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Electronic Supplementary Information

Multigram chromatography-free synthesis of octa(ethylene glycol) *p*-toluenesulfonate

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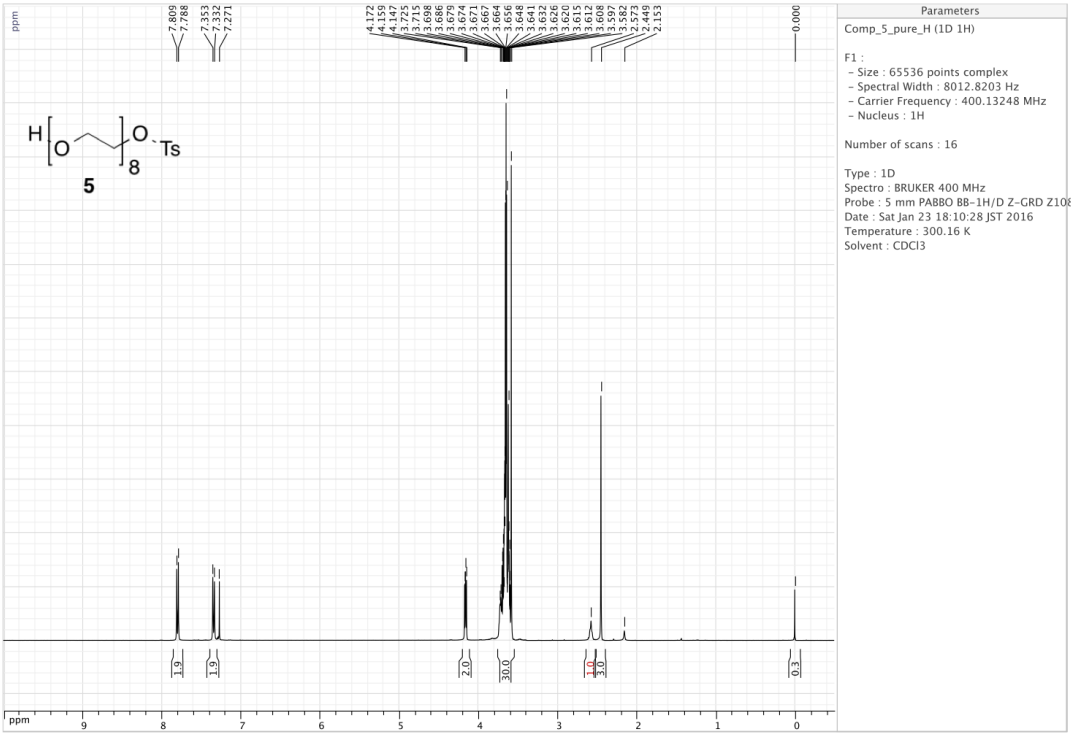
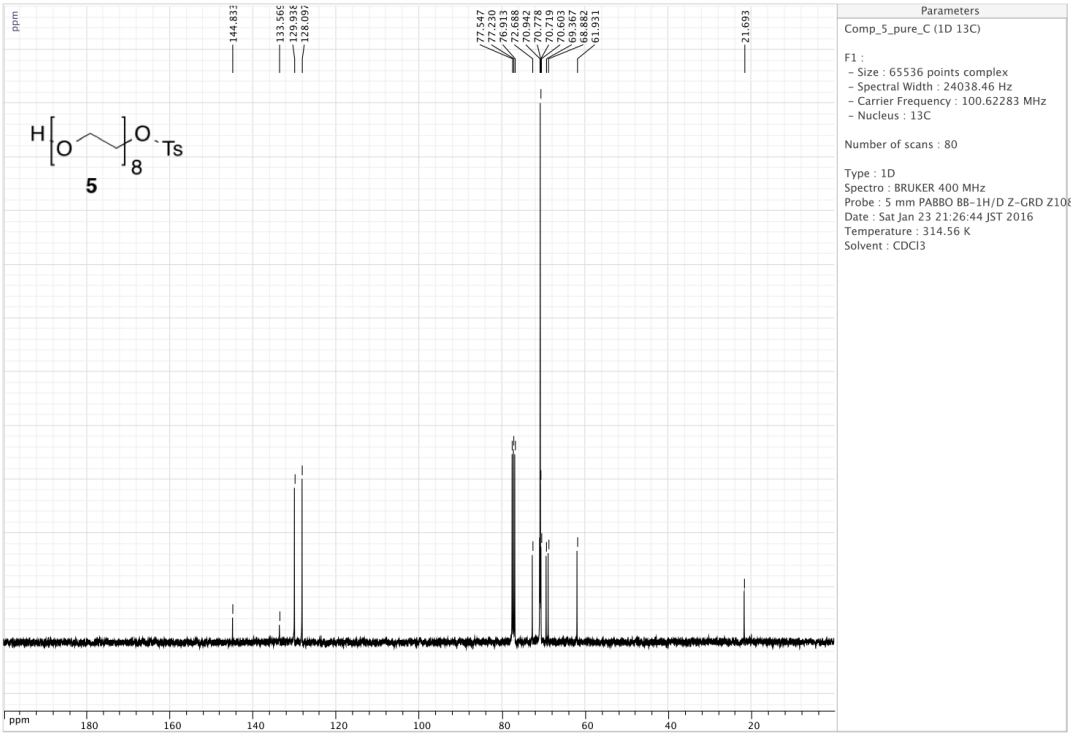
1. Analytical data for octa(ethylene glycol) *p*-toluenesulfonate (5)

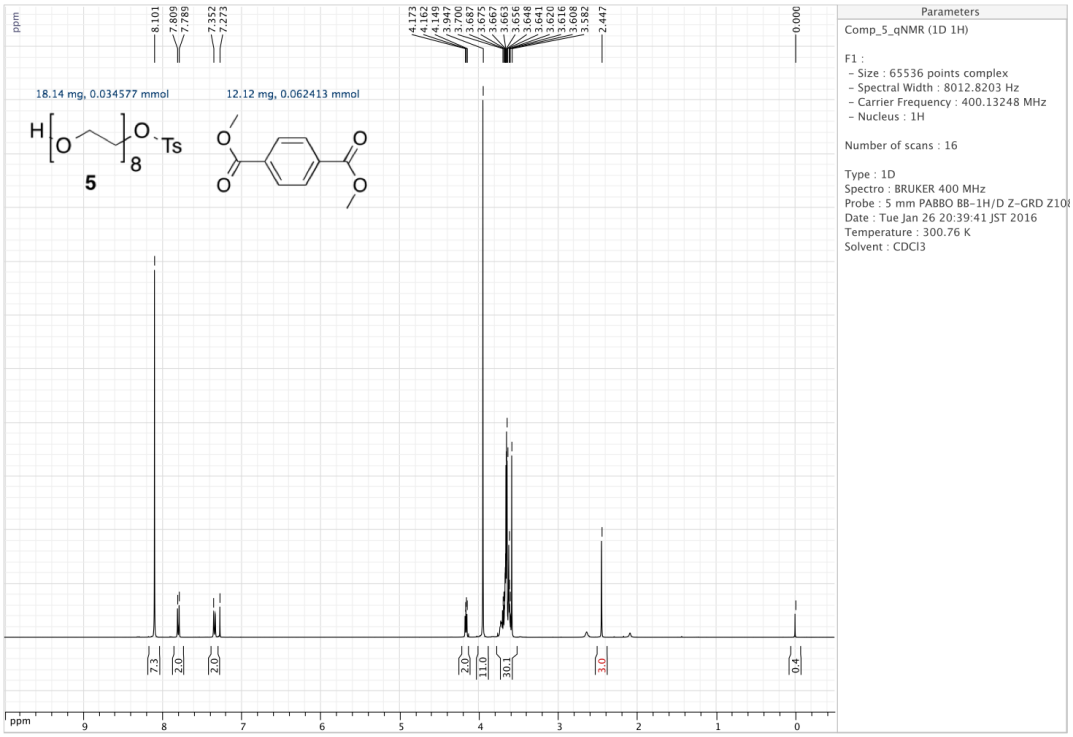
1.1 ^{1}H and ^{13}C NMR spectra



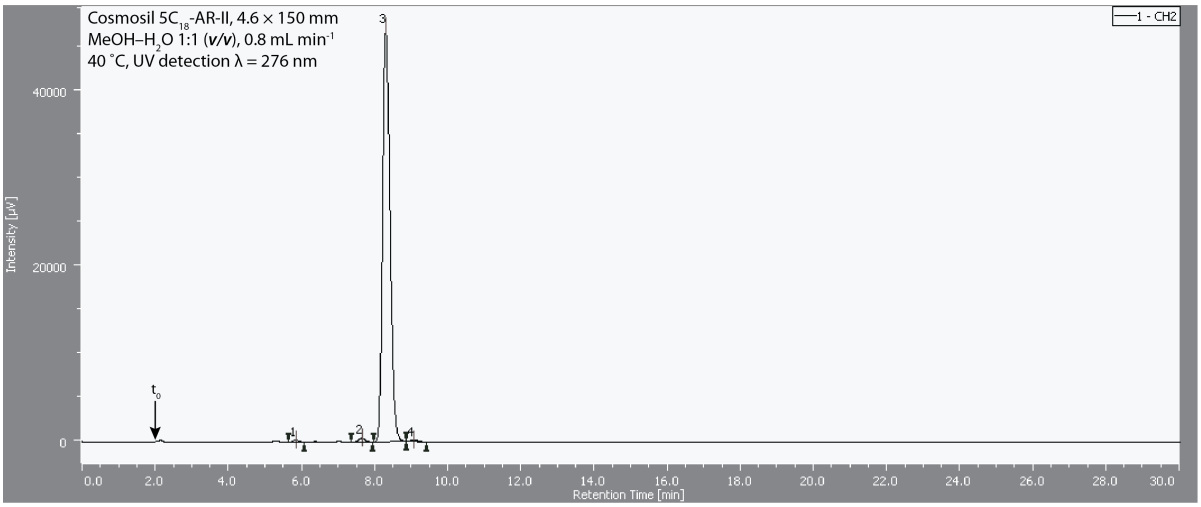


1.2 Quantitative NMR experiment (reference: dimethyl terephthalate)

Compound **5** (18.14 mg, 34.577 mmol) and dimethyl terephthalate (12.12 mg, 62.413 mmol) were dissolved in $CDCl_3$ (1 mL). ^1H NMR spectra (400 MHz) of the solution was recorded with relaxation delay D1 = 30 s. Molar ratio (by NMR): 1.8175; Molar ratio (weighted sample): 1.8050; purity calculated: 99.3%.



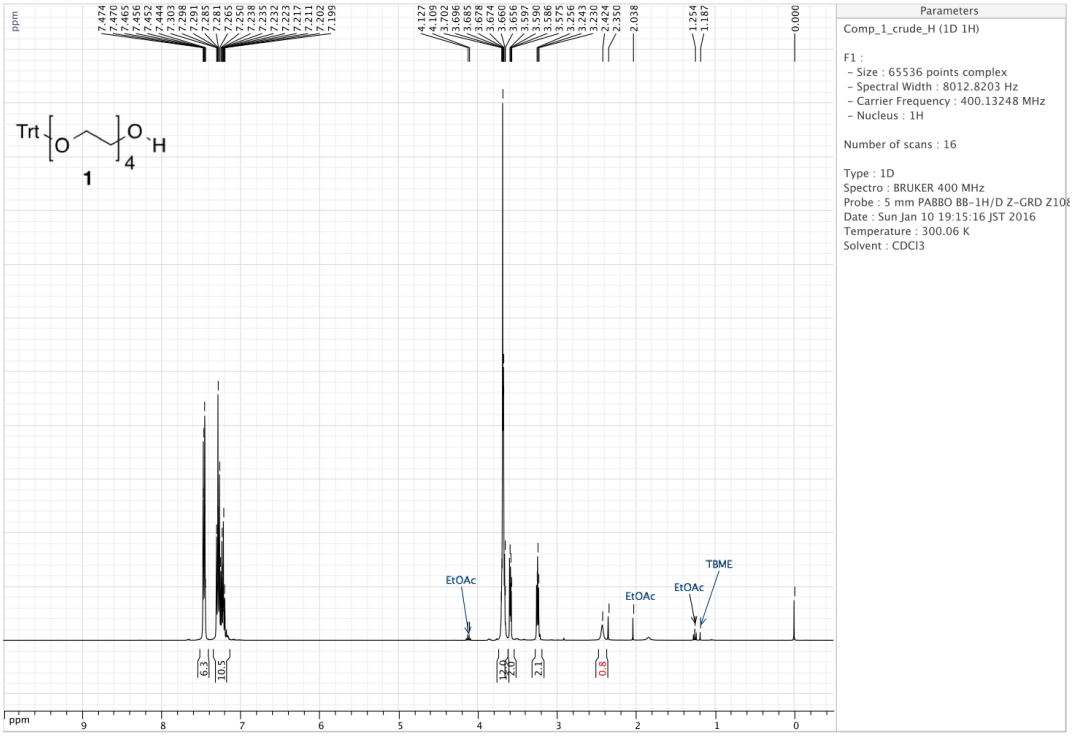
1.3 HPLC analysis of oligomeric purity



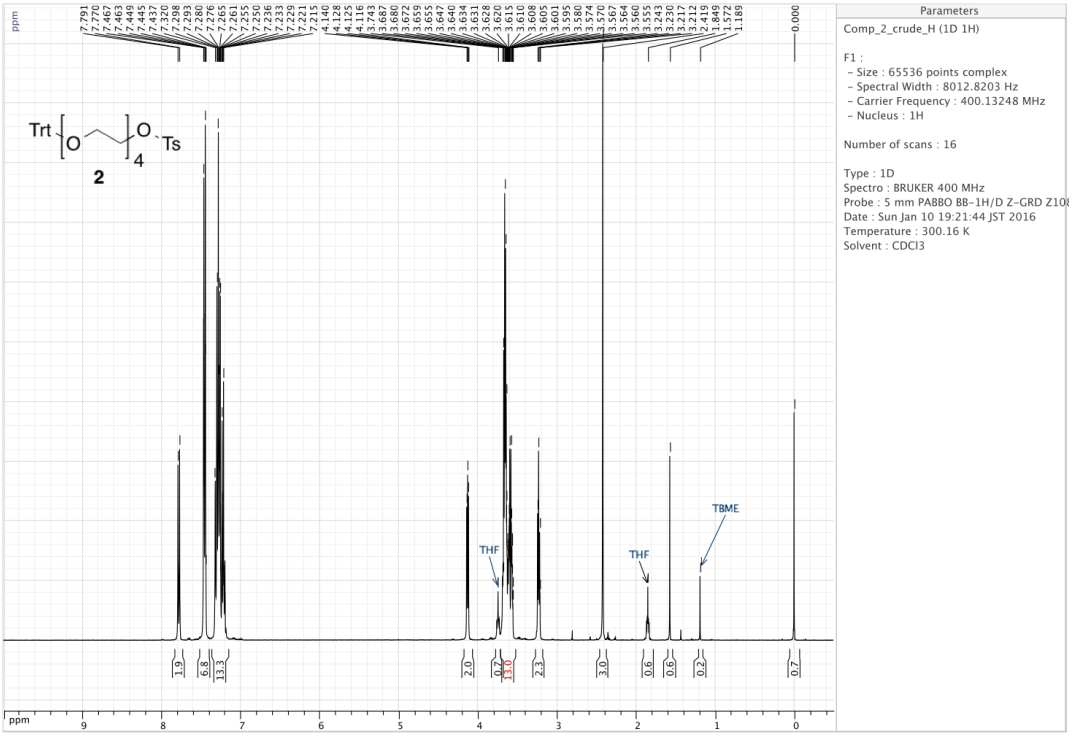
#	ピーク名	CH	tR	面積	高さ	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	2	5.842	2325	229	0.345	0.476	N/A	7470	6.185	1.075	
2	Unknown	2	7.650	5431	444	0.805	0.924	N/A	9381	1.897	1.051	
3	Unknown	2	8.300	663806	47156	98.427	98.151	N/A	7998	2.123	1.238	
4	Unknown	2	9.083	2850	215	0.423	0.448	N/A	9707	N/A	1.117	

2. ^{1}H NMR spectra of crude intermediate compounds

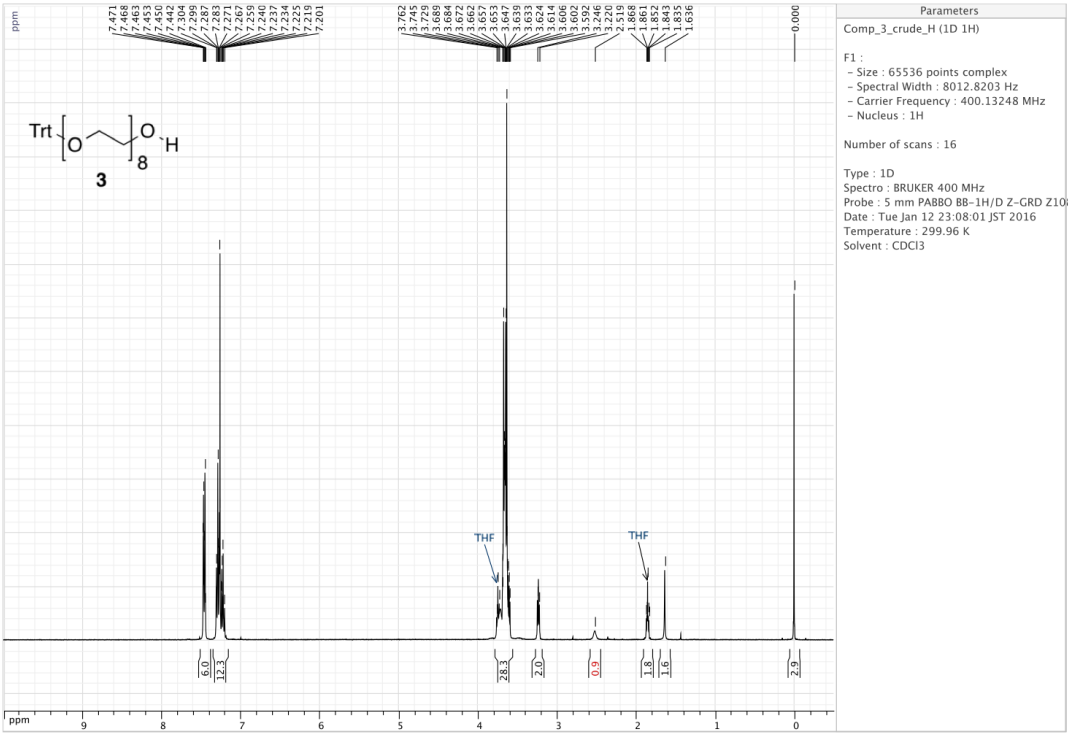
2.1 Tetra(ethylene glycol) trityl ether (**1**)



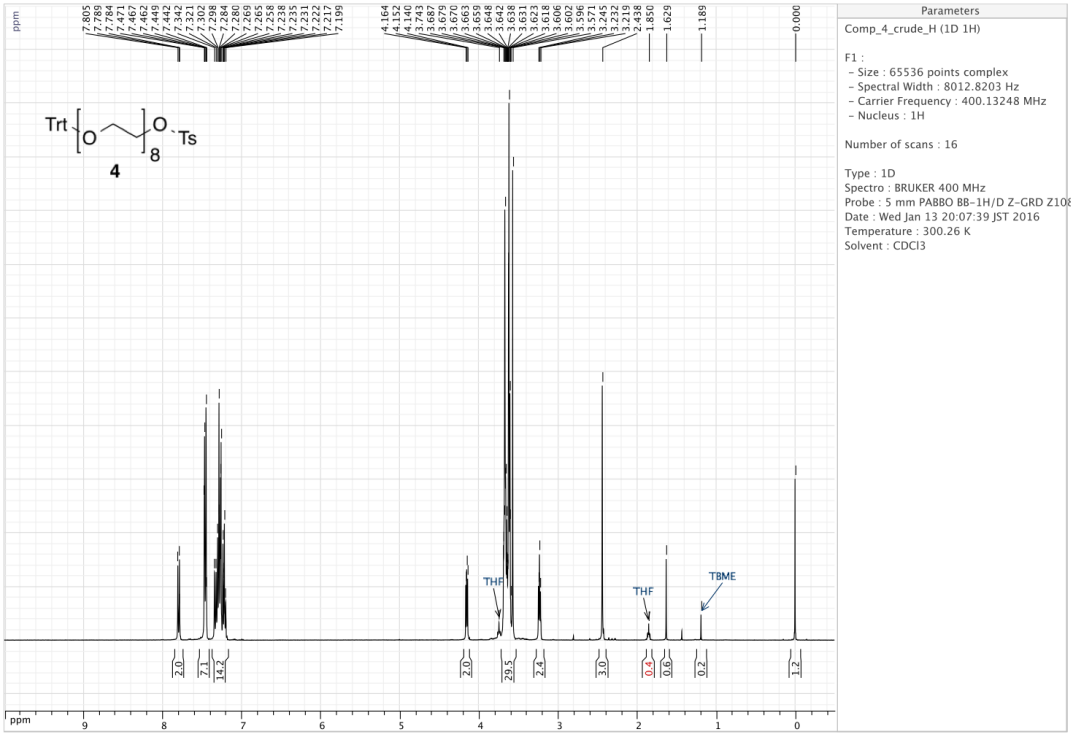
2.2 Tetra(ethylene glycol) trityl ether *p*-toluenesulfonate (**2**)



2.3 Octa(ethylene glycol) trityl ether (**3**)

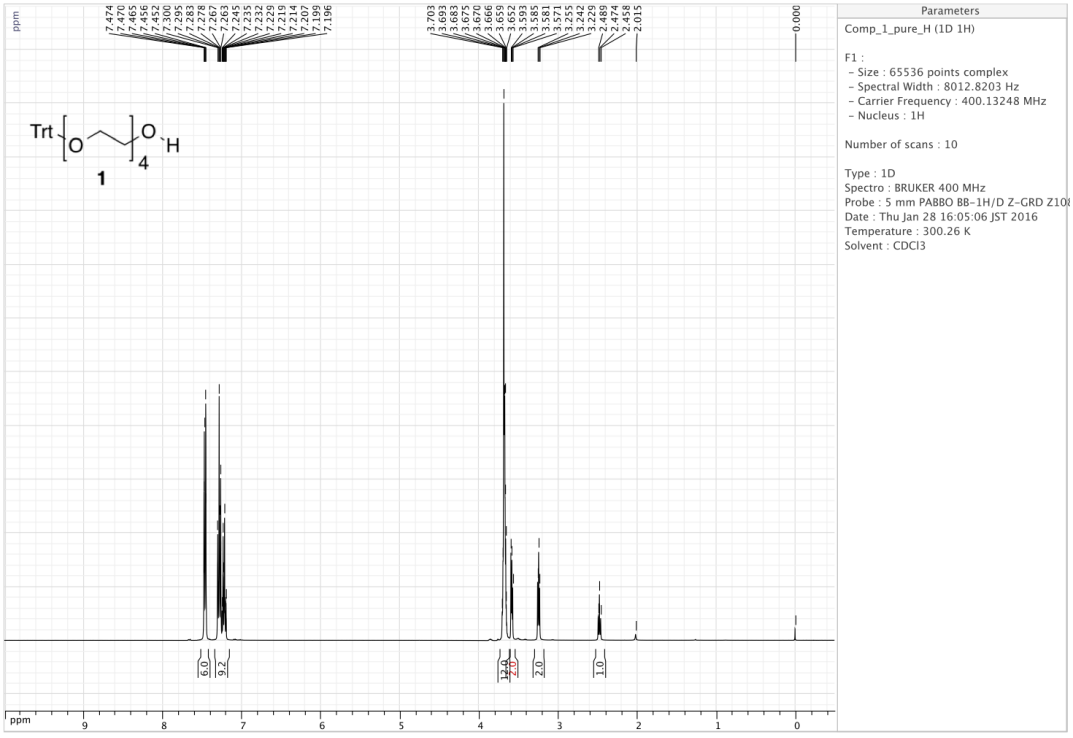


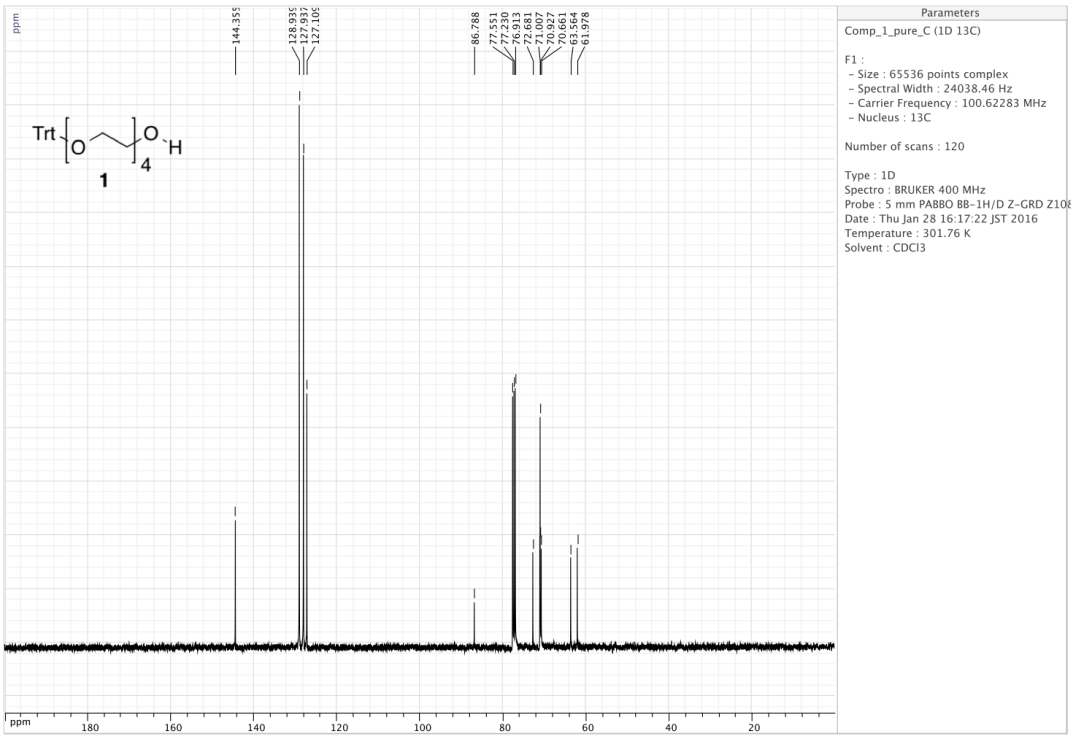
2.4 Octa(ethylene glycol) trityl ether *p*-toluenesulfonate (**4**)



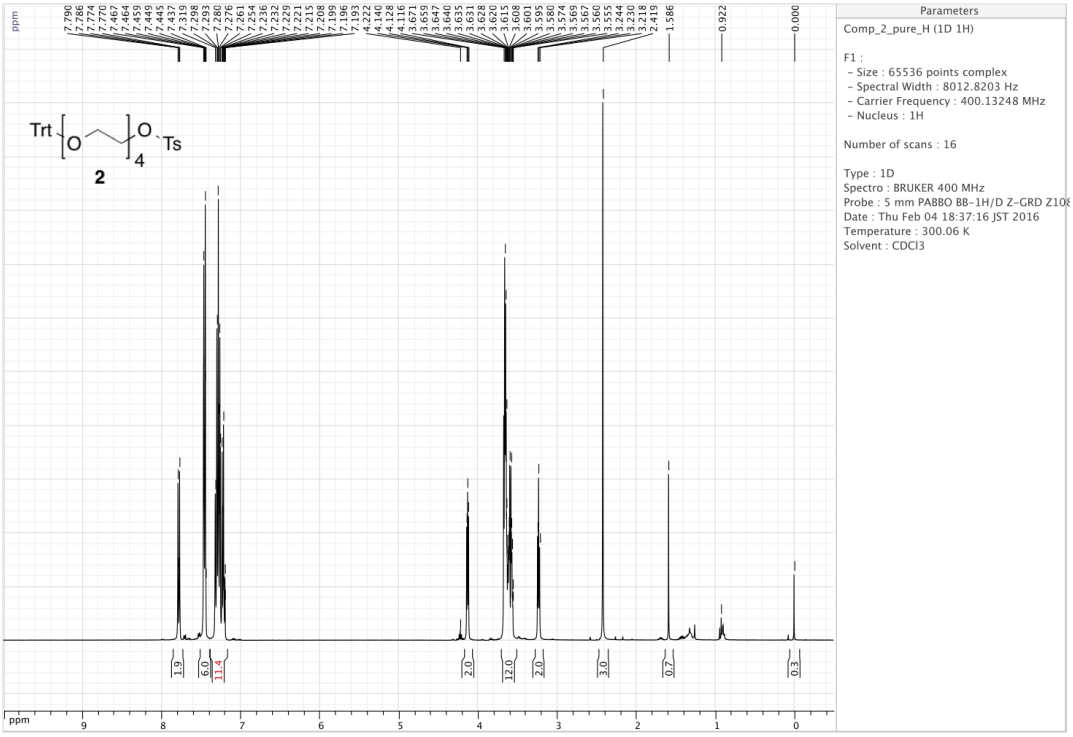
3. ^{1}H and ^{13}C NMR spectra of pure intermediate compounds

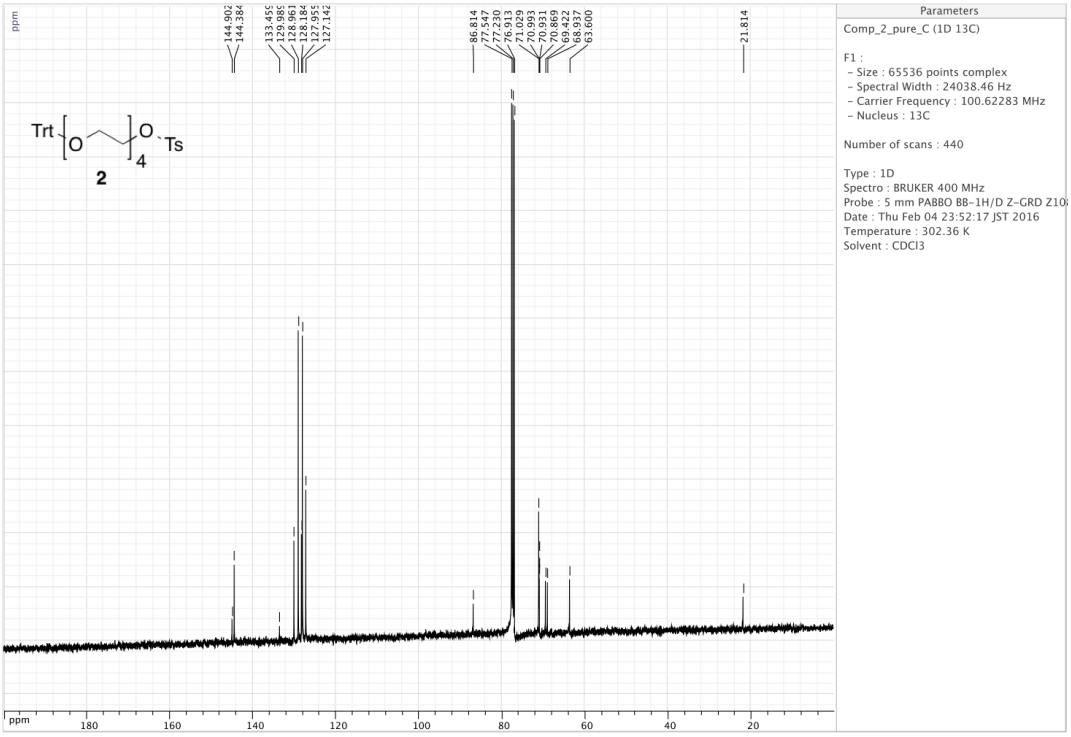
3.1 Tetra(ethylene glycol) trityl ether (**1**)



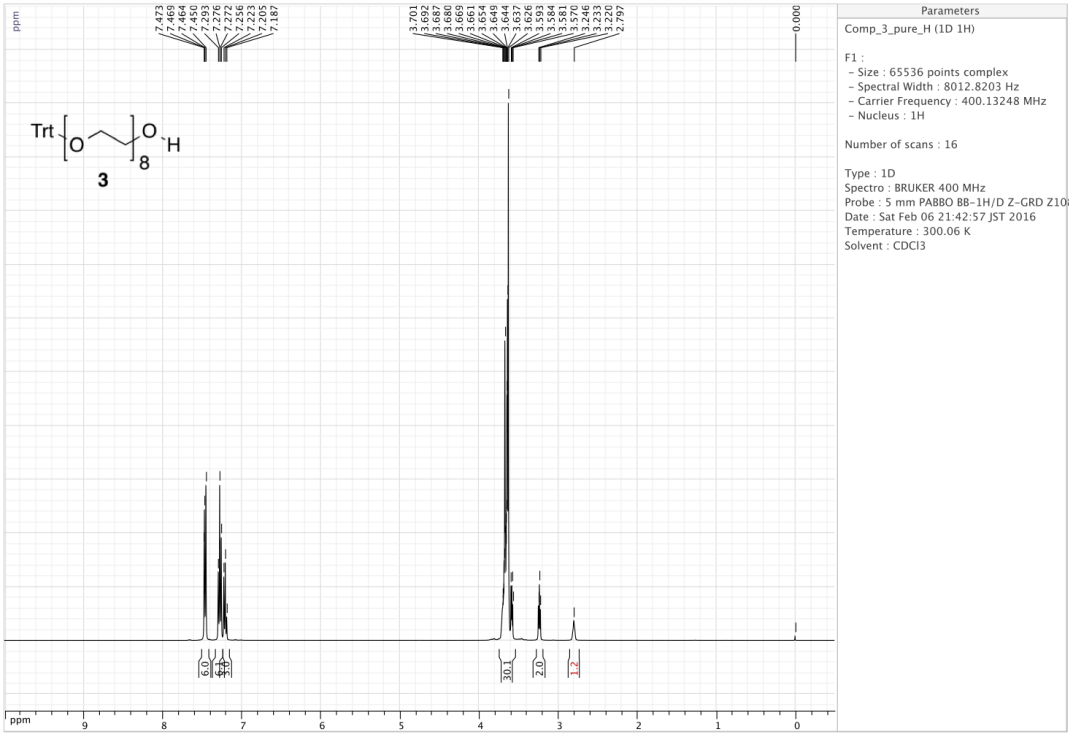


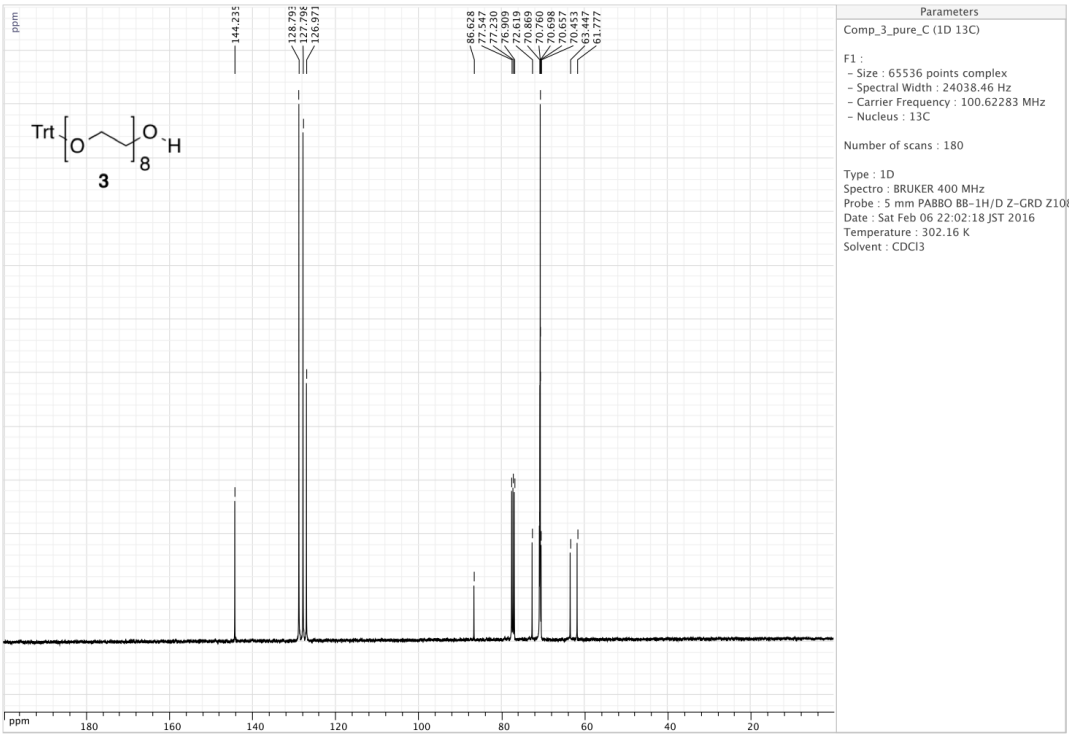
3.2 Tetra(ethylene glycol) trityl ether *p*-toluenesulfonate (**2**)



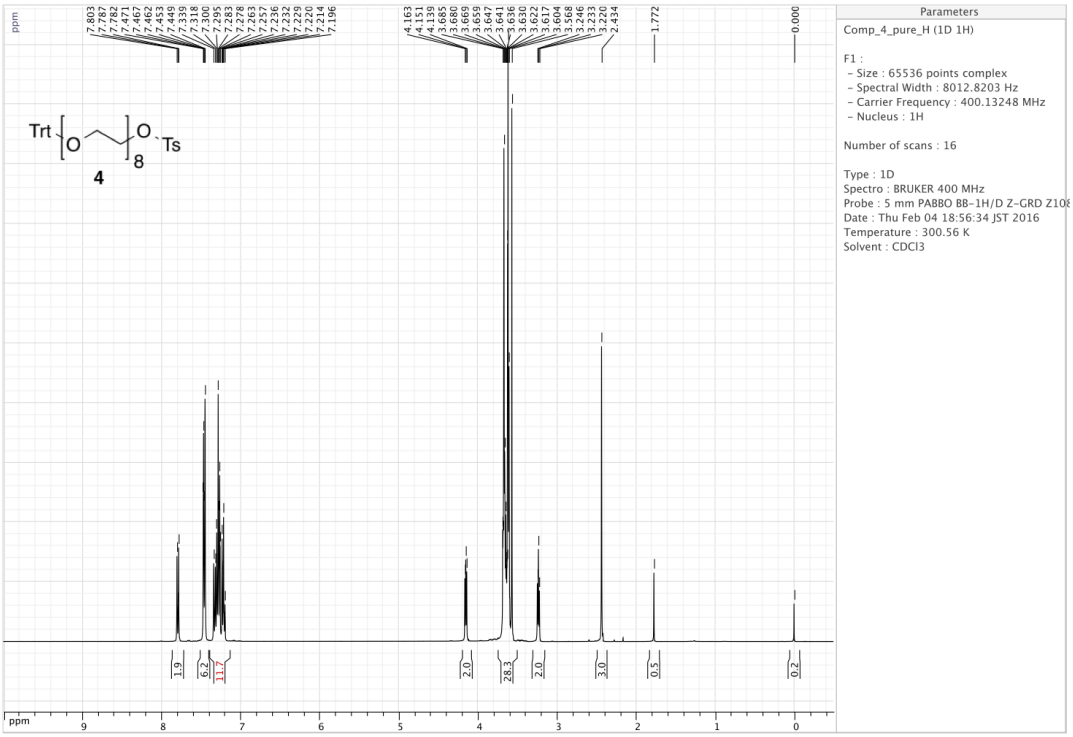


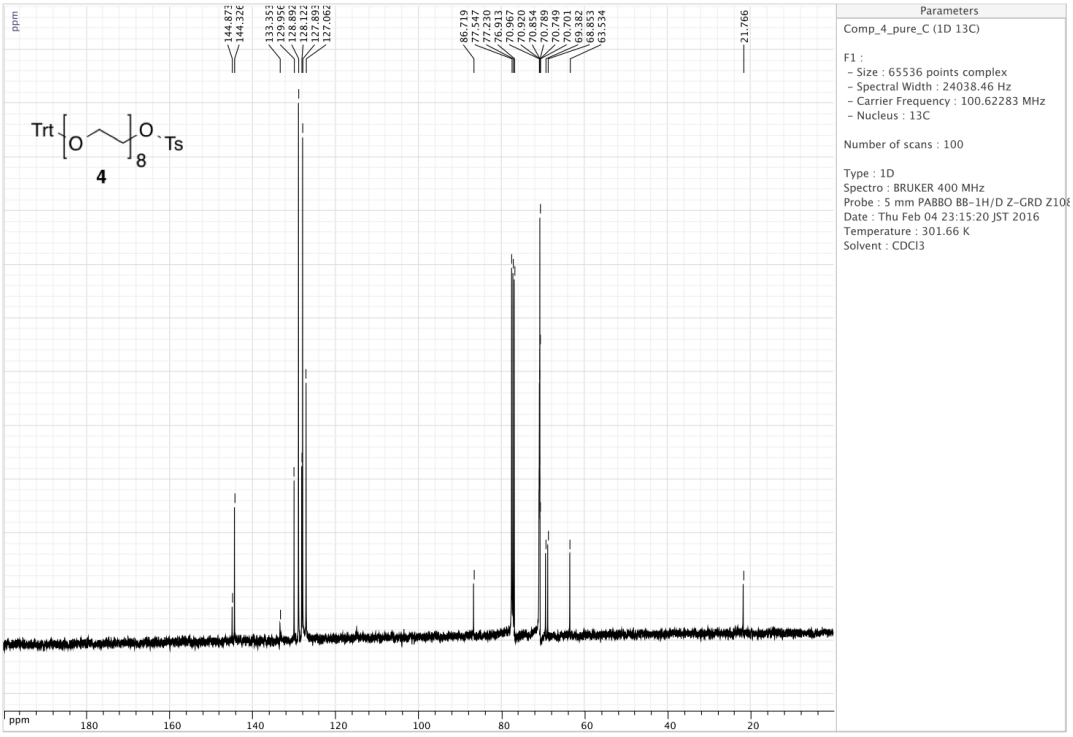
3.3 Octa(ethylene glycol) trityl ether (**3**)





3.4 Octa(ethylene glycol) trityl ether *p*-toluenesulfonate (**4**)





4. Independent procedure reproduction

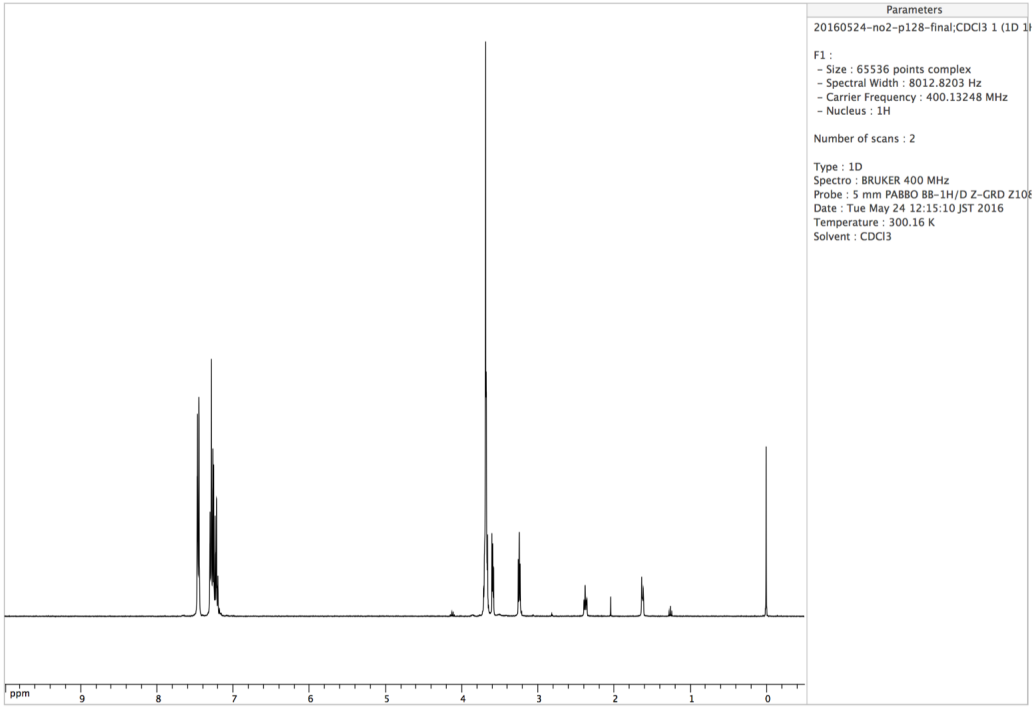
The above procedure was repeated on a 50% scale, starting from 12.5 g of trityl chloride. All amounts were reduced by half and the other parameters were maintained unchanged. Tetra(ethylene glycol) from the same lot was used.

Table S1: Products yields obtained during the procedure reproduction

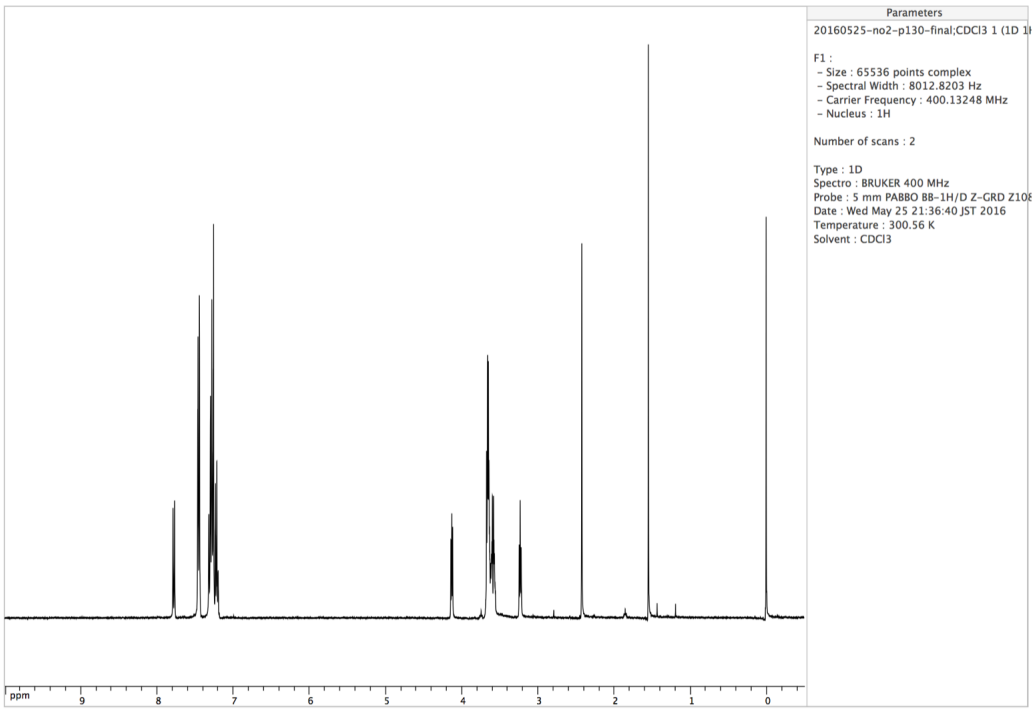
Reaction product	Expected yield	Obtained yield	^{1}H NMR
1	19.3–20.3 g	19.1 g	correct
2	25.0–26.0 g	25.0 g	correct
3	24.8–26.3 g	25.3 g	correct
4	30.0–31.8 g	30.6 g	correct
5	16.8–17.8 g	17.3 g	correct

The overall yield of the reproduced process was 73.5% (expected 71–76%) over 5 steps. The oligomer purity determined by HPLC was 98.3% (expected 98.4%). Below crude ^{1}H NMR spectra of compounds **1**–**4** and the data of the isolated final product **5** (^{1}H NMR and HPLC) are provided.

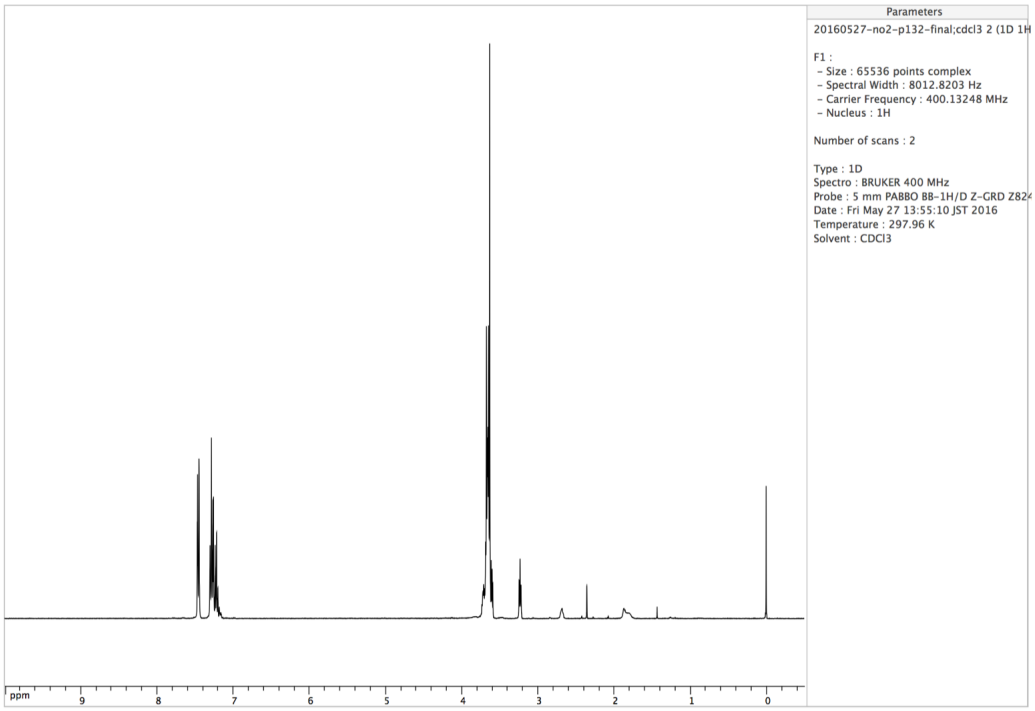
4.1 ^{1}H NMR of tetra(ethylene glycol) trityl ether (**1**)



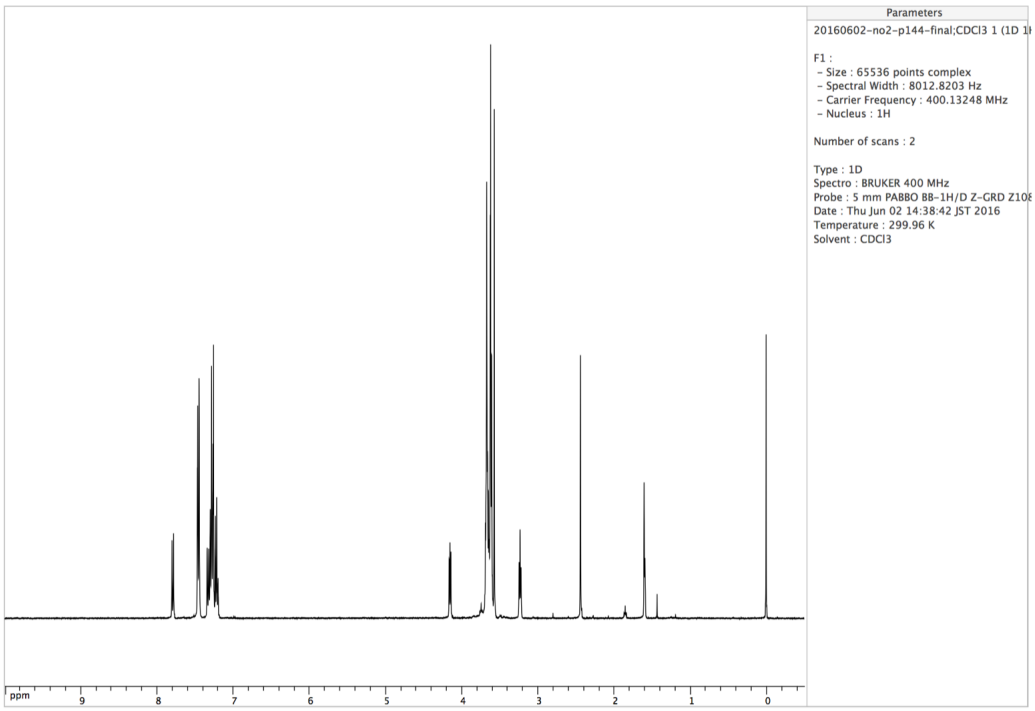
4.2 ^{1}H NMR of tetra(ethylene glycol) trityl ether *p*-toluenesulfonate (**2**)



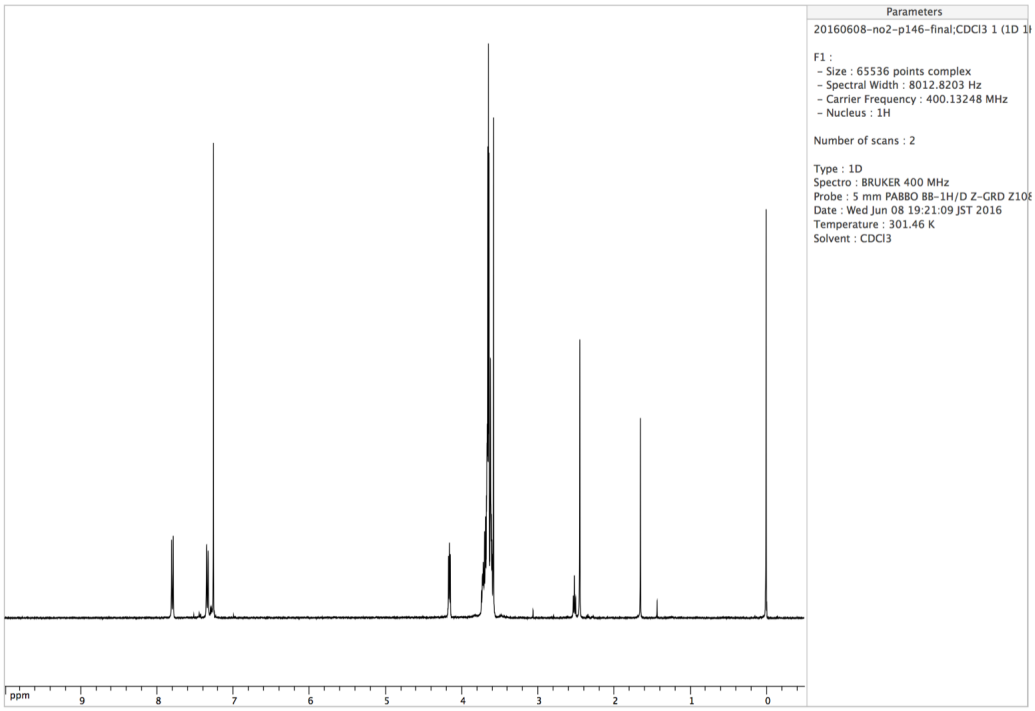
4.3 ^{1}H NMR of octa(ethylene glycol) trityl ether (**3**)



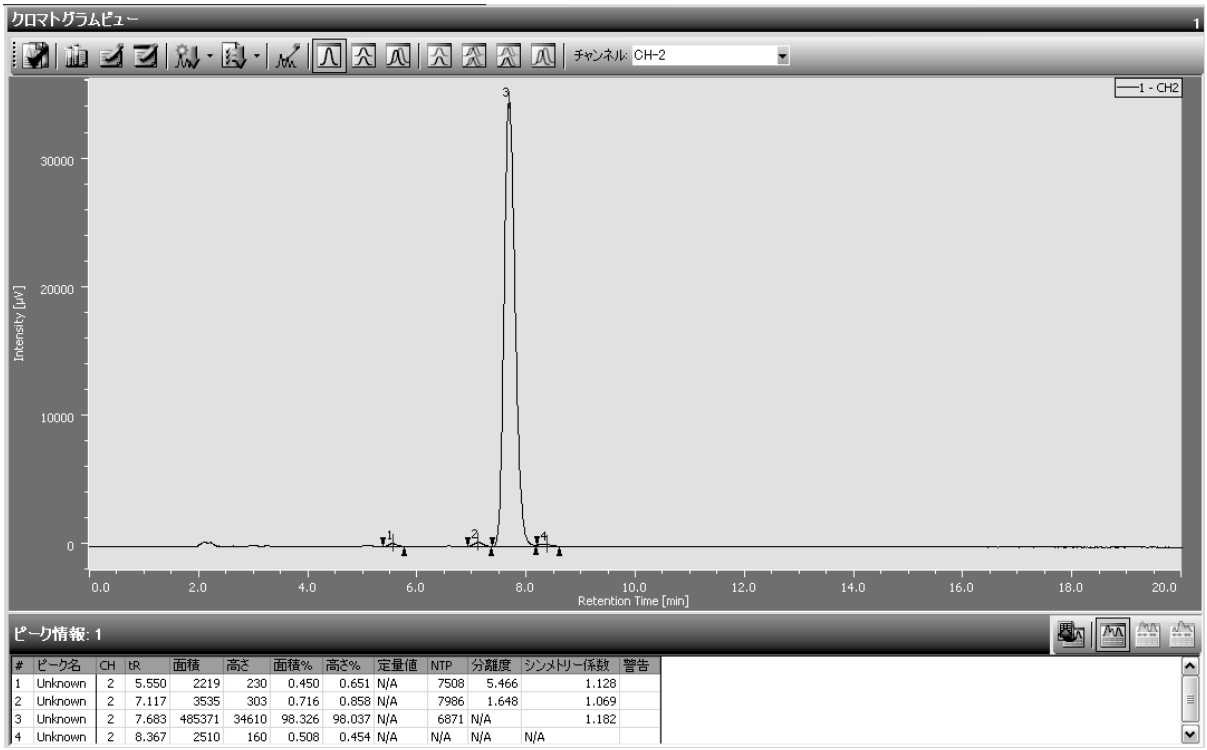
4.4 ^{1}H NMR of octa(ethylene glycol) trityl ether *p*-toluenesulfonate (**4**)



4.5 Octa(ethylene glycol) *p*-toluenesulfonate (**5**)



4.6 HPLC of octa(ethylene glycol) *p*-toluenesulfonate (**5**)



#	ピーク名	CH	tR	面積	高さ	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	2	5.550	2219	230	0.450	0.651	N/A	7508	5.466	1.128	
2	Unknown	2	7.117	3535	303	0.716	0.858	N/A	7986	1.648	1.069	
3	Unknown	2	7.683	485371	34610	98.326	98.037	N/A	6871	N/A	1.182	
4	Unknown	2	8.367	2510	160	0.508	0.454	N/A	N/A	N/A	N/A	

5. Detailed comments on octa(ethylene glycol) *p*-toluenesulfonate extraction process

In the final stage of compound **5** synthesis, the crude product is partitioned between ethyl acetate and brine. This process is repeated several times, until the desired compound is completely extracted from the aqueous layer. If only ethyl acetate and brine were present in the mixture, very likely just a single extraction would be sufficient. However, there is also a small volume of methanol remaining after the previous operation and this solvent, miscible with both ethyl acetate and water, decreases efficiency of the extraction process. Due to that several repeated extractions are usually required, as explained in the experimental part of the manuscript. Here we show quantitative experimental data regarding the partitioning process of **5** between ethyl acetate and brine.

A stock solution of compound **5** (1% *v*/*v*) in ethyl acetate (4 mL) was prepared. A sample (100 μL) of this solution was diluted with methanol (3.0 mL) and the UV absorbance spectrum of the diluted solution was recorded in range 240–300 nm in triplicate (reference sample "A"). Three samples of the stock solution (1.0 mL) were mixed with saturated brine, methanol and/or water as follows:

- Sample "B": saturated brine (0.5 mL);
- Sample "C": saturated brine (0.5 mL), methanol (0.1 mL);
- Sample "D": saturated brine (0.5 mL), methanol (0.1 mL), water (0.05 mL).

The mixtures were shaken well and, once the layers separated completely, samples of the organic layers (100 μL) were diluted with methanol (3.0 mL) and UV absorbance spectra of the diluted solutions were recorded.

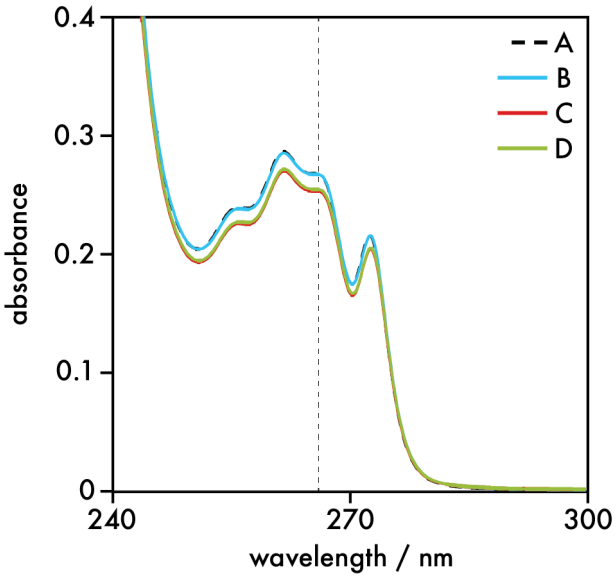


Figure S1: UV absorbance spectra of PEG_8-Ts before (A) and after washing with different aqueous solutions (B–D)

In order to visualize the residual concentrations of compound **5** in the analyzed solutions, UV absorption at 266 nm was compared. With respect to the reference sample "A" (A_{266} = 0.270 ± 0.001, 100%), the sample washed exclusively with brine was hardly affected by the process ("B", A_{266} = 0.267 ± 0.001, 98.8%), while the sample containing additional methanol ("C", A_{266} = 0.253 ± 0.001, 93.8%) contained lower concentration of the analyte. Interestingly, the presence of additional water–methanol mixture ("D", A_{266} = 0.256 ± 0.001, 94.8%) did not decrease the analyte concentration any further.

In summary, this experiment shows that the presence of methanol, remaining likely after incomplete evaporation under reduced pressure, decreases efficiency of the extraction process and additional repetition are required to collect all the product from the aqueous layer.