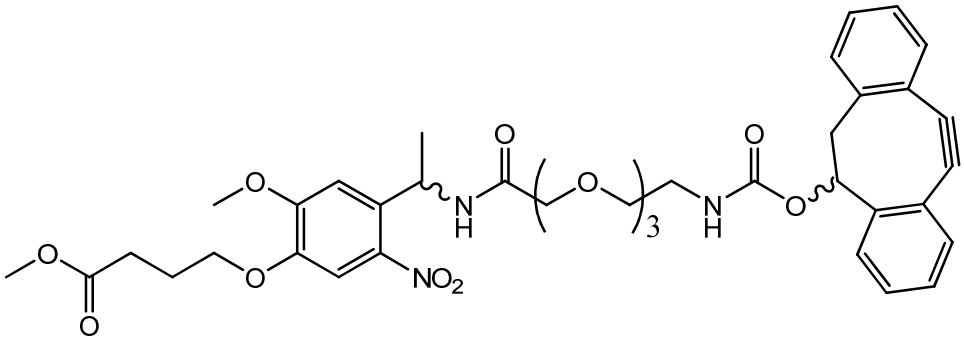
4-[2-Methoxy-5-nitro-4-(1-aminoethyl)phenoxy]butanoicacid methyl ester hydrochloride **5**: In a 250 ml round bottom flask equipped with a gas inlet and a stirring bar 8.2 g of trifluoroacetamide **4**[9] (20.1 mmol) were dissolved in 100 ml of a 0.36 M soln. of HCl in dry MeOH[22] under an atmosphere of nitrogen. The resulting mixture was refluxed for 36 h, cooled to rt and the volatiles removed in a stream of air. The residual white solid was triturated with diethyl ether, filtered and crystallized from ethanol to yield 6.77 g of pure title compound **5** (19.4 mmol, 97 %) as wooly colorless crystals. mp: 191.5°C (EtOH). Anal. calcd for $C_{14}H_{21}ClN_2O_6$: N, 8.03; C, 48.21; H, 6.07; found: N, 7.87; C, 48.25; H, 6.21. IR (NaBr): 3440, 2924, 1739, 1582, 1525, 1339, 1281, 1225, 1053 cm^{-1}. FAB-MS: m/z 313 $[M\text{-}Cl^-]^+$, 296 $[M\text{-}NH_3\text{-}Cl^-]^+$. ^{1}H-NMR (400.1 MHz, MeOH-d_4): δ 7.68 (s, 1H, aryl), 7.32 (s, 1H, aryl), 5.13 (q, 1H, J = 6.8 Hz, C**H**NH_4Cl), 4.14 (t, 2H, J = 6.1 Hz, aryl-OC**H**$_2$), 4.02 (s, 3H, C**H**$_3$), 3.68 (s, 3H, C**H**$_3$), 2.55 (t, 2H, J = 7.3 Hz, C**H**$_2$COOMe), 2.16-2.08 (m, 2H, C**H**$_2$), 1.73 (d, 3H, C**H**$_3$CHNH_4Cl). ^{13}C-NMR (100.6 MHz, MeOH-d_4): δ 175.3 (**C**OOMe), 155.6, 149.8, 142.6, 128.2, 110.8, 110.6 (aryl), 69.6 (aryl-O**C**H_2), 57.3 (aryl-O**C**H_3), 52.2 (COO**C**H_3), 47.6 (**C**HN), 31.2 (Bu-**C**H_2), 25.5 (Bu-**C**H_2), 20.0 (NCH**C**H_3).



7

4-{4-[14-(tert.-Butoxycarbonyl)amino-4-oxo-6,9,12-trioxa-3-azatetradec-2-yl]-2-methoxy-5-nitrophenoxy}butanoic acid methyl ester **7**: In a 50 ml round bottom flask equipped with a stirring bar 922 mg of methyl ester **6**[20] (2.87 mmol) were saponified with 1 M aq. NaOH in methanol at rt for 1 h. The mixture was acidified with solid $NaHSO_4$, transferred to a separatory funnel and extracted 5 times with DCM. The combined organic layers were dried with Na_2SO_4 and the solvent evaporated. The crude free acid was dissolved in 15 ml dry THF and transferred to a vessel equipped with a gas inlet and a stirring bar. Then 504 mg HOBt (3.73 mmol, 1.3 eq.) were added, and the solution cooled to -20°C. Subsequently, 770 mg DCC (3.73 mmol, 1.3 eq.) were added and the solution stirred for 6 h at -20°C. Thereafter, 1 g of nitroaromatic **5** (2.87 mmol, 1 eq.) was added together with 1.5 ml DIPEA (8.61 mmol, 3 eq.) and the mixture stirred for additional 14 h at rt. Then the precipitate of DC-urea was filtered off, the mixture transferred to a separatory funnel and diluted with ethyl acetate. The organic layer was separated and washed twice with 1 M $NaHSO_4$-soln., once each with sat. $NaHCO_3$-soln. and brine, dried over Na_2SO_4 and the solvent removed under reduced pressure. The residual viscous yellow oil was subjected to column chromatography eluting with $CHCl_3$

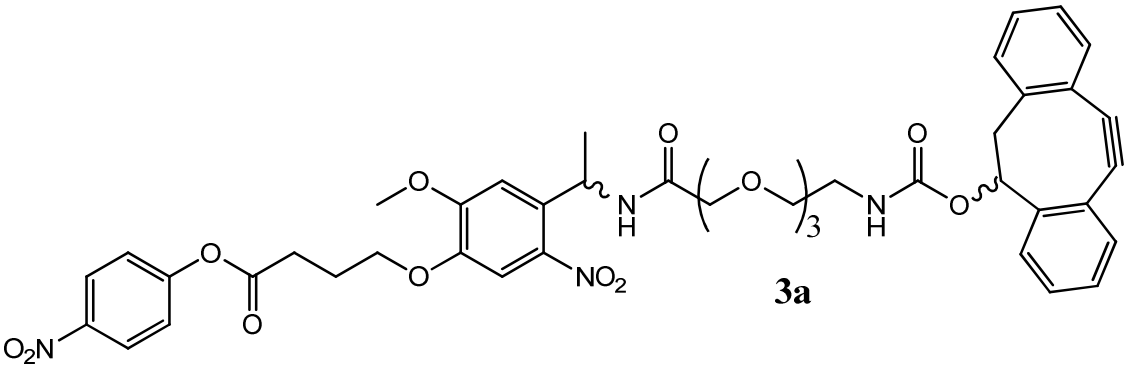
containing 1 *v*% MeOH yielding 1.52 g of pure title compound **7** (2.60 mmol, 91 %) as pale yellow viscous oil. R_f: 0.32 ($CHCl_3$+*v*1% MeOH). IR (neat): 3357, 2974, 2935, 2875, 1712, 1518, 1456, 1366, 1274, 1176, 870, 758 cm^{-1}. FT-ICR-MS: m/z $[M+Na]^+$ calcd for $C_{27}H_{43}N_3O_{12}Na$: 624.2739 found: 624.2743. ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ 7.63-7.57 (m, 1H, CON**H**), 7.52 (s, 1H, aryl), 6.96 (s, 1H, aryl), 5.65-5.56 (m, 1H, aryl-C**H**N), 4.96 (s, broad, 1H, OCON**H**), 4.06 (t, 2H, J = 6.2 Hz, aryl-OC**H**$_2$), 4.01 (d, 1H, J = -15.8 Hz, OC**H**$_2$CON), 3.89 (s, 3H, C**H**$_3$), 3.89 (d, 1H, J = -15.8 Hz, OC**H**$_2$CON), 3.74-3.58 (m, 8 H, EG-chain-C**H**$_2$), 3.66 (s, 3H, C**H**$_3$), 3.48 (t, 2H, J = 5.2 Hz, EG-chain-C**H**$_2$), 3.27-3.21 (m, 2H, C**H**$_2$NHBoc), 2.51 (t, 2H, J = 7.2 Hz, C**H**$_2$COOMe), 2.18-2.10 (m, 2H, C**H**$_2$), 1.53 (d, 3H, J = 6.9 Hz, C**H**$_3$CHN), 1.40 (s, 9H, *t*Bu). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 173.4 (**C**OOMe), 169.3 (**C**ON), 156.0 (O**C**ONH), 153.9, 147.0, 140.6, 134.3, 110.4, 109.9 (aryl), 79.3 (*t*Bu), 71.1, 70.6, 70.4, 70.4, 70.3, 70.2 (EG-**C**H$_2$), 68.3 (aryl-O**C**H$_2$), 56.4 (aryl-O**C**H$_3$), 51.7 (COO**C**H$_3$), 46.1 (**C**HN), 40.4 (**C**H$_2$NHBoc), 30.4 (Bu-**C**H$_2$), 28.5 (*t*Bu), 24.3 (Bu-**C**H$_2$), 21.4 (aryl-NCH**C**H$_3$).



9

4-{4-[14-(11,12-didehydro-5,6-dihydrodibenzo[a,e]cycloocten-5-oxycarbonylamino)-4-oxo-6,9,12-trioxa-3-azatetradec-2-yl]-2-methoxy-5-nitrophenoxy}butanoic acid methyl ester **9**: In a 50 ml round bottom flask equipped with a stirring bar 1.45 g of nitroaromatic **7** (2.41 mmol) were *N*-Boc-deprotected using 20 *v*% TFA in dry DCM for 1 h and the volatiles subsequently removed in a stream of air. After drying in vacuum over night the corresponding ammonium derivative was dissolved in 10 ml dry DMF in a round bottom flask equipped with a gas inlet and a stirring bar under an atmosphere of nitrogen. To the solution were added 1.26 ml DIPEA (7.23 mmol, 3 eq.) and 929 mg of activated carbonate **8**[11b] (2.41 mmol, 1 eq.) and the mixture stirred at rt for 24 h. Thereafter the shiny yellow solution was diluted with ethyl acetate, transferred to a separatory funnel, washed twice with 1 M $NaHSO_4$-soln., three times with 5% Na_2CO_3-soln. and once with brine, dried over Na_2SO_4 and the solvent removed under reduced pressure. The residue was subjected to column chromatography eluting with $CHCl_3$ containing 1.5 *v*% MeOH yielding 1.62 g of pure title compound **9** (2.17 mmol, 90%) as pale yellow foam. R_f: 0.43 ($CHCl_3$+*v*2% MeOH). IR (NaBr): 3365, 2934, 1729, 1672, 1520, 1336, 1273, 1216, 1104, 1029, 760 cm^{-1}. FT-ICR-MS: m/z $[M+Na]^+$ calcd for $C_{39}H_{45}N_3O_{12}Na$: 770.2896 found: 770.2894. ^{1}H-NMR from the mixture of diastereomers (400.1 MHz, Benzol-d_6): δ 7.77 (t, 1H, J = 8.2 Hz, CON**H**), 7.71-7.62 (m, 1H, aryl), 7.34 (s, 1H, aryl), 7.30-7.11 (m, 4H, aryl), 7.08-6.91 (m, 4H, aryl), 6.41-6.34/5.83-5.74 (m/m, 1H, Bn-C**H**O), 6.35/5.91 (s/s, broad, 1H, OCON**H**), 6.05-5.94 (m, 1H, Bn-C**H**N), 4.10-2.71 (m, 22H), 3.90 (dd, 1H, J = -15.7 Hz/7.3 Hz, Bn-C**H**$_2$), 2.95 (dd, 1H, J = -15.7 Hz/3.8 Hz, Bn-C**H**$_2$), 2.29-2.22 (m, 2H, C**H**$_2$COOMe), 1.88-1.79 (m, 2H, C**H**$_2$), 1.51/1.56-1.37 (d/m, 3H, J = 6.6 Hz, C**H**$_3$CHN). ^{13}C-

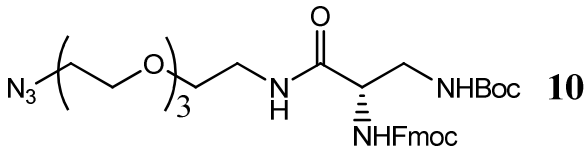
NMR from the mixture of diastereomers (100.6 MHz, Benzol-d_6): δ 172.8 (**C**OOMe), 169.3 (**C**ON), 155.7 (O**C**ONH), 154.1, 153.0, 151.6, 147.5, 141.4, 134.6, 130.4, 128.1, 127.9, 127.3, 127.2, 127.0, 126.5, 126.2, 124.3, 124.2, 121.9, 113.6, 110.8, 110.6, 109.6 (aryl), 77.8, 77.1 (benzyl-**C**HO), 70.9, 70.5, 70.1, 70.1, 70.0 (EG-**C**H_2), 67.8 (aryl-O**C**H_2), 55.8/55.8 (aryl-O**C**H_3), 51.1 (COO**C**H_3), 46.8, 46.2 (**C**HN/benzyl-**C**H_2), 41.1 (**C**H_2NHBoc), 30.4 (Bu-**C**H_2), 24.6 (Bu-**C**H_2), 21.4 (**C**H_3).



3a

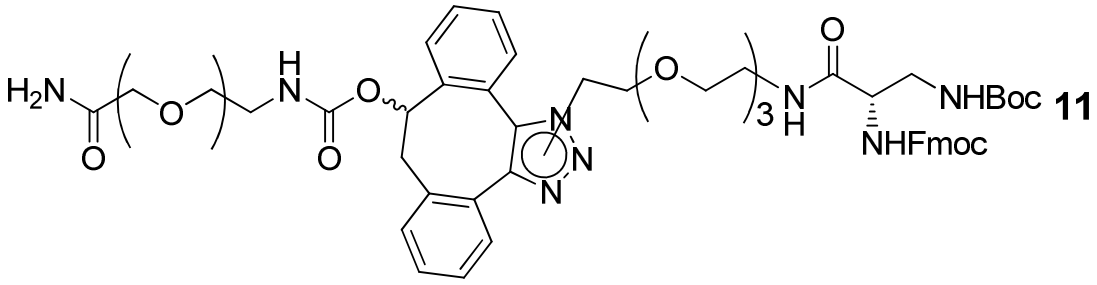
4-{4-[14-(11,12-Didehydro-5,6-dihydrodibenzo[a,e]cycloocten-5-oxycarbonylamino)-4-oxo-6,9,12-trioxa-3-azatetradec-2-yl]-2-methoxy-5-nitrophenoxy}butanoic acid 4-nitophenyl ester **3a**: In an 25 ml round bottom flask 1.54 g of nitroaromatic **9** (2.06 mmol) were dissolved in 4.5 ml THF/MeOH 1:1 *v*/*v*. To the solution were added 184 mg LiOH*H_2O (4.39 mmol, 2.1 eq.) dissolved in 4.5 ml water and the mixture stirred for 90 min. at rt.[23] Then the solution was acidified by adding 1 M $NaHSO_4$-soln. and transferred to a separatory funnel. The aqueous layer was extracted five times with DCM, the combined organic layers dried with Na_2SO_4 and the solvent evaporated under reduced pressure. Subsequently, in a 25 ml round bottom flask equipped with a gas inlet and a stirring bar the crude acid was dissolved in 10 ml dry THF under an atmosphere of nitrogen. To the solution were added 315 mg *p*-nitrophenol (2.27 mmol, 1.1 eq.) and after cooling to -20°C 638 mg DCC (3.09 mmol, 1.5 eq.). The mixture was then stirred for 6 h at -20°C and additional 14 h at rt. After filtration of the precipitated DC-urea the solution was diluted with ethyl acetate, transferred to a separatory funnel, washed twice with 1M $NaHSO_4$-soln. and once each with sat. $NaHCO_3$-soln. and brine. After removal of the solvent under reduced pressure, the residue was subjected to column chromatography eluting with toluene/acetone 7:3 *v*/*v* yielding 1.05 g of pure title compound **9** (1.23 mmol, 60%) as pale yellow foam. R_f: 0.34 (toluene/acetone 7:3 *v*/*v*). IR (NaBr): 3407, 2933, 1763, 1723, 1673, 1522, 1346, 1273, 1211, 1130, 760 cm^{-1}. FT-ICR-MS: m/z $[M+Na]^+$ calcd for $C_{44}H_{46}N_4O_{14}Na$: 877.2903 found: 877.2905. ^{1}H-NMR from the mixture of diastereomers (400.1 MHz, Benzene-d_6): δ 7.84-7.75 (m, 3H, *p*NP/CON**H**), 7.66-7.55 (m, 1H, aryl), 7.38 (s, 1H, aryl), 7.28-7.09 (m, 4H, aryl), 7.06-6.89 (m, 4H, aryl), 6.79-6.73 (m, 2H, *p*NP) 6.38-6.33/5.75-5.66 (m/m, 1H, Bn-C**H**O), 6.30/5.85 (s/s, broad, 1H, OCON**H**), 6.03-5.93 (m, 1H, Bn-C**H**N), 4.08-2.70 (m, 19H), 3.88 (dd, 1H, J = -15.8 Hz/5.1 Hz, Bn-C**H**$_2$), 2.92 (dd, 1H, J = -15.8 Hz/3.8 Hz, Bn-C**H**$_2$), 2.41 (t, 2H, J = 7.1 Hz, C**H**$_2$COOMe), 1.94-1.80 (m, 2H, C**H**$_2$), 1.50/1.56-1.34 (d/m, 3H, J = 6.6 Hz, C**H**$_3$CHN). ^{13}C-NMR from the mixture of diastereomers (100.6 MHz, Benzene-d_6): δ 170.2 (**C**OOMe), 169.4 (**C**ON), 155.8, 155.5, 154.1 (O**C**ONH/aryl), 153.0, 151.6, 147.4, 145.5, 141.4, 135.1, 130.4, 128.1, 127.9, 127.4, 127.3, 126.6, 126.3, 125.1, 124.3, 124.2, 122.4, 121.9, 113.6, 110.7, 110.6, 109.7 (aryl), 77.8, 77.2 (benzyl-**C**HO), 70.9, 70.8, 70.6, 70.5, 70.1, 70.1 (EG-**C**H_2), 67.7 (aryl-O**C**H_2), 55.8 (aryl-

O**C**H_3), 46.7, 46.1 (**C**HN/benzyl-**C**H_2), 41.2 (**C**H_2NHBoc), 31.0 (Bu-**C**H_2), 24.5 (Bu-**C**H_2), 21.5 (**C**H_3).



10

(S)-N-α-(9-Fluorenyl)methoxycarbonyl-N`-β-tert.-butoxycarbonyl-β-aminoalanyl-11-azido-3,6,9-trioxaundecyl amide **10**: In a 100 ml round bottom flask equipped with a gas inlet and a stirring bar 5 g of α-Fmoc-β-Boc-L-β-aminoalanine (7.98 mmol) were dissolved in 50 ml dry THF under an atmosphere of nitrogen. Then the solution was cooled to 0°C and 1.62 g PFP (8.78 mmol, 1.1 eq.) were added followed by 2.15 g DCC (10.4 mmol, 1.3 eq.) and stirring continued for 6 h at 0°C. Thereafter 1.92 g of 2-{2-[2-(Azidoethoxy)ethoxy]ethoxy}amine[24] (8.78 mmol, 1.1 eq.) and 2.08 ml DIPEA (12.0 mmol, 1.5 eq.) were added and the slurry stirred for additional 14 h at rt. After filtration from the DC-urea precipitate the solution was diluted with ethyl acetate and transferred to a separatory funnel. The organic layer was washed twice each with 1 M $NaHSO_4$-soln. and sat. NaHCO3-soln., once with brine, dried with Na_2SO_4 and the solvent removed under reduced pressure. The residue was purified by column chromatography eluting with toluene/acetone 3:1-7:3 *v/v* yielding 3.2 g of pure title compound **10** (5.11 mmol, 64%) as colorless resin. R_f: 0.29 (toluene/acetone 3:1 *v/v*). $[\alpha]_D^{20}$= -12.5 (c=1.0, $CHCl_3$). IR (NaBr): 3319, 2871, 2108, 1689, 1661, 1536, 1450, 1307, 1163, 739 cm^{-1}. FT-ICR-MS: m/z $[M+Na]^+$ calcd for $C_{31}H_{42}N_6O_8Na$: 649.2956 found: 649.2950.^{1}H-NMR (400.1 MHz, $CDCl_3$): δ 7.75 (d, 2H, J = 7.5 Hz, Fmoc), 7.62-7.57 (m, 2H, Fmoc), 7.39 (t, 2H, J = 7.5 Hz, Fmoc), 7.30 (dt, 2H, J = 7.5 Hz/0.9 Hz, Fmoc), 6.96 (s, broad, 1H, CON**H**), 6.32 (s, broad, 1H, CON**H**), 5.29 (s, broad, 1H, CON**H**), 4.44-4.24 (m, 2H, Fmoc-C**H**$_2$O/α-C**H**), 4.20 (t, 1H, J = 7.2 Hz, Fmoc-C**H**), 3.65-3.40 (m, 16H, EG-chain-C**H**$_2$/β-C**H**), 3.34 (t, 2H, J = 5.2 Hz, C**H**$_2$$N_3$), 1.44 (s, 9H, *t*Bu). ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 170.2 (**C**ONH), 157.2, 156.6 (O**C**ONH), 143.9, 143.8, 141.4, 127.8, 127.2, 125.2, 120.1 (aryl), 80.1 (*t*Bu), 70.7, 70.7, 70.6, 70.4, 70.0, 69.6 (EG-**C**H_2), 67.3 (Fmoc-**C**H_2O), 56.4 (α-**C**H), 50.7 (**C**$H_2$$N_3$), 47.2 (Fmoc-**C**H), 42.9, 39.5 (**C**H_2N), 28.4 (*t*Bu).



11

{12-[[[8,9-dihydro-1-[2-[2-[2-[[3-(tert.-butoxycarbonyl)amino-2-[(9-fluorenyl)methoxycarbonyl]aminopropanamido]ethoxy]ethoxy]ethoxy]ethyl]-1H-dibenzo[3,4:7,8]cycloocta[1,2-d]triazol-9-yl]oxy]carbonyl]amino}-3,6,10-trioxadodecanoic acid amide **and** *{12-[[[8,9-dihydro-3-[2-[2-[2-[[3-(tert.-butoxycarbonyl)amino-2-[(9-fluorenyl)methoxycarbonyl]aminopropanamido]ethoxy]ethoxy]ethoxy]ethyl]-1H-dibenzo[3,4:7,8]cycloocta[1,2-d]triazol-9-yl]oxy]carbonyl]amino}-3,6,10-trioxadodecanoic acid amide* **11**: Triazole-loaded TOYOPEARL® was irradiated according to the procedure

described above and the remaining solid support filtered off. Then dioxane was removed under reduced pressure and the aqueous residue transferred to a separatory funnel. The aq. layer was extracted five times with DCM, the combined organic layers dried over Na_2SO_4 and the solvent removed under reduced pressure leaving **11** as colorless foam in analytical purity. R_f: 0.34 ($CHCl_3$+6*v*%MeOH). $[\alpha]_D^{20}$= -5.3 (c=1.0, $CHCl_3$). FT-ICR-MS: m/z $[M+Na]^+$ calcd for $C_{56}H_{70}N_8O_{14}Na$: 1101.4904 found: 1101.4900. HPLC: 8.65 min., 98.2 %. ^{1}H-NMR from the mixture of regioisomers/diastereomers (400.1 MHz, $CDCl_3$): δ 7.74 (d, 2H, J = 7.6 Hz, Fmoc), 7.62-7.46 (m, 4H, Fmoc/aryl), 7.45-7.34 (m, 2H, aryl), 7.38 (t, 2H, J = 7.4 Hz, Fmoc), 7.33-6.99 (m, 7H, Fmoc/aryl/CON**H**), 6.37 (s, broad, 1H, CON**H**), 6.25-6.15 (m, 1H, CON**H**), 6.06/5.98-5.91 (m, 1H, CONH), 5.71-5.62/5.60-5.49 (m, 1H, OCON**H**), 4.76-4.67/4.63-4.41 (m, 2H, Bn-C**H**O/α-C**H**), 4.41-4.24 (m, 3H, Fmoc-OC$\mathbf{H}_2$/C$\mathbf{H}_2$), 4.19 (t, 1H, J = 7.2 Hz, Fmoc-C**H**), 4.05-3.84 (m, 4H, OC$\mathbf{H}_2$CONH$_2$/Bn-C$\mathbf{H}_2$), 3.74-3.17/3.01 (m/t, 28H, J = 12.1 Hz, EG-C$\mathbf{H}_2$/β-C$\mathbf{H}_2$), 1.42 (s, 9H, *t*Bu). ^{13}C-NMR from the mixture of regioisomers/diastereomers (100.6 MHz, $CDCl_3$): δ 173.4, 170.3 (**C**ONH), 157.2, 156.7, 156.0, 155.4 (O**C**ONH), 147.9, 146.3 (aryl), 143.9/143.9, 141.4 (Fmoc), 137.3, 135.8, 135.6, 134.6, 134.4, 133.6, 132.8, 132.2, 131.5, 130.3, 129.9, 129.6, 129.4, 129.1, 128.9, 128.7, 128.6 (aryl), 127.8 (Fmoc), 127.7, 127.3 (aryl), 127.2 (Fmoc), 126.8, 126.5, 125.3 (Fmoc), 124.9, 124.5 (aryl), 120.1 (Fmoc), 79.9 (*t*Bu), 71.7, 71.1, 71.0, 70.7, 70.6, 70.4, 70.4, 70.3, 70.2, 70.2, 70.0, 69.7, 69.2 (EG-**C**H_2), 67.3 (Fmoc-OC$\mathbf{H}_2$), 56.1 (α-**C**H), 48.6, 48.3, 48.2 (**C**H_2N), 47.2 (Fmoc-**C**H), 43.3, 42.9, 40.9, 39.4, 37,9, 37.3 (**C**H_2N), 28.4 (*t*Bu).

4. References

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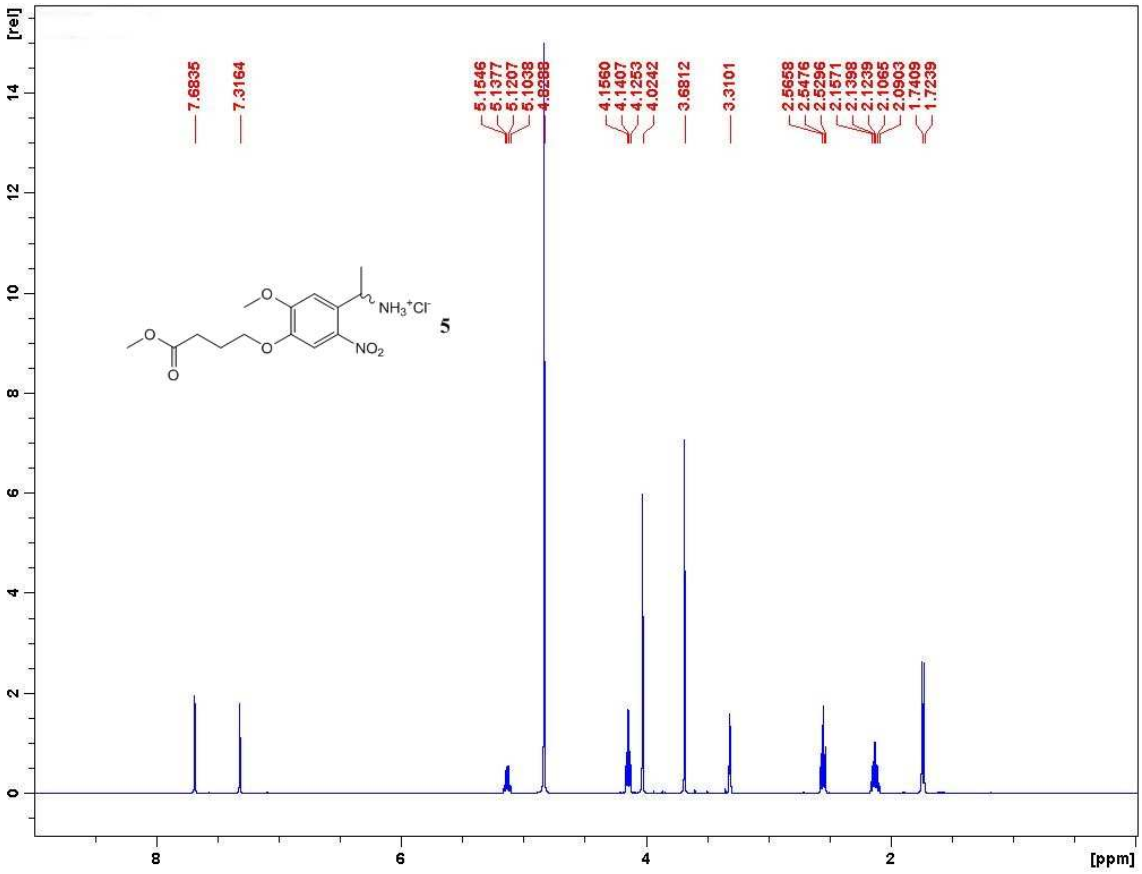
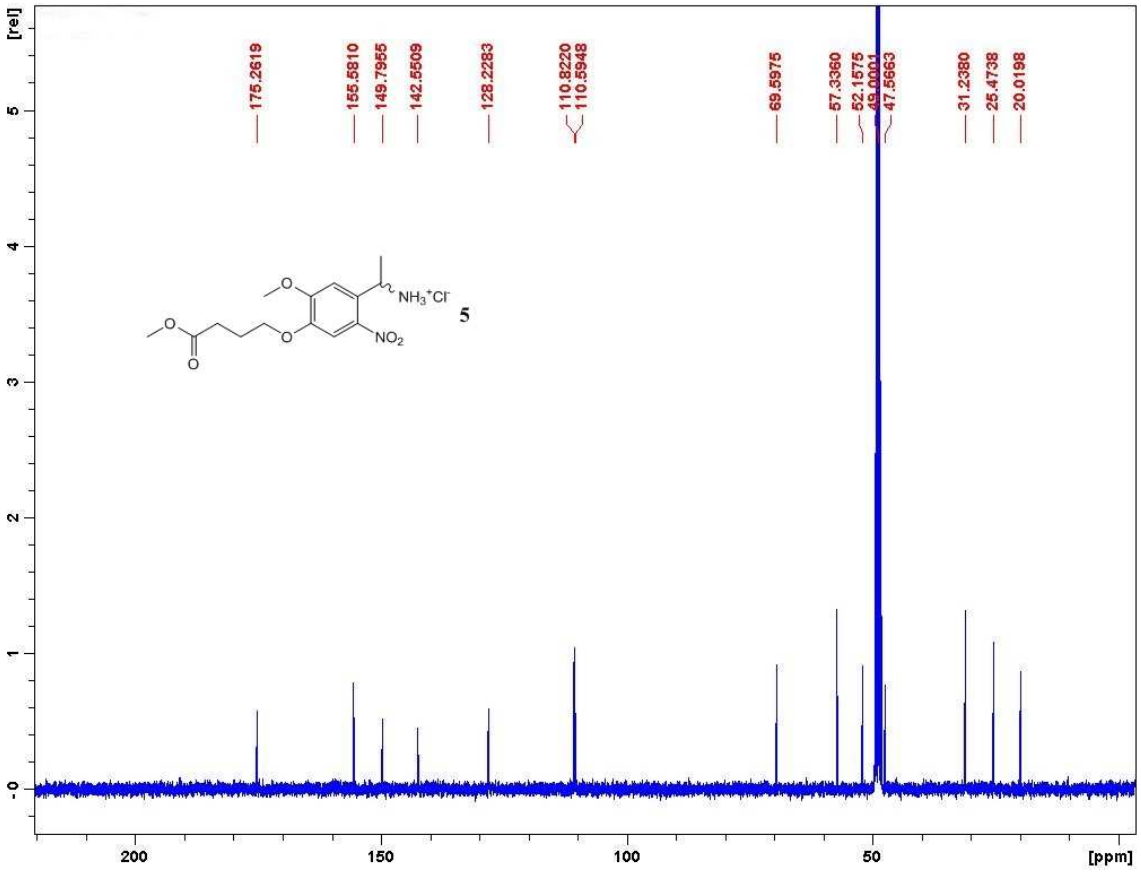
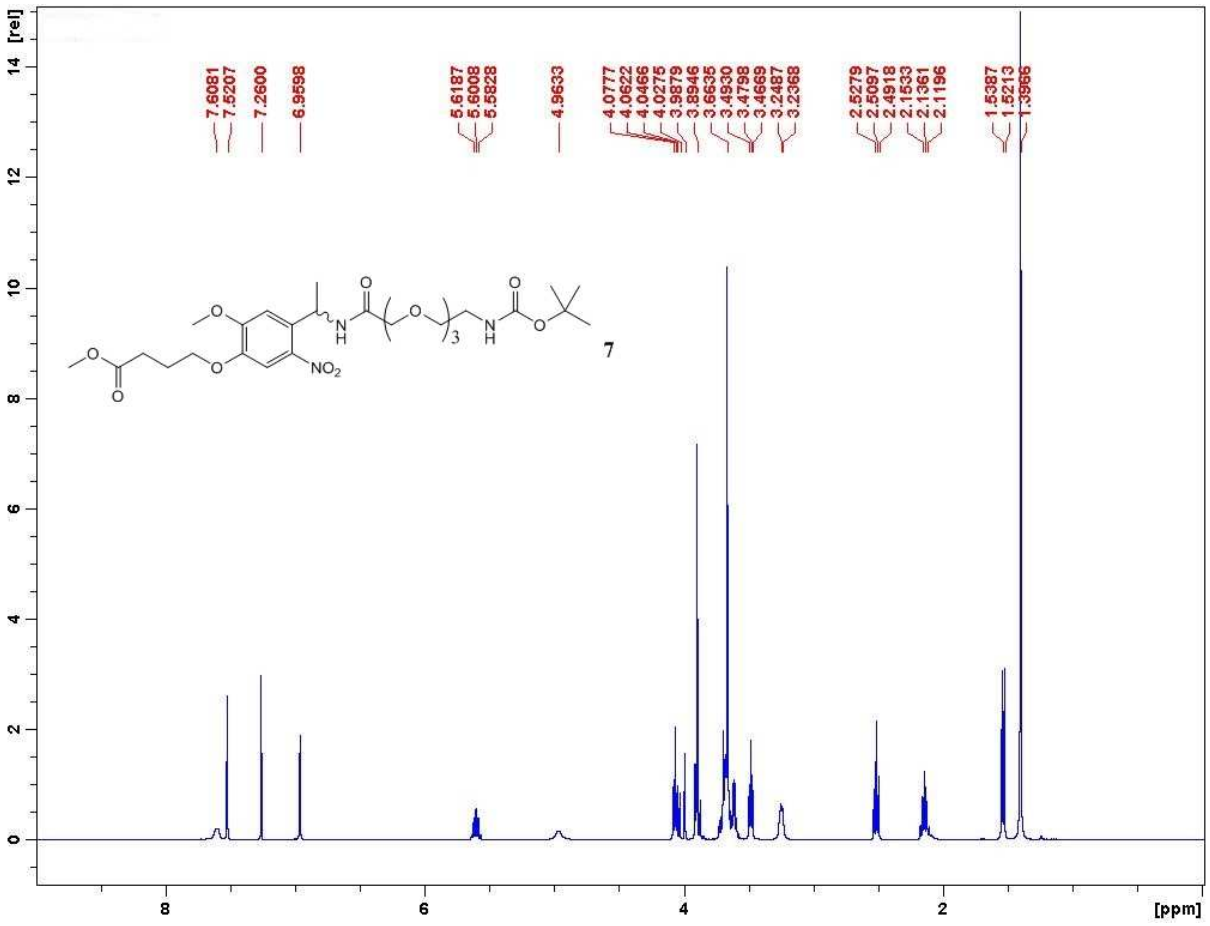
5. NMR-Spectra of compounds prepared



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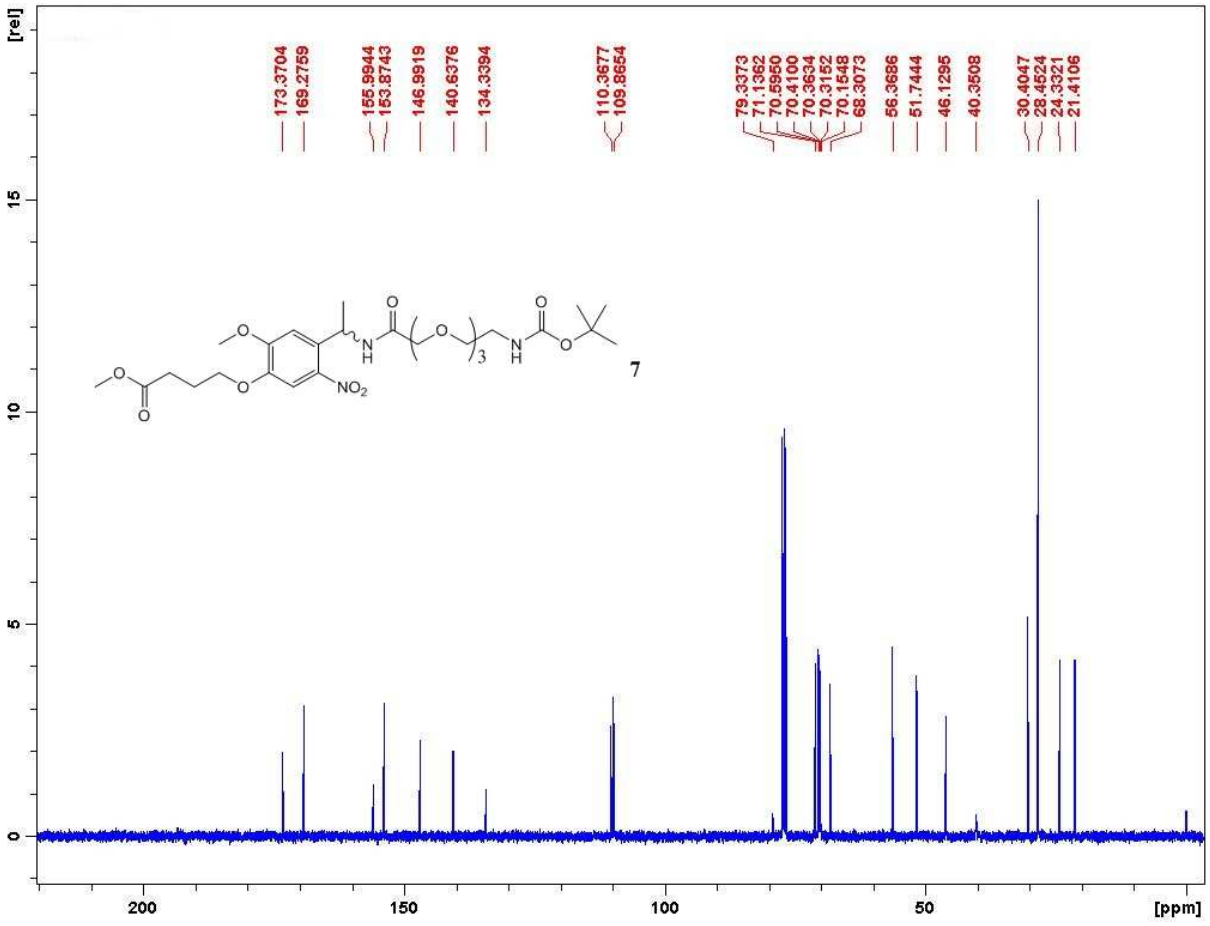
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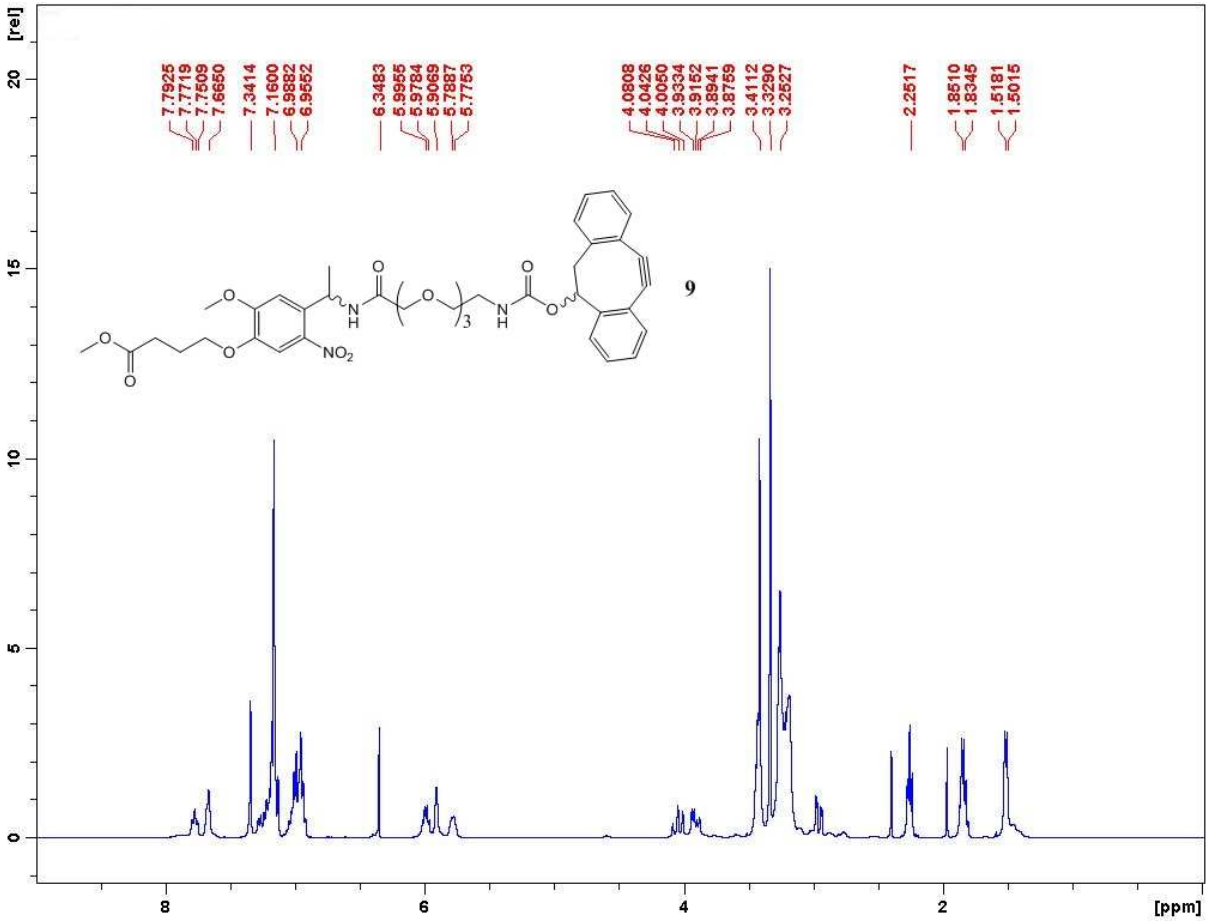
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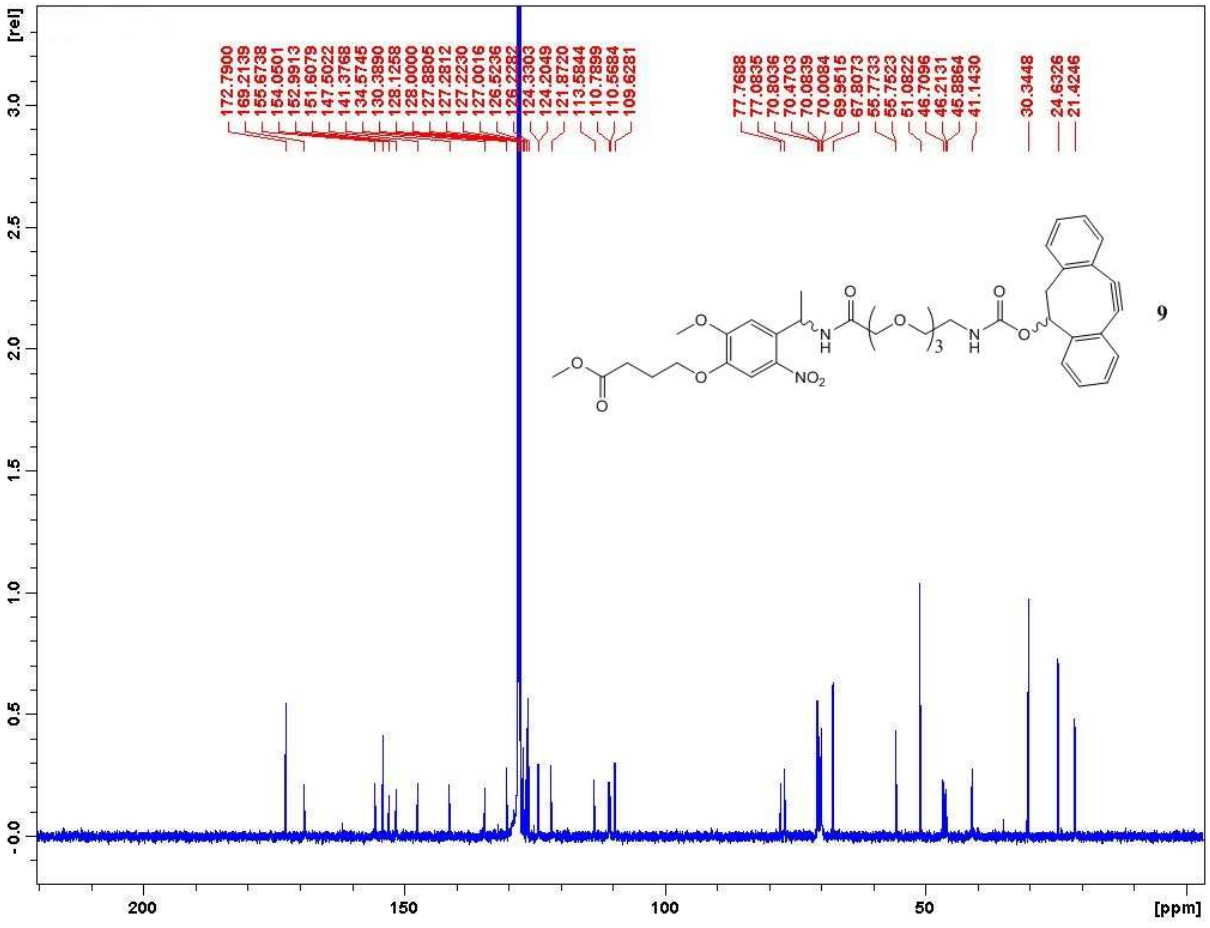
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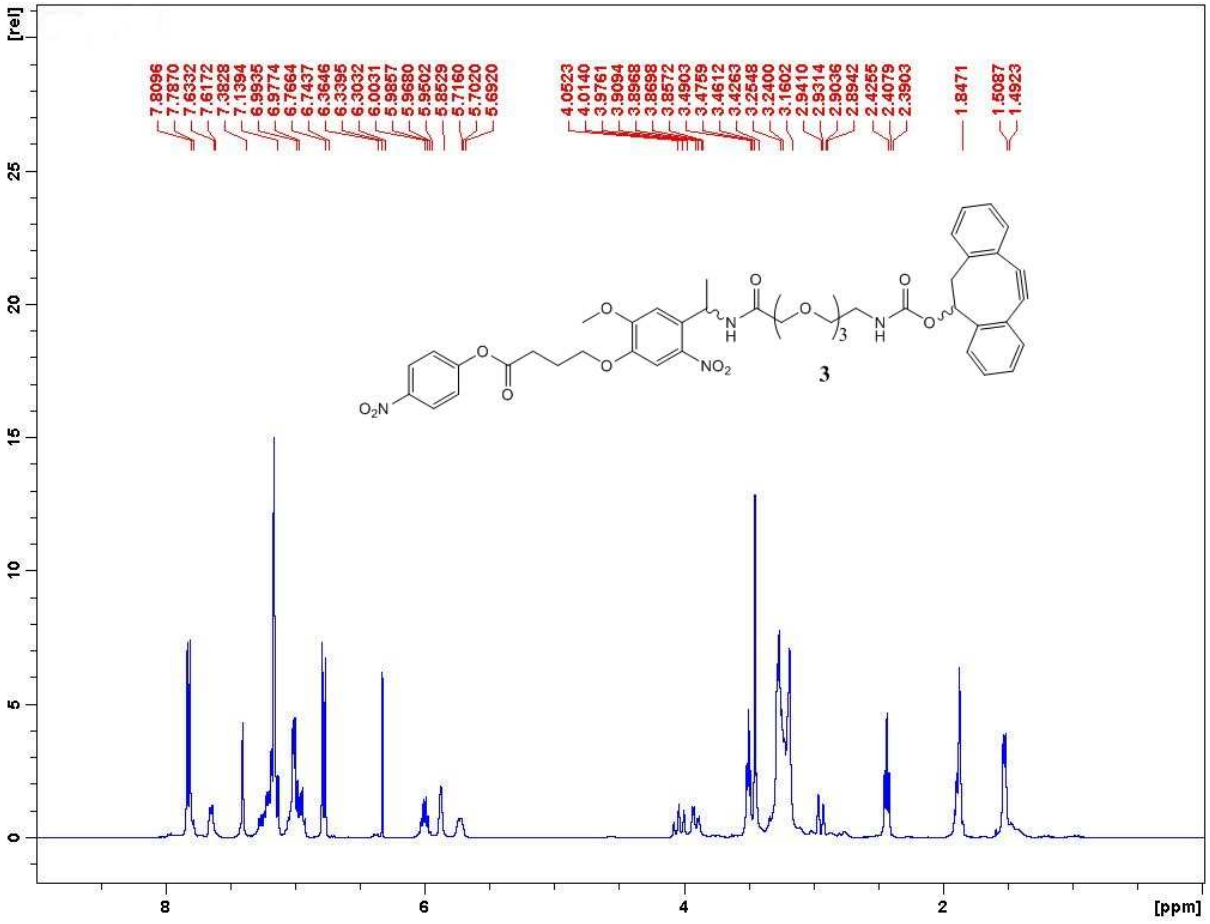
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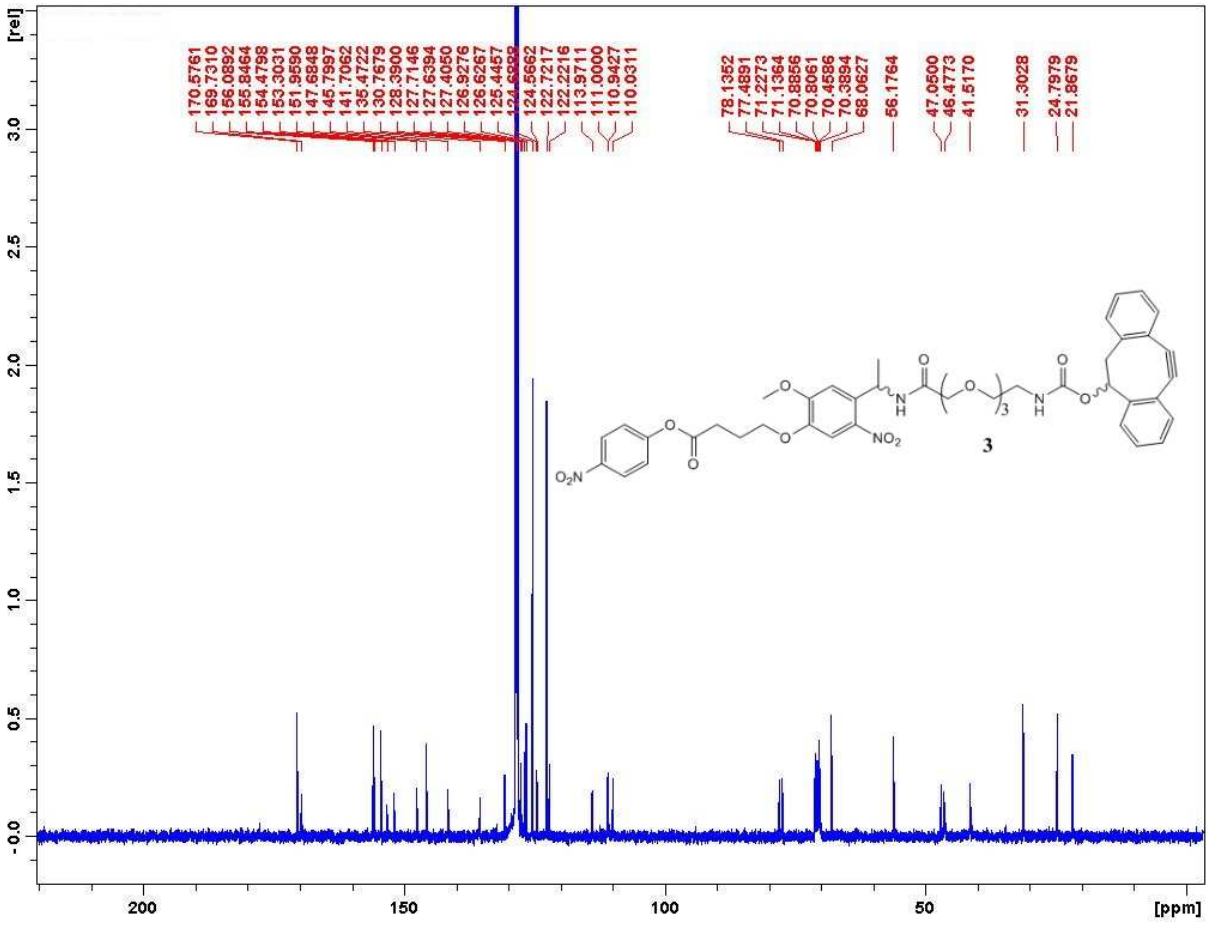
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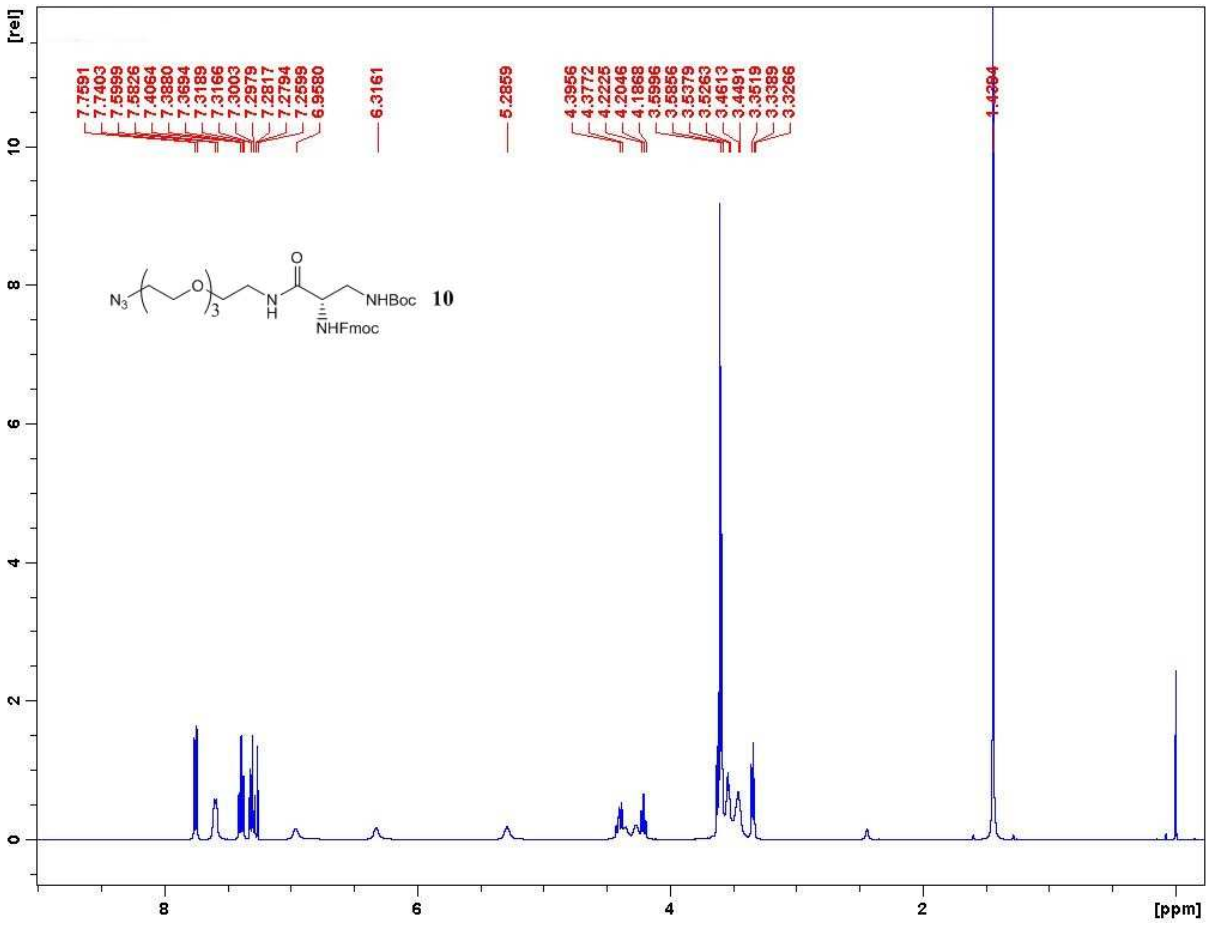

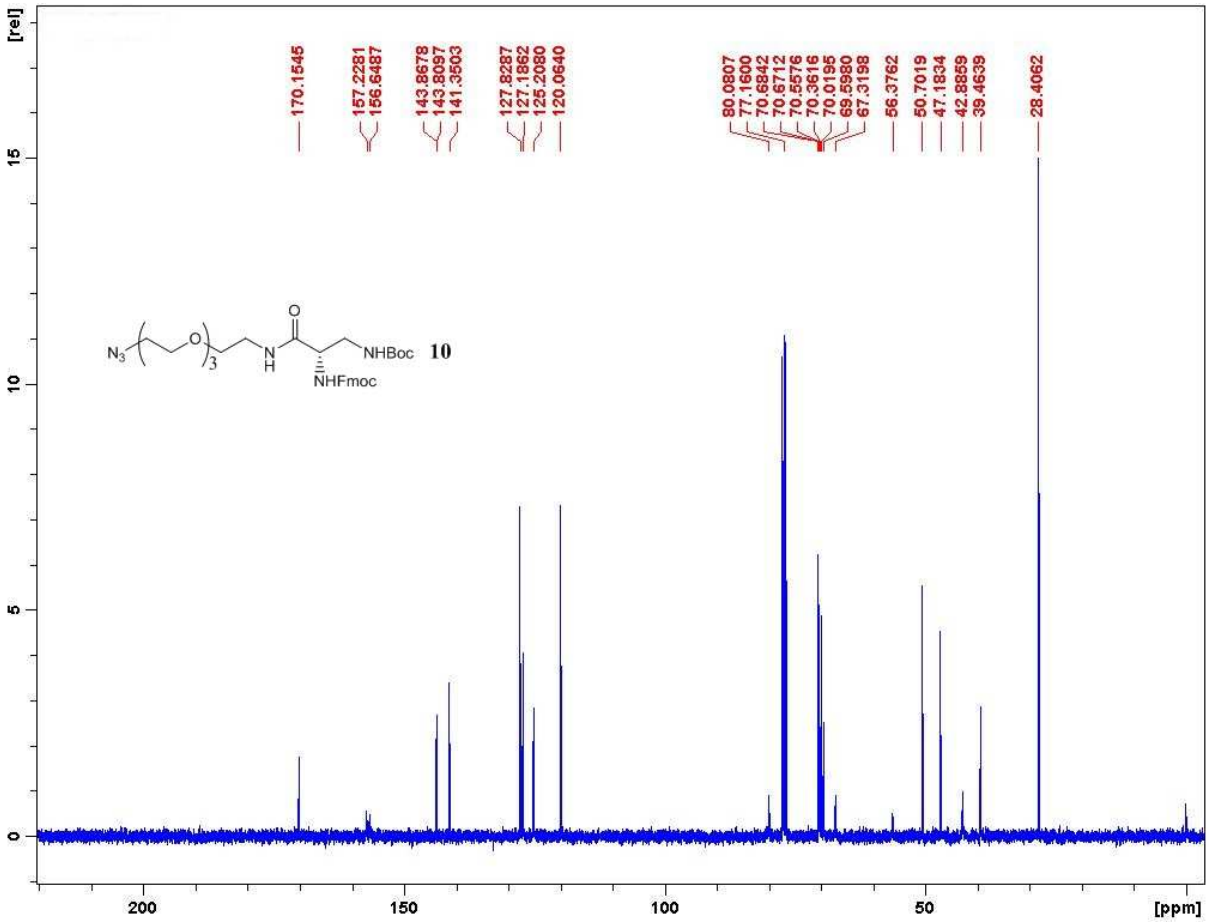

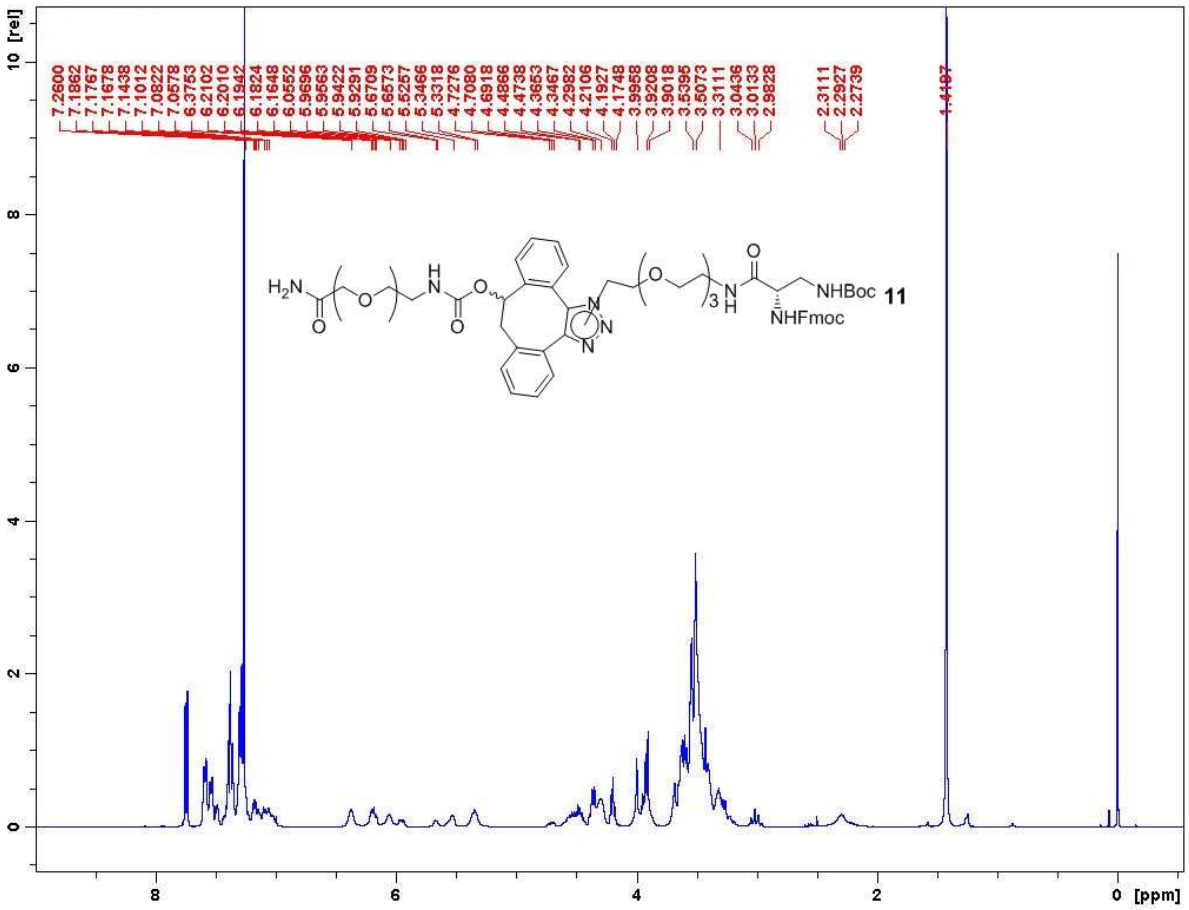
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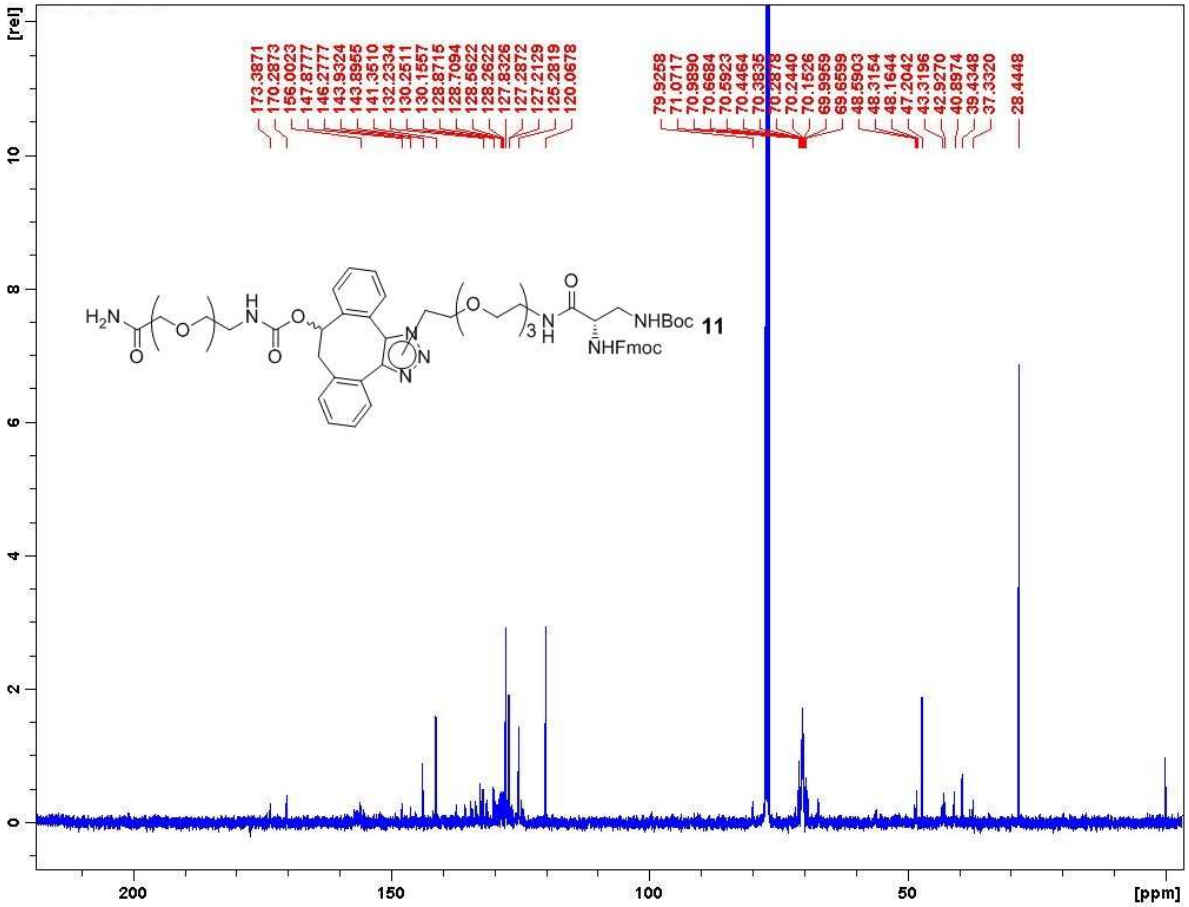
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