Electronic Supplementary Information

Chromatography-free synthesis of monodisperse oligo(ethylene glycol) mono-*p*-toluenesulfonates and quantitative analysis of oligomer purity

Adam M. Wawro,[†] Takahiro Muraoka,[†‡§] Kazushi Kinbara[†‡]*

[†]*Institute of Multidisciplinary Research for Advanced Materials, Tohoku University*
2-1-1 Katahira, Aoba-ku, Sendai 980-8577, Japan

[‡]*Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology*
4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan

[§]*PRESTO, Japan Science and Technology Agency*
4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

1. Chromatography-free process: details and comments

The chromatography-free synthesis of PEG-Ts requires attention during reaction setting and workup, since accidentally generated impurities might have to be removed by column chromatography later. Here we list the most important points to care about.

The quality of the purchased PEG and trityl chloride is essential for a positive outcome. Special attention should be paid to the basic building block, PEG_4, as its initial dispersity, i.e. presence of PEG_3 and PEG_5, affects the quality of the final product. In this study PEG_4 from a single lot was used for all the experiments (Sigma, item no. 110175, lot no. MKBP3393V).

In general, four main reaction types can be recognized: initial trityl protection, tosylation, chain elongation, one more tosylation and final trityl deprotection.

The first reaction, protection of PEG_4 with trityl chloride, is generally simple and, as long as all of the starting material is consumed, no troubles are expected. Although this type of reaction is often carried out at elevated temperature or in a presence of DMAP, no such modifications were necessary in this case. During the workup, remaining PEG_4 is removed by extraction with brine and after the extraction one should confirm absence of PEG_4 by TLC (silica, EtOAc, I_2; $R_f = 0$). The product appearance depends on the quality of TrtCl used. Based on our experience, the product is usually obtained as yellowish oil, but the source of yellow hue could not be identified.

The second reaction, tosylation, is performed according to a modified procedure developed by Ouchi and coworkers.[1] In the original procedure, slight excess of the PEG-type reagent was used in order to consume all TsCl. Alternatively, excess of TsCl could be used, but then chromatographic purification was required. Using equimolar amount is rather unsafe, as even small deviation in the reactant purity can affect the final result of the whole chromatography-free process. However, we observed that if in this heterogeneous system certain ratios of THF, water and NaOH are used, PEG tosylation is significantly faster than TsCl hydrolysis at 0 °C. Under the same conditions, at room temperature, TsCl hydrolyzes slowly, while the reaction product, PEG tosylate, does not hydrolyze at observable rate. Therefore, keeping reaction stirred at low temperature until all the starting material is consumed, followed by warming to rt and stirring overnight results in selective hydrolysis of the excess of TsCl. Importantly, vigorous stirring seemed to be crucial for this process. When the mixture was left still for several hours, partial cleavage of trityl group was observed, probably caused by HCl released in organic layer, which was not immediately neutralized by the basic aqueous phase. For workup, EtOAc or MTBE may be used instead of Et_2O. In the case of EtOAc, it should be fully removed by evaporation before being transferred to the following step. Because drying with Na_2SO_4 is rather inefficient for PEG derivatives in THF at high concentrations, the remaining water has to be removed

[1] M. Ouchi, Y. Inoue, Y. Liu, S. Nagamune, S. Nakamura, K. Wada and T. Hakushi, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 1260–1262.

by azeotropic co-evaporation with toluene. The tosylation reaction is repeated also at least once after the PEG chain extension. The reaction conditions and workup are generally the same, however we observed that longer PEGs tend to undergo tosylation faster. It is probably due to different polarity and thus different distribution on the organic–aqueous interface, where the reaction supposedly takes place.

The third reaction, Williamson ether synthesis, is important for keeping the monodispersity of the product as low as possible. We did not find using *t*-BuOK in DMF instead of NaH in THF advantageous. At 40 °C, using NaH in THF, the reaction was completed in 4 days. At higher temperatures (50 °C or ca. 70 °C) the reaction progress was swifter, resulting in completion within less than one day, but moderately more intense depolymerization was observed as well. Therefore, if one prefers time-efficiency to monodispersity, the temperature should be elevated. During the reaction workup, unreacted PEG_4 should be removed completely, as in the case of the first step. In general, PEG-Trt derivatives have very low affinity towards aqueous phase, so the product is retained in the organic phase during the extraction.

The final process is the trityl group cleavage by catalytic hydrogenation. During this step all the accumulated side products are transformed into free PEG chains. The desired PEG monotosylate becomes the least hydrophilic PEG derivative in the mixture. The other product, triphenylmethane, is selectively removed by washing with hexane, as even more hydrophobic PEG monosubstituted derivatives have very low solubility in this solvent. The completion of washing is simply confirmed by lack of UV absorption of the hexane phase at 254 nm, simply using fluorescent TLC plate. The following extraction with ethyl acetate and water separates PEG-Ts from free PEGs. The separation is efficient, as long as the temperature is kept around 20 °C or below. At higher temperatures free PEGs, known for their thermoresponsive behavior, may be difficult to wash away completely. The successful separation can be confirmed by mass spectrometry.

Finally, it should be noted that the trityl-containing intermediates should not be stored at room temperature for longer time. Importantly, the intermediate compounds in a crude form show better stability than if isolated and purified by chromatography on silica. In that latter case we observed spontaneous trityl cleavage during one-week storage, probably catalyzed by suspended silica particles.

2. Monodispersity analysis

Because ionization events depend heavily on molecular structure of the analyte, supposedly distribution of charges between major and minor components of the mixture depends on the structure as well. Thus, the monodispersity values obtained from mass-spectrometry-based methods for compounds with significantly different chemical structures should not be compared directly without any comments. On the contrary, HPLC systems with UV detectors are suitable for such analysis, provided that molar absorption coefficient of the oligomers of interest does not change with chain length and sample concentration is in range at which the Lambert-Beer law applies.

To confirm that molar absorption coefficient ε of PEG_n-Ts does not depend on the PEG chain in the considered length range, we recorded UV spectra of four oligomers (n = 4, 8, 12, 16) in water-methanol mixture (1:1)(Figure S1). Although in the whole analyzed range (240-300 nm) the ε values were similar for all four oligomers, the most suitable region for quantitative analysis is above λ = 266 nm.

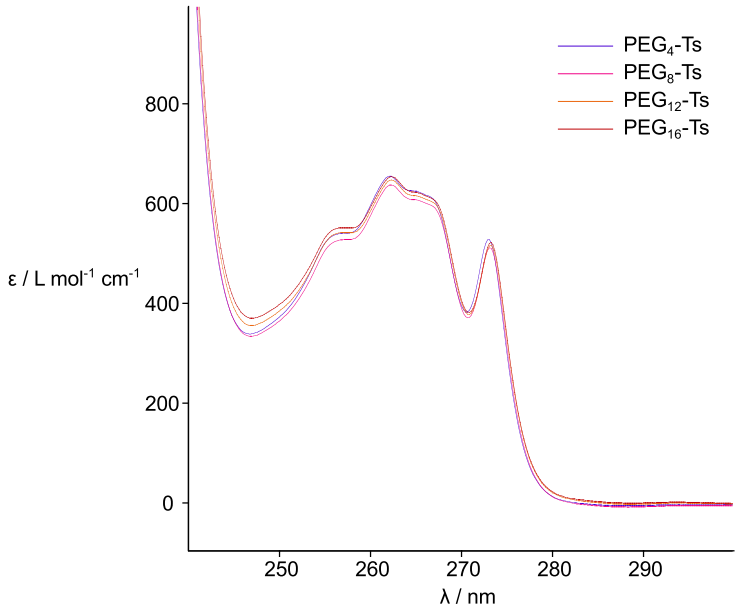


Figure S1: Molar absorption coefficients ε of PEG_n-Ts oligomers.

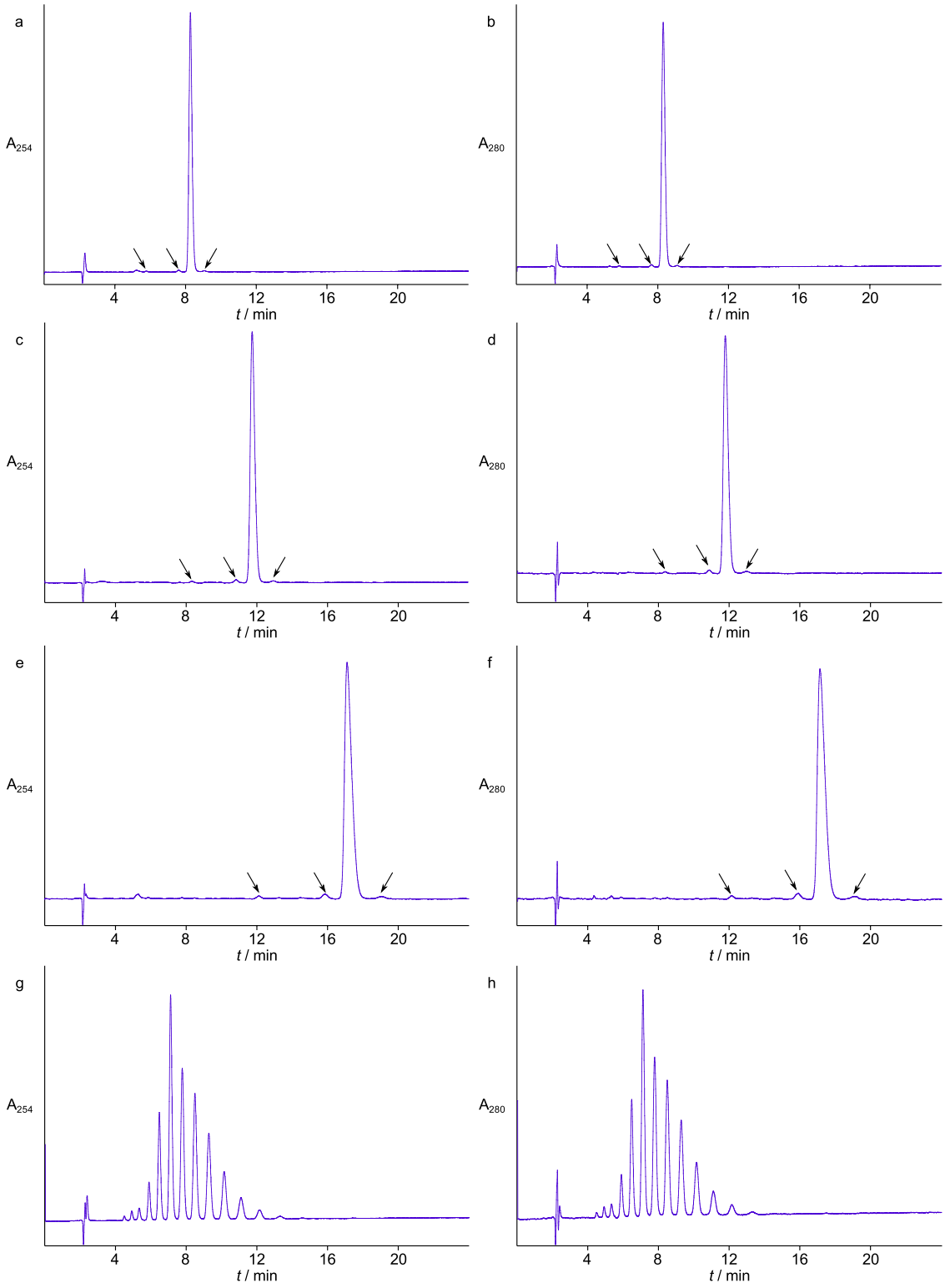


Figure S2: RP-HPLC chromatograms of a PEG_n-Ts with UV absorbance detection at 254 and 280 nm. (a) PEG_8-Ts@254 nm; (b) PEG_8-Ts@280 nm; (c) PEG_{12}-Ts@254 nm; (d) PEG_{12}-Ts@280 nm; (e) PEG_{16}-Ts@254 nm; (f) PEG_{16}-Ts@280 nm; (g) PEG400-Ts@254 nm; (h) PEG400-Ts@280 nm. Arrows mark peaks corresponding to minor oligomers.

During HPLC analysis, in order to discriminate PEG-Ts peaks from other compounds in the mixture, we set the detector at two wavelengths: general (254 nm) and more specific (280 nm)(Figure S2). It can be seen that there are three most significant impurities: $PEG_{(n-1)}$-Ts, $PEG_{(n+1)}$-Ts and $PEG_{(n-4)}$-Ts. The relative abundance of specific oligomers in all three products is shown in Table S1. As expected, the amount of impurities rises with the PEG chain length. Because the reasons why the impurities are present are different, the ratios between the amounts show non-linear correlation. $PEG_{(n+1)}$-Ts is generated only from traces of PEG_5 present in the starting material. $PEG_{(n-1)}$-Ts is produced from initially present PEG_3 as well as a result of depolymeryzation, so its amount rises quicker than the amount of $PEG_{(n+1)}$-Ts. $PEG_{(n-4)}$-Ts comes from uncompleted Williamson reaction or PEG_4 not completely removed during workup and may slightly vary from batch to batch.

Table S1: Oligomer composition of PEG_n-Ts analyzed with various methods.

sample	component	MALDI-L[a]	MALDI-R[b]	HPLC[c]
PEG_8-Ts (5)	PEG_4-Ts	0.4%	0.1%	0.2%
	PEG_7-Ts	0.4%	0.2%	0.7%
	PEG_8-Ts	**98.8%**	**99.4%**	**98.7%**
	PEG_9-Ts	0.4%	0.3%	0.5%
PEG_{12}-Ts (8)	PEG_8-Ts	0.2%	0.1%	0.3%
	PEG_{11}-Ts	0.8%	0.3%	0.9%
	PEG_{12}-Ts	**98.3%**	**99.3%**	**98.2%**
	PEG_{13}-Ts	0.7%	0.3%	0.6%
PEG_{16}-Ts (11)	PEG_{12}-Ts	0.2%	0.2%	0.7%
	PEG_{15}-Ts	0.8%	0.4%	1.5%
	PEG_{16}-Ts	**98.3%**	**99.1%**	**97.0%**
	PEG_{17}-Ts	0.6%	0.3%	0.9%

a) MALDI source in a linear mode, b) MALDI source in a reflectron mode, c) detection at 280 nm. All values rounded half up to 0.1%.

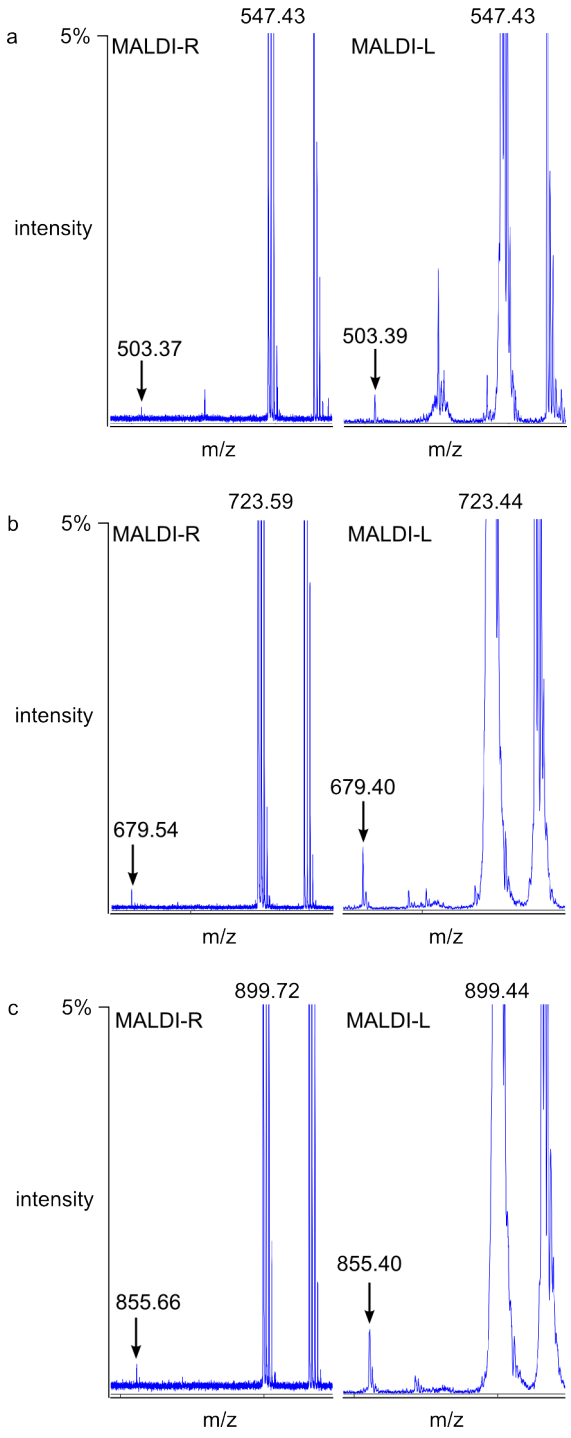


Figure S3: Magnifications of a) PEG_8-Ts, b) PEG_{12}-Ts, c) PEG_{16}-Ts MS spectra recorded with different methods: MALDI in reflectron mode (left) and MALDI in linear mode (right). The intensity was scaled to 5% of the main $[M+Na]^+$ peak. Peaks of relevant $PEG_{(n-1)}$-Ts impurities are marked with arrows.

3. Synthesis

The chromatography-free method described here produces pure tosylates **5**, **8** and **11**. Intermediates **1-4**, **6**, **7**, **9** and **10** contain some symmetric PEG-type impurities that are completely removed during the final hydrogenation step (see synthesis of **5**, **8** or **11**). Because of that, the intermediates were used as obtained, without further purification. However, if required in pure state, the intermediate compounds can be purified by chromatography on silica, eluted with hexane–ethyl acetate or ethyl acetate–methanol, depending on the compound polarity. For clarity, the crude products that were used without purification are marked with an asterisk (*).

3.1 Preparation of TrtO-PEG$_4$-OH (**1**)

Tetra(ethylene glycol) (200 mL, 224 g, 1.15 mol) was placed in a 2-neck 1 L flask and dried by azeotropic evaporation with toluene (50 mL). The flask was equipped with a balloon, a septum, and a stir bar. The liquid was degassed under vacuum and dry pyridine (18 mL, 17.6 g, 0.22 mol) was added under argon atmosphere, followed by triphenylmethyl chloride (40.00 g, 0.1435 mol). The mixture was vigorously stirred for 3 h at rt. The reaction was quenched with water (200 mL). Crude product was extracted with toluene (100 mL) and the organic layer was washed with water-brine mixture (4:1, 100 mL), saturated aqueous solution of ammonium chloride (50 mL) and brine (4 × 50 mL). The absence of tetra(ethylene glycol) was confirmed by TLC [silica, EtOAc; R_f = 0 (PEG$_4$); R_f = 0.55 (**1**)]. The milky emulsion was filtered through a piece of filter paper, the filtrate was concentrated and pyridine was removed by azeotropic evaporation with toluene (3 × 50 mL) to afford **1** as colorless oil (*) (62.40 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46 (d, 6H, ^3J = 7.1 Hz), 7.26 (m, 9H), 3.68 (m, 12H), 3.59 (t, 2H, ^3J = 4.2 Hz), 3.24 (t, 2H, ^3J = 5.1 Hz), 2.36 (t, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.3 (*ipso*-C_{Ph}), 128.9 (*m*-C_{Ph}), 127.9 (*o*-C_{Ph}), 127.1 (*p*-C_{Ph}), 86.7 (CPh_3), 72.6 (CH_2CH_2OH), 70.9-70.6 (C_{PEG}), 63.5 (CH_2OTrt), 61.9 (CH_2OH). HRMS (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{27}H_{32}O_5K$ 475.1881; Found 475.1865.

3.2 Preparation of TrtO-PEG$_4$-OTs (**2**)

Compound **1** (62.40 g, not more than 0.1435 mol) was placed in a 1-neck 1 L flask with a stir bar, dissolved in THF (200 mL) and cooled to 0 °C on ice bath. Sodium hydroxide (20.0 g, 0.50 mol) was dissolved in water (60 mL), cooled to rt and added to the THF solution. The mixture was stirred on an ice bath for 20 min, then a solution of *p*-toluenesulfonyl chloride (30.0 g, 0.157 mol) in THF (60 mL) was added slowly through dropping funnel over 30 min. The mixture was stirred for 4 h at 0 °C. After consumption of compound **1** (confirmed by TLC [silica, 50% EtOAc–hexane; R_f = 0.1 (**1**); R_f = 0.55 (**2**)]) the ice bath was removed and the mixture was stirred at rt for 15 h to hydrolyze remaining tosyl chloride (confirmed by TLC [silica, 30% EtOAc–hexane; R_f = 0.2 (**2**); R_f = 0.6 (Trt-PEG$_4$-Trt); R_f = 0.7 (TsCl)]). Then water (30 mL) and diethyl ether (50 mL) were added, organic layer was separated,

washed with saturated aqueous solution of sodium hydrogen carbonate (50 mL) and brine (3 × 50 mL) and dried over sodium sulfate. Activated charcoal (0.5 g) was added to the yellow solution, solids were filtered off and the filtrate was concentrated to yield viscous yellowish oil (*) (79.33 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.78 (d, 2H, ^{3}J = 8.3 Hz), 7.46 (d, 6H, ^{3}J = 7.2 Hz), 7.26 (m, 11H), 4.12 (t, 2H, ^{3}J = 4.8 Hz), 3.62 (m, 12H), 3.23 (t, 2H, ^{3}J = 5.2 Hz), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.8 (*ipso*-C_{Ts}), 144.2 (*ipso*-C_{Ph}), 133.1 (*p*-C_{Ts}), 129.9 (*m*-C_{Ts}), 128.8 (*m*-C_{Ph}), 127.9 (*o*-C_{Ts}), 127.8 (*o*-C_{Ph}), 127.0 (*p*-C_{Ph}), 86.6 (CPh_3), 70.9-70.6 (C_{PEG}), 69.3 (CH_2CH_2OTs), 68.7 (CH_2CH_2OTs), 63.4 (CH_2OTrt), 21.7 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{38}O_7SNa$ 613.2230; Found 613.2232.

3.3 Preparation of TrtO-PEG_8-OH (**3**)

Sodium hydride (60% dispersion in paraffin oil, 7.35 g, 0.184 mol) was placed in a 2-neck 1 L flask under argon and washed with dry hexane (2 × 50 mL). Anhydrous THF (180 mL) was added carefully and the mixture was cooled to 0 °C on ice bath. Tetra(ethylene glycol) (200 mL, 224 g, 1.15 mol), dried previously by azeotropic evaporation with toluene (3 × 50 mL), was added through a dropping funnel over 30 min. As long as evolution of H_2 gas was observed, the addition was slow. Once the mixture became a clear solution, the remaining reactant was added more quickly. Then a solution of compound **2** (79.33 g, not more than 0.1435 mol, dried just before use with toluene, 3 × 50 mL) in dry THF (100 mL) was added through the same dropping funnel over 15 min. The ice bath was removed, the flask was equipped with a condenser and the mixture was stirred vigorously at 40 °C under argon on an oil bath for 4 days. After the consumption of compound **2** (confirmed by TLC [silica, 50% EtOAc–hexane; R_f = 0.05 (**3**); R_f = 0.55 (**2**)]) the mixture was cooled to rt, water (200 mL) and brine (200 mL) were added. The organic layer was separated and the aqueous layer was extracted with diethyl ether (50 mL). Combined organic layers were washed with water-brine 1:1 (50 mL) and brine (5 × 50 mL). The absence of tetra(ethylene glycol) was confirmed by TLC [silica, EtOAc; R_f = 0 (PEG_4)]. The solution was dried over sodium sulfate; activated charcoal powder (ca. 0.5 g) was added and filtered off. The filtrate was concentrated under vacuum to yield yellowish oil (*) (79.65 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46 (d, 6H, ^{3}J = 7.2 Hz), 7.26 (m, 9H), 3.63 (m, 30H), 3.23 (t, 2H, ^{3}J = 5.2 Hz), 2.71 (t, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.2 (*ipso*-C_{Ph}), 128.8 (*m*-C_{Ph}), 127.8 (*o*-C_{Ph}), 127.0 (*p*-C_{Ph}), 86.6 (CPh_3), 72.6 (CH_2CH_2OH), 70.9-70.4 (C_{PEG}), 63.4 (CH_2OTrt), 61.8 (CH_2OH). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{48}O_9Na$ 635.3191; Found 635.3188.

3.4 Preparation of TrtO-PEG_8-OTs (**4**)

Compound **3** (79.65 g, not more than 0.1435 mol) was placed in a 1-neck 1 L flask with a stir bar, dissolved in THF (200 mL) and cooled to 0 °C on ice bath. Sodium hydroxide (20.0 g, 0.5 mol) was dissolved in water (60 mL), cooled to rt and added to the THF solution. The mixture was stirred on an ice bath for 15 min, then a solution of *p*-toluenesulfonyl chloride (30.0 g, 0.157 mol) in THF (60 mL)

was added slowly through a dropping funnel over 30 min. The mixture was stirred for 1.5 h at 0 °C. After the consumption of compound **3** (confirmed by TLC [silica, EtOAc; R_f = 0.1 (**3**); R_f = 0.5 (**4**)]), the ice bath was removed and the mixture was stirred at rt for 12 h. Hydrolysis of *p*-toluenesulfonyl chloride was confirmed by TLC. Then water (50 mL) and Et_2O (50 mL) were added to the mixture. The organic layer was washed with a saturated aqueous solution of sodium hydrogen carbonate (50 mL) and brine (3 × 50 mL) and dried over sodium sulfate. The resulting clear solution was concentrated to yield yellowish oil (*) (96.32 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.79 (d, 2H, ^3J = 8.3 Hz), 7.45 (m, 6H, ^3J = 7.2 Hz), 7.27 (m, 11H), 4.15 (t, 2H, ^3J = 4.8 Hz), 3.62 (m, 28H), 3.23 (t, 2H, ^3J = 5.2 Hz), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.8 (*ipso*-C_{Ts}), 144.2 (*ipso*-C_{Ph}), 133.1 (*p*-C_{Ts}), 129.9 (*m*-C_{Ts}), 128.7 (*m*-C_{Ph}), 128.0 (*o*-C_{Ts}), 127.8 (*o*-C_{Ph}), 126.9 (*p*-C_{Ph}), 86.6 (CPh_3), 70.9-70.6 (C_{PEG}), 69.3 (CH_2CH_2OTs), 68.7 (CH_2CH_2OTs), 63.4 (CH_2OTrt), 21.7 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{42}H_{54}O_{11}SNa$ 789.3279; Found 789.3246.

3.5 Preparation of HO-PEG_8-OTs (**5**)

Compound **4** (94.56 g, not more than 0.1435 mol) was placed in a pressure reactor (500 mL) and dissolved in methanol (200 mL). 10% palladium on carbon powder (0.88 g) was added to the mixture, and then the reactor was sealed and charged with hydrogen gas (1.0 MPa). The mixture was stirred for 14 h at 50 °C. Then the reactor was recharged with hydrogen gas again (1.0 MPa) and the reaction was continued for 23 h at 50 °C. Then the reactor was cooled to rt, unsealed and the reaction mixture was filtered on a Kiriyama funnel. The solution was cooled to –20 °C, precipitated white crystals were filtered off and the filtrate was concentrated under reduced pressure. The residue was washed with hexane (10 × 100 mL) until triphenylmethane was removed completely (confirmed by TLC; no more UV absorption of the hexane solution). The solvent was removed, the residual yellowish oil was dissolved in ethyl acetate (120 mL) and washed with water (2 × 50 mL), brine (2 × 50 mL) and dried over sodium sulfate. Solvent was removed under reduced pressure to yield pure compound **5** as pale yellowish oil (54.03 g, 0.103 mol, 72% over 5 steps). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.80 (d, 2H, ^3J = 8.3 Hz), 7.35 (d, 2H, ^3J = 8.3 Hz), 4.16 (t, 2H, ^3J = 4.9 Hz), 3.65 (m, 30H), 2.62 (t, 1H, OH), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.9 (*ipso*-C_{Ts}), 133.0 (*p*-C_{Ts}), 129.9 (*m*-C_{Ts}), 128.1 (*o*-C_{Ts}), 72.6 (CH_2CH_2OH), 70.9-70.4 (C_{PEG}), 69.4 (CH_2CH_2OTs), 68.8 (CH_2CH_2OTs), 61.8 (CH_2OH), 21.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{40}O_{11}SNa$ 547.2184; Found 547.2167.

3.6 Preparation of TrtO-PEG_{12}-OH (**6**)

Sodium hydride (60% dispersion in paraffin oil, 1.85 g, 0.0463 mol) was placed in a 2-neck 300 mL flask under argon and washed with dry hexane (2 × 15 mL). Anhydrous THF (50 mL) was added carefully and the mixture was cooled to 0 °C on an ice bath. Tetra(ethylene glycol) (50 mL, 56 g, 0.288 mol), dried previously by azeotropic evaporation with toluene (2 × 15 mL), was added through a dropping funnel over 20 min. Then a solution of compound **4** (24.08 g, not more than 0.0359 mol,

dried just before use with toluene, 2 × 15 mL) in THF (25 mL) was added through the same dropping funnel over 15 min. Then the ice bath was removed, the flask was equipped with condenser and the mixture was stirred vigorously at 40 °C on oil bath for 4 days. After consumption of compound **4** (confirmed by TLC [silica, EtOAc; R_f = 0.5 (**4**)]) the mixture was cooled to rt, brine (100 mL) and water (ca. 20 mL, to make aqueous phase transparent) were added to the mixture. The organic layer was separated and the aqueous layer was extracted with diethyl ether (10 mL). Combined organic extracts were washed with brine (4 × 15 mL). The absence of tetra(ethylene glycol) was confirmed by TLC [silica, EtOAc; R_f = 0 (PEG_4)]. The solution was dried over sodium sulfate, activated charcoal powder was added and solids were filtered off. The filtrate was concentrated under reduced pressure to yield yellowish oil (*) (23.62 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46 (d, 6H), 7.26 (m, 9H), 3.63 (m, 46H), 3.23 (t, 2H), 3.08 (t, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 143.8 (*ipso*-C_{Ph}), 128.4 (*m*-C_{Ph}), 127.4 (*o*-C_{Ph}), 126.6 (*p*-C_{Ph}), 86.2 (CPh_3), 72.3 (CH_2CH_2OH), 70.5-70.0 (C_{PEG}), 63.0 (CH_2OTrt), 61.3 (CH_2OH). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{43}H_{64}O_{13}Na$ 811.4239; Found 811.4235.

3.7 Preparation of TrtO-PEG_{12}-OTs (**7**)

Compound **6** (23.62 g, not more than 0.0359 mol) was placed in a 1-neck 300 mL flask with a stir bar, dissolved in THF (50 mL) and cooled to 0 °C on ice bath. Aqueous solution (15 mL) of sodium hydroxide (5.0 g, 0.125 mol) was added to the THF solution. The mixture was stirred on an ice bath for 15 min, then a solution of *p*-toluenesulfonyl chloride (7.5 g, 0.0393 mol) in THF (15 mL) was added slowly through a dropping funnel over 15 min. The mixture was stirred for 1.5 h at 0 °C. After the consumption of compound **6** (confirmed by TLC [silica, 10% MeOH–EtOAc]), the ice bath was removed and the mixture was stirred at rt for 12 h. Hydrolysis of *p*-toluenesulfonyl chloride was confirmed by TLC [silica, 30% EtOAc–hexane; R_f = 0.7 (TsCl)]. Et_2O (15 mL) was added to the mixture and the organic layer was washed with brine (3 × 15 mL) and dried over sodium sulfate. The resulting solution was treated with powdered charcoal, filtered and concentrated to yield **7** as yellowish oil (*) (27.33 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.79 (d, 2H, ^3J = 8.4 Hz), 7.45 (m, 6H, ^3J = 7.2 Hz), 7.27 (m, 11H), 4.16 (t, 2H, 5.0 Hz), 3.62 (m, 44H), 3.24 (t, 2H, ^3J = 5.2 Hz), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.7 (*ipso*-C_{Ts}), 144.1 (*ipso*-C_{Ph}), 133.0 (*p*-C_{Ts}), 129.8 (*m*-C_{Ts}), 128.7 (*m*-C_{Ph}), 127.9 (*o*-C_{Ts}), 127.7 (*o*-C_{Ph}), 126.9 (*p*-C_{Ph}), 86.5 (CPh_3), 70.9-70.5 (C_{PEG}), 69.3 (CH_2CH_2OTs), 68.6 (CH_2CH_2OTs), 63.3 (CH_2OTrt), 21.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{50}H_{70}O_{15}SNa$ 965.4328; Found 965.4310.

3.8 Preparation of HO-PEG_{12}-OTs (**8**)

Compound **7** (27.33 g, not more than 0.0359 mol) was placed in a pressure reactor (500 mL) and dissolved in methanol (50 mL). 10% palladium on carbon powder (0.28 g) was added to the mixture and walls of the reactor were rinsed with methanol (10 mL). The reactor was sealed and charged with

hydrogen gas (1.4 MPa). The mixture was stirred for 15 h at 50 °C. Then the reactor was cooled to rt, unsealed and the reaction mixture was filtered on a Kiriyama funnel. The filtrate was cooled to –20 °C, the precipitated crystals were filtered off and the filtrate was washed with hexane (5 × 15 mL). The solvent was removed under reduced pressure and the residual oil was dissolved in ethyl acetate (50 mL), washed with brine (5 × 15 mL) and dried over sodium sulfate. Solvent was evaporated to yield pure compound **8** as pale yellowish oil (15.93 g, 0.0227 mol, 63% over 7 steps). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.80 (d, 2H, ^{3}J = 8.3 Hz), 7.34 (d, 2H, ^{3}J = 8.0 Hz), 4.16 (t, 2H, ^{3}J = 5.2 Hz), 3.66 (m, 46H), 2.73 (t, 1H, OH), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.8 (*ipso*-C_{Ts}), 133.1 (*p*-C_{Ts}), 129.9 (*m*-C_{Ts}), 128.0 (*o*-C_{Ts}), 72.6 (CH_2CH_2OH), 70.8-70.4 (C_{PEG}), 69.3 (CH_2CH_2OTs), 68.7 (CH_2CH_2OTs), 61.7 (CH_2OH), 21.7 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{56}O_{15}SNa$ 723.3232; Found 723.3213; $[M+2Na]^{2+}$ Calcd for $C_{31}H_{56}O_{15}SNa_2$ 373.1562; Found 373.1551.

3.9 Preparation of TrtO-PEG_{16}-OH (**9**)

Sodium hydride (60% dispersion in paraffin oil, 1.85 g, 0.0463 mol) was placed in a 2-neck 300 mL flask under argon and washed with dry hexane (2 × 20 mL). Anhydrous THF (50 mL) was added carefully and the mixture was cooled to 0 °C on an ice bath. Tetra(ethylene glycol) (50 mL, 56 g, 0.288 mol), dried previously by azeotropic evaporation with toluene (2 × 15 mL), was added to the mixture through a dropping funnel over 15 min. Then a solution of compound **7** (27.99 g, not more than 0.0359 mol, dried just before use with toluene, 2 x 15 mL) in THF (25 mL) was added through the same dropping funnel over 10 min. Then the ice bath was removed, the flask was equipped with a condenser and the mixture was stirred vigorously at 40 °C on an oil bath for 4 days. After the consumption of compound **7** (confirmed by TLC [silica, 10% MeOH–EtOAc]) the mixture was cooled to rt, brine (100 mL), water (ca. 20 mL, to make the aqueous phase transparent) and ethyl acetate (15 mL) were added. The organic layer was separated and washed with brine (6 × 15 mL). The absence of tetra(ethylene glycol) was confirmed by TLC [silica, EtOAc-MeOH 9:1; R_f = 0 (PEG_4)]. The solution was dried over sodium sulfate; activated charcoal powder (ca. 0.1 g) was added and filtered off. The filtrate was concentrated under reduced pressure to yield **9** as yellow oil (*) (27.76 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46 (d, 6H, ^{3}J = 7.2 Hz), 7.28 (m, 6H), 7.22 (m, 3H), 3.63 (m, 62H), 3.23 (t, 2H, ^{3}J = 5.2 Hz), 2.73 (t, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.1 (*ipso*-C_{Ph}), 128.7 (*m*-C_{Ph}), 127.7 (*o*-C_{Ph}), 126.9 (*p*-C_{Ph}), 86.5 (CPh_3), 72.5 (CH_2CH_2OH), 70.8-70.3 (C_{PEG}), 63.3 (CH_2OTrt), 61.7 (CH_2OH). HRMS (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{51}H_{80}O_{17}K$ 1003.5027; Found 1003.5024.

3.10 Preparation of TrtO-PEG_{16}-OTs (**10**)

Compound **9** (27.76 g, not more than 0.0359 mol) was placed in a 1-neck 500 mL flask with a stir bar, dissolved in THF (50 mL) and cooled to 0 °C on ice bath. Aqueous solution (15 mL) of sodium

hydroxide (5.0 g, 0.125 mol) was added to the THF solution. The mixture was stirred on an ice bath for 15 min, then a solution of *p*-toluenesulfonyl chloride (7.5 g, 0.0393 mol) in THF (15 mL) was added slowly through a dropping funnel over 15 min. The mixture was stirred for 1.5 h at 0 °C. After the consumption of compound **9** (confirmed by TLC [silica, 10% MeOH–EtOAc]), the ice bath was removed and the mixture was stirred at rt for 12 h. Hydrolysis of *p*-toluenesulfonyl chloride was confirmed by TLC [silica, 30% EtOAc–hexane; R_f = 0.7 (TsCl)]. Et_2O (25 mL) and water (ca. 10 mL, to make the aqueous phase transparent) was added and the organic layer was washed with brine (3 × 15 mL) and dried over sodium sulfate. The resulting solution was treated with powdered charcoal, filtered and concentrated to yield **10** as yellow oil (*) (31.77 g). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.79 (d, 2H, ^3J = 8.3 Hz), 7.46 (m, 6H, ^3J = 7.2 Hz), 7.27 (m, 11H), 4.14 (t, 2H, ^3J = 4.8 Hz), 3.62 (m, 60H), 3.23 (t, 2H, ^3J = 5.2 Hz), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.7 (*ipso*-C_{Ts}), 144.0 (*ipso*-C_{Ph}), 133.0 (*p*-C_{Ts}), 129.7 (*m*-C_{Ts}), 128.6 (*m*-C_{Ph}), 127.9 (*o*-C_{Ts}), 127.7 (*o*-C_{Ph}), 126.8 (*p*-C_{Ph}), 86.4 (CPh_3), 70.8-70.4 (C_{PEG}), 69.2 (CH_2CH_2OTs), 68.6 (CH_2CH_2OTs), 63.3 (CH_2OTrt), 21.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{58}H_{86}O_{19}SNa$ 1141.5376; Found 1141.5353.

3.11 Preparation of HO-PEG_{16}-OTs (**11**)

Compound **10** (31.77 g, not more than 0.0359 mol) was placed in a pressure reactor (500 mL) and dissolved in methanol (65 mL). 10% palladium on carbon powder (0.31 g) was added to the mixture and walls of the reactor were rinsed with methanol (10 mL). The reactor was sealed and charged with hydrogen gas (1.4 MPa). The mixture was stirred for 18 h at 50 °C. Then the reactor was cooled to rt, unsealed and the reaction mixture was filtered through Celite pad on Kiriyama funnel. The filtrate volume was reduced under reduced pressure by ca. 1/3, cooled to –20 °C, the precipitated crystals were filtered off and the solvent was removed under reduced pressure. The residue was washed with hexane (8 × 30 mL) until all triphenylmethane was removed. The residue was dissolved in ethyl acetate (300 mL), washed with brine-water (130 mL brine + 20 mL water), brine (8 × 50 mL) and dried over sodium sulfate. Solvent was evaporated to yield compound **11** as pale yellowish oil crystallizing upon standing (19.55 g, 0.0223 mol, 62% over 9 steps). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.79 (d, 2H, ^3J = 8.4 Hz), 7.35 (d, 2H, ^3J = 8.4 Hz), 4.16 (t, 2H, ^3J = 5.0 Hz), 3.66 (m, 62H), 2.80 (t, 1H, OH), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.5 (*ipso*-C_{Ts}), 132.8 (*p*-C_{Ts}), 129.6 (*m*-C_{Ts}), 127.6 (*o*-C_{Ts}), 72.3 (CH_2CH_2OH), 70.4-70.0 (C_{PEG}), 69.0 (CH_2CH_2OTs), 68.3 (CH_2CH_2OTs), 61.3 (CH_2OH), 21.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{39}H_{72}O_{19}SNa$ 899.4281; Found 899.4259; $[M+2Na]^{2+}$ Calcd for $C_{39}H_{72}O_{19}SNa_2$ 461.2086; Found 461.2079.

3.12 Preparation of TsO-PEG_8-OCH_2CH_2COOt-Bu (**12**)

Compound **5** (2.182 g, 4.159 mmol) was dried by co-evaporation with toluene, dissolved in dry toluene (15 mL) and the mixture was cooled to 0 °C on an ice bath. *Tert*-butyl acrylate (1 mL, 0.875 g, 6.83 mmol) and powdered potassium hydroxide (40 mg, 0.71 mmol) were added under argon

atmosphere and the mixture was stirred at 0 °C for 3 h. Then it was diluted with ethyl acetate (15 mL), the organic layer was washed with water and brine and passed through 1 cm thick silica layer on Kiriyama funnel. The filtrate was concentrated under reduced pressure to give compound **12** as colorless oil (2.373 g, 3.635 mmol, 87%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.80 (d, 2H, ^{3}J = 8.4 Hz), 7.34 (d, 2H, ^{3}J = 8.0 Hz), 4.16 (t, 2H, ^{3}J = 4.8 Hz, $SOCH_2$), 3.72-3.58 (m, 34H, PEG CH_2), 2.50 (t, 2H, ^{3}J = 6.6 Hz, $COCH_2$), 2.45 (s, 3H, $ArCH_3$), 1.45 (s, 9H, CCH_3). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 170.9 (CO), 144.8 (CS), 133.1 (*C*CH_3), 129.9, 128.0, 80.5 (*C*$(CH_3)_3$), 70.6, 69.3, 68.7, 66.9, 36.3 (*C*CO), 28.1 (C(*C*$H_3)_3$), 21.7 (C*C*H_3). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{52}O_{13}SNa$ 675.3021; Found 675.3021.

3.13 Preparation of TsO-PEG_8-OCH_2CH_2CHO (**13**)

Compound **12** (187.8 mg, 0.288 mmol) was dried by co-evaporation with toluene, dissolved in dry toluene under argon atmosphere and the mixture was cooled to –78 °C. Diisobutylaluminum hydride (1 M solution in toluene, 380 μL, 0.380 mmol) was added slowly to the solution and the mixture was stirred for 1 h. The reaction was quenched carefully with water (10 μL). The mixture was warmed to 0 °C, 15% aqueous NaOH solution (10 μL) was added and then the mixture was slowly warmed to rt. More water (40 μL) was added and after stirring for 15 min the mixture was dried over anhydrous magnesium sulfate. The solution was concentrated under reduced pressure and the residue was purified by column chromatography on silica (MeOH-CH_2Cl_2, 3:97) to give compound **13** (partially in a form of methanol hemiacetal) as colorless oil (87.2 mg, 0.150 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 9.78 (s, 1H, CHO), 7.80 (d, 2H, ^{3}J = 8.4 Hz), 7.36 (d, 2H, ^{3}J = 8.4 Hz), 4.16 (t, 2H, ^{3}J = 4.8 Hz), 3.82 (t, 2H, ^{3}J = 6.4 Hz), 3.70-3.54 (m, 32H), 2.68 (t, 2H, ^{3}J = 6.0 Hz, C*H*$_2$CHO), 2.45 (s, 3H). MeOH-hemiacetal unique peaks: 4.68 (1H, m, C*H*(OH)OCH_3), 3.58 (3H, s, CH(OH)OC*H*$_3$), 1.99 (1H, m, diastereotopic C*H*$_2$CH(OH)), 1.80 (1H, m, diastereotopic C*H*$_2$CH(OH)). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 201.2 (CHO), 144.8, 133.1, 129.9, 128.0, 70.6, 69.3, 68.7, 64.9, 43.9 (*C*H_2CHO), 21.7. MeOH-hemiacetal unique peaks: 97.3 (*C*H(OH)OCH_3), 67.2, 54.6 (OCH_3), 35.8. HRMS (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{26}H_{44}O_{12}SK$ 619.2185; Found 619.2173. Hemiacetal form: Calcd for $C_{27}H_{48}O_{13}SK$ 651.2447; Found 651.2448.

3.14 Preparation of TsO-PEG_8-OCH_2CH_2COOH (**14**)

Compound **12** (122.6 mg, 0.188 mmol) was dissolved in a mixture of dichloromethane (1 mL) and trifluoroacetic acid (0.5 mL). The solution was stirred for 1 h at rt. The volatiles were removed under reduced pressure to yield **14** as colorless oil quantitatively. Traces of the remaining trifluoroacetic acid were removed by passing through a thin layer of silica. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.80 (d, 2H, ^{3}J = 8.4 Hz), 7.35 (d, 2H, ^{3}J = 8.4 Hz), 4.16 (t, 2H, ^{3}J = 4.8 Hz), 3.78-3.58 (m, 2H), 2.62 (t, 2H, ^{3}J = 6.2 Hz, CH_2CO), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 175.3, 144.9,

133.0, 129.9, 128.0, 70.4, 69.3, 68.7, 66.4, 34.8 (CH_2CO), 21.6. HRMS (ESI-TOF) m/z: $[M-H]^-$ Calcd for $C_{26}H_{43}O_{13}S$ 595.2430; Found 595.2419.

3.15 Preparation of TsO-PEG$_8$-OCH$_2$CH$_2$SO$_2$CHCH$_2$ (**15**)

Compound **5** (127 mg, 0.242 mmol) was dissolved in dry THF (3 mL) under argon atmosphere. Divinyl sulfone (200 µL, 235 mg, 1.99 mmol) was added to the mixture, followed by powdered potassium *tert*-butoxide (25 mg, 0.223 mmol). The mixture was stirred at rt for 15 min, filtered, and the precipitate was washed with dichloromethane. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica (MeOH-CH_2Cl_2, 4:96) to give product **15** as colorless oil (84.0 mg, 0.131 mmol, 54%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.80 (d, 2H, ^3J = 8.4 Hz), 7.35 (d, 2H, ^3J = 8.4 Hz), 6.83 (dd, 1H, ^3J = 9.9, 16.6 Hz), 6.38 (d, 1H, ^3J = 16.6 Hz, CH_2 *E*), 6.09 (d, 1H, ^3J = 9.9 Hz, CH_2 *Z*), 4.16 (t, 2H, ^3J = 4.8 Hz), 3.90 (t, 2H, ^3J = 5.6 Hz, C*H*$_2$CH$_2$SO$_2$), 3.70-3.58 (m, 30H), 3.26 (t, 2H, ^3J = 5.6 Hz, CH_2SO_2), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 144.9, 138.1 (CH), 133.1, 129.9, 128.7 (*C*H$_2$CH), 128.0, 70.6, 69.4, 68.7, 64.7, 55.1 (CH_2SO_2), 21.7. HRMS (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{27}H_{46}O_{13}S_2K$ 681.2011; Found 681.2009.

3.16 Preparation of HO-PEG$_8$-N$_3$ (**16**)

Compound **5** (887 mg, 1.69 mmol) and sodium azide (200 mg, 3.08 mmol) were dissolved in acetonitrile (15 mL) under argon atmosphere. The mixture was stirred at 80 °C for 24 h, cooled to rt and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica (MeOH-CH_2Cl_2, 4:96) to give product **16** as colorless oil (643 mg, 1.63 mmol, 96%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 3.75-3.60 (m, 30H), 3.39 (t, 2H, ^3J = 5.0 Hz, CH_2N_3), 2.78 (t, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 72.6, 70.7, 70.4, 70.1, 61.7, 50.7 (CH_2N_3). HRMS (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{16}H_{33}O_8N_3K$ 434.1899; Found 434.1931.

3.17 Preparation of HO-PEG$_8$-NH$_2$ (**17**)

To a solution of compound **16** (145 mg, 0.367 mmol) in methanol (2 mL) 10% palladium carbon (5 mg) was added and the mixture was stirred under hydrogen atmosphere (1 bar) overnight. Then it was filtered through Celite ands concentrated under reduced pressure to give product **17** as pale yellowish oil (128 mg, 0.346 mmol, 95%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 5.17, 3.75-3.60 (m, 32H), 3.07. ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 72.3, 70.1, 69.1, 60.8, 40.4 (CH_2NH_2). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{36}O_8N$ 370.2435; Found 370.2459.

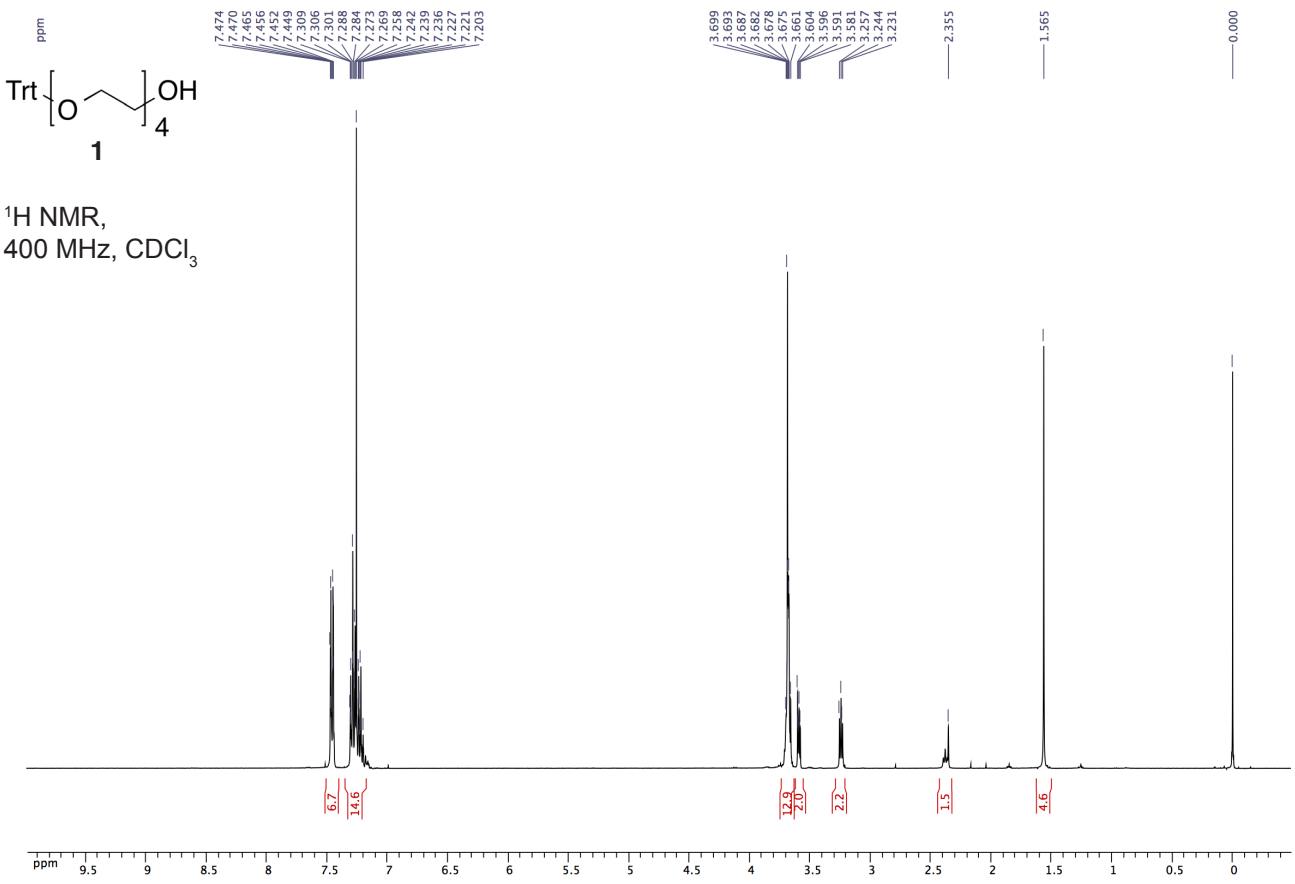
3.18 Preparation of HO-PEG$_8$-SH (**18**)

To a solution of compound **5** (186 mg, 0.355 mmol) in dry DMF (1 mL) potassium thioacetate (54 mg, 0.473 mmol) was added under argon atmosphere. The mixture was stirred at rt overnight, diluted

with *tert*-butyl methyl ether (5 mL) and filtered. The filtrate was concentrated under reduced pressure to give yellow oil. The oil was dissolved in dry methanol (2 mL) under argon atmosphere, potassium carbonate (123 mg, 0.89 mmol) was added to the solution and the mixture was stirred at rt for 2 h. Then it was diluted with *tert*-butyl methyl ether (5 mL), acidified with 3 drops of concentrated hydrochloric acid and dried over anhydrous sodium sulfate. Subsequent filtration and concentration under reduced pressure afforded yellowish oil containing impure **18** (114 mg, 0.295 mmol, 82%), partially oxidized to the corresponding disulfide. The pure thiol **18** was obtained after purification using column chromatography on silica (MeOH-CH_2Cl_2, 5:95) (83 mg, 0.215 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 3.73-3.60 (m, 30H), 2.69 (td, ^3J = 6.5, 8.3 Hz), 1.61 (t, ^3J = 8.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 72.9, 72.6, 70.5, 61.7, 24.3 (CH_2SH). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{34}O_8SNa$ 409.1867; Found 409.1874.

4. ^{1}H and ^{13}C NMR spectra

Every page contains two spectra of a single compound: ^{1}H on the top, and ^{13}C on the bottom. Because crude products **1**-**4**, **6**, **7**, **9** and **10** contain symmetric PEG-type impurities, the peak integration does not always match the expected value. The impurities are visible at ESI-MS spectra.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OH
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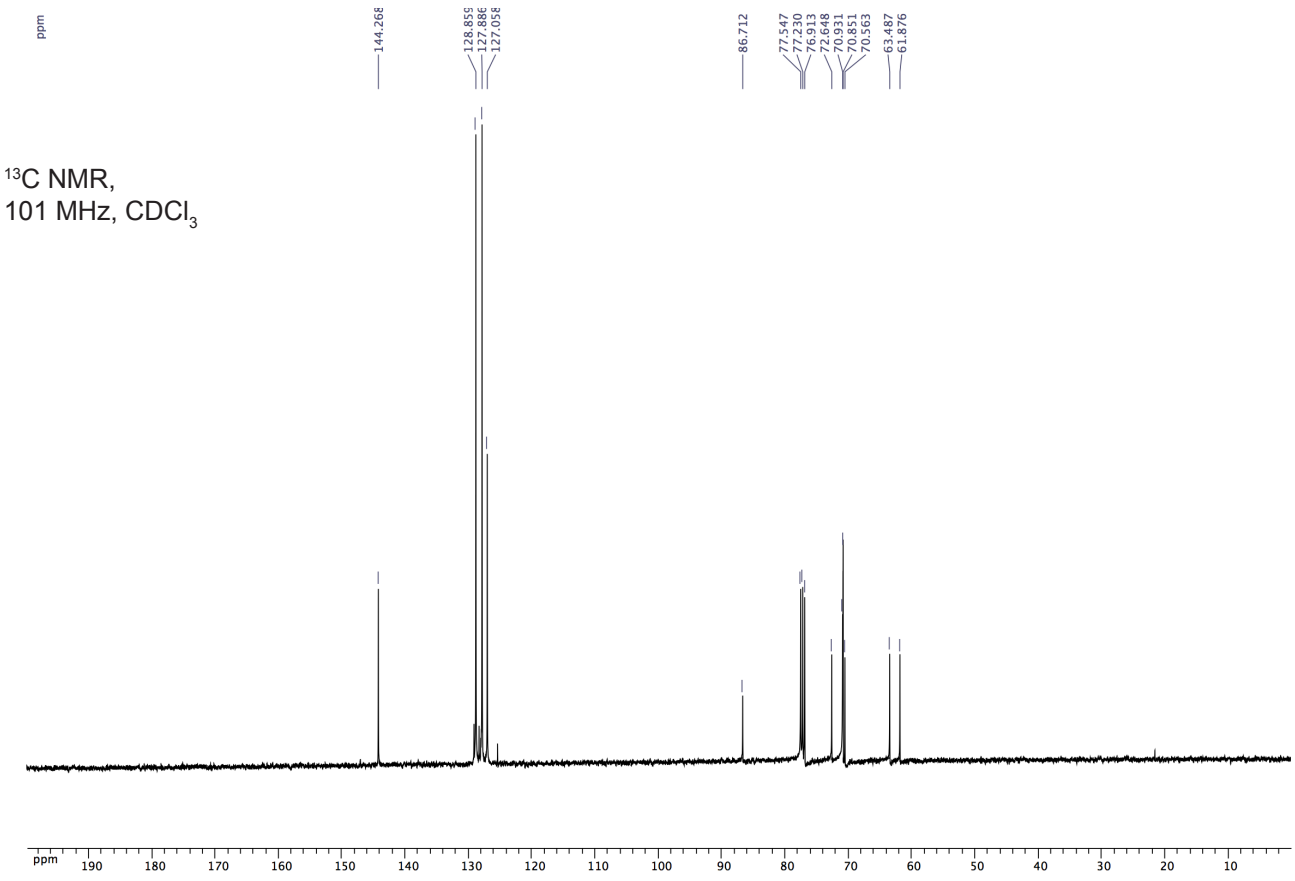
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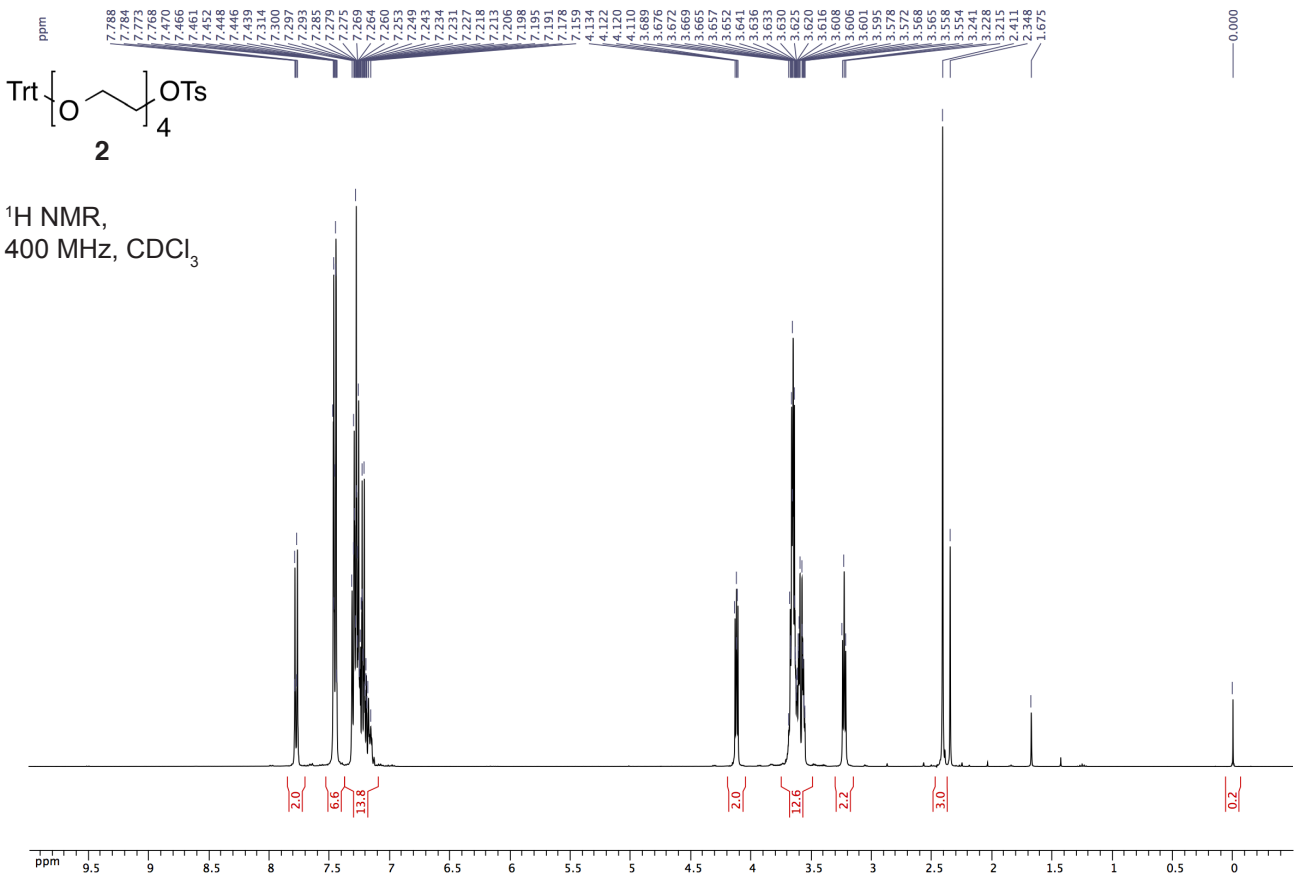
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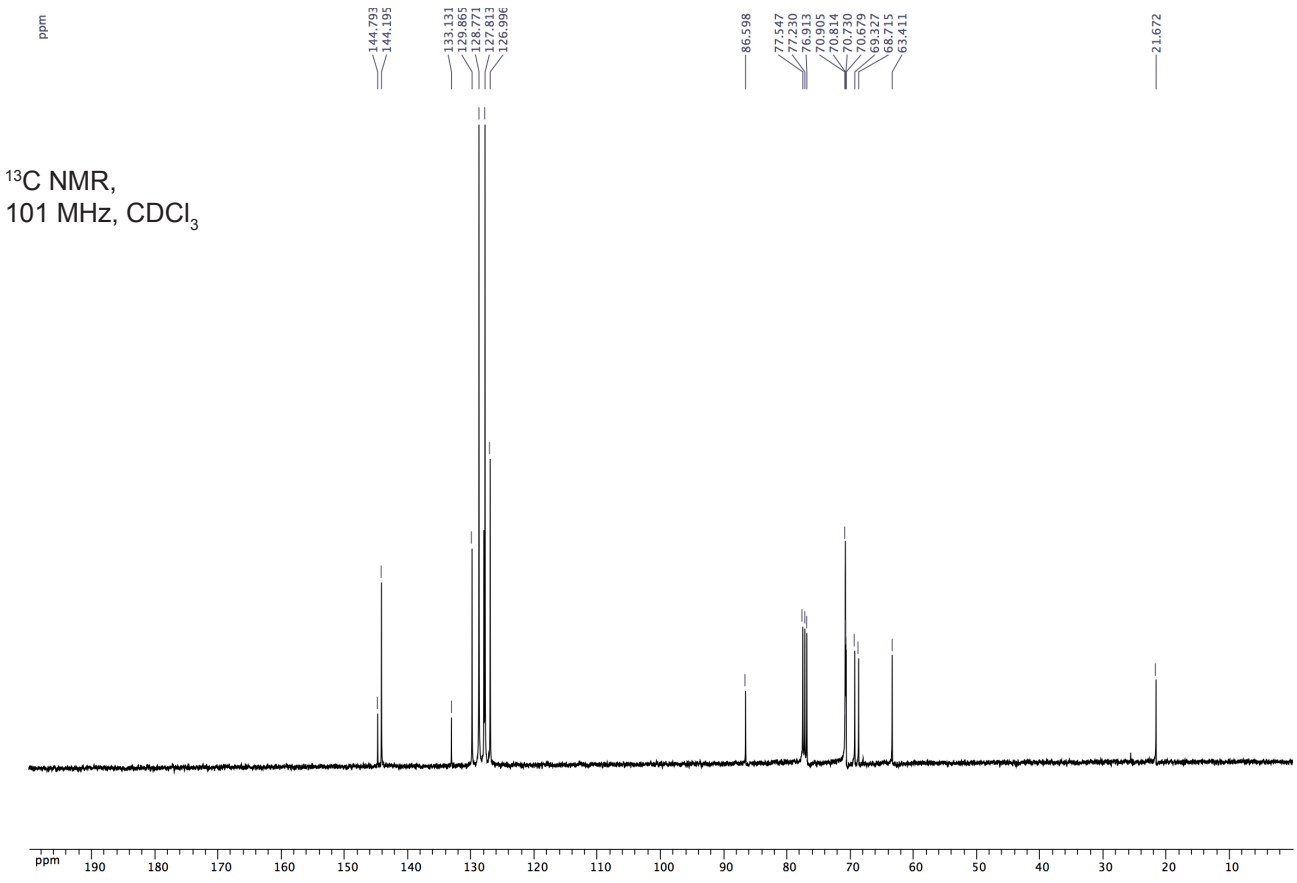
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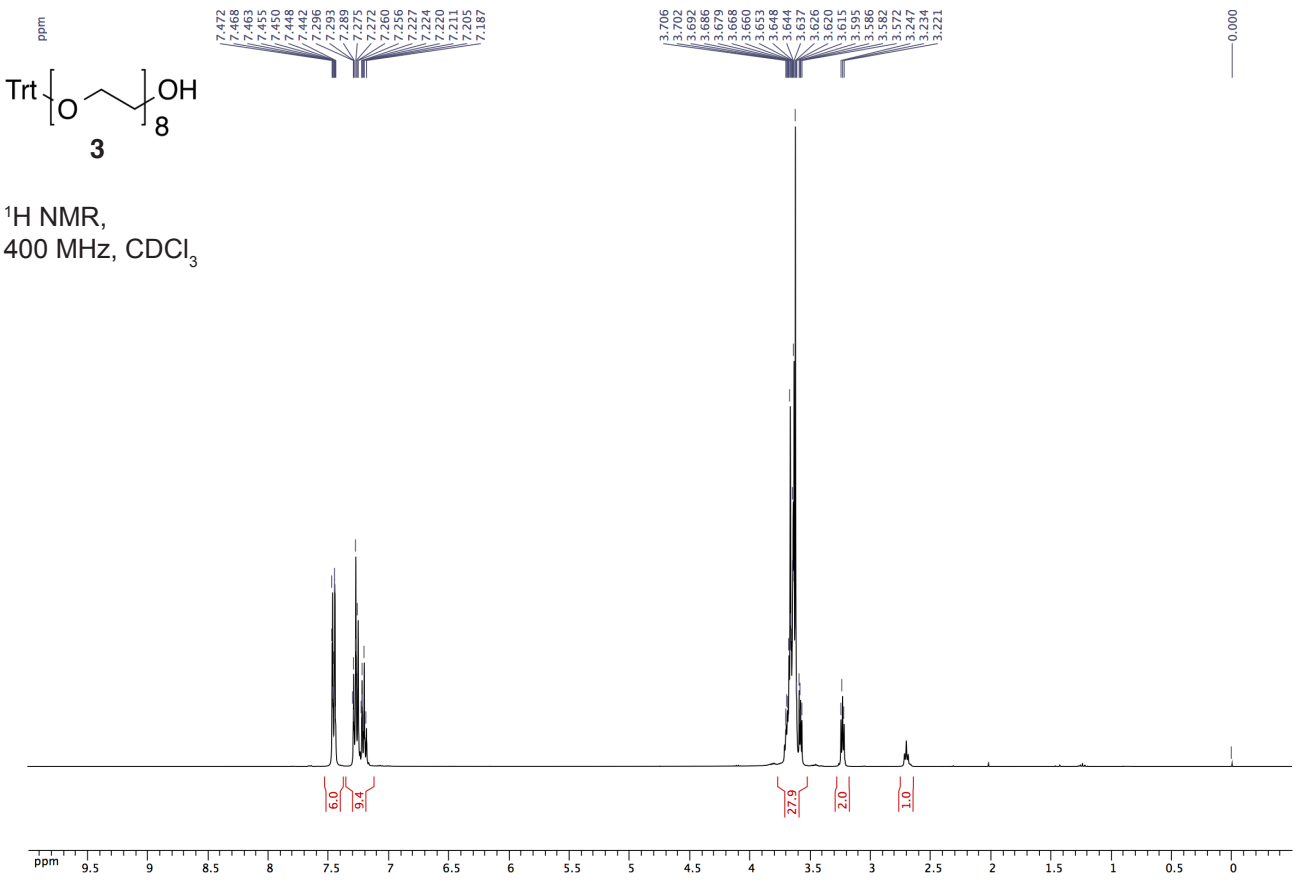

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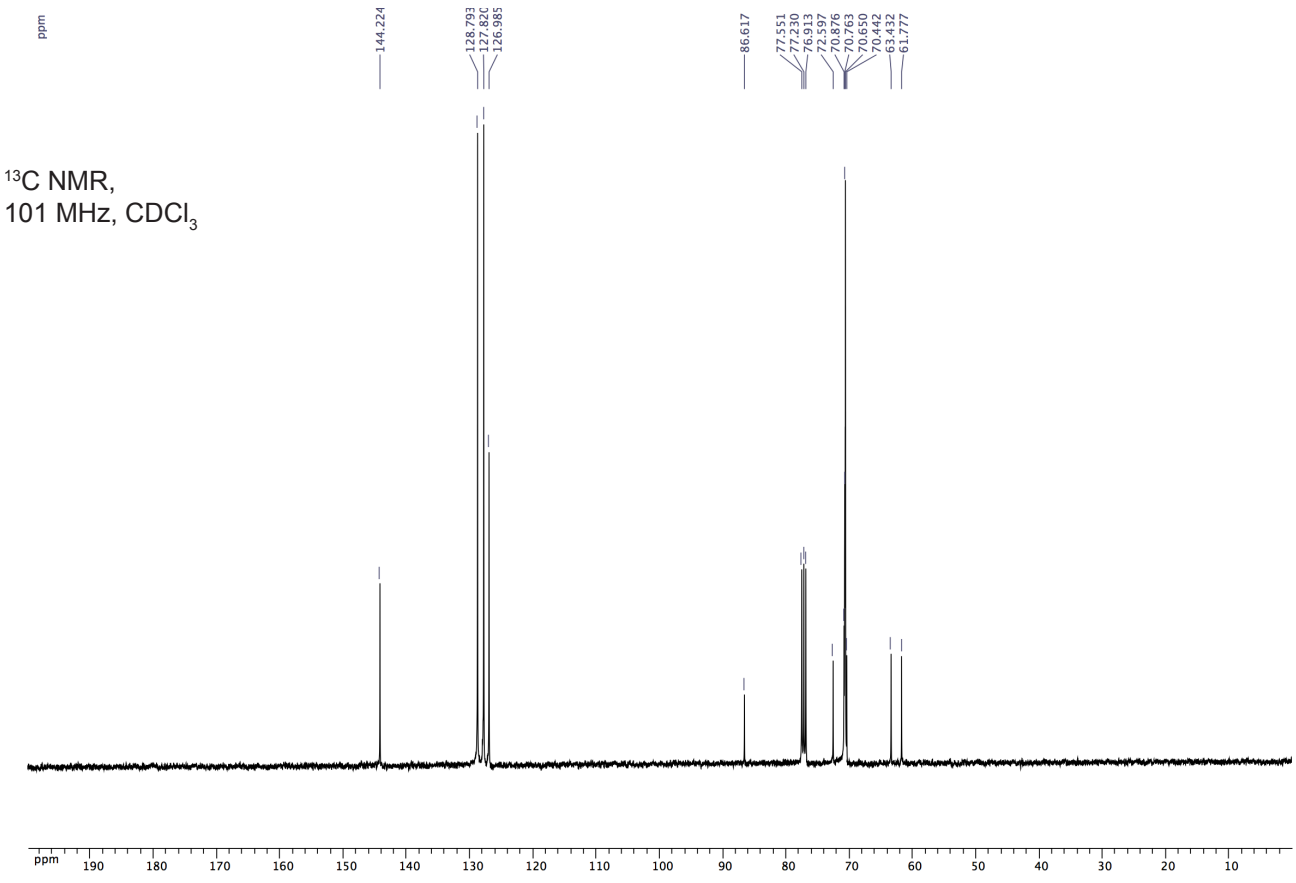

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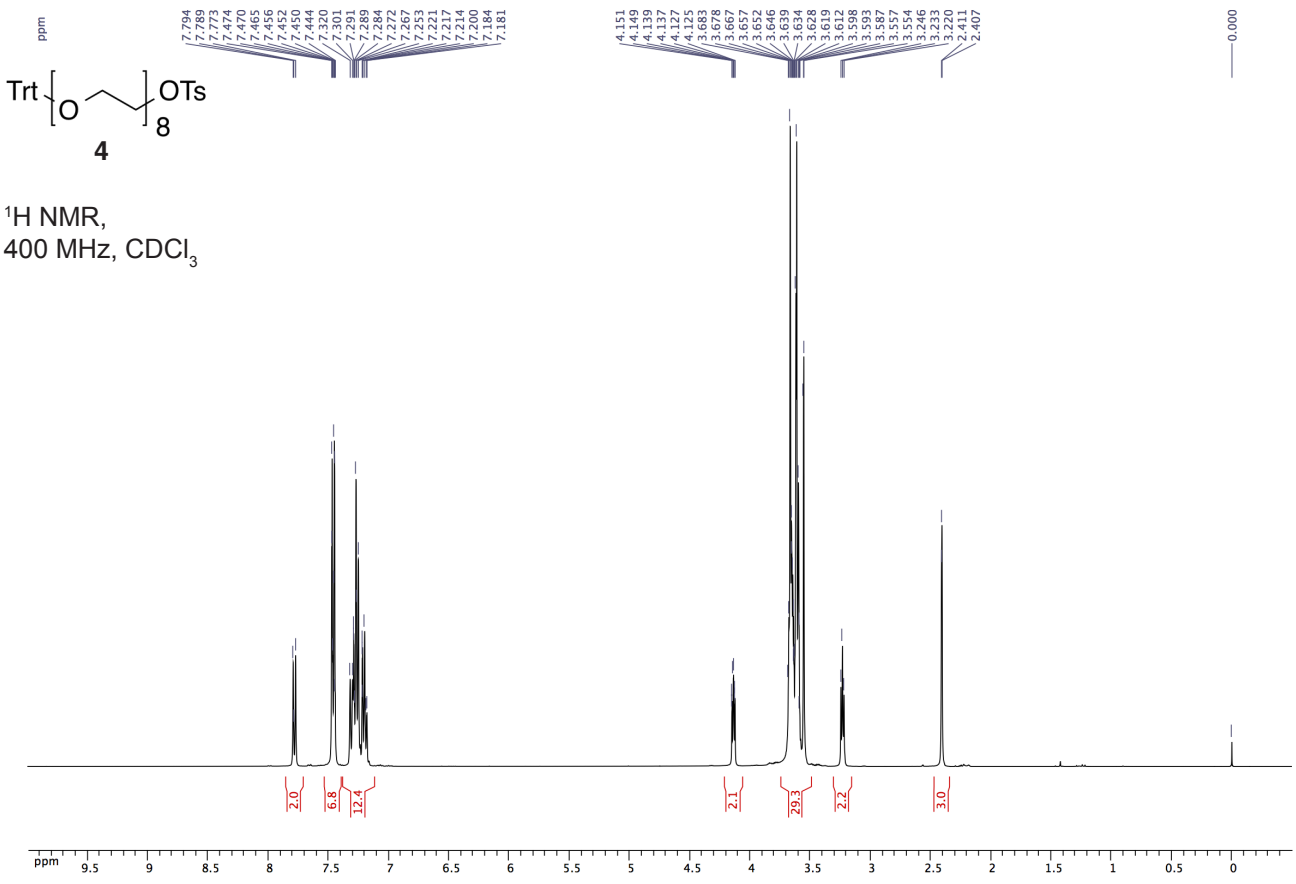

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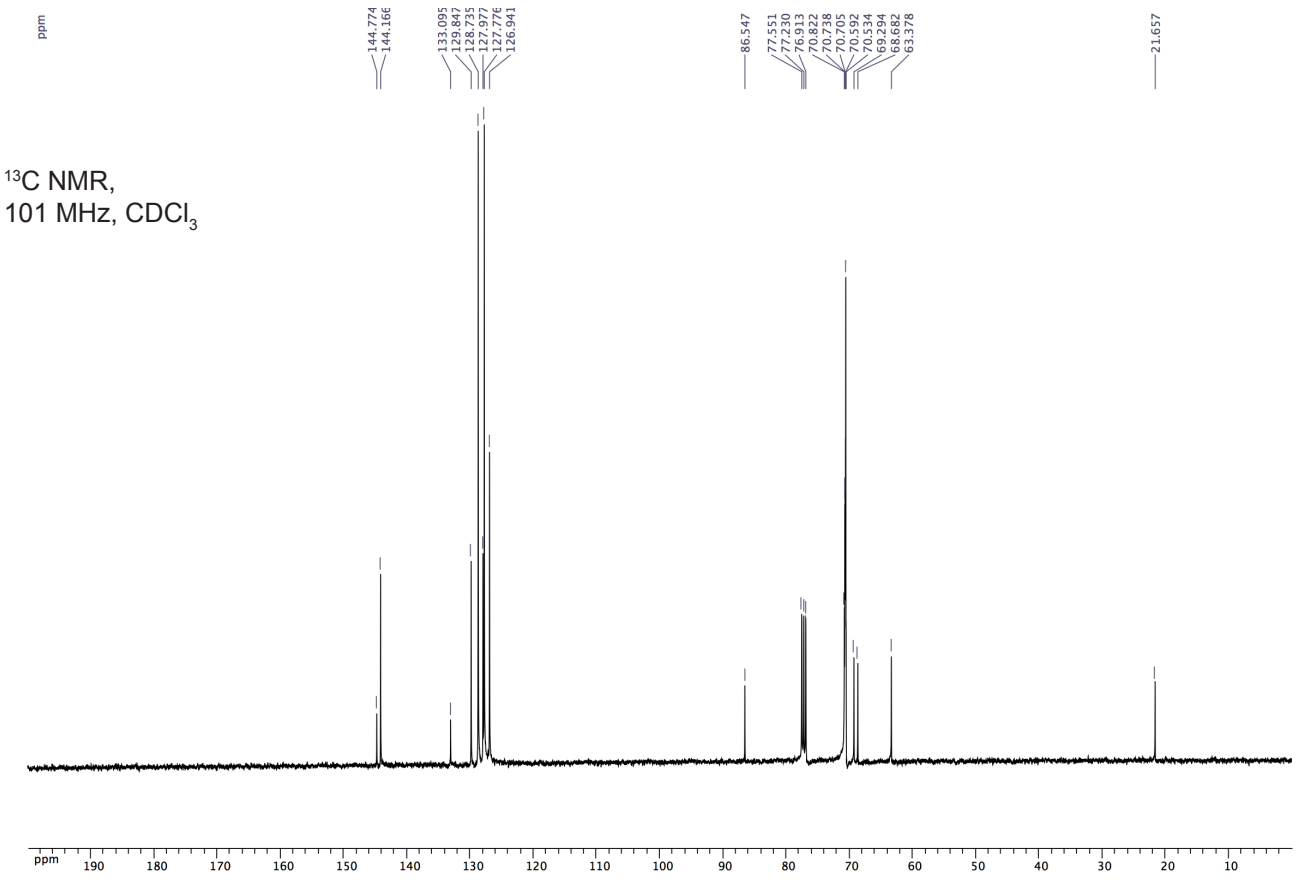

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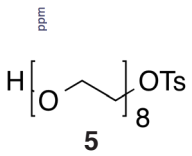

5

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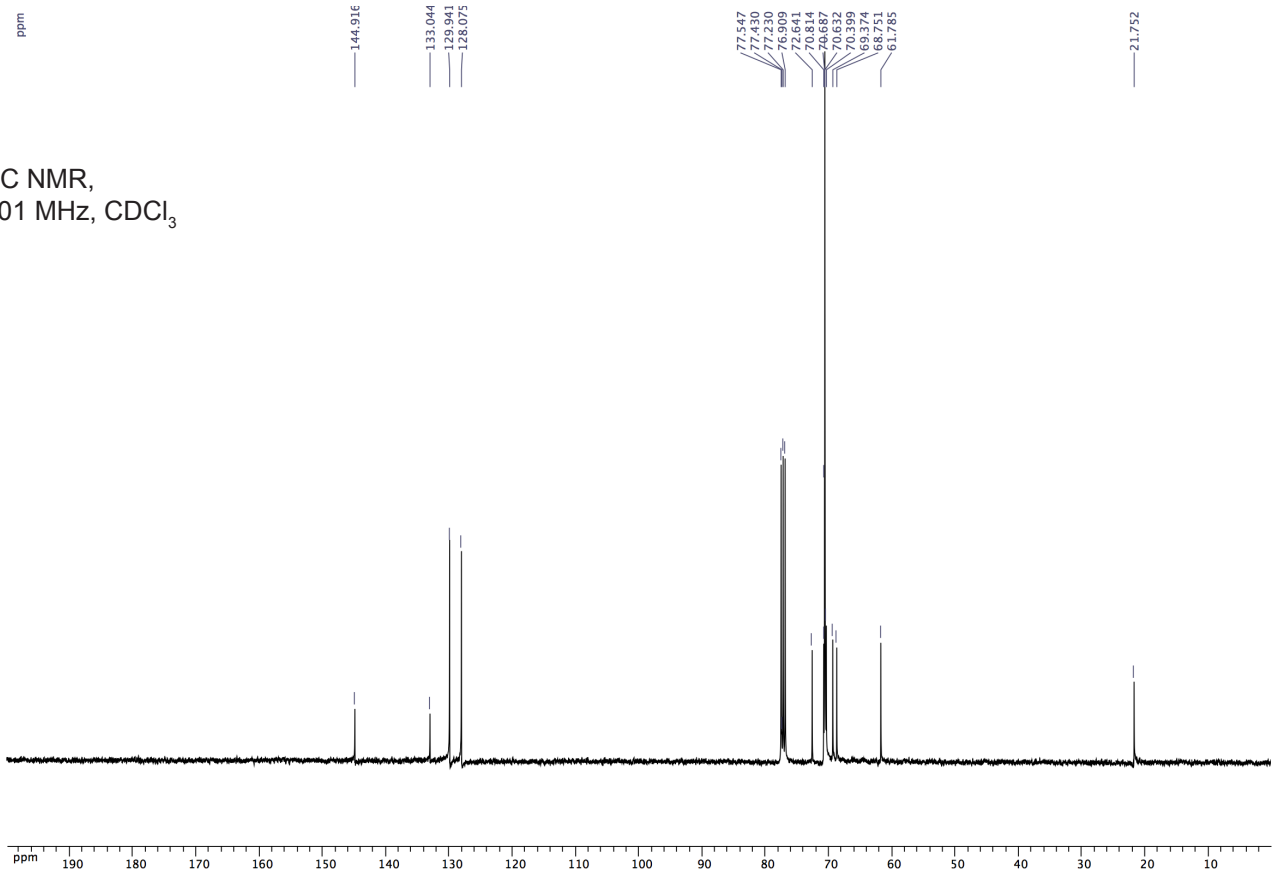
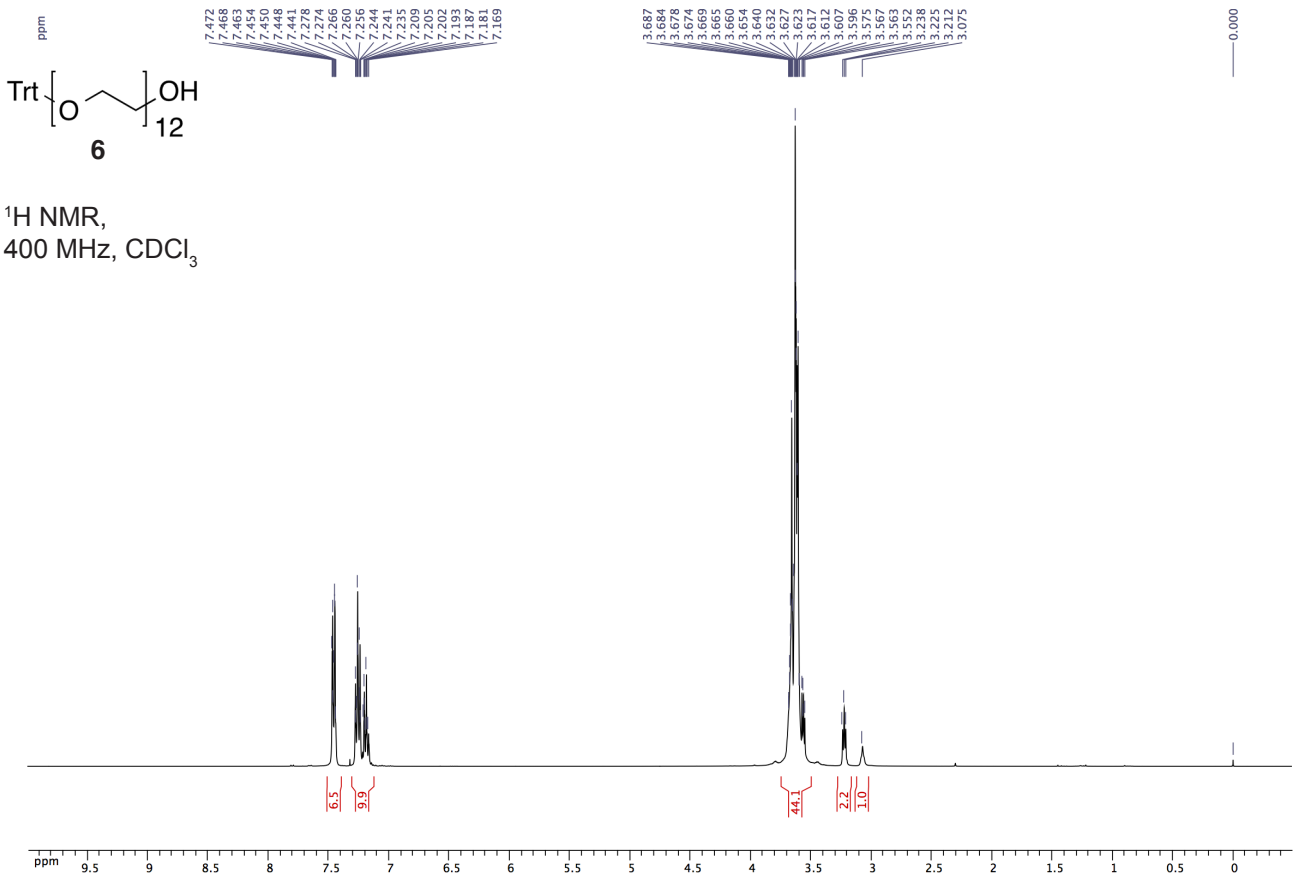
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$





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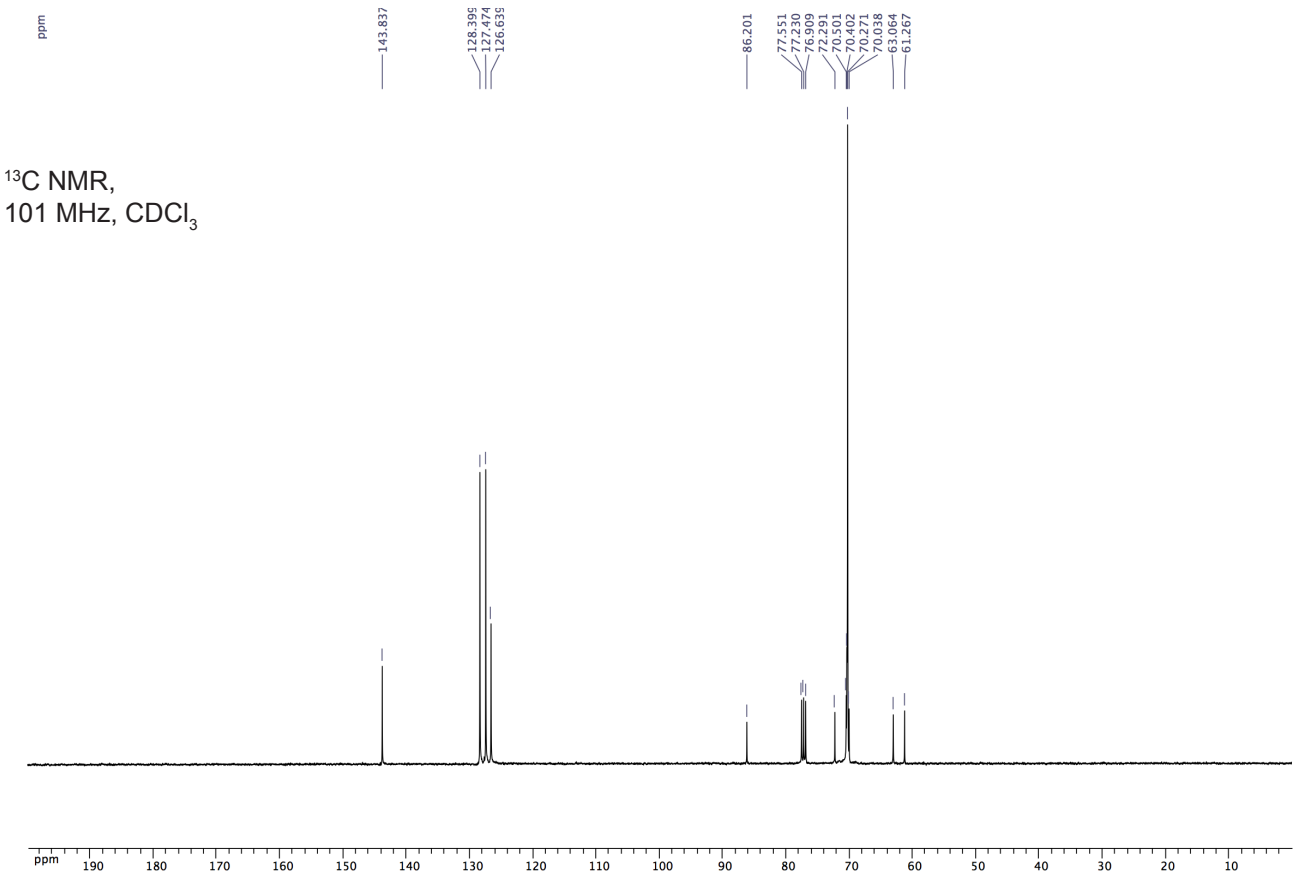
400 MHz, $CDCl_3$



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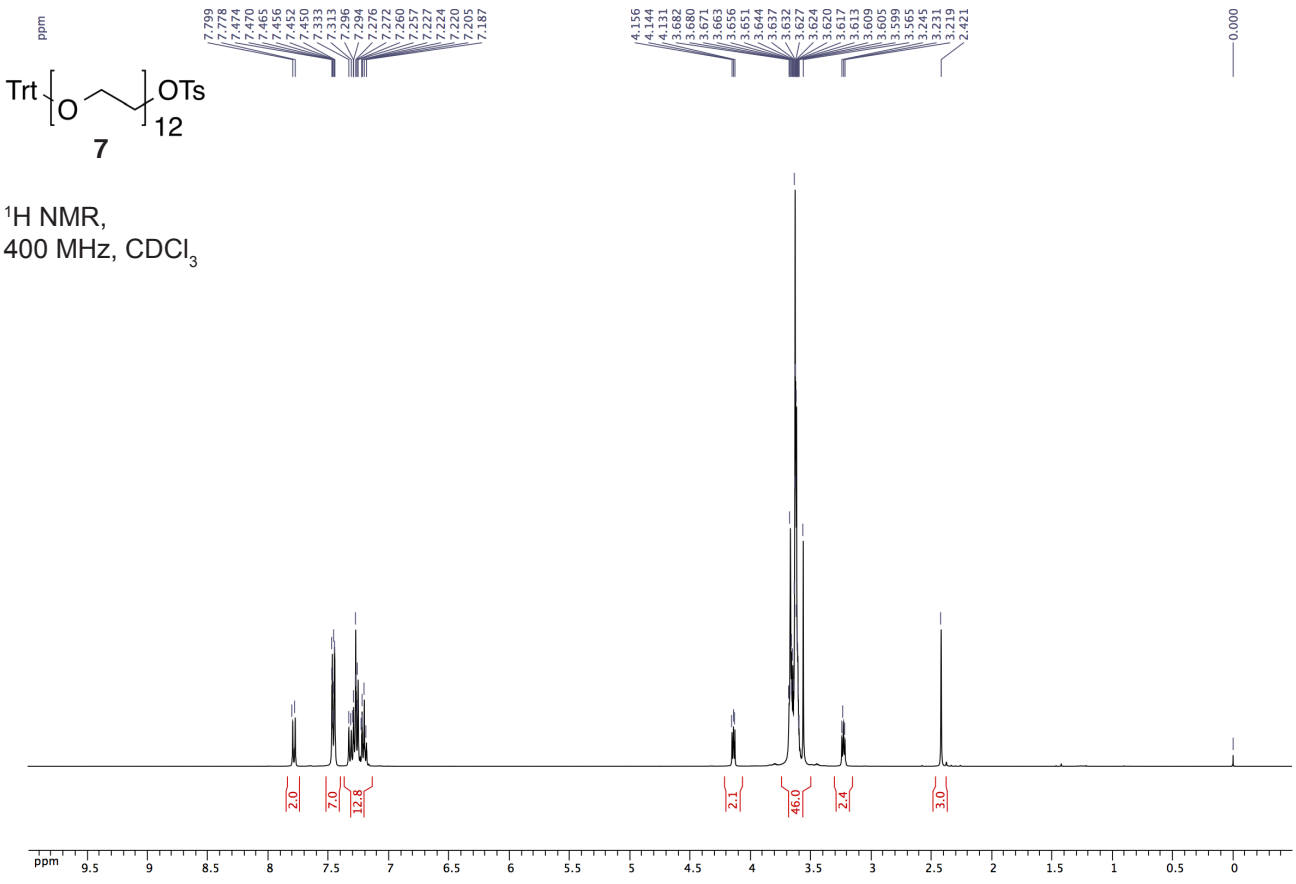
101 MHz, $CDCl_3$



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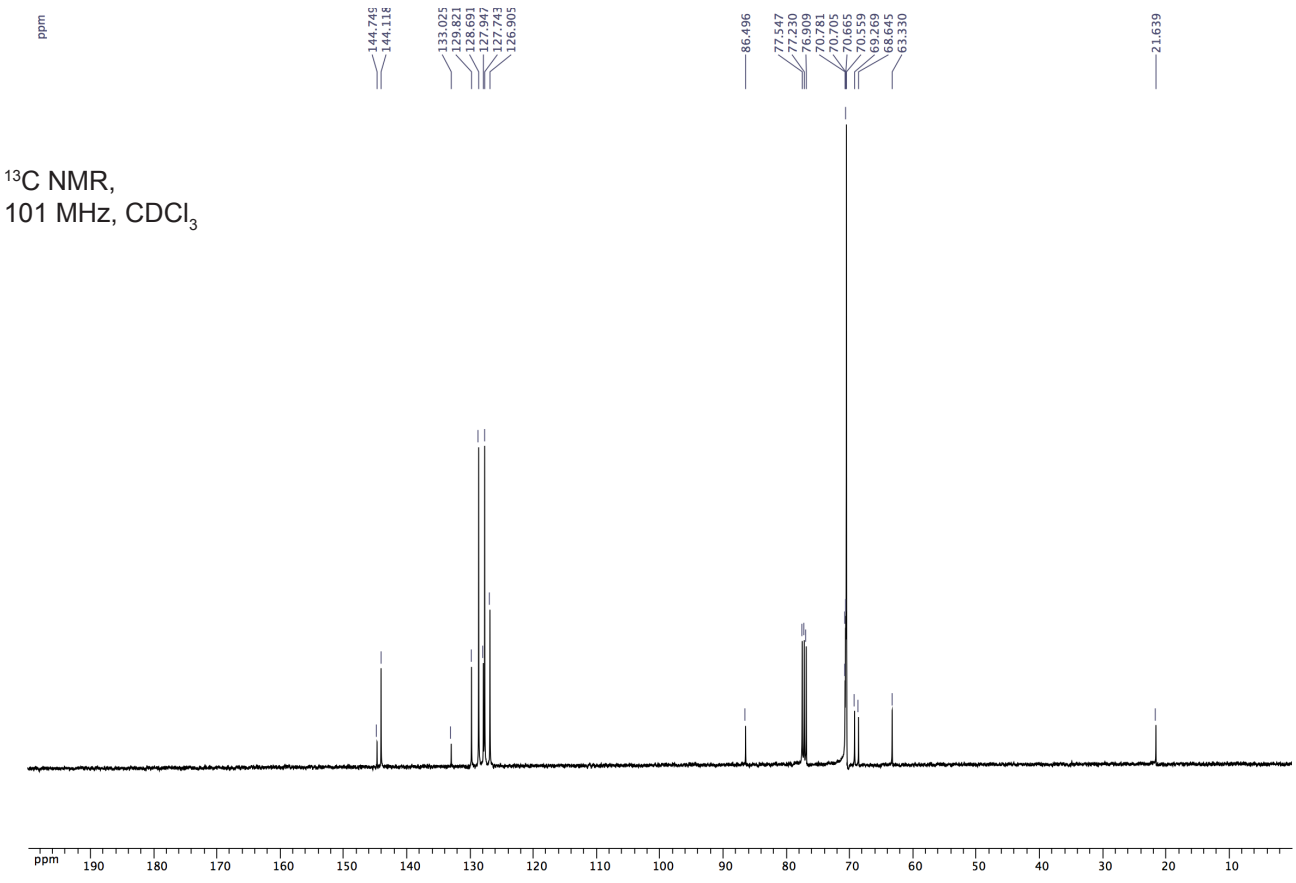
400 MHz, $CDCl_3$



^{13}C NMR,
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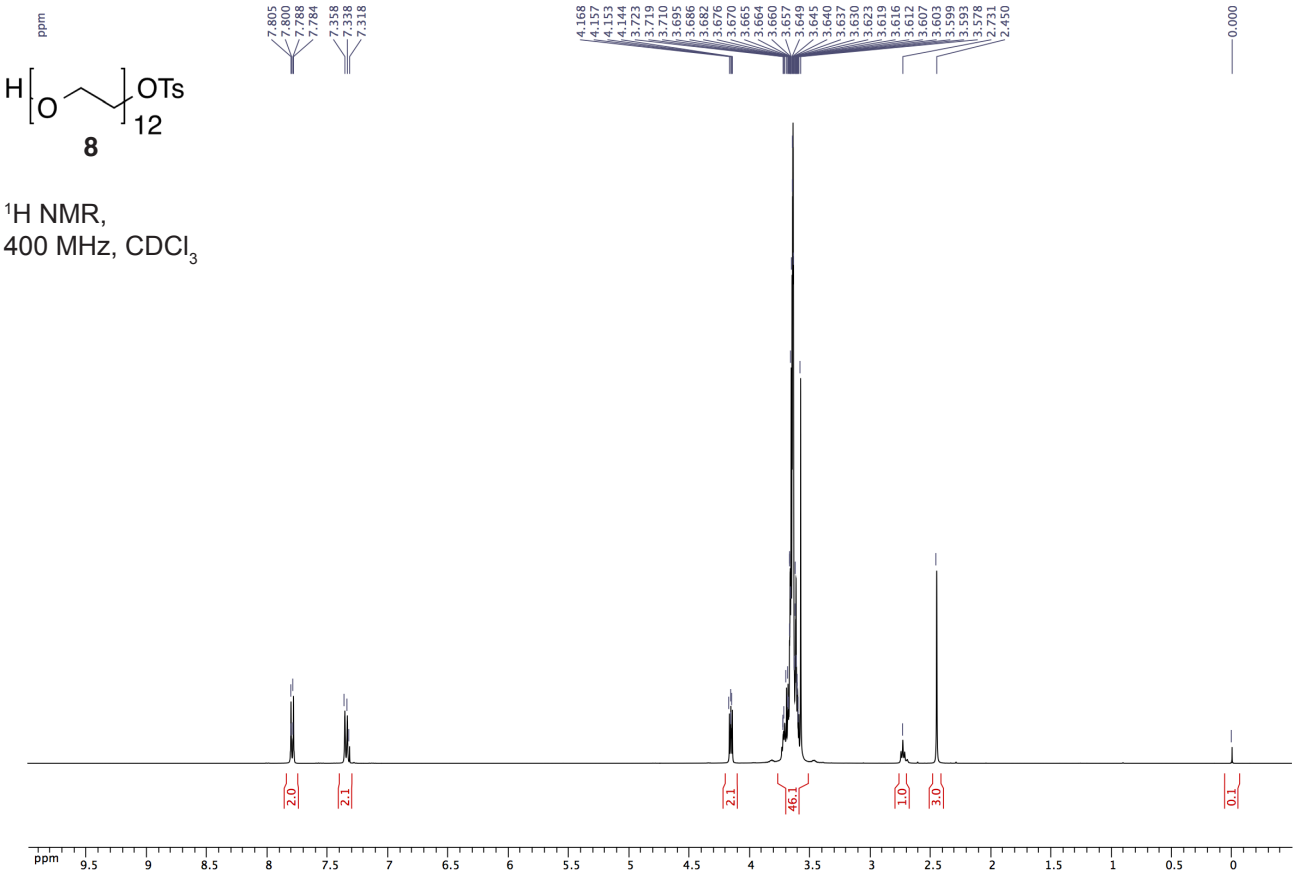
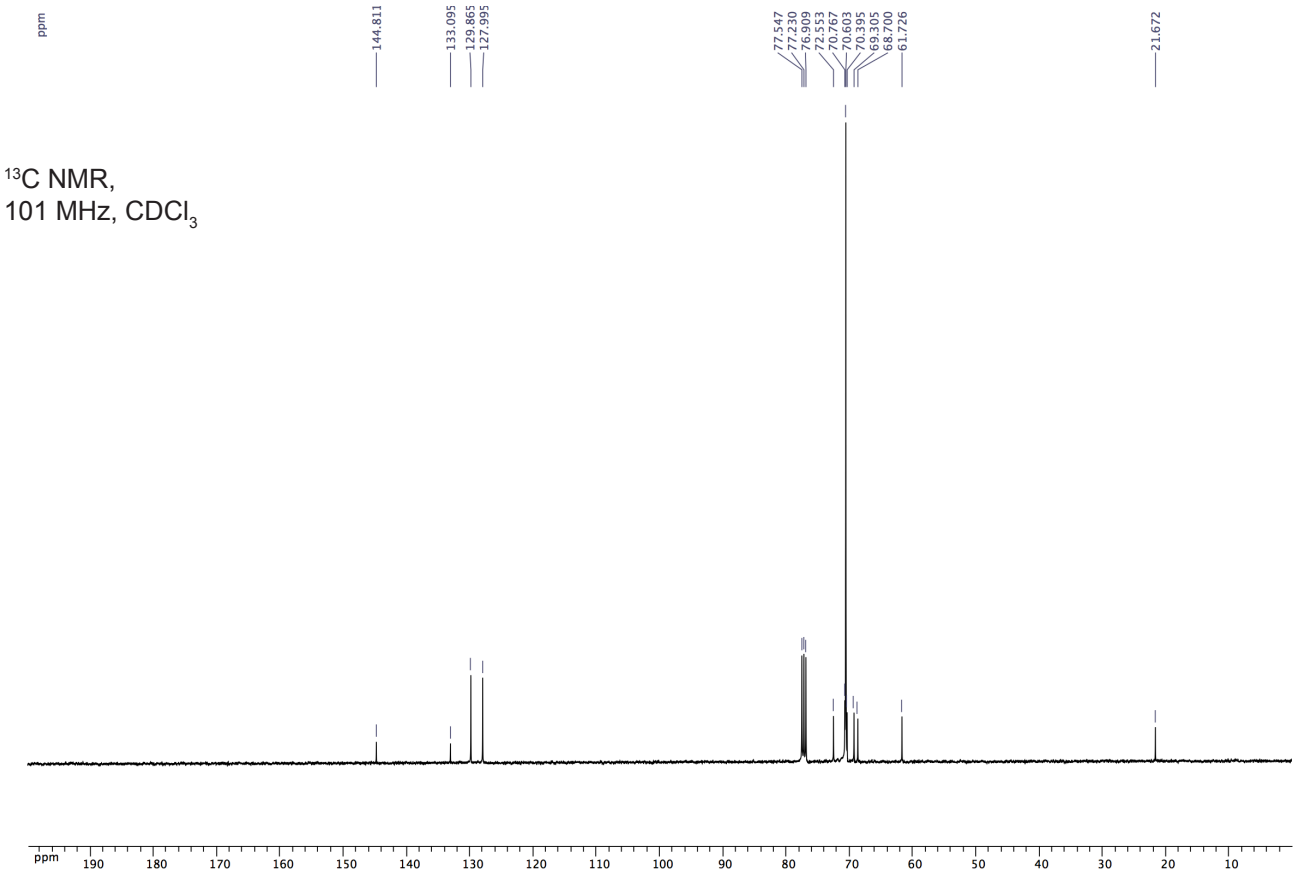
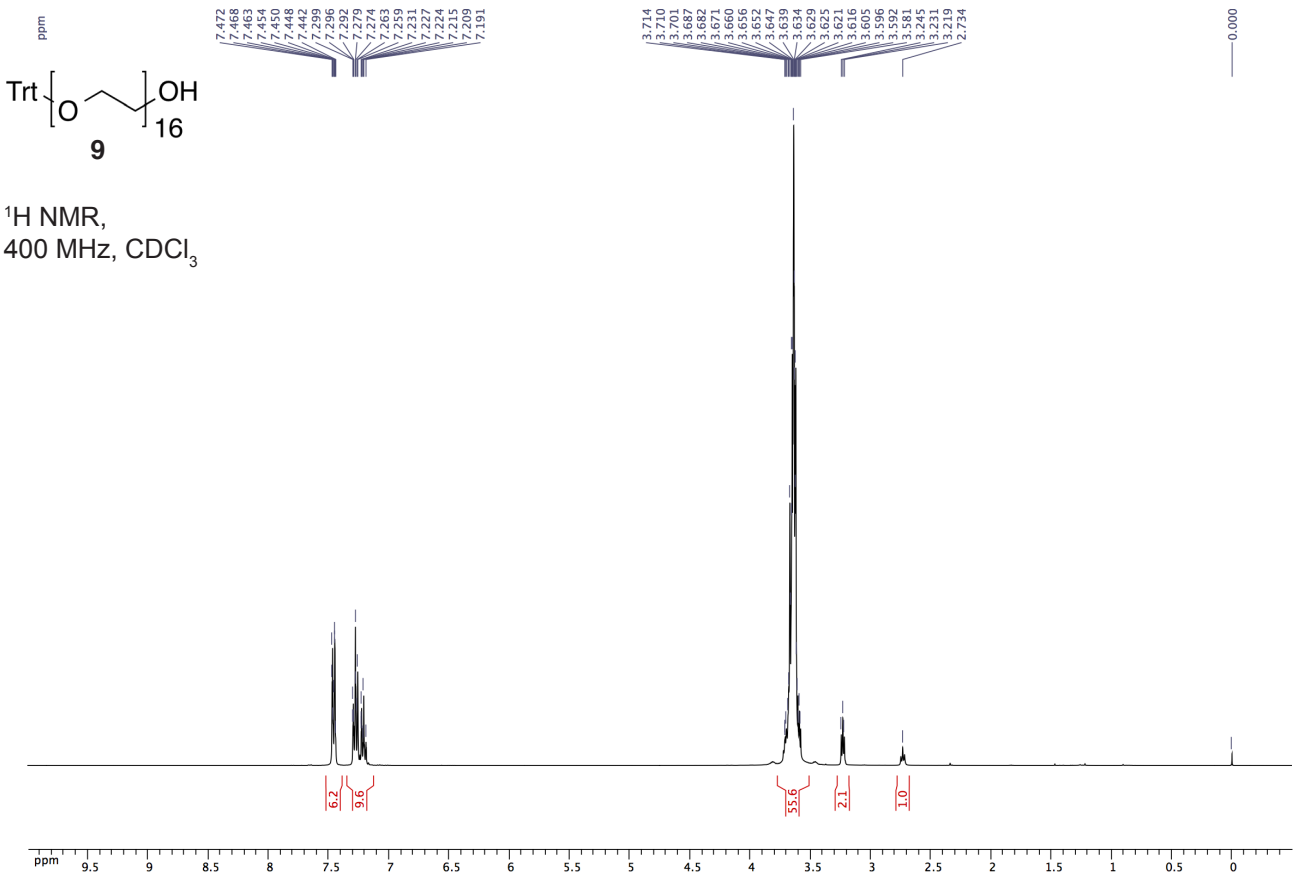


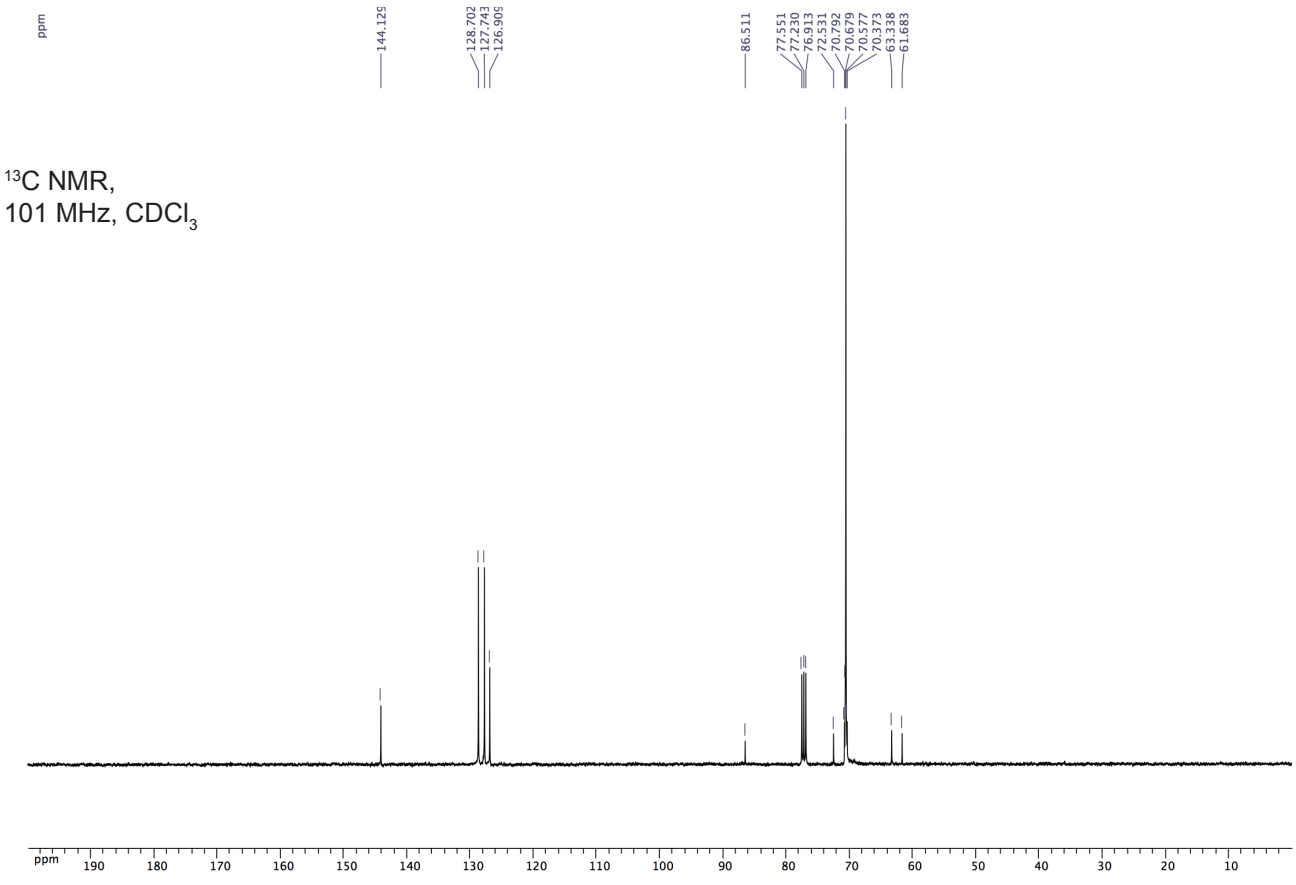
^{1}H NMR,
400 MHz, $CDCl_3$



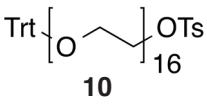
^{13}C NMR,
101 MHz, $CDCl_3$



^{1}H NMR,
400 MHz, $CDCl_3$



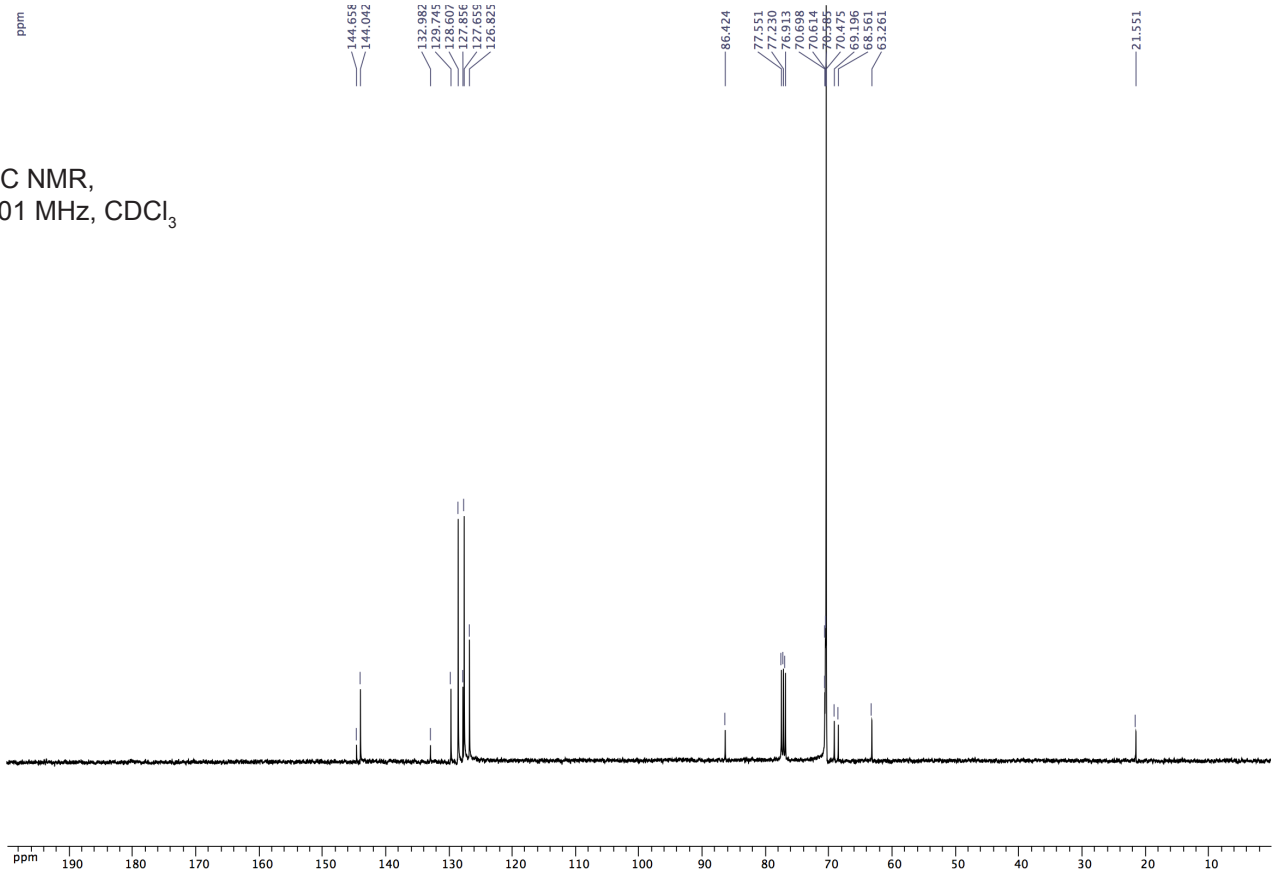
^{13}C NMR,
101 MHz, $CDCl_3$

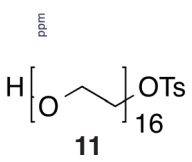


10

^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

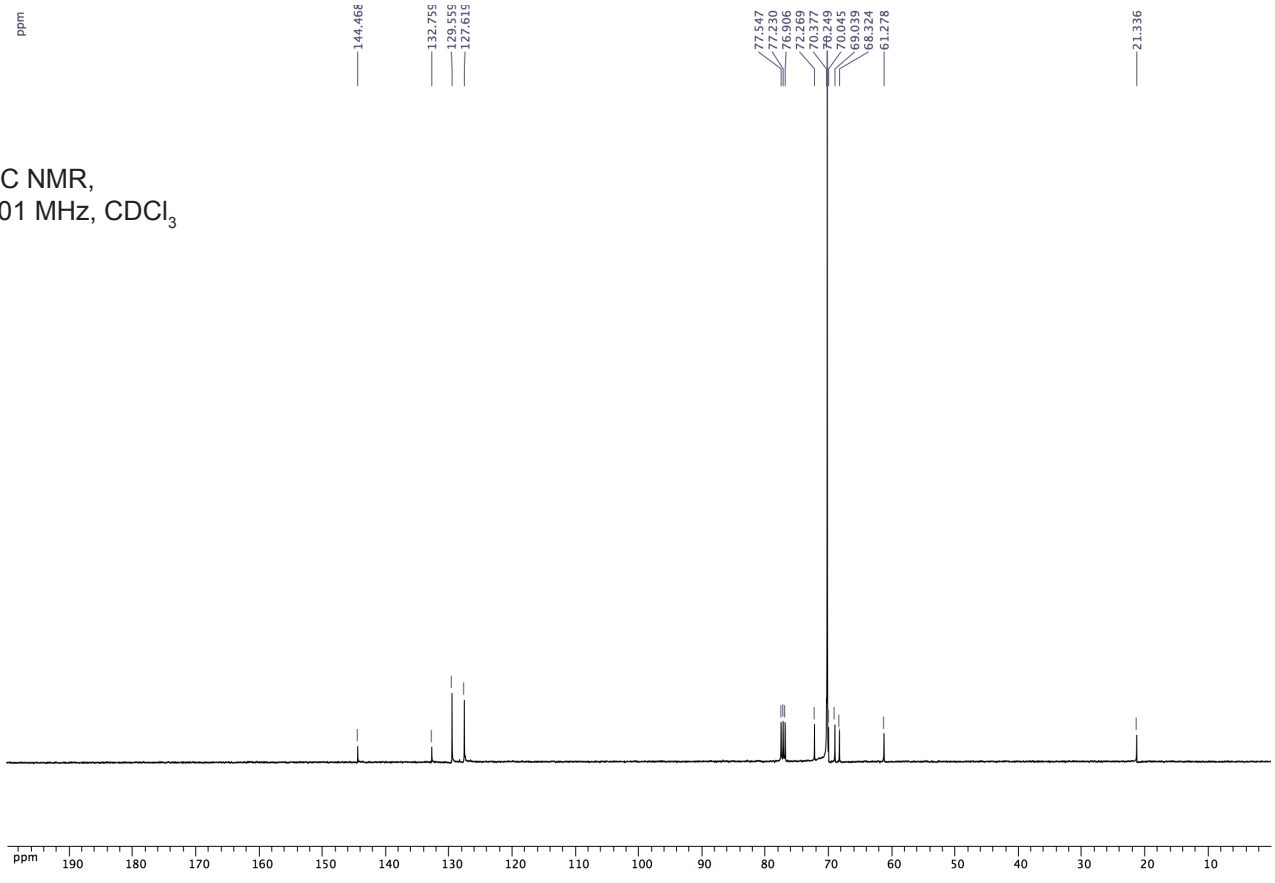


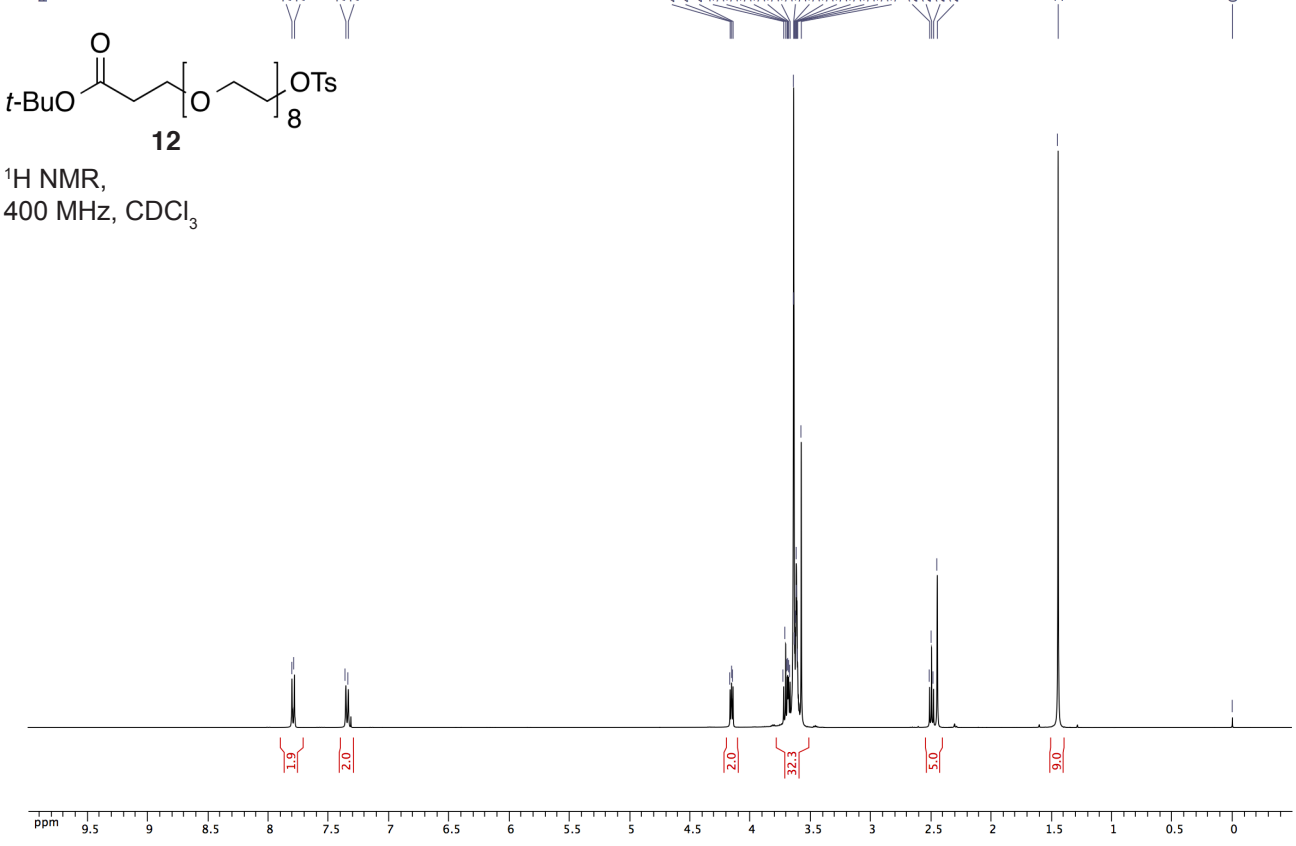


11

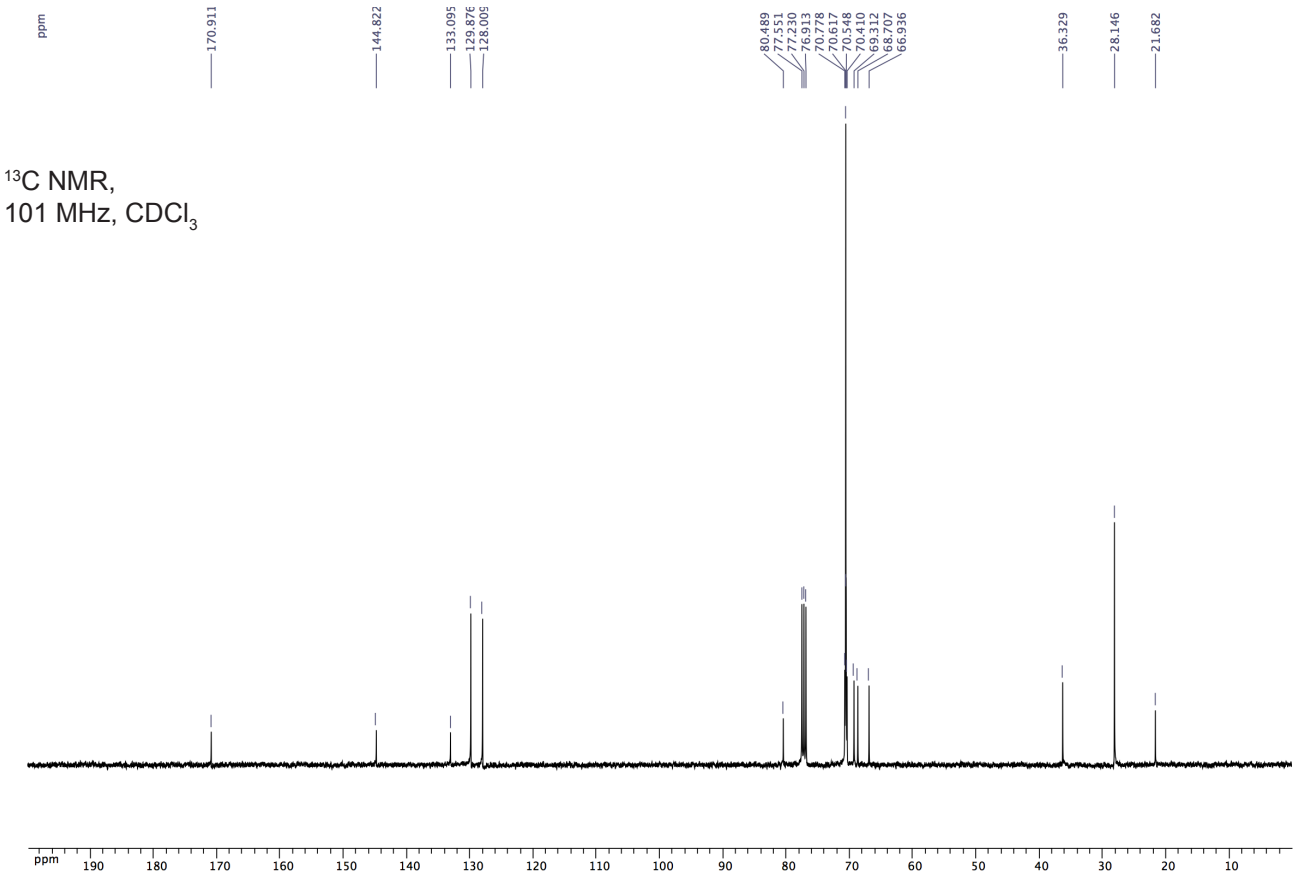
^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

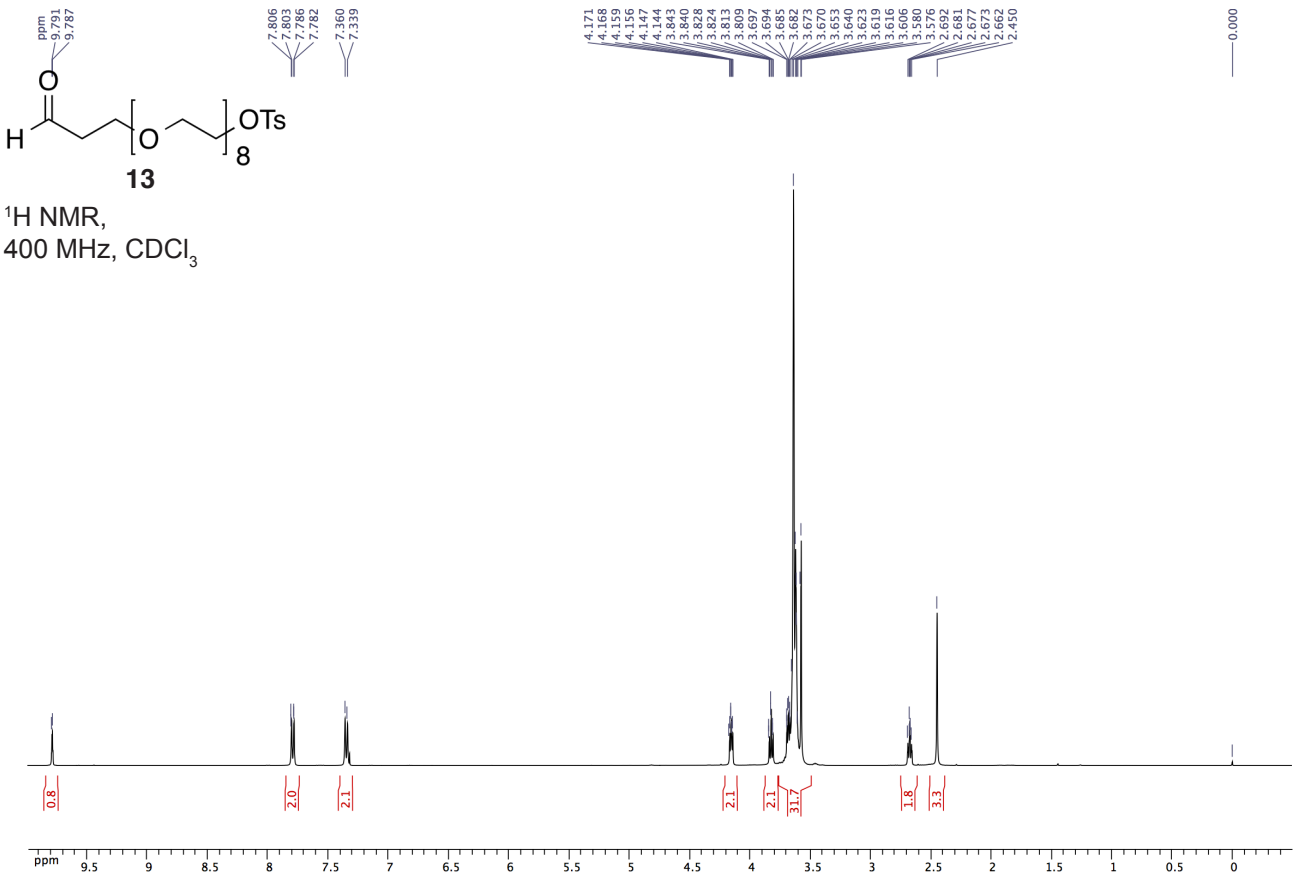




^{1}H NMR,
400 MHz, $CDCl_3$

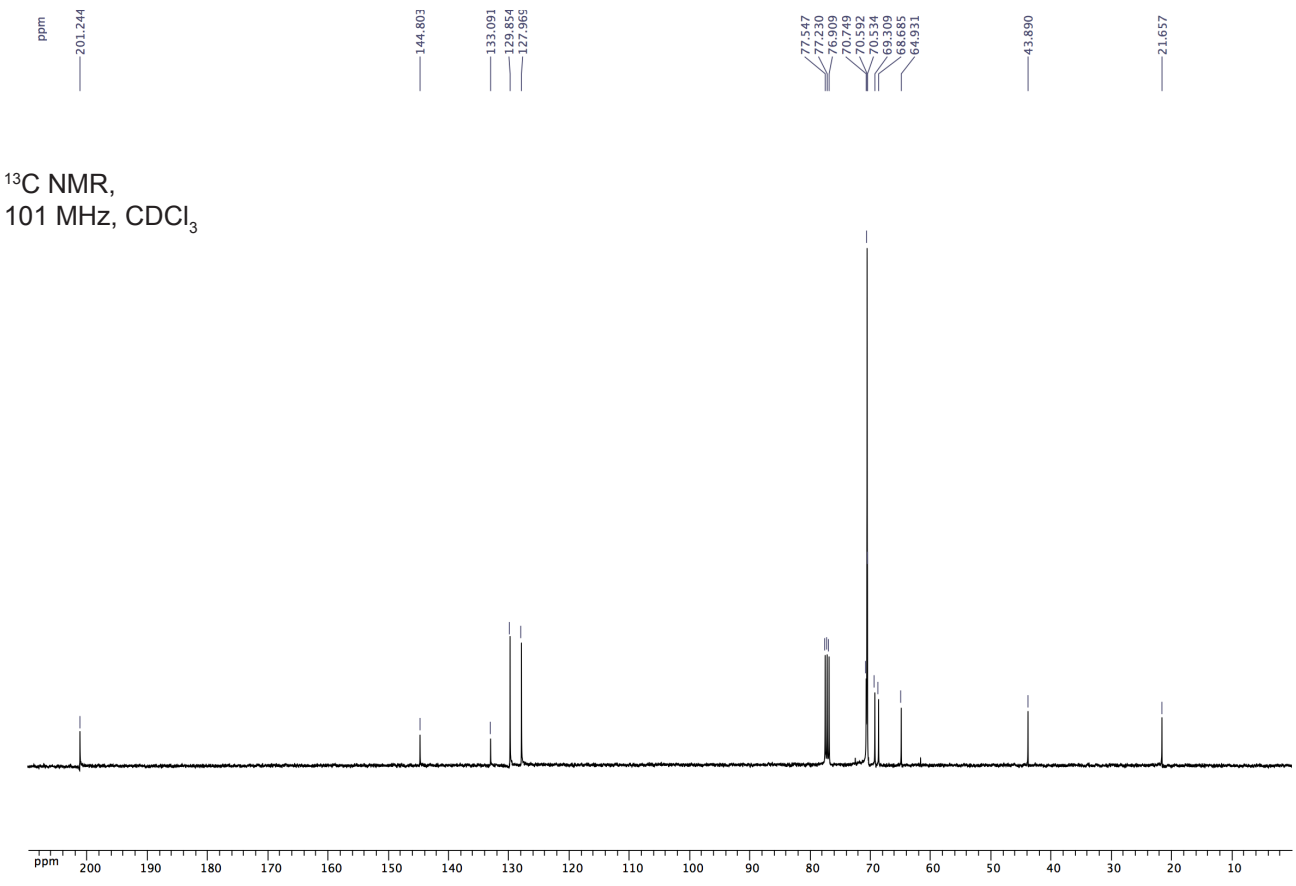


^{13}C NMR,
101 MHz, $CDCl_3$

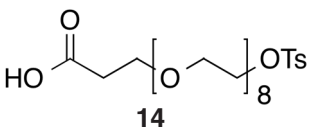


13

^{1}H NMR,
400 MHz, $CDCl_3$



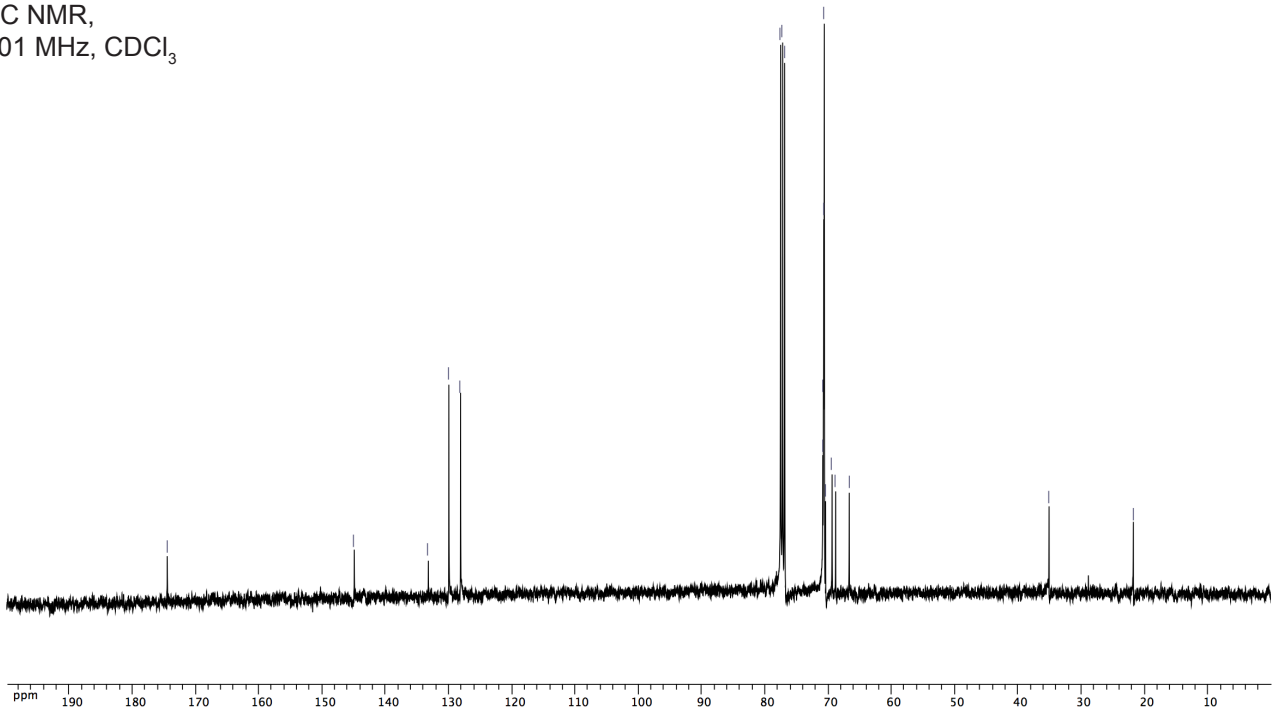
^{13}C NMR,
101 MHz, $CDCl_3$

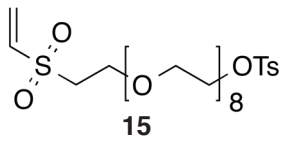


14

^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

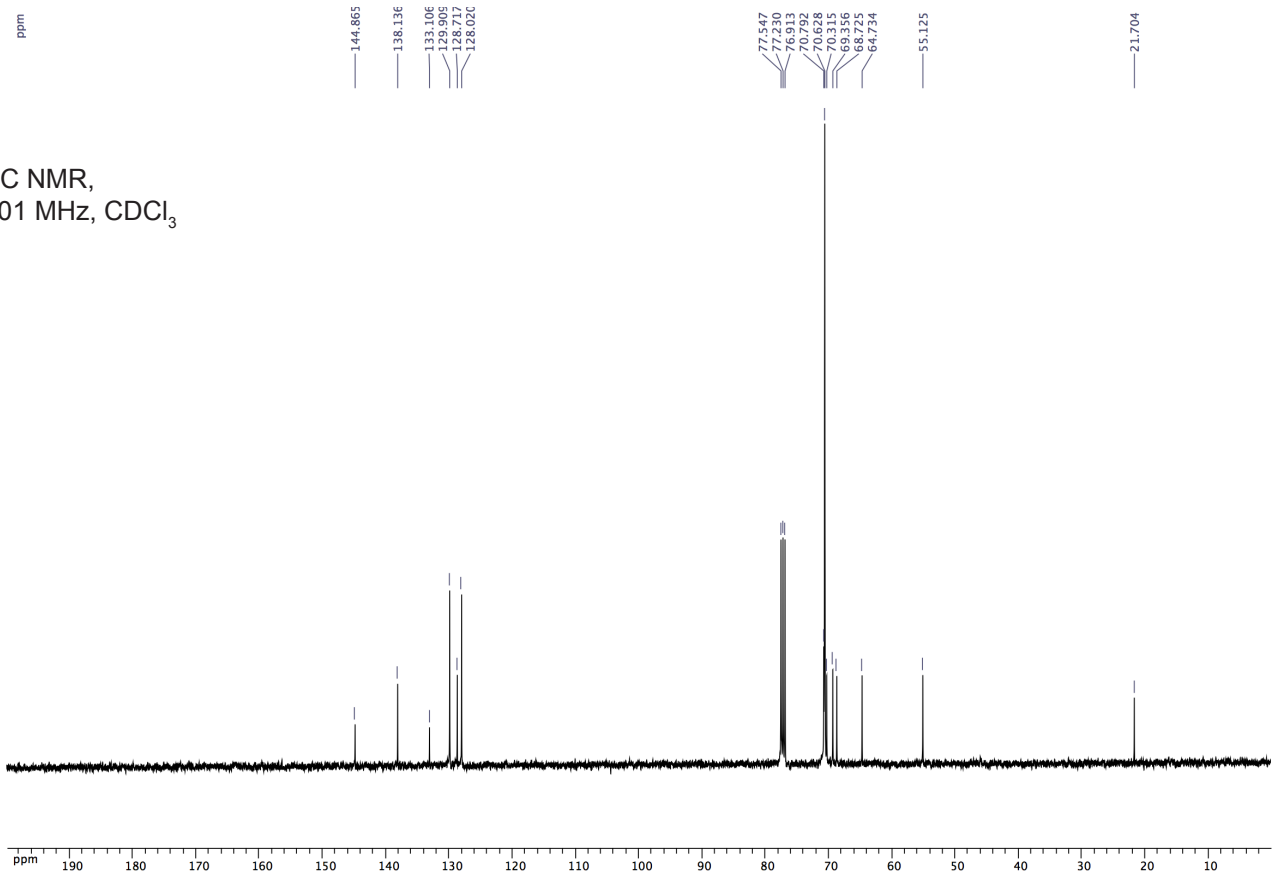


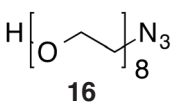


15

^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

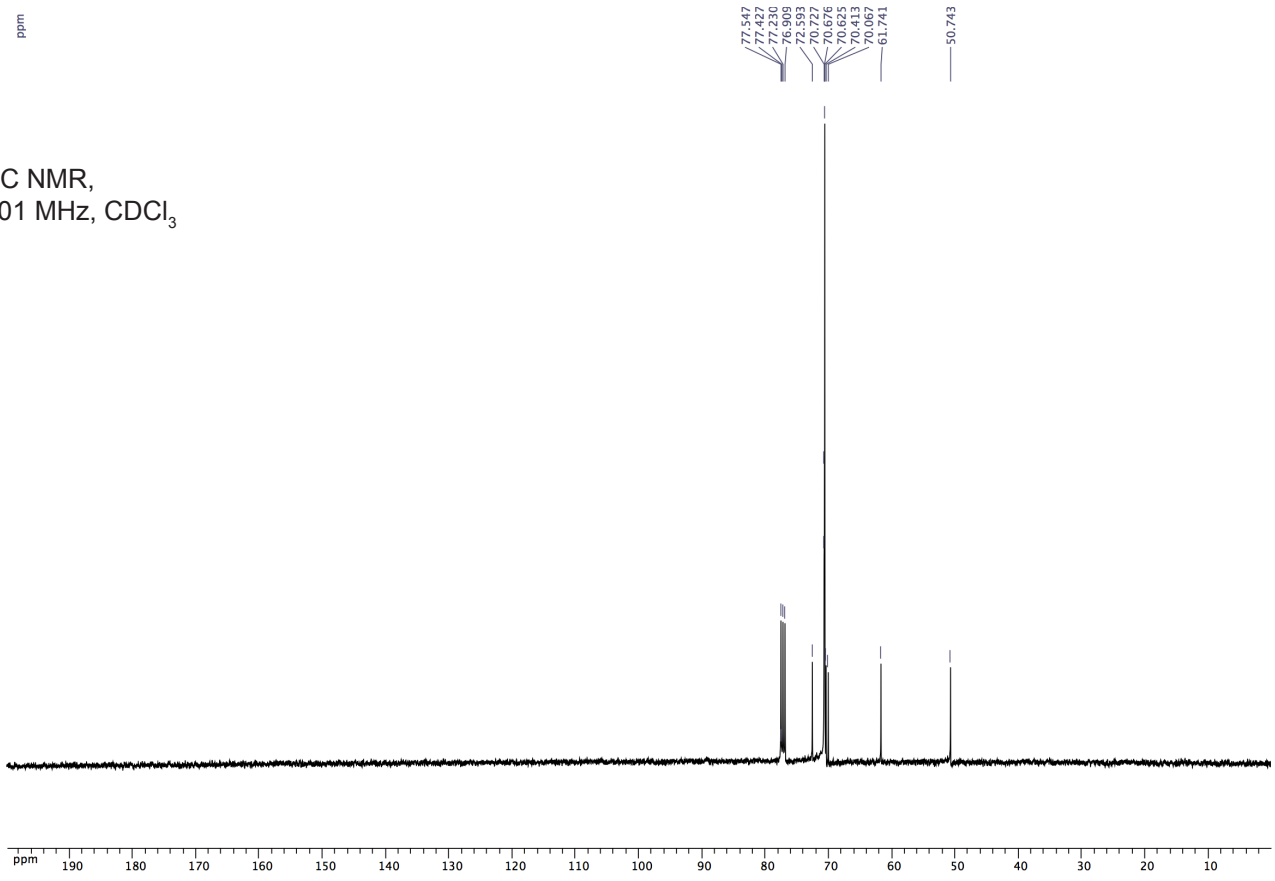


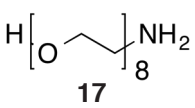


16

^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

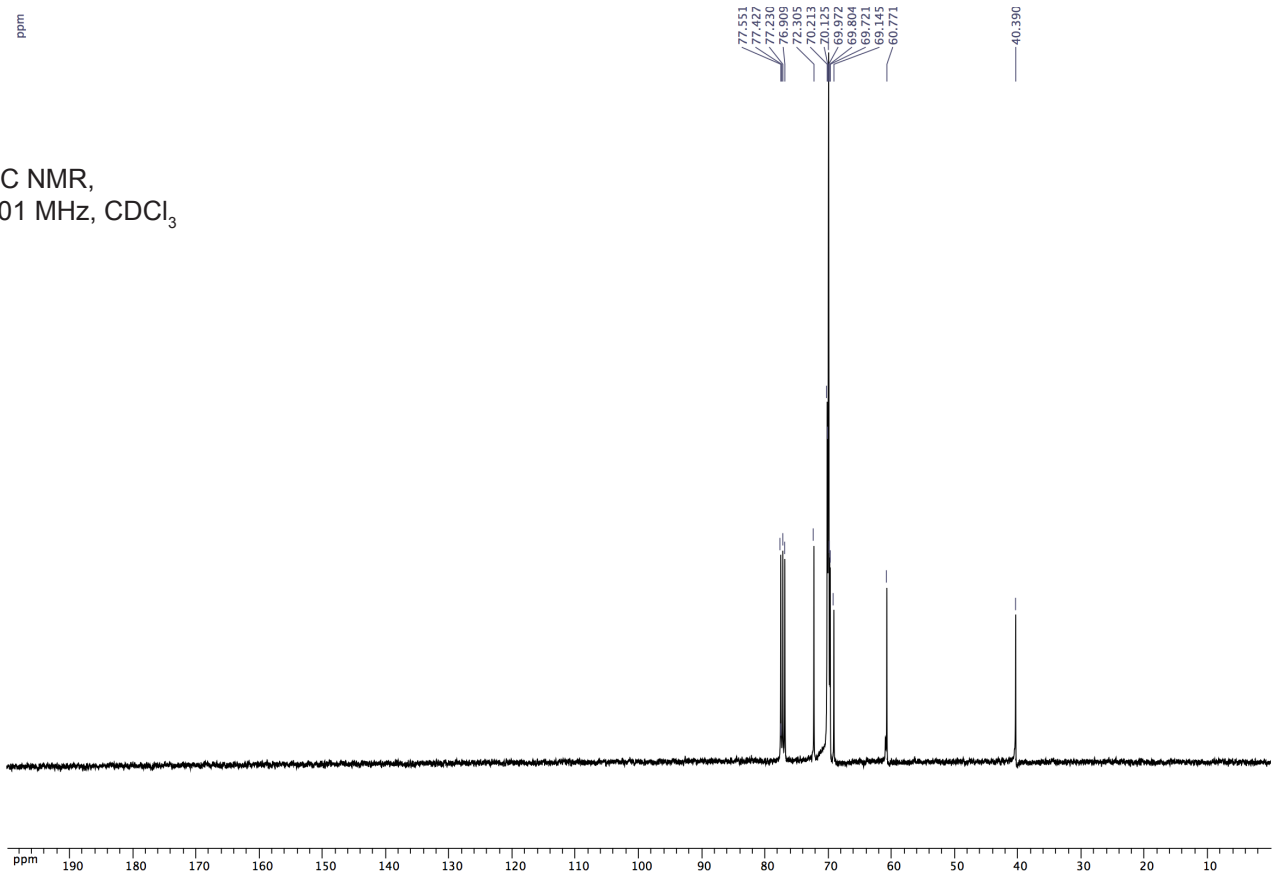


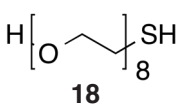


17

^{1}H NMR,
400 MHz, $CDCl_3$

^{13}C NMR,
101 MHz, $CDCl_3$

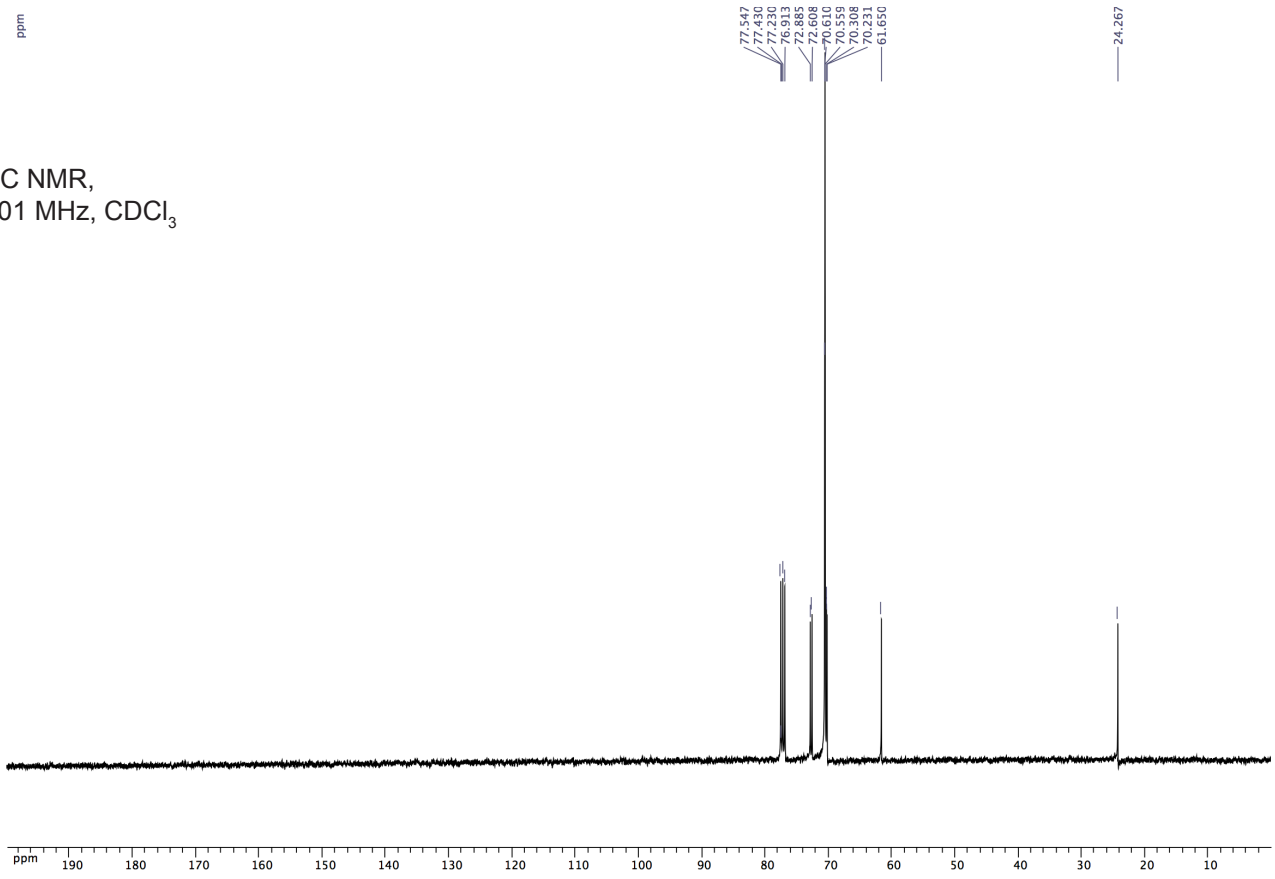




18

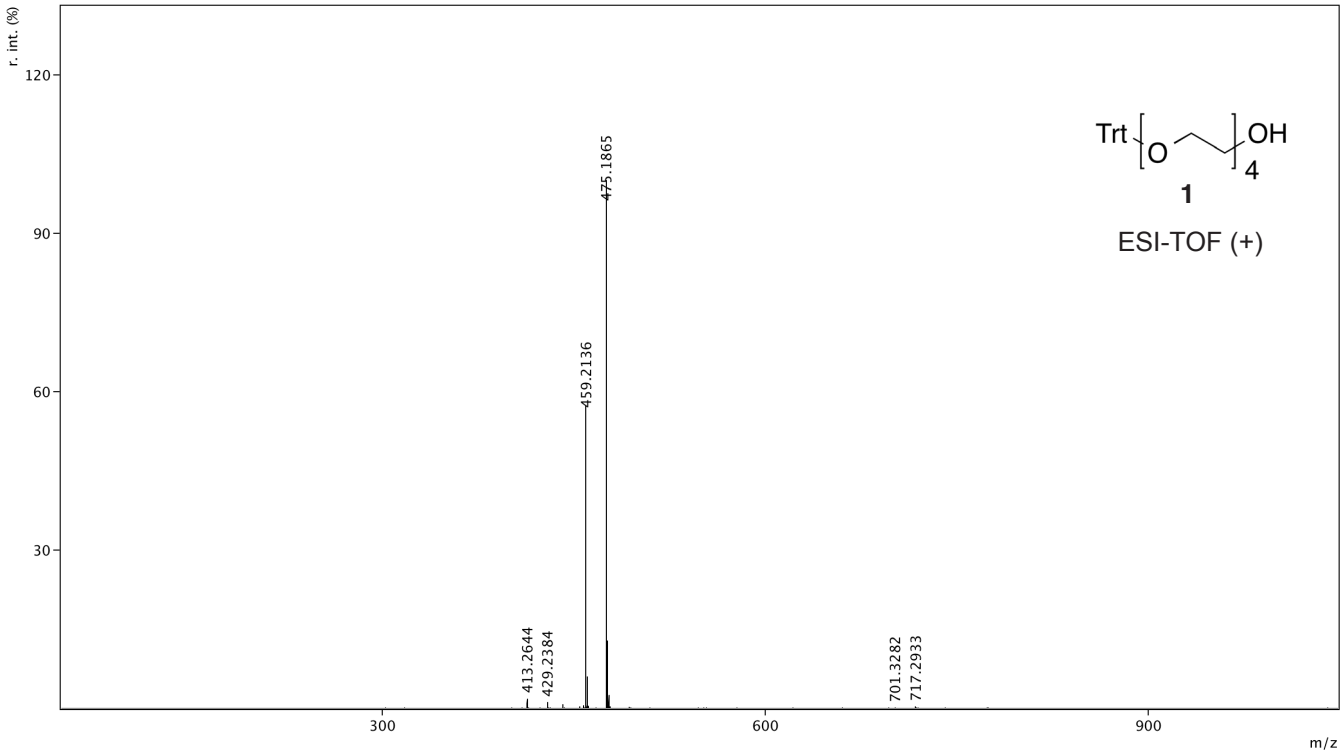
^{1}H NMR,
400 MHz, $CDCl_3$

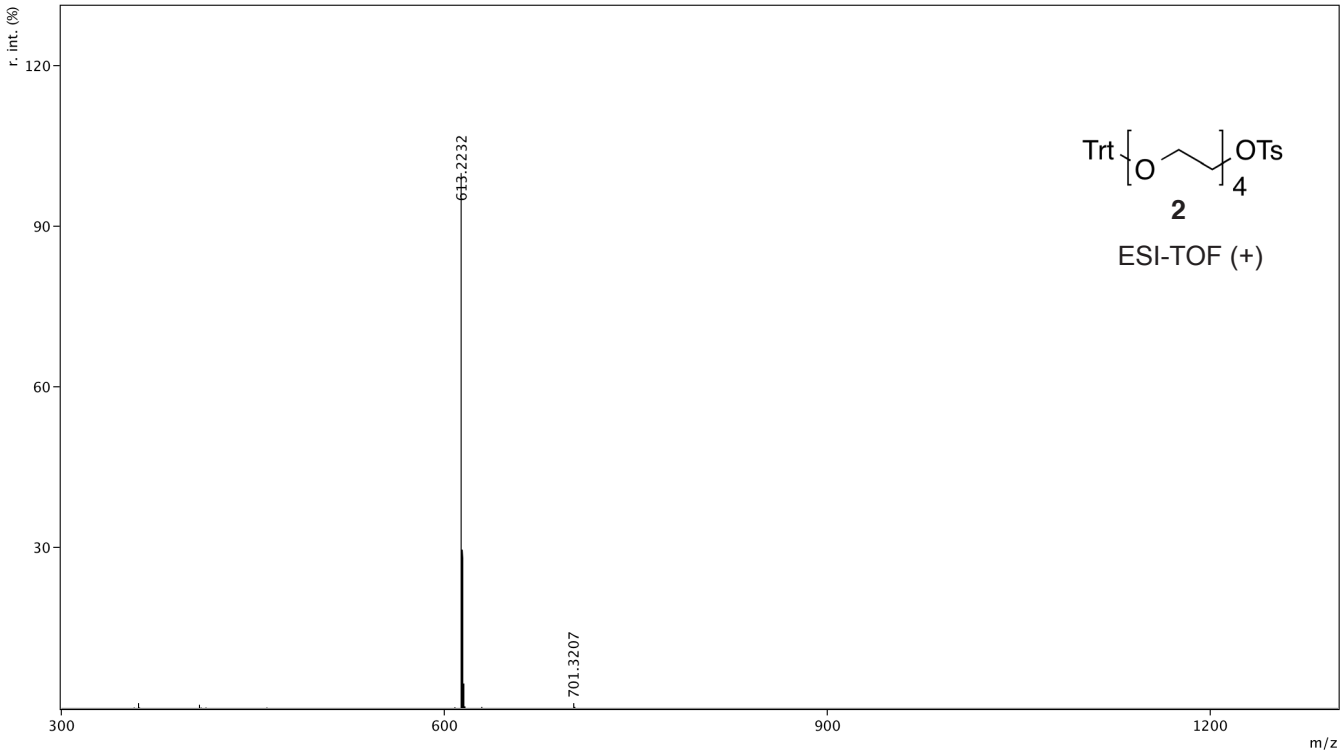
^{13}C NMR,
101 MHz, $CDCl_3$

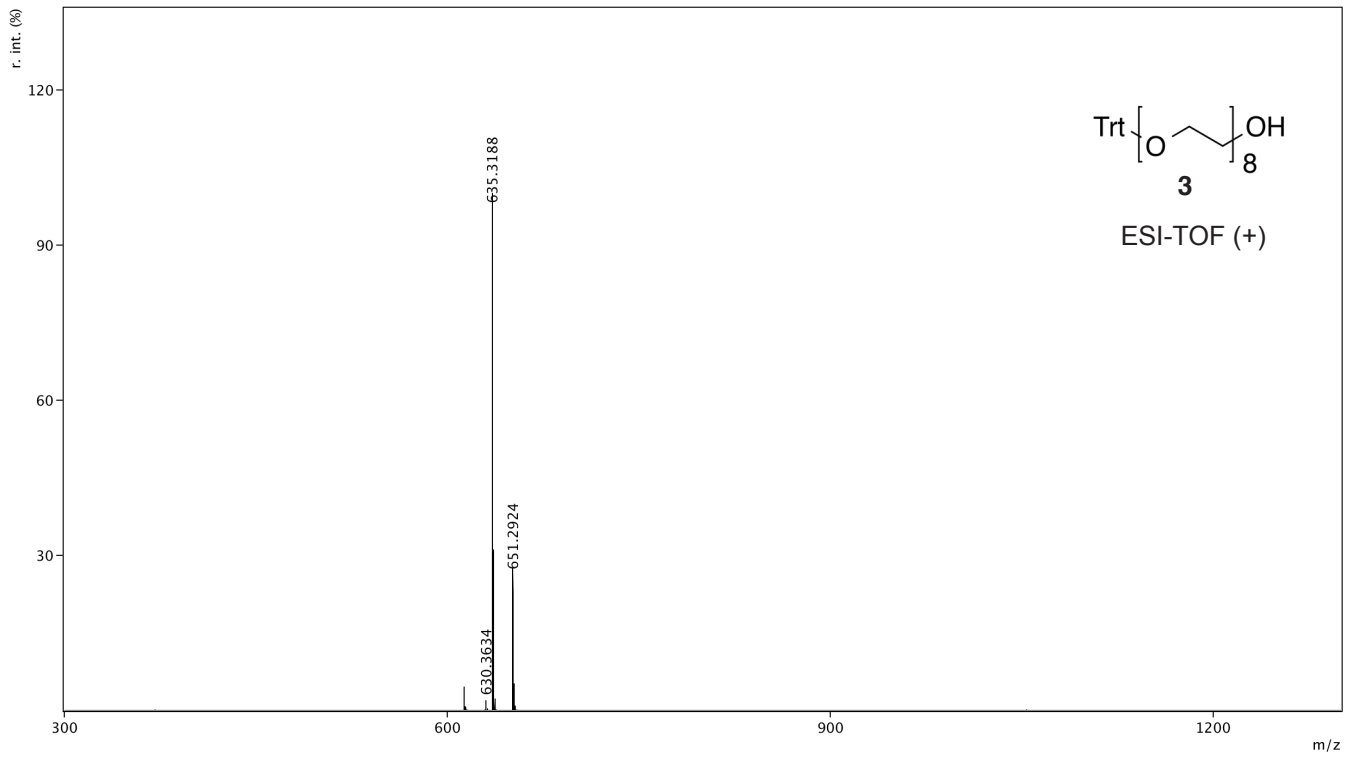


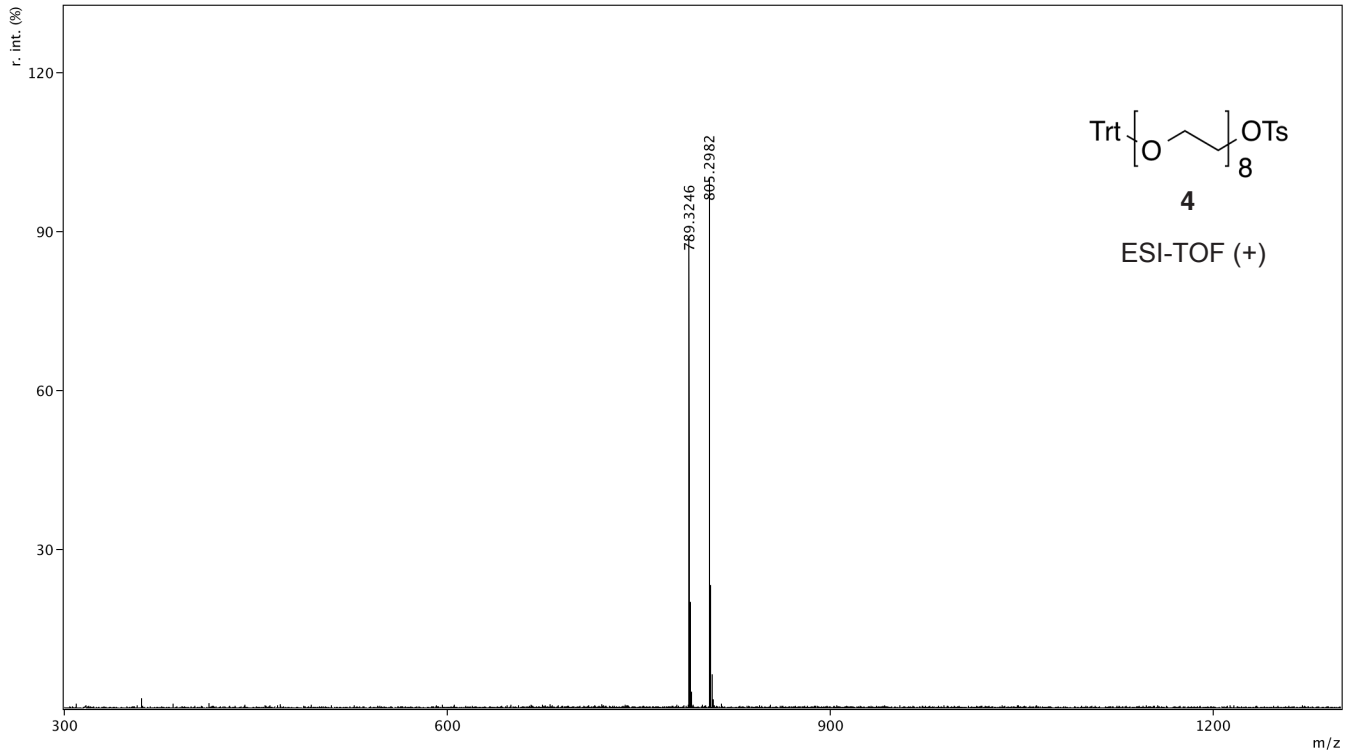
5. ESI-MS spectra

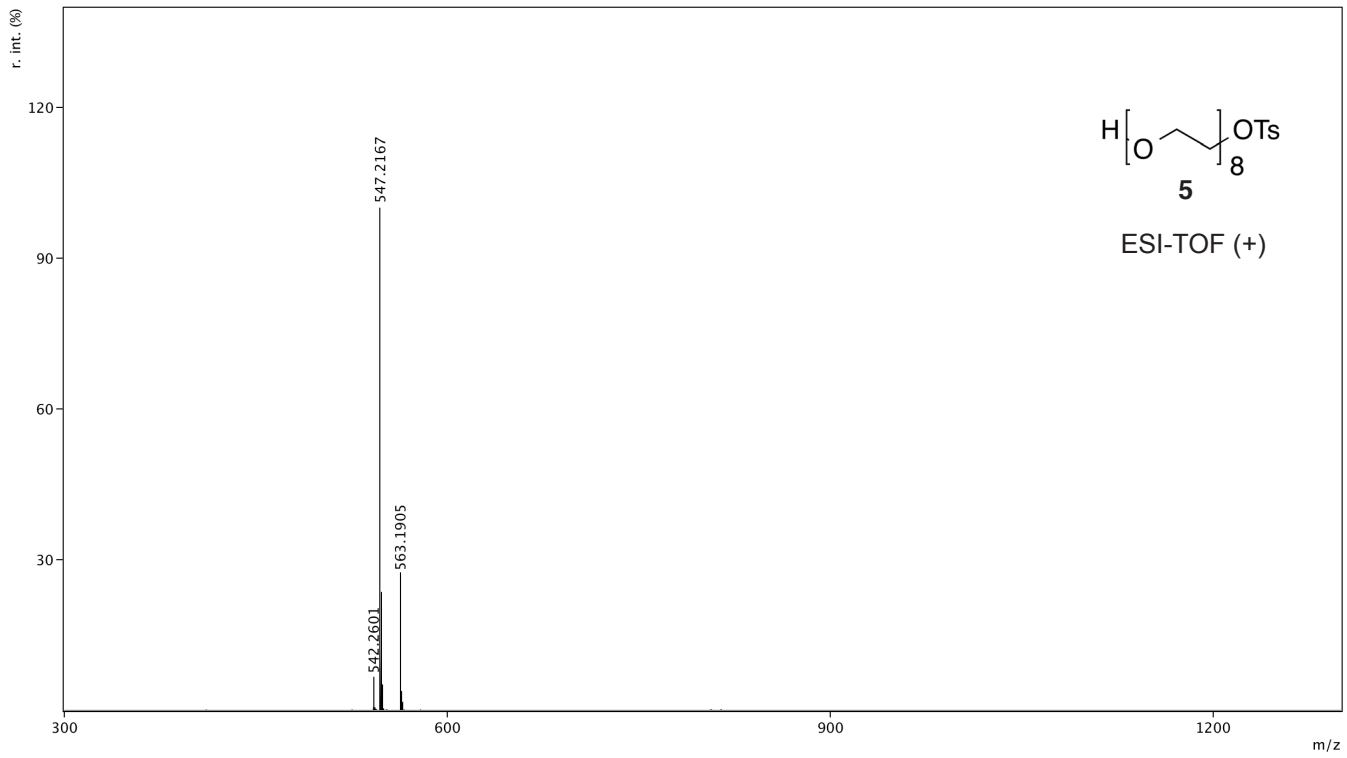
ESI-MS high-resolution data presented below were used for compound identification, not monodispersity analysis.

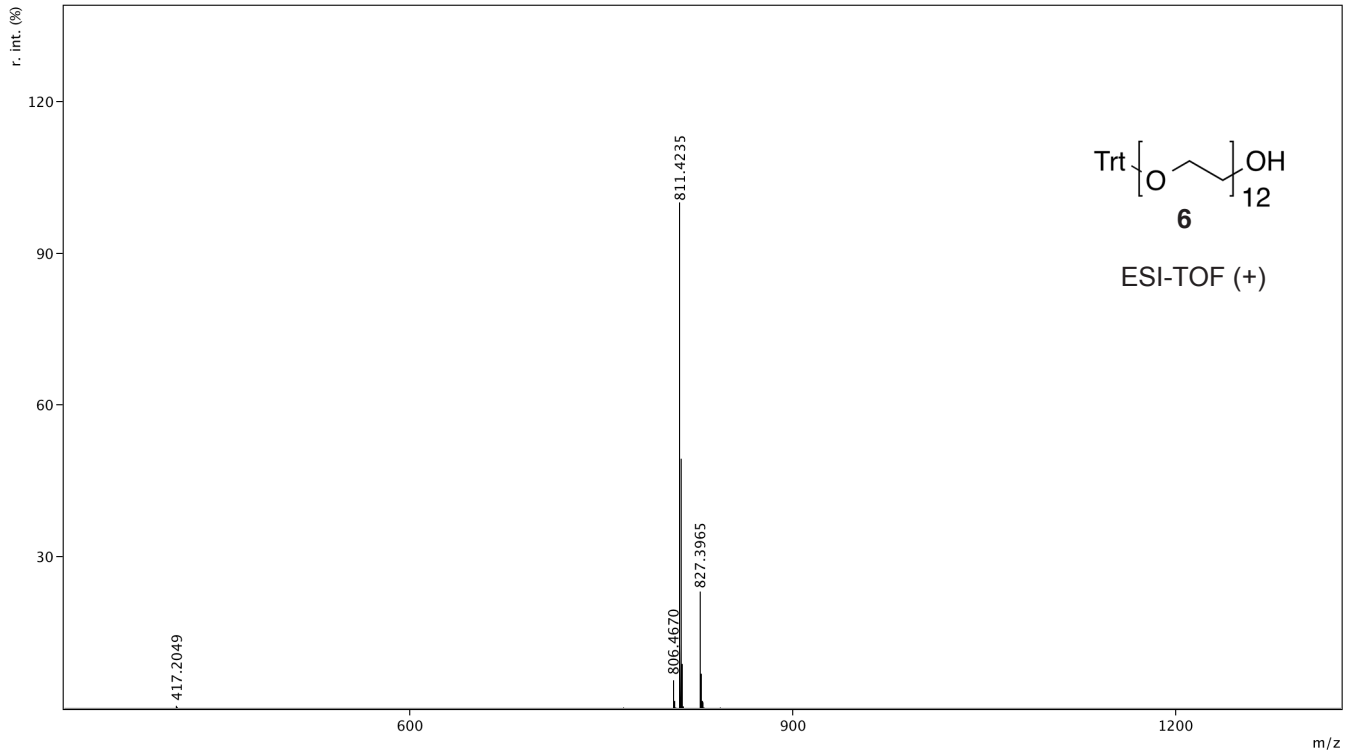

r. int. (%)
120
90
60
30
475.1865
459.2136
413.2644
429.2384
701.3282
717.2933
300
600
900
m/z
Trt
O
OH
4
1
ESI-TOF (+)

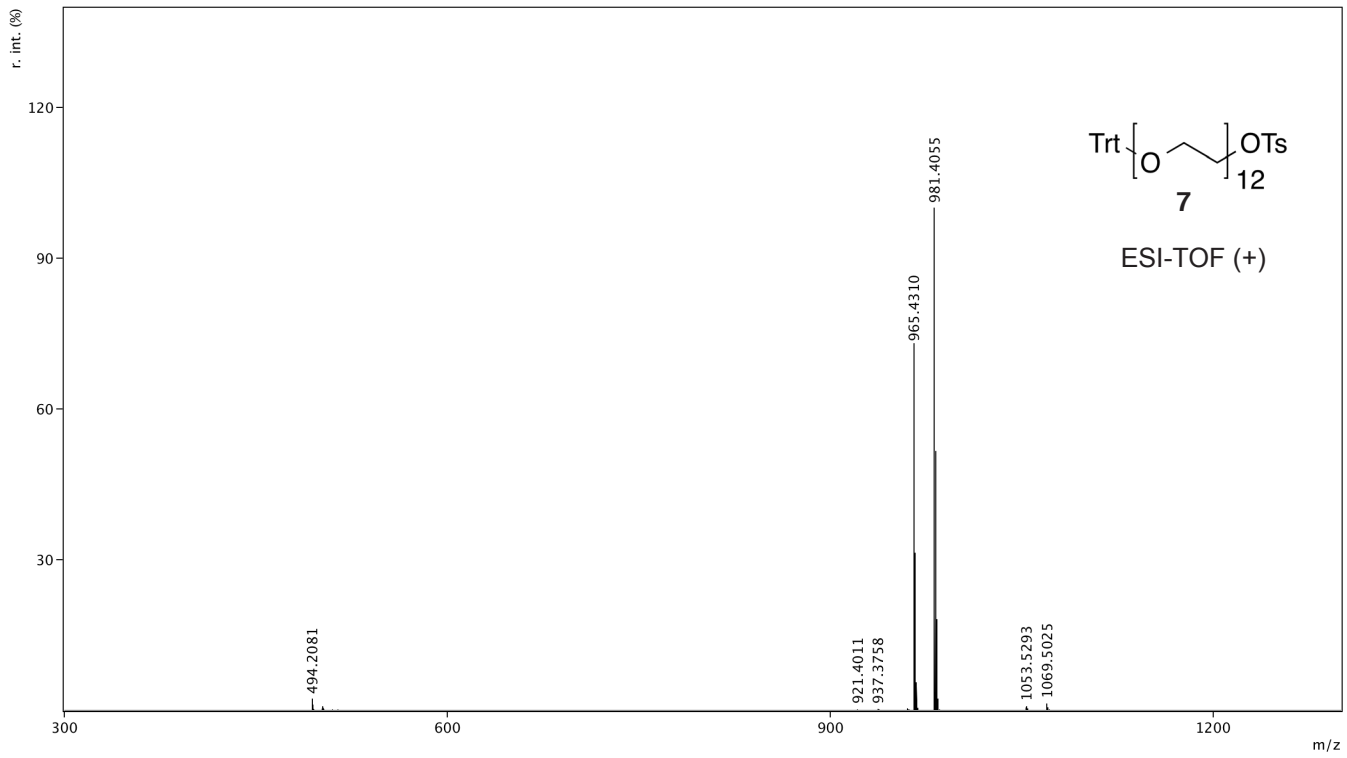

r. int. (%)
120
90
60
30
613.2232
701.3207
300
600
900
1200
m/z
Trt
O
OTs
4
2
ESI-TOF (+)

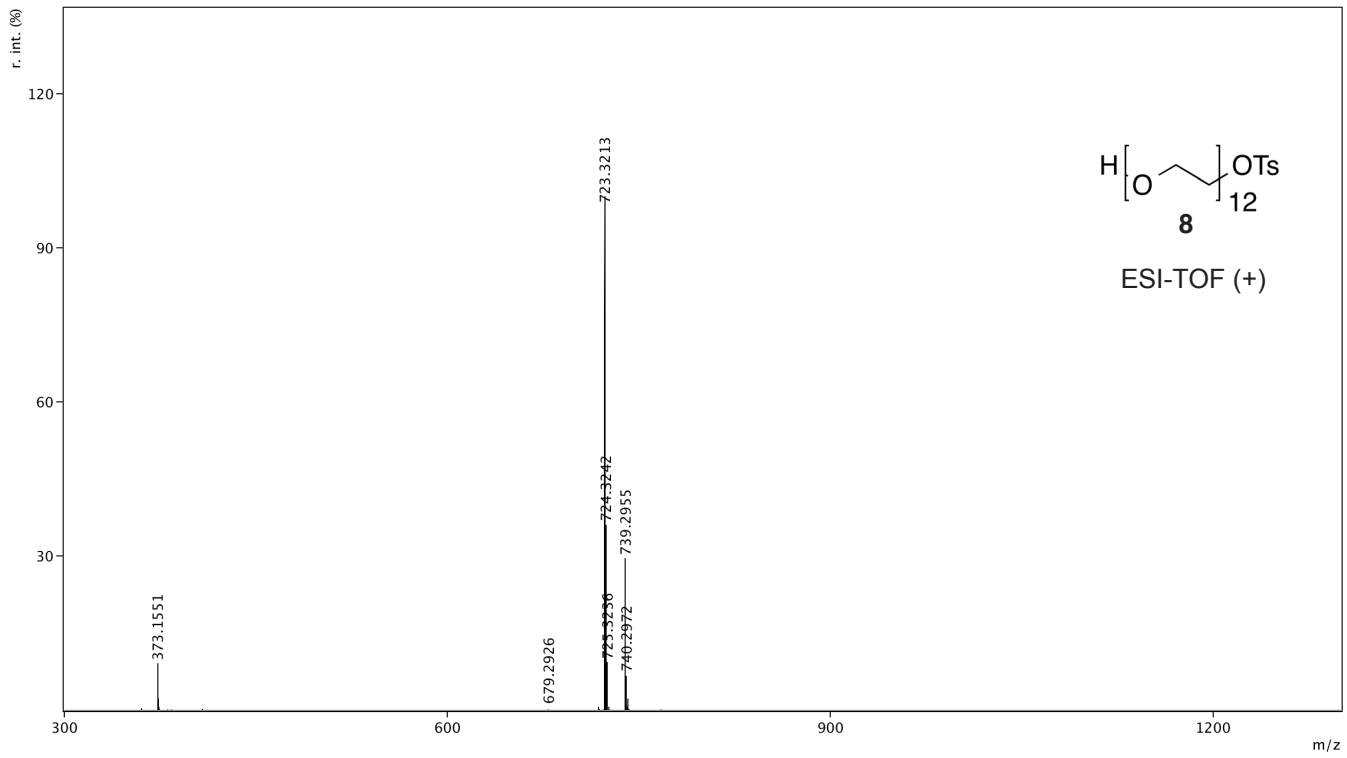

r. int. (%)
120
90
60
30
635.3188
651.2924
630.3634
300
600
900
1200
m/z
Trt
O
OH
8
3
ESI-TOF (+)

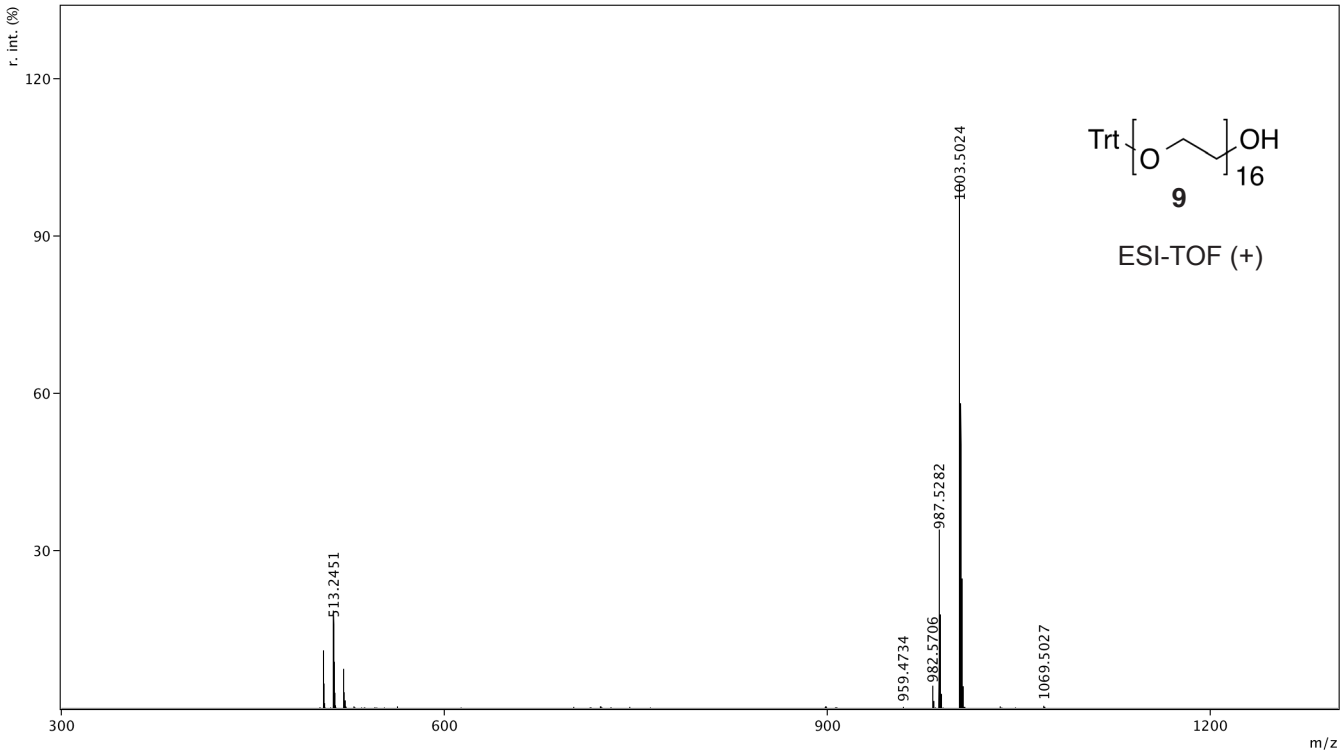

r. int. (%)
120
90
60
30
789.3246
805.2982
300
600
900
1200
m/z
Trt
O
OTs
8
4
ESI-TOF (+)

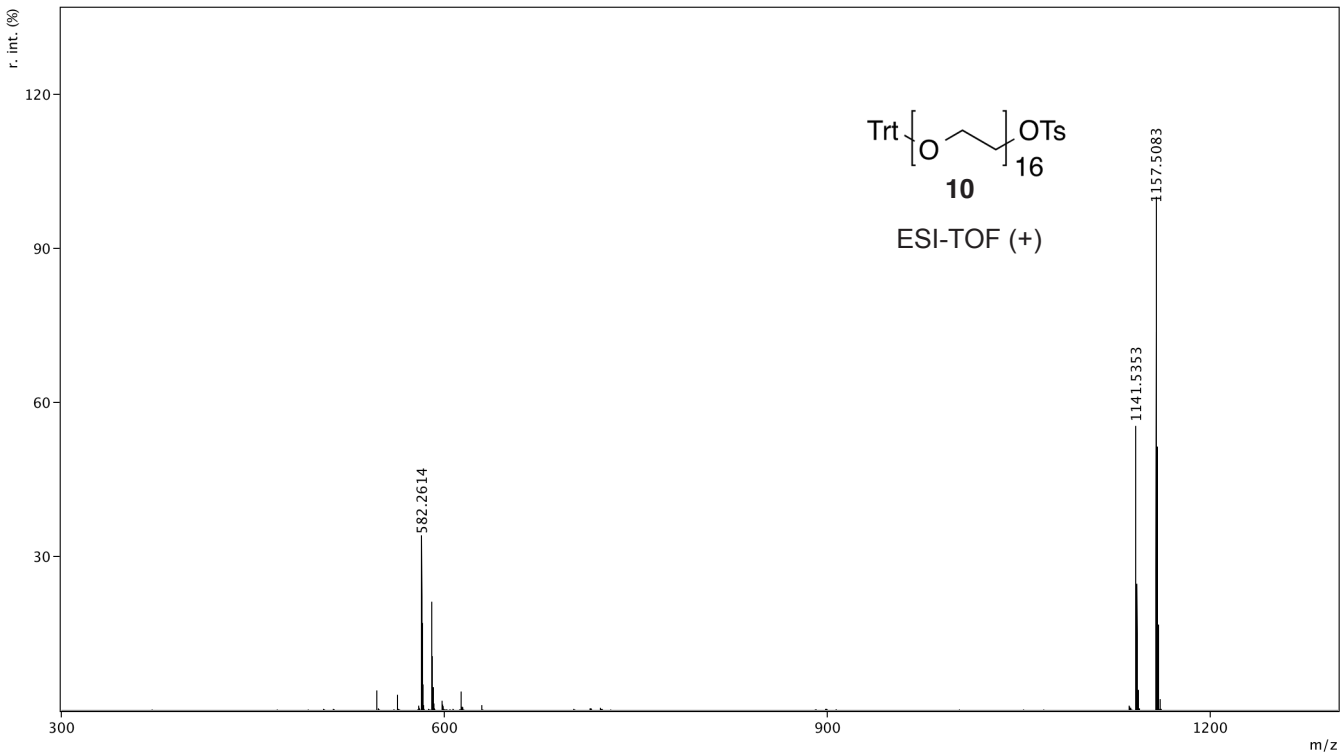

r. int. (%)
120
90
60
30
547.2167
563.1905
542.2601
300
600
900
1200
m/z
H
O
OTs
8
5
ESI-TOF (+)

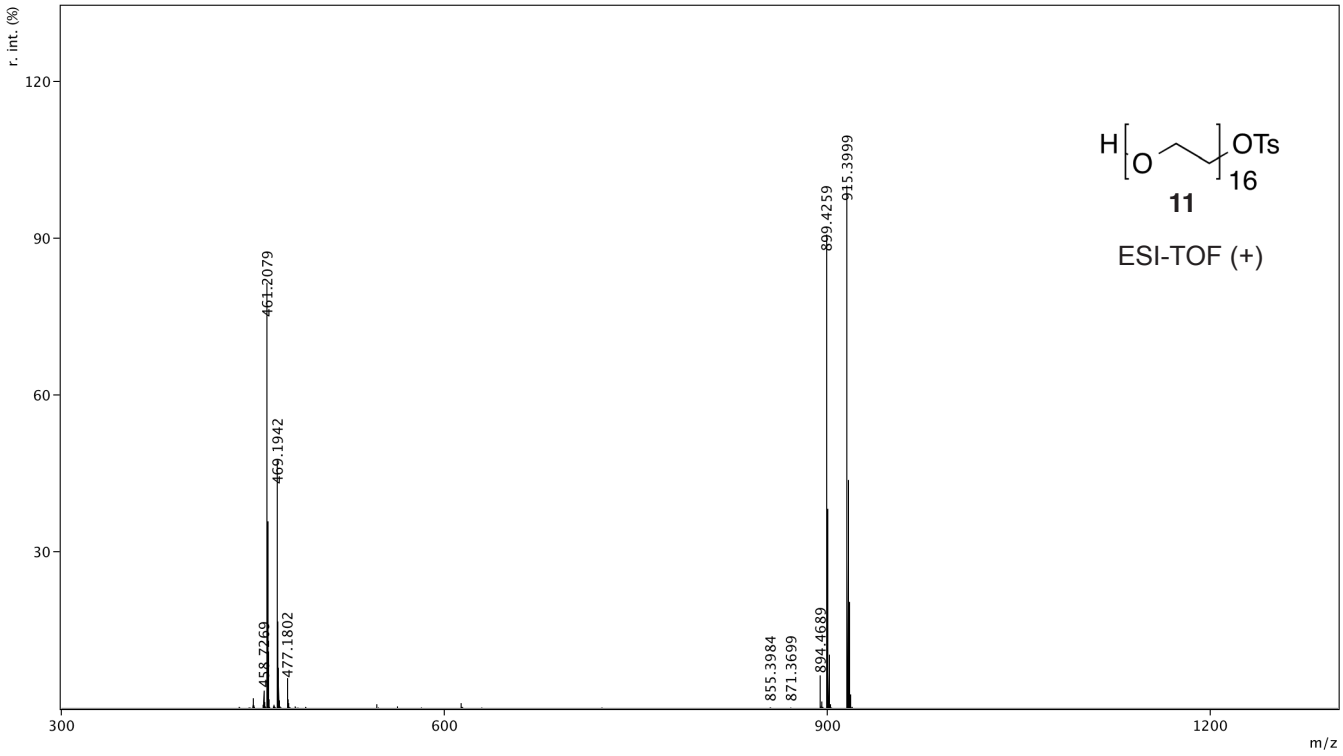

r. int. (%)
120
90
60
30
811.4235
827.3965
806.4670
417.2049
600
900
1200
m/z
Trt
O
OH
12
6
ESI-TOF (+)

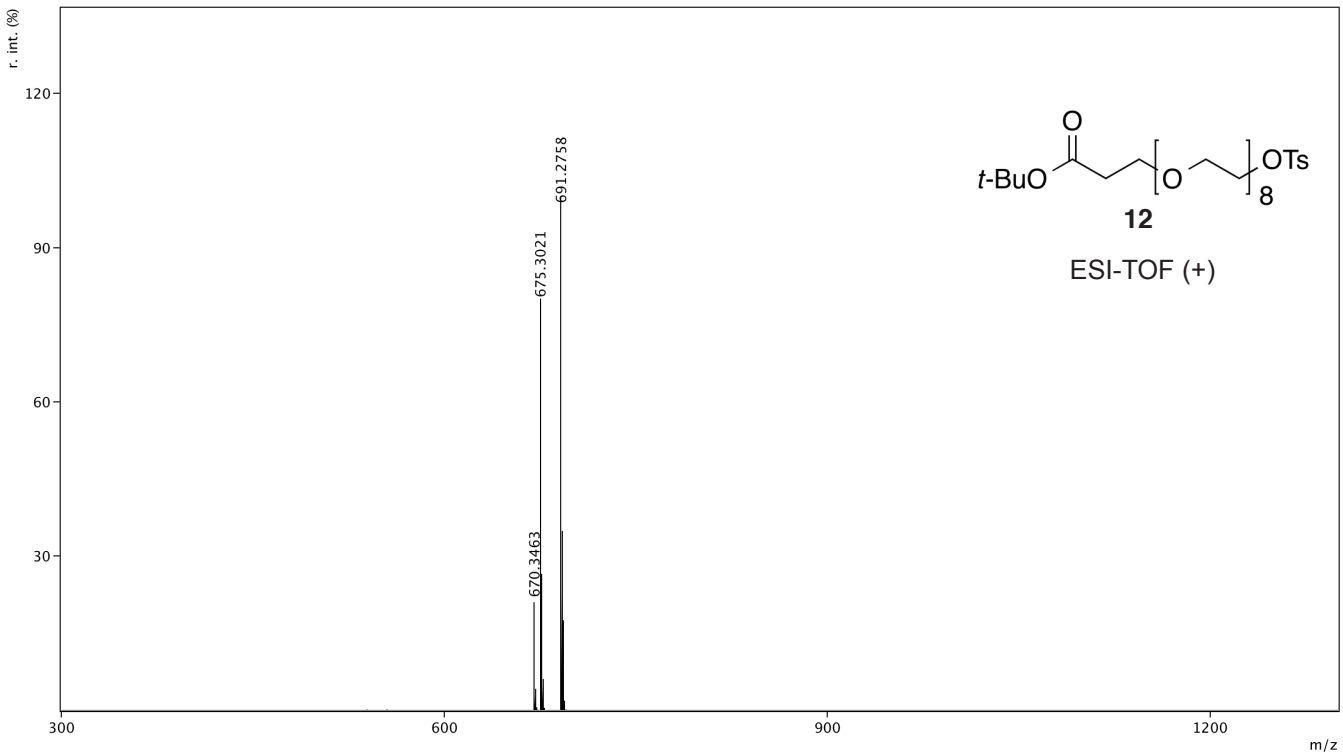

r. int. (%)
120
90
60
30
494.2081
921.4011
937.3758
965.4310
981.4055
1053.5293
1069.5025
300
600
900
1200
m/z
Trt
O
OTs
12
7
ESI-TOF (+)

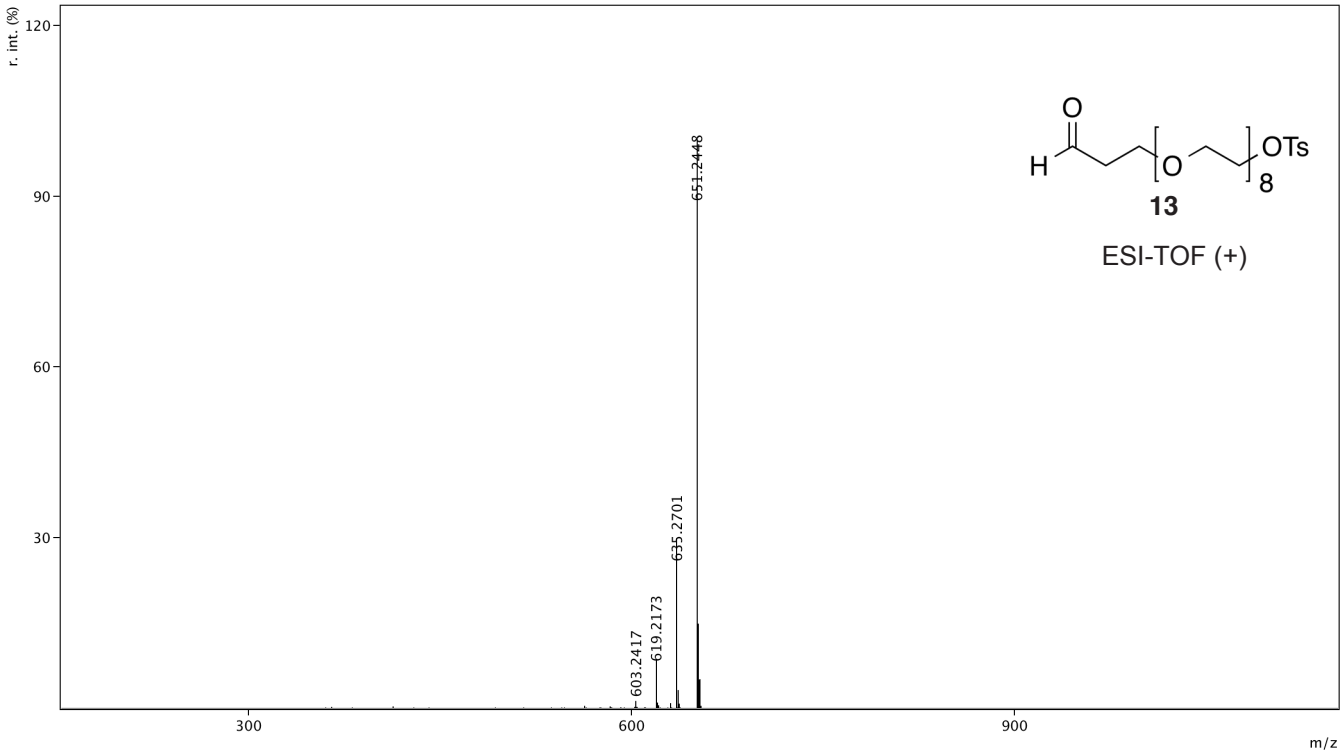

r. int. (%)
120
90
60
30
373.1551
679.2926
723.3213
724.3242
739.2955
740.2972
300
600
900
1200
m/z
H
O
OTs
12
8
ESI-TOF (+)

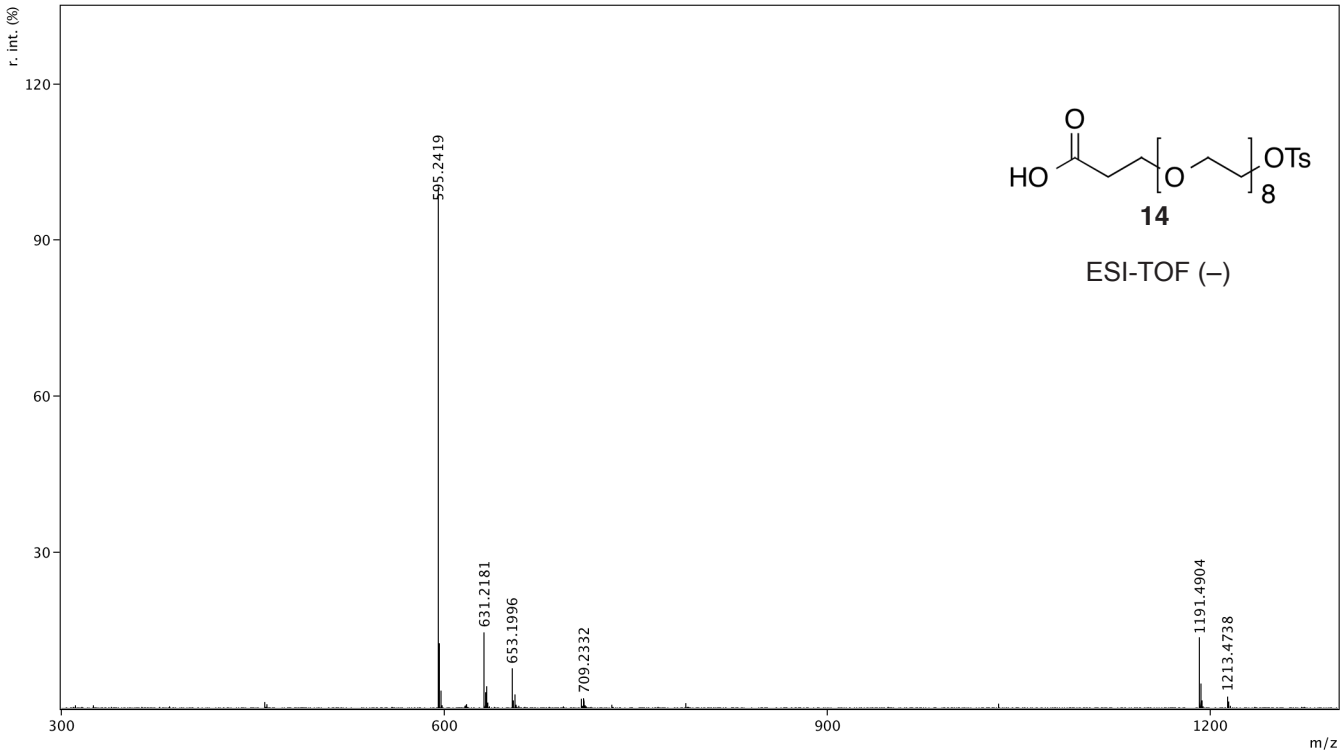

r. int. (%)
120
90
60
30
513.2451
959.4734
982.5706
987.5282
1003.5024
1069.5027
300
600
900
1200
m/z
Trt
O
OH
16
9
ESI-TOF (+)

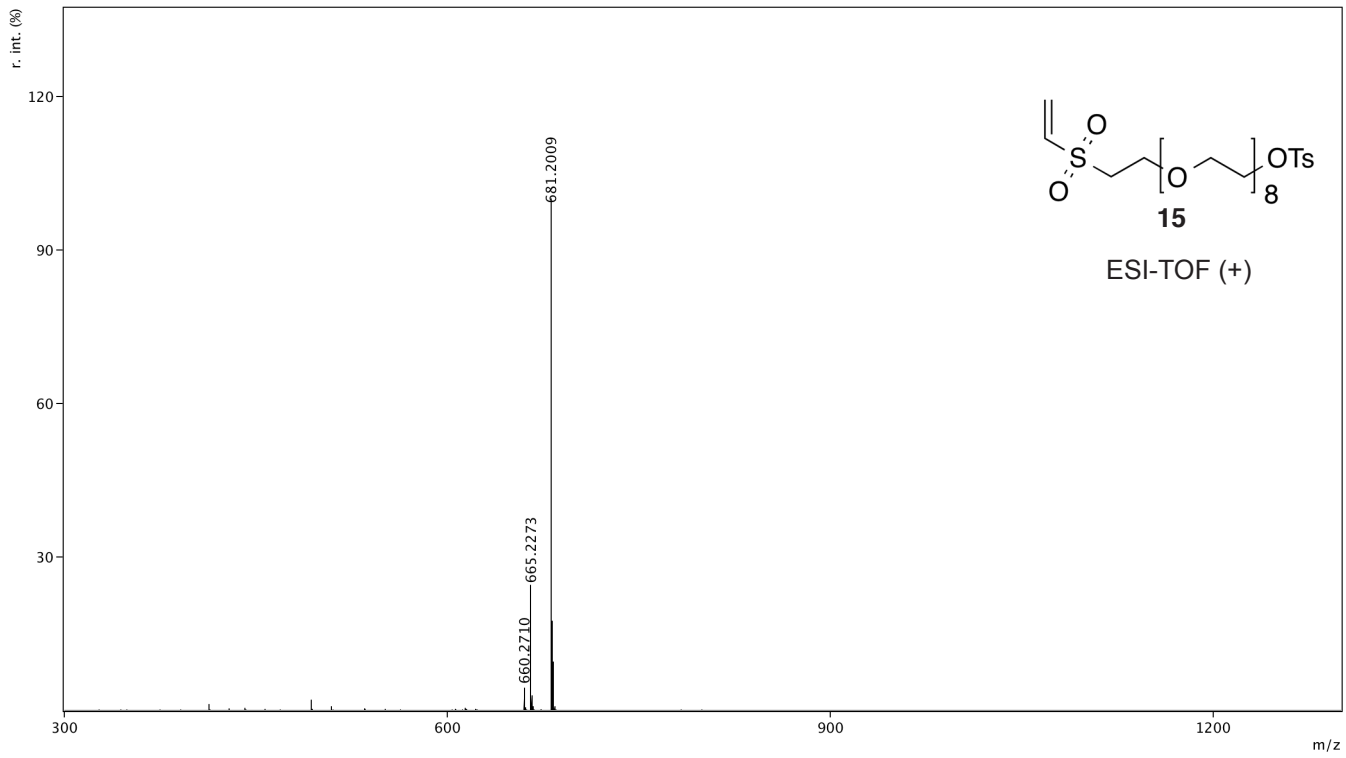

r. int. (%)
120
90
60
30
582.2614
1141.5353
1157.5083
300
600
900
1200
m/z
Trt
O
OTs
16
10
ESI-TOF (+)

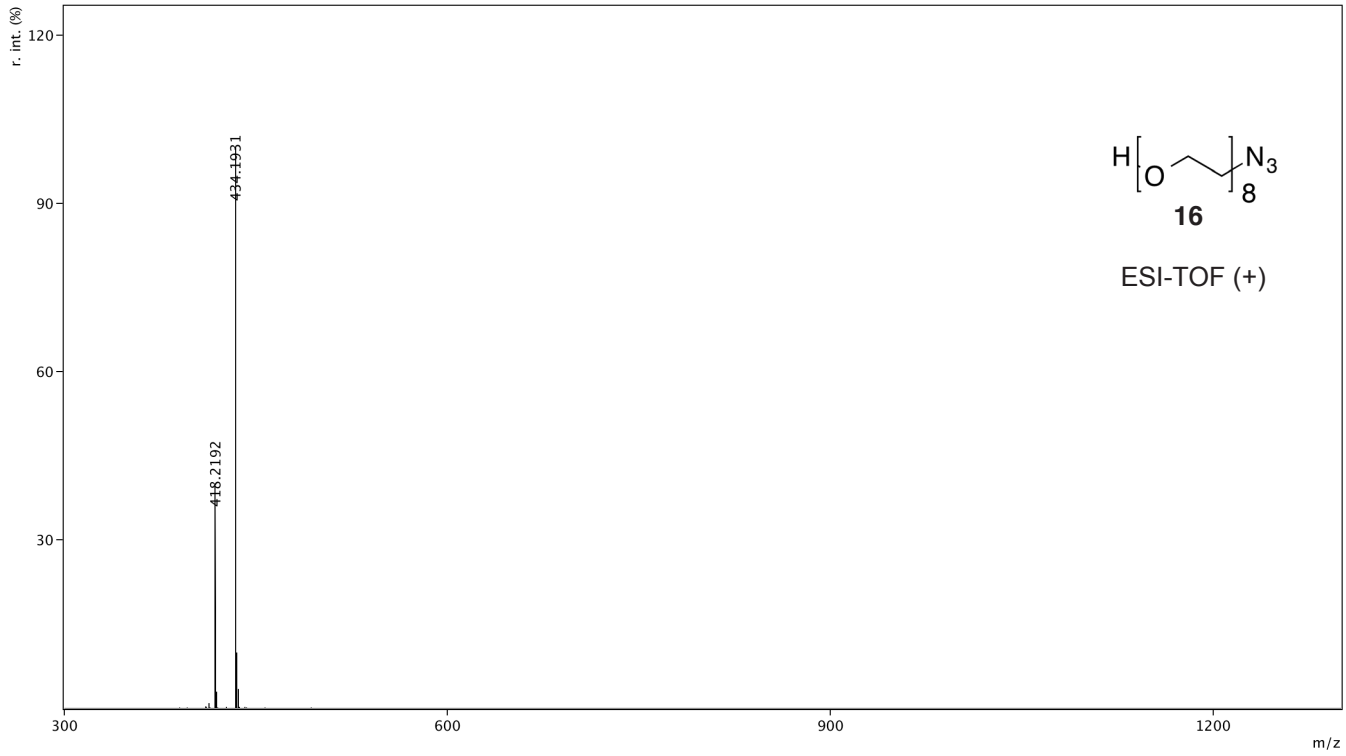

r. int. (%)
120
90
60
30
461.2079
469.1942
458.7269
477.1802
855.3984
871.3699
894.4689
899.4259
915.3999
300
600
900
1200
m/z
H
O
OTs
16
11
ESI-TOF (+)

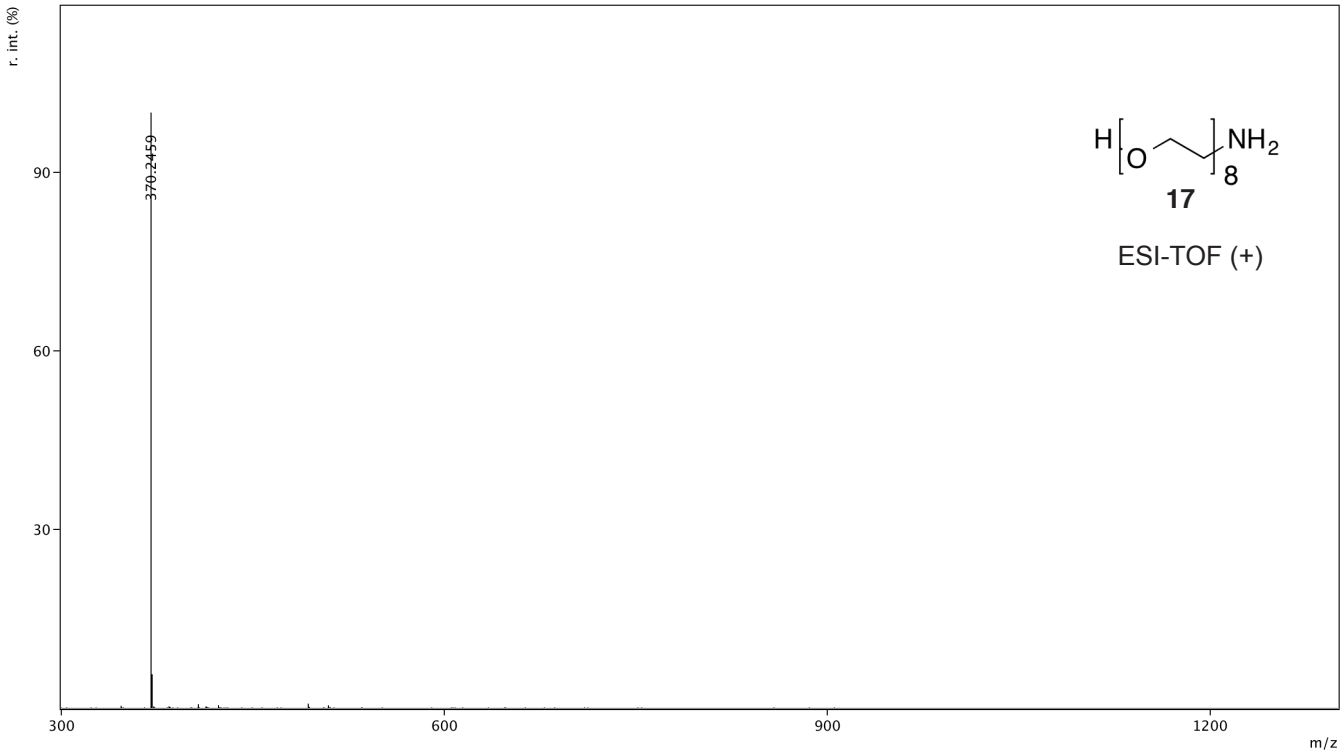

r. int. (%)
120
90
60
30
670.3463
675.3021
691.2758
300
600
900
1200
m/z
O
t-BuO
O
OTs
8
12
ESI-TOF (+)

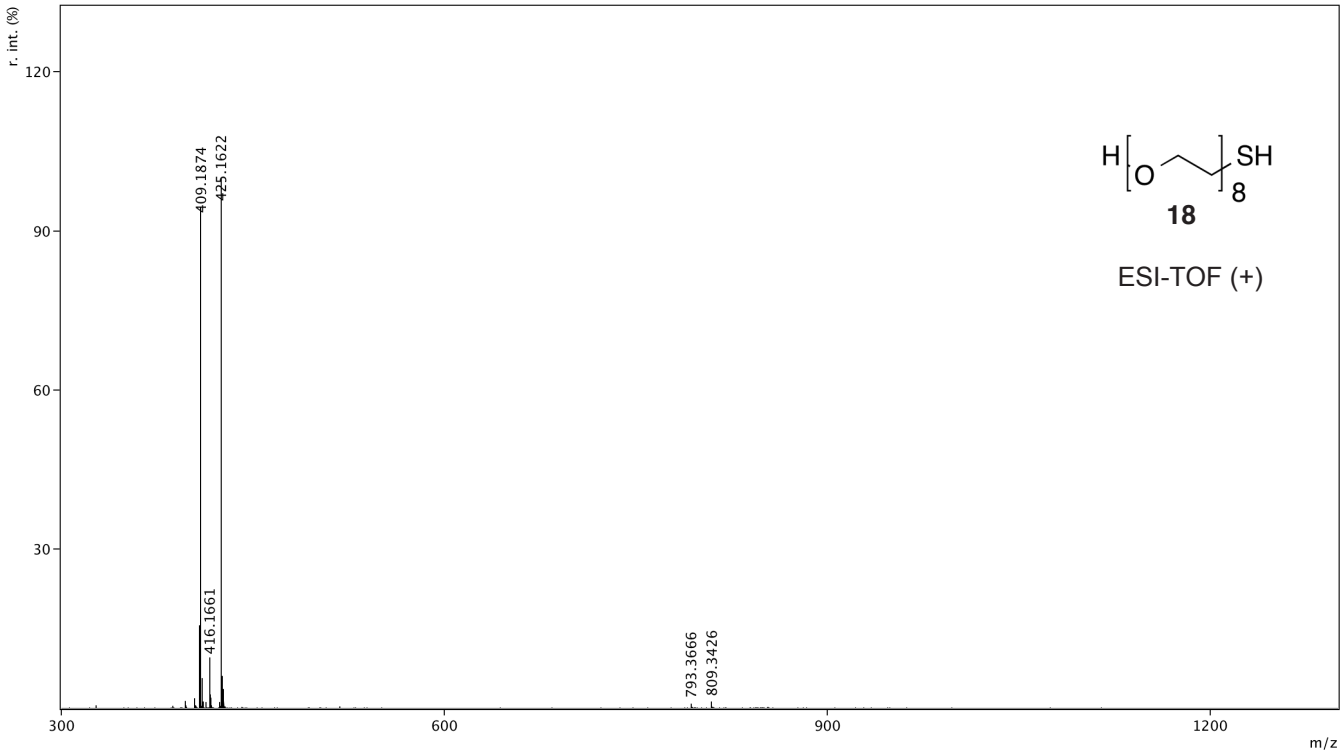

r. int. (%)
120
90
60
30
651.2448
635.2701
619.2173
603.2417
300
600
900
m/z
O
H
O
OTs
8
13
ESI-TOF (+)


r. int. (%)
120
90
60
30
595.2419
631.2181
653.1996
709.2332
1191.4904
1213.4738
300
600
900
1200
m/z
O
HO
O
OTs
8
14
ESI-TOF (–)


r. int. (%)
120
90
60
30
681.2009
665.2273
660.2710
300
600
900
1200
m/z
O
S
O
O
OTs
8
15
ESI-TOF (+)


r. int. (%)
120
90
60
30
434.1931
418.2192
300
600
900
1200
m/z
H
O
N3
8
16
ESI-TOF (+)


r. int. (%)
370.2459
90
60
30
300
600
900
1200
m/z
H
O
8
NH2
17
ESI-TOF (+)


r. int. (%)
120
409.1874
425.1622
90
60
416.1661
30
793.3666
809.3426
300
600
900
1200
m/z
H
O
8
SH
18
ESI-TOF (+)