Iterative Synthesis of Monodisperse PEG Homostars and Linear Heterobifunctional PEG

Supplementary Information

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Contents

General Experimental Memoranda

^{1}H- and ^{13}C-NMR spectra were recorded on a Brüker AV-400 spectrometer. Chemical shifts in ppm are referenced with respect to residual solvent signals: δ_H ($CHCl_3$) 7.25 ppm, δ_H (CHD_2OD) 3.31 ppm; δ_C ($CDCl_3$) 77.50 ppm, δ_C (CD_3OD) 49.15 ppm. The splitting patterns for ^{1}H-NMR spectra are denoted as follows; s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), b (broad) and combinations thereof. Coupling constants (J) are in Hertz (Hz). ^{13}C-NMR assignments (C, CH, CH_2 and CH_3) and ^{1}H-NMR assignments, where given, were established with the aid of DEPT-135, HSQC and COSY experiments. $CDCl_3$ was purchased from *VWR* and CD_3OD from *Merck*. All NMR of Dmtr-derivatives was conducted in the presence of a small amount of Et_3N, and these purified compounds were always stored with a trace of added Et_3N. Mass spectra were recorded on *Micromass* MALDI micro MX, or *Micromass* LCT Premier (ESI) mass spectrometers. Reagents were purchased from *Sigma-Aldrich Ltd.* and used as supplied, except where specified: the HPLC assay supplied for tetragol (**1**) indicated *ca*. 99.2% purity, with 0.5% trigol and 0.2% pentagol; sublimed grade of KO*t*-Bu was used. Reactions were carried out under anhydrous conditions under a nitrogen atmosphere. Dichloromethane, acetonitrile, THF and DMF were dried and stored over baked 4Å molecular sieves. Triethylamine, diethyl ether, methanol, isopropanol and *N*-methyl imidazole were used as supplied. Flash chromatography was conducted in a 9 cm diameter, porosity 3 glass sinter funnel: Geduran® (Si 60) from *Merck* was used for normal phase columns, and *Merck* silanised silica for reverse phase columns. Thin layer chromatography was carried out using *Merck* silica gel 60 F_{254} aluminium-backed plates; compounds were visualised using UV light or $KMnO_4$ stain, $R_f \pm$ *ca.* 0.05.

Synthetic Procedures

(4,4'-Dimethoxytriphenylmethyl)tetra(ethylene glycol), 3.

Tetragol (**1**, 58.27 g, 300 mmol) was co-evaporated from anhydrous MeCN (3 × 80 mL) in a 1 L round-bottomed flask and was re-dissolved in MeCN (100 mL). To this was added triethylamine (12.5 mL, 90 mmol) followed by solid DmtrCl (20.31 g, 60 mmol). The reaction was stirred overnight and the next day concentrated aq. ammonia (2 mL), then silanised silica (200 mL) were added. With gentle swirling, the slurry was diluted by slow addition of water (1 L). The silica was collected in a large glass sinter and washed first with water (250 mL), then with water-MeCN (1:3, 750 mL + 1 mL conc. NH_3). The crude product was eluted from the silica with MeCN (750 mL), the solvent stripped off, and the oily residue co-evaporated from MeCN (3 × 80 mL).

The residue was re-dissolved in ether (750 mL). To this was added powdered anhydrous calcium chloride (150 g) and the suspension stirred vigorously overnight.[S1] The next day the solids were collected in a large sinter funnel, washing with further ether (250 mL), and discarding the filtrate; if any product is detected in the filtrate by TLC, re-treat the filtrate with calcium chloride. The solids were placed in a 3 L beaker and the inorganic material dissolved in water (2L + 2 mL conc. NH_3). Silanized silica was added (160 mL) and, after gentle stirring, the silica was collected in a large sinter funnel. The silica was washed with water (250 mL), then water-MeCN (3:1, 250 mL), discarding the filtrate, and finally the pure product was washed from the silica with MeCN (750 mL + 0.5 mL Et_3N; on a smaller scale extraction into CH_2Cl_2 is more practical. The MeCN was evaporated, and the residue re-evaporated from MeCN (3 × 80 mL), to give the *title compound* (27.77 g, 95%).

R_f(EtOH-$CHCl_3$ 1:19 + trace Et_3N) **3** 0.42; DmtrO-Peg$_4$-ODmtr 0.74. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (bd, *J*=7.5, 2H), 7.38 (d, *J*=8.8, 4H), 7.30 (bt, *J*=7.5, 2H), 7.22 (bt, *J*=7.3, 1H), 6.85 (d, *J*=8.8, 4H), 3.80 (s, 6H), 3.74-3.68 (m, 12H), 3.61 (t, *J*=4.6, 2H), 3.26 (t, *J*=5.2, 2H), 2.71 (t, *J*=6.1, 1H, O***H***). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.38 (2C), 145.10 (1), 136.33 (2C) (5×Dmtr ***C***), 130.08 (4C), 128.21 (2C), 127.76 (2C), 126.67 (1C), 113.04 (4C) (13×Dmtr ***C***H), 85.95 (Dmtr Ar$_3$***C***O), 72.53 (O***C***H$_2$CH$_2$OH), 70.76 (2C), 70.72 (2C), 70.41 (1C) (5×***C***H$_2$O), 63.15 (***C***H$_2$ODmtr), 61.74 (OCH$_2$***C***H$_2$OH), 55.21 (2×O***C***H$_3$). *m/z* (ESI+) $[M+H]^+$ = 519.2349, calc. $C_{29}H_{36}NaO_7^+$ = 519.2359.

(4,4'-Dimethoxytriphenylmethyl)tetra(ethylene glycol) toluenesulfonate, 4.

Dmtr-tetragol (**3**, 28.36 g, 57.1 mmol) was evaporated from acetonitrile (3 × 50 mL) in a 500 mL round-bottomed flask and was re-dissolved in CH_2Cl_2 (180 mL). To this was added first Et_3N (15.9 mL, 114 mmol) then *p*-toluene sulfonyl chloride (14.13 g, 74.3 mmol) and the reaction was stirred over night. The next day the CH_2Cl_2 was stripped off under reduced pressure and the resultant oil washed from the flask into a 2 L conical flask with isopropanol (600 mL). To this was added triethylamine (16 mL), then *N*-methylimidazole (16 mL) and finally water (200 mL). After stirring vigorously for 2 hr, silanised silica (250 mL) was added followed by slow addition of water (1 L) and the silica was collected in a large sinter funnel. The silica was washed with water (1 L) and the filtrate discarded. The silica was then washed with 95% MeCN-water (1.5 L) and the filtrate concentrated *in vacuo* to give the *title compound* as a pale yellow oil (32.85 g, 88%).

R_f (EtOH-$CHCl_3$ 1:19 + trace Et_3N) 0.69. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.81 (d, *J*=8.3, 2H), 7.49 (dd, *J*=7.4, 1.3, 2H), 7.37 (d, *J*=8.9, 4H), 7.34 (d, *J*=8.1, 2H), 7.29 (bt, *J*=7.6, 2H), 7.21 (bt, *J*=7.2, 1H), 6.84 (d, *J*=8.9, 4H), 4.15 (t, *J*=4.9, 2H), 3.80 (s, 6H), 3.68-3.58 (m, 12H), 3.25 (t, *J*=5.2, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.40 (2C), 145.11 (1C) (3×Dmtr $\boldsymbol{C}$), 144.81 (Ts $\boldsymbol{C}$), 136.32 (2×Dmtr $\boldsymbol{C}$), 132.97 (Ts $\boldsymbol{C}$), 130.08 (4×Dmtr $\boldsymbol{C}$H), 129.84 (Ts $\boldsymbol{C}$H), 128.21 (2×Dmtr $\boldsymbol{C}$H), 127.97 (Ts $\boldsymbol{C}$H), 127.76 (2C), 126.68 (1C), 113.04 (4C) (7×Dmtr $\boldsymbol{C}$H), 85.92 (Dmtr $Ar_3\boldsymbol{C}O$), 70.75 (4C), 70.61 (1C) (5×$\boldsymbol{C}H_2O$), 69.28 ($\boldsymbol{C}H_2OTs$), 68.67($\boldsymbol{C}H_2O$), 63.13 ($\boldsymbol{C}H_2$ODmtr), 55.21 (2×O$\boldsymbol{C}H_3$), 21.64 (Ts $\boldsymbol{C}H_3$). *m/z* (ESI+) $[M+H]^+$ = 673.2416, calc. $C_{36}H_{42}O_9S^+$ = 673.2447.

(4,4'-Dimethoxytriphenylmethyl)octa(ethylene glycol), 5.

Dmtr-tetragol tosylate (**4**, 32.85 g, 50.5 mmol) and tetragol (**1**, 110.9 g, 571 mmol) were co-evaporated from acetonitrile (3 × 100 mL) in a 1 L round-bottomed flask. The resultant oil was re-dissolved in DMF (220 mL) and potassium *tert*-butoxide (9.64 G, 86 mmol) was added. The next day saturated ammonium chloride (25 mL) was added and the mixture was transferred to a 2 L conical flask. To this mixture were added first silanised silica (300 mL), then slowly water (1.5 L) and the silica was collected in a large sinter funnel. The silica was washed first with water (1 L) followed by MeCN-water (1:4, 1 L + a little conc. ammonia) and the washings discarded. Finally the silica was washed with acetone-water (19:1, 1.7 L + a trace Et_3N), the filtrate concentrated in vacuo, and the residual oil co-evaporated from MeCN (3 × 300 mL). The crude product (31.83 g) was fractionated by normal phase chromatography in two batches. Half the crude product was loaded onto a column of flash silica (250 mL) in a large sinter funnel which was eluted with a gradient of EtOH-CH_2Cl_2 (1:199 to 9:191 v/v, containing a trace of Et_3N), and this procedure was repeated on the second batch. Combining appropriate fractions, recovered starting material (**4**, 3.79 g, 11.5 %), DmtrO-Peg$_{12}$-ODmtr (1.24 g, 3.7%) and the *title compound* (**5**, 23.63 g, 61.4%) were all isolated as pale yellow oils. This procedure may be conducted on three times the scale with ease to obtain crude product that is then purified chromatographically as required.

R_f (EtOH-$CHCl_3$ 1:19 + trace Et_3N) **5** 0.33; Dmtr-OPeg$_{16}$O-Dmtr 0.40.^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (dd, *J*=7.2, 1.4, 2H), 7.33 (d, *J*=8.8, 4H), 7.25 (t, *J*=7.5, 2H), 7.17 (t, *J*=7.3, 1H), 6.80 (d, *J*=8.9, 4H), 3.76 (s, 6H), 3.69 (t, *J*=9.2, 2H), 3.67-3.62 (m, 26H), 3.58 (t, *J*=9.2), 3.21 (t, *J*=5.3, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.35 (2C), 145.07 (1C), 136.32 (2C) (5×Dmtr $\boldsymbol{C}$), 130.03 (4C), 128.18 (2C), 127.69 (2C), 126.60 (1C), 112.99 (4C) (13×Dmtr $\boldsymbol{C}$H), 85.88 (Dmtr $Ar_3\boldsymbol{C}O$), 72.60 (O$\boldsymbol{C}H_2CH_2OH$), 70.73 (1C), 70.70 (1C), 70.67 (1C) 70.63 (1C), 70.58 (2C), 70.53 (6C), 70.32 (1C) (13×$\boldsymbol{C}H_2O$), 63.11 ($\boldsymbol{C}H_2$ODmtr), 61.53 ($OCH_2\boldsymbol{C}H_2OH$), 55.14 (2×O$\boldsymbol{C}H_3$). *m/z* (ESI+) $[M+Na]^+$ = 695.3405, calc. $C_{37}H_{53}O_{11}Na^+$ = 695.3407.

(4,4'-Dimethoxytriphenylmethyl)octa(ethylene glycol) toluenesulfonate, 6.

Dmtr-octagol (**5**, 5.85 g, 8.70 mmol) was evaporated from acetonitrile (3 × 20 mL) in a 100 mL round-bottomed flask and then re-dissolved in CH_2Cl_2 (36 mL). To this was added first Et_3N (2.43 mL, 17.4 mmol) followed by *p*-toluene sulfonyl chloride (2.152 g, 11.3 mmol) and the reaction was stirred for 72 hr at RT. Following this the CH_2Cl_2 was stripped off under reduced pressure, and to the resultant oil in a 1 L conical flask were added isopropanol (70 mL), Et_3N (1 mL), *N*-methylimidazole

(2 mL) and finally water (70 mL). After stirring vigorously for 2 hr, silanized silica (47 mL) was added followed by slow addition of water (900 mL), and the silica was collected in a large sinter funnel. The silica was washed with MeCN-water (1:2 v/v, 600 mL) and the filtrate discarded. The silica was then washed with MeCN-water (750 mL, 1:19 v/v) and the filtrate concentrated *in vacuo* to give the *title compound* (**6**, 7.29 g, 101%) as a pale yellow oil.

R_f (EtOH-CHCl$_3$ 1:19 + trace Et$_3$N) 0.53. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.80 (d, *J*=8.3, 2H), 7.46 (dd, *J*=7.7, 1.4, 2H), 7.37-7.33 (m, 6H), 7.28 (t, *J*=7.5, 2H), 7.20 (tt, *J*=7.2, 1.0, 1H), 6.82 (d, *J*=9.0, 4H), 4.16 (t, *J*=4.9, 2H), 3.79 (s, 6H), 3.69-3.61 (m, 24H), 3.58 (s, 4H), 3.23 (t, *J*=5.2, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 158.37 (2C), 145.08 (1C) (3×Dmtr ***C***), 144.75 (Ts ***C***), 136.33 (2×Dmtr ***C***), 133.03 (Ts ***C***), 130.05 (4×Dmtr ***C***H), 129.80 (Ts ***C***H), 128.20 (2×Dmtr ***C***H), 127.96 (Ts ***C***H), 127.71 (2C), 126.62 (1C), 113.02 (4C) (7×Dmtr ***C***H), 85.91 (Dmtr Ar$_3$***C***O), 70.72 (3C), 70.69 (1C), 70.64 (1C), 70.59 (2C), 70.54 (5C), 70.50 (1C) (13×***C***H$_2$O), 69.23 (***C***H$_2$OTs), 68.66 (***C***H$_2$O), 63.14 (***C***H$_2$ODmtr), 55.18 (2×O***C***H$_3$), 21.62 (Ts ***C***H$_3$). *m/z* (ESI+) [M+Na]$^+$ = 849.3512, calc. $C_{44}H_5NaO_{13}S^+$ = 849.3496.

Tris-1,3,5-[(4,4'-dimethoxytriphenylmethyl)octa(ethylene glycol)methyl]benzene, 7.

Dmtr-octagol (**5**, 9.284 g, 13.8 mmol) in a 1 L round bottomed flask was evaporated from MeCN (3 × 50 mL), then re-dissolved in THF (30 mL). To this solution was added solid potassium *tert*-butoxide (1.423 g, 12.8 mmol) and, after the powder had dissolved, this was followed by solid 1,3,5-tri(bromomethyl)benzene (**2**, 1.234 g, 3.45 mmol). After 2 hr the reaction was quenched with sat. ammonium chloride (4 mL). A large sinter funnel was charged with a bed of silanised silica (200 mL) in water. The reaction was diluted with alternating water and MeCN to achieve a solution (final volume of 400 mL) just at the point of turbidity, and this was carefully loaded onto the silica bed. The column was eluted with a gradient of MeCN-water (4:6 to 8:2 v/v containing 0.25 mL conc. ammonia per 100 mL). The appropriate fractions were combined and the MeCN stripped off on the rotary evaporator. The residual emulsion was diluted with brine and extracted into CH$_2$Cl$_2$ (× 4). The organic layer was dried over Na$_2$SO$_4$ and evaporated to dryness to give the *title compound* (**7**, 7.130 g, 96.9%).

R_f (MeOH-CHCl$_3$ 1:19 + trace Et$_3$N) 0.32; Dmtr-OPeg$_8$OH 0.45. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.47 (d, *J*=7.3, 1.1, 6H, Dmtr), 7.35 (d, *J*=8.9, 12H, Dmtr), 7.28 (t, *J*=7.5, 6H, Dmtr), 7.24 (s, 3H, Hub), 7.20 (t, *J*=7.3, 3H, Dmtr), 6.82 (d, *J*=8.9, 12H, Dmtr), 4.55 (s, 6H, ArC***H$_2$***OEG), 3.78 (s, 18H, 6×ArOC***H$_3$***), 3.68-3.62 (m, 90H, 45×C***H$_2$***O), 3.23 (t, *J*=5.3, 6H, 3×C***H$_2$***ODmtr). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 158.37 (6×Dmtr ***C***), 145.10 (3×Dmtr ***C***), 138.59 (3×Hub ***C***), 136.32 (6×Dmtr ***C***), 130.06 (12×Dmtr ***C***H), 128.18 (6×Dmtr ***C***H), 127.75 (6×Dmtr ***C***H), 126.65 (3×Dmtr ***C***H), 126.33 (3×Hub ***C***H), 113.02 (12×Dmtr ***C***H), 85.89 (3×Dmtr Ar$_3$***C***O), 73.07 (3×Ar***C***H$_2$OEG), 70.74 (3C), 70.70 (6C), 70.63 (3C), 70.58 (27C), 70.54 (3C), 69.53 (3C) (45×***C***H$_2$O), 63.12 (3×***C***H$_2$ODmtr), 55.19 (6×O***C***H$_3$). *m/z* (MALDI-ToF+) [M+Na]$^+$ = 2155, calc. $C_{120}H_{162}NaO_{33}{}^+$ = 2155.1.

Tris-1,3,5-[octa(ethylene glycol)methyl]benzene, 8.

To tris(Dmtr-octagolmethyl)benzene (**7**, 5.947 g, 2.79 mmol) dissolved in CH$_2$Cl$_2$ (71 mL) was added pyrrole (1.93 mL, 27.9 mmol) and dichloroacetic acid (920 µL). After 2 hr, the reaction was quenched with sat. NaHCO$_3$(aq) (ca. 100 mL), extracted with CHCl$_3$ (× 5), and dried over Na$_2$SO$_4$. The solvent was evaporated, the mixture re-dissolved in CH$_2$Cl$_2$ with trace TEA and loaded onto a bed of silica (400 mL) in a large sinter funnel. The silica was washed with the CHCl$_3$, until pyrrole and Dmtr-pyrrole had eluted, as confirmed by TLC, and the filtrate was discarded. The product was washed from the silica with MeOH-CHCl$_3$ (1:9 v/v, *ca.*1.5 L), and the solvent was evaporated *in vacuo* to give the *title compound* (**8**, 3.131g, 91.9%) as a colorless oil.

R_f (MeOH-CHCl$_3$ 1:9) 0.34. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.23 (s, 3H, Hub), 4.54 (s, 6H, 3×ArC***H$_2$***OEG), 3.71 (t, *J*=4.6, 6H, 3×C***H$_2$***O), 3.68-3.62 (m, 84H, 42×C***H$_2$***O), 3.60 (t, *J*=4.6, 6H, 3×C***H$_2$***O), 2.85 (s, 3H (ex), 3×O***H***). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 138.57 (3×Hub ***C***), 126.33 (3×Hub ***C***H), 73.06 (3×Ar***C***H$_2$OEG), 72.58 (3×O***C***H$_2$CH$_2$OH), 70.54 (36C), 70.28 (3C), 69.50 (3C) (42×***C***H$_2$O), 61.67 (3×OCH$_2$***C***H$_2$OH). *m/z* (MALDI-ToF+) [M+Na]$^+$ = 1248, calc. $C_{57}H_{108}NaO_{27}{}^+$ = 1247.7.

Tris-1,3,5-[(4,4'-dimethoxytriphenylmethyl)hexadeca(ethylene glycol)methyl]benzene, 9.

Tris(octagolmethyl)benzene (**8**, 2.500 g, 2.041 mmol) and DmtrO-EG$_8$-OTs (**6**, 16.88 g, 20.41 mmol) were separately co-evaporated from MeCN (3 x 10 mL and 3 × 50 mL, respectively), then re-dissolved in DMF (20 + 21 mL) and combined in a two-necked round-bottomed flask. A 60 % dispersion of NaH in mineral oil (490 mg) was washed with 60-80 °C petroleum ether (3 × 5 mL), decanting the supernatant and allowing the powder (294 mg, 12.25 mmol) to dry under a stream of N$_2$, and then added to the reaction mixture. The reaction was held at 30 °C for 12.5 hours, then quenched by careful addition of sat. NH$_4$Cl (*ca.* 2 mL) until effervescence ceased. The solution was transferred to a 500 mL Erlenmeier flask, silanised silica was added (*ca.* 200 mL), and the solution was diluted by slow addition of water (up to 500 mL) with gentle swirling to prevent phase separation. The slurry was then carefully poured onto further silanised silica (300 mL, in water basified with conc. ammonia) in a large sinter funnel. The silanised silica bed was washed with water (ca. 2 L) and the crude product mixture was then eluted with acetone (*ca.* 2.5 L), the solvent stripped off *in vacuo* and residual water was co-evaporated from MeCN (*ca.* 4 × 300 mL) until a single phase was obtained. The product mixture, containing unreacted Dmtr-EG$_8$-OTs (**6**) as well as Dmtr-EG$_{16}$-Dmtr was separated by normal phase chromatography with flash silica (400 mL) using a MeOH-CHCl$_3$ gradient, containing a trace of Et$_3$N. Combination of the relevant fractions afforded the *title compound* (6.03 g, 92.7%) and recovered building block, Dmtr-EG$_8$-OTs (**6**, 10.50 g, 12.7 mmol) as well as Dmtr-EG$_{16}$-Dmtr (0.47 g, 0.35 mmol).

R_f (MeOH-CHCl$_3$ 1:9 + trace Et$_3$N) 0.63; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.46 (dd, *J*=7.2, 1.4, 6H, Dmtr), 7.34 (d, *J*=8.9,12H, Dmtr), 7.27 (bt, *J*=7.8, 6H, Dmtr), 7.23 (s, 3H, Hub), 7.19 (tt, *J*=7.3, 1.2, 3H, Dmtr), 6.81 (d, *J*=8.9, 12H, Dmtr), 4.54 (s, 6H, 3×ArC***H***$_2$OEG), 3.78 (s, 18H, 6×ArOC***H***$_3$), 3.69-3.63(m, 186H, 93×C***H***$_2$O), 3.22 (t, *J*=5.2, 3×C***H***$_2$ODmtr); ^{13}C NMR (101 MHz, CDCl$_3$) δ = 158.35 (6×Dmtr ***C***), 145.07 (3×Dmtr ***C***), 138.58 (3×Hub ***C***), 136.32 (6×Dmtr ***C***), 130.04 (12×Dmtr ***C***H), 128.18 (6×Dmtr ***C***H), 127.71 (6×Dmtr ***C***H), 126.61 (3×Dmtr ***C***H), 126.29 (3×Hub ***C***H), 113.01 (12×Dmtr ***C***H), 85.89 (3×Dmtr Ar$_3$***C***O), 73.07 (3×Ar***C***H$_2$OEG), 70.75 (3C), 70.70 (3C), 70.65 (3C), 70.56 (78C), 69.53 (3C) (93×***C***H$_2$O), 63.13 (3×***C***H$_2$ODmtr), 55.18 (6×O***C***H$_3$). *m/z* (MALDI-ToF+) $[M+Na]^+$ = 3213, calc. $C_{168}H_{258}NaO_{57}^+$ = 3211.7.

Bis-(4,4'-dimethoxytriphenylmethyl)hexadeca(ethylene glycol).

R_f (EtOH-CHCl$_3$ 1:19 + trace Et$_3$N) 0.39; R_f (MeOH-CHCl$_3$ 1:9 + trace Et$_3$N) 0.75; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.46 (dd, *J*=7.3, 1.3, 4H), 7.34 (d, *J*=8.9, 8H), 7.25 (bt, *J*=7.5, 4H), 7.17 (bt, *J*=7.3, 2H), 6.80 (d, *J*=8.9, 8H), 3.74 (s, 12H), 3.66-3.62 (m, 60H), 3.22 (t, *J*=5.2, 4H). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 158.37 (4C), 145.10 (2C), 136.30 (4C) (10×Dmtr ***C***), 130.03 (8C), 128.17 (4C), 127.71 (4C), 126.62 (2C), 113.01 (8C) (26×Dmtr ***C***H), 85.88 (2×Dmtr Ar$_3$***C***O), 70.76 (2C), 70.70 (4C), 70.66 (2C), 70.56 (22) (30×***C***H$_2$O), 63.14 (2×***C***H$_2$ODmtr), 55.14 (4×O***C***H$_3$). *m/z* (ESI+) $[M+NH_4]^+$ = 1344.7, calc. $C_{74}H_{106}NO_{21}^+$ = 1344.73.

Tris-1,3,5-[hexadeca(ethylene glycol)methyl]benzene, 10.

To tris(Dmtr-hexadecagolmethyl)benzene (**9**, 5.96 g, 1.87 mmol) dissolved in DCM (48 mL) were added pyrrole (1.30 mL, 18.7 mmol) and dichloroacetic acid (0.62 mL, 1.3 vol%). After 2 hours, the solution was partitioned with sat. NaHCO$_3$ (*ca.* 100 mL), and the aqueous layer was extracted with CHCl$_3$ (5 × 75 mL). The combined organic layers were dried over Na$_2$SO$_4$ and the solvent was evaporated *in vacuo*. The residue was absorbed onto a column of flash silica (200 mL) in a large sinter funnel. The silica was washed with MeOH-CHCl$_3$ (3:47 v/v, up to 1 L until all Dmtr-pyrrole had eluted) and the eluent discarded. The silica was then washed with MeOH-CHCl$_3$ (1:4 v/v, *ca.* 3 L) until no further product eluted, as determined by TLC. The filtrate was evaporated to dryness *in vacuo* to give the *title compound* (3.72 g, 87.2%) as a waxy colourless solid.

R_f (MeOH-CHCl$_3$ 1:9) 0.44; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.23 (s, 3H, Hub), 4.54 (s, 6H, 3×ArC***H***$_2$OEG), 3.72 (t, *J*=4.5, 6H, 3×C***H***$_2$O), 3.68-3.60 (m, 186H, 93×C***H***$_2$O). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 138.58 (3×Hub ***C***), 126.30 (3×Hub ***C***H), 73.07 (3×Ar***C***H$_2$OEG), 72.55 (3×O***C***H$_2$CH$_2$OH), 70.55 (84C), 70.32 (3C), 69.52 (3C) (90×***C***H$_2$O), 61.70 (3×OCH$_2$***C***H$_2$OH). *m/z* (MALDI-ToF+) $[M+Na]^+$ = 2305, calc. $C_{105}H_{205}O_{51}{}^+$ = 2305.3.

Tris-1,3,5-[(4,4'-dimethoxytriphenylmethyl)tetracosa(ethylene glycol)methyl]benzene, 11.

This reaction was conducted using the same procedure as for the preparation of compound **9**, above: To tris(hexadecagolmethyl)benzene (**10**, 3.700 g, 1.62 mmol) and DmtrO-EG$_8$-OTs (**6**, 13.404 g, 16.21 mmol) in DMF (32.5 mL) was added of NaH (389 mg 60 % dispersion in mineral oil → 233 mg dry powder, 9.73 mmol). After 22 hr at 30 °C, the reaction was worked up and purified by normal phase chromatography to afford the *title compound* (5.45 g, 79.0%), plus a mixed fraction largely containing the *title compound* (0.51 g).

R_f (MeOH-CHCl$_3$ 1:9) 0.61; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.44 (dd, *J*=7.2, 1.4, 6H, Dmtr), 7.33 (d, *J*=8.9, 12H, Dmtr), 7.26 (bt, *J*=7.5, 6H, Dmtr), 7.22 (s, 3H, Hub), 7.18 (tt, *J*=7.3,1.2, 3H, Dmtr), 6.80 (d, *J*=8.9, 12H, Dmtr), 4.53 (s, 6H, 3×ArC***H₂***OEG), 3.77 (s, 18H, 6×ArOC***H₃***), 3.67-3.62 (m, 282H, 141×C***H₂***O), 3.21 (t, *J*=5.2, 6H, 3×C***H₂***ODmtr). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 158.34 (6×Dmtr ***C***), 145.06 (3×Dmtr ***C***), 138.57 (3×Hub ***C***), 136.30 (6×Dmtr ***C***), 130.03 (12×Dmtr ***C***H), 128.17 (6×Dmtr ***C***H), 127.70 (6×Dmtr ***C***H), 126.60 (3×Dmtr ***C***H), 126.27 (3×Hub ***C***H) 113.00 (12×Dmtr ***C***H), 85.88 (3×Dmtr Ar$_3$***C***O), 73.06 (3×Ar***C***H$_2$OEG), 70.74 (3C), 70.69 (3C), 70.63 (3C), 70.55 (129C), 69.52 (3C) (141×***C***H$_2$O), 63.12 (3×***C***H$_2$ODmtr), 55.17 (6×O***C***H$_3$). *m/z* (MALDI-ToF+) $[M+Na]^+$ = 4269.1, calc. $C_{216}H_{354}NaO_{81}{}^+$ = 4269.35.

Tris-1,3,5-[tetracosa (ethylene glycol)methyl]benzene, 12.

This reaction was conducted using the same procedure as for the preparation of compound **10**, above: To tris(Dmtr-tetracosagolmethyl)benzene (**11**, 5.45 g, 1.28 mmol) in DCM (33 mL) were added pyrrole (889 µL, 12.8 mmol) and dichloroacetic acid (423 µL, 1.3 vol%). After 2 hours, the reaction was worked up as above to give the *title compound* (3.16 g, 74.2%) as a colourless waxy solid.

R_f (MeOH-CHCl$_3$ 1:9) 0.43; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.25 (s, 3H, Hub), 4.56 (s, 6H, 3×ArC***H₂***OEG), 3.74 (t, *J*=4.5, 6H, 3×C***H₂***O), 3.70-3.62 (m, 282H, 141×C***H₂***O). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 138.59 (3×Hub ***C***), 126.32 (3×Hub ***C***H), 73.09 (3×Ar***C***H$_2$OEG), 72.56 (3×O***C***H$_2$CH$_2$OH), 70.57 (132C), 70.33 (3C), 69.54 (3C) (138×***C***H$_2$O), 61.73 (3×OCH$_2$***C***H$_2$OH). *m/z* (MALDI-ToF+) $[M+Na]^+$ = 3338.8, calc. $C_{153}H_{300}NaO_{75}{}^+$ = 3339.98.

Tris-1,3,5-[methoxytetracosa (ethylene glycol)methyl]benzene, 13.

Tris(tetracosagolmethyl)benzene (**12**, 480 mg, 0.144 mmol) was dissolved in DMF (1 mL) and to this was added MeI (89.5 µL, 1.44 mmol). A 60 % dispersion of NaH in mineral oil (35 mg) was washed with 60-80 °C petroleum ether (3 × 1 mL), decanting the supernatant and allowing the powder (21 mg, 0.86 mmol) to dry under a stream of N$_2$, and then added to the reaction mixture. The reaction was run at RT for 24 hours and subsequently quenched by very slow addition of sat. NaHCO$_3$ (*ca.* 7 drops). After 5 minutes, the volatiles were evaporated *in vacuo* (oil pump). The residue was diluted with brine and extracted CHCl$_3$ (5 × 10 mL), the combined organic layers dried over Na$_2$SO$_4$ and the solvent stripped off *in vacuo* to afforded the *title compound* (487 mg, 100%), which was used without further purification.

R_f (MeOH-CHCl$_3$ 1:9) 0.62; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.21 (s, 3H), 4.53 (s, 6H), 3.67-3.60 (m, 279H), 3.53 (t, *J*=4.7, 6H), 3.36 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$) δ = 138.56 (3×Hub ***C***), 126.28 (3×Hub ***C***H), 73.05 (3×Ar***C***H$_2$OEG), 71.90 (3C), 70.53 (138C), 69.51 (3C) (144×***C***H$_2$O), 59.00 (3× O***C***H$_3$). *m/z* (MALDI-ToF+) $[M+Na]^+$ = 3403.8, calc. $C_{156}H_{306}NaO_{75}{}^+$ = 3404.01.

Methoxytetracosa (ethylene glycol), 14.

To tris(MeO-EG$_{24}$-OCH$_2$)benzene (**13**, 85 mg, 0.025 mmol) and charcoal (36 mg) were added methanol (2 mL) then a freshly prepared solution of of palladium diacetate (4.0 mg) in THF (0.200 mL). The solution was hydrogenolyzed under 7 bar hydrogen at 80 °C for 16 hr. The following day the solids were removed by filtration through Celite, washing with MeOH-water (9:1 v/v, 8 mL), and the filtrate was evaporated at reduced pressure. The residue was co-evapoated from ethanol (3 × 2 mL), then taken up in chloroform, filtered and the solvent stripped off to give the *title compound* (**14**, 72 mg, 88%) as a waxy solid.

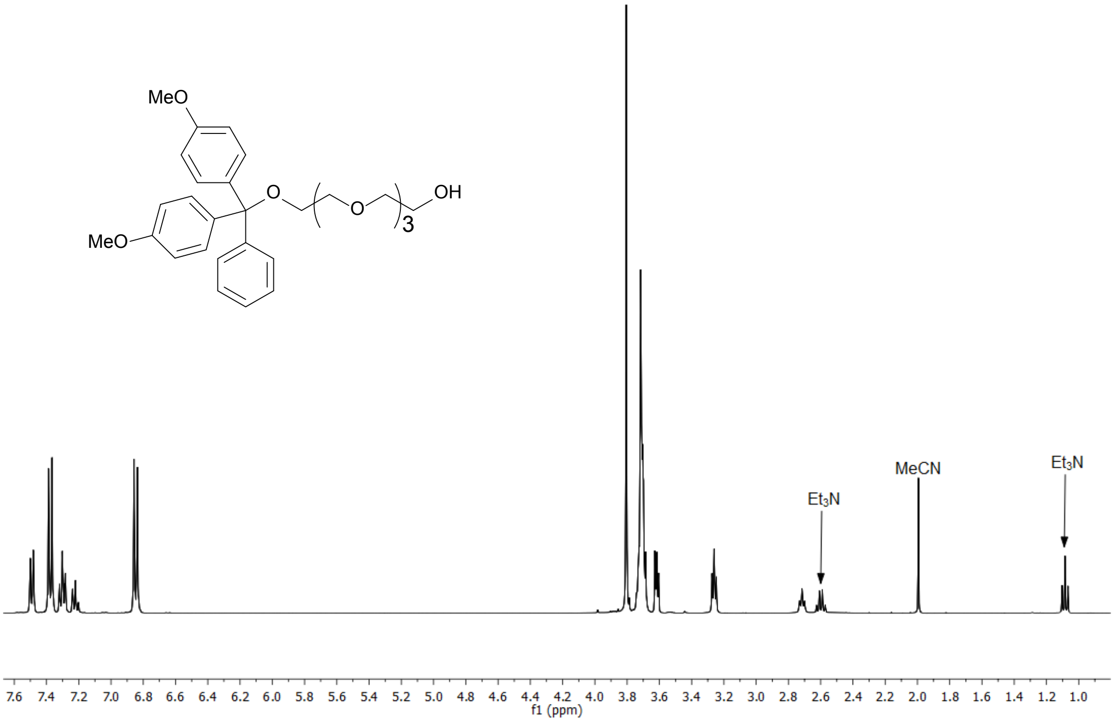
R_f (MeOH-CHCl$_3$ 1:9) 0.50 ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 3.67$ (t, *J*=4.5, 2H), 3.61-3.54 (m, 92H), 3.50 (t, *J*=4.7, 2H), 3.33 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) $\delta = 72.59$ (O***C***H$_2$CH$_2$OH), 71.86 (1C), 70.49 (44C), 70.21 (1C) (46×***C***H$_2$O), 61.55 (OCH$_2$***C***H$_2$OH), 58.96 (O***C***H$_3$). *m/z* (ESI+) $[M+Na]^+ = 1111.6442$, calc. $C_{49}H_{100}NaO_{25}^+ = 1111.6451$.

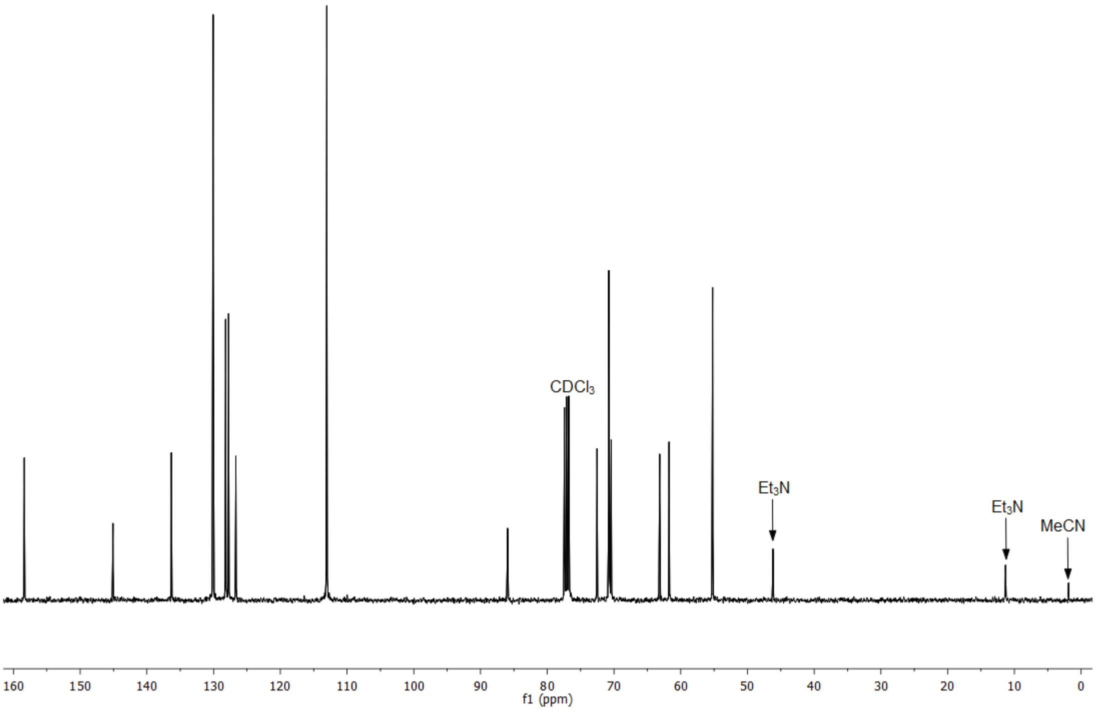
Supplementary references

S1. K. B. Sharpless, A. O. Chong and J. A. Scott, *J. Org. Chem.* 40, **1975**, 1252.

^{1}H & ^{13}C NMR Facsimiles

DmtrO-EG$_4$-OH, 3





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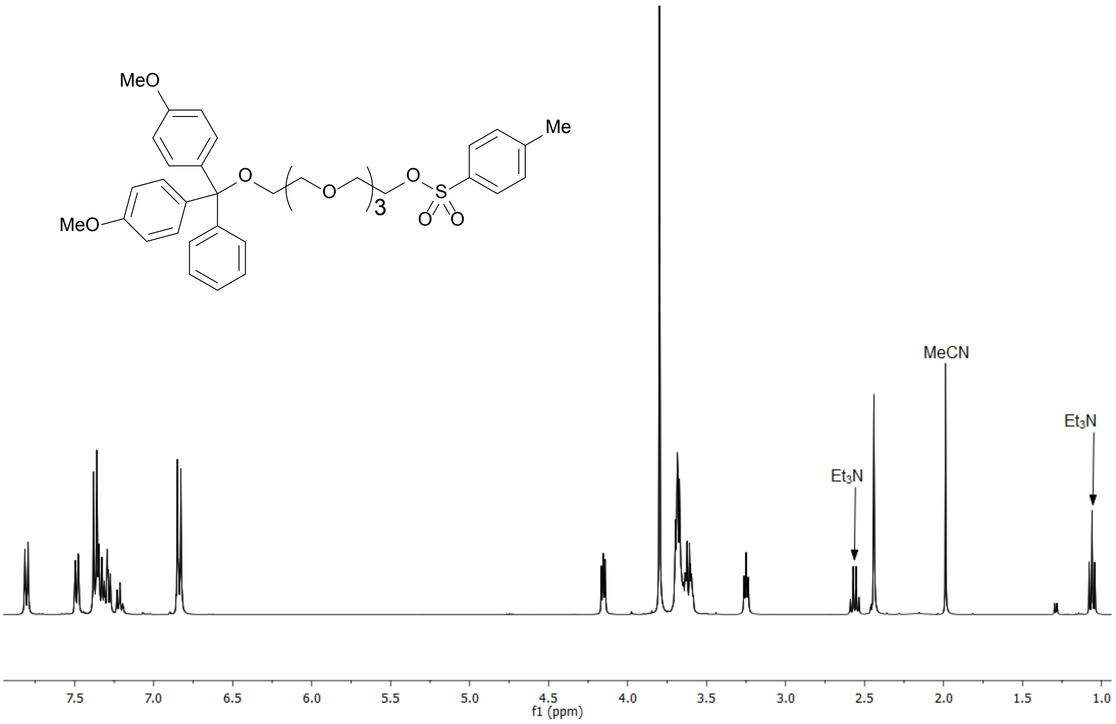

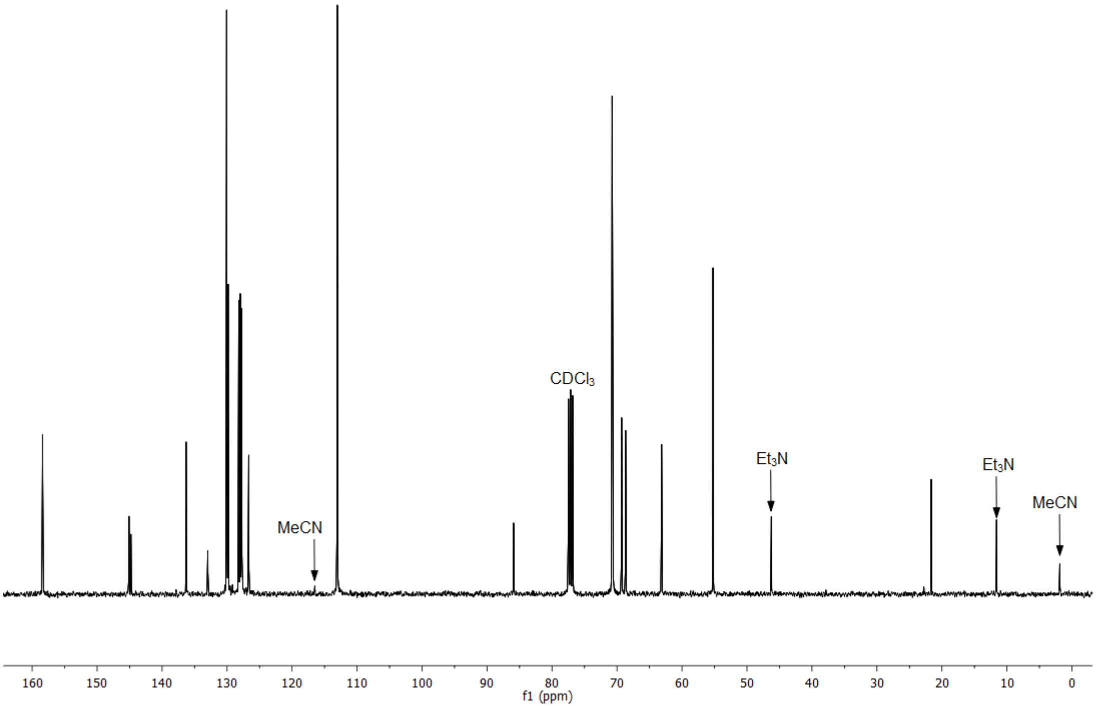

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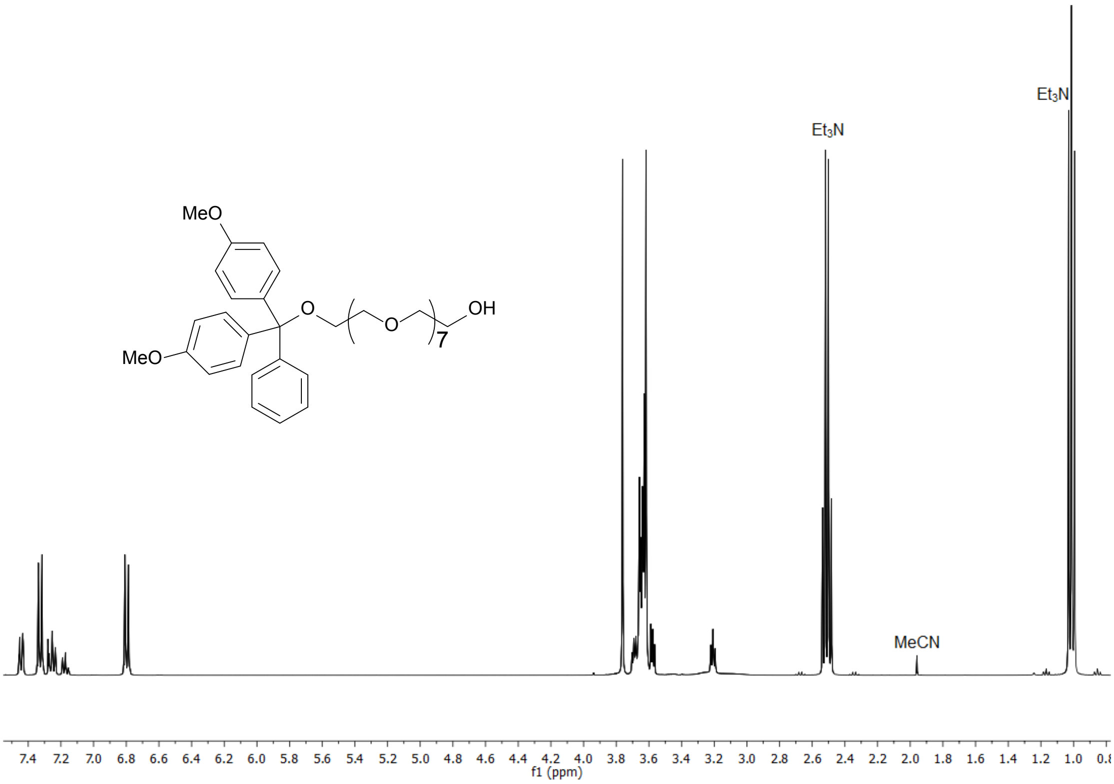

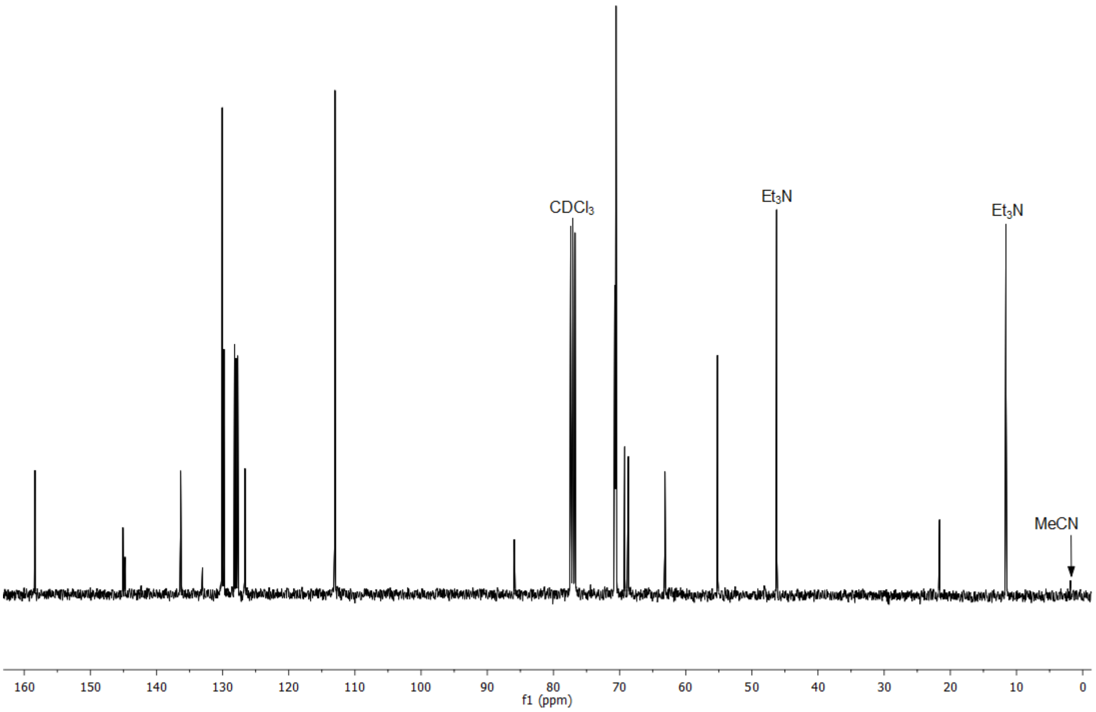

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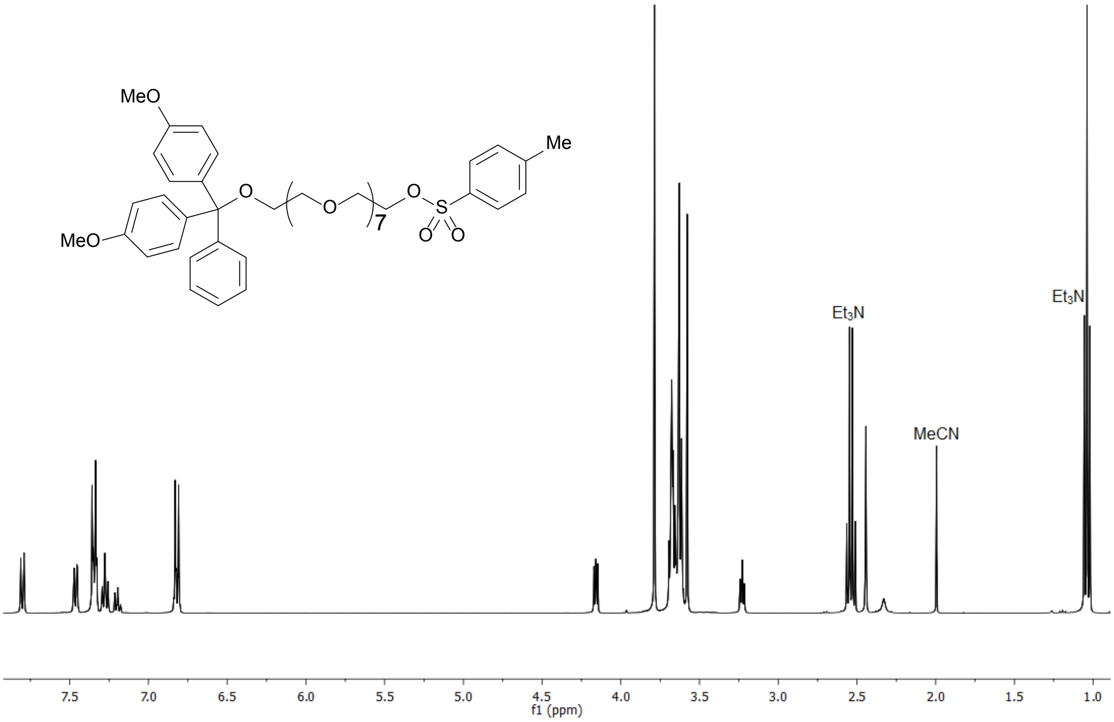
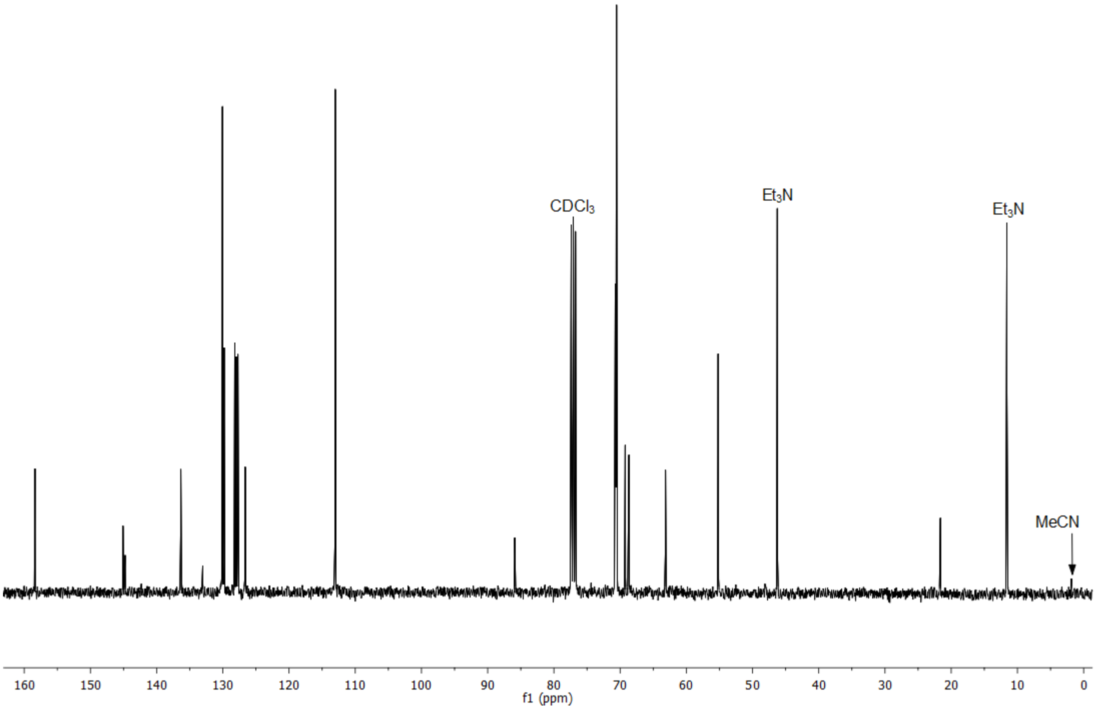
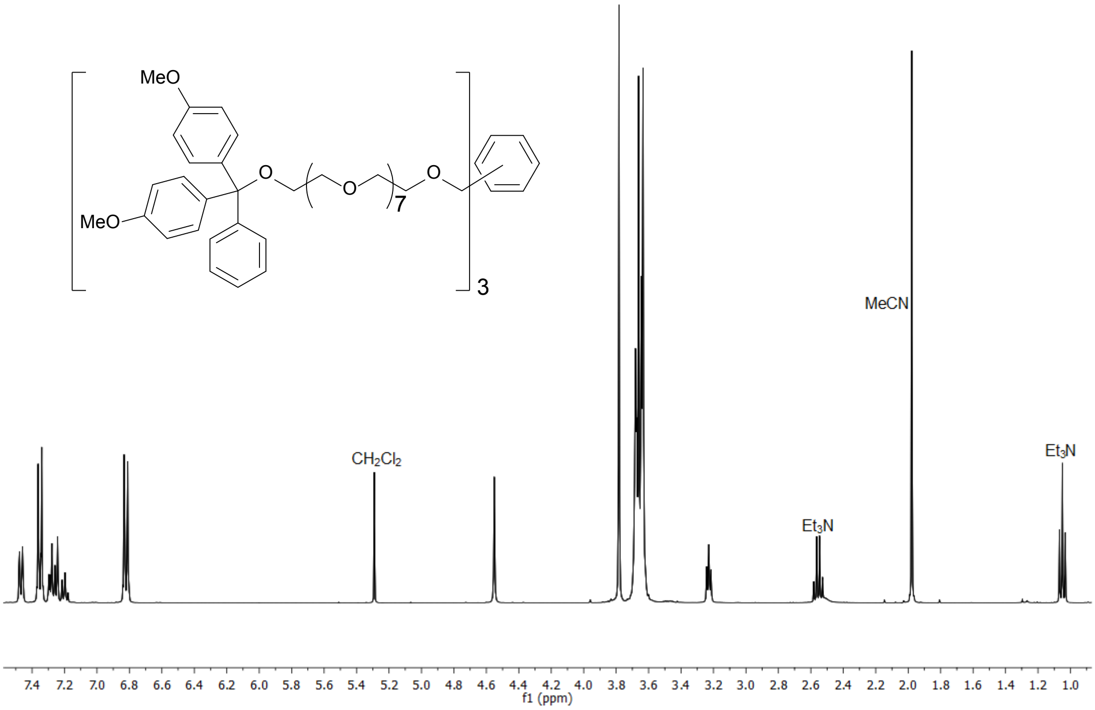
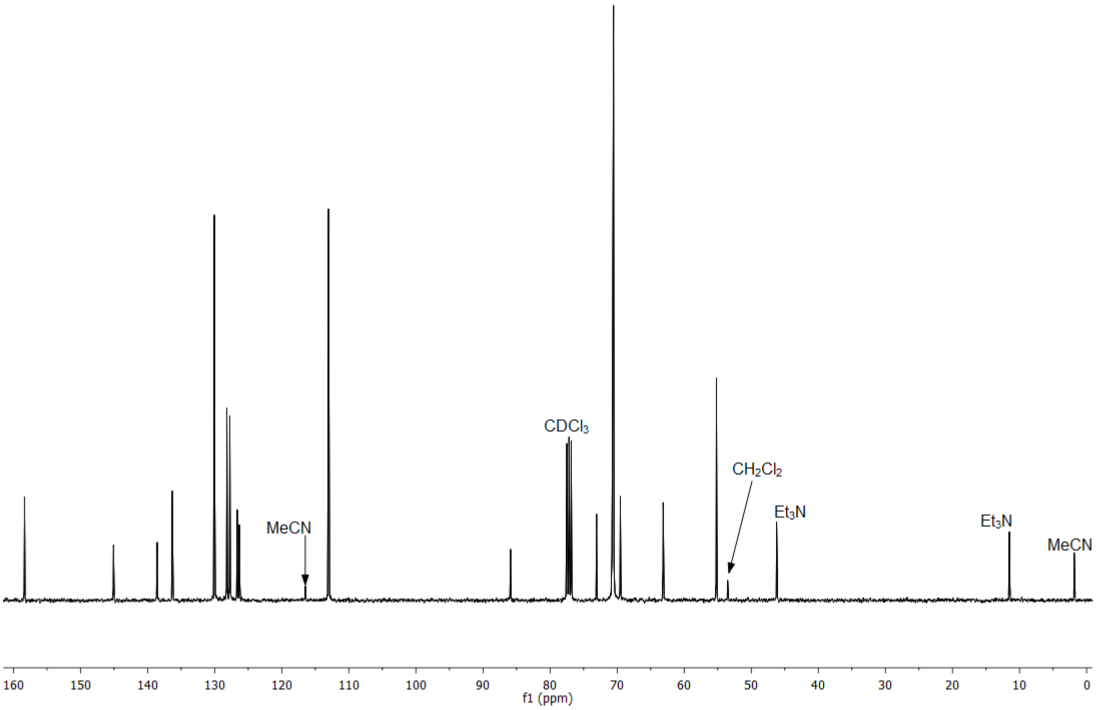




$C_6H_3(CH_2O\text{-}EG_8\text{-}ODmtr)_3$, 7





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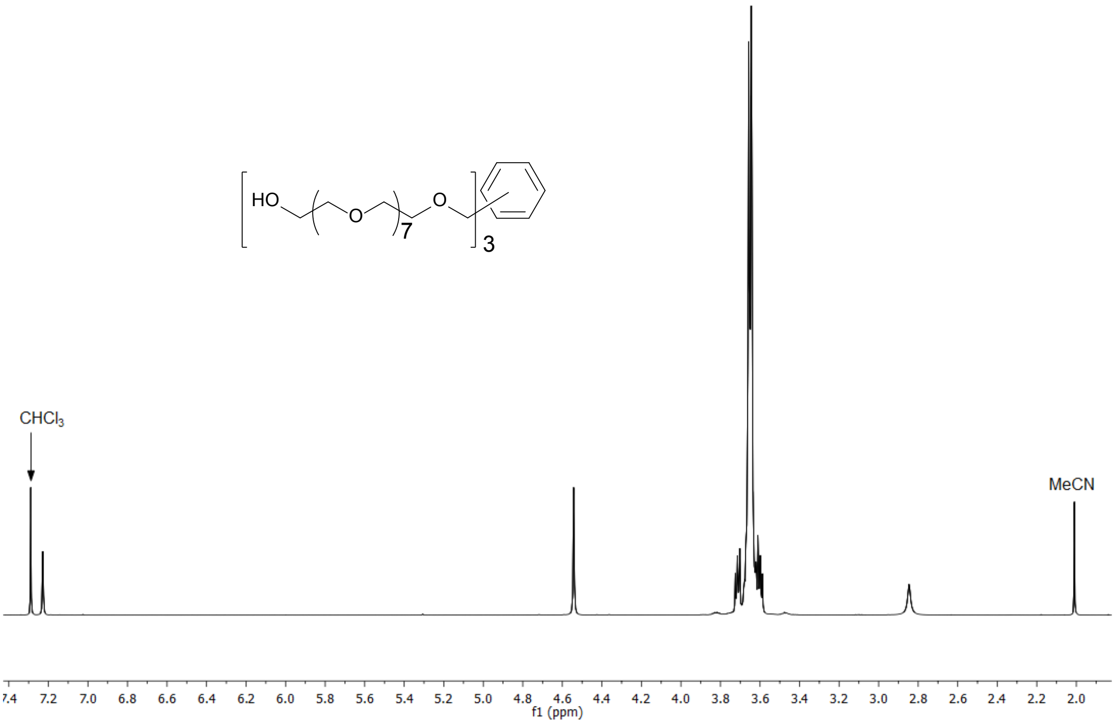

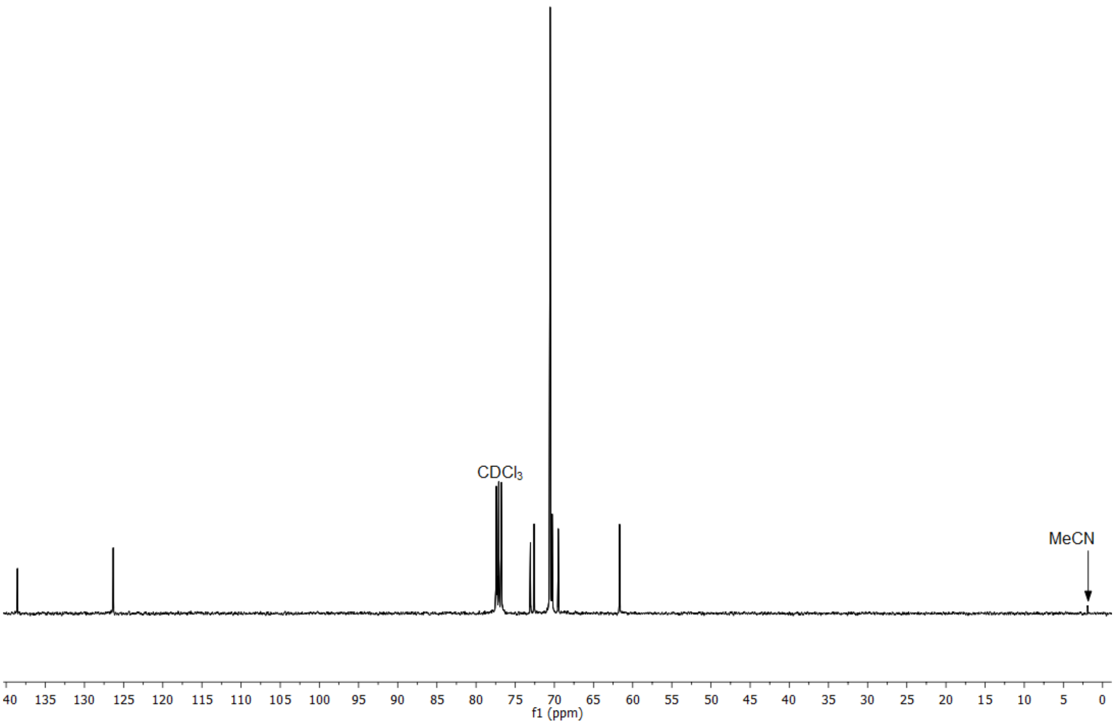

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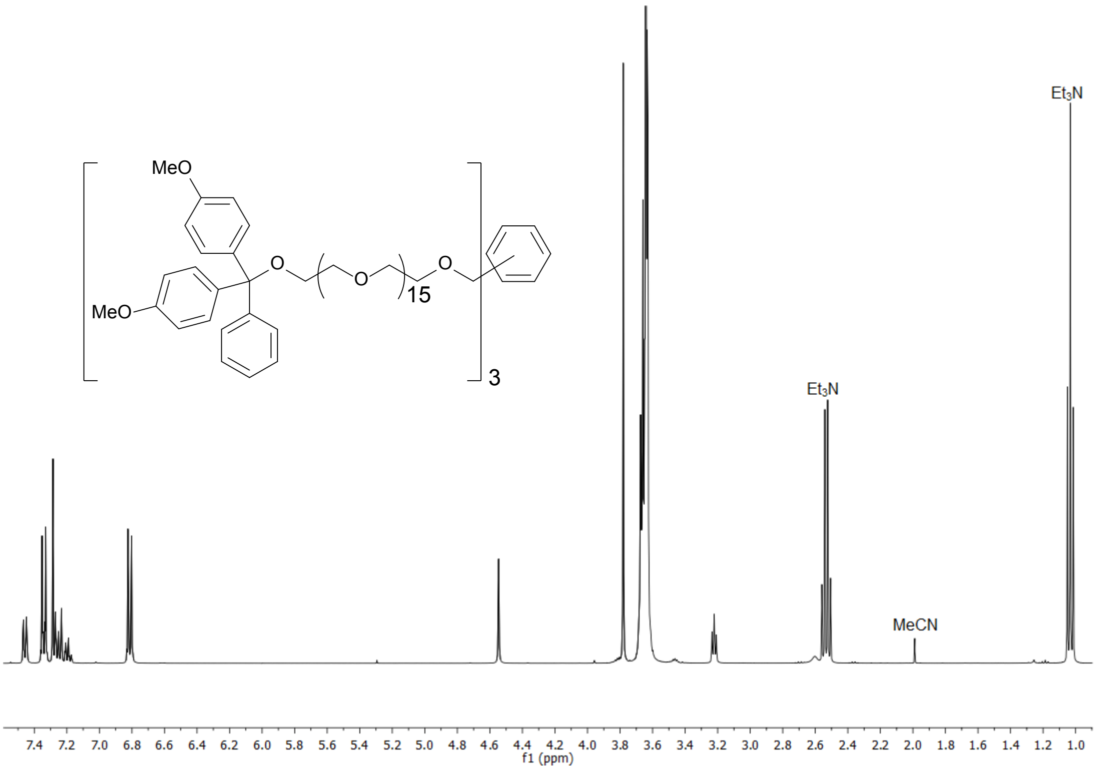

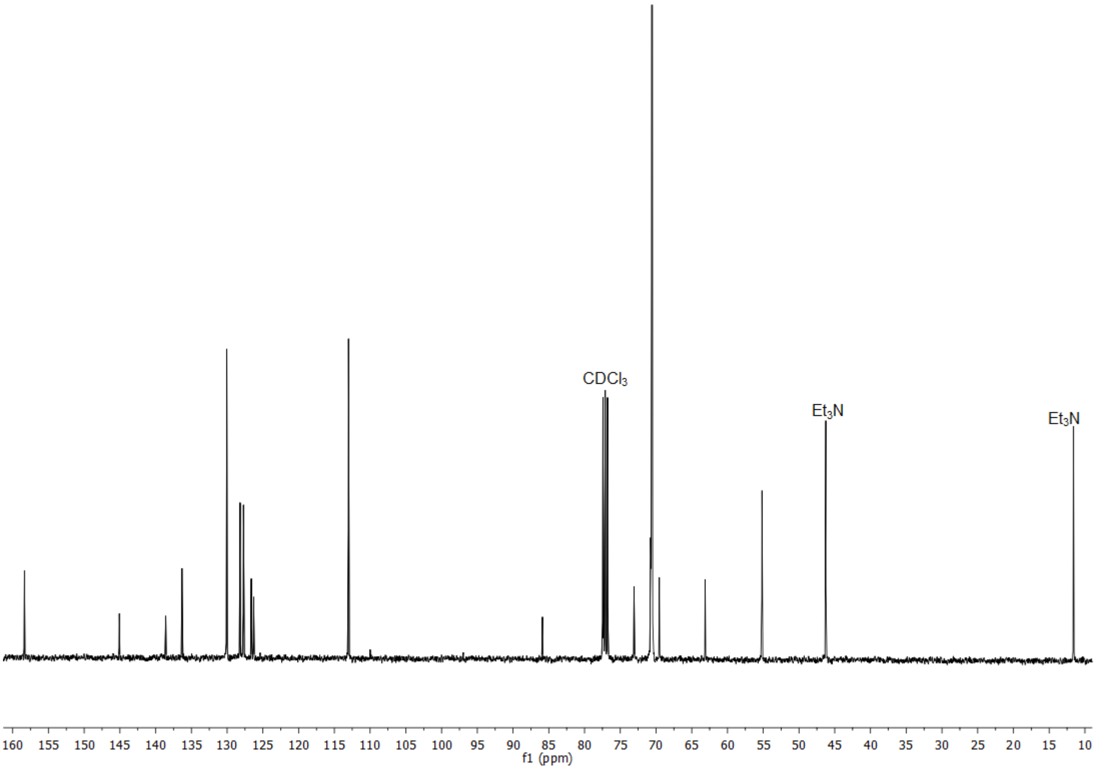

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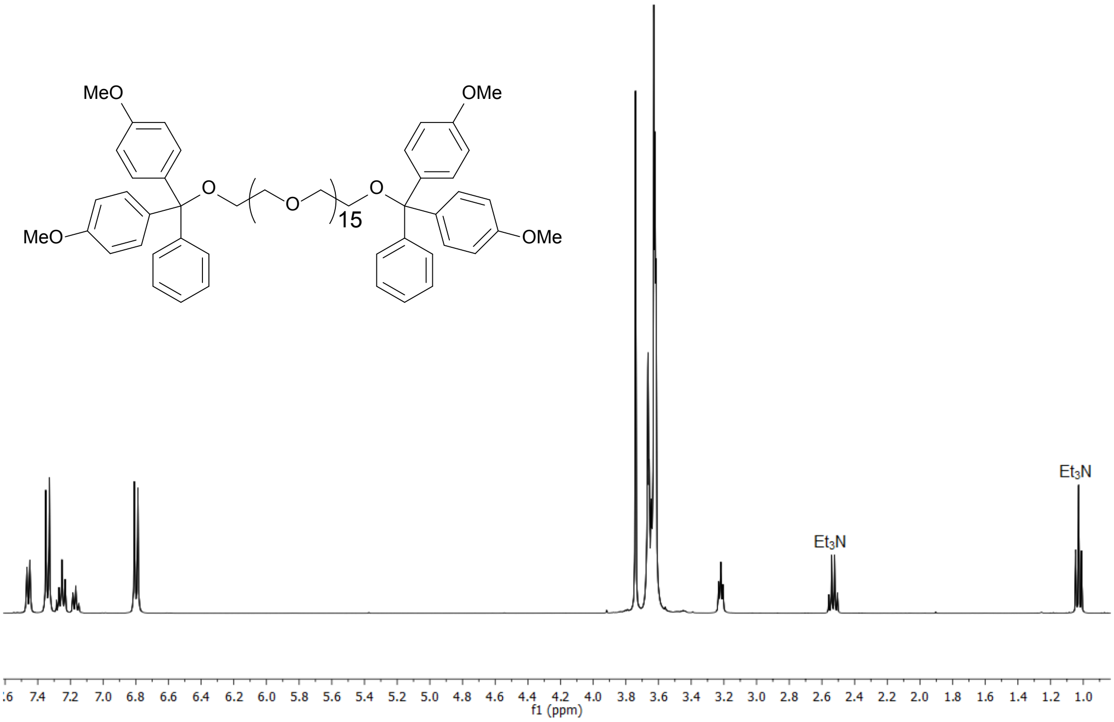

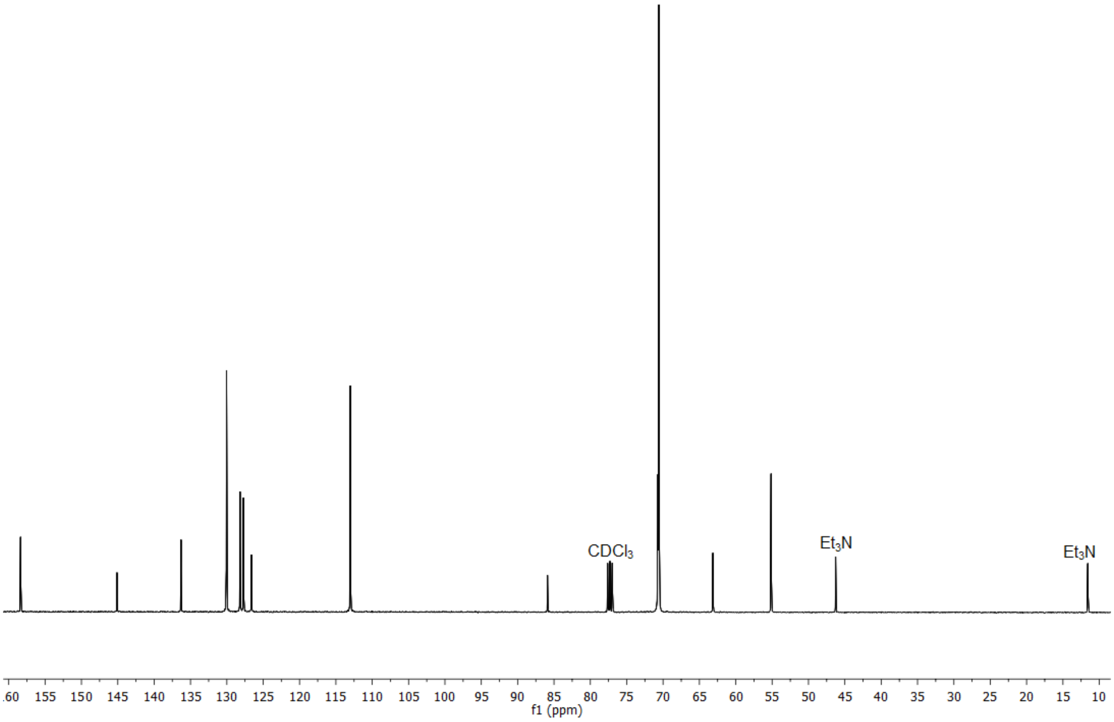

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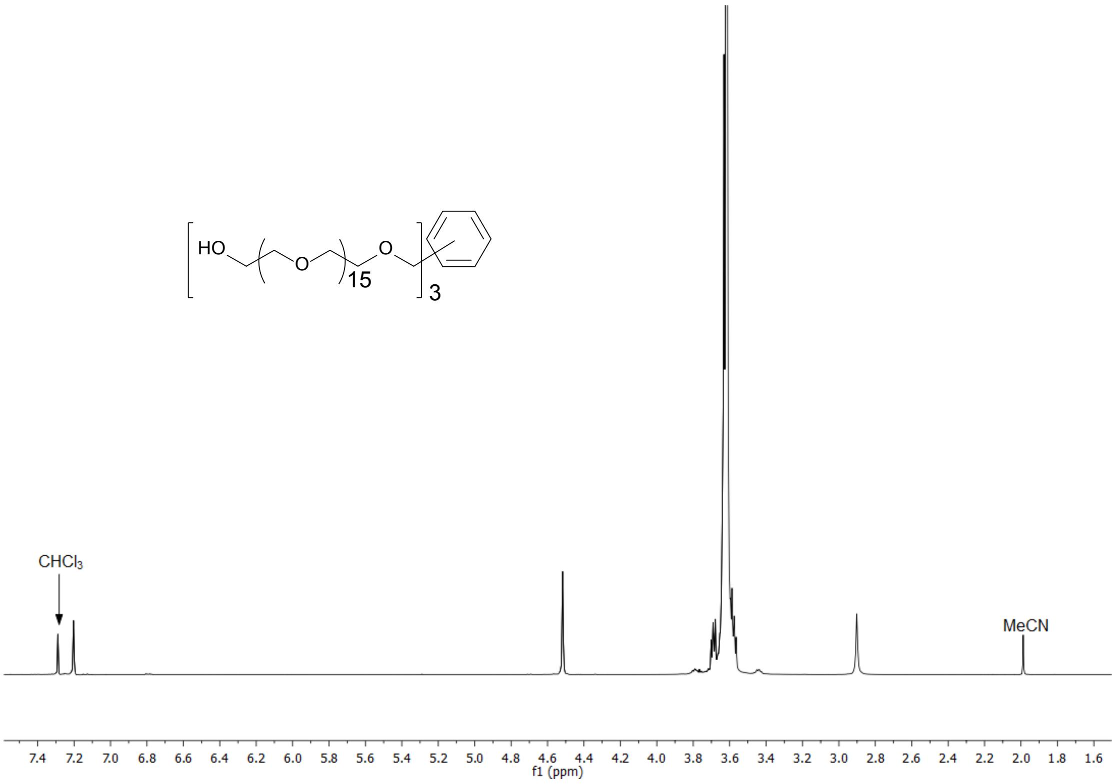

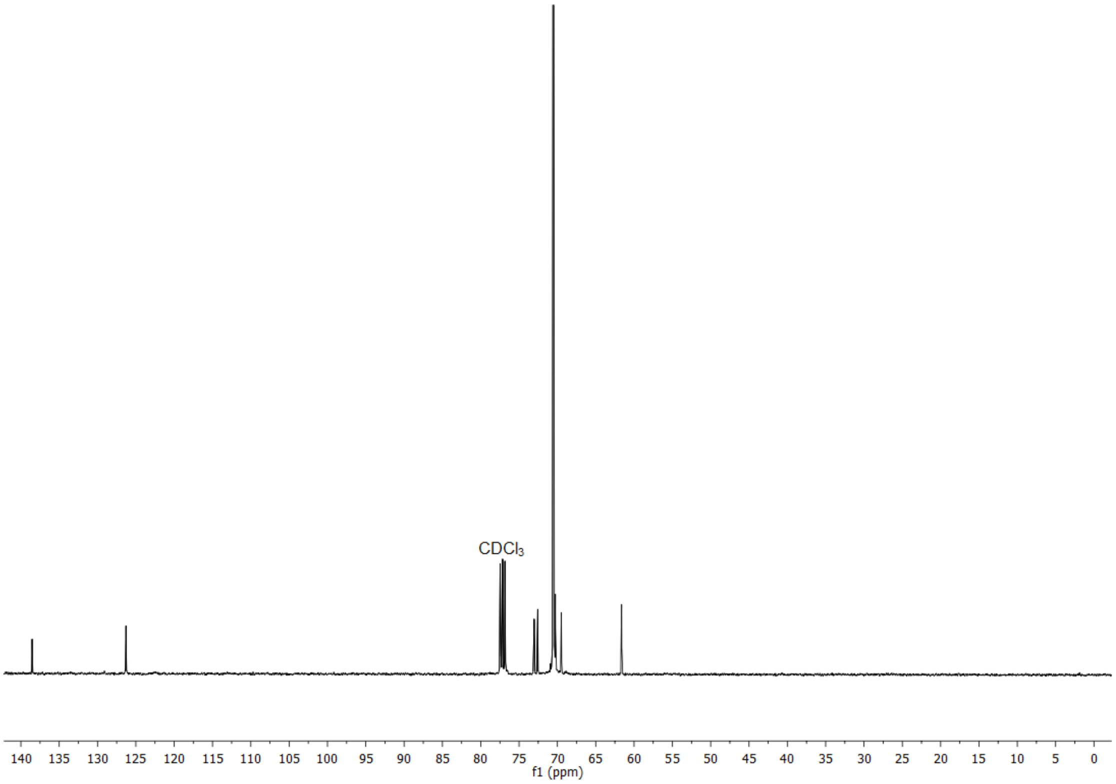

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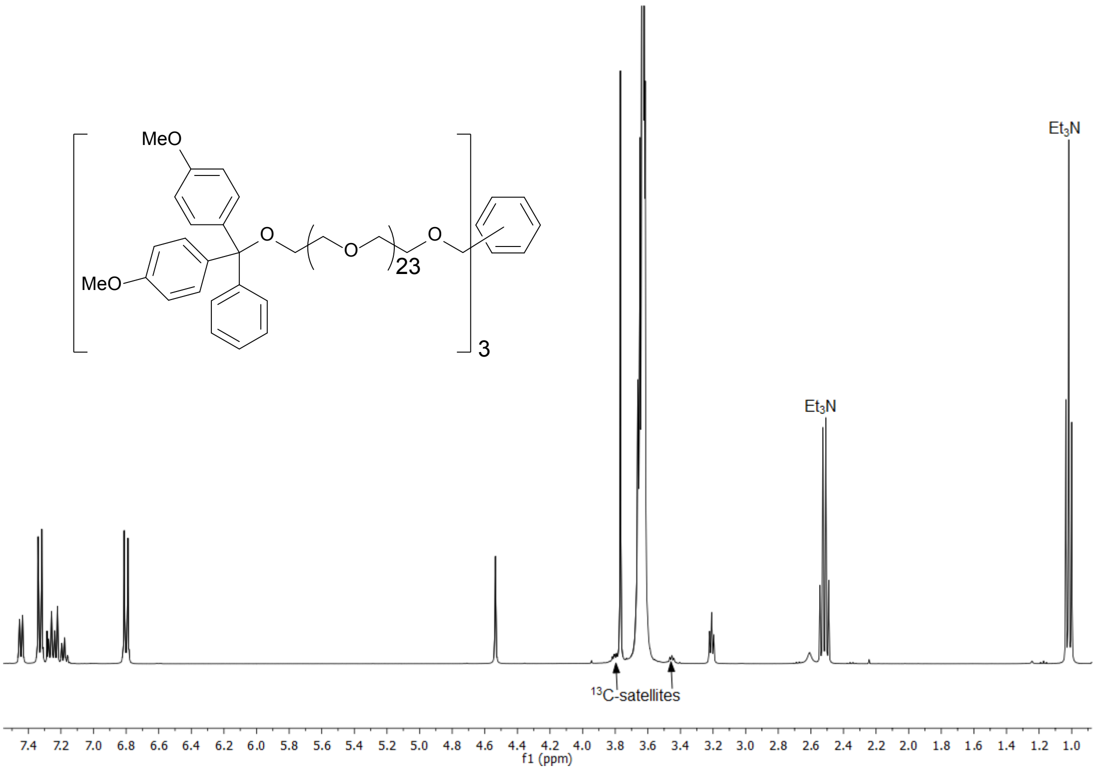

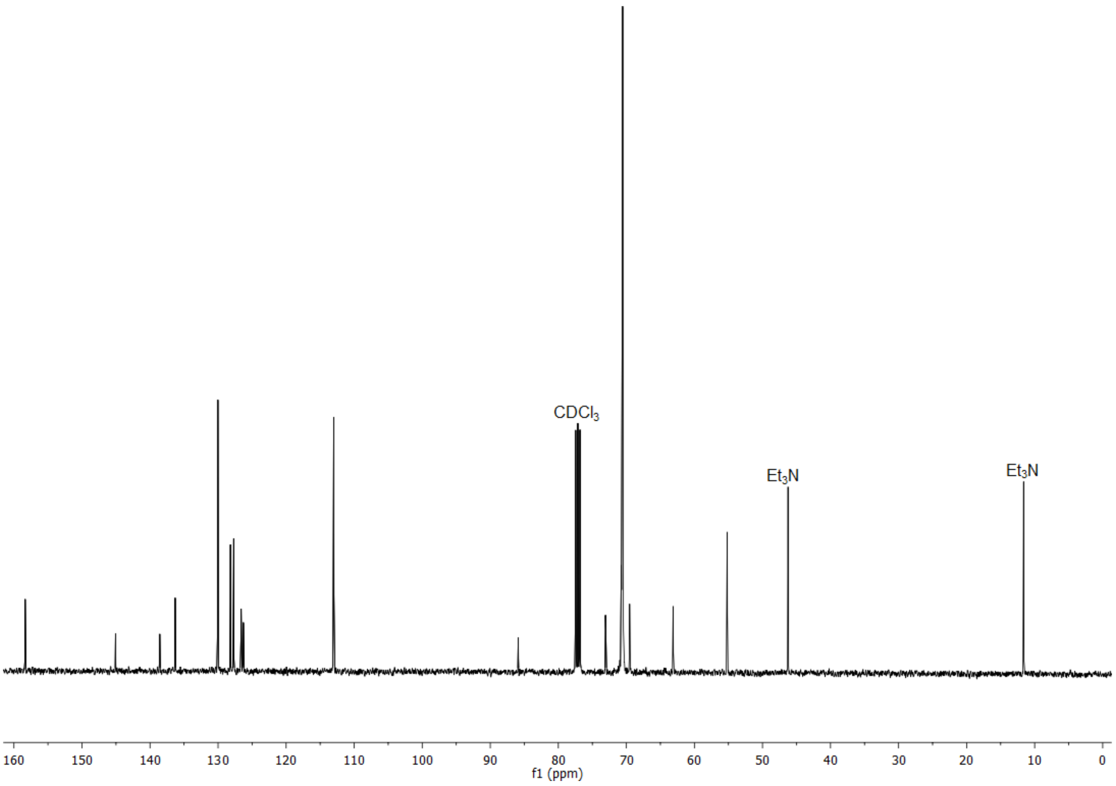

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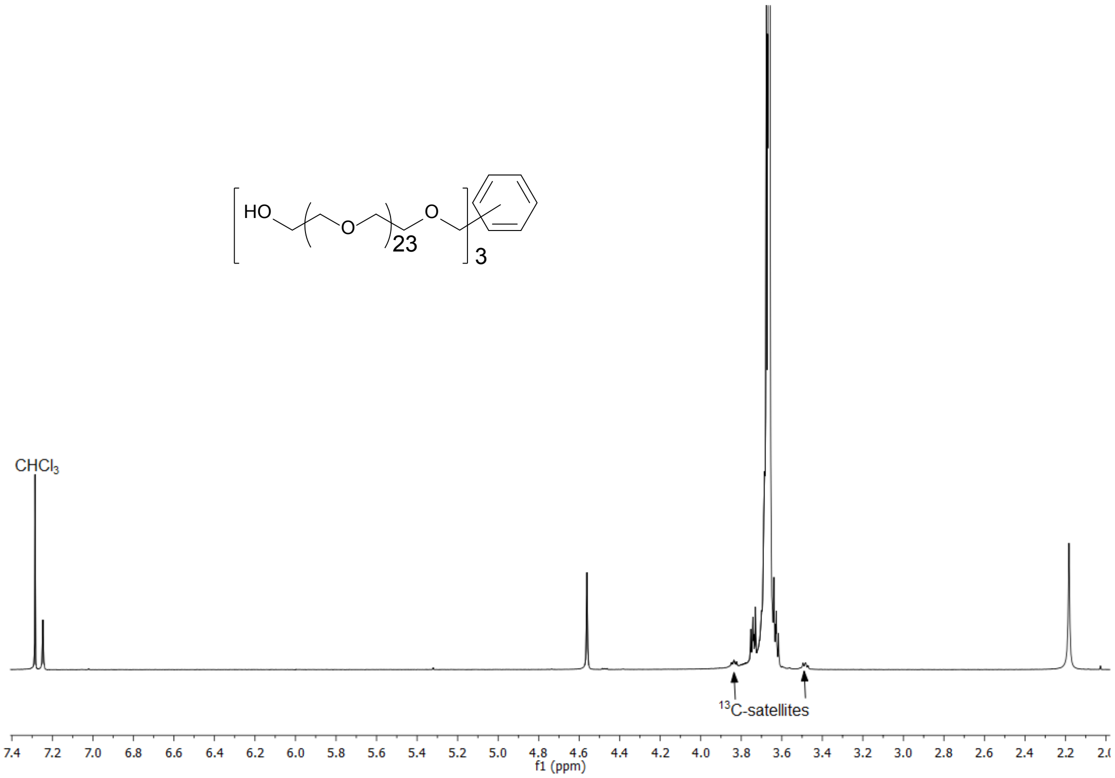

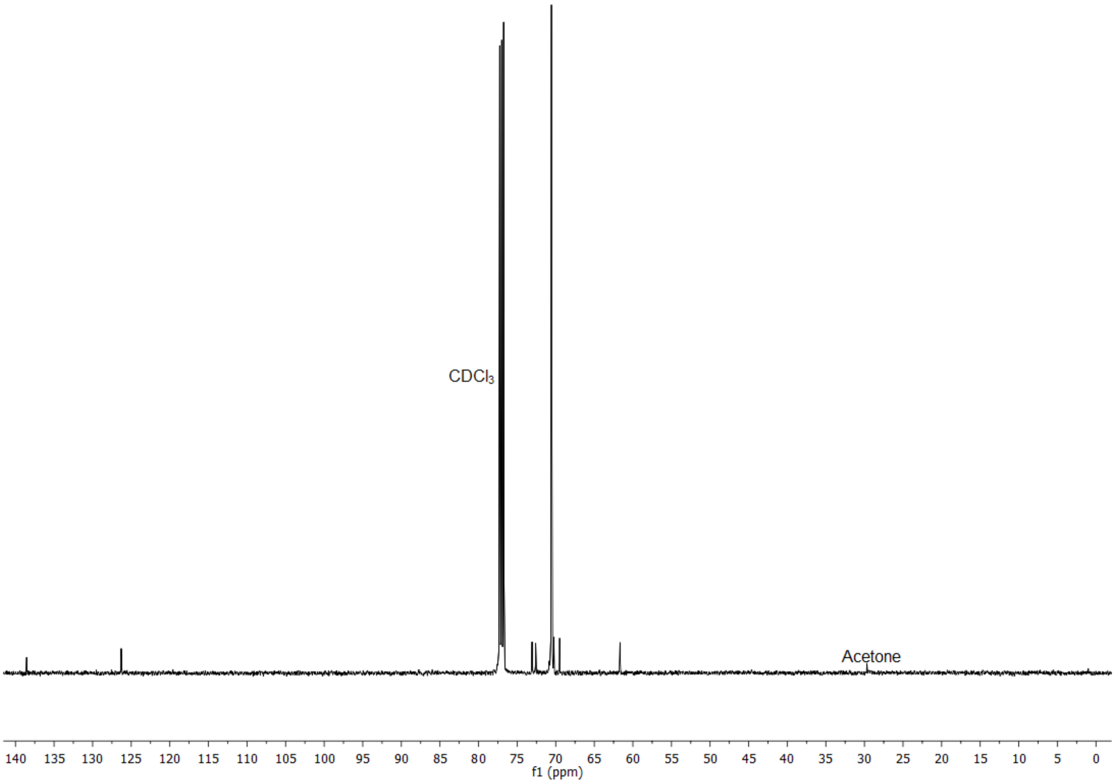

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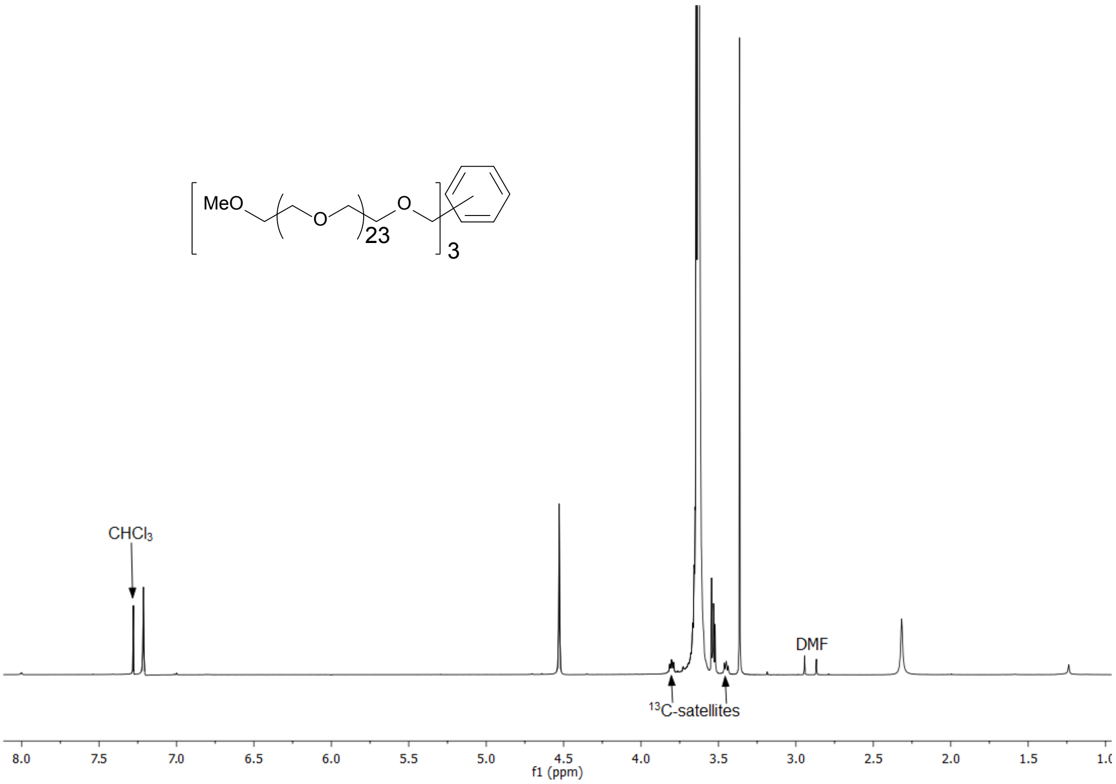

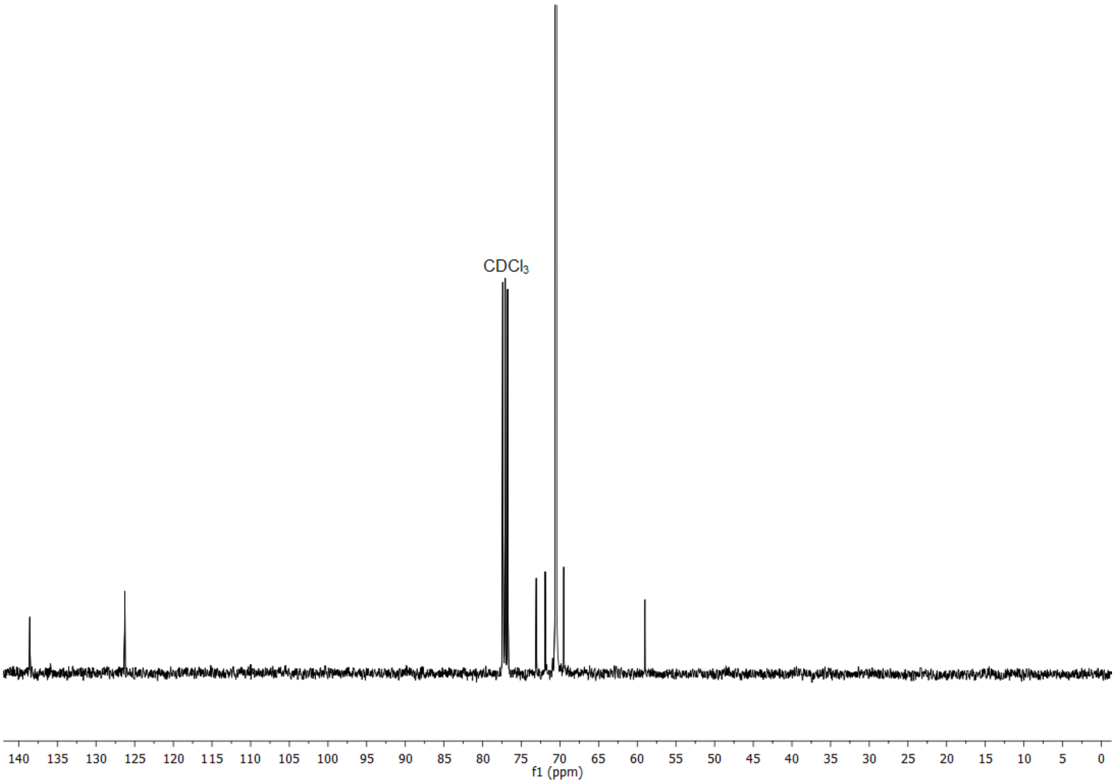

MeO-EG$_{24}$-OH, 14