Development of Hydrophilic Photolabile Hydroxyl Protecting Groups

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Experimental Procedures

General. Organic solutions were concentrated by rotary evaporation at ca. 12 Torr.. Flash column chromatography was performed employing 230-400 mesh silica gel. Thin-layer chromatography was performed using glass plates pre-coated to a depth of 0.25 mm with 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Infrared (IR) data are presented as frequency of absorption (cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were recorded on a 300 MHz and a 400 MHz NMR spectrometers; Chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances), coupling constant in Hertz (Hz), integration. UV absorbance was measured with 6×10^{-5} M solution in 1 cm cuvette.

Materials. Tetrahydrofuran, toluene, and acetonitrile were distilled from appropriate drying reagents under a nitrogen atmosphere at 760 Torr.. Other chemicals were obtained from commercial vendors and used without further purification.

Representative procedure of photochemical removal of the hydrophilic photolabile hydroxyl protecting groups

Procedure A (irradiation at pH 7): Into two Pyrex NMR tubes, an equal amount of the purified potassium salt **4a** (1.26 mg, 1.8 μmol, 3 mM) in 0.6 mL of D_2O was introduced respectively. One tube was irradiated with a 450 W medium-pressure mercury lamp equipped with a Pyrex filter sleeve in a Hanovia photoreactor for 12 min without deaeration. To both irradiated and non-irradiated tubes, an equal amount of DMAP (0.11mg, 0.9 μmol) was then added. NMR analysis of both tubes determined the yields of the PPG and methyl α-D-glucoside to be 93% and 96%, respectively.

Procedure B (irradiation at pH 12): The compound **7a** (16 mg, 0.021 mmol) was treated with an aqueous solution of KOH (1 M, 0.21 mmol) in CH_3OH at room temperature overnight. The solvent was removed, and the residue was dissolved in D_2O (2.28 mL). Into two Pyrex NMR tubes, 0.2 mL of the obtained solution with 0.4 mL D_2O was introduced respectively. One tube was irradiated with a 450 W medium-pressure mercury lamp equipped with a Pyrex filter sleeve in a Hanovia photoreactor for 12 min without deaeration. To both irradiated and non-irradiated tubes, an equal amount of DMAP (0.11mg, 0.9 μmol) was then added. NMR analysis of both tubes determined the yields of the PPG and methyl α-D-glucoside to be 92% and 96%, respectively.

Preparative photoreaction of release methyl *α*-D-glucoside (5a): The compound **7a** (93.3 mg, 0.12 mmol) was treated with KOH (83.4 mg, 1.3 mmol) in 0.52 mL of methanol at room temperature overnight. The solvent was then removed, and the residue was divided equally into two portions and transferred into two Pyrex test tubes (Φ1.5×12 cm) with 12 mL of H_2O respectively. The two test tubes were irradiated with a 450 W medium-pressure mercury lamp equipped with a Pyrex filter sleeve in a Hanovia reactor for 20 min without deaeration. The obtained solution was acidified with concentrated HCl to pH = 3 and then excess of CH_2N_2 in ethyl ether was added and adjusted to pH = 8. The organic phase was separated and concentrated. The residue was purified by flash column chromatography, eluted with petroleum ether/ethyl acetate = 3:1 to afford **8** (52.9 mg, 93%) with a trace amount of mono substituted aniline **9** (< 0.7 mg, < 2%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.26 (m, 10 H), 7.12 (t, *J* = 8.0 Hz, 1 H), 6.57–6.48 (m, 3 H), 3.69 (s, 1 H), 3.67 (s, 3 H), 3.11 (t, *J* = 6.8 Hz, 2 H), 2.85 (s, 1 H), 2.40 (t, *J* = 7.2 Hz, 2 H), 1.89 (p, *J* = 7.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.81, 148.08, 147.81, 146.95, 128.82, 127.96, 127.80, 127.12, 117.44, 112.85, 111.26, 82.05, 51.65, 43.24, 31.60, 24.60; IR(neat) 3403, 3058, 3024, 2951, 1725, 1605, 1490, 1447, 757, 702; HRMS (ESI) *m/e* calcd. for $C_{24}H_{26}NO_3$ 376.1913, found 376.1915.The aqueous phase was concentrated and the yield of methyl *α*-D-glucoside (**5a**) was 98%, determined by NMR analysis with the internal standard DMAP.

Preparation of 4a*:* A mixture of **7a** (450 mg, 0.58 mmol), 15 mL of CH_3OH, 3.9 mL of saturated K_2CO_3 and 5.8 mL H_2O was stirred at room temperature overnight. The solvent was removed, and the residue was extracted with CH_3OH (12 mL×5). The obtained crude product was purified by flash column chromatography to give **4a** (340 mg, 84%). R_f = 0.5 (DCM/MeOH = 3:1); ^{1}H NMR (300 MHz, CD_3OD) δ 7.58–7.41 (m, 4 H), 7.32–7.11 (m, 6 H), 7.07 (t, *J* = 7.9 Hz, 1 H), 6.83 (s, 1 H), 6.72–6.57 (m, 2 H), 4.77 (d, *J* = 3.6 Hz, 1 H), 3.76 (t, *J* = 7.9 Hz, 1 H), 3.64 (t, *J* = 9.2 Hz, 1 H), 3.56–3.39 (m, 5 H), 3.35 (s, 1 H), 3.30–3.15 (m, 5 H), 2.19 (t, *J* = 6.4 Hz, 4 H), 1.77 (m, 4 H); ^{13}C NMR (75 MHz, CD_3OD) δ 179.6, 148.8, 146.0, 145.9, 145.6, 129.8, 129.7, 129.4, 128.5, 127.8, 118.4, 114.8, 112.5, 100.9, 87.9, 75.3, 73.4, 72.5, 72.2, 64.9, 55.4, 51.5, 33.8, 24.2; IR(neat) 3383, 2933, 1699, 1598, 1576, 1495, 1447, 1147, 1050, 749, 708, 637; HRMS (ESI) *m/e* calcd. for $C_{34}H_{42}NO_{10}$ 624.2809, found 624.2810.

Synthesis of 17: A solution of 3-aminobenzoic acid (**16**) (5.486 g, 40 mmol) and concentrated H_2SO_4 (8.6 mL, 160 mmol) in methanol (50 mL) was refluxed for 3.3 d. The solvent was then removed and the residue was neutralized with NaOH (2 N) and saturated aqueous $NaHCO_3$ to pH = 7. The obtained mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated to provide the methyl ester (5.687 g, 94%).

A solution of the obtained ester (1.512 g, 10 mmol) and Et_3N (1.40 mL, 10 mmol) in DCM (50 mL) was treated with acetic chloride (0.757 mL, 10.5 mmol) dropwise at 0 °C. After 7 h at room temperature, the reaction mixture was washed with water and brine, dried over Na_2SO_4 and concentrated to provide the desired product (1.879 g, 97%) without further purification.

A solution of the above obtained acetylated ester (4.85 g, 25.1 mmol) in THF (100 mL) was treated with PhMgBr (50 mL, 2 M) dropwise at 0 °C under argon atmosphere. The reaction was stirred

overnight at room temperature. Work-up and recrystallization from petroleum ether and DCM provided the trityl alcohol as a white solid (4.1 g, 51%).

A solution of the obtained trityl alcohol (4 g, 12.6 mmol) was treated with NaOH (10 g, 250 mmol) in methanol (70 mL) and water (10 mL) and heated at 85 °C for 2.5 d. Workup and recrystallization of the product from DCM and petroleum ether gave the (3-aminophenyl)diphenylmethanol (**17**) as a pale yellow solid (3.25 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.19 (m, 10H), 7.09 (t, J = 8.0 Hz, 1 H), 6.64–6.55 (m, 3 H), 3.23 (br, d, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 146.9, 146.0, 128.8, 127.9, 127.8, 127.1, 118.5, 114.9, 114.1, 81.9; IR(neat) 3370, 3057, 1605, 1490, 1447, 1314, 1267, 1148, 1018, 756, 701; HRMS (ESI) *m/e* calcd. for $C_{19}H_{18}NO$ 276.1388, found 276.1395.

Synthesis of 18*:* A mixture of **17** (275 mg, 1 mmol), ethyl bromoacetate (0.66 mL, 6 mmol), Na_2HPO_4 (714 mg, 5 mmol) and NaI (60 mg, 0.4 mmol) in 5 mL of anhydrous acetonitrile was heated at 85 °C under argon for 19.5 h. Workup and flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 3:1, afforded **18** (391 mg, 87%) as a pale yellow oil. R_f 0.4 (petroleum ether/ethyl acetate = 3/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 10 H), 7.16 (t, J = 7.9 Hz, 1 H), 6.66 (d, J = 8.4 Hz, 1 H), 6.51 (m, 2 H), 4.11 (q, J = 7.1 Hz, 4 H), 4.03 (s, 4 H), 2.84 (s, 1 H), 1.21 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 148.0, 147.5, 146.9, 128.8, 127.9, 127.8, 127.1, 118.2, 112.6, 111.5, 82.1, 61.1, 53.5, 14.2; IR(neat) 3498, 2981, 1743, 1601, 1495, 1447, 1184, 1025, 755, 702; HRMS (ESI) *m/e* calcd. for $C_{27}H_{30}NO_5$ 448.2124, found 448.2134.

Synthesis of 19*:* A mixture of **17** (275 mg, 1 mmol), methylacrylate (0.9 ml, 10 mmol), hydroquinone (44 mg, 0.4 mmol) and AcOH (23 µL, 0.4 mmol) was heated at 105 °C for 4.5 d in a sealed tube. Direct flash column chromatography on silica gel, eluted with benzene/ ethyl acetate = 8:1, afforded a mixture of **19** and its corresponding monosubstituted aniline (269 mg, Di./Mono. > 10:1). Into the above obtained mixture of anilines in 2 mL DCM, AcCl (8 µL, 0.11 mmol) and Et_3N (15µL, 0.11 mmol) were added at 0 °C. The resultant solution was stirred at room temperature for 2.4 h. The solvent was removed and the residue was purified by flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 2:1, to afford **19** (204 mg, 46 %) as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 2/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 10 H), 7.16 (t, J = 8.0 Hz, 1 H), 6.64–6.56 (m, 2 H), 6.53 (s, 1 H), 3.63 (s, 6 H), 3.54 (t, J = 7.2 Hz, 4 H), 2.97 (s, 1 H), 2.45 (t, J = 7.2 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 148.2, 146.9, 146.2, 129.0, 127.9, 127.7, 127.0, 116.9, 112.6, 111.3, 82.1, 51.6, 46.9, 32.1; IR(neat) 2952, 1733, 1599, 1491, 1437, 1363, 1261, 1199, 1175, 996, 752, 702; HRMS (ESI) *m/e* calcd. for $C_{27}H_{30}NO_5$ 448.2124, found 448.2117.

Synthesis of 8*:* A mixture of **17** (2.99 g, 10.9 mmol), ethyl bromobutylate (7.5 mL, 65.2 mmol), Na_2HPO_4 (7.7 g, 54.3 mmol) and NaI (0.65 g, 4.3 mmol) in 11 mL of anhydrous DMF was heated at 70 °C under argon for 2 d. Workup and flash column chromatography on silica gel, eluted with benzene/ethyl acetate = 9:1, afforded **8** (4.19 g, 81%) as a pale yellow oil. R_f 0.4 (benzene/ethyl acetate = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.21 (m, 10H), 7.14 (t, J = 8.0 Hz, 1 H), 6.61 (dd, J = 7.9, 2.4 Hz, 1 H), 6.54 (s, 1 H), 6.48 (d, J = 7.7 Hz, 1 H), 3.64 (s, 6 H), 3.20 (t, J = 7.6 Hz, 4 H), 3.10 (s, 1 H), 2.23 (t, J = 7.2 Hz, 4 H), 1.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 148.1, 147.1, 147.0, 128.7, 127.9, 127.6, 126.9, 116.0, 112.3, 110.9, 82.1, 51.5, 50.2, 31.0, 22.2; IR(neat)

3505, 2951, 1733, 1599, 1575, 1494, 1447, 1366, 1174, 858, 751, 703; HRMS (ESI) *m/e* calcd. for $C_{29}H_{34}NO_5$ 476.2437, found 476.2434.

Synthesis of 20: A mixture of **18** (0. 326 g, 0. 73 mmol), Ac_2O (0.102 mL, 1.09 mmol), Et_3N (0.102 mL, 0.728 mmol) and MoO_2Cl_2 (1.4 mg, 7 μmol) in 1.2 mL of toluene was heated at 120 °C for 2 h. The mixture was washed with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated to give **20** (0.36 g, 100%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.17 (m, 10 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 6.77 (d, *J* = 8.8 Hz, 1 H), 6.60 (t, *J* = 2.2 Hz, 1 H), 6.50 (dd, *J* = 8.2, 2.7 Hz, 1 H), 4.13 (q, *J* = 7.1 Hz, 4 H), 4.04 (s, 4 H), 2.15 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 168.6, 147.3, 144.4, 143.3, 128.5, 128.4, 127.6, 127.1, 118.6, 113.0, 111.5, 89.9, 61.1, 53.7, 22.5, 14.2; IR(neat) 2982, 1747, 1604, 1495, 1449, 1368, 1220, 1184, 1024, 991, 977, 765, 700; MS (ESI) *m/e* 430.2 [M-59].

Synthesis of 21: A mixture of **19** (0. 132 g, 0. 295 mmol), Ac_2O (0.042 mL, 0.443 mmol), Et_3N (0.042 mL, 0.325 mmol) and MoO_2Cl_2 (1.8 mg, 9 μmol) in 0.44 mL of toluene was heated at 120 °C for 4 h. The mixture was quenched with water and extracted with DCM. The combined organic layers were dried over Na_2SO_4 and concentrated to give **21** (0.143 g, 99%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.33 (m, 4 H), 7.33–7.20 (m, 6H), 7.15 (t, *J* = 8.0 Hz, 1 H), 6.71 (d, *J* = 7.7 Hz, 1 H), 6.65 (s, 1 H), 6.57 (dd, *J* = 8.2, 2.5 Hz, 1 H), 3.65 (s, 6 H), 3.61 – 3.50 (t, *J* = 7.2 Hz, 4 H), 2.56 – 2.42 (t, *J* = 7.2 Hz, 4 H), 2.17 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 168.7, 145.9, 144.6, 143.4, 128.7, 128.4, 127.6, 127.2, 117.2, 112.9, 111.4, 90.0, 51.6, 47.0, 32.1, 22.5; IR(neat) 2952, 1733, 1601, 1576, 1495, 1436, 1367, 1229, 1018, 986, 766, 703; HRMS (ESI) *m/e* calcd. for $C_{29}H_{32}NO_6$ 490.2230, found 490.2236.

Synthesis of 22: A mixture of **8** (1.265 g, 2.66 mmol), Ac_2O (0.375 mL, 3.99 mmol), Et_3N (0.371 mL, 2.66 mmol) and MoO_2Cl_2 (5.3 mg, 0.0266 mmol) in 3 mL of toluene was heated at 120 °C for 5 h. The mixture was washed with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated to give **22** (2.396 g, 92%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.34 (m, 4 H), 7.34–7.18 (m, 6 H), 7.12 (t, *J* = 8.0 Hz, 1 H), 6.66 (d, *J* = 7.8 Hz, 1 H), 6.63–6.54 (m, 2 H), 3.64 (s, 6 H), 3.21 (t, *J* = 7.5 Hz, 4 H), 2.25 (t, *J* = 7.3 Hz, 4 H), 2.17 (s, 3 H), 1.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 168.8, 147.0, 144.4, 143.5, 128.6, 128.5, 127.5, 127.1, 116.5, 113.1, 111.2, 90.2, 51.5, 50.4, 31.3, 22.5, 22.4; IR(neat) 2952, 1738, 1600, 1497, 1437, 1367, 1230, 1018, 988, 766, 700; HRMS (ESI) *m/e* calcd. for $C_{31}H_{36}NO_6$ 518.2543, found 518.2553.

Preparation of 7a*:* A mixture of **22** (208 mg, 0. 60 mmol) and **10a** (64 mg, 0.20 mmol) in 0.2 mL of toluene was heated at 120 °C for 2.5 h. The solvent was removed and the residue was directly purified by flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 1:1, to afford **7a** (123 mg, 79 %) as a pale yellow oil. R_f 0.6 (petroleum ether/ethyl acetate = 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.0, 1.3 Hz, 4 H), 7.33–7.16 (m, 6 H), 7.12 (t, *J* = 8.0 Hz, 1 H), 6.72 (d, *J* = 7.7 Hz, 1 H), 6.68 (s, 1 H), 6.57 (dd, *J* = 8.2, 2.2 Hz, 1 H), 5.43 (dd, *J* = 10.1, 9.5 Hz, 1 H), 5.09 (dd, *J* = 10.2, 9.5 Hz, 1 H), 5.01 (d, *J* = 3.6 Hz, 1 H), 4.93 (dd, *J* = 10.2, 3.7 Hz, 1 H), 3.92 (ddd, *J* = 10.4, 5.1, 2.0 Hz, 1 H), 3.63 (s, 6 H), 3.46 (s, 3 H), 3.30–3.18 (m, 5 H), 3.14 (dd, *J* = 10.5, 5.2 Hz, 1 H), 2.26 (t, *J* = 7.3 Hz, 4 H), 2.09 (s, 3 H), 1.99 (s, 3 H), 1.80 (m, 4 H), 1.71 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 170.2, 170.1, 169.1, 147.2, 144.1, 144.0, 144.0, 128.7, 128.6, 128.5,

127.6, 126.8, 117.1, 113.3, 111.0, 96.5, 86.8, 71.1, 70.5, 69.0, 68.7, 62.0, 55.1, 51.5, 50.2, 31.2, 22.5, 20.7, 20.7, 20.4; IR(neat) 2952, 1755, 1599, 1495, 1439, 1369, 1225, 1172, 1039, 931, 749, 707; HRMS (ESI) *m/e* calcd. for $C_{42}H_{52}NO_{13}$ 778.3439, found 778.3445.

Preparation of 7b*:* A mixture of **22** (297 mg, 0. 57 mmol) and **10b** (133 mg, 0.38 mmol) in 0.6 mL of toluene was heated at 120 °C for 2 h. The solvent was removed and the residue was directly purified by flash column chromatography on silica gel, eluted with benzene/ethyl acetate = 9:1, to provide **7b** (256 mg, 83 %) as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.38 (m, 4 H), 7.34–7.17 (m, 6 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 6.74 (d, *J* = 7.6 Hz, 1 H), 6.65 (s, 1 H), 6.57 (dd, *J* = 8.3, 2.1 Hz, 1 H), 5.21 (dd, *J* = 9.8, 3.5 Hz, 1 H), 5.17 (dd, *J* = 3.5, 1.7 Hz, 1 H), 5.02 (t, *J* = 9.8 Hz, 1 H), 4.69 (d, *J* = 1.6 Hz, 1 H), 3.92–3.74 (m, 2 H), 3.68–3.49 (m, 7 H), 3.30–3.09 (m, 6 H), 2.25 (t, *J* = 7.2 Hz, 4 H), 2.14 (s, 3 H), 2.05 (s, 3 H), 1.98 (s, 3 H), 1.95–1.71 (m, 6 H), 1.16 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 170.1, 170.0, 169.8, 147.1, 144.9, 144.6, 144.5, 128.7, 128.6, 128.5, 127.6, 126.8, 116.9, 113.3, 111.0, 97.4, 86.7, 71.3, 69.9, 69.2, 66.1, 65.2, 60.1, 51.5, 50.4, 31.3, 30.0, 22.5, 20.9, 20.8, 20.7, 17.4; IR(neat) 2952, 1747, 1599, 1494, 1438, 1370, 1246, 1225, 1137, 1081, 1052, 747, 709; HRMS (ESI) *m/e* calcd. for $C_{44}H_{56}NO_{13}$ 806.3752, found 806.3749.

Preparation of 7c*:* A mixture of **22** (158 mg, 0. 30 mmol) and **10c** (198 mg, 2.15 mmol) was heated at 120 °C without a solvent for 4 h. The crude product was directly loaded onto a column for flash column chromatography on silica gel, eluted with petroleum ether /ethyl acetate = 2:1, then petroleum ether /ethyl acetate = 1:4. The product **7c** (77 mg, 42 %) was obtained as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/4); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (dt, *J* = 2.2, 1.4 Hz, 4 H), 7.35–7.16 (m, 6 H), 7.11 (t, *J* = 8.0 Hz, 1 H), 6.86 (s, 1 H), 6.64 (d, *J* = 8.2 Hz, 1 H), 6.56 (dd, *J* = 8.2, 2.3 Hz, 1 H), 3.86 (s, 1 H), 3.72–3.53 (m, 8 H), 3.33–3.16 (m, 6 H), 3.09 (s, 1 H), 2.37 (s, 1 H), 2.29 (t, *J* = 7.2 Hz, 4 H), 1.83 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 147.3, 144.7, 143.9, 143.8, 128.7, 128.6, 128.5, 127.7, 127.0, 126.9, 117.0, 112.5, 110.9, 87.1, 71.1, 65.3, 64.3, 51.6, 50.3, 31.2, 22.4; IR(neat) 3448, 2951, 1733, 1598, 1494, 1448, 1367, 1202, 1073, 863, 774, 750, 709, 638; HRMS (ESI) *m/e* calcd. for $C_{32}H_{40}NO_7$ 550.2805, found 550.2796.

Preparation of 7d*:* A mixture of **22** (233 mg, 0. 45 mmol) and **10d** (48 mg, 0.36 mmol) in 0.4 mL of toluene was heated at 120 °C for 2.5 h. The solvent was removed and the residue was purified by flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 1:2, then 1:4, to afford **7d** (179 mg, 97 %) as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.34 (m, 4 H), 7.34–7.18 (m, 6 H), 7.11 (t, *J* = 7.8 Hz, 1 H), 6.68 (s, 1 H), 6.64–6.54 (m, 2 H), 6.46 (d, *J* = 8.3 Hz, 1 H), 4.71 (dt, *J* = 8.0, 3.0 Hz, 1 H), 3.74 (s, 3 H), 3.69–3.57 (m, 7 H), 3.39 (dd, *J* = 9.3, 2.8 Hz, 1 H), 3.24 (t, *J* = 7.5 Hz, 4 H), 2.28 (t, *J* = 7.2 Hz, 4 H), 2.00 (s, 3 H), 1.82 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 171.1, 169.7, 147.2, 144.5, 143.6, 143.4, 128.7, 128.6, 128.5, 127.8, 127.7, 127.1, 127.1, 116.7, 112.9, 111.1, 86.8, 63.7, 52.6, 52.3, 51.6, 50.3, 31.2, 23.0, 22.5; IR(neat) 2952, 1738, 1679, 1598, 1495, 1436, 1372, 1207, 1096, 989, 861, 748, 709; HRMS (ESI) *m/e* calcd. for $C_{35}H_{43}N_2O_8$ 619.3019, found 619.3018.

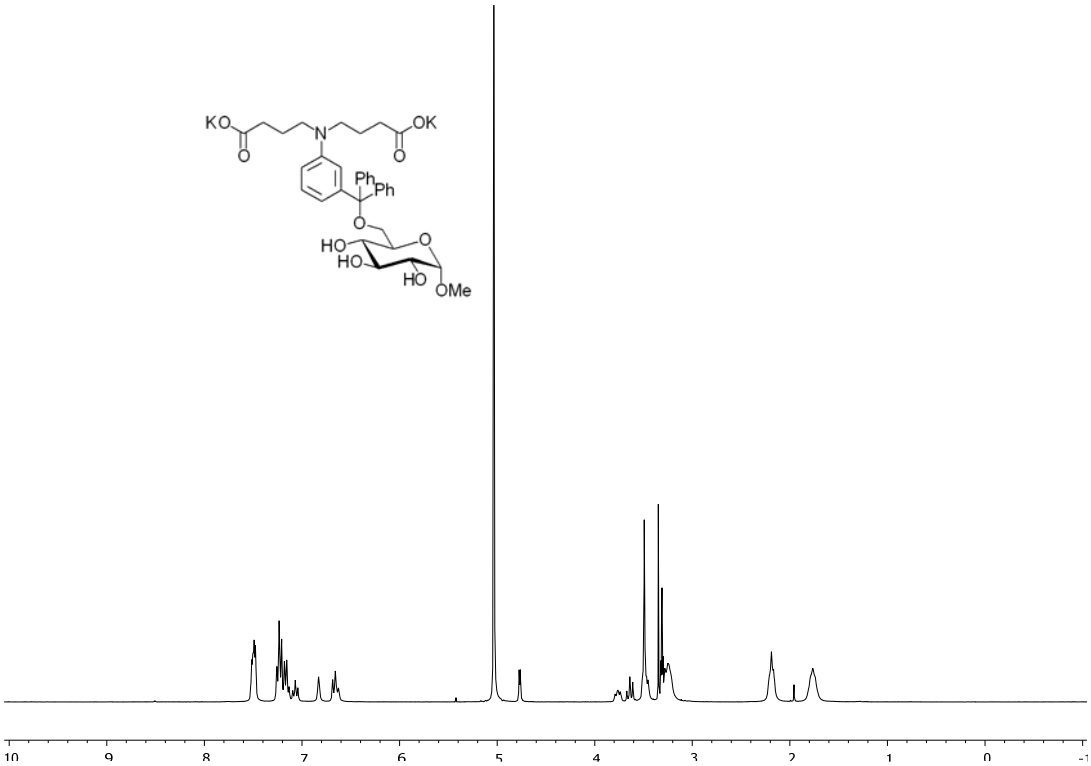
Preparation of 7e*:* A mixture of **22** (155 mg, 0. 3 mmol) and **10e** (24 mg, 0.1 mmol) in 0.2 mL of toluene was heated at 120 °C for 2.25 h. The solvent was removed and the residue was purified by flash column chromatography on silica gel, eluted with, then petroleum ether/ethyl acetate = 1:4, to

afford **7e** (57 mg, 81 %) as a colorless oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/4); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (br, s, 1 H), 7.58 (d, *J* = 1.2 Hz, 1 H), 7.51–7.39 (m, 4 H), 7.37–7.21 (m, 6 H), 7.15 (t, *J* = 8.2 Hz, 1 H), 6.73–6.66 (m, 2 H), 6.62 (dd, *J* = 8.4, 2.1 Hz, 1 H), 6.39 (t, *J* = 6.7 Hz, 1 H), 4.62 (m, 1 H), 4.07 (q, *J* = 3.2 Hz, 1 H), 3.65 (s, 6 H), 3.47 (qd, *J* = 10.5, 3.1 Hz, 2 H), 3.22 (t, *J* = 7.6 Hz, 4 H), 2.90 (br, s, 1 H), 2.42 (m, 1 H), 2.35–2.18 (m, 5 H), 1.81 (m, 4 H), 1.48 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 163.6, 150.2, 147.4, 144.2, 143.9, 143.3, 135.6, 128.7, 128.5, 127.9, 127.8, 127.2, 127.2, 117.3, 113.2, 111.6, 111.1, 87.7, 86.0, 84.7, 71.9, 63.5, 51.7, 50.4, 40.8, 31.2, 29.7, 22.5, 11.8; IR(neat) 3446, 2952, 1733, 1683, 1598, 1368, 1272, 1199, 708; HRMS (ESI) *m/e* calcd. for $C_{39}H_{46}N_3O_9$ 700.3234, found 700.3229.

Preparation of 11*:* A mixture of **20** (221 mg, 0. 45 mmol) and **10d** (48 mg, 0.3 mmol) in 0.4 mL toluene was heated at 120 °C for 3.6 h. The solvent was removed and the residue was purified by flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 2:3, to afford **11** (162 mg, 91 %) as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.17 (m, 10 H), 7.11 (t, *J* = 8.0 Hz, 1 H), 6.83 (dd, *J* = 2.5, 1.7 Hz, 1 H), 6.69 (d, *J* = 8.6 Hz, 1 H), 6.62 (d, *J* = 8.3 Hz, 1 H), 6.47 (dd, *J* = 8.1, 2.4 Hz, 1 H), 4.73 (dt, *J* = 8.5, 2.9 Hz, 1 H), 4.16 (q, *J* = 7.1 Hz, 4 H), 4.08 (d, *J* = 4.2 Hz, 4 H), 3.73 (s, 3 H), 3.60 (dd, *J* = 9.2, 3.0 Hz, 1 H), 3.37 (dd, *J* = 9.2, 2.9 Hz, 1 H), 2.04 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 170.9, 169.9, 147.4, 145.1, 143.1, 142.7, 128.7, 128.6, 127.7, 127.7, 127.2, 127.1, 118.6, 112.6, 111.1, 86.5, 63.6, 61.1, 53.8, 52.5, 52.3, 22.9, 14.1; IR(neat) 2983, 1747, 1676, 1603, 1496, 1449, 1373, 1342, 1184, 1096, 1027, 750, 708; HRMS (ESI) *m/e* calcd. for $C_{33}H_{39}N_2O_8$ 591.2706, found 591.2705.

Preparation of 12*:* A mixture of **21** (141 mg, 0. 29 mmol) and **10d** (31 mg, 0.19 mmol) in 0.4 mL of toluene was heated at 120 °C for 2 h. The solvent was removed and the residue was purified by flash column chromatography on silica gel, eluted with petroleum ether/ethyl acetate = 1:2, to afford **12** (104 mg, 91 %) as a pale yellow oil. R_f 0.5 (petroleum ether/ethyl acetate = 1/2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.18 (m, 10 H), 7.10 (t, *J* = 8.0 Hz, 1 H), 6.90 (s, 1 H), 6.78 (d, *J* = 8.1 Hz, 1 H), 6.61 (d, *J* = 8.6 Hz, 1 H), 6.54 (dd, *J* = 8.2, 2.4 Hz, 1 H), 4.73 (dt, *J* = 8.2, 2.9 Hz, 1 H), 3.72 (s, 3 H), 3.69 – 3.57 (m, 10 H), 3.48 (ddd, *J* = 33.7, 9.2, 2.9 Hz, 2 H), 2.54 (t, *J* = 8.6 Hz, 4 H), 2.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 171.1, 169.9, 146.2, 145.8, 143.0, 142.8, 128.9, 128.8, 128.7, 127.8, 127.7, 127.3, 127.2, 117.2, 112.3, 110.9, 86.6, 63.8, 52.7, 52.3, 51.7, 47.0, 32.3, 23.0; IR(neat) 2952, 1738, 1679, 1599, 1576, 1495, 1436, 1373, 1204, 1176, 1155, 1095, 1035, 996, 766, 734, 709, 639; HRMS (ESI) *m/e* calcd. for $C_{33}H_{39}N_2O_8$ 591.2706, found 591.2712.

4a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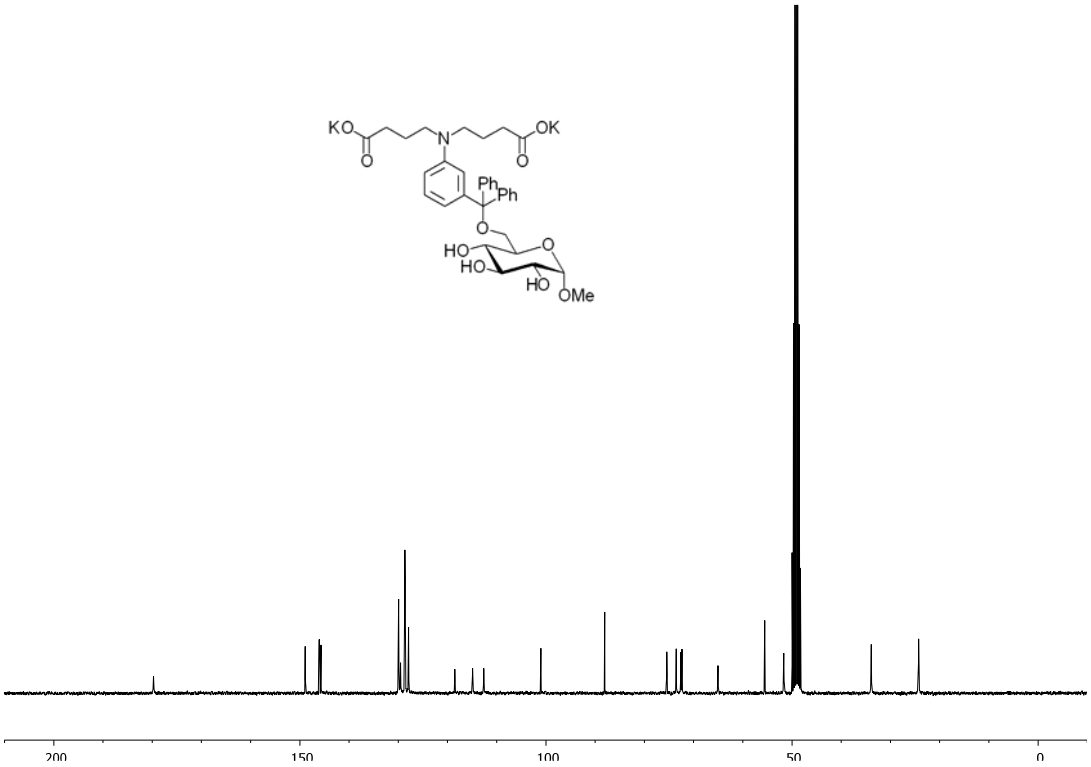
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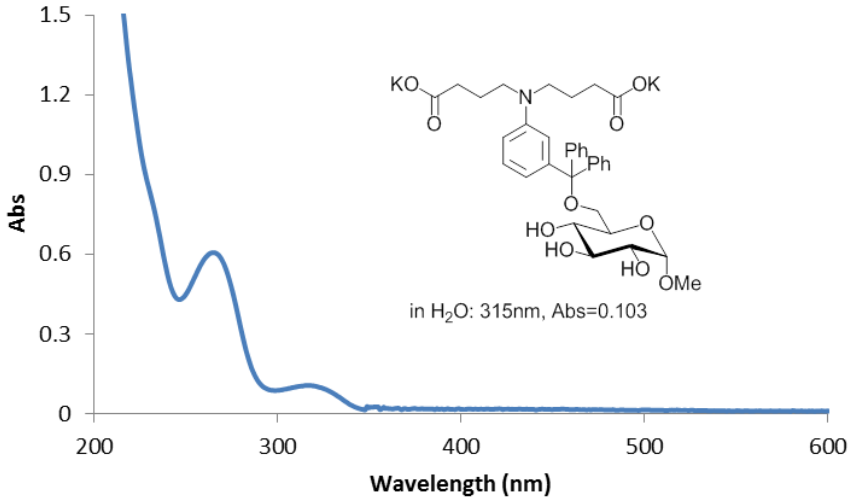
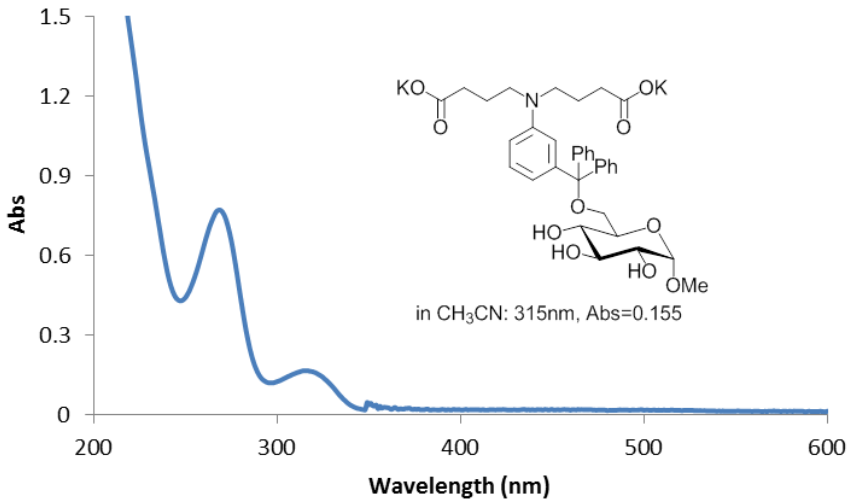
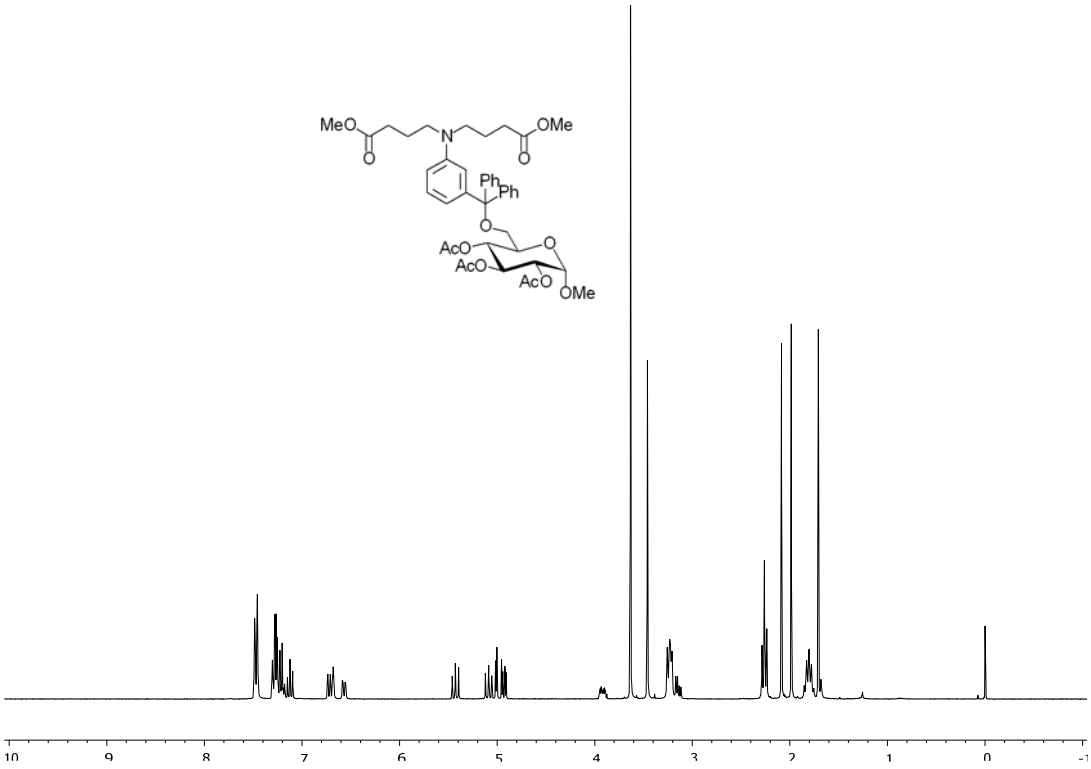


$\varepsilon_{H2O,\ 315\ nm} = 1.7 \times 10^3\ M^{-1}cm^{-1}$



$\varepsilon_{MeCN,\ 315\ nm} = 2.6 \times 10^3\ M^{-1}cm^{-1}$

7a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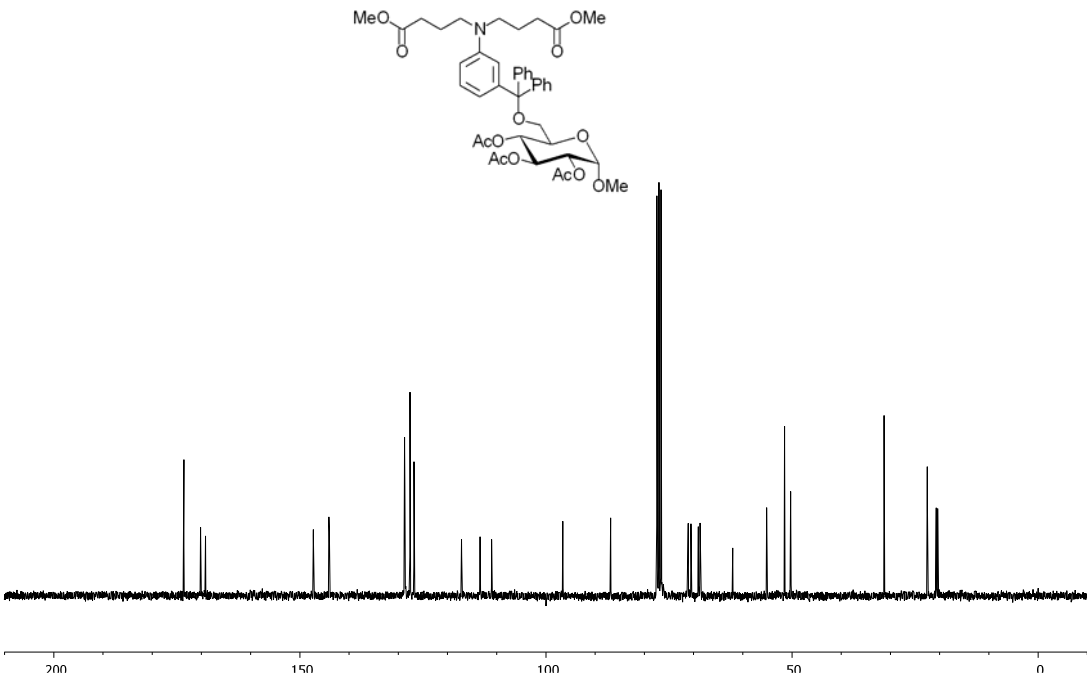
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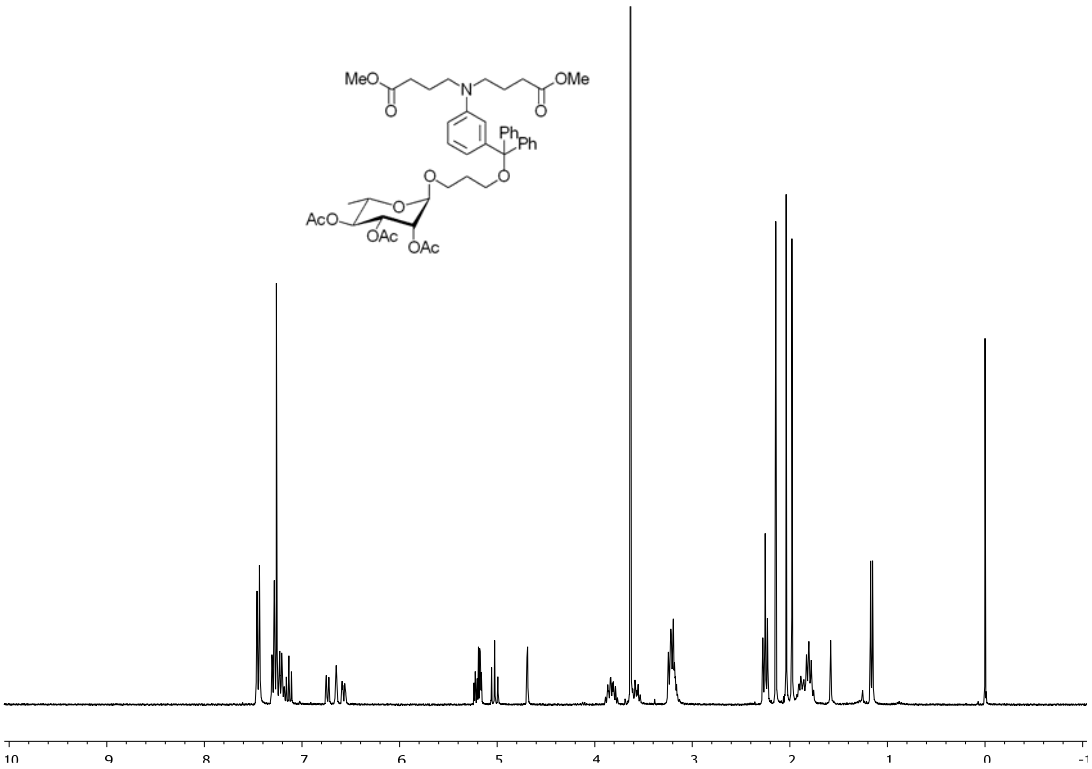
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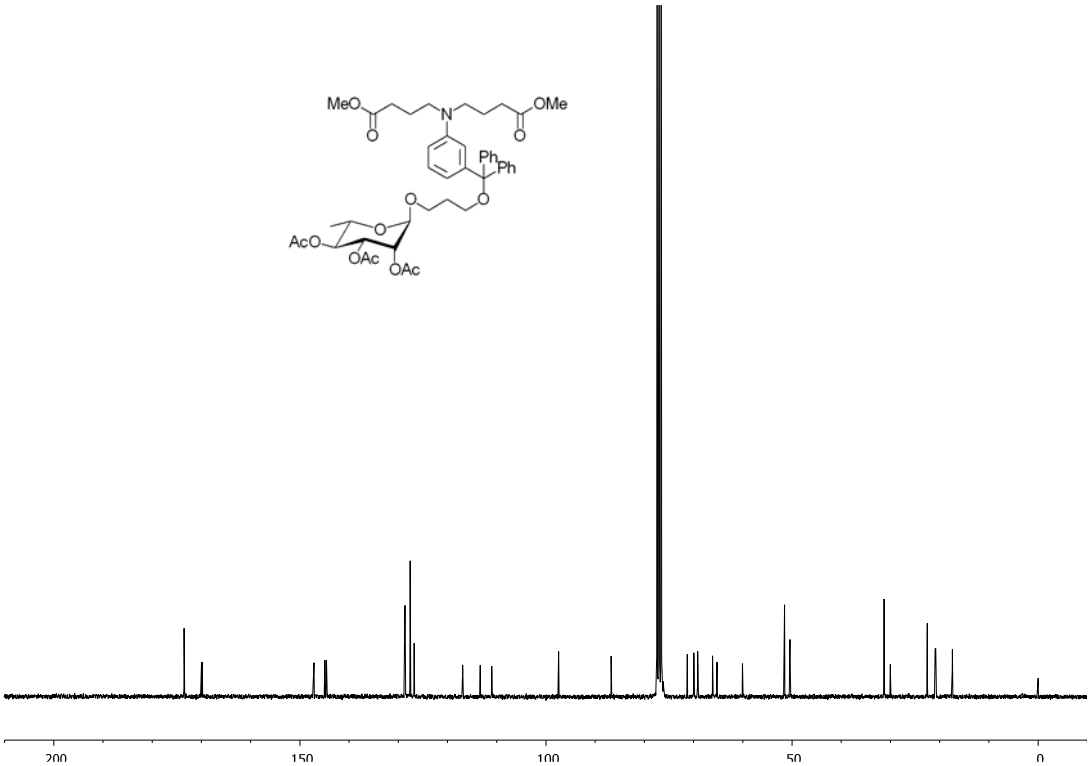
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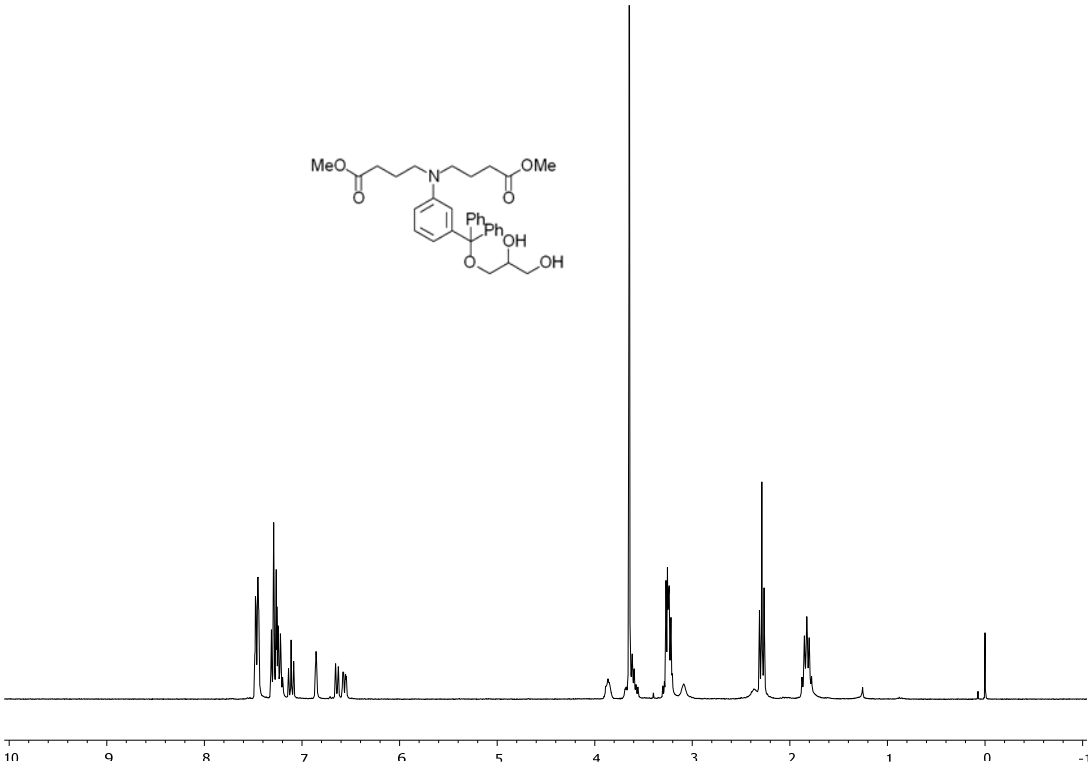

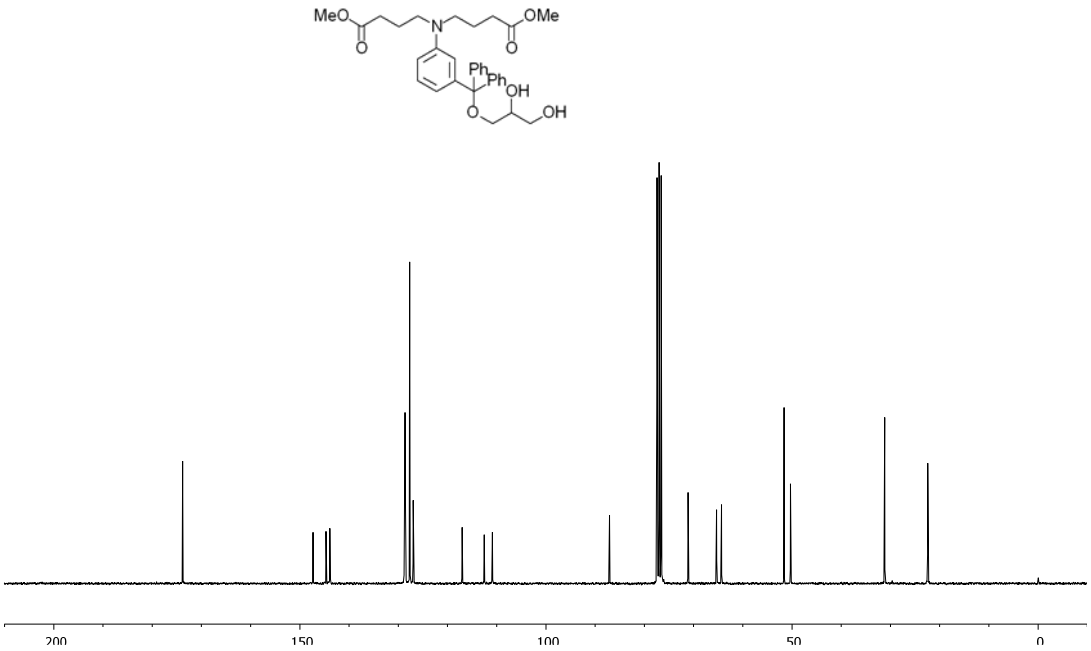

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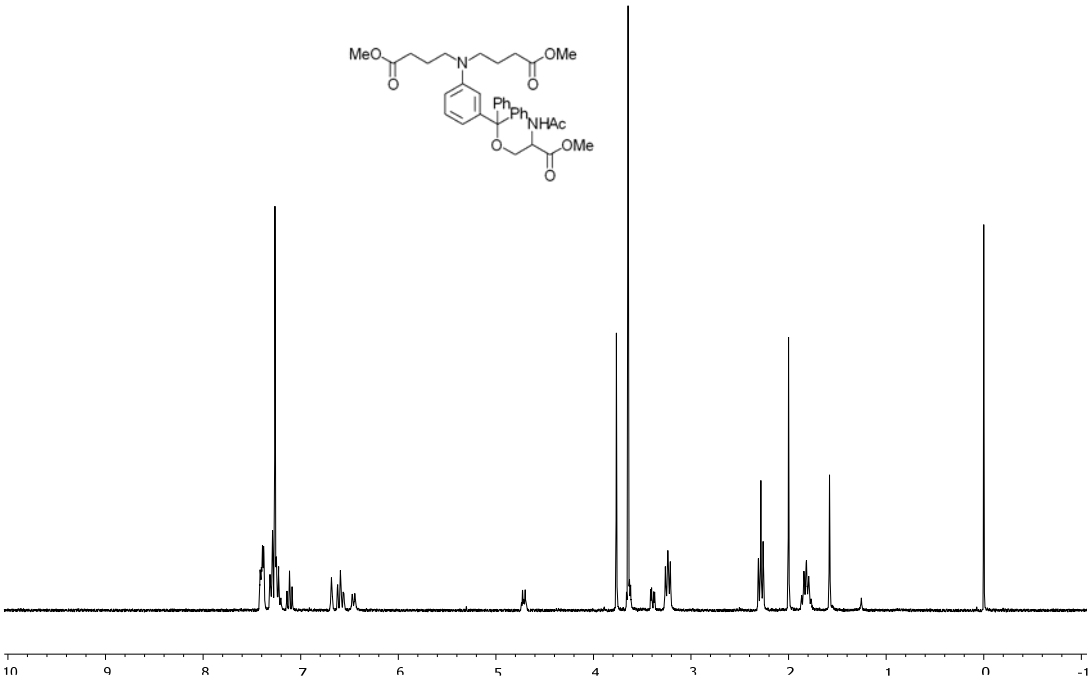
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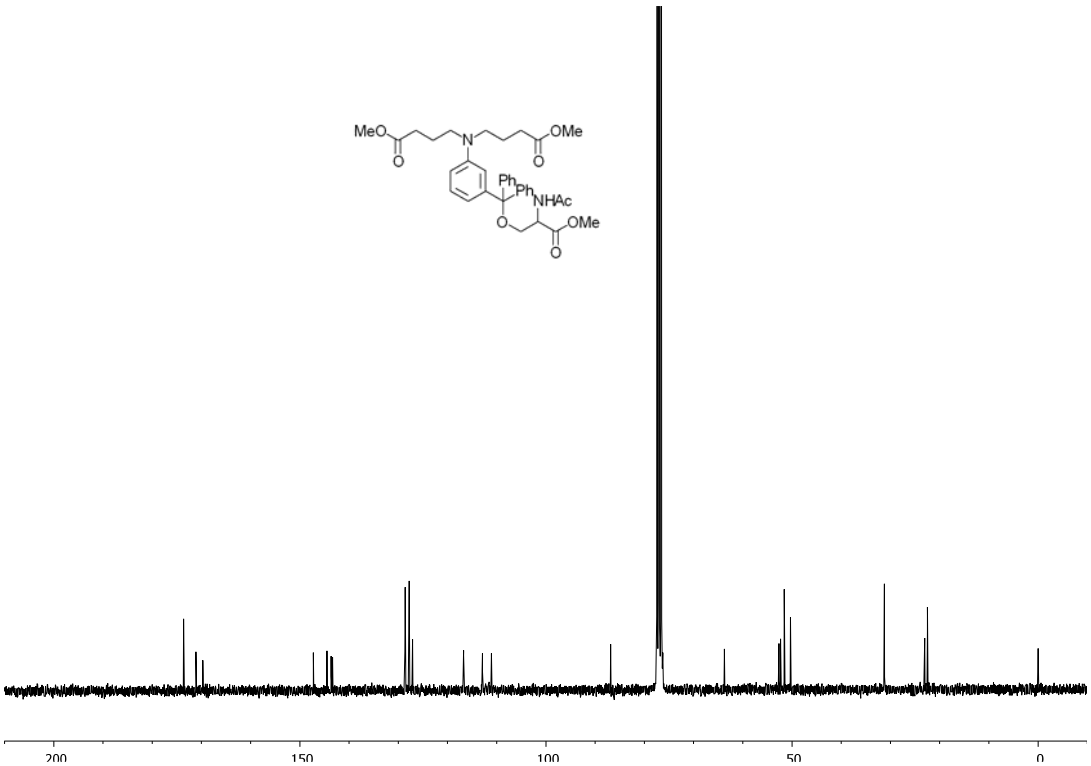
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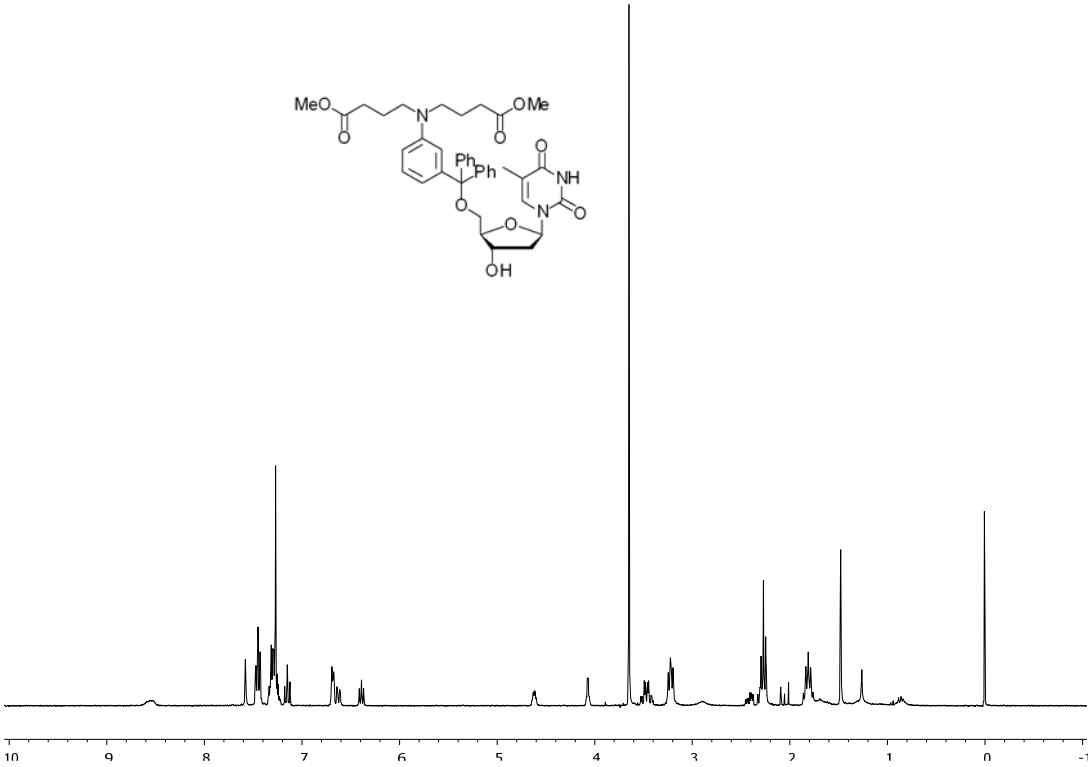
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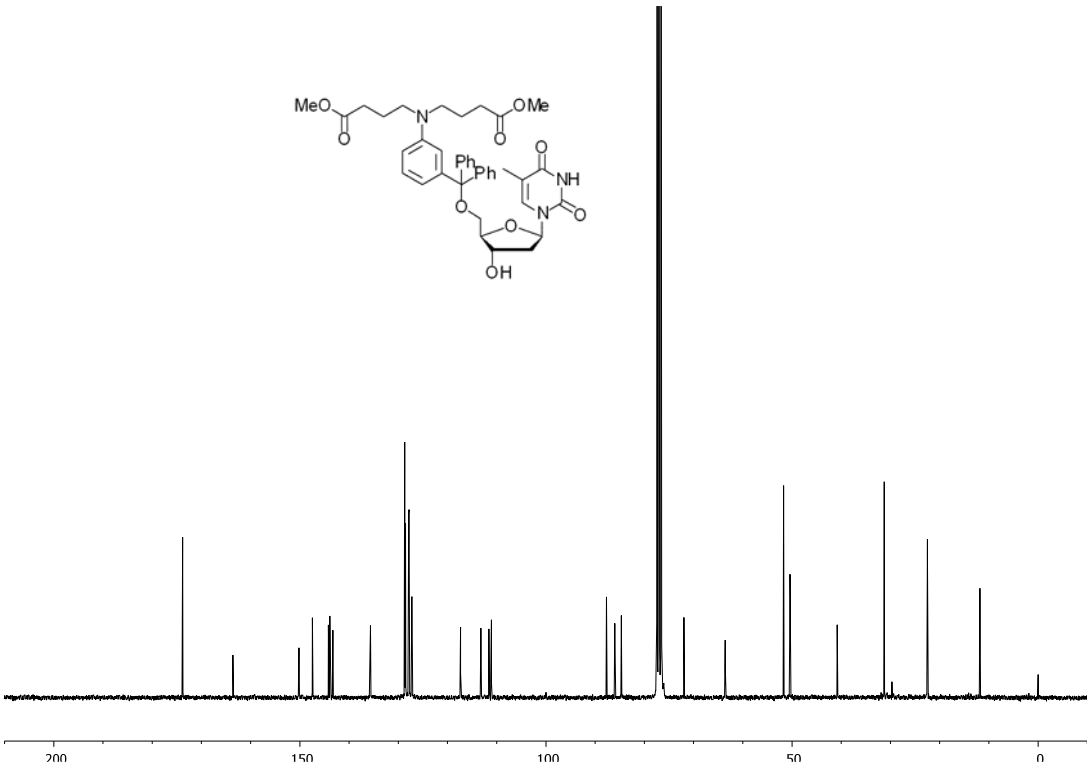
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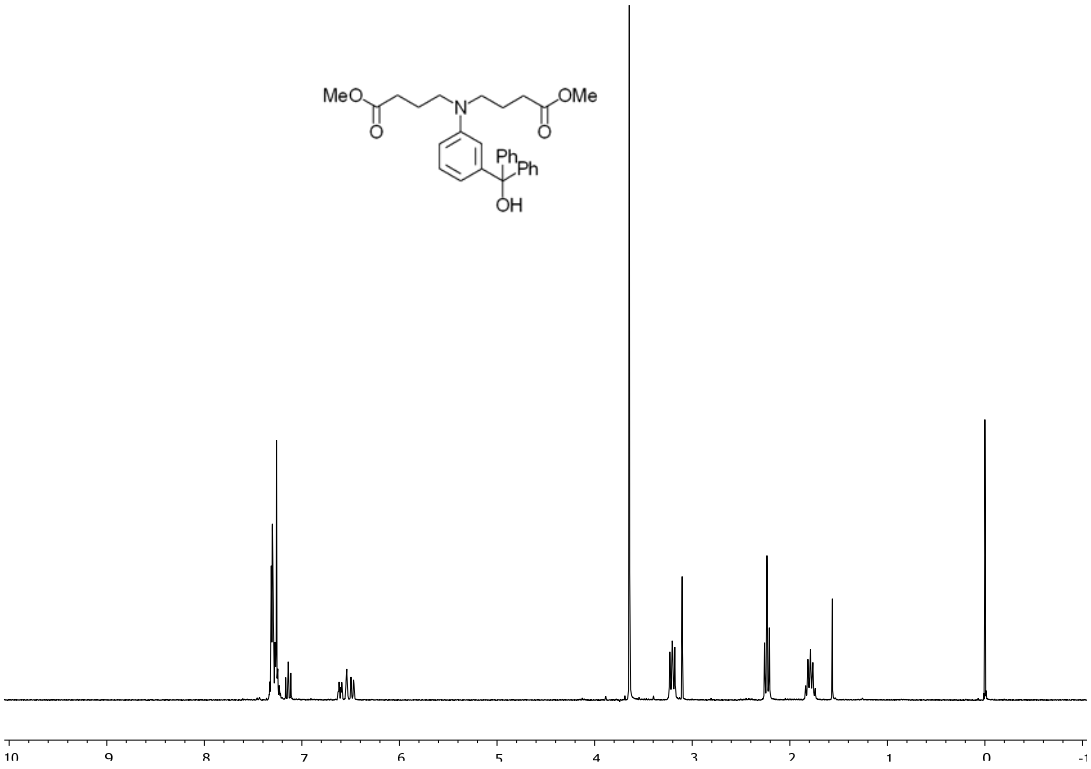
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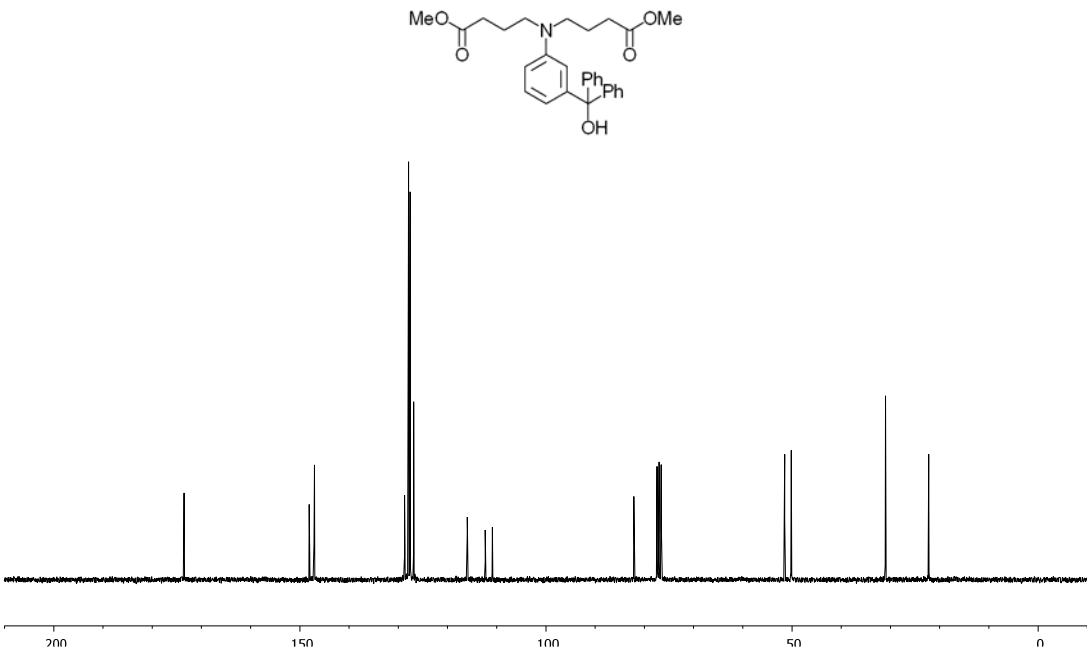
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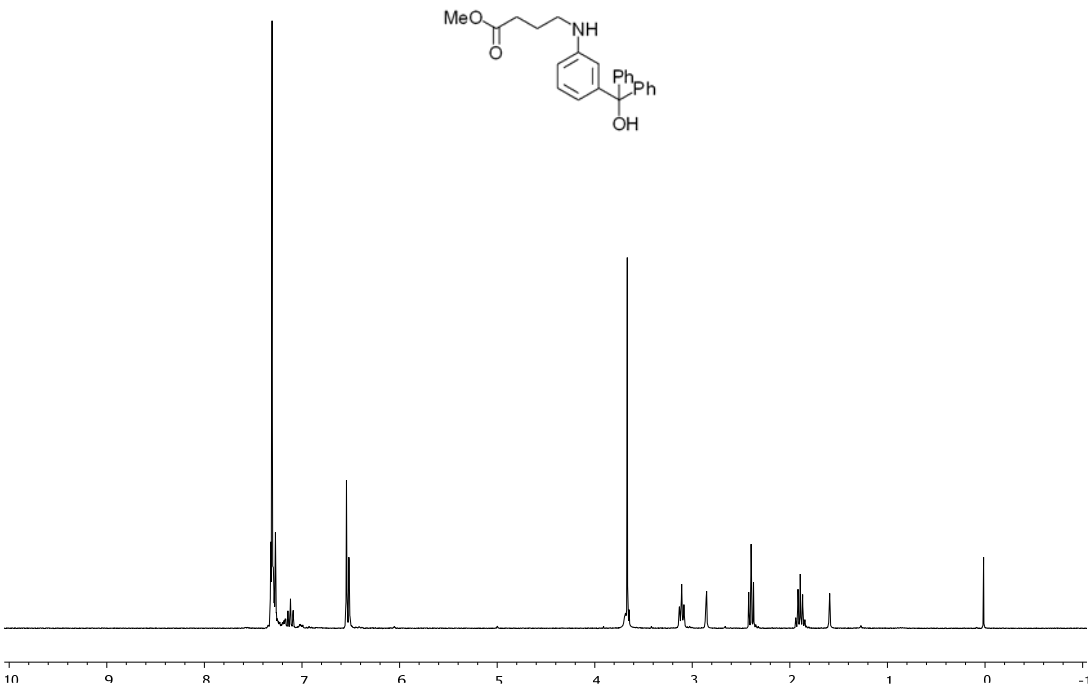

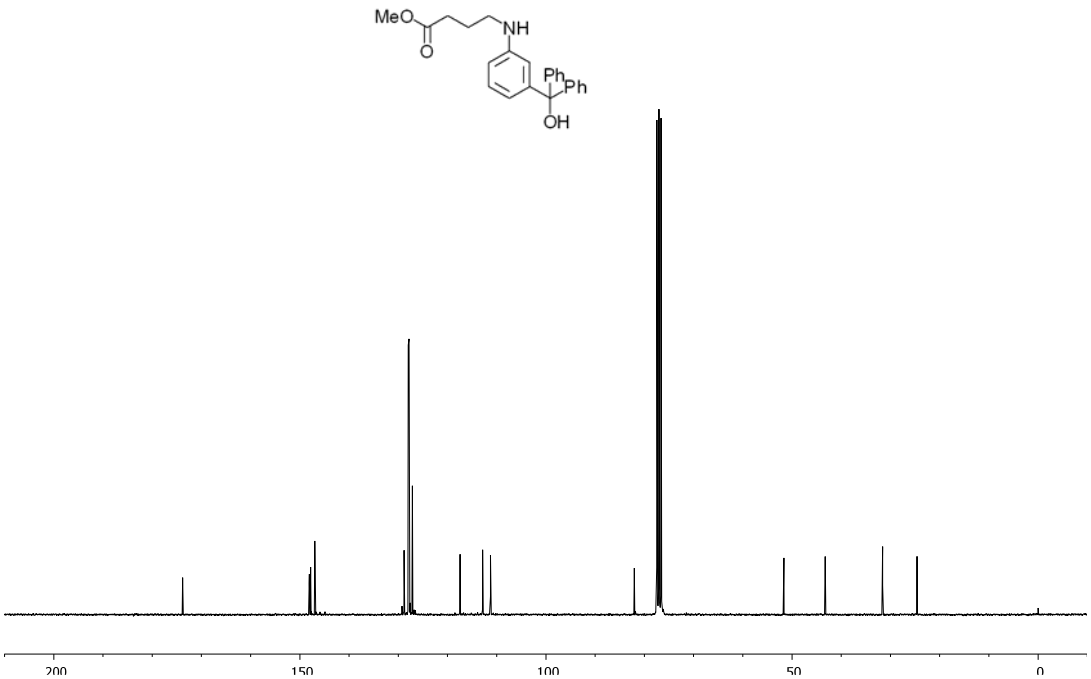

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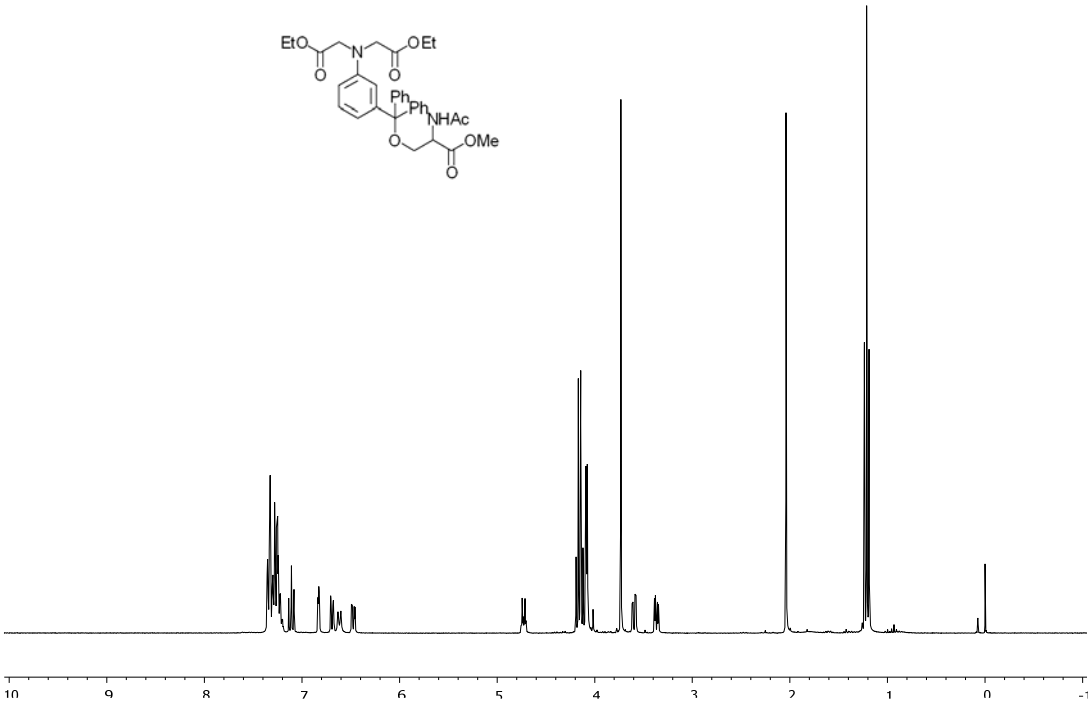
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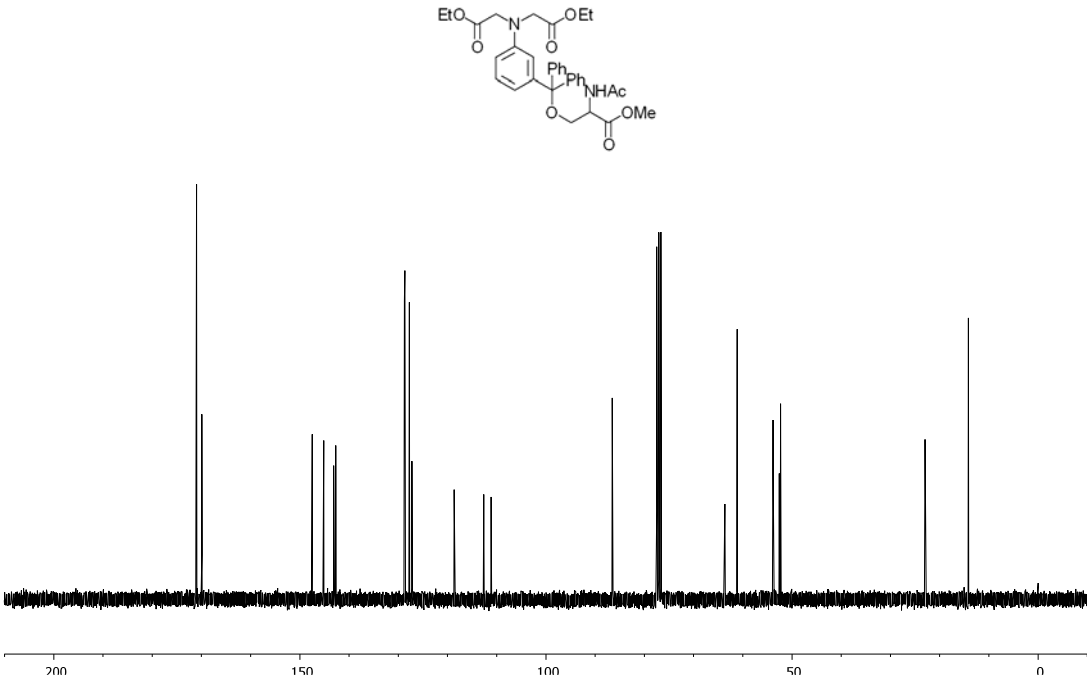
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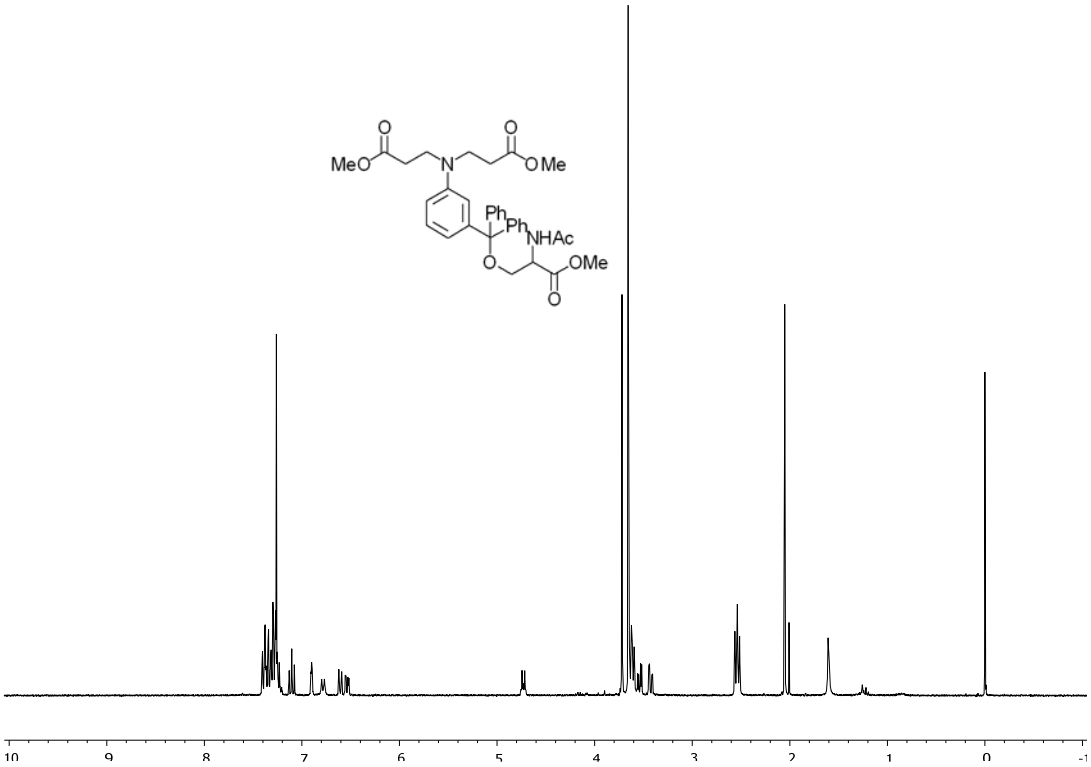
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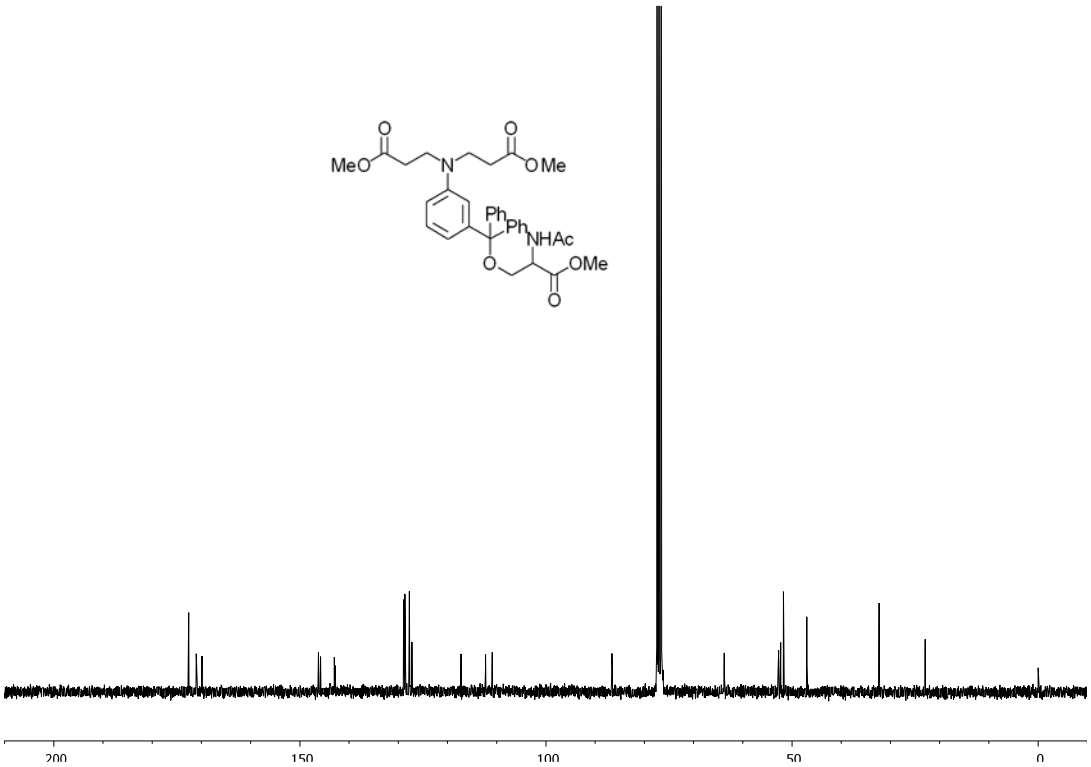
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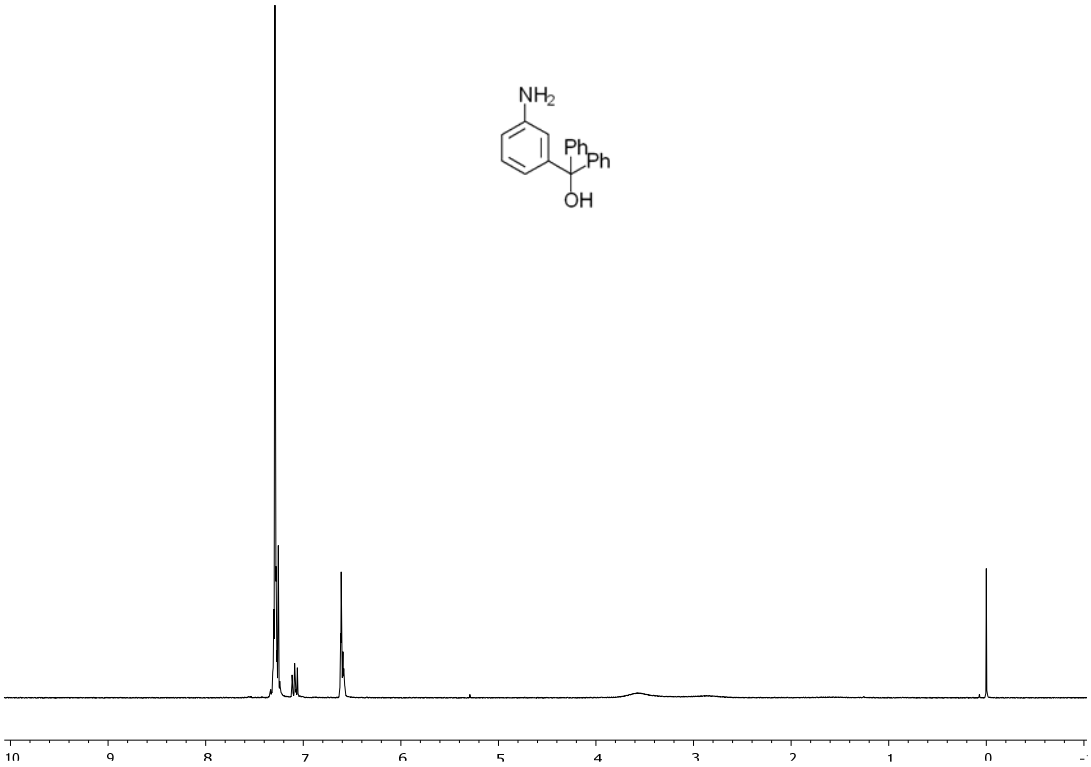

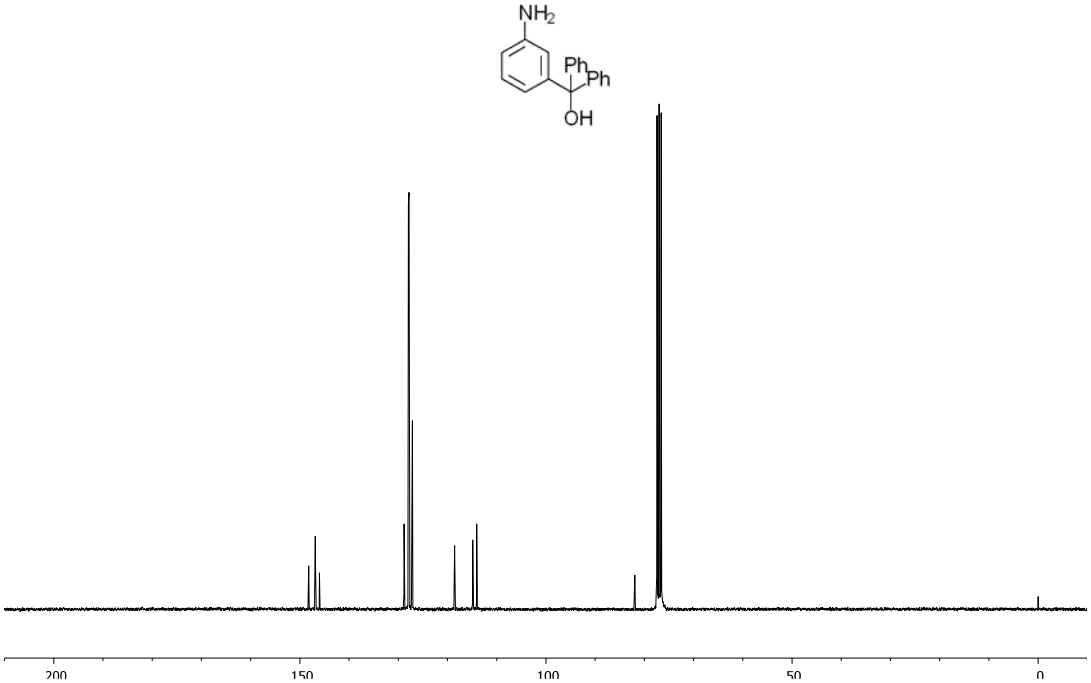

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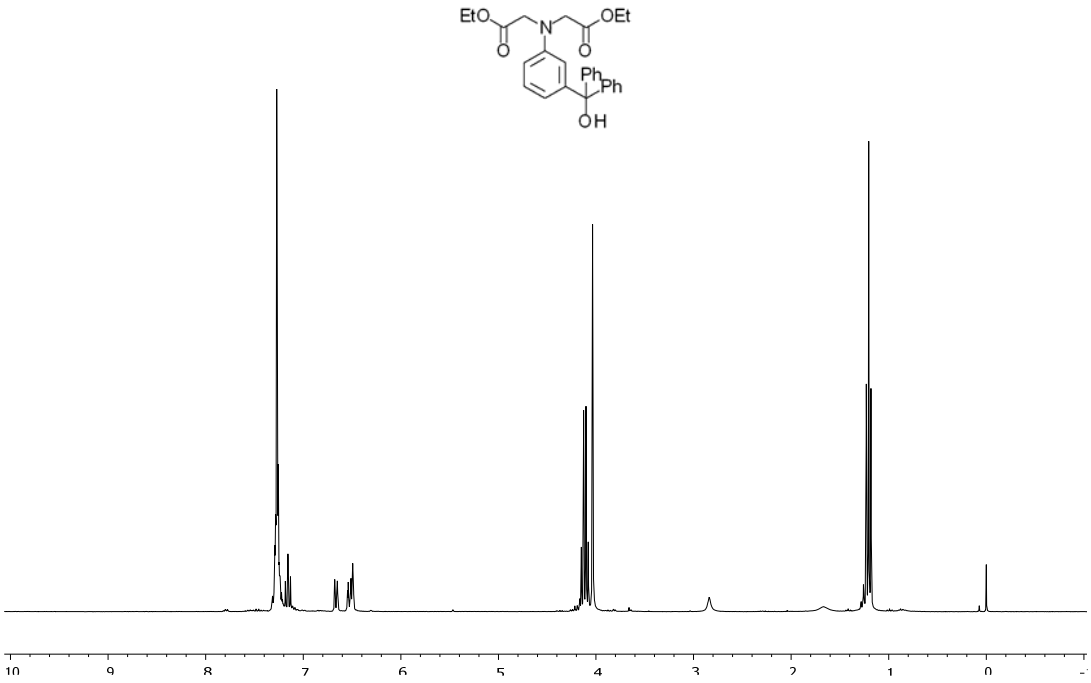
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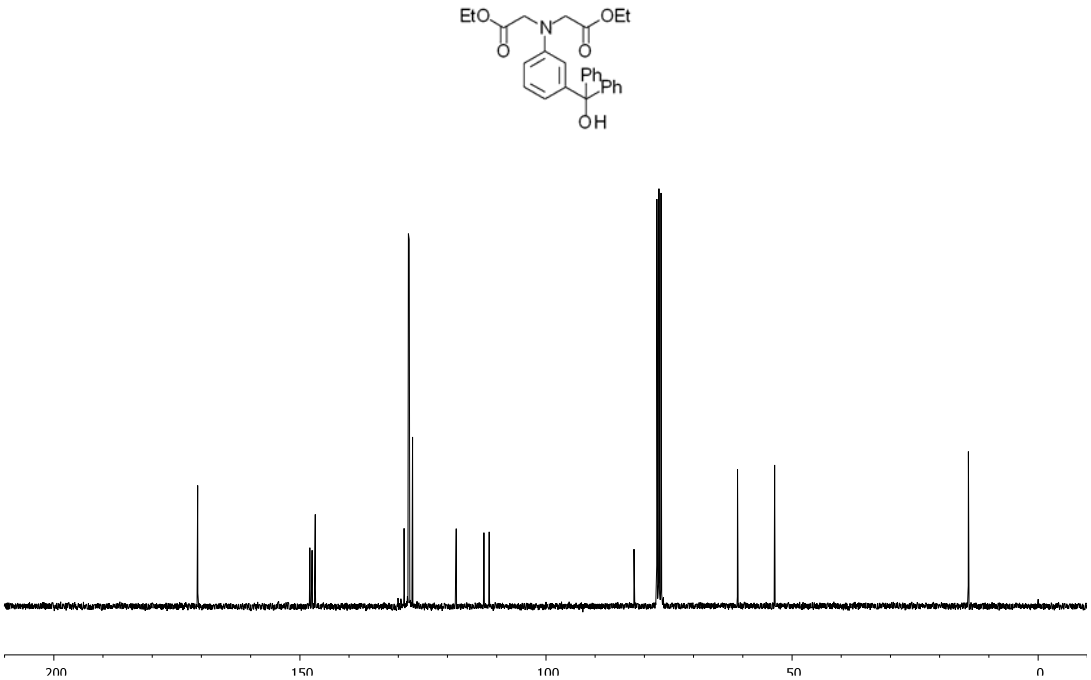
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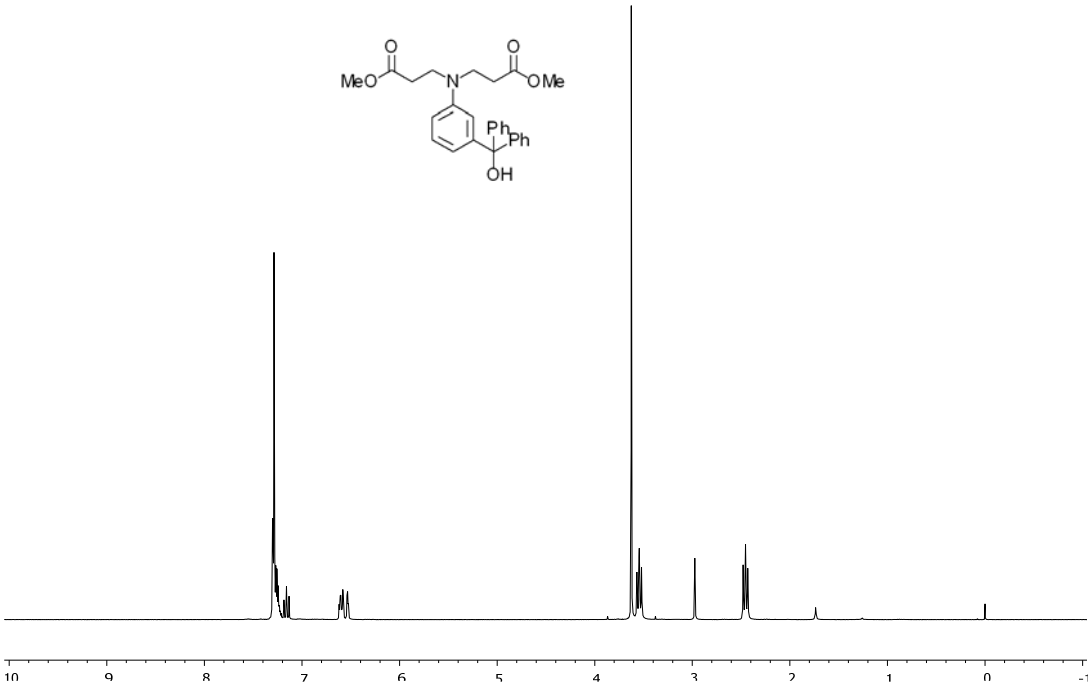
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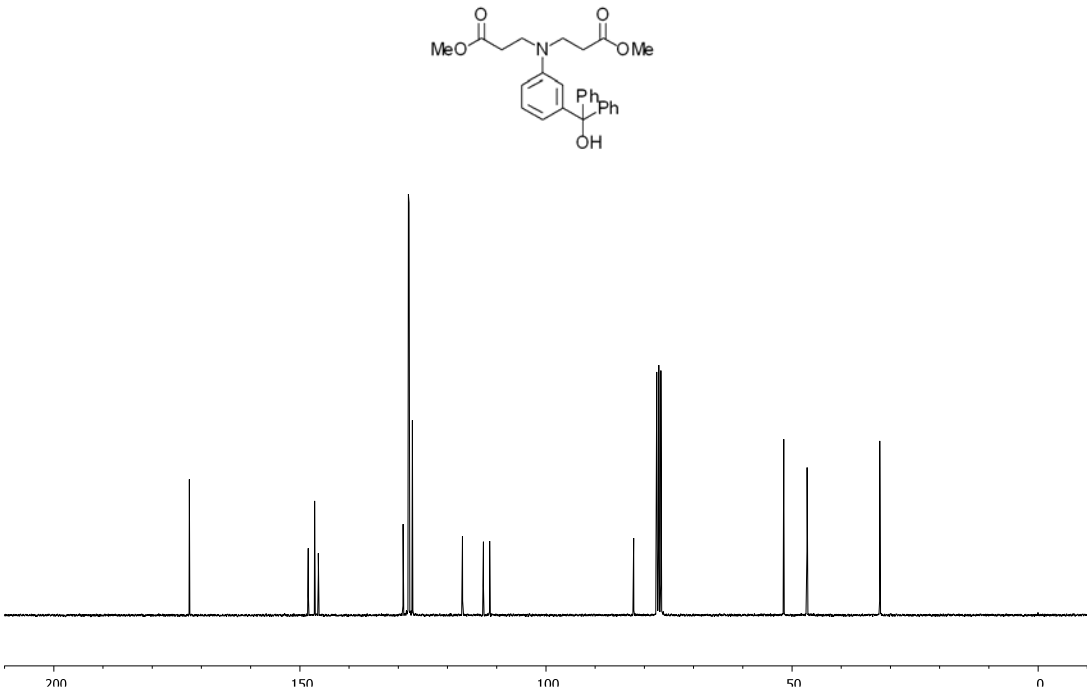
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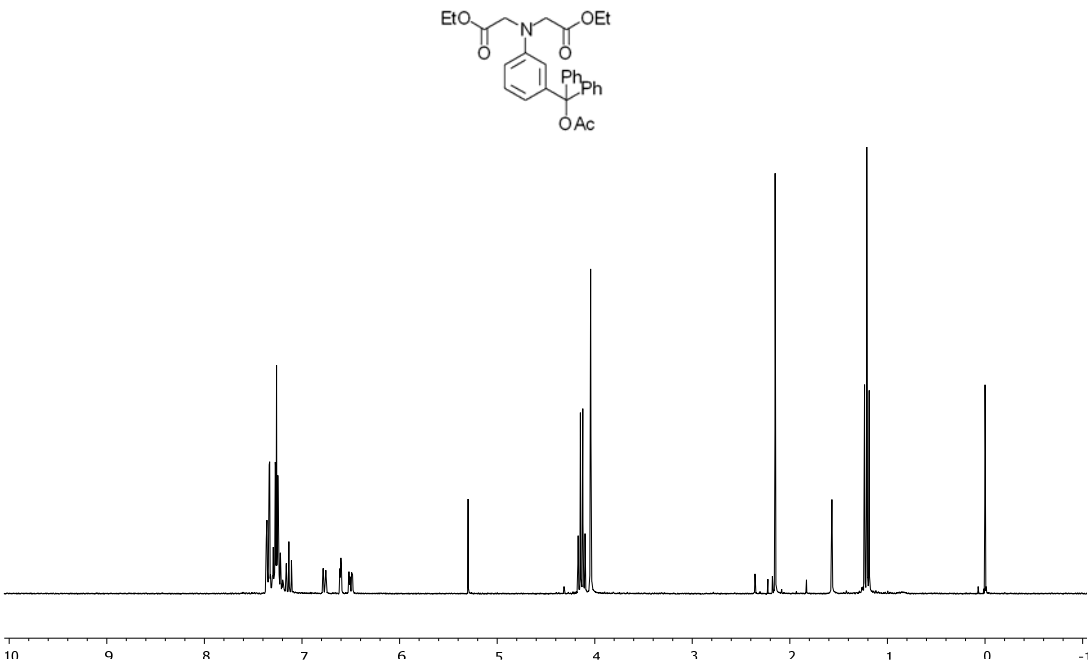
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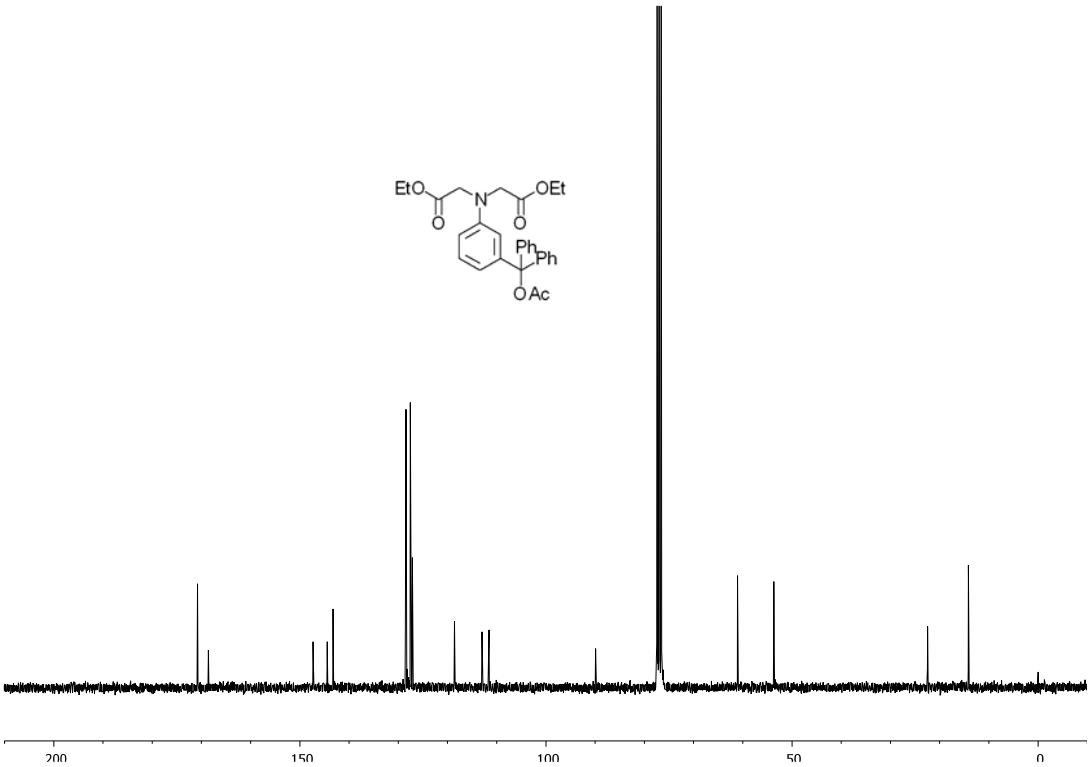
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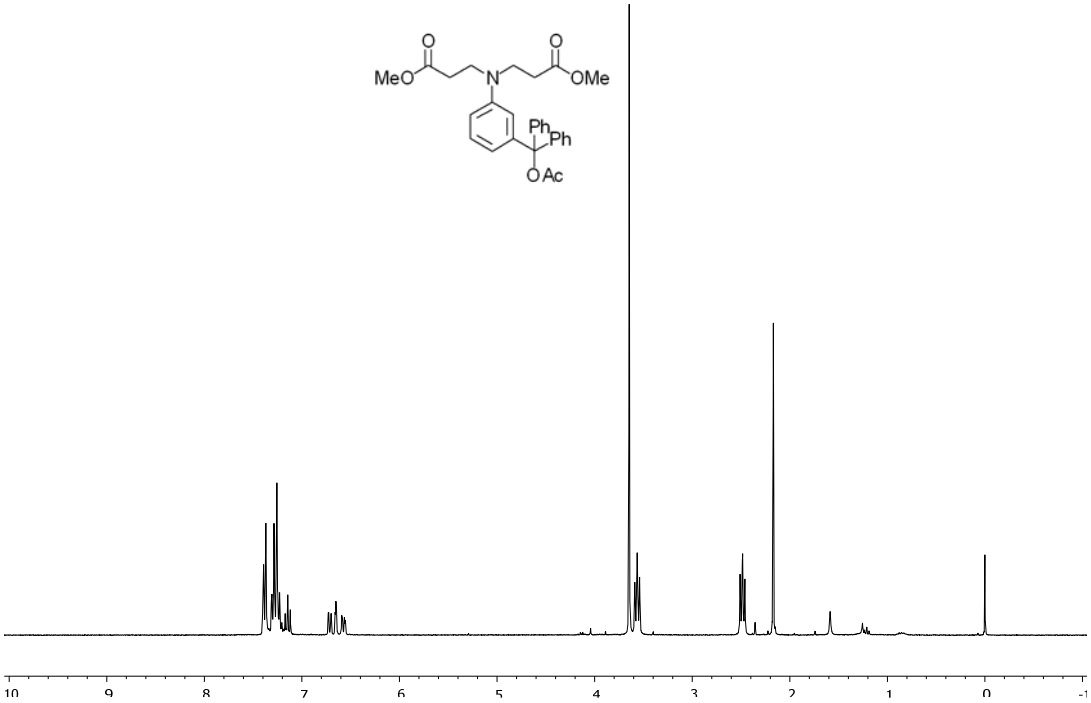
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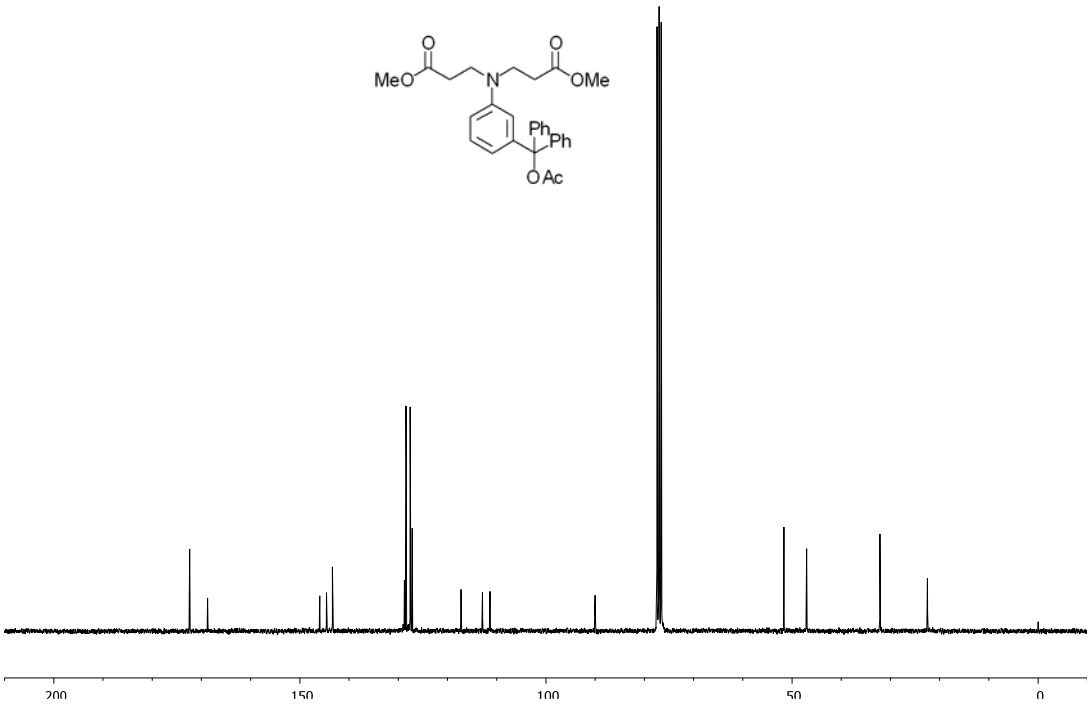
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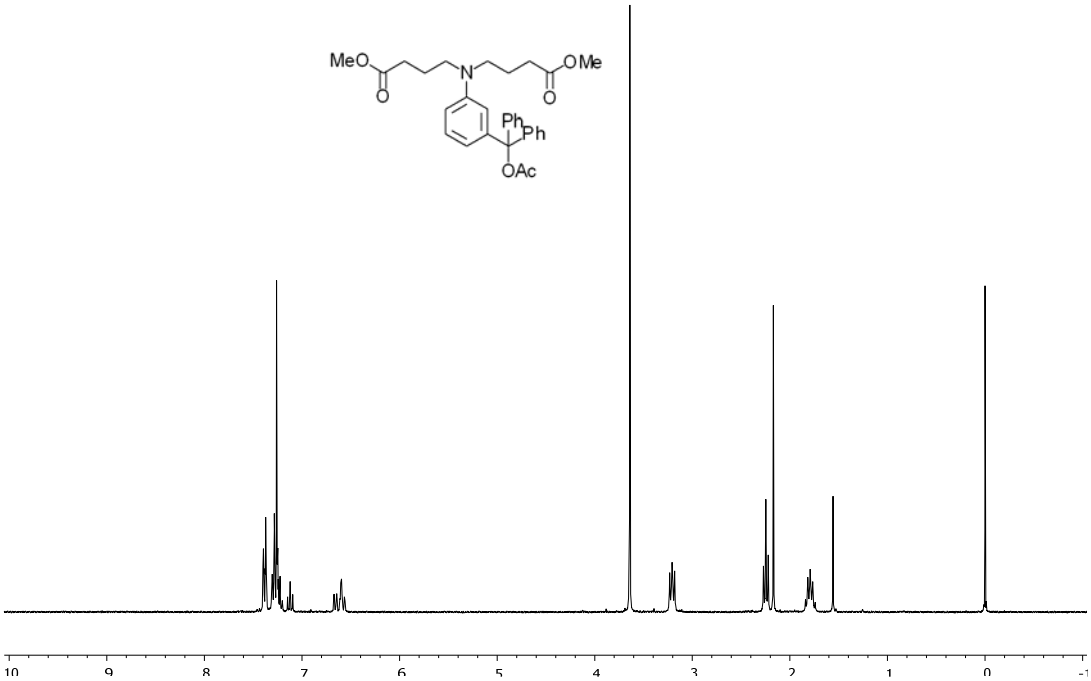
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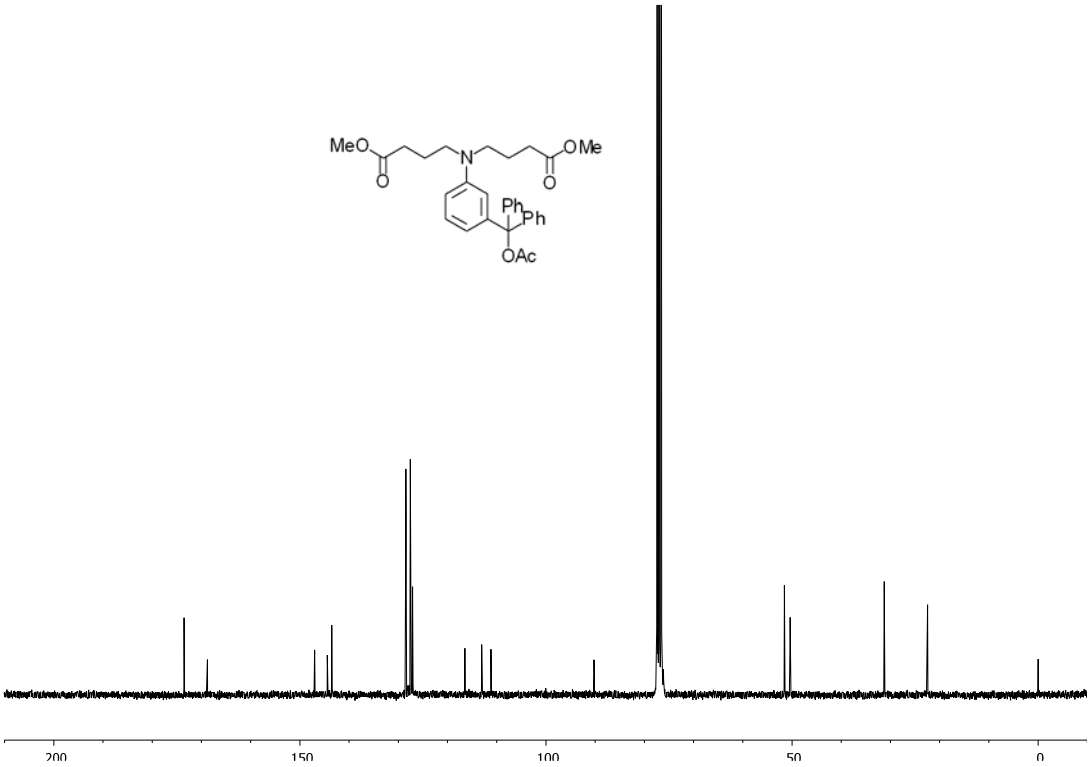
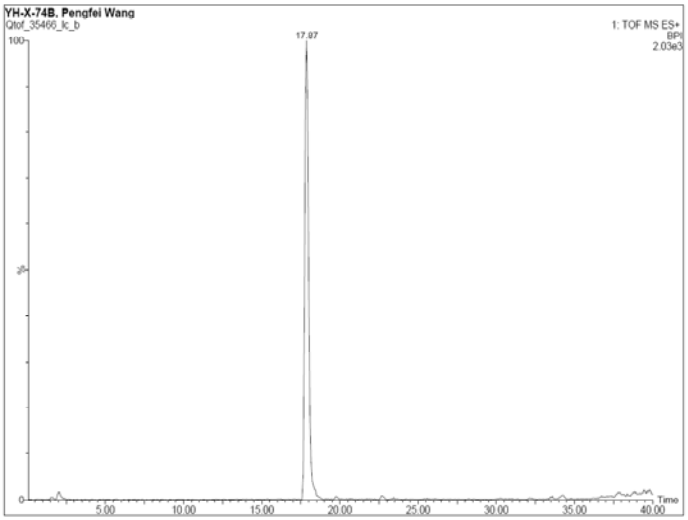

MeO
O
N
OMe
O
Ph
Ph
OAc
200
150
100
50
0

LCMS profile of the photoreaction of 4a (pH ~12)



Waters Alliance 2795 LC Gradient Timetable

Time	A%	B%	C%	D%
0.00	90.0	10.0	0.0	0.0
1.00	90.0	10.0	0.0	0.0
31.00	20.0	80.0	0.0	0.0
32.00	0.0	100.0	0.0	0.0
40.00	0.0	100.0	0.0	0.0
41.00	90.0	10.0	0.0	0.0
56.00	90.0	10.0	0.0	0.0

Waters Alliance 2795 LC Mobile Phase

SolventsA%	90.0 Solvent A
B%	10.0 Solvent B
C%	0.0 Solvent C
D%	0.0 Solvent D
Flow Ramp	2.00
Flow (ml/min)	0.200
Stop Time (mins)	56.00
Min Pressure (Bar)	0
Max Pressure (Bar)	300

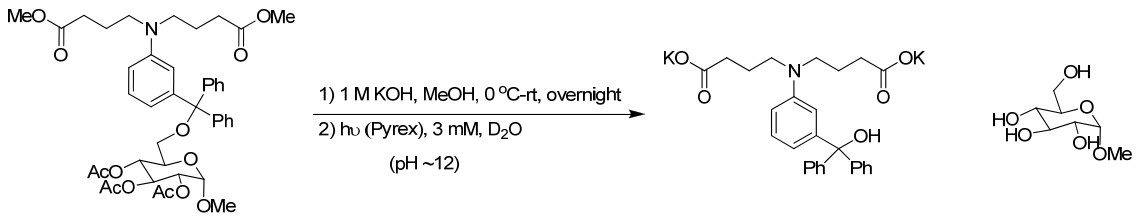
Degasser OnStroke Volume 130.0 µl

Mobile phase

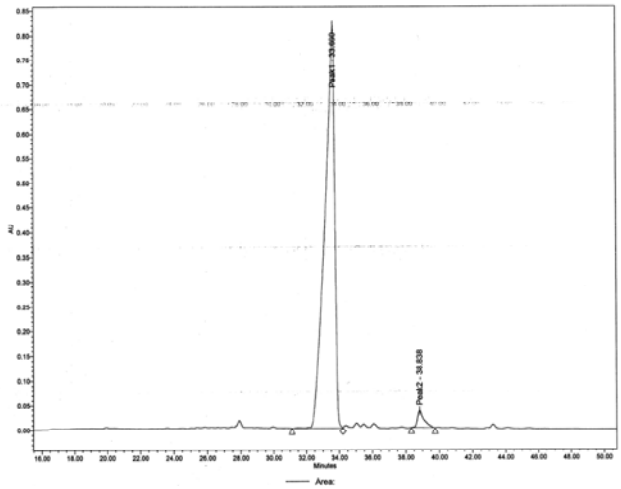
A=95%H_2O, 5%ACN and 0.1% formic acid

B=95%ACN, 5%H_2O and 0.1% formic acid.

HPLC Profiles

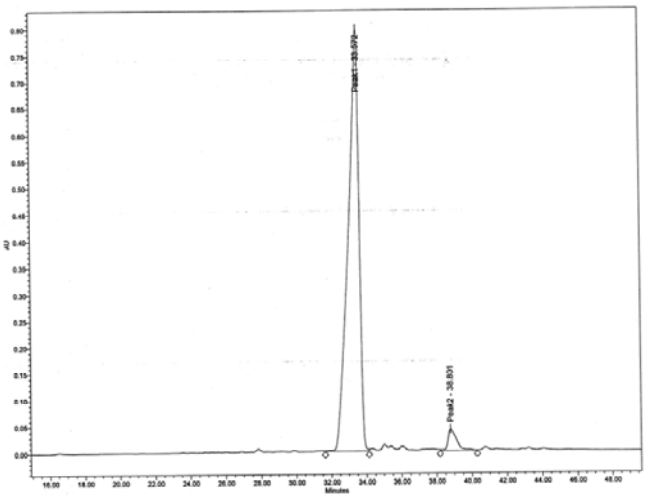


Irradiation time = 12 min

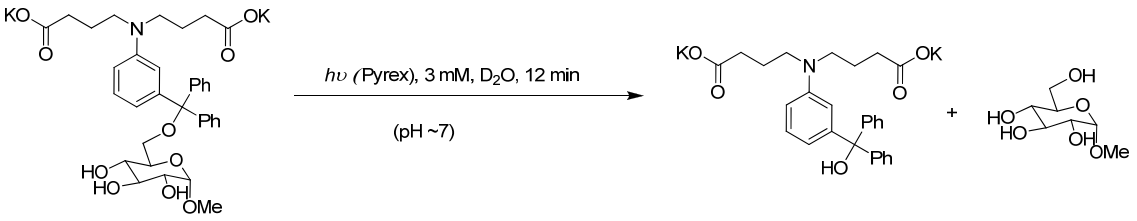


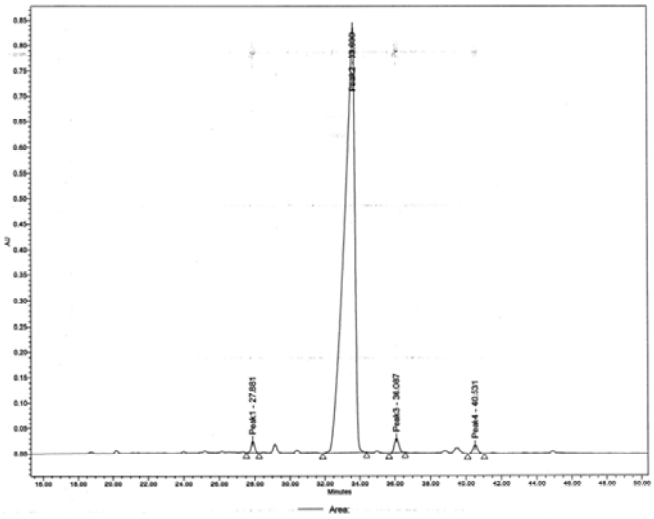
	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1	Peak1	33.660	34165472	97.39	817340	BV			Found	Q20
2	Peak2	38.838	914121	2.61	33363	BB			Found	Q20

Irradiation time = 20 min



	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1	Peak1	33.572	33851265	96.11	798305	VV			Found	Q20
2	Peak2	38.801	1368329	3.89	40622	VV			Found	Q20





	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1	Peak1	27.881	321725	0.89	23258	BB			Found	Q20
2	Peak2	33.630	35062825	96.81	835536	BB			Found	Q20
3	Peak3	36.087	509538	1.41	28375	BB			Found	Q20
4	Peak4	40.531	325310	0.90	17169	BB			Found	Q20