Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Huisgen-based conjugation of water-soluble porphyrins to deprotected sugars: towards mild strategies for the labelling of glycans

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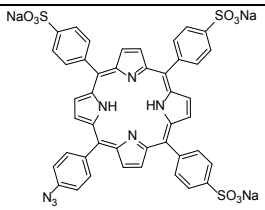
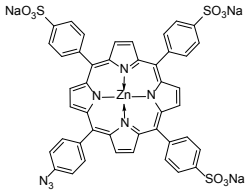
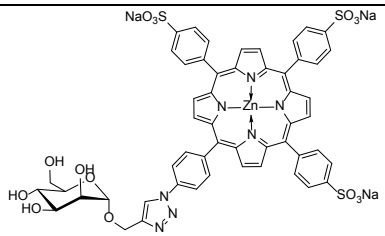
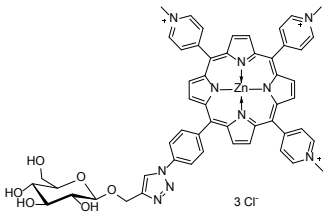
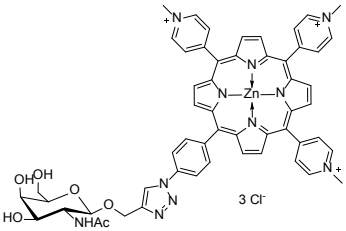
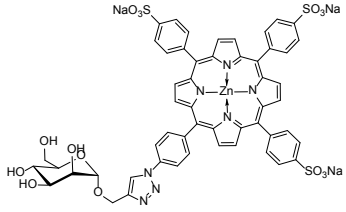
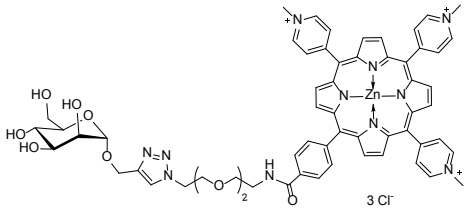
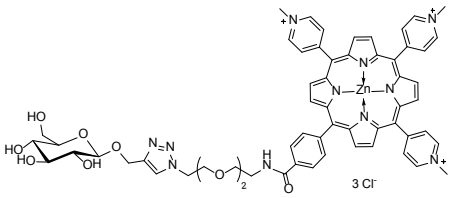
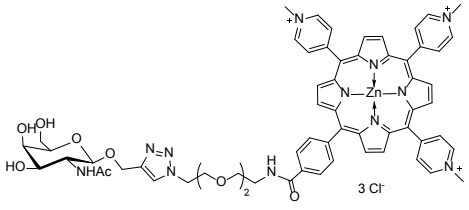
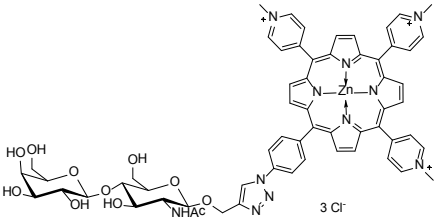
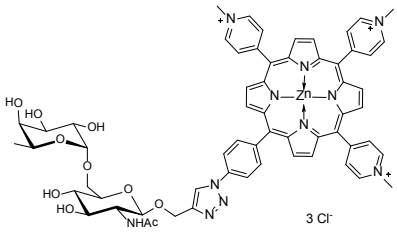
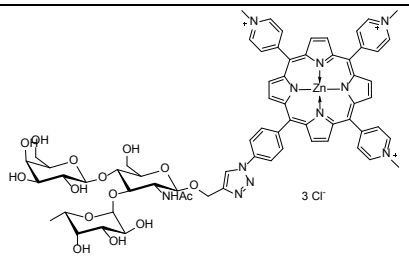
2a		**2**	
10		**11**	
12		**13**	
14		**15**	
16		**17**	
18		**19**	

Experimental

General Remarks

^{1}H and ^{13}C NMR spectra were recorded on JEOL Eclipse 400 and JEOL Lambda 400 spectrometers (operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C). $CDCl_3$, DMSO-d_6,

and MeOH-d_3 were used as solvents. Chemical shifts (δ) are reported in parts per million (ppm), referenced to either $CHCl_3$ (^{1}H, 7.26 ppm; ^{13}C, 77.16 ppm) or DMSO (^{1}H, 2.50 ppm; ^{13}C, 39.52 ppm) or MeOH (^{1}H, 3.31 ppm; ^{13}C, 49.00 ppm). Coupling constants (J) are recorded in Hz and significant multiplicities described by singlet (s), doublet (d), triplet (t), quadruplet (q), broad (br), multiplet (m), or doublet of doublets (dd). ESI mass spectra were performed on a Thermofisher LTQ orbitrap XL (EPSRC Mass Spectrometry Service, Swansea), or on a Varian 500-MS ion trap spectrometer, equipped with a Varian Prostar 212LC binary gradient pumping system and a Varian ProStar 410 autosampler. A standard Varian ESI source was used operating in +ve ion mode. Data was acquired and processed using Varian Workstation software. MALDI mass spectra were performed either on an Applied Biosystems Voyager DE-STR MALDI-TOF (EPSRC National Mass Spectrometry Facilities, Swansea, UK), or on a Bruker Reflex IV MALDI-TOF, operated in reflectron mode and monitoring positive ions. I the latter case, data was acquired and processed using Bruker Compass software. 1,8-Dihydroxy-9,10-dihydroanthracen-9-one (dithranol) was used as the matrix. UV−visible spectra were recorded on a Varian Cary spectrophotometer. Fluorescence spectra were recorded on a Cary Eclipse Fluorimeter. Flash chromatography was carried out on silica gel 60 (MP Biomedicals, 32−63 μm). Analytical TLC was carried out on aluminium sheets pre-coated with silica gel 60 (Fluka, 0.2 mm thick). Chemical reagents were purchased from Sigma-Aldrich, Fluka, Acros, Lancaster, and Alfa Aesar at the highest grade of purity available, and were used as received unless otherwise stated. Dichloromethane and THF were dried by filtration through alumina and storage over activated molecular sieves.[1] All other solvents were purchased from Fisher Scientific and used as received. Deionised water was obtained from a Millipore Milli-Q system. Gel filtrations were performed on Sephadex® G-25 medium, using pre-packed PD-10 columns (GE Healthcare, UK), using deionised water as the eluent. Filtrations through membranes were performed on Sartolon® polyamide filters, 25 mm, 0.20 μm pores. Solid phase extractions were performed on Supelco Discovery DSC-18 cartridges (1 g). RP-HPLC analyses were performed on a system consisting of a Perkin Elmer series 200 LC pump, and a Perkin Elmer 785A UV/vis detector. The separations were performed on a Gemini C18, 5μ, 150 x 4.6 mm, 110 Å (Phenomenex, UK), equipped with a SecurityGuard C18 (ODS) 4 x 3.0 mm ID guard column (Phenomenex, UK) at a flow rate of 1 mL/min. Method A: the mobile phase consisted of 0.1% TFA in water (solvent A) and 0.1% TFA in acetonitrile (solvent B). Gradient: 0.0–10.0 min 0-95% solvent B, 10.0–15.0 min 95% solvent B, 15.0–15.1 min at 95-5% solvent B, 15.1–18.0 min 5% solvent B. Method B: the mobile phase consisted of 0.1M NH_4AcO in water (solvent A) and 0.1M NH_4AcO in 50% aqueous AcCN (solvent B). Gradient: 0–15.0 min 2-100% solvent B, 15.0–18.0 min 100% solvent B, 18.0–18.1 min 100-2% solvent B, 18.1–20.0 min 2% solvent B.

5-(4-azidophenyl)-10,15,20-tris(4-methylpyridiniumyl)porphyrinato zinc(II) trichloride,[2] 5-(4-aminophenyl)-10,15,20-tris(4-sulfonatophenyl)porphyrin trisodium,[4] were synthesised following procedures reported in the literature.

Synthesis

5-[4-azidophenyl]-10,15,20-*tris*(4-sulfonatophenyl)porphyrinato trisodium, 2a: To an ice-cold solution of 5-[4-aminophenyl]-10,15,20-*tris*(4-sulfonatophenyl)porphyrin trisodium (200 mg, 0.21 mmol) in TFA (10 mL), sodium nitrite (30 mg, 0.42 mmol) was added and the mixture was stirred for 30 minutes at 0 °C. Sodium azide (55 mg, 0.84 mmol) was then added and stirring at 0 °C was continued for further 30 minutes. Ethyl acetate (40 mL) was added to the mixture and the resulting precipitate was collected by filtration through cotton wool. The solid was taken in DCM/TEA (95/5) to neutralise the residual TFA, and the solvent was evaporated. The residue was taken in ethanol, the resulting solution was filtered through paper, and the solvent was evaporated. The solid was taken in water (3 mL), $Zn(OAc)_2$ was added and the mixture is stirred for 30 minutes at room temperature. THF was then added to the mixture and the precipitate was filtered through paper and dissolved in methanol, the resulting solution wais filtered through paper, and the porphryrin was precipitated by addition of ethyl acetate. The compound was purified by crystallisation from methanol/diethyl ether. (Purple solid, 168 mg, 77%, two steps). M.p.(°C): > 300. HPLC: (Method B) t_R: 9.84; NMR: (d_6-DMSO) δ: 8.80 (8H, *β-H*), 8.22 (d, 2H, *J* 6.9, *5-o-Ar*), 8.14 (d, 6H, *J* 7.8, *10+15+20-m-Ar*), 8.03 (d, 6H, *J* 7.8, *10+15+20-m-Ar*), 7.55 (d, 2H, *J* 6.9, *5-m-Ar*); ^{13}C NMR: (d_6-DMSO) δ: 149.3, 149.2, 147.2, 142.8, 139.5, 138.9, 135.5, 133.6, 131.7, 131.5, 123.8, 120.0, 119.4, 117.5; MALDI-MS (-ve, CHCA) (m/z): calcd. for $[C_{44}H_{24}N_7O_9S_3Zn]^{3-}$/3: 318.0035, found: 318.0038 $[M- 3Na]^{3-}$/3; UV/vis: (H_2O) λ (%): 422 (100), 557 (14.4), 597 (11.7); log ε_{422}: 5.16

5-[4-2-(2-(2-Azidoethoxy)ethoxy)ethanaminocarbonyl]phenyl]-10,15,20-tris(4-pyridyl)porphyrin: To a stirred solution of 5-[4-(Succinimide-N-oxycarbonyl)phenyl]-10,15,20-tri-(4-pyridyl) porphyrin (100 mg, 0.135 mmol) in dry DMSO (10 ml) was added 2-(2-(2-azidoethoxy)ethoxy)ethanamine (65 mg, 0.33 mmol), and anhydrous potassium carbonate (58 mg, 0.416 mmol). The mixture was stirred for two days at 40 ˚C, protected from light and atmospheric moisture. Water (10 ml) was added, and the mixture centrifuged. The resulting solid was precipitated from methanol over dichloromethane to yield a purple solid (88 mg, 82 %). Rf: (silica, 5 % MeOH in DCM): 0.35. ^{1}H NMR ($CDCl_3$, d_4-MeOH): δ 8.92-8.97 (6H, m, 10,15,20-*m-Ar*), 8.49-8.92 (8H, m, *β-H*), 8.17-8.26 (m, 4H, *5-Ar*), 8.15 (6H, m, 10,15,20-*o-Ar*), 7.77 (1H, m, N*H*), 3.56-3.84 (10H, m, O*CH*$_2$). ^{13}C-NMR: ($CDCl_3$) δ: 168.1, 150.5, 147.9, 144.7, 134.6, 134.2, 129.9, 125.8, 120.5, 117.4, 117.1, 70.6, 70.2, 70.1, 70.0, 50.6, 40.4. HRMS (ESI^+): calcd. for $C_{48}H_{39}N_{11}O_3Na$: 840.3130, found: 840.3125. UV/vis: (DCM) λ (%): 417 (100), 513 (5.4), 547 (2.4), 588 (2.6), 642 (0.8). log ε_{417}: 5.58.

5-[4-2-(2-(2-azidoethoxy)ethoxy)ethanaminocarbonyl]phenyl]-10,15,20-*tris*(1-methyl-pyridinium-4-yl)porphyrinato zinc (II) trichloride, 3: To a stirred solution of 5-[4-2-(2-(2-azidoethoxy)ethoxy)ethanaminocarbonyl]phenyl]-10,15,20-tris(4-pyridyl)porphyrin (87 mg, 0.106 mmol) in DMF (10ml) was added methyl iodide (2 ml, 32 mmol) via syringe. The reaction mixture was stirred at 40 °C overnight. The mixture was cooled to room temperature and cold diethyl ether (100 ml) was added. The mixture was filtered through cotton wool, and the residue redissolved in methanol. A solution of zinc acetate (107 mg, 0.59 mmol) in water (10 ml) was added and the

mixture was stirred at room temperature for 3 hours, and NH_4PF_6 added. The resulting solution was filtered and the precipitate redissolved in acetone. Tetrabutylammonium chloride was added, and the resulting solution filtered. The product was precipitated from diethyl ether over methanol to yield the product as a green solid (84 mg, 77.5 %). Rf: 0.49 (silica, 1/1/8 satd. aq. KNO_3/water/MeCN). 1H NMR (DMSO-d6): δ 9.38-9.49 (6H, m, 10,15,20-*m-Ar*), 8.85-9.04 (14H, m, β-*H* and 10,15,20-*o-Ar*), 8.30-8.36 (2H, d, *J* 8.32, *5-o-Ar*), 8.23-8.29 (2H, d, *J* 8.26, *5-m-Ar*), 4.73 (9H, m, NCH_3), 3.57-3.74 (10H, m, OCH_2), 3.42 (2H, m, CH_2N_3). ^{13}C-NMR: (d_6-DMSO) δ: 166.8, 159.0, 150.5, 148.9, 148.7, 148.5, 145.4, 144.2, 134.6, 134.3, 133.6, 132.7, 132.2, 122.8, 116.0, 115.4, 70.3, 70.0, 69.6, 50.6, 48.2. HRMS (ESI$^+$): calcd. for $C_{51}H_{46}N_{11}O_3Zn$: 308.1020 found 308.1025. UV/vis: (H_2O) λ (%): 434 (100), 563 (8.1), 607 (3.6). logε_{434}: 5.26.

General procedure for the synthesis of porphyrin-carbohydrate conjugates under Huisgen conditions: 5-{[4-(β-D-mannopyranosyl)-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20- *tris*[1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride, 10: A solution of 5-(4-azidopheny)-10,15,20- *tris*[(1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride (40 mg, 0.05 mmol) and 1-β-D-propargyloxymannose (15 mg, 0.07 mmol) is treated with $CuSO_4 \cdot 5H_2O$ (3.5 mg, 0.01 mmol) and sodium ascorbate (5.5 mg, 0.03 mmol), and the resulting solution is stirred at room temperature for 20 minutes, whereupon TLC shows that conversion of the starting porphyrin is complete. The mixture is diluted with 10% aqueous NH_4PF_6, and the crude porphyrin is recovered by centrifugation. The solid is dissolved in acetone and porphyrin is precipitated again as the trichloride salt by drop-wise addition of a 20% solution of tetrabutylammonium chloride in acetone. The porphyrin is recovered by centrifugation, and purified my crystallisation from methanol/diethyl ether. (Green solid, 50 mg, 93%). M.p.(°C): > 300. HPLC (Method A): t_R: 6.55; ^{1}H NMR: (d_6-DMSO + D_2O) δ: 9.40 (6H, br, *10+15+20-m-Ar*), 9.16 (1H, s, 5_T-*H*), 9.04 and 8.98 (8H, 2m, *β-H*), 8.89 (6H, m, *10+15+20-o-Ar*), 8.38 (4H, m, *5-o-Ar* + *5-m-Ar*), 4.89 (1H, br s, *H-1*), 4.88 (1H, m, OC*H*(H)), 4.71 (9H, m, CH_3), 4.70 (1H, m, OCH(*H*)), 3.77 (1H, d, $J_{6',6}$ 10.7, *H-6'*), 3.71 (1H, br, *H-2*), 3.60-3.45 (3H, m, *H-3*, *H-4*, *H-5*), 3.50 (1H, m, *H-6*); ^{13}C NMR: (d_6-DMSO) δ: 158.9, 148.9, 148.8, 148.5, 145.7, 144.2, 133.0, 132.7, 132.4, 122.3, 99.2, 74.9, 71.5, 71.0, 67.5, 61.5, 59.7, 48.5; MALDI-MS (+ve, dithranol) (m/z): calcd. for $C_{53}H_{47}N_7O_6Zn$: 983.295, found: 983.519 [M- 3Cl]$^+$; UV/vis: (H_2O) λ (%): 434 (100), 563 (13.7), 609 (9.8); log ε_{434}: 5.44

5-{[4-(β-D-glucopyranosyl)-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20- *tris*[1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride, 11: The title compound was obtained following the general procedure. (Green solid, 46 mg, 91 %). M.p.(°C): > 300 (decomp.). HPLC (Method A): t_R: 6.44; ^{1}H NMR: (d_6-DMSO/ D_2O) δ: 9.40 (6H, m, *10+15+20-m-Ar*), 9.16 (1H, s, 5-triazole-H), 9.05 and 9.00 (8H, 2m, *β-H*), 8.90 (6H, *10+15+20-o-Ar*), 8.39 (4H, m, *5-o-Ar* + *5-m-Ar*), 5.05 (1H, d, *J* 12.1, OC*H*(H)), 4.89 (1H, d, *J* 12.2, OCH(*H*)), 4.72 (CH_3), 4.42 (1H, d, $J_{1,2}$ 8.4, *H-1*), 3.72 (1H, d, $J_{6',6}$ 12.1, *H-6'*), 3.53 (1H, dd, $J_{6,6'}$ 11.9, $J_{6,5}$ 6.0, *H-6*), 3.25 - 3.11 (4H, m, *H-2,3,4,5*); ^{13}C NMR: (d_6-DMSO) δ: 158.9, 150.6, 148.9, 148.8, 148.5, 146.0, 144.2, 142.7, 136.9, 135.9, 133.1, 132.8, 132.7, 132.4, 123.5, 122.3, 118.9, 116.1, 102.8, 77.4, 77.0, 73.9, 70.6, 62.1, 61.6, 48.4; MALDI-MS

(+ve, dithranol) (m/z): calcd. for $C_{53}H_{47}N_7O_6Zn$: 983.295, found: 983.331 [M- 3Cl]$^+$; UV/vis: (H_2O) λ (%): 434 (100), 564 (17.4), 611 (14.2); log ε_{434}: 5.33

5-{4-[(2-acetamido-2-deoxy-β-D-glucopyranosyl)-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20- *tris*[1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride, 12: The title compound was obtained following the general procedure. (Green solid, 45 mg, 91 %). M.p.(°C): > 300. HPLC (Method A): t_R: 6.52; ^{1}H NMR: (d_6-DMSO/ D_2O) δ: 9.52 (1H, s, 5-triazole-H), 9.50, 9.43, 9.32 (3 br, 14H, *β-H* and *10+15+20-Ar*), 8.77 (br, 4H, *5-Ar*), 8.24 (1H, d, *J* 9.9, N*H*), 5.02 (1H, d, *J* 12.4, OC*H*(H)), 4.86 (1H, d, *J* 12.4, OCH(*H*)), 4.71 (CH_3), 4.62 (1H, d, $J_{1,2}$ 7.9 Hz, *H-1a*), 4.23 (1H, br, *H-1b*), 3.91 (1H, d, $J_{6',6}$ 11.0, *H-6'a*), 3.71 (1H, dd, $J_{6,6'}$ 11.0, $J_{6,5}$ 4.5, *H-6a*), 3.65-3.33 (10H, m (under solvent peak), *H-6b*, *H-2a/b*, *H-3a/b*, *H-5a/b*, *H-4a/b*), 1.86 (3H, s, OCH_3); ^{13}C NMR: (d_6-DMSO) δ: 170.1, 158.9, 148.9, 148.8, 148.5, 145.8, 144.2, 142.7, 135.9, 133.0, 132.7, 132.4, 132.1, 123.4, 122.3, 118.9, 116.1, 115.4, 100.9, 77.6, 74.6, 71.1, 61.9, 61.6, 55.8, 48.3, 23.6; MALDI-MS (+ve, dithranol) (m/z): calcd. for $C_{56}H_{50}N_{11}O_6Zn$: 1024.3321, found: 1024.3321 [M-3Cl]$^+$; UV/vis: (H_2O) λ (%): 434 (100), 566 (19.3), 615 (16.3); log ε_{421}: 5.17

5-{[4-(β-D-mannopyranosyl)-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20-*tris*(4-sulfonatophenyl)porphyrinato zinc(II) trisodium, 13: The title compound was obtained following the general procedure. The desired compound was recovered from the reaction mixture by addition of acetone and filtration of the solid. The residue was taken in ethanol, the resulting solution was filtered through paper, and the precipitation of the porphyrin was induced by addition of acetone. The solid was filtered and dried *in vacuo*. (Purple solid, 33 mg, 63 %). M.p.(°C): > 300. HPLC (Method B): t_R: 8.99; ^{1}H NMR: (d_6-DMSO/ D_2O) δ: 9.59 (1H, s, 5-triazole-H), 9.31-9.24 (8H, m, *β-H*), 8.84 (d, 2H, *J* 9.0, *5-o-Ar*), 8.71 (d, 2H, *J* 9.0, *5-m-Ar*), 8.53 (d, 6H, *J* 8.7, *10+15+20-m-Ar*), 8.71 (d, 6H, *J* 8.7, *10+15+20-m-Ar*), 4.91 (1H, d, *J* 12.1 Hz, OCH(*H*)), 4.89 (1H, d, $J_{1,2}$ 1.2, H-1), 4.78 (1H, d, *J* 12.1, OC*H*(H)), 3.80-3.45 (6H, m, *H-6/6'*, *H-5*, *H-4*, *H-3*, *H-2*); ^{13}C NMR: (d_6-DMSO) δ: 150.1, 149.9, 149.8, 149.7, 147.2, 145.5, 143.6, 136.6, 135.9, 134.2, 132.4, 132.1, 124.4, 123.4, 120.9, 120.7, 120.6, 119.4, 118.9, 99.7, 74.7, 70.7, 67.4, 59.7; MALDI-MS (-ve, dithranol) (m/z): $[C_{58}H_{38}N_7O_{15}S_3Zn]^{3-}$/3: 390.6965, found: 390.6966 [M- 3Na]$^{3-}$/3; UV/vis: (H_2O) λ (%): 422 (100), 558 (12.2), 595 (10); log ε_{422}: 5.44

5-{4[(β-D-mannopyranosyl)-oxymethyl)-2-{2-[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]ethoxy}ethanaminocarbonyl}phenyl)-10,15,20-*tris*(1-methylpyridinium-4-yl)porphyrinato zinc(II) trichloride, 14: The title compound was obtained following the general procedure. (Green solid, 2.9x10^{-2} mmol scale, 35 mg, 96 %). ^{1}H NMR: (d_6-DMSO/ D_2O) δ: 9.32-9.50 (6H, m, *10,15,20-m-Ar*), 8.84-9.07 (14H, m, *β-H* and *10,15,20-o-Ar*), 8.29-8.34 (2H, d, *J* 8.06, *5-o-Ar*), 8.22-8.28 (d, 2H, *J* 8.43, *5-m-Ar*), 8.14 (s, 1H, triazole *H-5*), 4.75 (br s, 1H,H-1), 4.71 (9H, s, NCH_3), 4.68 (1H, d, OC*H*(H)), 4.56 (2H, t, J 5.0, OCH_2), 4.53 (1H, d, *J* 12.2, OCH(*H*)), 3.89 (2H, t, *J* 5.0, OCH_2), 3.67 (1H, d, *J* 11.0, *H-6'*), 3.60-3.70 (8H, m, OCH_2), 3.61 (1H, br, *H-2*), 3.45 (1H, m (under solvent), *H-3*), 3.43 (1H, m (under solvent), *H-6*), 3.41 (2H, m (under solvent peak), *H-4*, *H-5*). ^{13}C-NMR (d_6-DMSO/ D_2O): δ 166.8, 158.97, 150.46, 148.88, 148.75, 148.47, 144.20, 144.00, 134.57, 134.29, 133.73, 132.66, 132.26, 126.26, 125.06, 116.09, 115.42, 99.57, 74.79, 71.51, 70.77, 70.13, 69.58, 69.29, 67.59, 65.50, 62.04, 61.82, 59.59, 49.99, 48.27. MALDI-MS (+ve, CHCA) (m/z): 1271 [M+Na]$^+$. UV/vis: (H_2O) λ (%): 435 (100), 563 (7.7), 611 (4.1). log ε_{435}: 5.20.

5-(4-[(β-D-glucopyranosyl)-oxymethyl]-2-{2-[2-(1*H*-1,2,3-triazol-1-yl)ethoxy]ethoxy}ethanaminocarbonyl]phenyl}-10,15,20-*tris*(1-methylpyridinium-4-yl)porphyrinato zinc (II) trichloride, 15: The title compound was obtained following the general procedure. (Green solid, 2.9x10^{-2} mmol scale, 34 mg, 93 %). ^{1}H NMR: (*d*$_6$-DMSO/ D_2O) δ: 9.35-9.45 (6H, m, *10,15,20-m-Py*), 8.85-9.06 (14H, m, *β-H* and *10,15,20-o-Ar*), 8.29-8.37 (2H, d, *J* 8.32, *5-o-Ar*), 8.22-8.28 (2H, d, *J* 8.26, *5-m-Ar*), 8.15 (1H, s, triazole *H-5*), 4.87 (1H, d, *J* 12.2, OC*H*(H)), 4.71 (9H, s, NCH_3), 4.65 (1H, d, *J* 12.2, OCH(*H*)), 4.57 (2H, t, OCH_2), 4.27 (1H, d, $J_{1,2}$ 7.8, *H-1*), 3.89 (2H, m, CH_2N$_3$), 3.72 (2H, m, *H-6* and N*H*), 3.70-3.60 (8H, m, OCH_2), 3.45 (1H, m, *H-6'*), 3.16-3.05 (3H, m, *H-2*, *H-3*, *H-4*), 3.00 (1H, m, *H-5*). ^{13}C-NMR (*d*$_6$-DMSO/ D_2O) δ: 166.9, 159.0, 150.5, 148.9, 148.7, 148.5, 145.3, 144.2, 134.6, 134.3, 133.7, 132.7, 132.2, 126.7, 125.2, 122.8, 116.1, 115.4, 102.6, 77.3, 77.5, 74.0, 70.6, 70.2, 70.1, 69.6, 69.3, 62.0, 61.7, 50.0, 48.3. MALDI-MS (+ve, CHCA): 1142 [M-3Cl]$^+$. UV/vis: (H_2O) λ (%): 437 (100), 563 (7.5), 610 (4.0). log ε$_{437}$: 5.29.

5-{4[(2-acetamido-2-deoxy-β-D-glucopyranosyl)-oxymethyl)-2-{2-[2-(1*H*-1,2,3-triazol-1-1yl)ethoxy]ethoxy}ethanaminocarbonyl}phenyl)-10,15,20-*tris*(1-methylpyridinium-4-yl)porphyrinato zinc(II) trichloride, 16: The title compound was obtained following the general procedure. (Green solid, 2.9x10^{-2} mmol scale, 36 mg, 97 %). ^{1}H NMR (*d*$_6$-DMSO/D_2O) δ: 9.37-9.46 (6H, m, *10,15,20-m-Ar*), 8.84-9.07 (14H, m, *β-H* and *10,15,20-o-Ar*), 8.30-8.37 (2H, d, *J* 8.16, *5-o-Ar*), 8.22-8.29 (2H, d, *J* 7.55, *5-m-Ar*), 8.05 (1H, s, triazole *H-5*), 7.75 (1H, m, N*H*), 4.82 (1H, d, *J* 12.2, OC*H*(H)), 4.71 (9H, m, NCH_3), 4.61 (1H, d, *J* 12.2, OCH(*H*)), 4.56 (2H, t, OCH_2), 4.41 (1H, d, $J_{1,2}$ 8.4, *H-1*), 3.89 (2H, m, OCH_2), 3.69 (1H, m, *H-6'*), 3.59-3.69 (8H, m, OCH_2), 3.44 (2H, m (under solvent peak), *H-6*, *H-2*), 3.30 (1H, t, $J_{3,2}$ = $J_{3,4}$ 8.7, *H-3*), 3.13 (m, 1H, *H-5*), 3.08 (1H, m, *H-4*), 1.79 (3H, s, CH_3). ^{13}C-NMR (DMSO-d$_6$/D_2O): δ 169.7, 166.8, 159.0, 150.5, 148.9, 148.8, 148.5, 145.4, 144.2, 134.6, 134.2, 133.7, 132.7, 132.2, 126.1, 125.0, 122.8, 116.1, 115.7, 100.9, 77.7, 74.2, 71.4, 70.2, 70.0, 69.6, 69.3, 65.5, 61.9, 61.7, 55.8, 50.0, 48.3, 23.7. MALDI-MS (+ve, CHCA) (m/z): 1183 [M-3Cl]$^+$. UV-vis (H_2O): λ (%): nm 436 (100), 563 (7.8), 610 (4.5). logε$_{436}$: 5.21.

5-{4-[(β-D-glucopyranosyl-(1→4)-(2-acetamido-2-deoxy-β-D-galactopyranosyl))-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl)-10,15,20-*tris*(1-methylpyridinium-4-yl)porphyrinato zinc(II) trichloride, 17: The title compound was obtained following the general procedure. (Green solid, 54 mg, 73 %). M.p.(°C): > 300. HPLC (Method A): t_R: 6.40; ^{1}H NMR: (*d*$_6$-DMSO) δ: 9.89 (6H, m, *10+15+20-m-Ar*), 9.51 (1H, s, 5-triazole-H), 9.50 and 9.34 (8H, 2br, *β-H*), 8.77 (4H, br, *5-Ar*), 8.29 (1H, d, *J* 9.8, N*H*), 5.02 (1H, d, *J* 12.4, OC*H*(H)), 4.86 (1H, d, *J* 12.4, OCH(*H*)), 4.71 (9H, br, NCH_3), 4.62 (1H, d, $J_{1,2}$ 7.9, *H*-1a), 4.23 (1H, br s, *H*-1b), 3.91 (1H, d, $J_{6',6}$ 11.0, *H*-6'a), 3.71 (1H, d, $J_{6,6'}$ 11.0, $J_{6,5}$ 4.5, *H*-6a), 3.65-3.33 (10H, m (under solvent peak), *H*-6b, *H*-2a/b, *H*-3a/b, *H*-5a/b, *H*-4a/b), 1.86 (3H, s, OCH_3); ^{13}C NMR: (*d*$_6$-DMSO) δ: 169.8, 158.9, 148.9, 148.8, 148.5, 145.7, 144.2, 142.7, 135.9, 133.8, 133.1, 132.7, 132.4, 123.4, 122.3, 118.9, 116.1, 115.5, 104.5, 100.7, 81.9, 76.1, 75.7, 73.6, 72.3, 71.1, 68.6, 61.9, 60.9, 55.2, 23.6; MALDI-MS (+ve, CHCA) (m/z): calcd. for $C_{61}H_{60}N_{11}O_{11}Zn$: 1186.37, found: 1186.37 [M- 3Cl]$^+$; UV/vis: (H_2O) λ (%):434 (100), 563 (18.8), 611 (15.7); log ε$_{434}$: 5.39

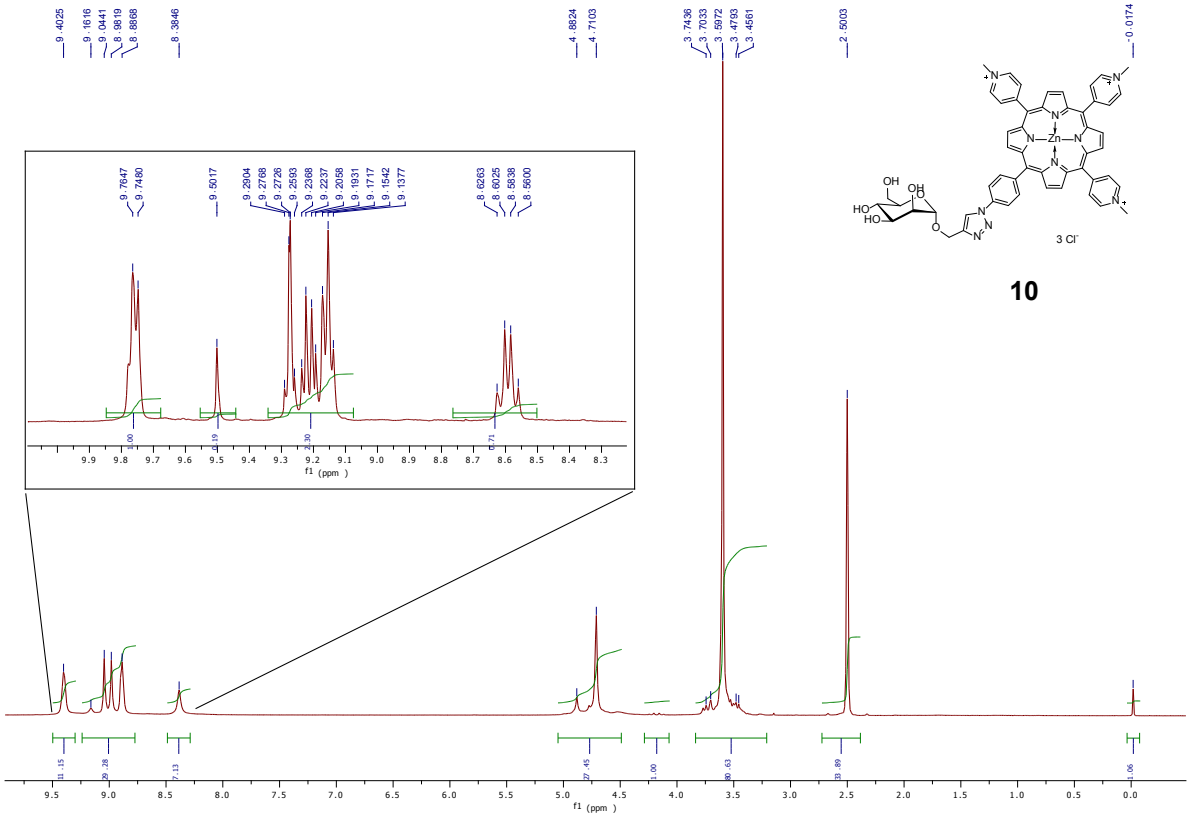
5-{4-[(α-L-fucopyranosyl-(1→6)-(2-acetamido-2-deoxy-β-D-glucopyranosyl))-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20-*tris*[1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride, 18: The title compound was obtained following

the general procedure. (Green solid, 1.79x10^{-2} mmol scale, 17 mg, 74 %). M.p.(°C): > 300 (decomp.); ^{1}H NMR: (*d*$_6$-DMSO) δ: 8.85 (8H, *β-H*), 8.26 (d, 2H, *J* 8.4, *5-o-Ar*), 8.19 (d, 6H, *J* 7.7, *10+15+20-m-Ar*), 8.06 (d, 6H, *J* 7.7, *10+15+20-m-Ar*), 7.58 (d, 2H, *J* 8.6, *5-m-Ar*); ^{13}C NMR: (*d*$_6$-DMSO) δ: 170.1, 158.9, 148.9, 148.8, 148.5, 145.8, 144.2, 136.9, 135.9, 132.7, 132.4, 123.4, 118.9, 116.1, 115.4, 100.9, 77.6, 74.6, 71.1, 61.9, 61.6, 55.8, 48.3, 23.6; MALDI-MS (-ve, CHCA) (m/z): calcd. for $C_{61}H_{60}N_{11}O_{10}Zn$: 1170.38, found: 1170.40 [M- 3Cl]$^{+}$; UV/vis: (H_2O) λ (%): 431 (100), 563 (8.1), 615 (6.0); log ε$_{421}$: 5.33

5-{4-[(α-L-fucopyranosyl-(1→3)-[(β-D-galactopyranosyl-(1→4)]-(2-acetamido-2-deoxy-β-D-glucopyranosyl))oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl-10,15,20-*tris*[1-methylpyridinium)-4-yl]porphyrinato zinc(II) trichloride, 19: The title compound was obtained following the general procedure. (Green solid, 3.45x10^{-2} mmol scale, 37 mg, 75 %). M.p.(°C): > 300 (decomp). HPLC (Method A): t_R: 6.40; ^{1}H NMR: (*d*$_6$-DMSO) δ: 9.89 (8H, br, *β-H*), 9.07 (1H, s, 5-triazole-H), 8.26 (d, 2H, *J* 8.4, *5-o-Ar*), 8.19 (d, 6H, *J* 7.7, *10+15+20-m-Ar*), 8.06 (d, 6H, *J* 7.7, *10+15+20-m-Ar*), 7.58 (d, 2H, *J* 8.6, *5-m-Ar*), 5.01 (1H, d, *J* 12.6, OC*H*(H)), 4.86 (1H, d, *J* 12.6, OCH(*H*)), 4.86 (1H, d $J_{1,2}$ = 3.0, H-1c), 4.70 (N-CH$_3$), 4.68 (1H, br, H-1a), 4.34 (1H, d, $J_{1,2}$ 6.8, H-1b), 3.86 (2H, br, H-6a), 3.76 (1H, m, H-2a), 3.74 (13H, m (under solvent peak), H-6b/6'b, H-2b/c, H-3a/b/c, H-5a/b/c, H-4a/b/c), 1.85 (3H, s, NHCOCH$_3$), 1.02 (3H, d, $J_{6,5}$ 6.1, H-6c); ^{13}C NMR: (*d*$_6$-DMSO) δ: 158.8, 148.9, 148.5, 144.2, 135.8, 132.7, 122.3, 118.9, 116.1, 115.4, 75.2, 74.3, 74.1, 72.2, 71.4, 70.0, 68.9, 67.9, 60.4, 48.3; MALDI-MS (+ve, CHCA) (m/z): calcd. for $C_{67}H_{70}N_{11}O_{15}Zn$: 1332.4, found: 1332.4 [M- 3Cl]$^{+}$; UV/vis: (H_2O) λ (%): 419 (100), 563 (20.1), 608 (16.8); log ε$_{421}$: 5.34

5-{4-[(α-L-fucopyranosyl-(1→6)-(2-acetamido-2-deoxy-β-D-glucopyranosyl))-oxymethyl]-1*H*-1,2,3-triazol-1-yl}phenyl)-10,15,20-*tris*(4-sulfonatophenyl)porphyrinato zinc(II) trisodium, 20: The title compound was obtained following the general procedure. (Dark purple solid, 3.45x10^{-2} mmol scale, 30 mg, 71 %). M.p.(°C): > 300 (decomp). HPLC (Method B): t_R: 9.34; ^{1}H NMR: (*d*$_6$-DMSO + D_2O) δ: δ 9.45 (1H, s, 5-triazole-*H*), 9.45-9.22 (8H, m, *β-H*), 8.78 (d, 2H, *J* 8.9, *5-o-Ar*), 8.70 (d, 2H, *J* 8.9, *5-m-Ar*), 8.51 (d, 6H, *J* 8.6, *10+15+20-m-Ar*), 8.38 (d, 6H, *J* 8.6, *10+15+20-m-Ar*), 4.95 (1H, d, *J* 12.3, OCH(*H*), 4.85 (1H, d, *J* 12.3, OC*H*(H)), 4.79 (1H, d, $J_{1,2}$ 2.3, H-1B), 4.49 (1H, d, $J_{1,2}$ 8.6, H-1A), 4.00 (1H, q, $J_{5,6}$ 6.0, H-5B), 3.97 (1H, d, $J_{6',6}$ 11.6, H-6'A), 3.60 (1H, m, H-6A), 3.69 - 3.55 (4H, (under solvent) m, H-2A, H-2B, H-3B, H-4B), 3.42 (1H, app t, $J_{3,2}$=$J_{3,4}$ 8.2, H-3A), 3.34 (1H, m, H-5A), 3.15 (1H, app t, $J_{4,3}$=$J_{4,5}$ 8.6 Hz, H-4A), 1.85 (3H, s, COCH3), 1.12 (3H, d, $J_{6,5}$ 6.3, H-6B); ^{13}C NMR: (*d*$_6$-DMSO) δ: 170.2, 149.9, 149.8, 149.6, 147.2, 143.6, 136.6, 135.9, 134.2, 132.3, 124.4, 123.5, 120.7, 120.6, 118.9, 100.5, 76.1, 72.0, 70.2, 68.9, 66.6, 55.7, 23.6; MALDI-MS (-ve, CHCA) (m/z): calcd. for $[C_{61}H_{51}N_7O_{19}S_3Zn]^{3-}$/3: 453.0580, found: 453.0582 [M- 3Na]$^{3-}$/3; UV/vis: (H_2O) λ (%): 424 (100), 554 (13.2), 595 (10.6); log ε$_{422}$: 5.36

Spectra



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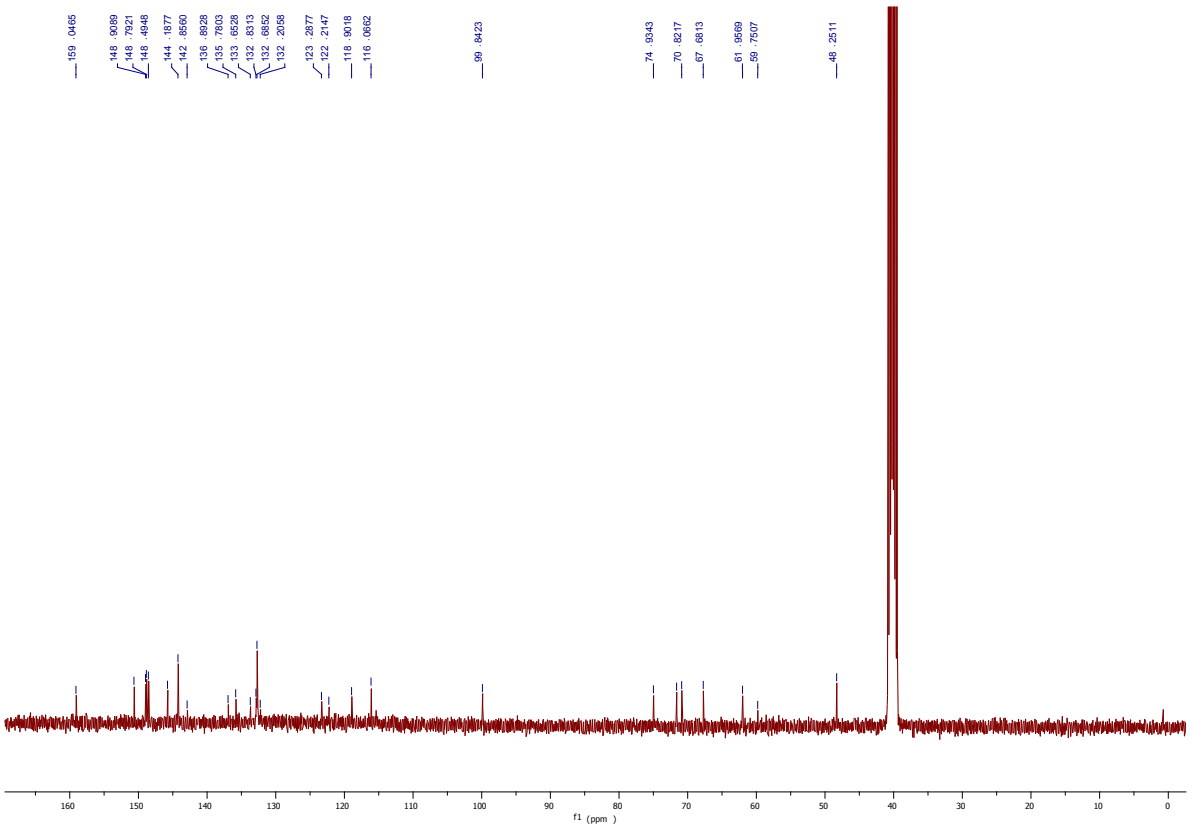

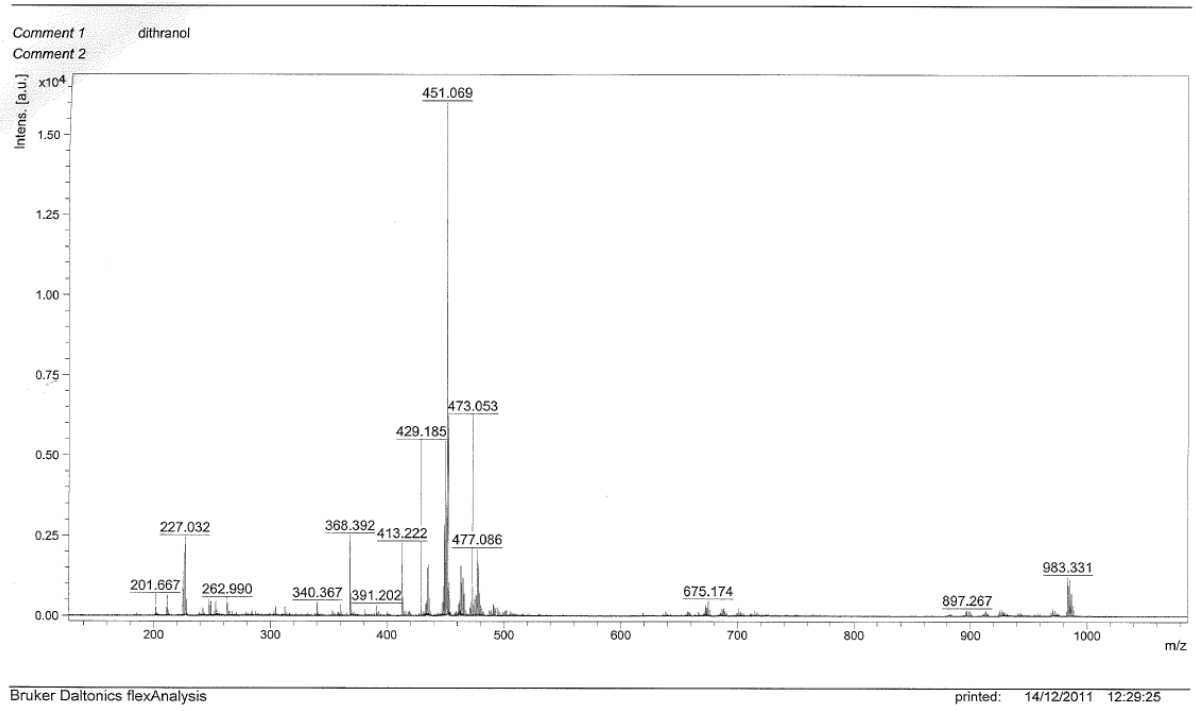
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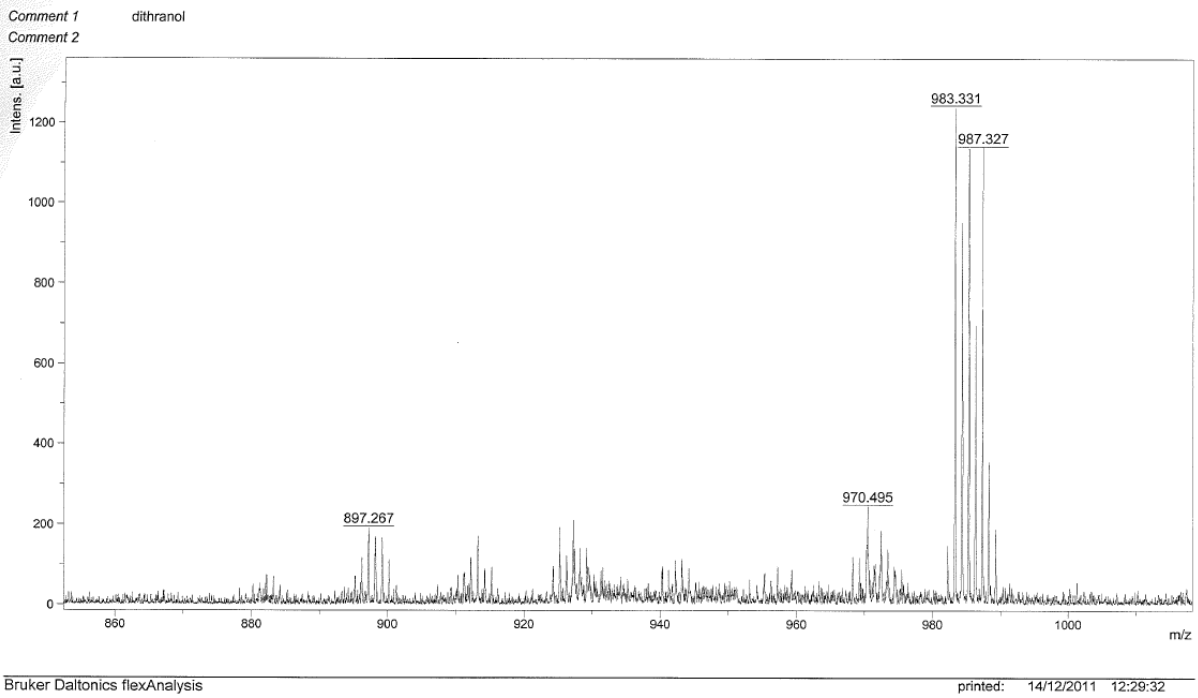
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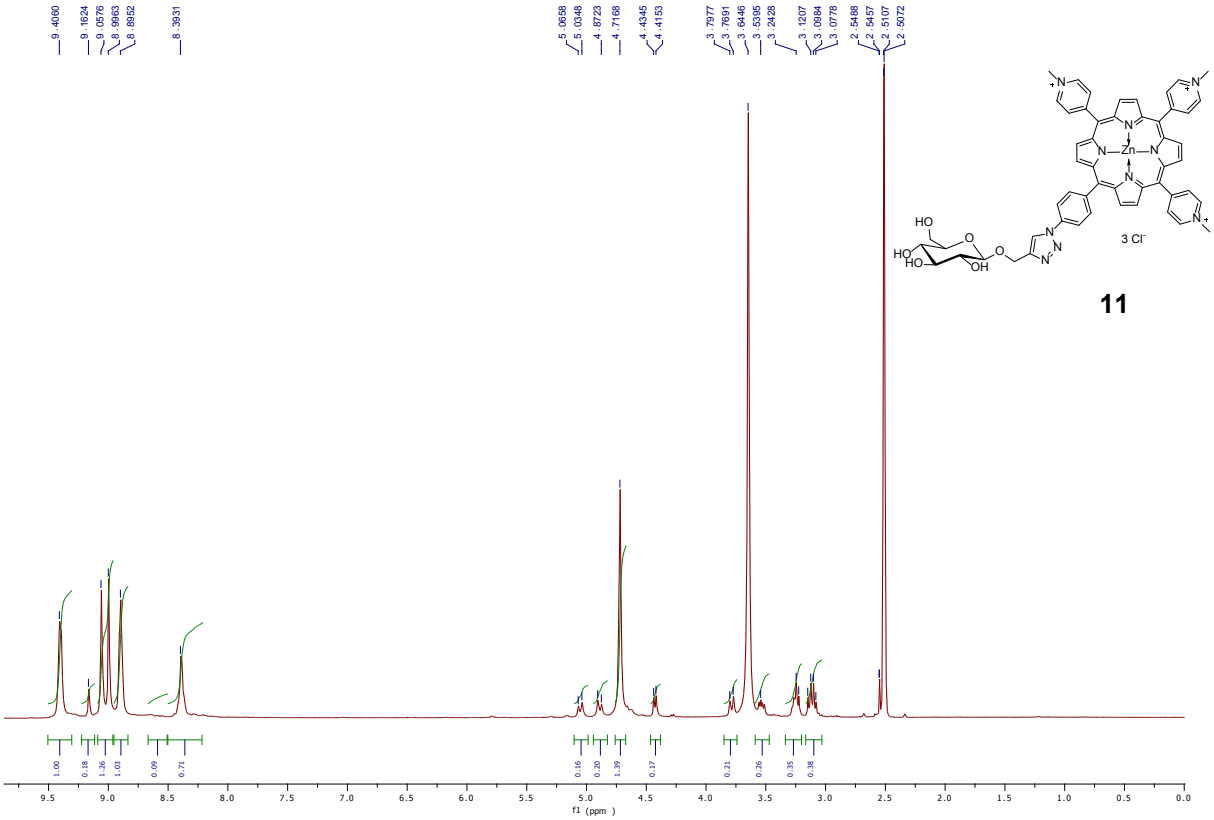

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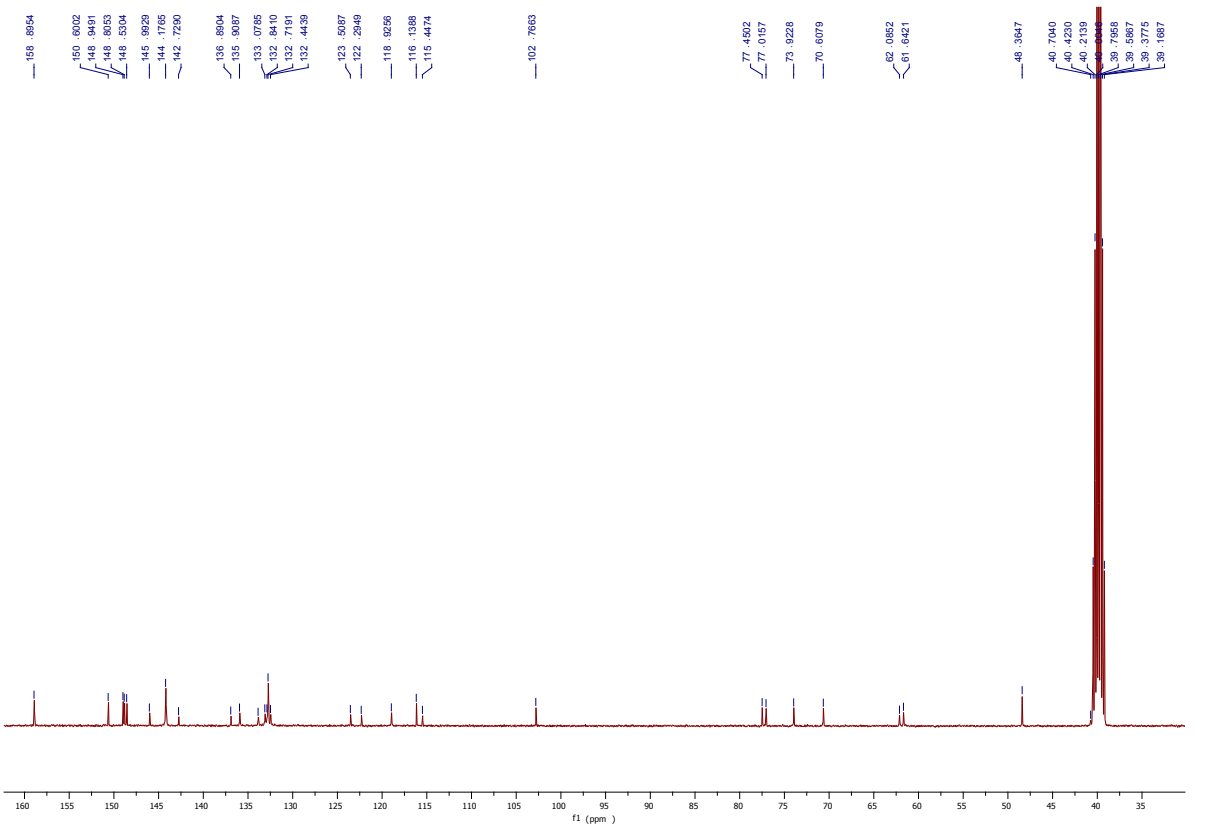

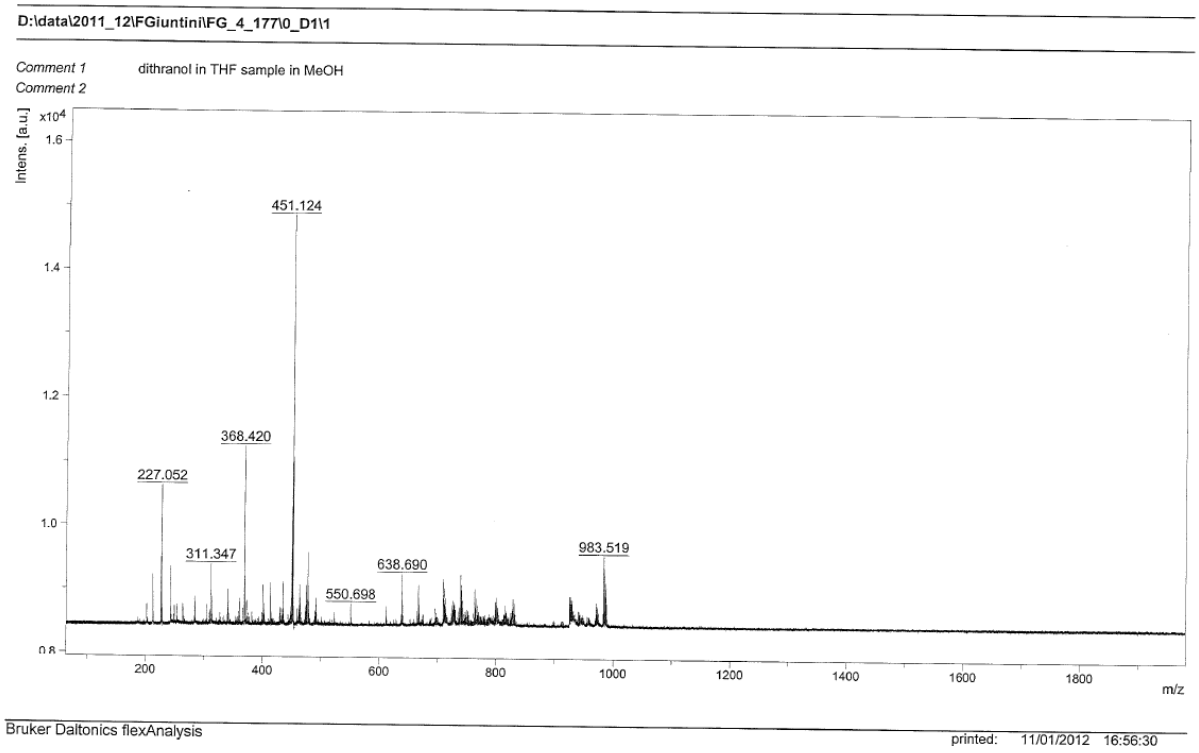

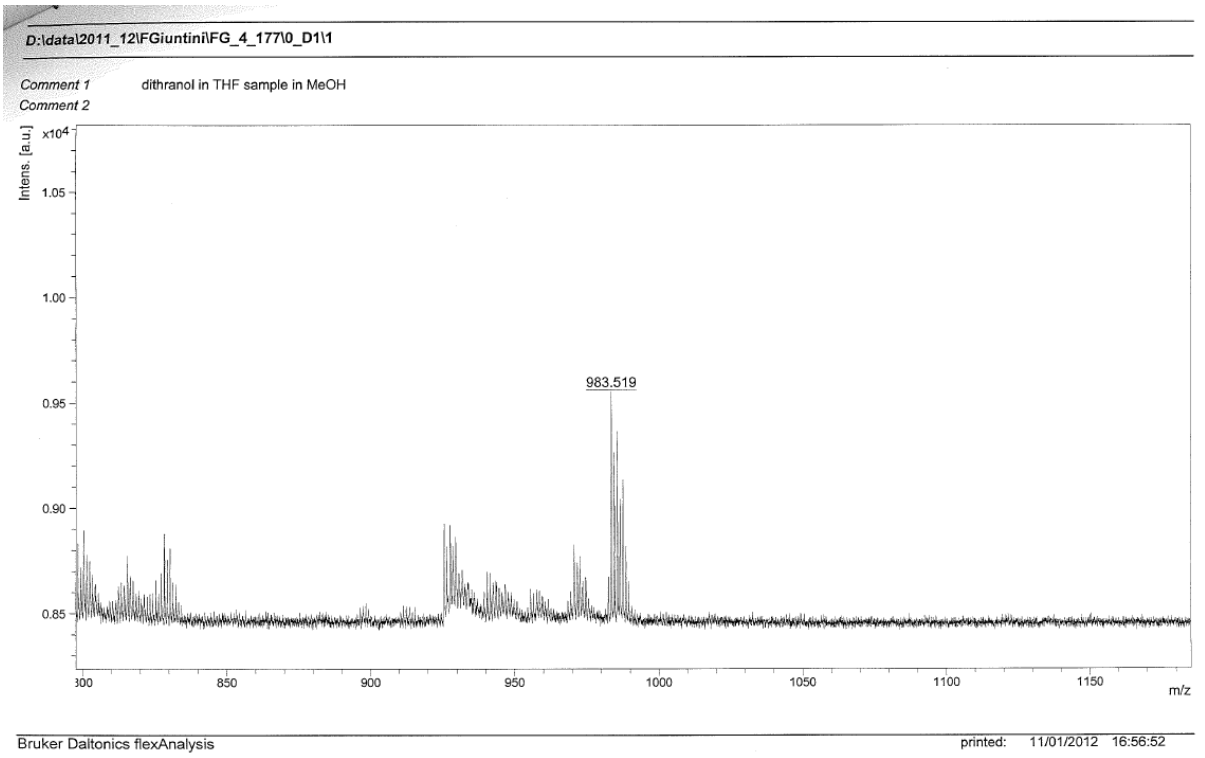

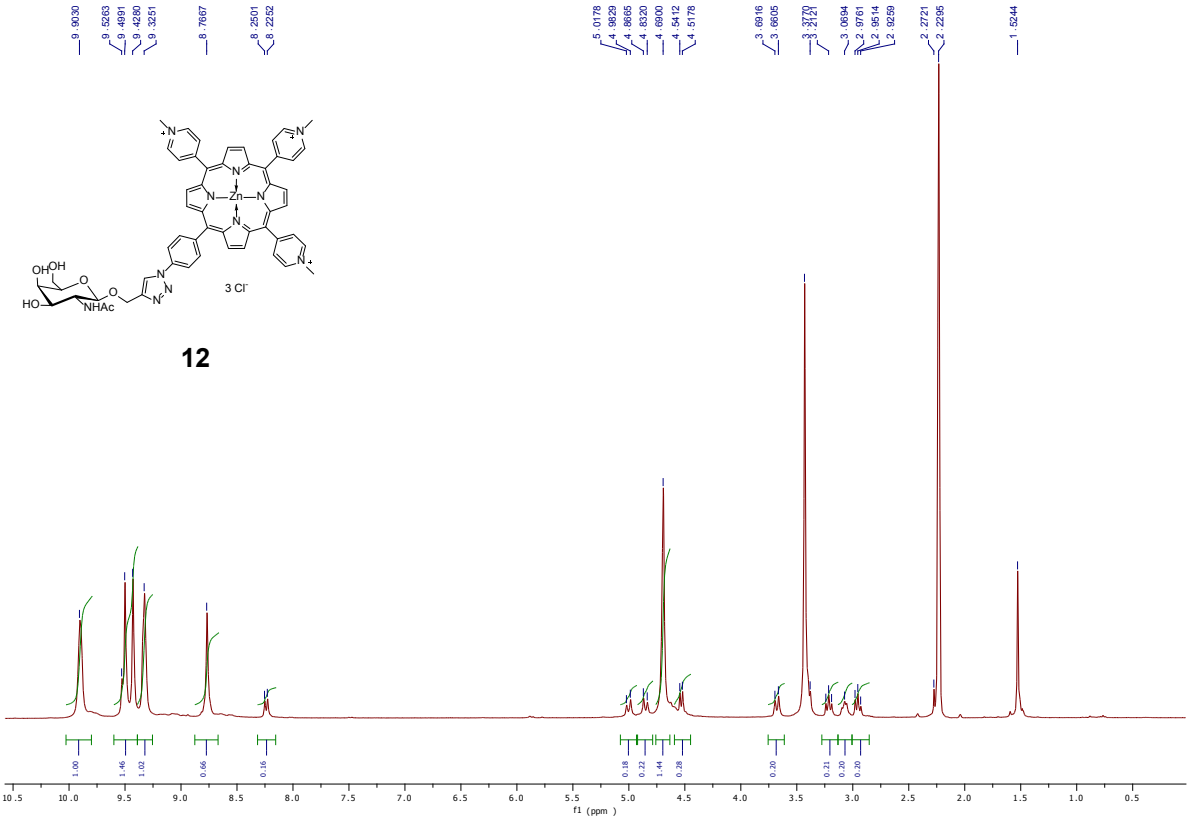

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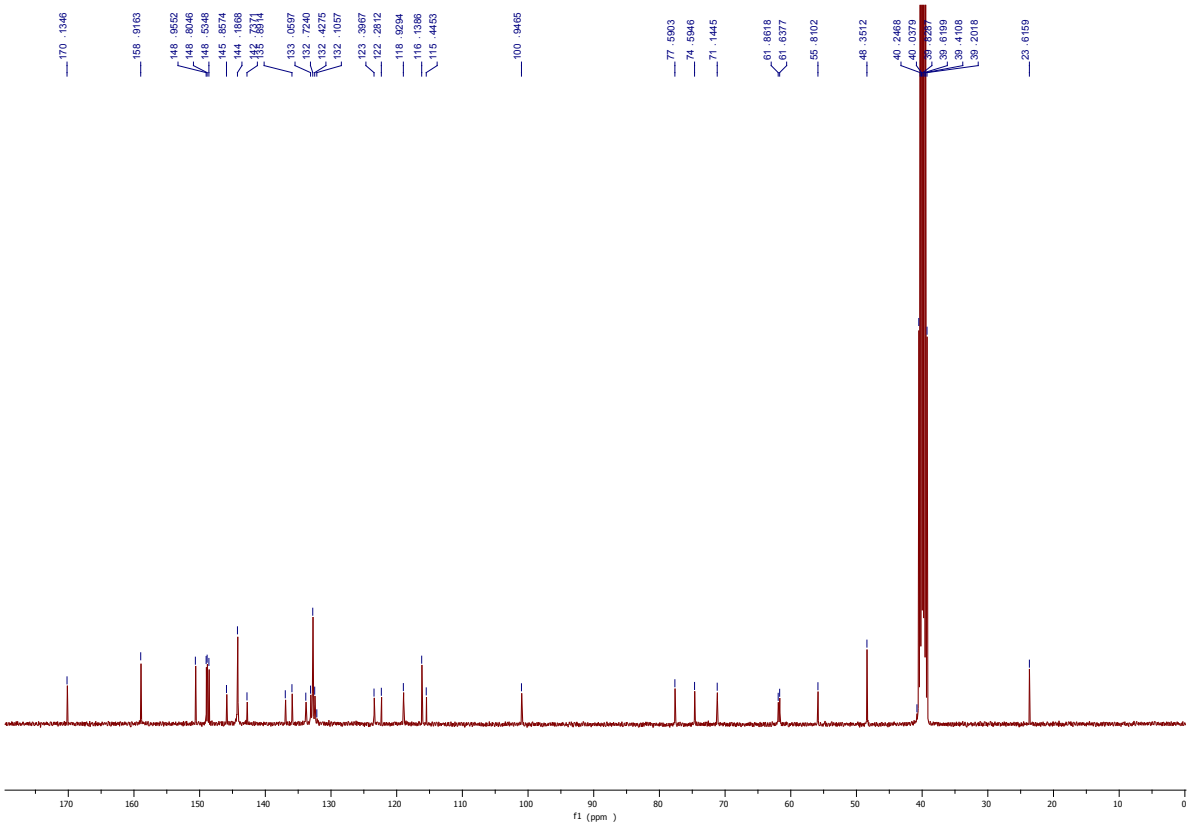

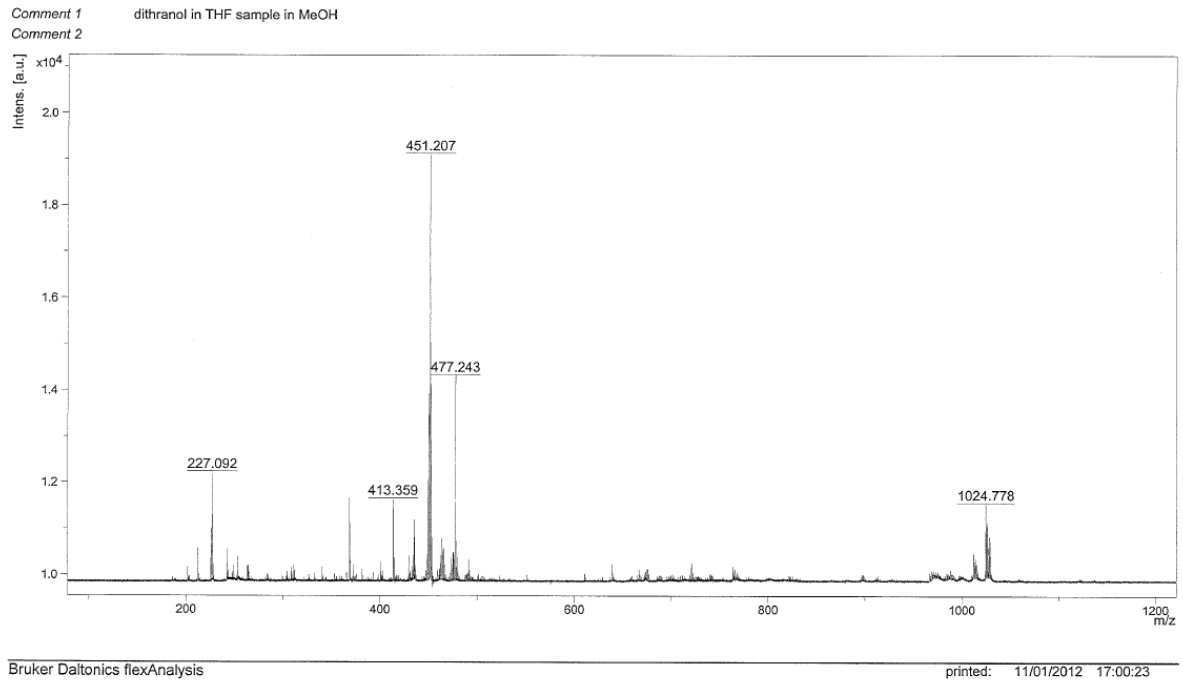

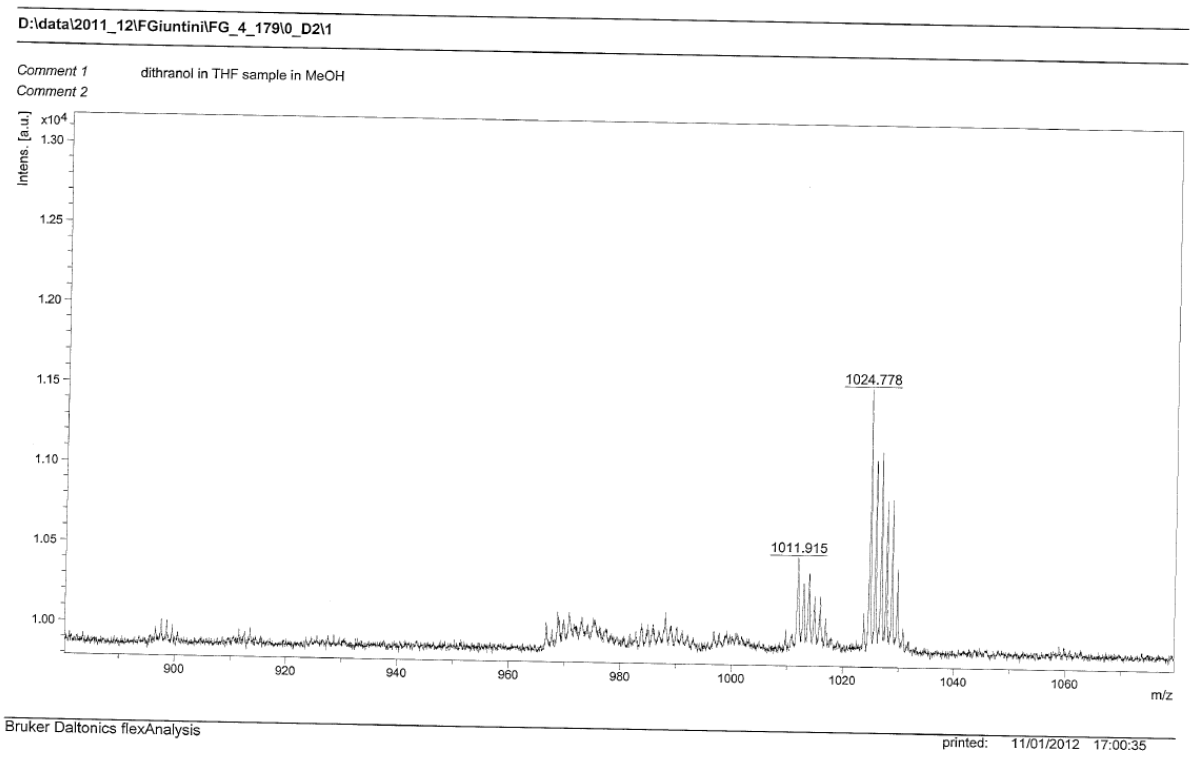

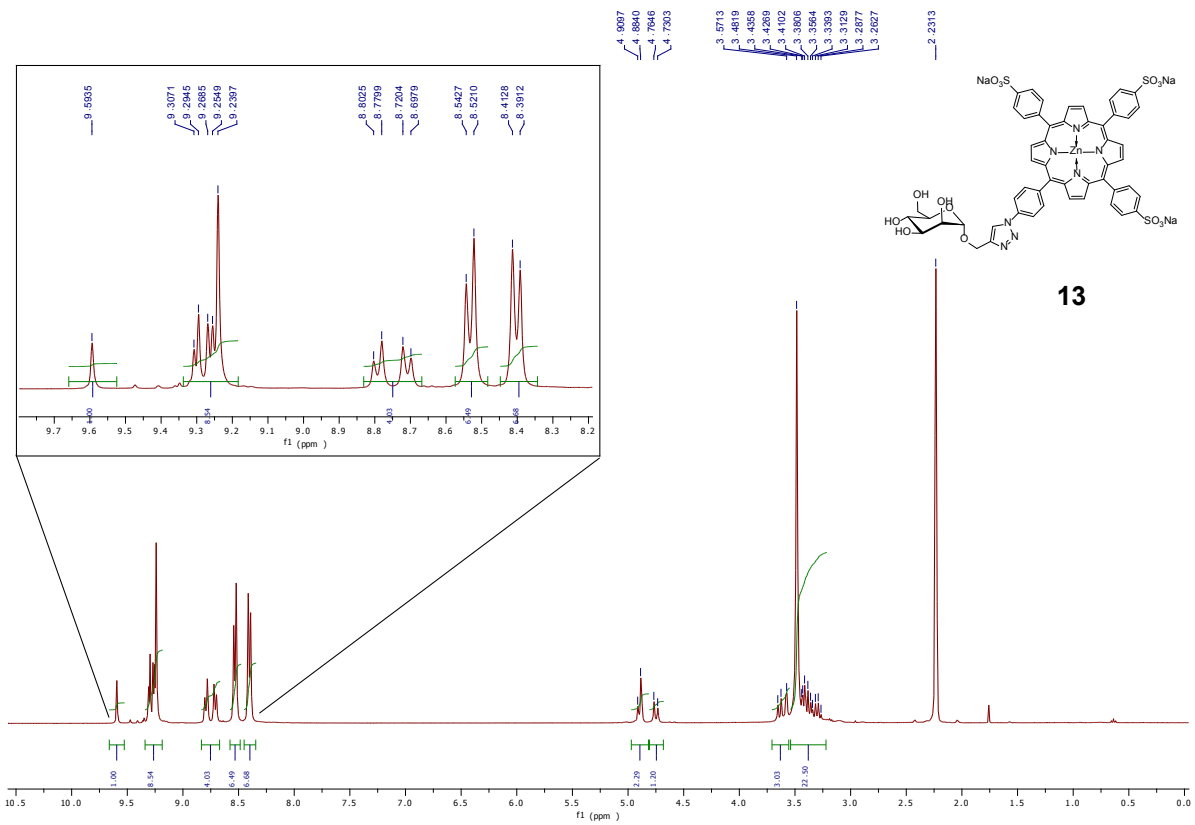

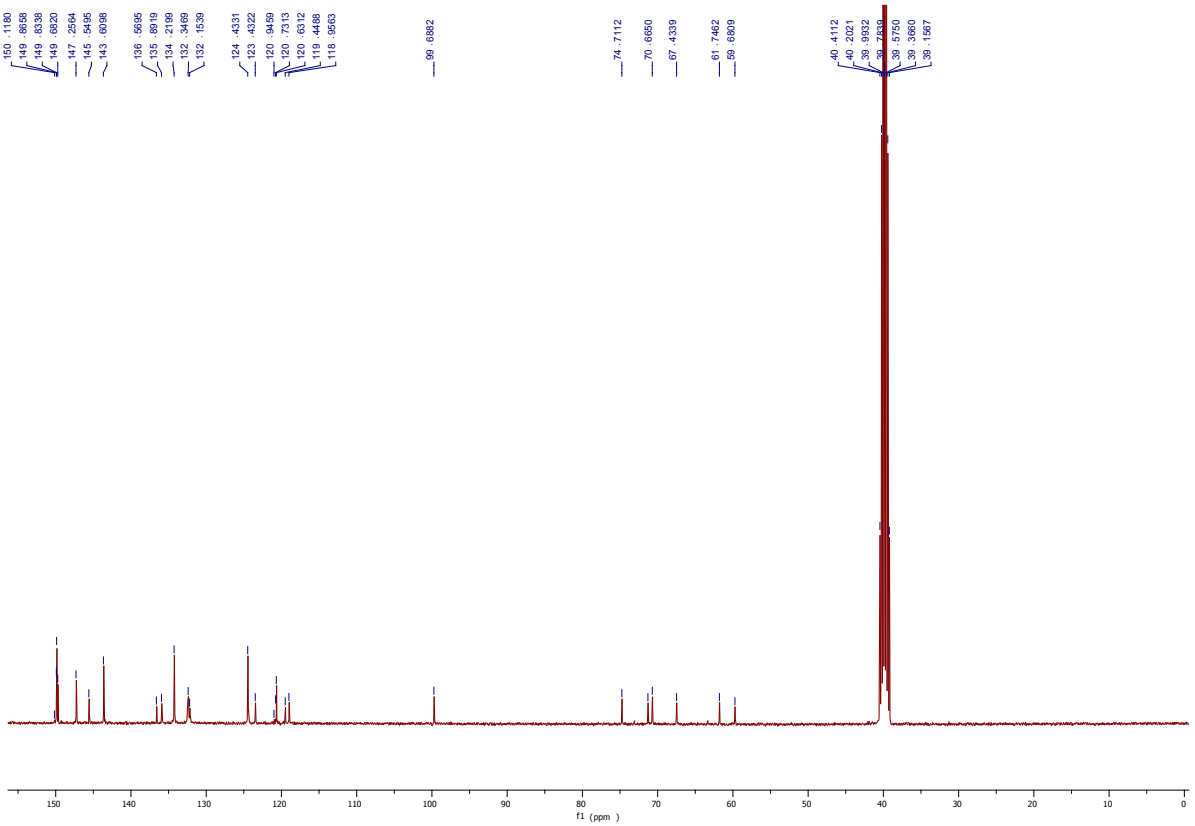

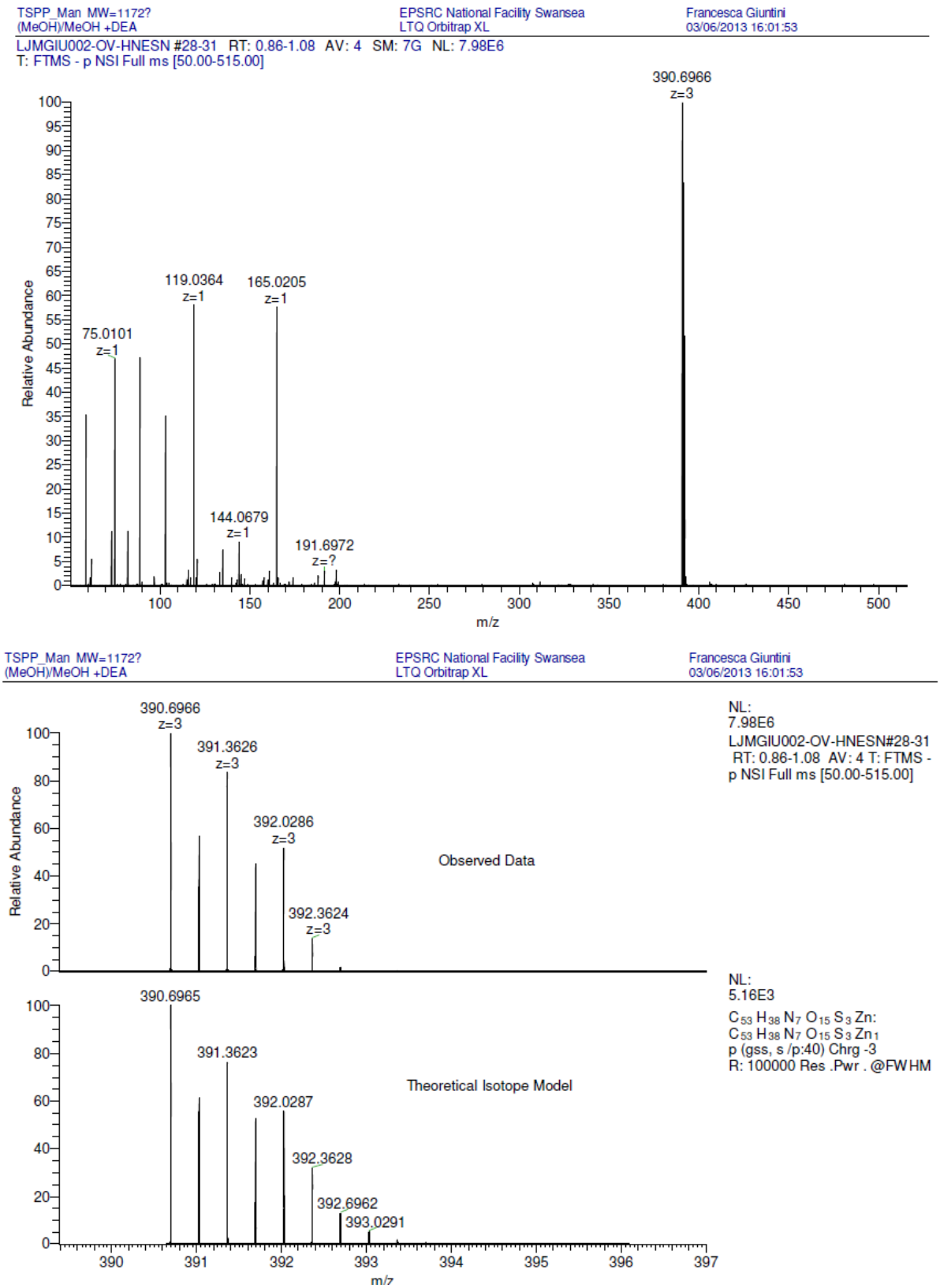
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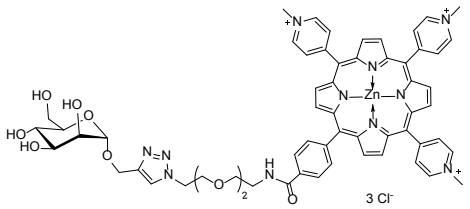

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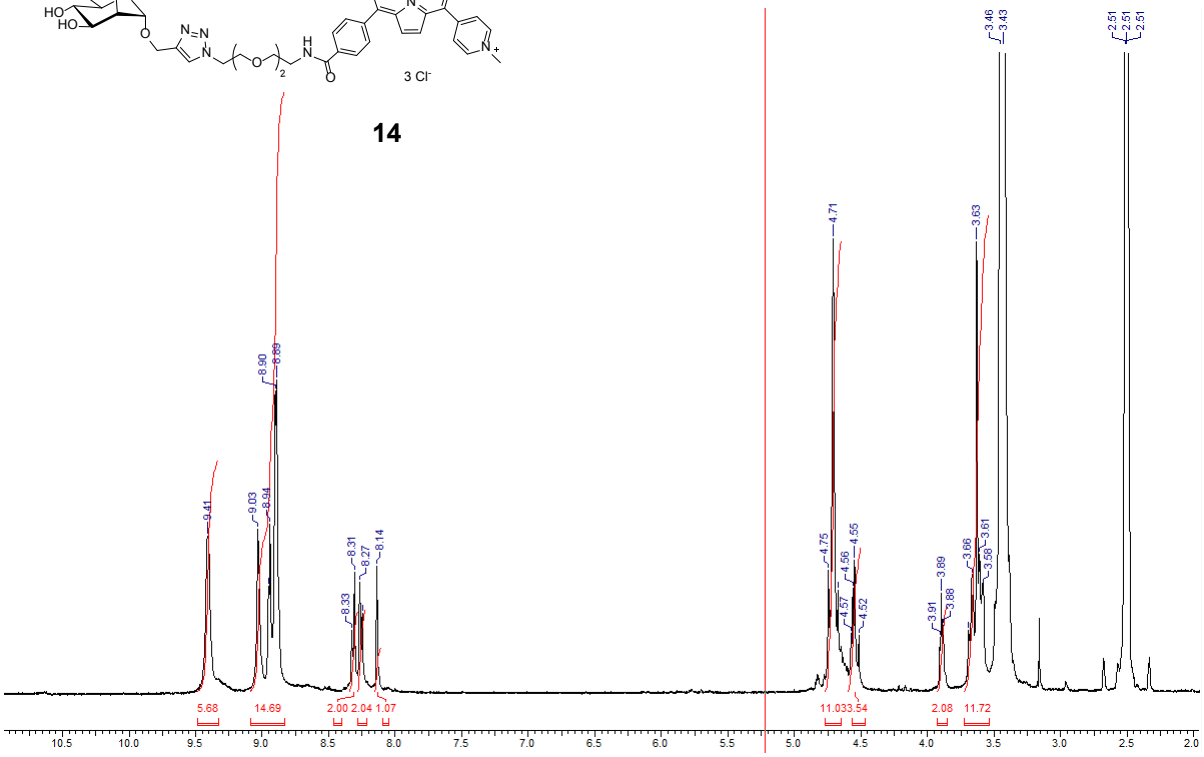

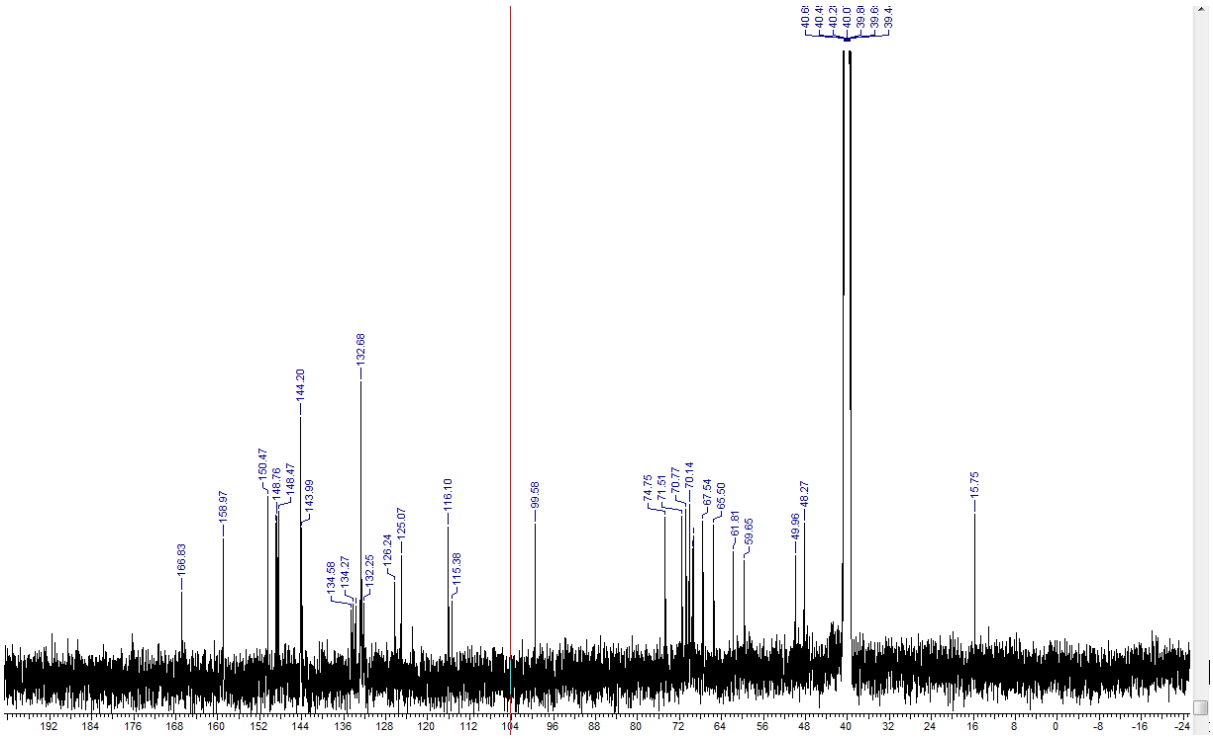

FBE698 - CHCA

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

Acquisition Date 19/02/2013 11:31:19

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Method	KDH_MSService_LoMassMethod
Submission Name	rwb39992fb
Instrument	solariX
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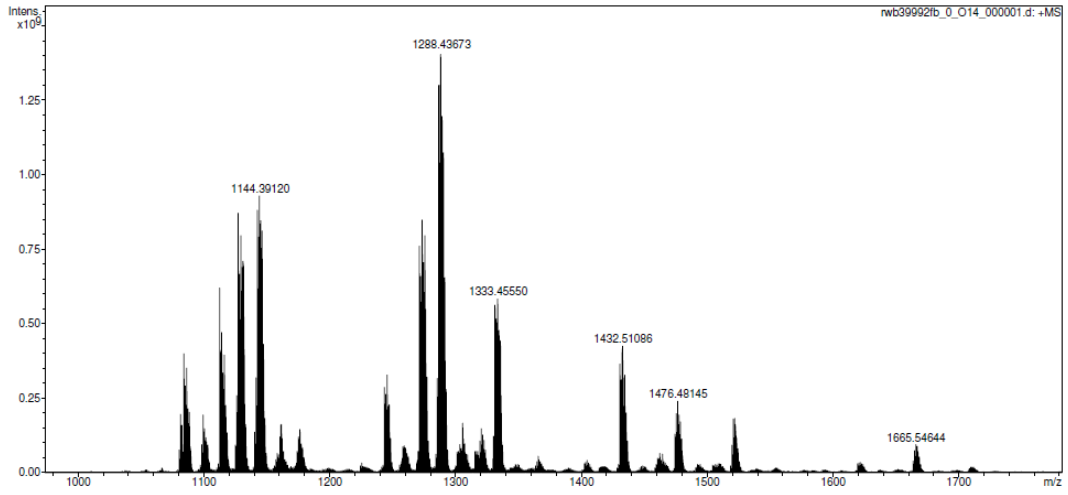

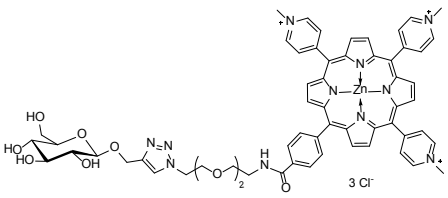
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OH
O
N=N
N
H
N
O
O
2
O
3 Cl-

15

9.41
9.40
9.03
8.90
8.89
8.33
8.31
8.27
8.15
4.88
4.85
4.71
4.66
4.56
4.55
4.28
4.26
3.90
3.89
3.88
3.67
3.63
3.61
3.49
3.17
3.14
3.12
3.11
3.07
3.05
3.01
2.99
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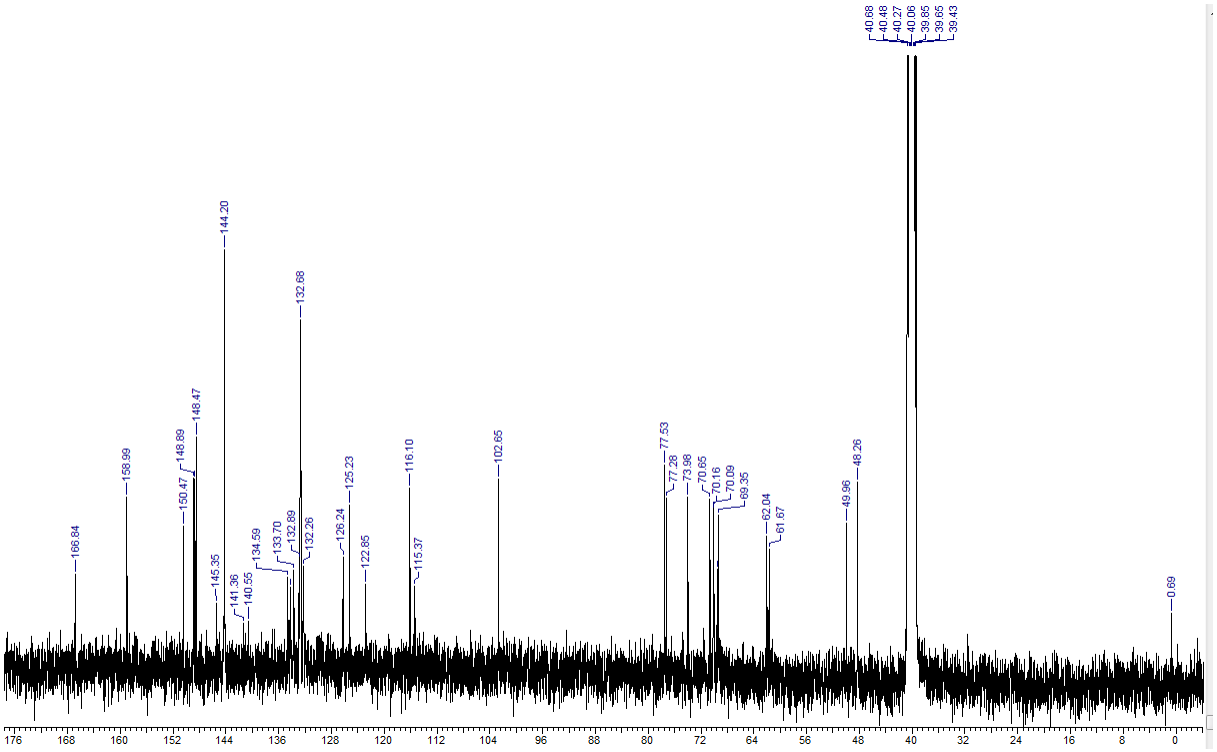
2.39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132.89
132.26
132.68
126.24
125.23
122.85
116.10
115.37
102.85
77.53
77.28
73.98
70.65
70.16
70.09
69.35
62.04
61.67
49.96
48.26
40.68
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39.65
39.43
0.69

FBE697 - CHCA

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

Acquisition Date 19/02/2013 10:37:37

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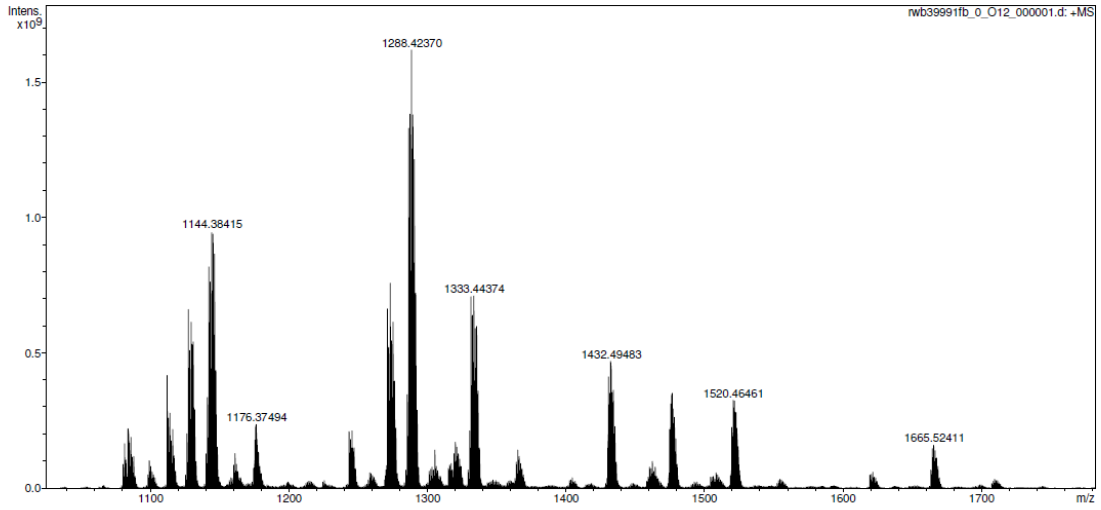

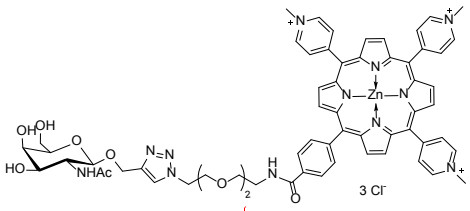

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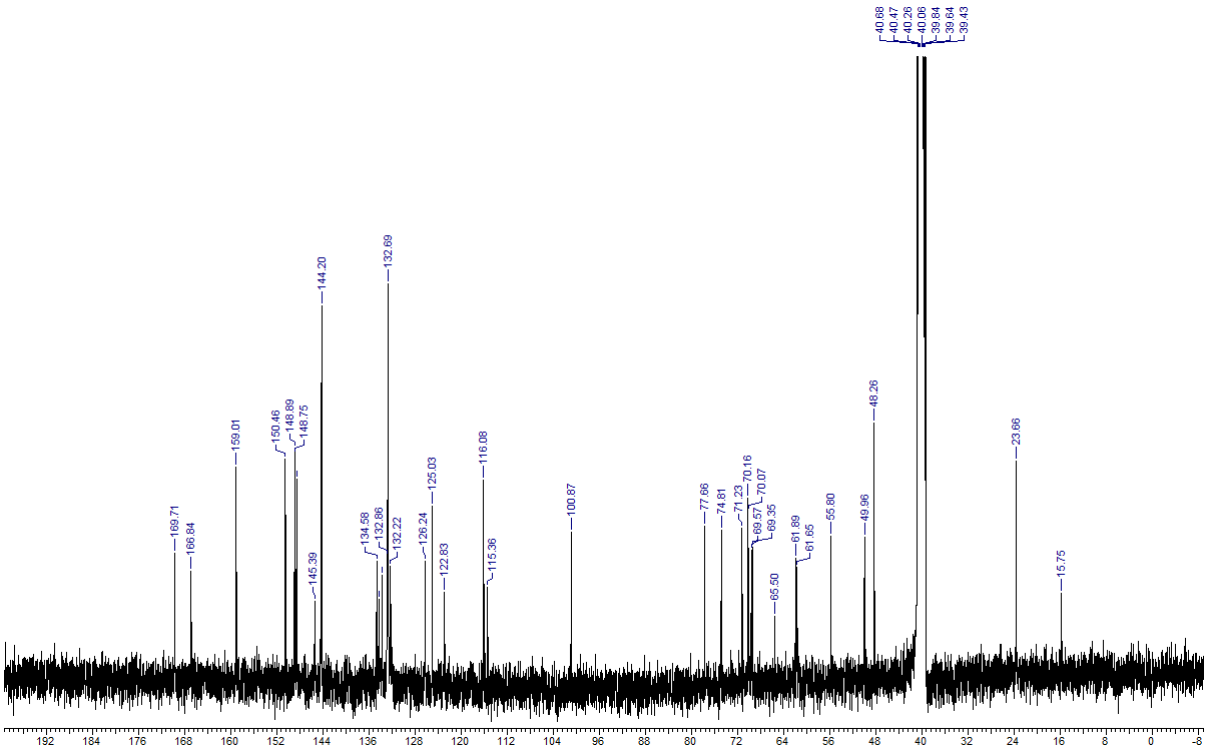

FBE699 - CHCA

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

Analysis Filename	rwb39993fb_0_O15_000001.d	Acquisition Date	19/02/2013 11:32:04
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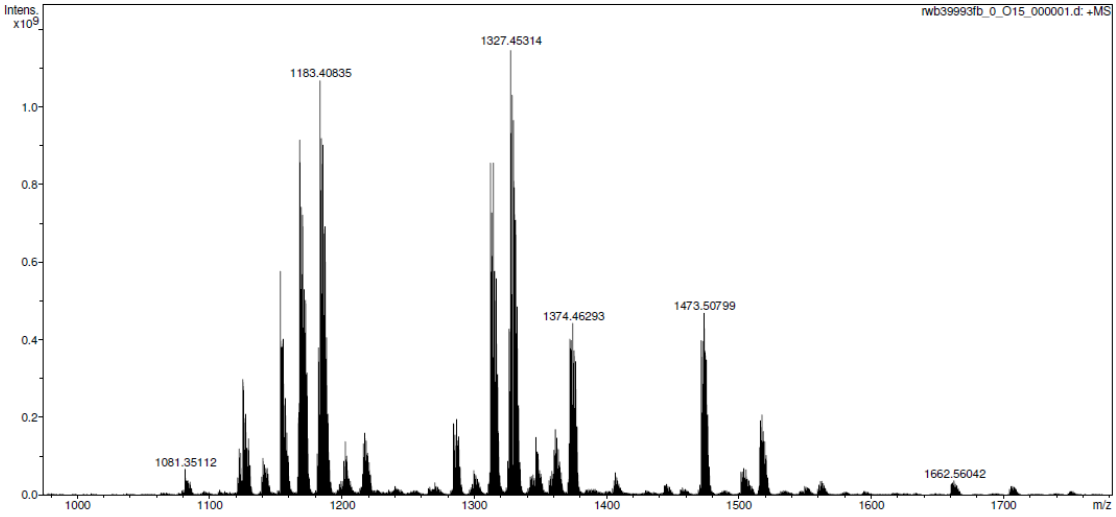

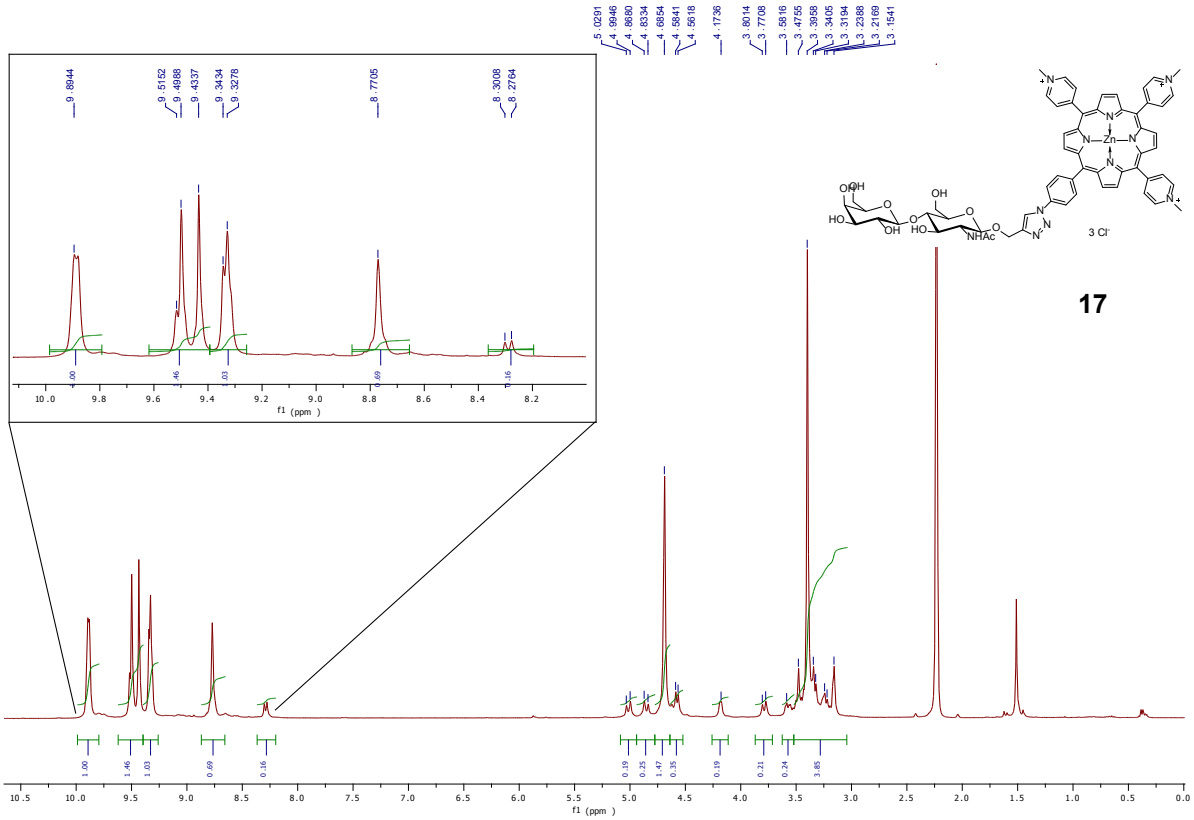

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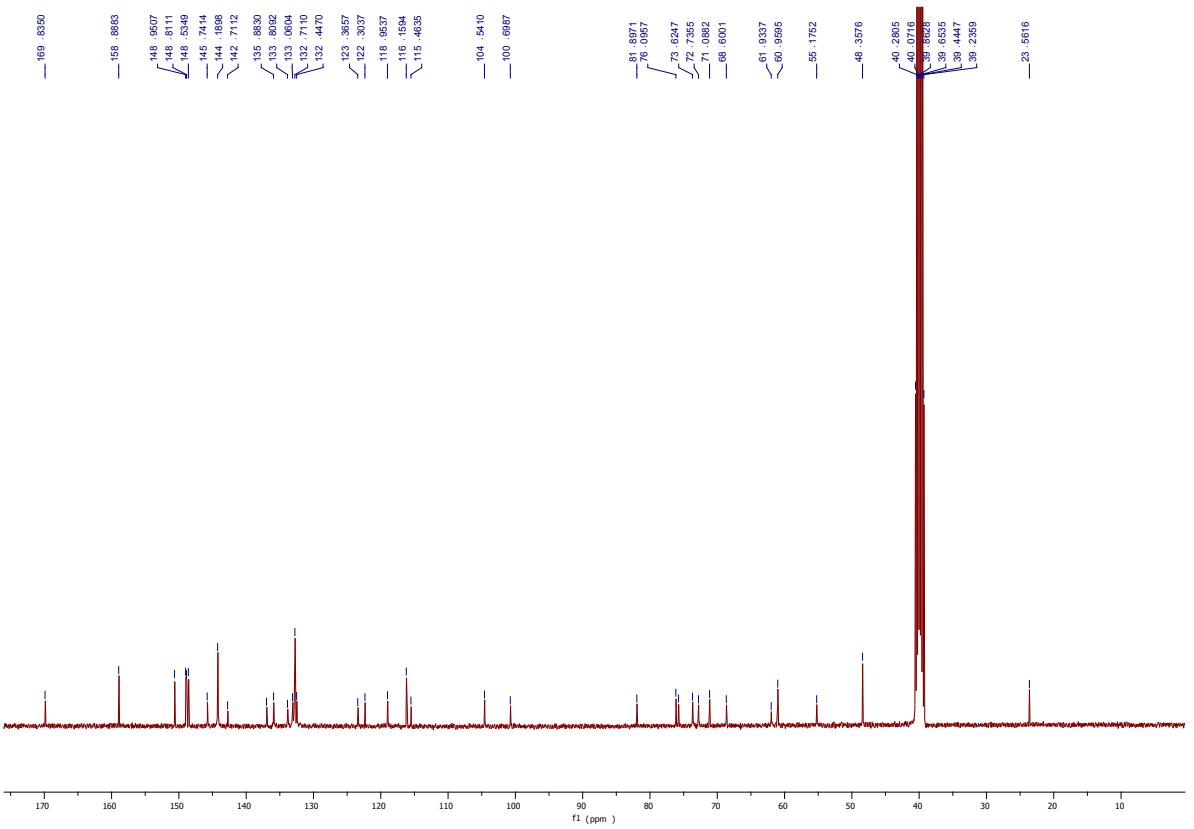

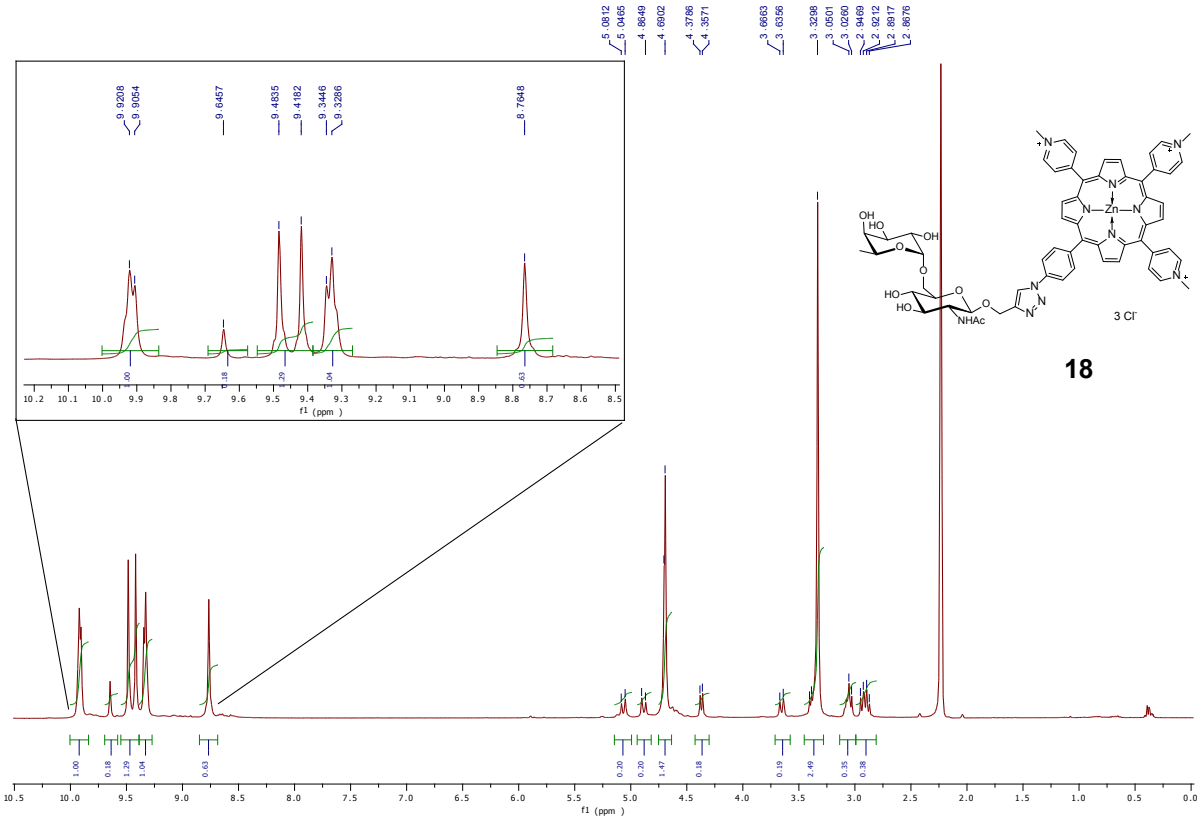

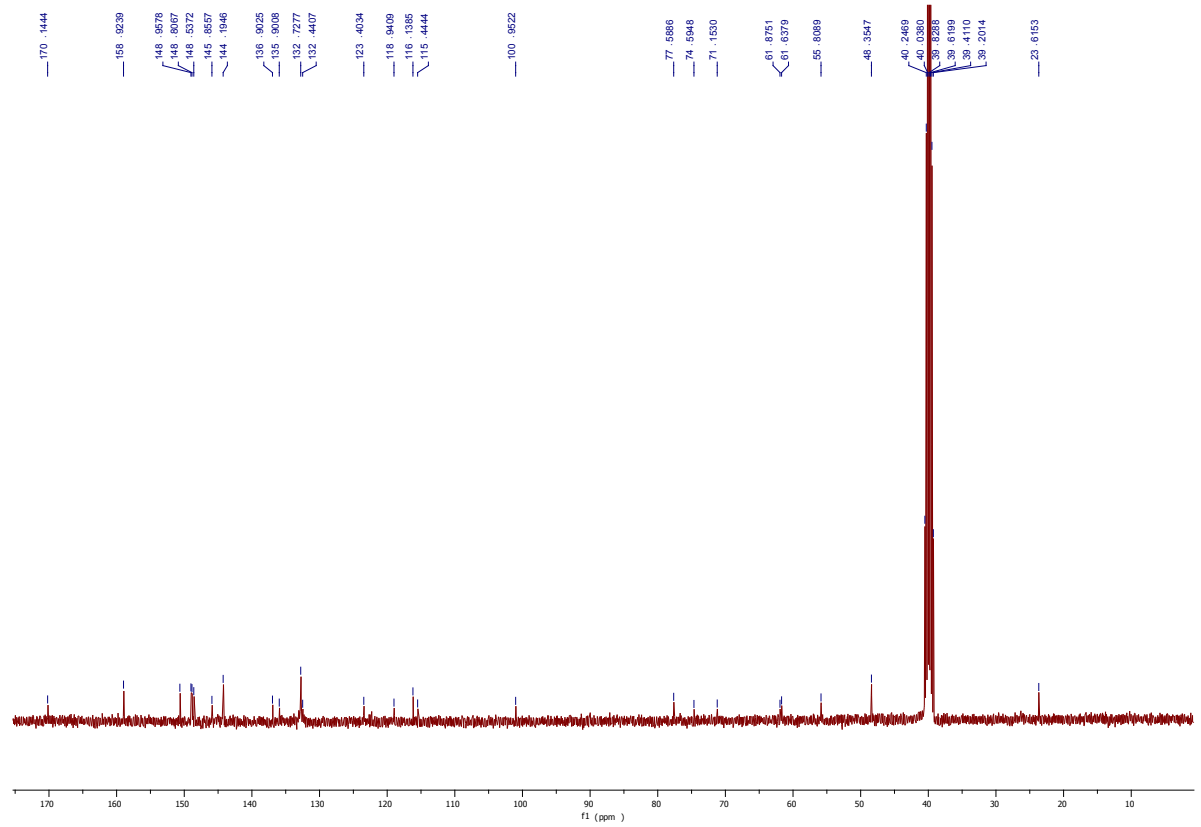

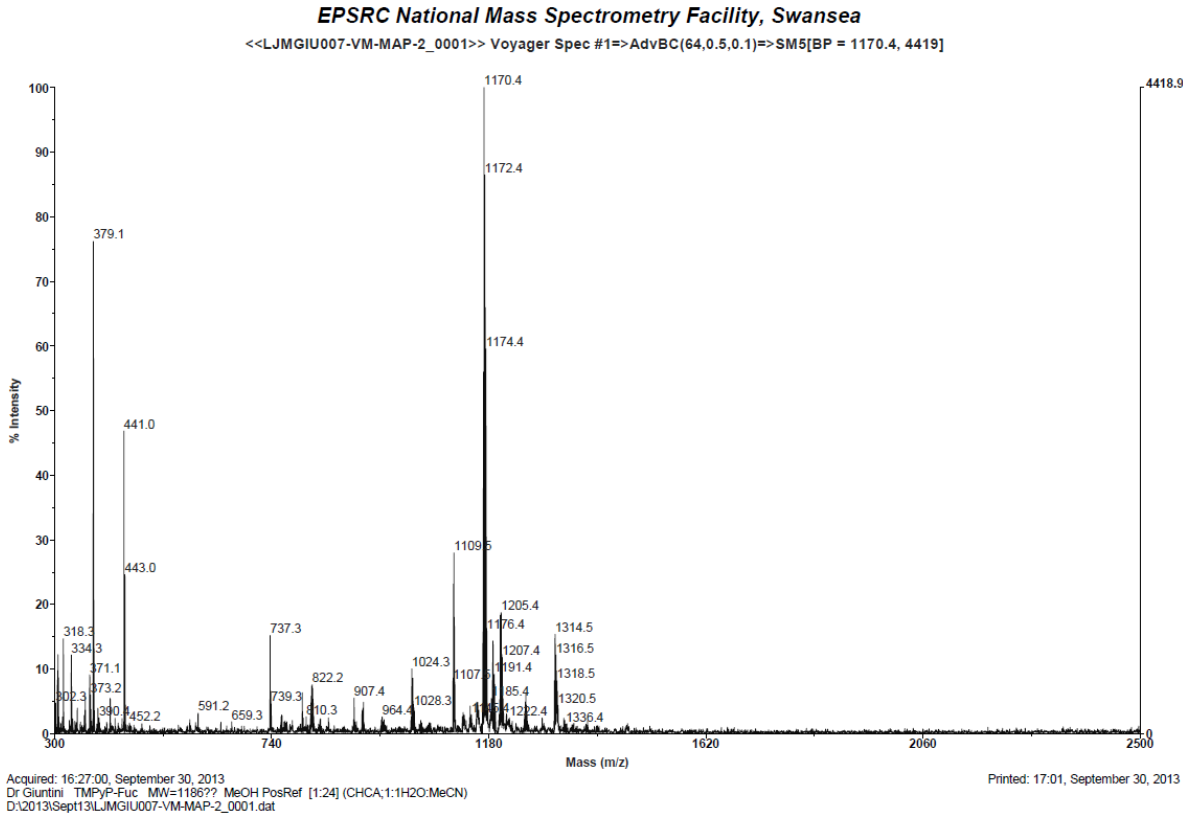
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% Intensity
Mass (m/z)
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4418.9
1172.4
379.1
1174.4
441.0
1109.5
443.0
1205.4
318.3
737.3
1176.4
1314.5
334.3
1207.4
1316.5
1024.3
371.1
1191.4
822.2
1318.5
373.2
907.4
1107.5
1085.4
739.3
1028.3
1320.5
591.2
659.3
1222.4
1336.4
452.2
964.4
Acquired: 16:27:00, September 30, 2013
Printed: 17:01, September 30, 2013
Dr Giuntini TMPyP-Fuc MW=1186?? MeOH PosRef [1:24] (CHCA;1:1H2O:MeCN)
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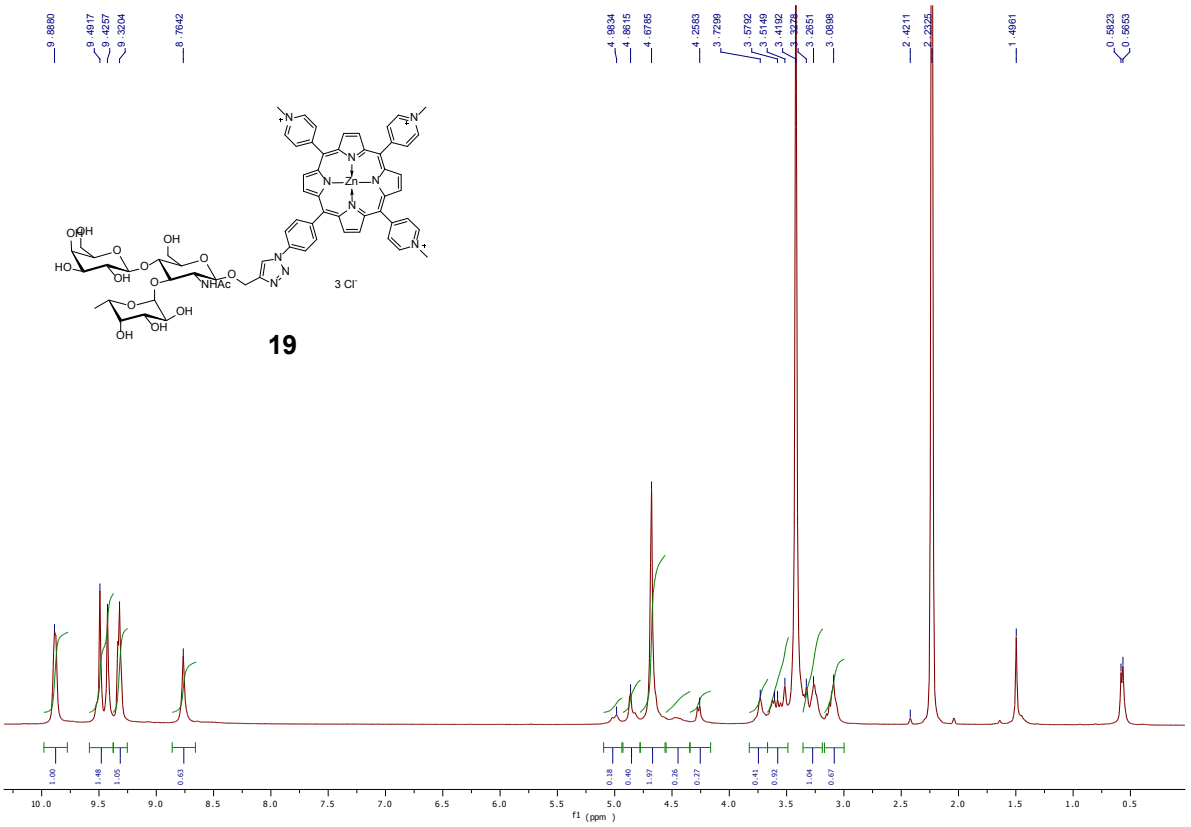
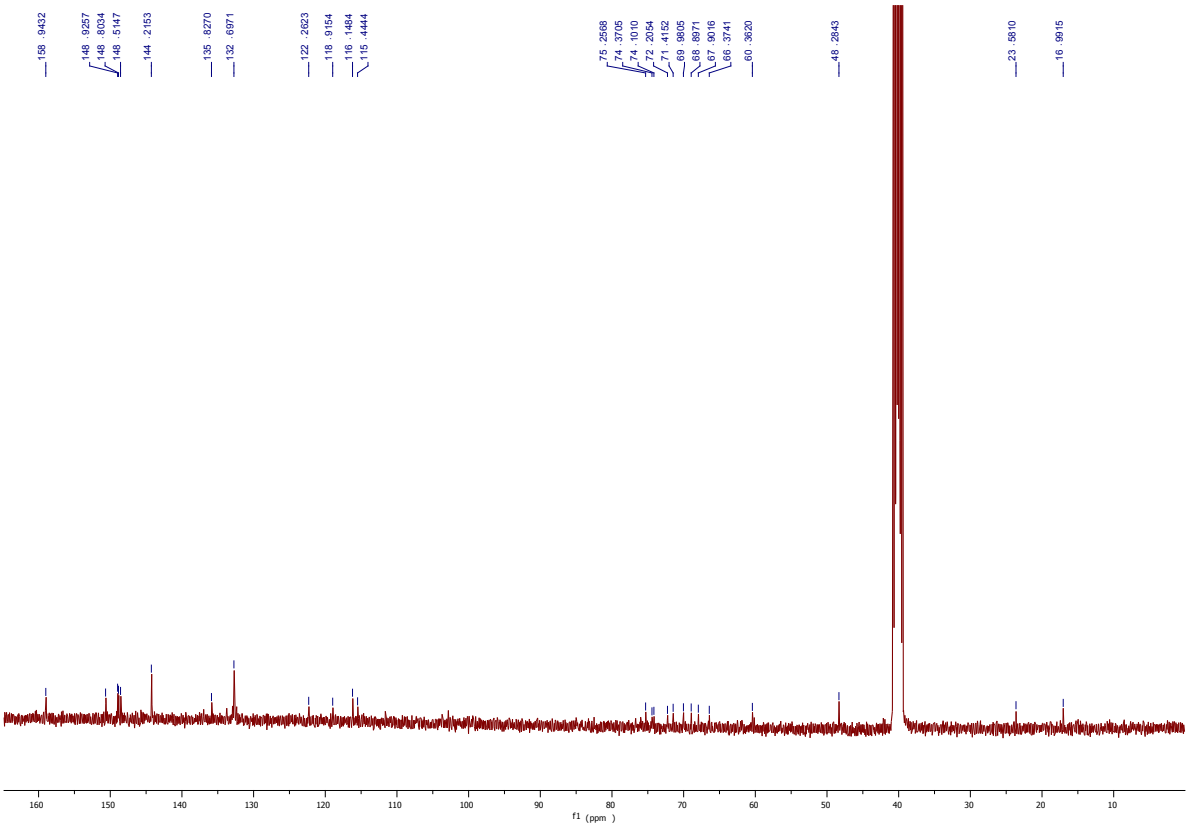
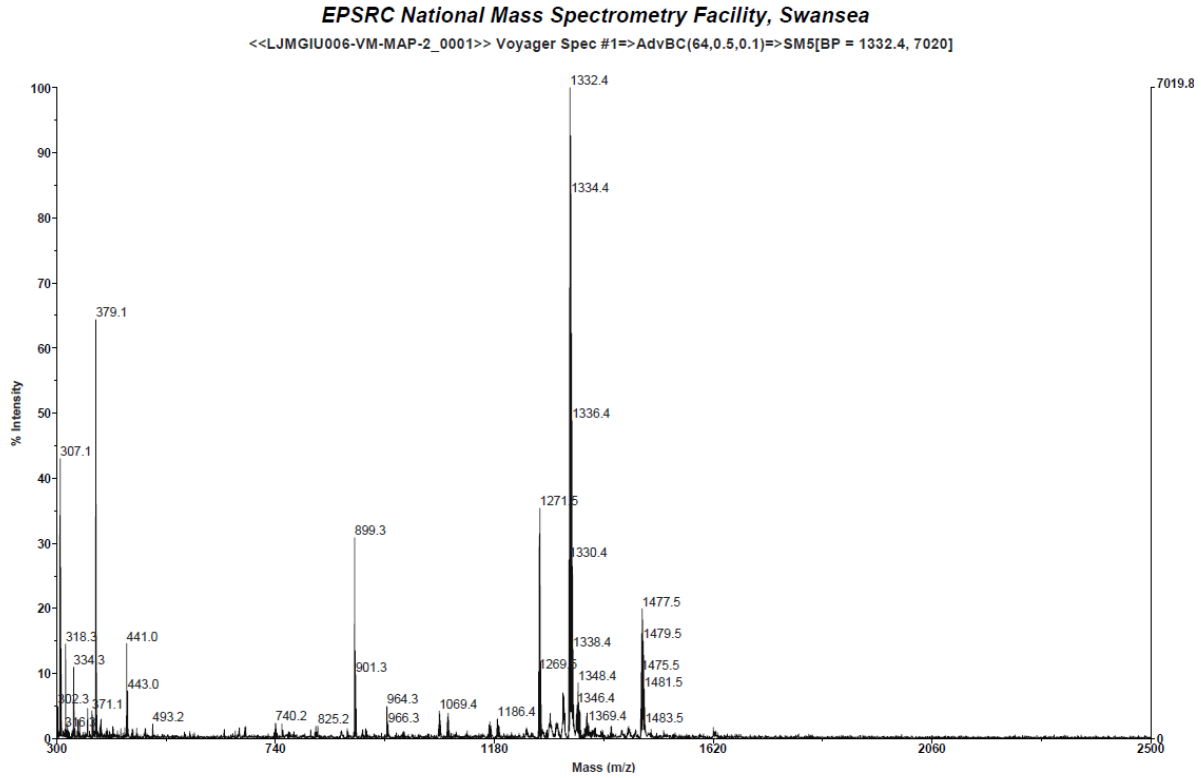


19

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Mass (m/z)
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1336.4
307.1
1271.5
899.3
1330.4
1477.5
1479.5
318.3
441.0
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334.3
901.3
1269.6
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1348.4
1481.5
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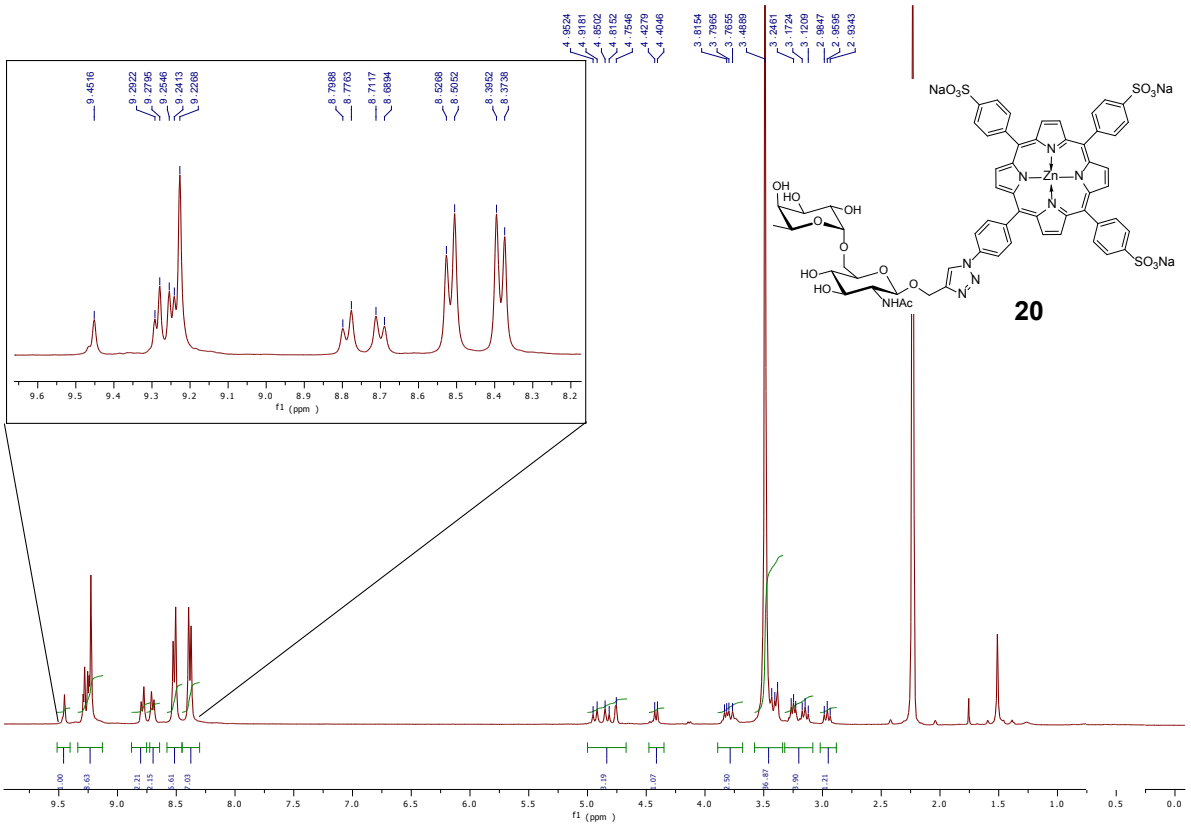
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SO3Na
N
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Zn
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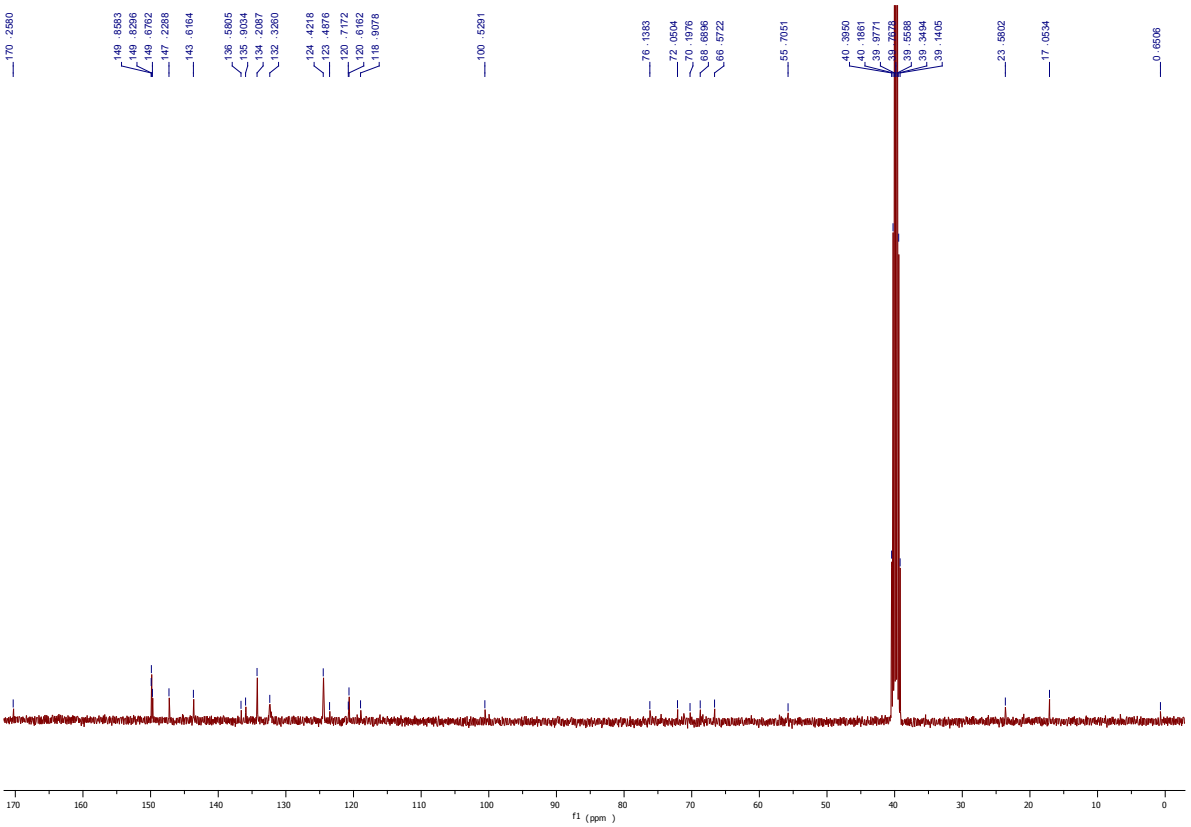
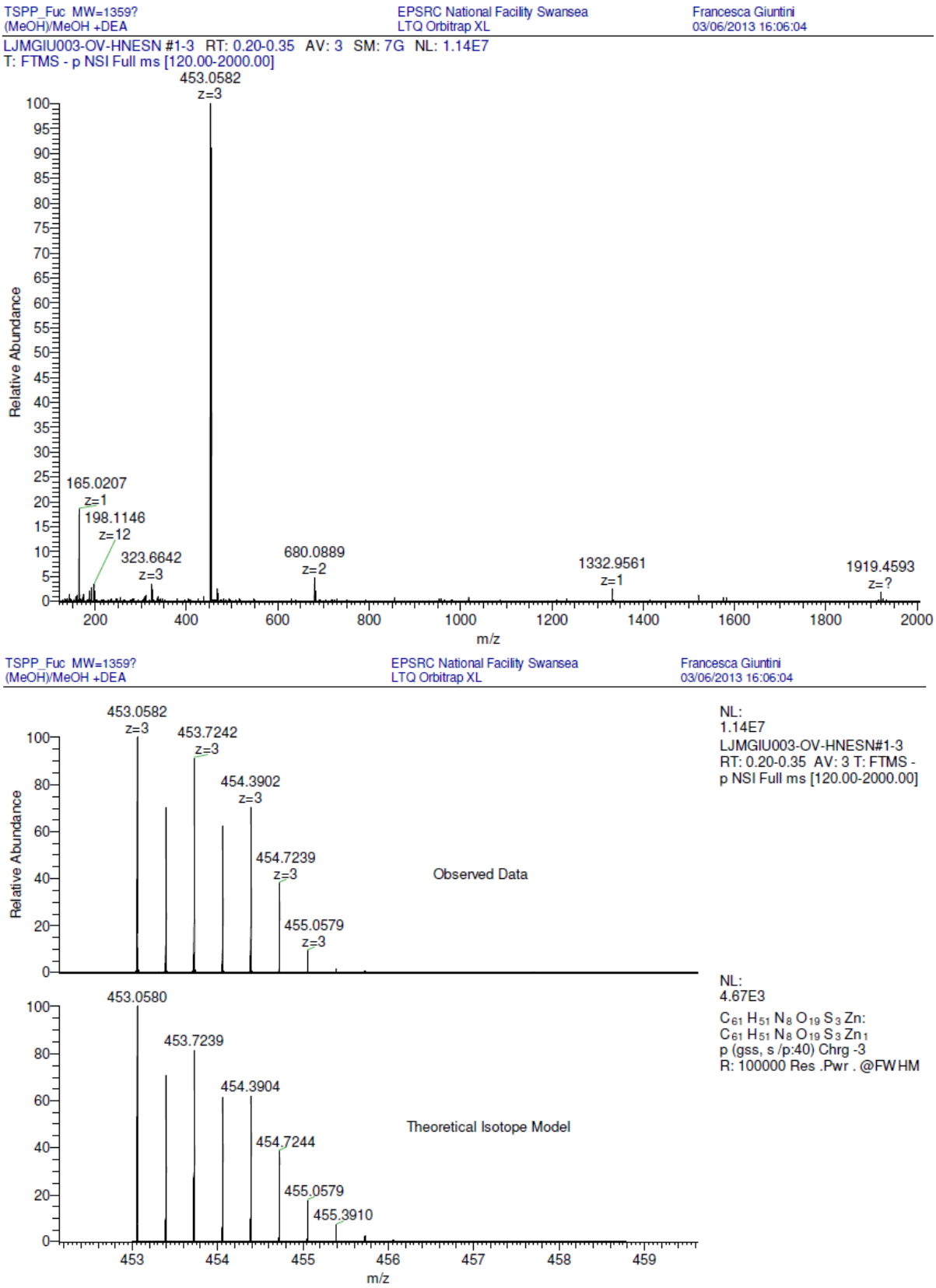
N
OH
HO
OH
O
O
HO
HO
O
NHAc
N
N
N
20
f1 (ppm)


f1 (ppm)



1. D. B. G. Williams and M. Lawton, *The Journal of Organic Chemistry*, 2010, **75**, 8351-8354.
2. F. Giuntini, F. Dumoulin, R. Daly, V. Ahsen, E. M. Scanlan, A. S. P. Lavado, J. W. Aylott, G. A. Rosser, A. Beeby and R. W. Boyle, *Nanoscale*, 2012, **4**, 2034-2045.

3. A. Schubert, T. Klütsch and D. Cech†, *Nucleosides and Nucleotides*, 1997, **16**, 277-289.
4. Y. Chen, T. Parr, A. E. Holmes and K. Nakanishi, *Bioconjugate Chem.*, 2008, **19**, 5-9.