Supporting Information

Light-Induced Hetero Diels-Alder Cycloaddition: A Facile and Selective Photo-Click Reaction

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General Methods. All organic solvents were dried and freshly distilled before use. Purification of products by column chromatography was performed using 40-63 μm silica gel. All NMR spectra were recorded on 400 MHz instrument in CDCl3 and referenced to TMS unless otherwise noted. Solutions for photolyses were prepared using HPLC grade water and acetonitrile. Both preparative and analytical photolyses were carried out using mini-Rayonet photochemical reactor equipped with 8 fluorescent UV lamps (4W; 254, 300, or 350 nm). Isolated pure photoproducts were then used as calibration standards for HPLC analyses of reaction mixtures. Quantum efficiencies of photochemical reactions were measured using ferrioxalate actinometry.[1] Buffer solutions were prepared using literature pKa values of the buffer acids and activity co-efficient recommended by Bates.[2]

Kinetic experiments. Rate measurements of *o*NQM reactions were conducted using LKS.60 kinetic spectrometer (Applied Photophysics) by following spectral changes at 310 nm. Generation of *o*NQMs was achieved by photolyses of *o*NQM precursors utilizing 7 ns fourth harmonic (266 nm) pulse from the Brilliant B Nd:YAG laser. 0.1 mM solutions of *o*NQM precursors **2a-c** and corresponding alkenes were purged with nitrogen for 15 min prior to flash photolysis. The sample solution was thermostatted at 25 ± 0.05 ^{0}C. Pseudo-first order rate constant for the formation and decay of *o*NQM were obtained by least-square separate fitting of experimental data to a single exponential function.

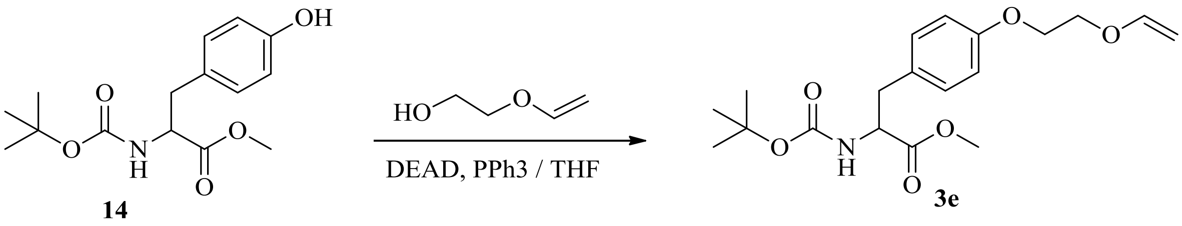
Fluorescent measurements: Fluorescent spectra of ca 10μM solution **2a** in doubly deionized water were recorded at λ_{ex} = 305 nm. The excitation source slit and the detector slit were set to 2 nm and 5 nm respectively. The fluorescence quantum yield was determined using 2-naphthol as the standard reference.[3] The fluorescent lifetime of **2a** was measured using LKS.60 spectrometer with 266 nm excitation.

Preparative Photolyses: A solution of **2** (0.3 mmol) and vinyl ether **3** (0.45 mmol) in 50% aqueous acetonitrile (300 mL) was irradiated with 16 fluorescent UV lamps (RPR-2537A^o) for 20 min. Photolysate was extracted with ethyl acetate, and dried over sodium sulfate. Solvents were removed in vacuum and residue purified by column chromatography (EtOAc – hexanes).

Analytical photolyses were performed by irradiating 0.1mM solution of *o*NQM **2** in 50% aqueous acetonitrile (3 mL) in the presence of alkenes **3a**, **8-12**, as well as **13**, with 300 nm lamps for 3 min (15% conversion) and 20 min (> 99% conversion).

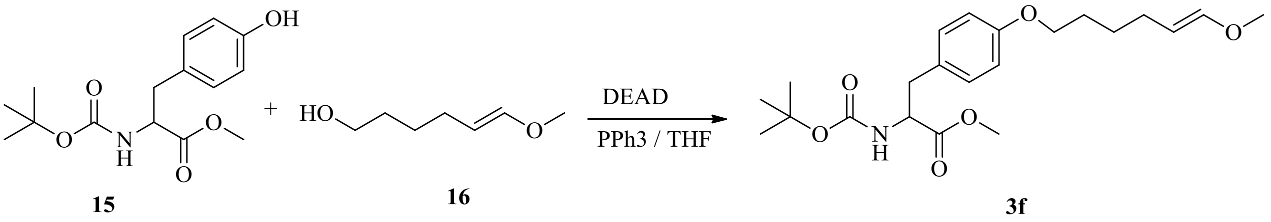
Materials: Ethyl vinyl ether, olefins **8-11**, 2-hydroxyethyl vinyl ether (**3b**), isopropenyl methyl ether (**3c**) and triethyleneglycol monomethyl ether were purchased from VWR; N-Boc-tyrosine methyl ester was purchased from sigma-Aldrich. Ethyl(3-hydroxy-2-naphthalenyl)methyl ether,[4] 3-hydroxy-2-naphthalenemethanol (**2a**),[4] phenyl vinyl ether **12**,[5] enamine **13**,[6] 1-ethoxy-1-heptene (**3d**),[7] 1-iodo-2-(2-(2-methoxyethoxy)ethoxy)ethane (**18**),[8] methyl 3,5-dihydroxy-2-naphthoate (**17**),[9] and 6-methoxyhex-5-en-1-ol (**16**)[10] were prepared according to literature procedures.

Synthesis of vinyloxy-derivatized tyrosine 3e:



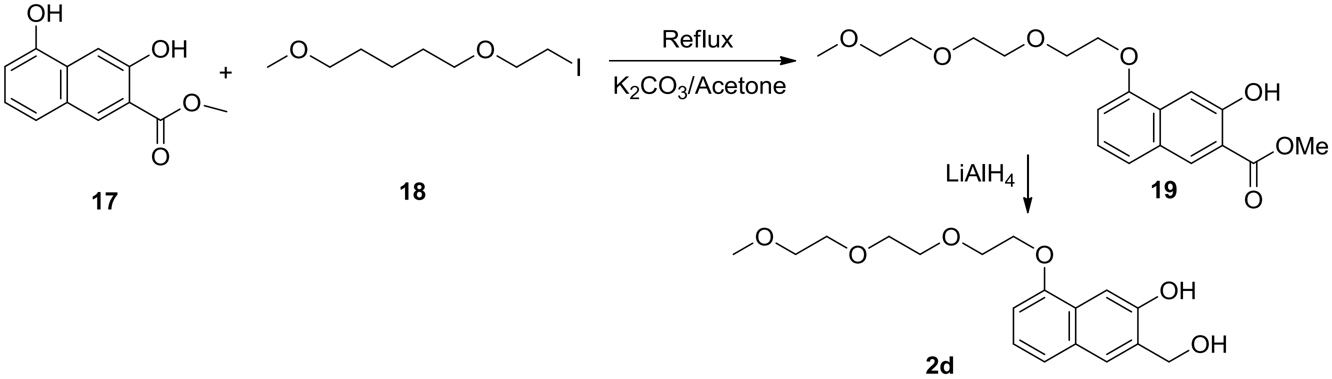
PPh$_3$ (1.1 g, 4.1 mmol) was slowly added to a solution of protected tyrosine **14** (1 g, 3.4 mmol) and 2-hydroxyethyl vinyl ether (**3b**, 329 mg, 3.7 mmol) in dry THF at 0^0C, followed by the addition of DEAD (710 mg, 4.1 mmol). The reaction mixture was allowed to reach room temperature and stirred for 4h. The reaction was quenched with water and the product was extracted with ethyl ether. The ethereal solution was washed with brine, dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The product was purified by column chromatography (5% EtOAc in CHCl$_3$) to yield 1.1 g of **3e** (87%). ^{1}H NMR: 7.02 (d, J = 4.8 Hz, 2H), 6.84 (d, J = 4.8 Hz, 2H), 6.50-6.55 (m, 1H), 4.98-4.50 (m, 1H), 4.50-4.55 (m, 1H), 4.21-4.25 (m, 1H), 4.17-4.18 (m, 2H), 4.00-4.10 (m, 3H), 3.69 (s, 3H), 2.96-3.07 (m, 2H), 1.41 (s, 9H). ^{13}C NMR: 28.49, 37.71, 52.29, 54.78, 66.65, 80.04, 87.26, 114.98, 128.72, 130.46, 151.83, 155.29, 157.93, 172.56. EI-MS *m/z*: 365 (0.1), 309 (1), 292 (2), 248 (45), 232 (1), 206 (6), 177 (100), 162 (1), 151 (1), 135 (6), 117 (3), 107 (90), 88 (10), 73 (40), 71 (35). FW calc. (C$_{19}$H$_{27}$NO$_6$): 365.1838, EI-HRMS: 365.1827

Synthesis of tyrosine appended vinyl ether 3f:



PPh_3 (1.81 g, 6.9 mmol) was added to a solution of **16** (trans isomer) (750 mg, 5.8 mmol) and **15** (1.88 g, 6.4 mmol) in dry THF at 0^0C. DEAD (1.2 mg, 1.1 mL, 6. 9 mmol) was slowly added to the reaction mixture under vigorous stirring. The reaction mixture was allowed to reach r.t and was stirred for 4h, quenched with water, and the product was extracted by ethyl ether. The ether solution was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The product was purified by column chromatography (5% ether in dichloromethane) to yield 1.65 g of the vinyl ether **3f** (70%).^{1}H NMR, *trans* isomer: 7.02 (d, J= 8.8Hz, 2H), 6.82 (d, J= 8.8Hz, 2H), 6.32 (d, J=12.8 Hz, 1H), 4.96 (d, J= 8Hz, 1H), 4.71-4.77 (m, 1H), 4.52-4.57 (m, 1H), 3.93 (t, J= 6Hz, 2H), 3.72 (s, 3H), 3.51 (s, 3H), 2.97-3.08 (m, 2H),1.98-2.03 (m, 2H), 2.75-1.82 (m, 2H), 1.48-1.55 (m, 2H) 1.43 (s, 9H); ^{13}C NMR, *trans* isomer: 27.37, 27.63, 28.53, 28.82, 37.68, 52.39, 54.76, 56.13, 68.00, 80.10, 102.82, 114.77, 127.95, 130.47, 147.54, 155.32, 158.41, 172.68. EI-MS *m/z*: 407 FW calc. ($C_{22}H_{33}NO_6$): 407.2308, EI-HRMS: 407.2298.

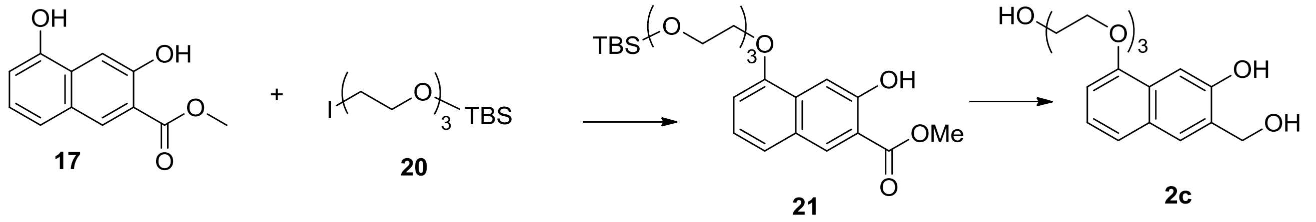
Synthesis of 3-(hydroxymethyl)-8-(PEG3-Me)naphthalen-2-ol (2d).



Methyl 3-hydroxy-5-(PEG3-Me)-2-naphthoate (**19**). 860 mg of potassium carbonate (6.2 mmol) was added to a solution of **17** (1.35 g, 6.2 mmol) in acetone (100 mL). Iodide **18** (1.70 g, 6.2 mmol) in 20 mL acetone was added dropwise, and reaction mixture was refluxed for 4 h. Most of the solvent was removed under reduced pressure and the residue was redissolved in ethyl ether (200 mL) . Organic layer was washed with brine, dried over anhydrous magnesium sulfate, and solvents were in vacuum. The residue was purified by column chromatography (EtOAc : hexanes 1:4) to yield 1.58g (70%) of **19** as yellow oil. ^{1}H NMR: 10.30 (s, 1H), 8.27 (s, 1H), 7.62 (s, 1H), 7.25 (d, J= 8.0 Hz, 1H), 7.08 (t, J= 8.0 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 4.14 (t, J = 4.8 Hz, 2H), 3.85-3.88 (m, 5H), 3.69-3.71 (m, 2H), 3.56-3.62 (m, 4H), 3.44-3.46 (m, 2H), 3.27 (s, 3H). ^{13}C NMR: 52.47, 57.93, 60.89, 68.67, 69.52, 69.63, 69.96, 70.87, 105.88 106.19, 113.25, 120.35, 122.70, 126.88, 129.43, 130.73, 152.16, 155.06, 169.21EI-MS *m/z*: 365 (17), 364 (100), 333(5), 287 (5), 257 (7), 243 (7), 218 (25), 200 (3), 186 (55), 147 (30), 129 (15), 113 (12), 103 (50), 73 (5). FW calc. ($C_{19}H_{24}O_7$): 364.1522, EI-HRMS: 364.1524.

3-(Hydroxymethyl)-8-(PEG3-Me)naphthalen-2-ol (**2d**). 1.2 equivalent of $LiAlH_4$ (0.187 g, 4.9 mmol) was added to a solution of **19** (1.50 g, 4.1 mmol) in dry THF (75 mL) at 0^0C. The reaction mixture was warmed to r.t., stirred for 4 h, and quenched with 5% HCl (20 mL). The reaction mixture was extracted with 75 mL of ethyl ether (3 times); the combined organic layer was washed with brine, dried over anhydrous magnesium sulfate, and solvents were removed under reduced pressure. The residue was purified by column chromatography (EtOAc) to yield 1.27g (92%) of **2b**. ^{1}H NMR: 7.57 (s, 1H), 7.40 (s, 1H), 7.19 (d, J= 8.0 Hz, 1H), 7.03 (t, J= 8.0 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 4.78 (s, 2H), 4.13 (m, 2H), 3.78 (m, 2H), 3.65-3.66 (m, 2H), 3.52-3.58 (m, 4H), 3.41-3.42 (m, 2H), 3.22 (s, 3H). ^{13}C NMR: 58.78, 63.02, 67.84, 69.56, 70.28, 70.41, 70.69, 71.70, 104.85 105.58, 120.32, 123.00, 126.57, 126.73, 128.79, 129.21, 153.12, 153.23. EI-MS *m/z*: 337 (20), 336 (100), 318 (7), 273 (3), 242 (7), 198 (8), 172 (20), 144 (15), 115 (23), 103 (17), 73 (5). FW calc. ($C_{18}H_{24}O_6$):336.1573, EI-HRMS found: 336.1575.

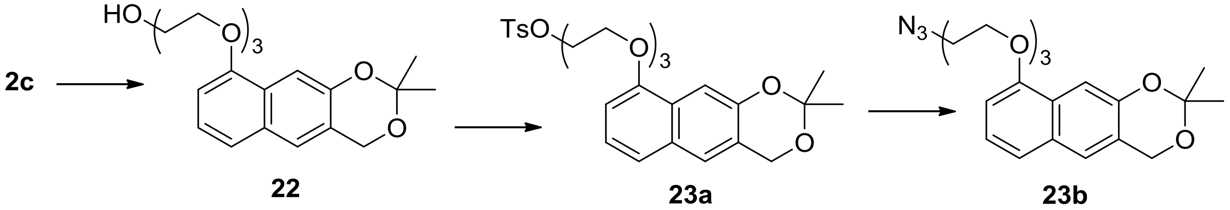
Preparation of *o*NQM precursor 2c:



Methyl 3-hydroxy-5-(PEG3-TBS)-2-naphthoate (**21**). Potassium carbonate (1.13 g, 8.17 mmol) was added to a solution of **17** (0.75 g, 3.4 mmol) in acetone (10 mL). followed by 1.4 g (3.75 mmol) of **20**.[11] The reaction mixture was refluxed for 4 h, solvent was removed under reduced pressure, and the residue was re-dissolved in ether. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was removed in vacuum. The residue was purified by column chromatography (EtOAc – hexanes 1:1) to yield 1.03 g (65%) of **15** as pale yellow oil.^{1}H NMR: 10.35 (s, 1H), 8.38 (s, 1H), 7.69 (s, 1H), 7.32 (d,8 Hz, 1H), 7.15 (t, 7.6 Hz, 1H), 6.77 (d, 8 Hz 1H), 4.21-4.23 (m, 2H), 3.93-3.97(m, 2H), 3.70-3.73 (m, 4H), 3.65-3.67 (m, 2H), 3.51-3.53 (m, 2H), 0.83 (s, 9H), 0.00 (s, 6H). ^{13}C NMR: -5.21, 18.41, 25.97, 52.58, 62.77, 68.06, 69.81, 70.89, 71.16, 72.78, 107.09, 107.31, 121.46, 123.80, 128.024, 130.61, 131.85, 153.33, 156.19, 170.36. EI-MS *m/z*: 464 (M+, 1), 449 (1), 417 (3), 409 (6), 407 (20), 376 (27), 375 (100), 331 (4), 287 (5), 259 (8), 257 (10), 243 (12), 213 (25), 185 (14), 169 (3), 157 (5), 129 (6), 101 (7), 88 (4), 73 (31). FW calc. ($C_{24}H_{36}O_7Si$): 464.2230, EI-HRMS found: 464.2240.

3-(Hydroxymethyl)-8-(PEG3)naphthalen-2-ol (**2c**). A solution of **21** (1 g, 2.15 mmol) in 20 mL of THF was added to a stirred suspension of $LiAlH_4$ (0.100g, 2.58 mmol) in dry THF (50 mL) at 0^0C. The reaction mixture was stirred at r.t. for 4h, quenched with 5% HCl, and extracted with ether. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and solvent was removed under reduced pressure. The residue was dissolved in 10 mL of acetonitrile and stirred with 2.5 equivalents of aq. HF (52% in water). 100 mL of EtOAc was added to the reaction mixture; the organic layer was washed with saturated aq. $NaHCO_3$, brine, dried over anhydrous magnesium sulfate, and solvents were removed under reduced pressure. The residue was purified by column chromatography (EtOAc) to yield 0.59 g (85%) of **2c** as pale yellow oil.^{1}H NMR (DMSO-d8): 9.80 (s, 1H), 7.73 (s, 1H), 7.41 (s, 1H), 7.32 (d,8 Hz, 1H), 7.12 (t, 7.6 Hz, 1H), 6.80 (d, 8 Hz 1H), 5.13 (t, J=5.6 Hz, 1H), 4.59-4.60 (m, 3H), 4.19-4.21 (m, 2H), 3.84-3.86 (m, 2H), 3.63-3.66 (m, 4H), 3.54-3.57 (m, 2H), 3.40-3.47 (m, 4H).^{13}C NMR (DMSO-d8): 58.60, 60.32, 67.55, 69.23, 69.95, 70.22, 72.46, 102.79, 104.77. 119.89, 122.60, 125.17, 125.24, 128.72, 132.05, 152.75. EI-MS *m/z*: 322(M$^+$,90), 304 (25), 259 (5), 242 (5), 216 (12), 198 (25), 172 (7), 144 (50), 115 (70), 89 (100), 85 (60), 71 (5). FW calc. ($C_{17}H_{22}O_6$): 322.1416, EI-HRMS: 322.1413.

Preparation of azide derivative 21b:

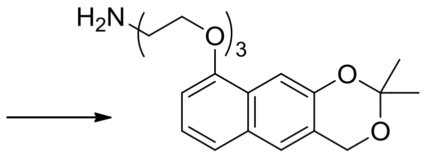


9-(PEG3)-2,2-dimethyl-4H-naphtho[2,3-d][1,3]dioxine (**22**). 2,2-Dimethoxypropane (0.480g, 4.65 mmol) and catalytic amount of TsOH were added to a solution of **2c** (0.5g, 1.55 mmol) in acetone (15 mL) and stirred overnight at r.t. Solvent was removed under reduced pressure and residue was dissolved in dichloromethane. The dichloromethane solution was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (55% EtOAc in hexanes) to yield 0.465 g (90%) of **22** as pale yellow oil. ^{1}H NMR: 7.65 (s, 1H), 7.41 (s, 1H), 7.29 (d,8 Hz, 1H), 7.18 (t, 7.6 Hz, 1H), 6.71 (d, 8 Hz 1H), 5.05 (s, 2H), 4.24-4.27 (m, 2H), 3.95-3.97 (m, 2H), 3.78-3.80 (m, 2H), 3.70-3.74 (m, 4H), 3.61-3.63 (m, 2H),1.59 (s, 6H).^{13}C NMR: 25.16, 61.38, 62.03, 68,04470.51, 70.70, 71.24, 72.75, 100.03, 104.91, 107.27, 120.14, 121.74, 123.29, 123.88, 126.44, 129.72, 149.65, 153.83. DIP- EI-MS *m/z*:362 (M+, 30), 304 (100), 273 (7), 259 (5), 216 (20), 198 (30), 174 (35), 172 (40), 144 (25), 115 (45), 85 (40), 87 (52), 73 (12). FW calc. ($C_{20}H_{26}O_6$): 362.1729, EI-HRMS: 362.1729.

9-(PEG3-Tos)-2,2-dimethyl-4H-naphtho[2,3-d][1,3]dioxine (**23a**). Triethylamine (0.2 g, 28μL, 2 mmol) and p-tosyl chloride (228 mg, 1.2 mmol) were added to a solution of **22** (0.362 g, 1 mmol) in dichloromethane (7 mL) and was stirred overnight at r.t. Solvent was removed under reduced pressure and the residue was re-dissolved in dichloromethane. The dichloromethane solution was washed with brine, dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography using (EtOAc-hexanes 1:4) to yield 0.423 mg (82%) of **23a** as pale yellow oil. ^{1}H NMR (CD_3CN): 7.77 (d, 8 Hz, 2H), 7.53 (s, 1H), 7.49 (s, 1H), 7.34-7.39 (m, 3H), 7.24 (t, 7.6 Hz, 1H), 6.82 (d, 8 Hz 1H), 5.05 (s, 2H), 4.21-4.24 (m, 2H), 4.11-4.12 (m, 2H), 3.88-3.90 (m, 2H), 3.63-3.64 (m, 4H), 3.53-3.55 (m, 2H),2.39 (s, 3H), 1.55 (s, 6H). ^{13}C NMR (CD_3CN): 20.95, 24.64, 61.07, 68.35, 68.62, 69.76, 70.30, 70.59, 70.75, 100.24, 105.37, 106.45, 120.13, 122.39, 123.85, 124.21, 126.32, 128.07, 129.87, 130.31, 133.33, 145.63, 149.99, 153.82. EI-MS *m/z*: 515(M^+, 3), 458 (15), 424 (12), 422 (12), 368 (40), 366 (42), 323 (7), 287 (10), 259 (50), 242 (32), 199 (50), 198 (40), 171 (25), 144 (25), 115 (60), 109 (90), 107 (100), 91 (25). FW calc. ($C_{27}H_{32}O_8S$): 516.1818, EI-HRMS found: 516.1812.

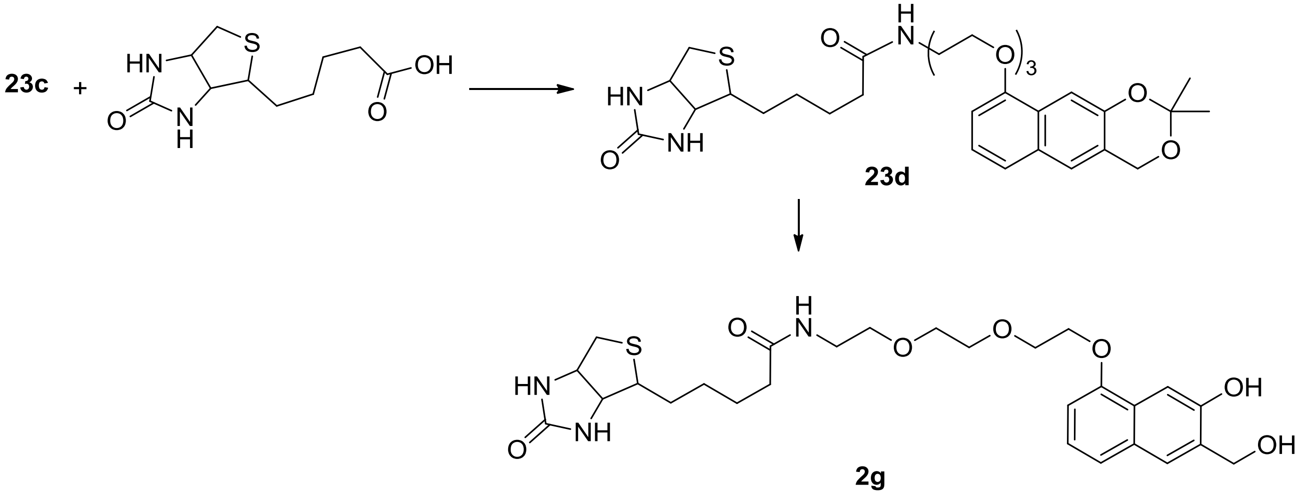
9-(PEG3-azide)-2,2-dimethyl-4H-naphtho[2,3-d][1,3]dioxine (**23b**). NaN_3 (0.06 g, 0.94 mmol) was added to a solution of **23a** (0.4 g, 0.78 mmol) in DMF (5 mL) and stirred at 60°C overnight. Solvent was removed under reduced pressure and the residue was dissolved in ether. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (EtOAc – hexanes, 4 : 6) to yield 0.240 mg (80%) of **23b** as pale yellow oil. ^{1}H NMR (CD_3CN): 7.58 (m, 2H), 7.35 (d,8 Hz, 1H), 7.24 (t, 7.6 Hz, 1H), 6.83 (d, 8 Hz 1H), 5.06 (s, 2H), 4.24-4.26 (m, 2H), 3.93-3.95 (m, 2H), 3.73-3.76 (m, 2H), 3.66-3.67 (m, 4H), 3.66-3.69 (m, 2H),1.57 (s, 6H). ^{13}C NMR (CD_3CN): 24.64, 50.93, 61.09, 68.36, 69.78, 69.94, 70.58, 70.90, 100.24, 105.36, 106.47, 120.13, 122.41, 123.86, 124.22128.01, 129.88, 150.02, 153.85. EI-MS *m/z*: 387(M^+, 30), 359 (40), 318 (7), 301 (100), 260 (15), 212 (50), 199 (50), 185 (35), 170 (35), 144 (38), 129 (36), 115 (77), 73 (92). FW calc. ($C_{20}H_{25}N_3O_5$): 387.1794, EI-HRMS found: 387.1787.

23b



23c

9-(PEG3-amine)-2,2-dimethyl-4H-naphtho[2,3-d][1,3]dioxine (**23c**). A solution of **23b** (0.2g, 0.52 mmol) in ether (30 mL) was added to a stirred suspension of $LiAlH_4$ (0.038g, 1 mmol) in dry ether at 0^0C, stirred for 4 h at r.t., quenched with 5% HCl, and extracted with ether. The ether solution was washed with brine, dried over anhydrous magnesium sulfate, and solvent was removed under reduced pressure to yield 152 mg (81%) of amine **23c** as yellow oil. ^{1}H NMR (CD_3CN): 7.51 (s, 1H), 7.49 (m, 2H), 7.33 (d,8 Hz, 1H), 7.23 (t, 7.6 Hz, 1H), 6.80 (d, 8 Hz 1H), 5.03 (s, 2H), 4.20-4.22 (m, 2H), 3.88-3.90 (m, 2H), 3.68-3.70 (m, 2H), 3.59-3.60 (m, 2H), 3.41-3.43 (m, 2H), 2.73 (br s, 2H), 2.10 (br s, 2H), 1.55 (s, 6H).^{13}C NMR (CD_3CN): 26.08, 41.61, 62.49, 69.76, 71.75, 72.21, 72.27, 101.66, 106.77, 107.90, 121.57, 123.79, 125.27, 125.64, 127.74, 131.28, 151.41, 156.24. EI-MS *m/z*: 361(M^+ , 100), 343 (7), 326 (5), 303 (75), 286 (18), 260 (7), 244 (12), 228 (15), 201 (37), 186 (60), 172 (37), 144 (26), 128 (26), 115 (70), 103 (6), 88 (12), 70 (35). FW calc. ($C_{20}H_{27}NO_5$): 361.1889, EI-HRMS found: 361.1889.



9-(PEG3-biotin)-2,2-dimethyl-4H-naphtho[2,3-d][1,3]dioxine (**23d**). 1.2 equivalents of EDC.HCl (54 mg, 0.28 mmol) and catalytic amount of DMAP were added to a solution of D-biotin (56 mg, 0.23 mmol) in 5 mL of dry DMF, followed by a dropwise addition of a solution of amine **23c** (90 mg, 0.25 mmol) in 2mL of DMF. The reaction mixture was stirred for 12 h at r.t. and DMF was removed in vacuum. The residue was re-dissolved in dichloromethane, washed with $NaHCO_3$ solution, brine, dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography using (10% MeOH in dichloromethane) to yield 0.12 g (83%) of **23d** as yellow oil. ^{1}H NMR (CD_3CN): 7.62 (s, 1H), 7.42 (s, 1H), 7.28 (t, 8Hz, 1H), 7.19 (t, 8 Hz, 1H), 6.92 (t, 8 Hz, 1H), 6.77 (s, 1H), 6.72 (d, 8 Hz 1H), 5.87 (s, 1H), 5.04 (s, 2H), 4.36-4.39 (m, 1H), 4.24-4.25 (m, 2H), 4.08-4.11 (m, 1H), 3.93-3.94 (m, 2H), 3.65-3.67 (m, 2H), 3.56-3.59 (m, 2H), 3.41-3.43 (m, 2H), 2.91-2.93 (m, 1H), 2.74-2.78 (m, 1H), 2.63-2.66 (m, 2H), 2.15 (t, 7.8 Hz, 2H), 1.55 (s, 6H), 1.53-1.63 (m, 4H), 1.27-1.30 (m, 2H).^{13}C NMR (CD_3CN): 25.21, 25.75, 28.26, 36.1839.40, 40.70, 60.39, 61.38, 61.91, 68.11, 70.03, 70.24, 70.43, 70.93, 100.10, 104.98, 107.14, 120.27, 121.85, 123.42, 123.97, 126.36, 129.72, 149.72, 153.76, 164.35, 173.53. FW calc. ($C_{30}H_{41}N_3O_7S$): 587.2665, EI-HRMS found: 587.2676.

3-(Hydroxymethyl)-8-(PEG3-biotin)naphthalen-2-ol (**2g**). 60 mg of Amberlyst resin was added to a solution of **23d** (100 mg, 0.17 mmol) in 5 mL of methanol and stirred for 2 h at r.t. The resin was removed by filtration through cotton plug and the methanol solution was passed through a short silica gel column to yield 93 mg (95%) of pure **2g** as yellow oil. ^{1}H NMR (Methanol-d4): 7.90 (t, 8 Hz, 1H), 7.73 (s, 1H), 7.52 (s, 1H), 7.32 (d, 8Hz, 1H), 7.14 (t, 8 Hz, 1H), 6.75 (d, 8 Hz 1H), 4.87 (s, 2H), 4.30-4.33 (m, 1H), 4.20-4.22 (m, 2H), 4.09-4.07 (m, 1H), 3.92-3.93 (m, 1H), 3.73-3.74 (m, 2H), 3.62-3.64 (m, 2H), 3.52-3.55 (m, 2H), 3.32-3.36 (m, 2H), 2.96-2.99 (m, 1H), 2.74-2.79 (m, 1H), 2.60-2.63 (m, 2H), 2.12 (t, 7.8 Hz, 2H), 1.42-1.62 (m, 4H), 1.23-1.32 (m, 2H).^{13}C NMR (Methanol-d4): 25.60, 28.23, 28.49, 35.58, 39.23, 39.88, 55.72, 60.21, 62.10, 67.89, 69.48, 69.89, 70.14, 70.82, 96.13, 103.55, 105.06, 120.30, 122.84, 126.27, 126.43, 129.68, 130.74, 153.23, 153.40, 164.82, 174.97. FW calc. ($C_{27}H_{37}N_3O_7S$): 547.2352, EI-HRMS found: 547.2349.

2-Ethoxy-3,4-dihydro-*2H*-benzo[*g*]chromene (**5a**). The adduct **5a** was isolated from photolysate in 87% yield by chromatography (EtOAc : hexanes, 1:4) as colorless oil. ^{1}H NMR: 7.86 (d, 7.6 Hz, 1H), 7.78 (d, 7.6Hz, 1H), 7.66 (d, 8.8Hz, 1H), 7.48-7.52(m, 1H), 7.34-7.38 (m, 1H), 7.08 (d, 8.8Hz, 1H), 5.38 (t, 2.8Hz, 1H), 3.90-3.94 (m, 1H), 3.67-3.71 (m, 1H), 3.08-3.15 (m, 2H), 2.20-2.26 (m, 1H), 2.11-.15 (m, 1H), 1.20 (t, 7. Hz, 3H).; ^{13}C NMR: 15.38, 17.69, 26.63, 64.02, 97.06, 114.45, 119.31, 122.22, 123.54, 126.47, 127.93, 128.60, 129.15, 133.70, 149.85; EI-MS *m/z*: 229(M^+ +1), 228(M+), 183, 182(base peak), 181, 154,153,152, 128, 115, 102, 85, 72, 57, 55, 44; FW calc. ($C_{15}H_{16}O_2$): 228.1150, EI-HRMS found 228.1142.

2-((3,4-Dihydro-*2H*-benzo[*g*]chromen-2-yl)oxy)ethanol (**5b**). The adduct **5b** was isolated from photolysate in 89% yield by chromatography (EtOAc : hexanes, 1:9) as colorless oil. ^{1}H NMR (CD_3CN): 7.70-7.78 (m, 2H), 7.62 (s, 1H), 7.37-7.41 (m, 1H), 7.31-7.34 (m, 1H), 7.24 (s, 1H), 5.42 (t, 2.8Hz, 1H), 3.84-3.89 (m, 1H), 3.70-3.75 (m, 1H), 3.53-3.66 (m, 2H), 3.11 3.20(m, 1H), 2.87-2.93 (m, 1H), 2.74 (t, J = 6Hz, 1H) 2.02-2.16 (m, 2H); ^{13}C NMR (100 MHz, CD_3CN): 20.85, 26.65, 61.25, 70.11, 98.08, 111.66, 123.92, 125.37, 125.80, 126.44, 127.26, 127.87, 129.25, 133.76, 151.31; EI-MS *m/z*: 245 (10), 244 (80), 183 (40), 182 (70), 181 (100), 171 (10), 105 (10), 158 (70), 141 (75), 128 (80), 115 (20), 100 (20), 87 (75), 72 (25), 63 (15), 51 (10), 45 (30). FW calc. ($C_{15}H_{16}O_3$): 244.1099, EI-HRMS found: 244.1102.

2-Methoxy-2-methyl-3,4-dihydro-*2H*-benzo[*g*]chromene (**5c**). The adduct **5c** was isolated from photolysate in 85% yield by chromatography (EtOAc : hexanes, 1:9) as colorless oil. ^{1}H NMR (CD_3CN): 7.69 (m, 2H), 7.55 (s, 1H), 7.69 (d, 8.3Hz, 1H), 7.36 (m, 1H), 7.29 (m, 1H), 7.23 (s, 1H), 3.28 (m, 3H), 3.16-3.25 (m, 1H), 2.82-2.88 (m, 1H), 2.12-2.12 (m, 1H), 1.91-1.97 (m, 1H), 1.59 (t, 3H); ^{13}C NMR (100 MHz, CD_3CN): 21.79, 21.75, 31.90, 48.66, 99.03, 111.68, 117.60, 123.87, 125.10, 125.71, 126.43, 127.23, 127.81, 129.26, 133.69, 151.82; EI-MS *m/z*: 229(M^+ +1), 229(5), 228 (27), 213 (6), 197 (25), 196 (48), 195 (40), 181 (100), 168 (10), 157 (250, 150 (20), 141 (15), 128 (55), 115 (15), 102 (10), 90 (12), 76 (12), 63 (12), 51 (12), 43 (50). FW calc. ($C_{15}H_{16}O_2$): 228.1150, EI-HRMS found: 228.1146.

2-Ethoxy-3-butyl-3,4-dihydro-*2H*-benzo[*g*]chromene (**5d**). The adduct **5d** (mixture of diastereomers) was isolated from photolysate in 88% yield by chromatography (EtOAc : hexanes, 1:9) as colorless oil. ^{1}H NMR (CD_3CN): **Diastereomer 1** (Major): 7.70-7.75 (m, 2H), 7.59 (s, 1H), 7.36-7.40 (m, 1H), 7.30-7.33 (m, 1H), 7.22 (s, 1H), 5.11 (d, J= 3.2 Hz, 1H), 3.82-3.94(m, 1H), 3.66-3.76(m, 1H), 3.18-3.23 (m, 1H), 2.68-2.72 (m, 1H) 2.00-2.03 (m, 1H); 1.21-1.48(m, 8H),1.16 (t, J = 6.8 Hz, 3H), 0.88 (t, J = 6.8 Hz, 3H). **Diastereomer 2** (Minor): 7.70-7.75 (m, 2H), 7.59 (s, 1H), 7.36-7.40 (m, 1H), 7.30-7.33 (m, 1H), 7.22 (s, 1H), 5.22 (d, J= 3.2 Hz, 1H), 3.82-3.94(m, 1H), 3.66-3.76(m, 1H), 2.87-2.93 (m, 1H), 2.74-2.83 (m, 2H) 2.00-2.03 (m, 1H); 1.21-1.48(m, 8H),1.13 (t, J = 6.8 Hz, 3H), 0.94 (t, J = 6.8 Hz, 3H).^{13}C NMR (CD_3CN): **Diastereomer 1** (Major): 13.62, 14.92, 22.59, 26.53, 26.65, 30.43, 32.96, 36.10, 63.97, 101.38, 111.39, 123.87, 124.68,125.79, 126.49, 127.28, 128.36, 129.47, 133.88, 151.28 **Diastereomer 2** (Minor): 13.62, 14.92, 22.59, 26.53, 26.65, 30.43, 32.96, 36.10, 63.97, 101.38, 111.39, 123.86, 125.53, 125.78, 126.44,127.32, 127.90, 129.29, 133.87, 151.27. EI-MS (*m/z)*: **Diastereomer 1** (Major): 299 (20), 298 (100), 254 (10), 239 (80), 209 (10), 195 (40), 181 (75), 169 (15), 157 (30), 141 (20), 128 (35), 115 (10), 95 (15), 57 (10), 41 (17). **Diastereomer 2** (Minor): 299 (20), 298 (100), 240 (15), 239 (75), 195 (30), 181 (70), 157 (25), 141 (20), 128 (35), 95 (10), 55 (10), 43 (12). FW calc. ($C_{20}H_{26}O_2$): 298.1933, EI-HRMS: 298.1934

3,3-Dimethyl-3,4-dihydro-2H-benzo[g]chromen-2-ol (**5f**) was isolated from photolysate in 85% yield by chromatography (EtOAc : hexanes, 1:9) as colorless oil. ^{1}H NMR: 7.67-7.71 (m, 2H), 7.54 (s, 1H), 7.35-7.38 (m, 1H), 7.29-7.34 (m, 1H), 7.23 (s, 1H), 5.17(d. J = 4Hz, 1H),3.06 3.10(m, 1H), 2.95 (d, J = 4Hz, 1H), 2.61-2.65 (m, 1H), 1.14 (s, 1H) 1.03 (s, 3H); ^{13}C NMR: 23.98, 24.39, 32.84, 35.57, 98.97, 111.62, 123.79, 123.85, 125.72, 126.61, 127.21, 128.35, 129.42, 133.74, 149.98; EI-MS *m/z*: 229 (M^+ +1), 228 (50), 195 (10), 183 (10), 158 (25), 157 (100), 128 (35), 115 (10), 71 (10), 43 (12). FW calc. ($C_{15}H_{16}O_2$): 228.1150, EI-HRMS found: 228.1145.

Tyrosine adduct 5g was isolated from photolysate in 87% yield by chromatography (EtOAc : hexanes, 1 : 2) as colorless oil. ^{1}H NMR (CD_3CN): 7.72 (d, 8 Hz, 1H), 7.69 (d, 8 Hz, 1H), 7.59 (m, 1H), 7.37 (t, 6 Hz,1H), 7.29 (t, 6 Hz, 1H), 7.21 (s, 1H), 7.17 (d, 7.2 Hz, 2H), 6.73 (d, 7.2 Hz, 2H), 5.44 (t, 2.4Hz, 1H), 4.26-4.32 (m, 1H), 4.03-4.11 (m, 3H), 3.95-4.00 (m, 1H) 3.05-3.12 (m, 1H), 2.96-3.00 (m, 1H), 2.78-2.90 (m, 1H), 2.01-2.11 (m, 2H), 1.34 (s, 9H); ^{13}C NMR (CD_3CN): 20.67, 26.49, 27.66, 36.57, 51.82, 55.25, 66.78, 67.56, 97.85, 111.67, EI-MS *m/z*: 521 (M+, 7), 466 (3), 447 (24), 421 (5), 404 (8), 362 (3), 333 (70), 227 (82), 183 (100), 155 (15), 153 (12), 128 (12), 107 (37), 91 (7), 78 (5). FW calc. ($C_{30}H_{35}NO_7$): 521.2414, EI-HRMS found: 521.2408.

Tyrosine adduct 5h (a mixture of diastereomeres) was isolated from photolysate in 89% yield by chromatography (EtOAc : hexanes, 1 : 2) as colorless oil. ^{1}H NMR: **Diastereomer 1** (major): 7.67-7.70 (m, 2H), 7.53 (s, 1H), 7.35 (t, J=7.6 Hz, 1H), 7.29(t, J=7.6 Hz, 1H), 7.25 (d, J=4.8Hz, 1H), 6.96 (d, J=8Hz, 2H), 6.73 (d, J=8Hz,2H), 5.00-5.02 (m, 1H), 4.97 (d, J=2.4Hz, 1H), 4.51-4.56(m, 1H), 3.71(s, 3H), 3.62-3.65(t, , J=6.4Hz, 2H), 3.52(s, 3H), 3.24-3.29(m, 1H), 2.93-3.05 (m, 2H), 2.64-2.69(m, 1H), 2.03-2.16(m, 1H), 1.42 (s, 9H), 1.25-1.63 (m, 6H). **Diastereomer 2** (minor): 7.67-7.70 (m, 2H), 7.52 (s, 1H), 7.35 (t, J=7.6 Hz, 1H), 7.29(t, J=7.6 Hz, 1H), 7.25 (d, J=4.8Hz, 1H), 6.96 (d, J=8Hz, 2H), 6.73 (d, J=8Hz,2H), 5.05 (d, J=2.4Hz, 1H),5.00-5.02 (m, 1H), 4.51-4.56(m, 1H), 3.71(s, 3H), 3.68-3.72, (t, J=6.4Hz, 2H), 3.48(s, 3H), 2.93-3.05 (m, 2H), 2.86-2.94 (m, 1H), 2.68-2.72 (m, 1H) 2.86-2.88 (m, 1H); 2.64-2.69(m, 1H), 2.03-2.16(m, 1H), 1.42 (s, 9H), 1.25-1.63 (m, 6H). ^{13}C NMR: **Diastereomer 1** (major): 172.81, 155.47, 155.29, 150.52, 133.7, 130.61, 129.42, 128.47, 127.90, 127.20, 126.59, 125.70, 123.87, 123.77, 115.71, 111.85, 102.11, 80.34, 62.98, 55.95, 54.83, 52.46, 37.78, 35.89, 32.92, 30.35, 28.53, 26.59, 23.46. **Diastereomer 2** (minor): 172.81, 155.47, 155.29, 150.58, 133.7, 130.61, 129.26, 128.47, 127.83, 127.29, 126.54, 125.67, 124.74, 123.84, 115.71, 111.91, 100.83, 80.34, 63.04, 56.09, 54.83, 52.46, 37.78, 36.59, 33.03, 31.35, 28.53, 27.40, 23.29. FW calc. ($C_{33}H_{41}NO_7$): 563.2883, EI-HRMS found: 563.2898.

2-Ethoxy-9-(PEG3-Me)-3,4-dihydro-*2H*-benzo[*g*]chromene (**5i**) was isolated from photolysate in 86% yield by chromatography (EtOAc : hexanes, 1 : 2) as colorless oil. ^{1}H NMR (CD_3CN): 7.56 (s, 1H), 7.52 (s, 1H), 7.32 (d, J= 8 Hz, 1H), 7.20 (t, J= 8 Hz, 1H), 6.8 (d, J= 7.2 Hz, 1H), 5.38 (t, 2.8Hz, 1H), 4.25 (m, 2H), 3.83-3.92 (m, 3H), 3.65-3.71 (m, 3H), 3.57-3.63 (m, 4H), 3.45-3.48 (m, 2H),3.29 (s, 3H) 3.05-3.15 (m, 1H), 2.82-2.92 (m, 1H), 2.05 (m, 2H), 1.16 (t, 7.2 Hz, 3H); ^{13}C NMR (CD_3CN): 14.84, 20.87, 26.76, 58.17, 63.74, 64, 69.68, 70.35, 70.49, 70.81, 71.91, 97.58, 104.82, 106.36, 119.78, 123.89, 125.63, 125.86, 127.71, 129.15, 130.21, 151.17, 153.71;EI-MS *m/z*: 391 (15), 390 (50), 345 (20), 344 (100), 314 (5), 285 (10), 244 (20), 198 (35), 197 (32), 169 (15), 147 (17), 115 (13), 103 (15). FW calc. ($C_{22}H_{30}O_6$): 390.2042, EI-HRMS found: 390.2048.

Biological Methods

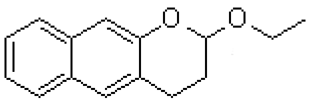
Materials: MTT (3-4,5-dimethylthiazole-2,5-diphenyl tetrazolium bromide) dye was purchased from Calbiochem (USA). All other chemical reagents were of analytical grade. A stock solution of **2c** in DMF was employed for biological experiments. Final concentrations of DMF in the media never exceeded 0.56% to avoid toxic effects.

Cell culture conditions: Human Jurkat cells (Clone E6−1; ATCC) were cultured in RPMI 1640 medium (ATCC) with l-glutamine (2 mM), adjusted to contain sodium bicarbonate (1.5 g/L), glucose (4.5 g/L), HEPES (10 mM), and sodium pyruvate (1 mM) and supplemented with penicillin (100 u/ml)/streptomycin (100 µg/mL; Mediatech) and fetal bovine serum (FBS, 10%; Hyclone). Cells were maintained in a humid 5% CO_2 atmosphere at 37 °C.

Evaluation of cell viability after photoactivation: Jurkat cells were harvested and washed with Dulbelco's PBS, pH 7.4 (DPBS) and transferred to round-bottom tubes (1×10^6 cells/sample). Cells in the absence or presence of compound **2c** (30 µM) were exposed to light (350 nm) for 2 mins. Cells were washed twice with DPBS (500 µl) and transferred to a 96-well plate (100,000 cells/well) in fresh culture medium (100 µl/well) and incubated for 5 h. Next, the culture medium was removed and the purple insoluble formazan formed was dissolved in 2-propanol (100 µl). The OD at 560 nm was measured using a microplate reader (BMG Labtech). Data points were collected in triplicate and expressed as normalized values for control cells (100%).

Table 1. Effect of UV irradiation of compound **2c** on cell viability

Cell treatment	**% Viable cells (Mean ± SD)**
	2 min exposure
Control cells	100.0 ± 5.1
Cells + UV	90.5 ± 3.5
Cells + **2c**	96.7 ± 5.7
Cells + **2c** + UV	93.9 ± 6.8



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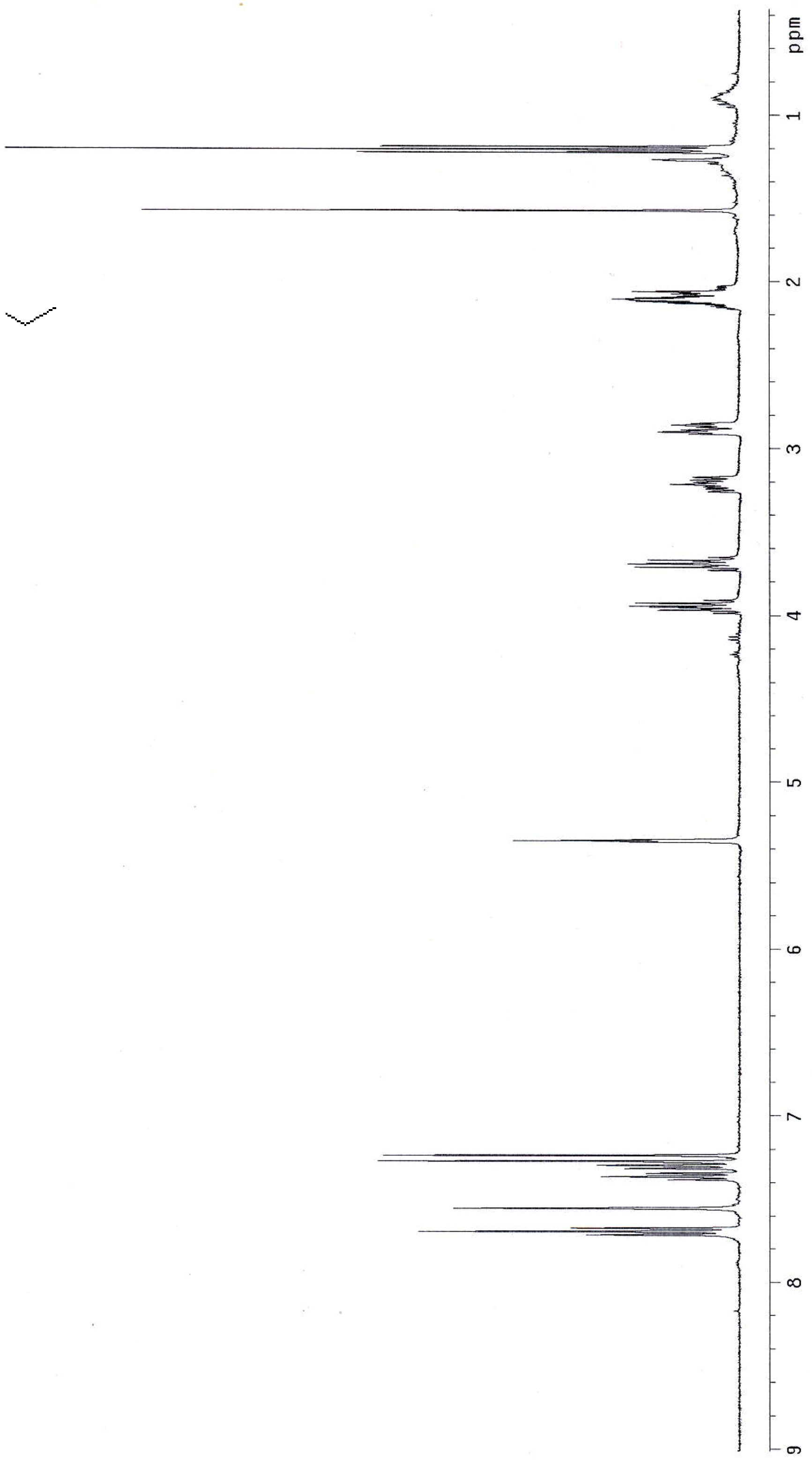

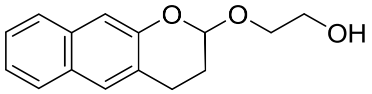

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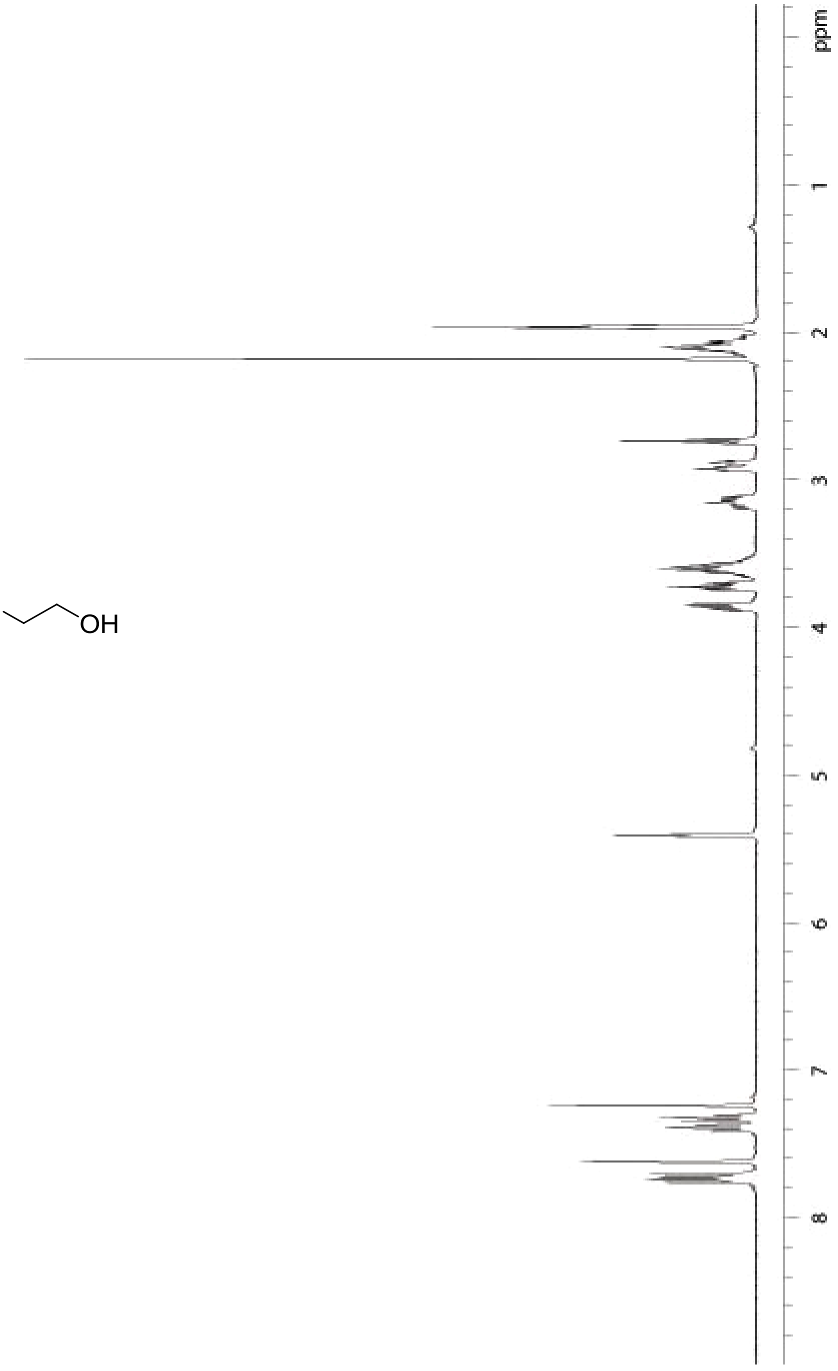

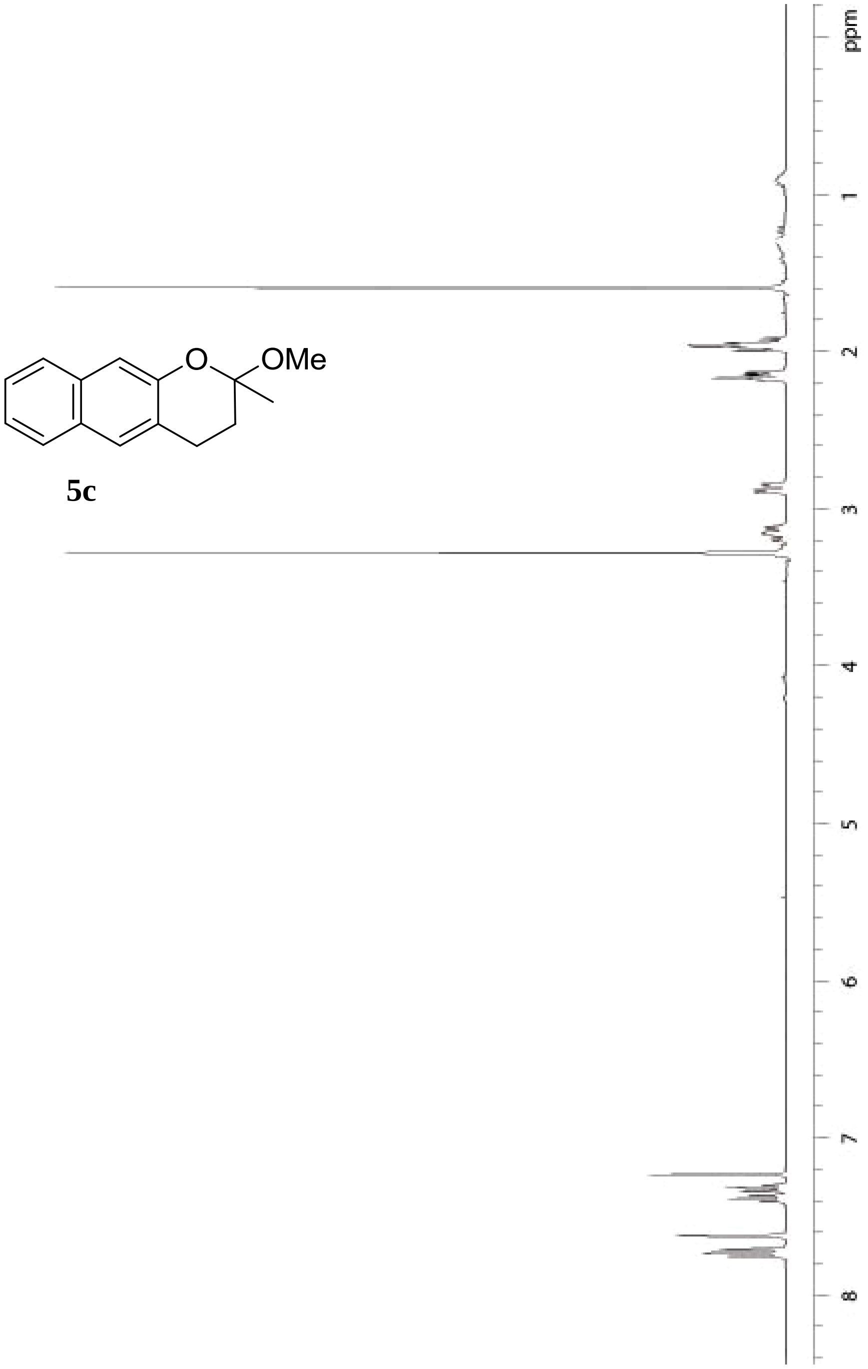

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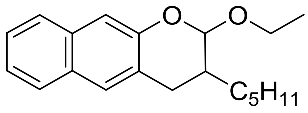

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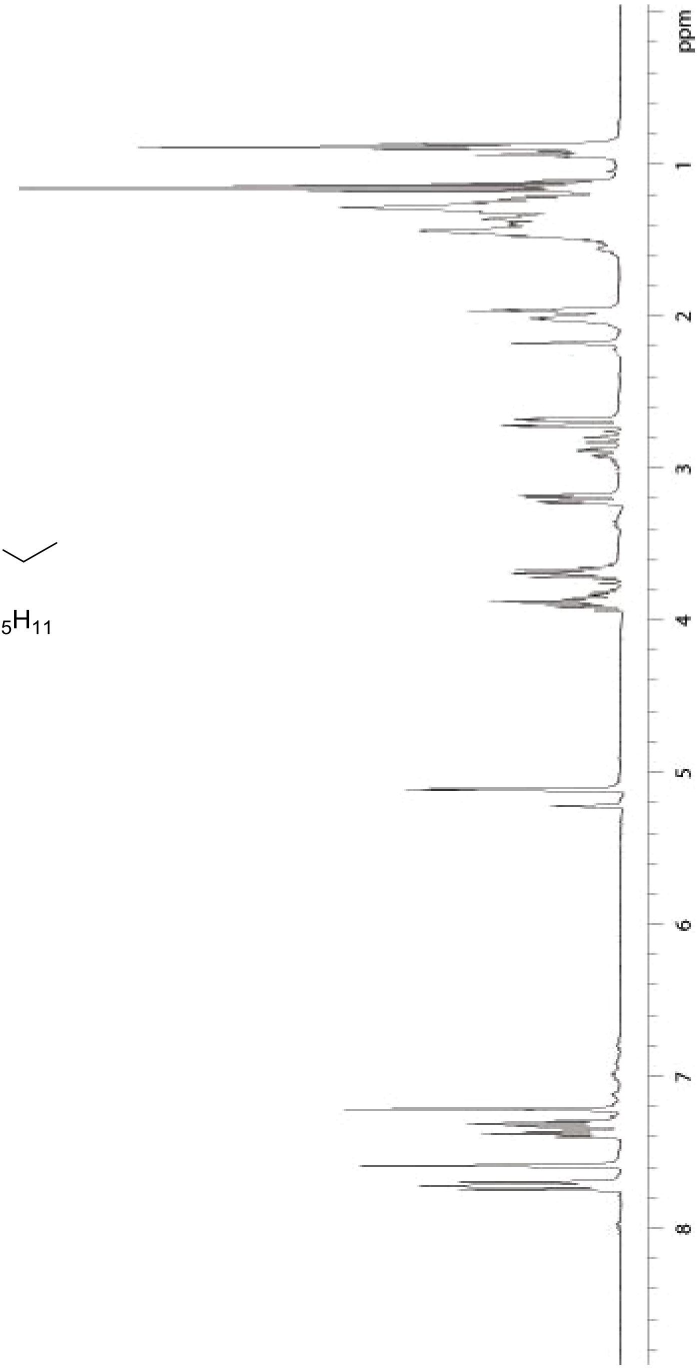

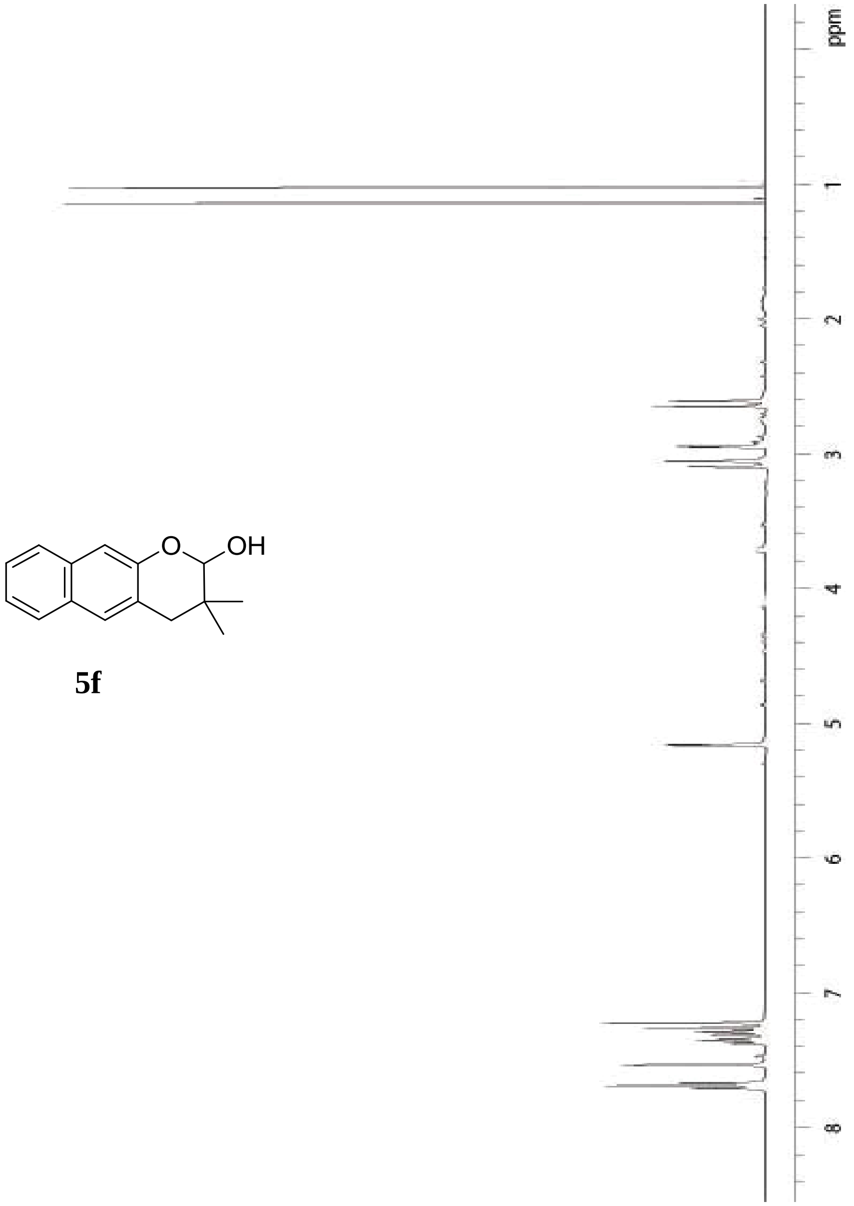

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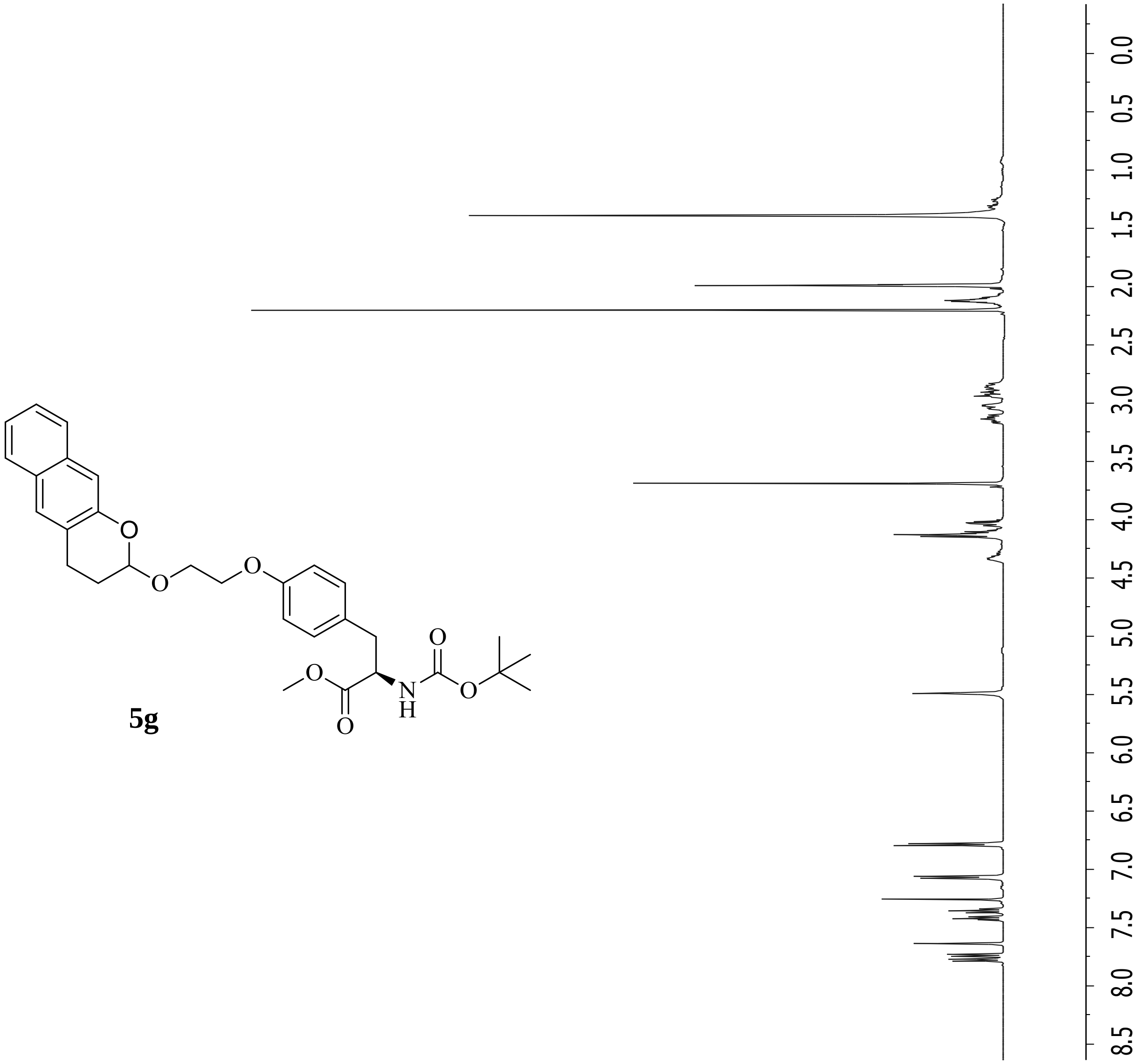

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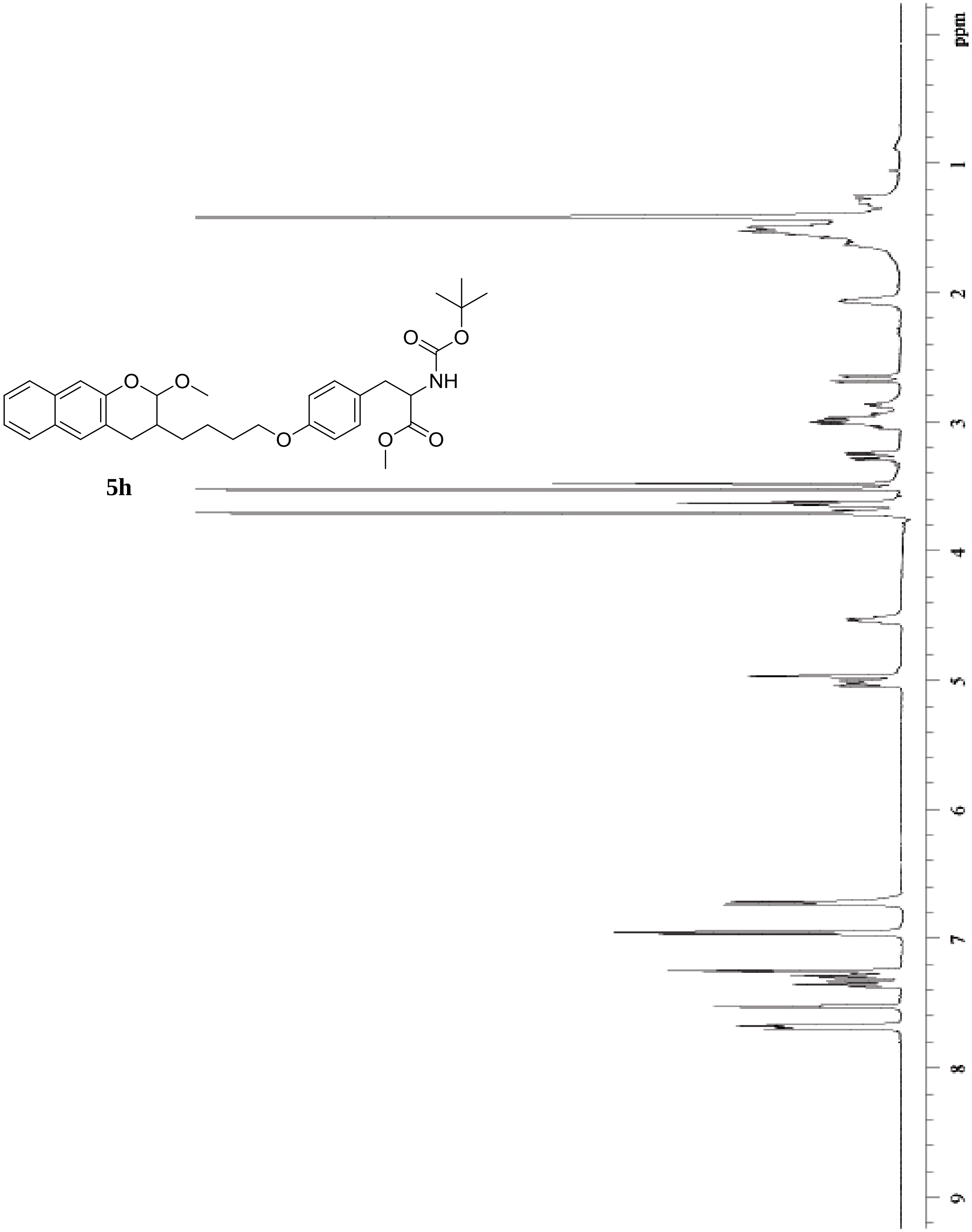

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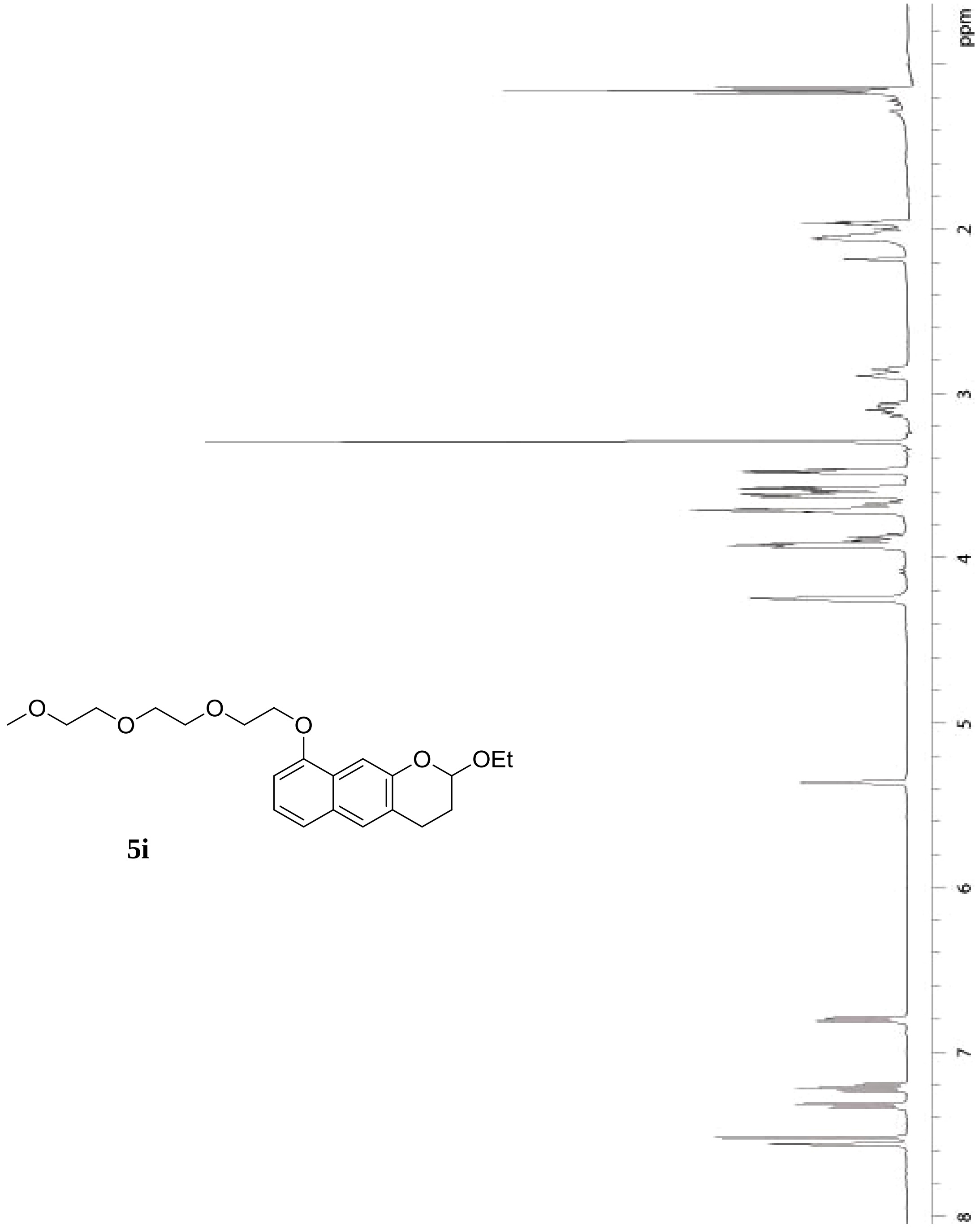

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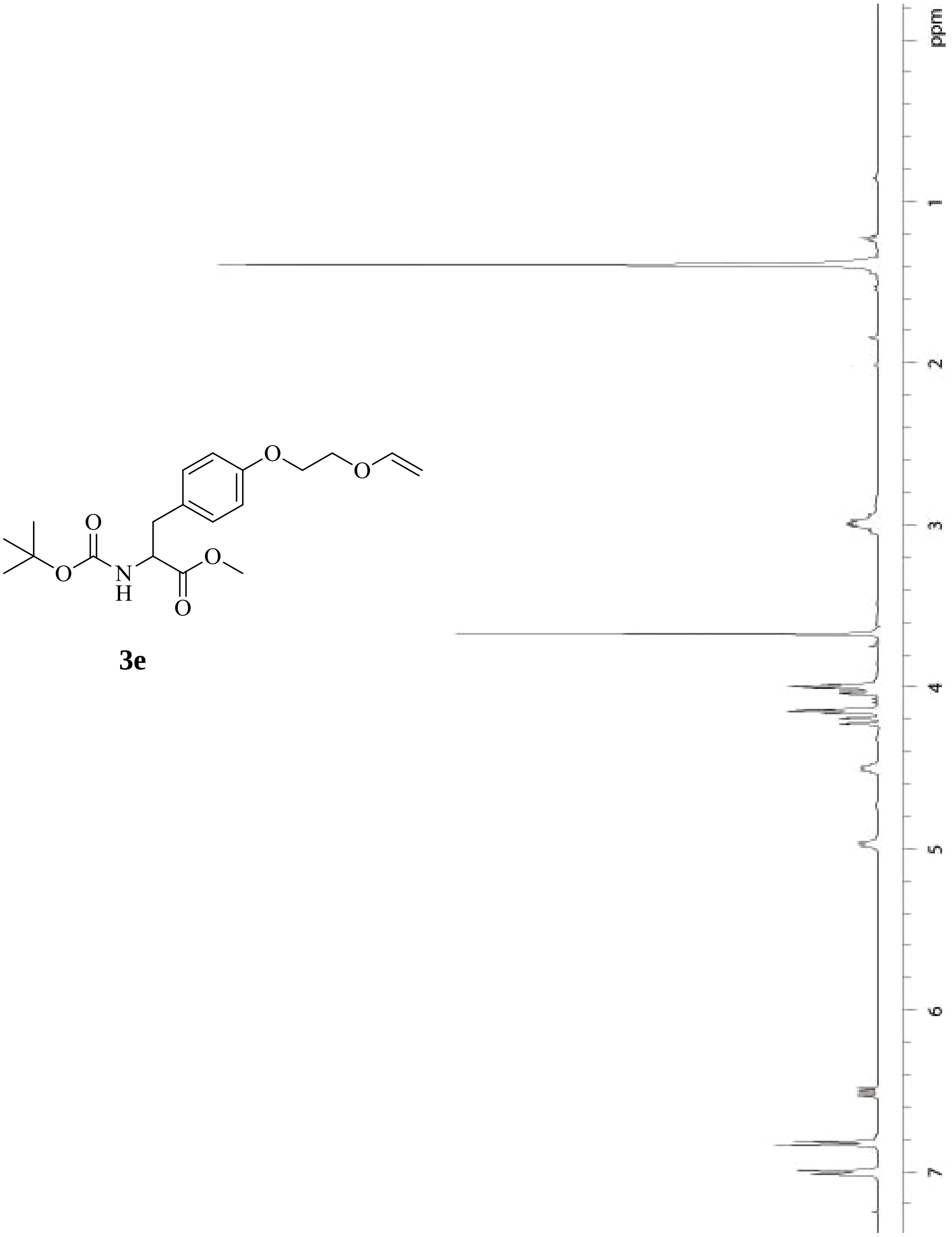

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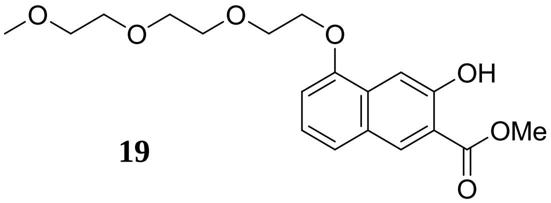

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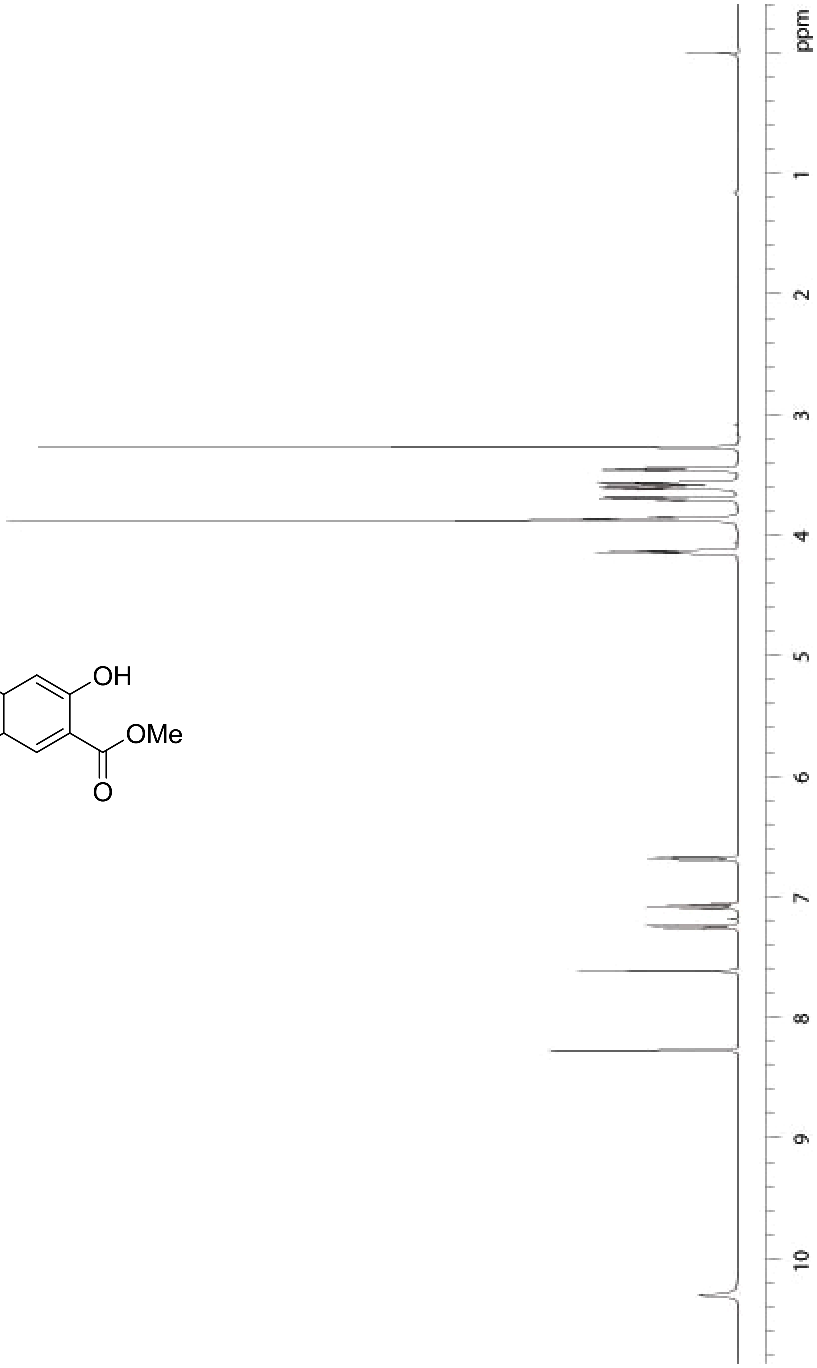

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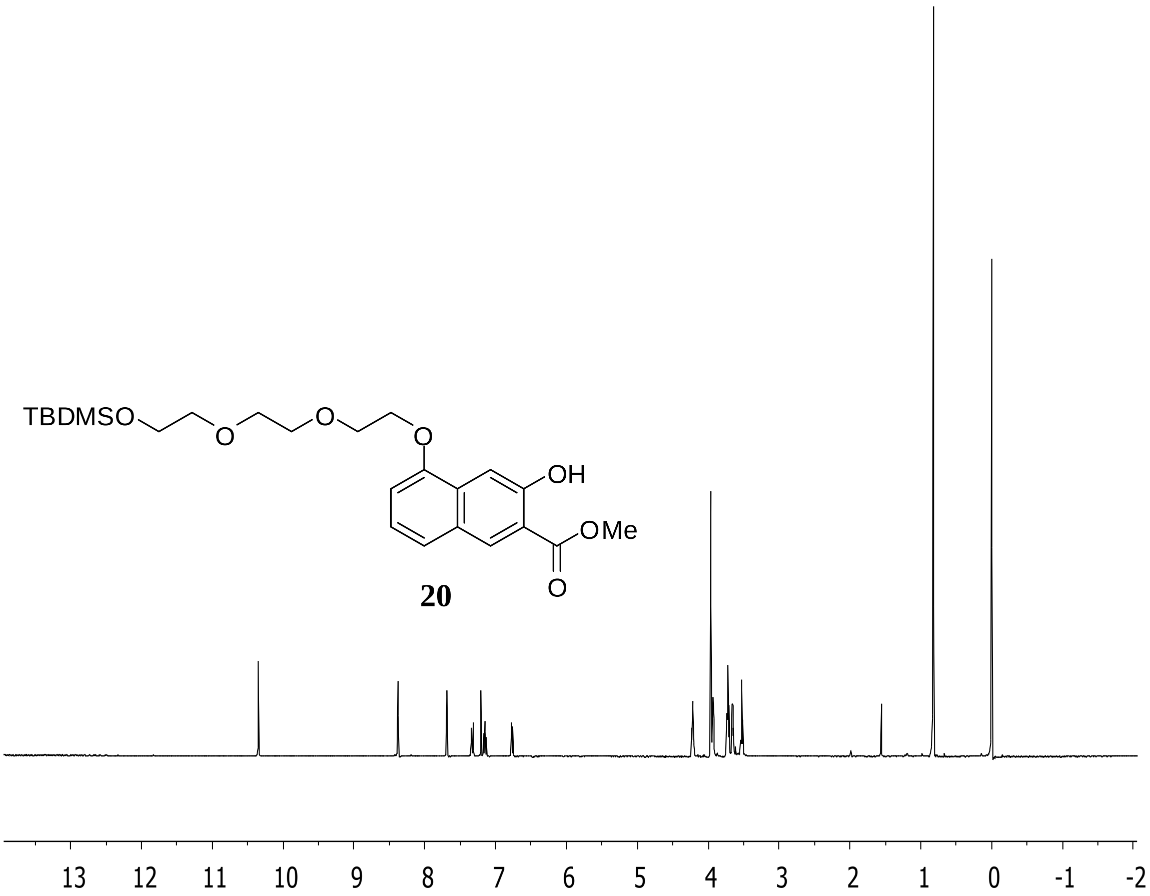

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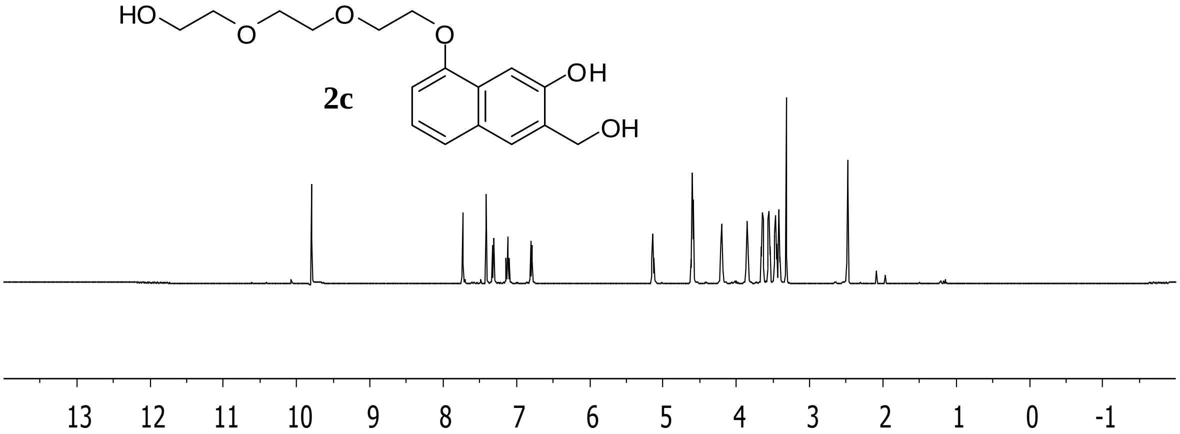

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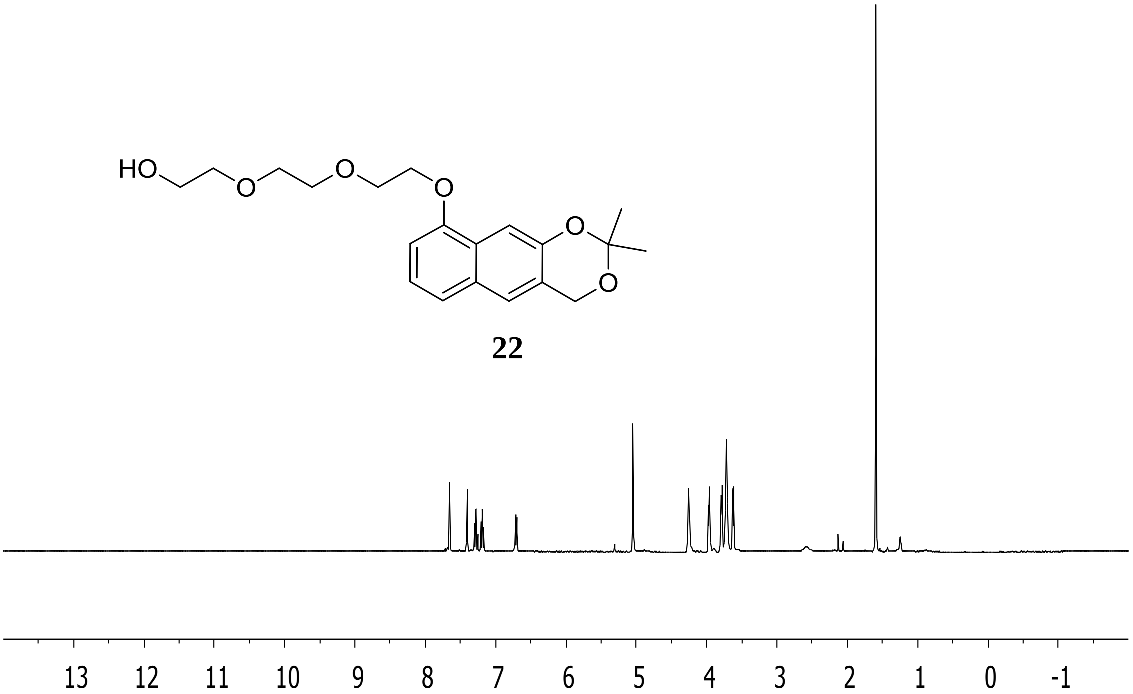

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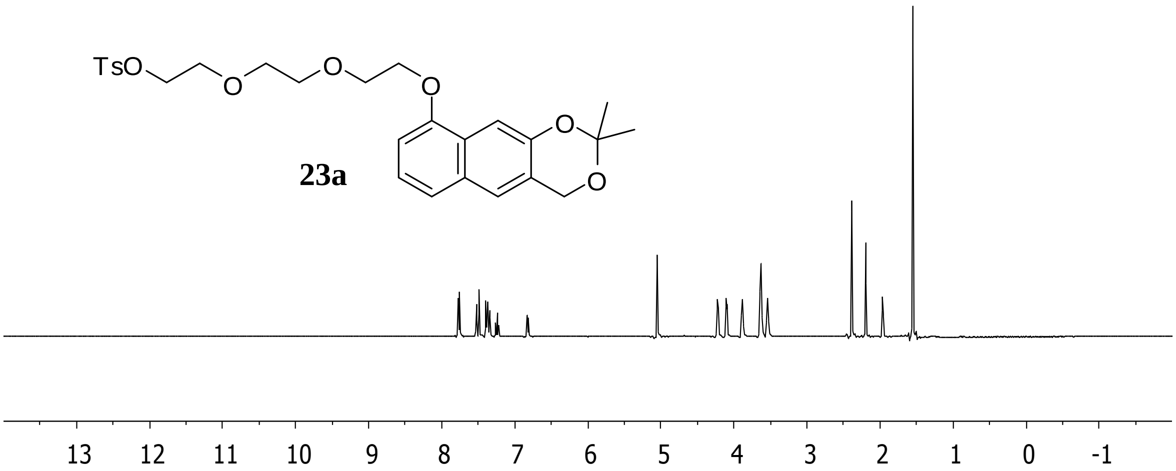

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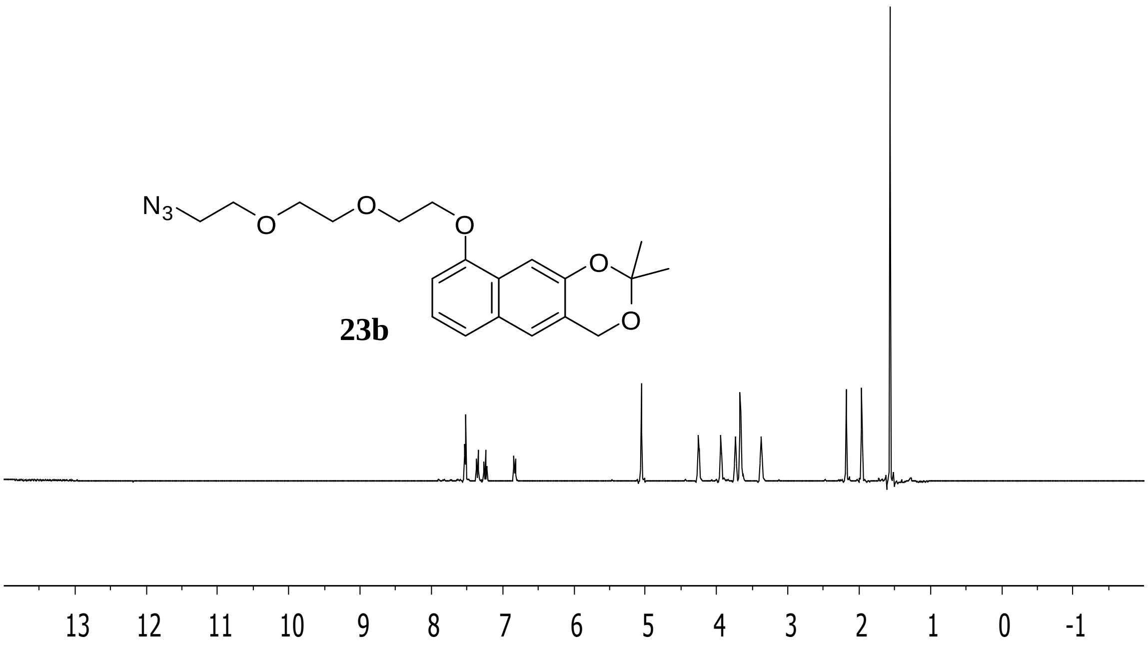

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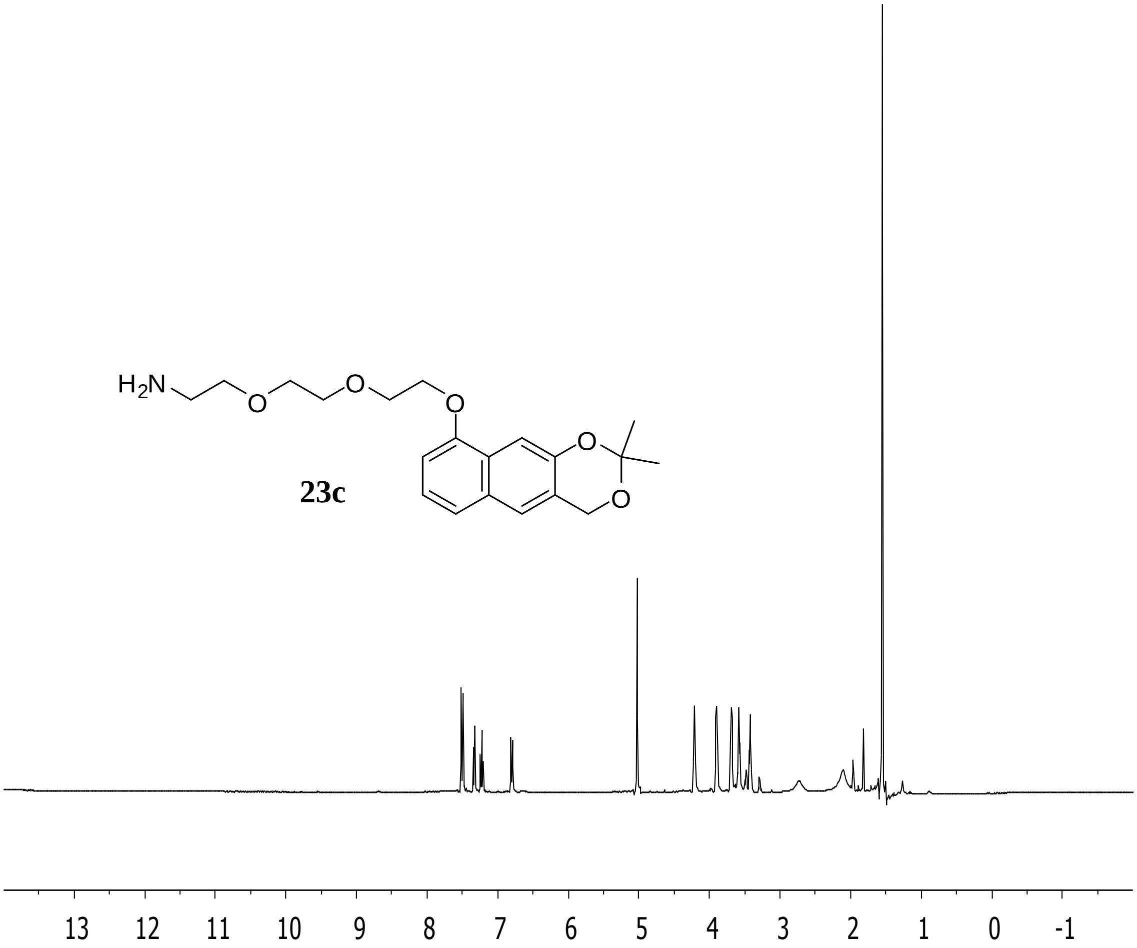

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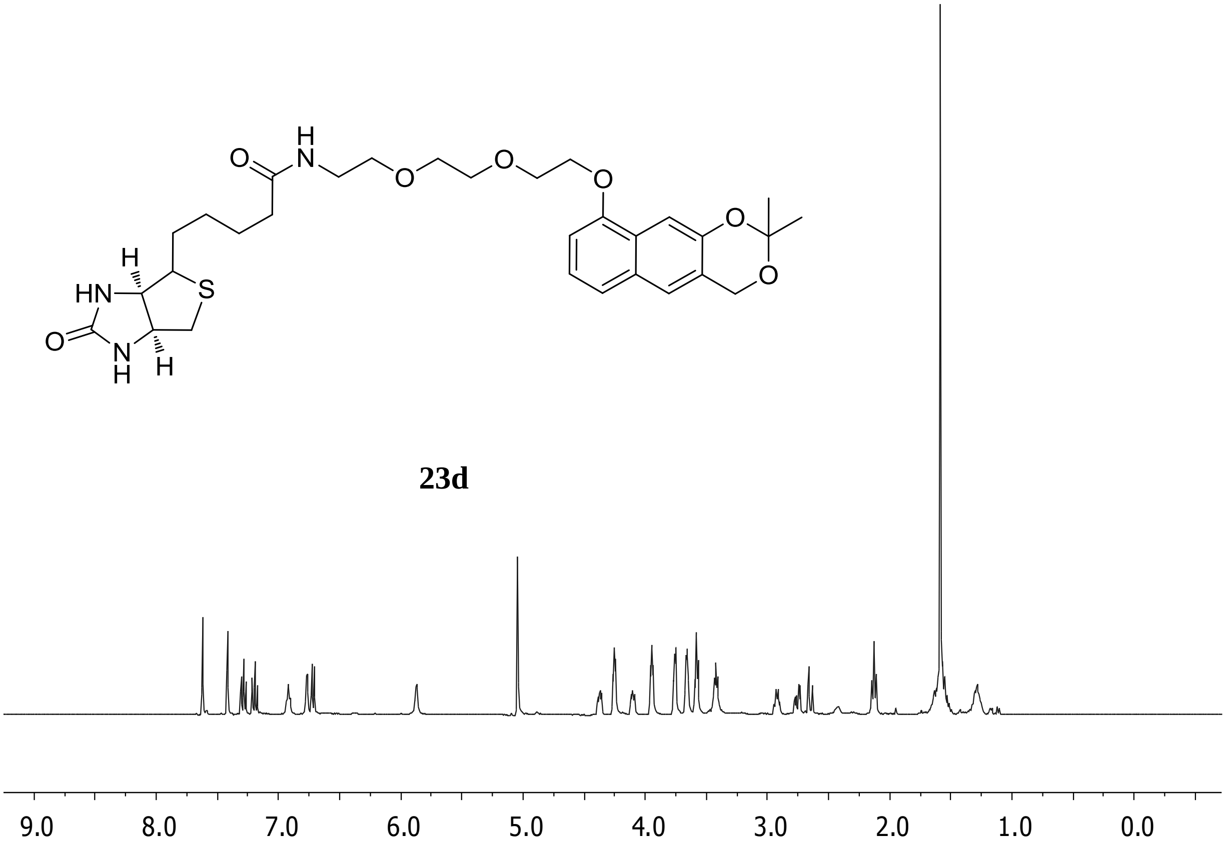
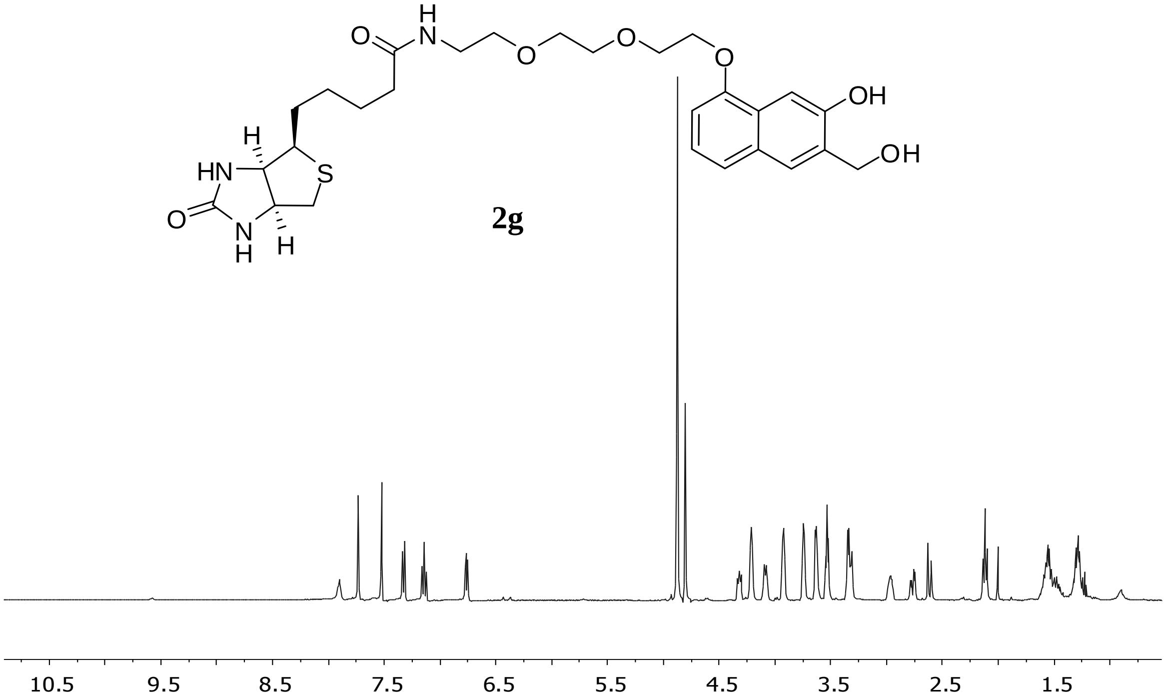


23d



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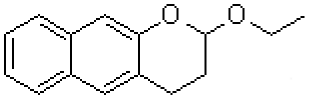

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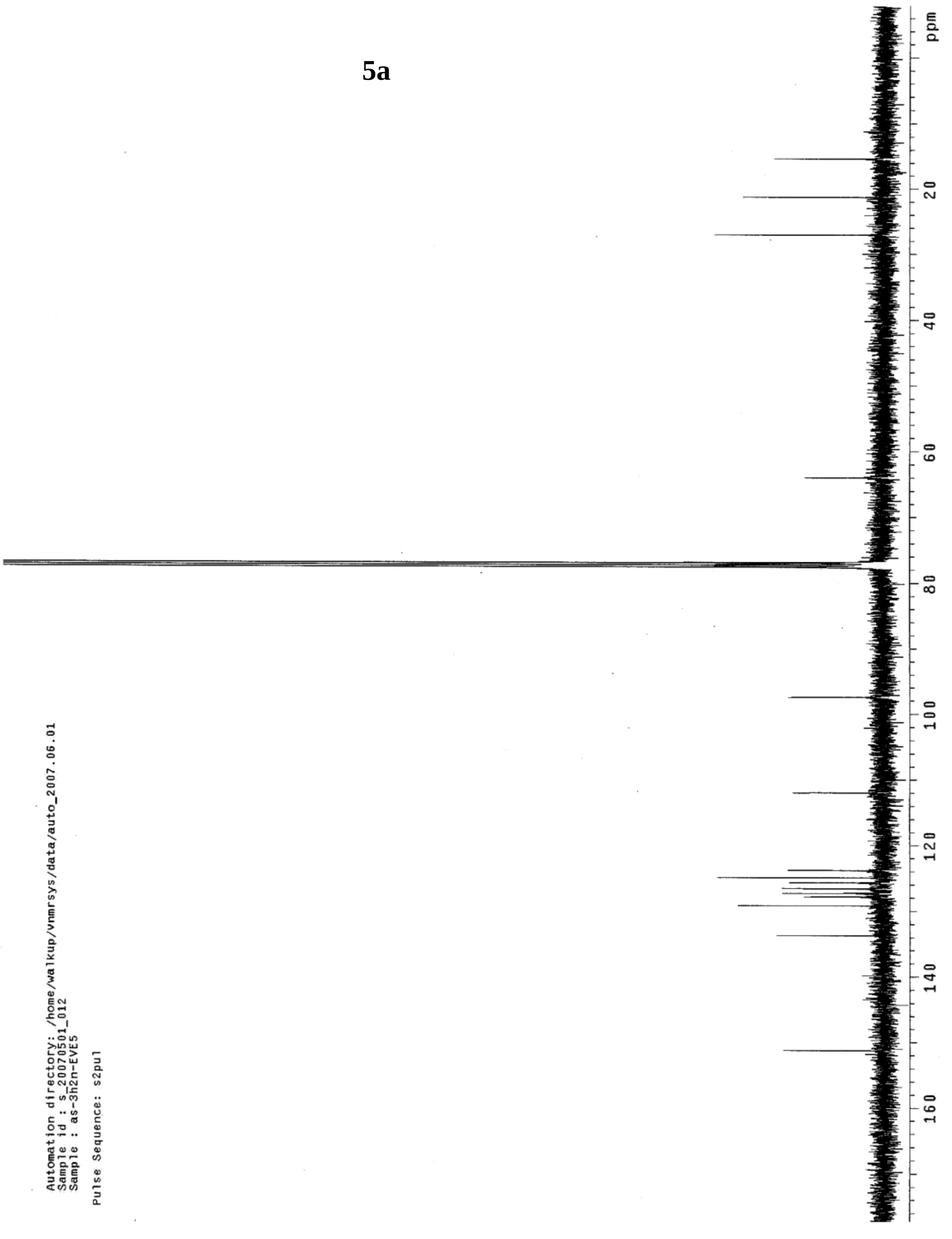

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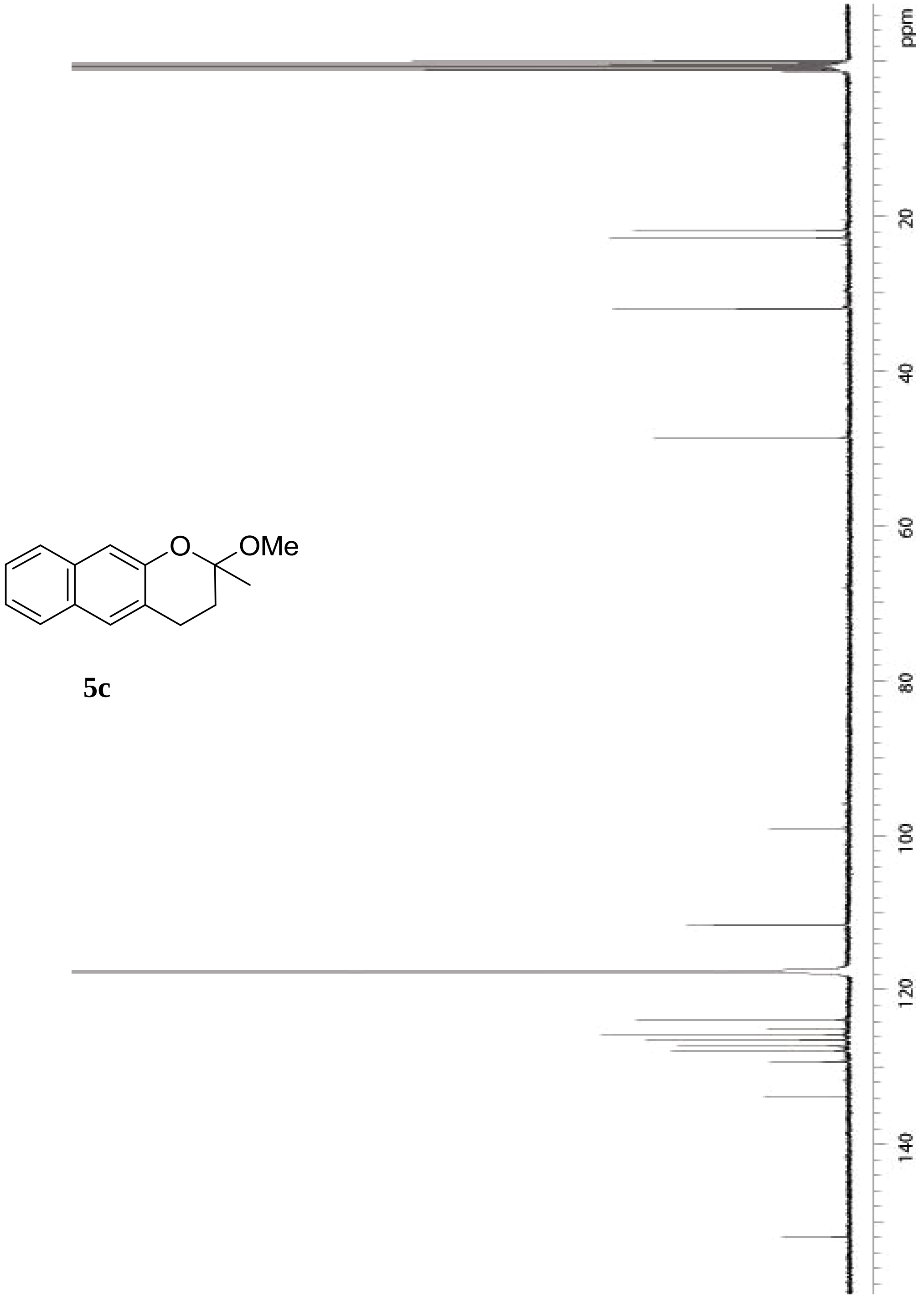
Sample id : s_20070501_012
Sample : as-3h2n-EVE5

Pulse Sequence: s2pul

5b



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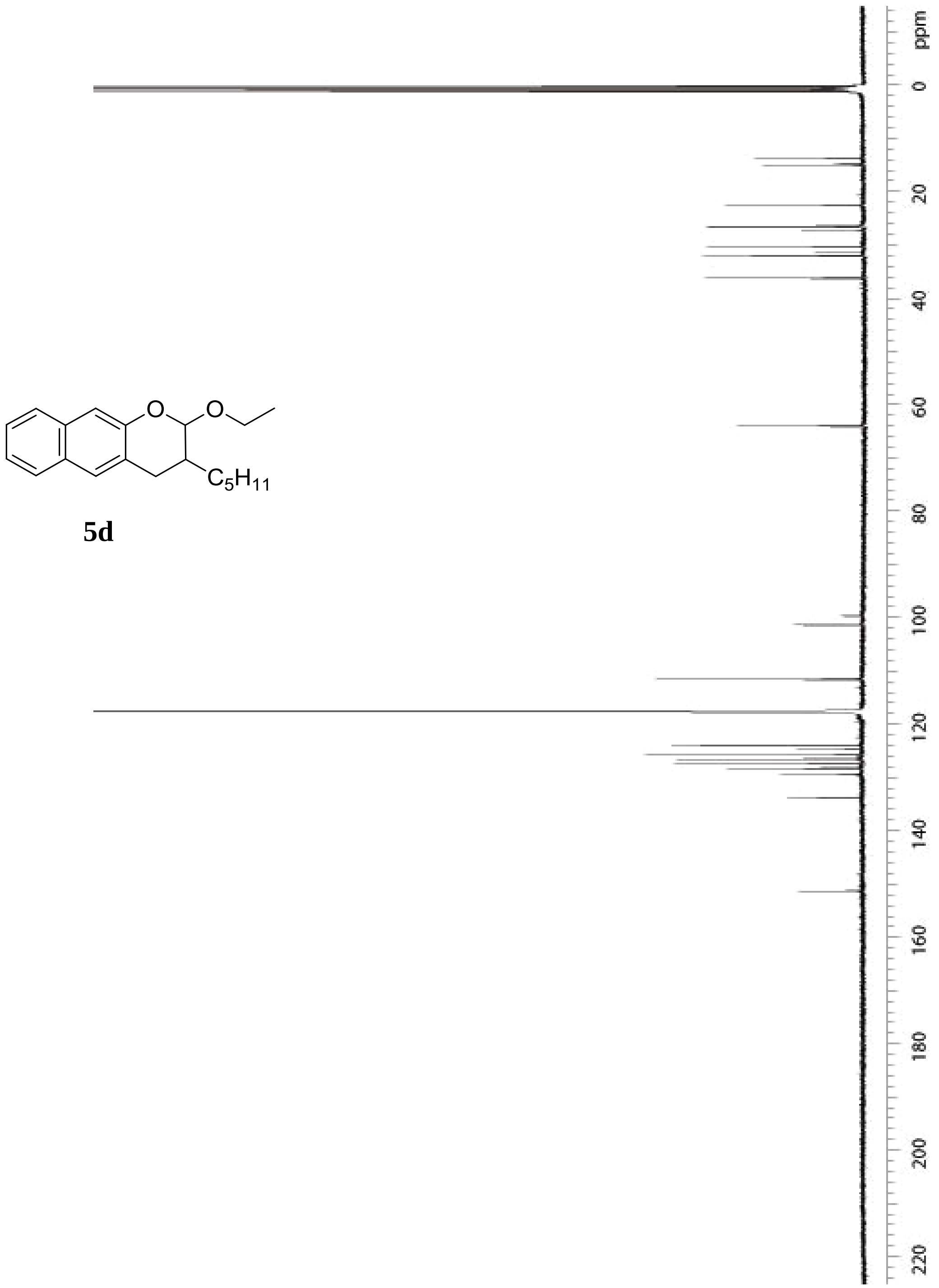

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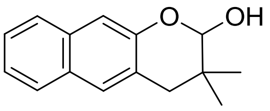

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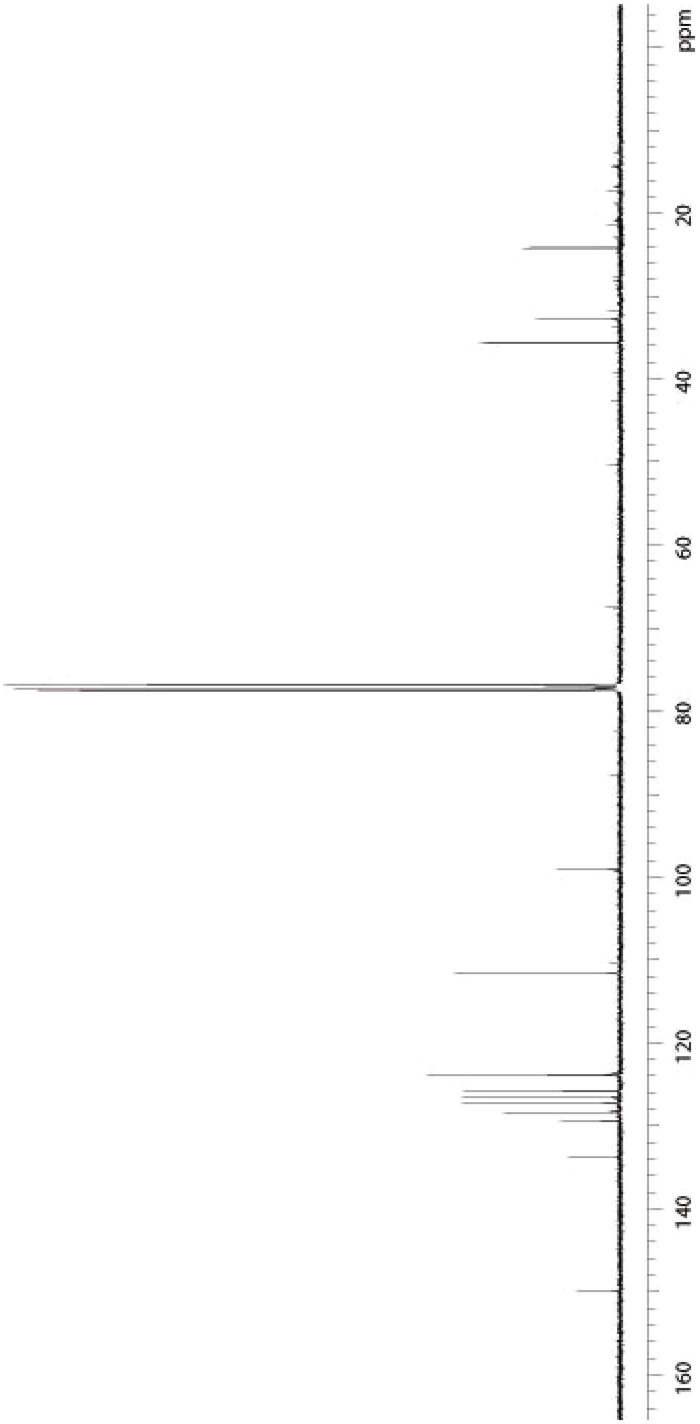

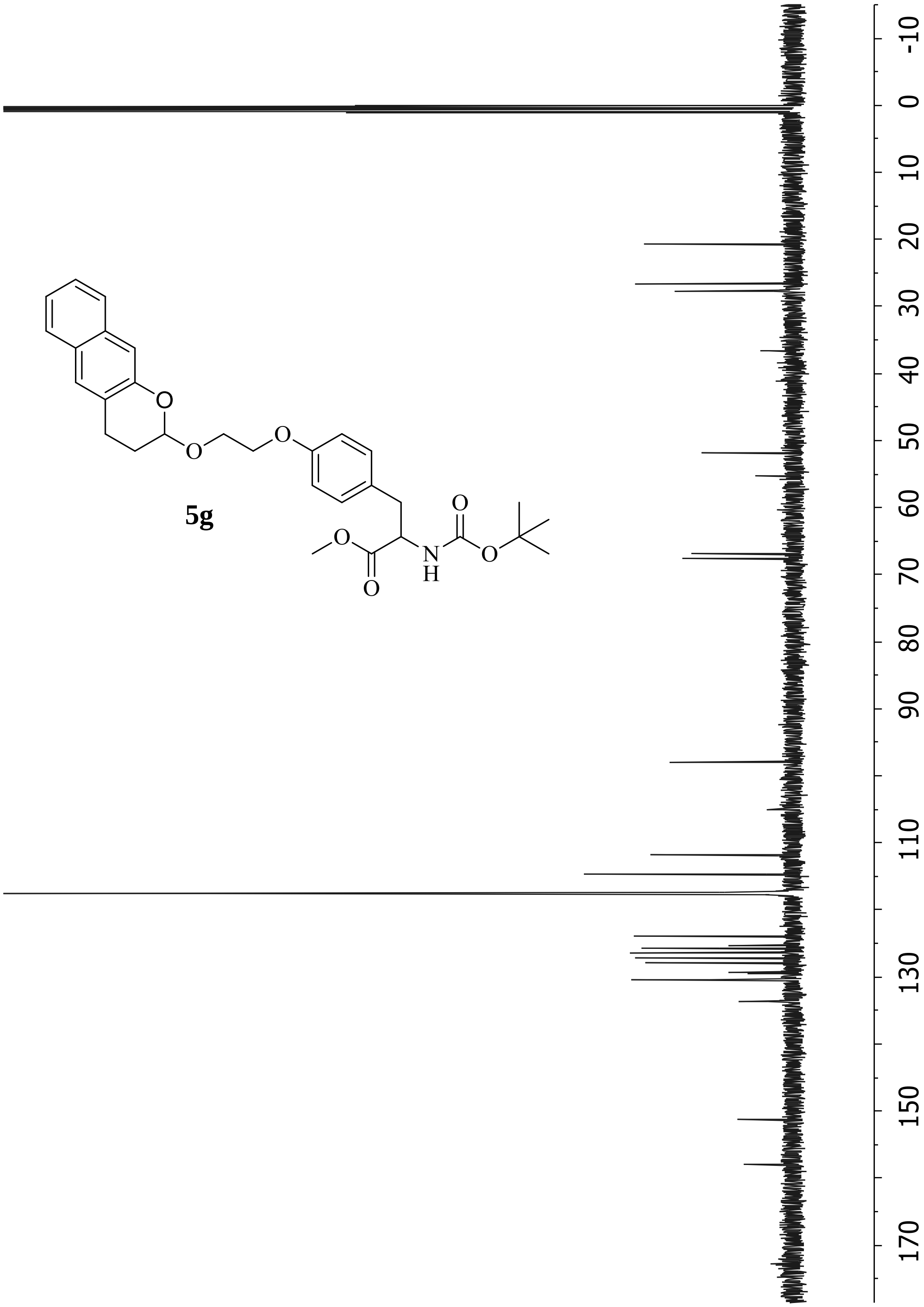
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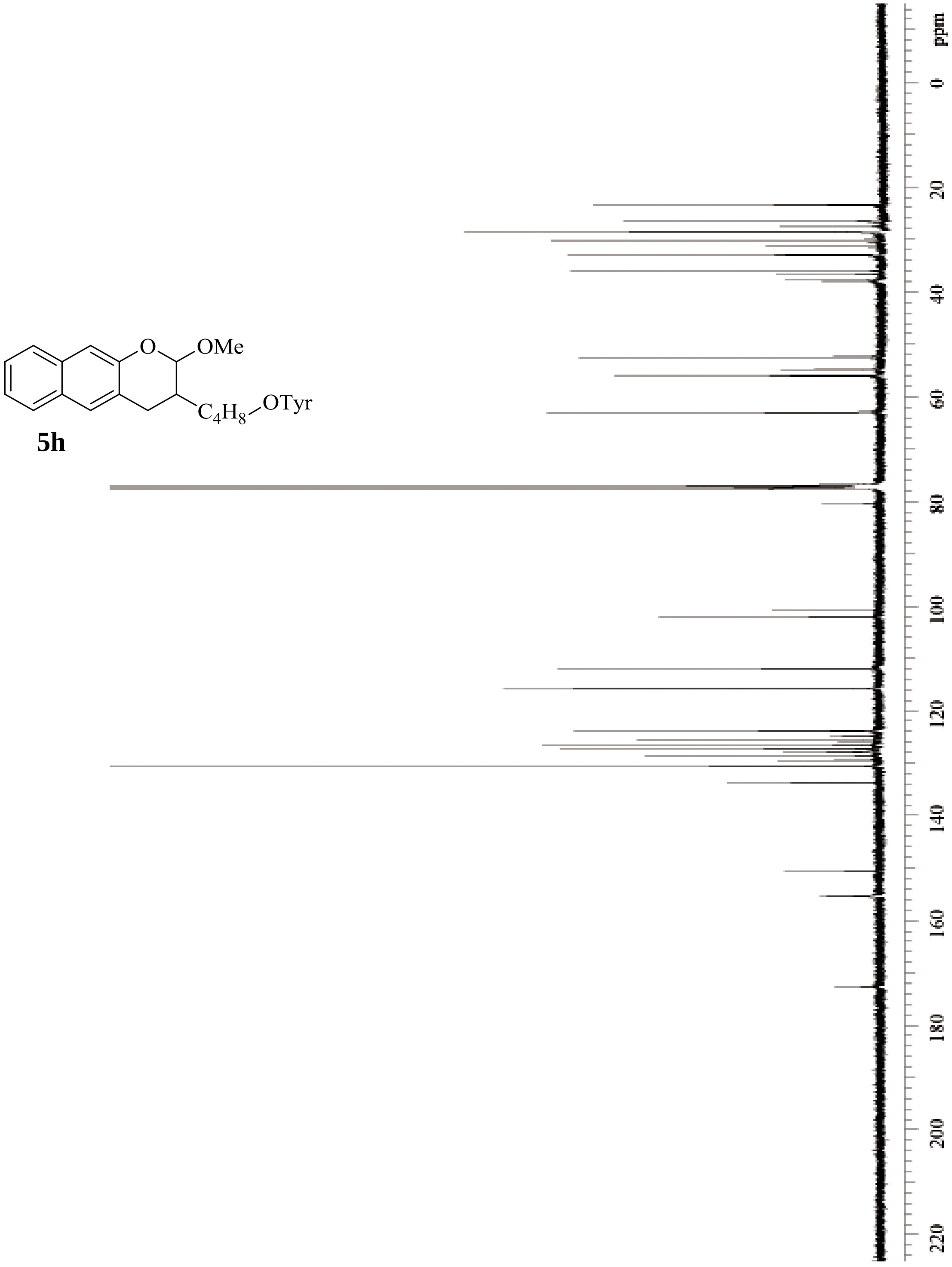

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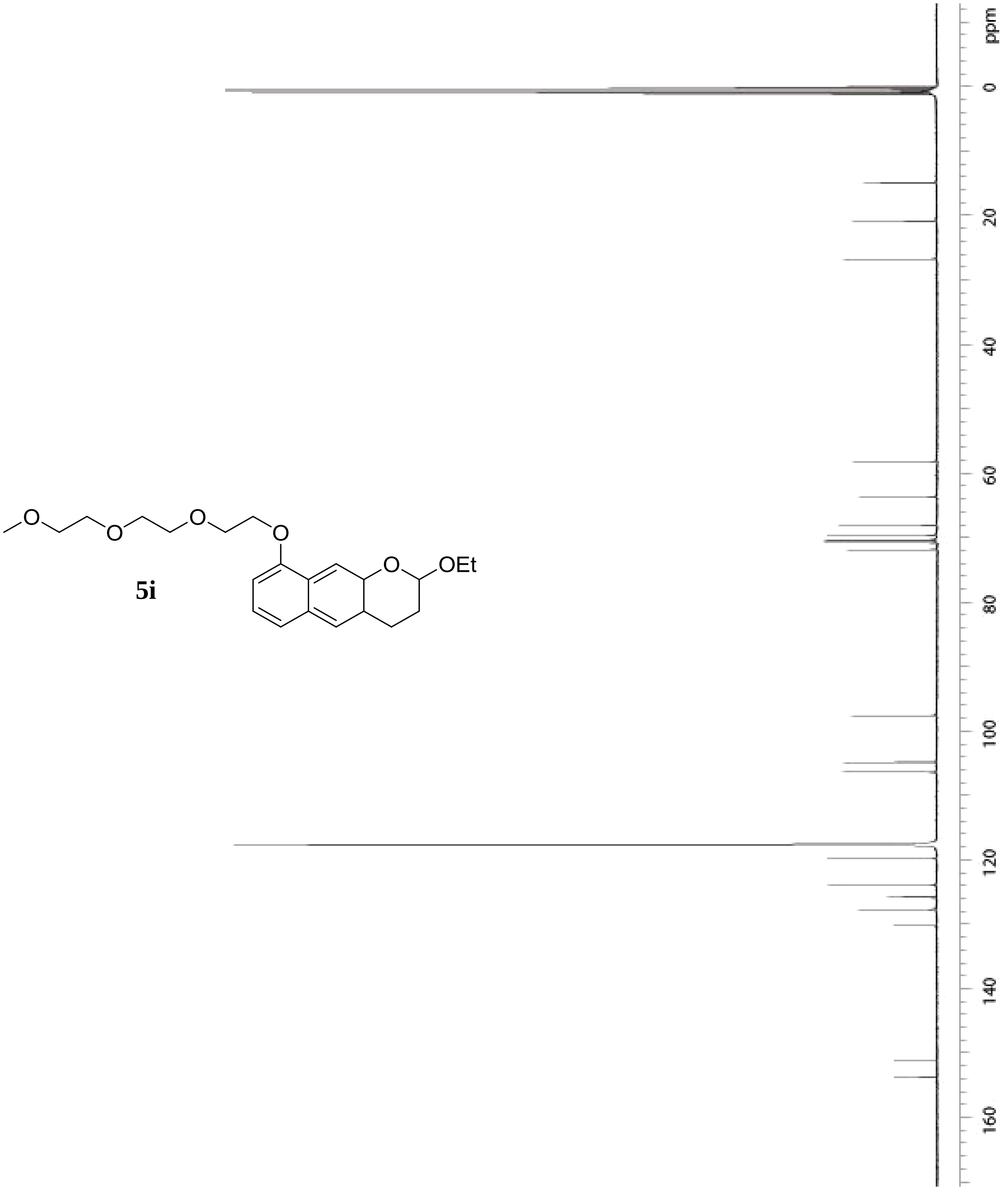

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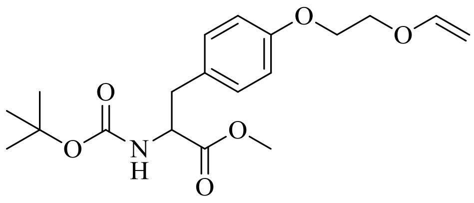

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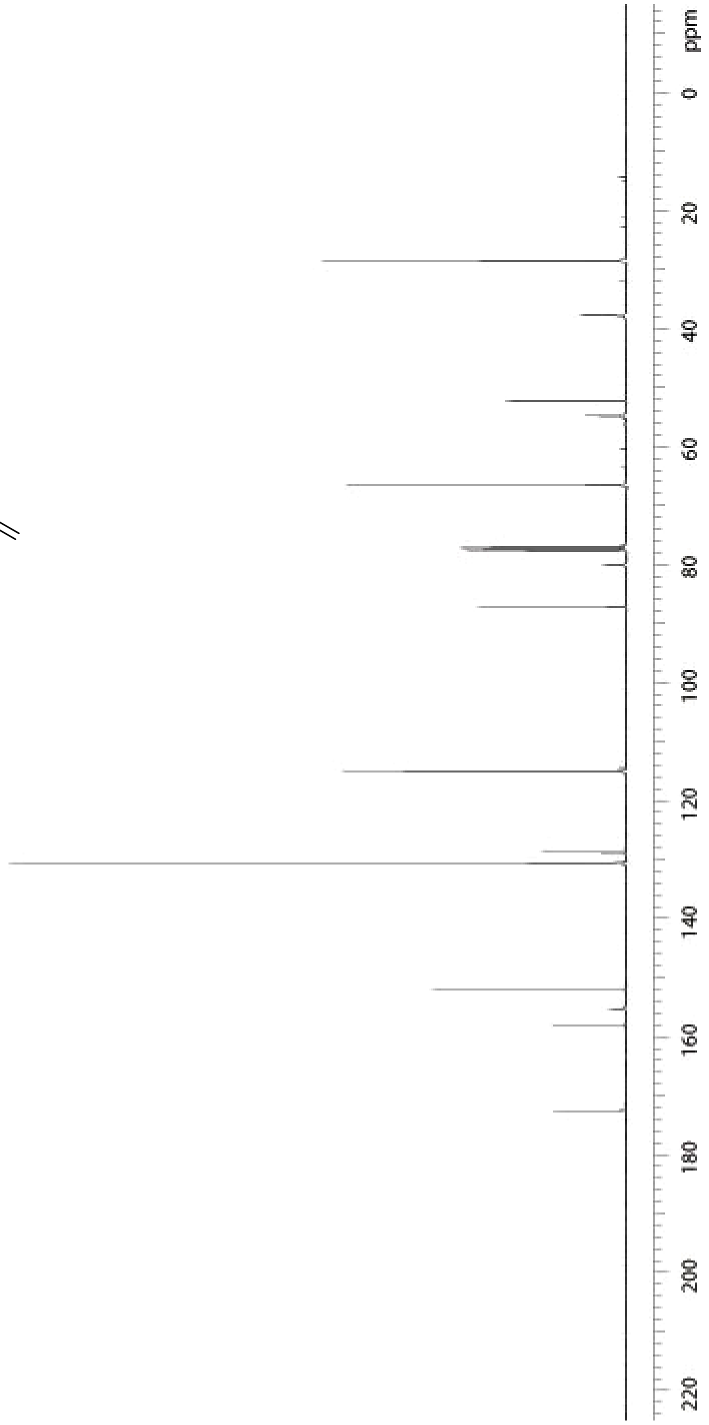

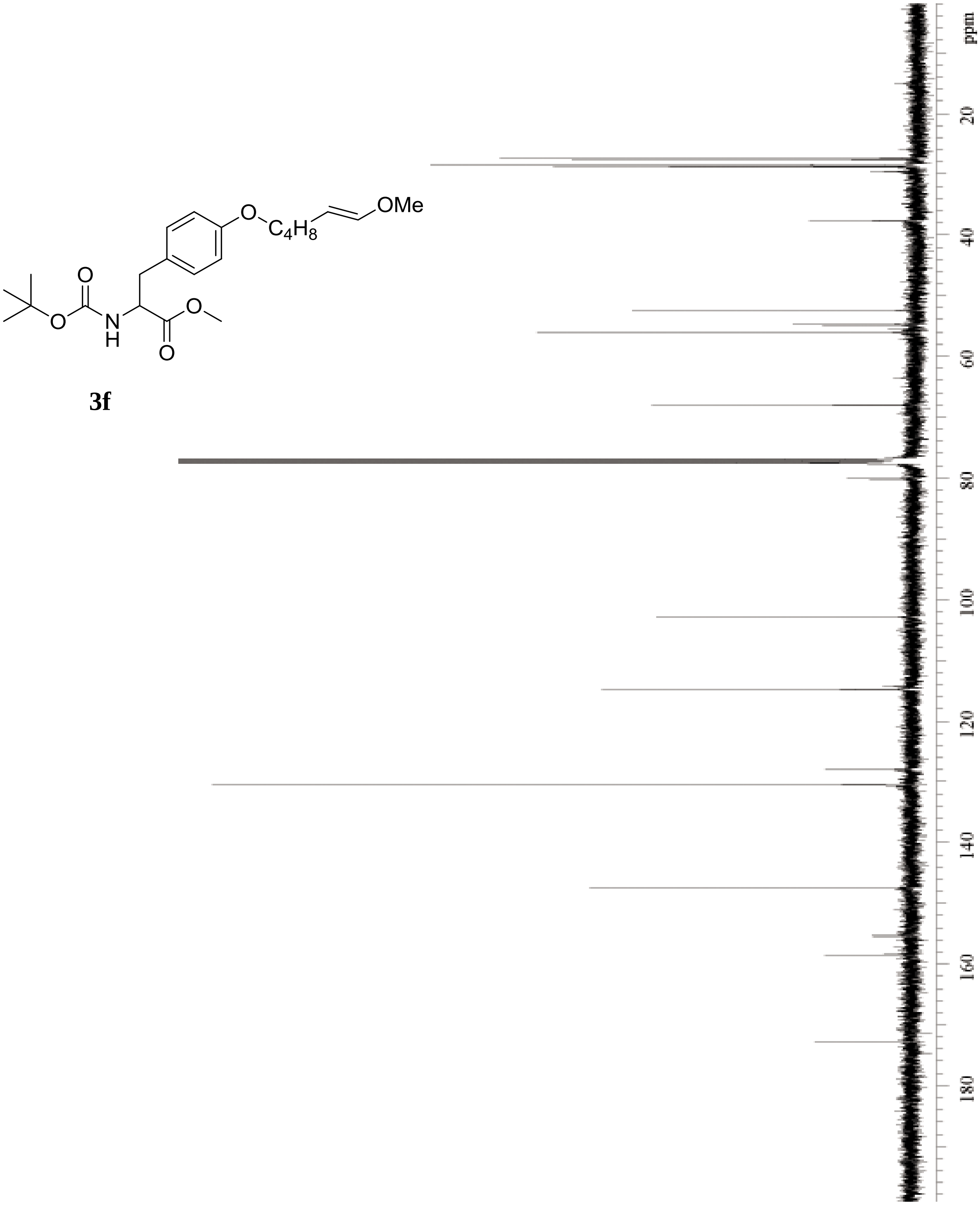

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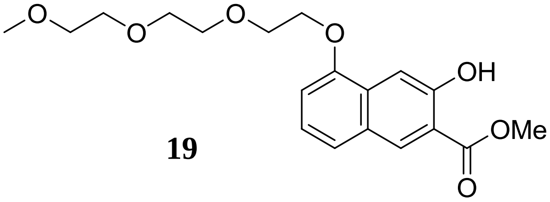

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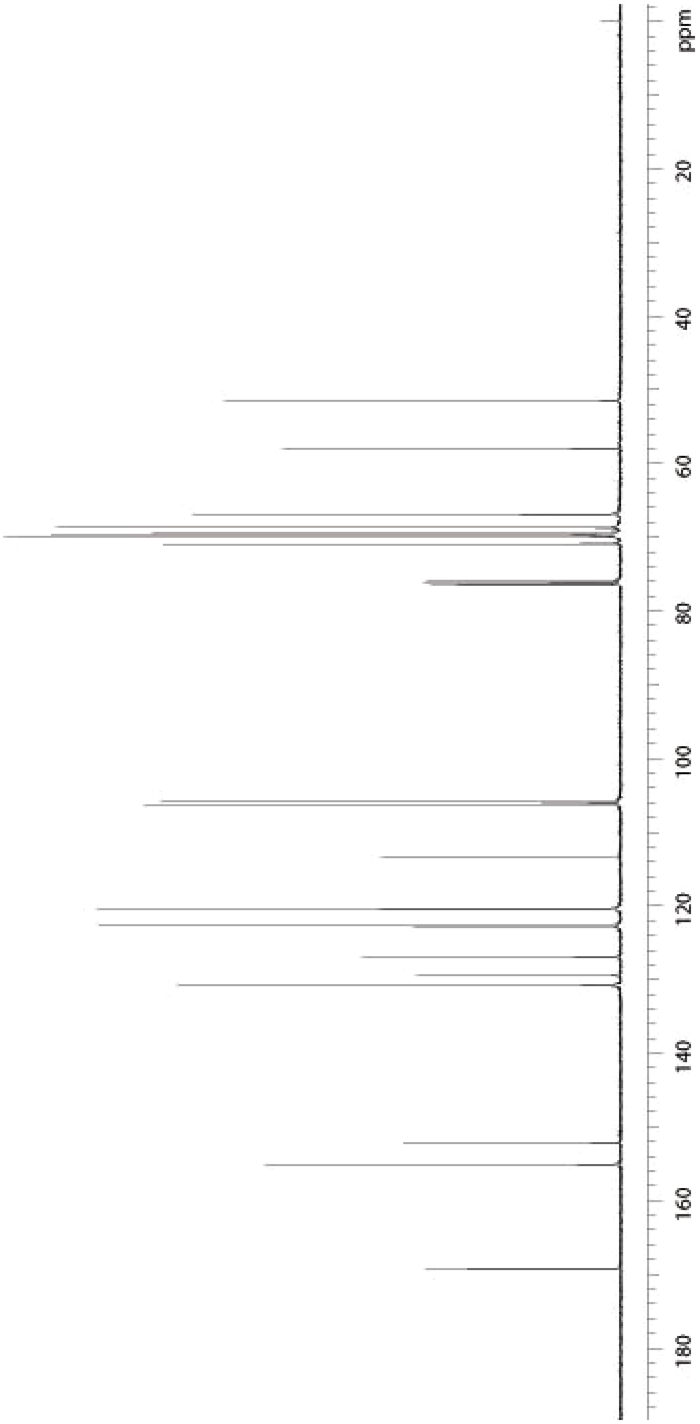

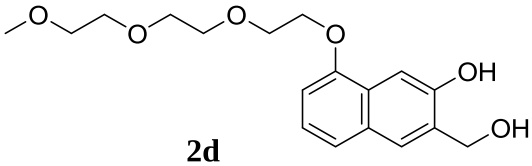

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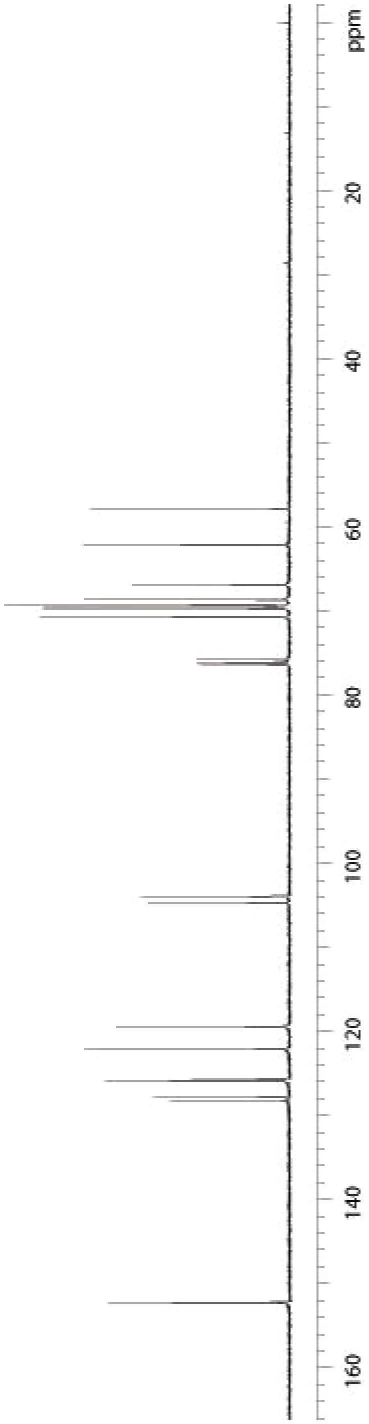

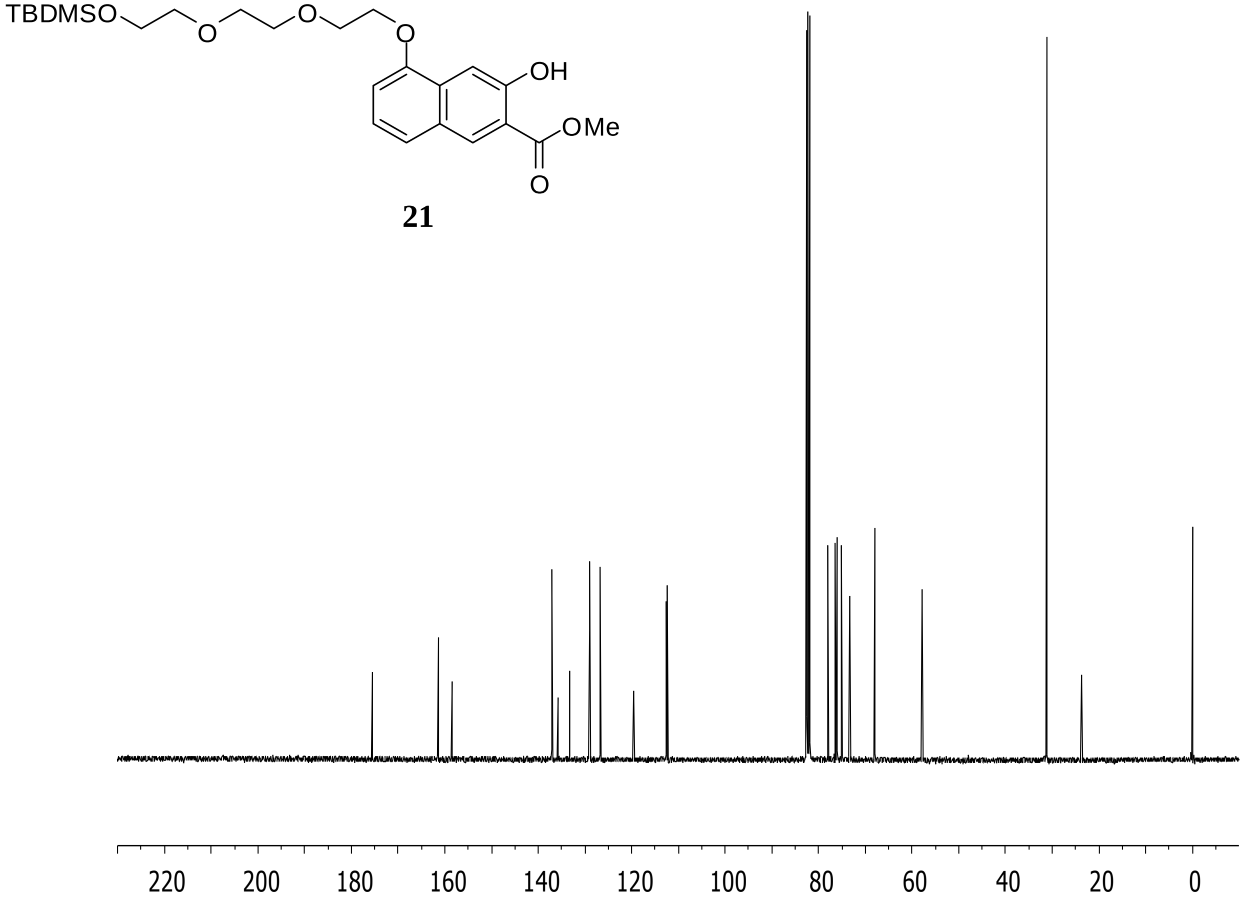

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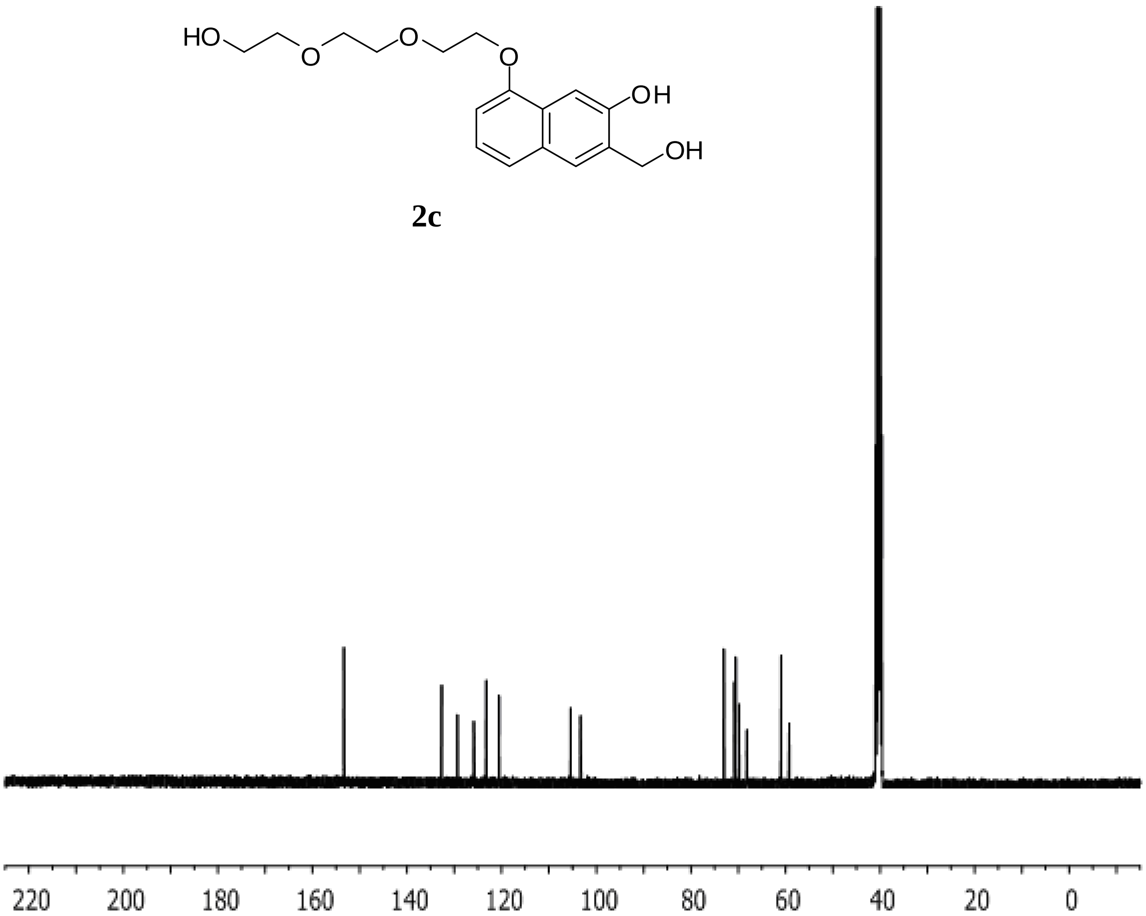

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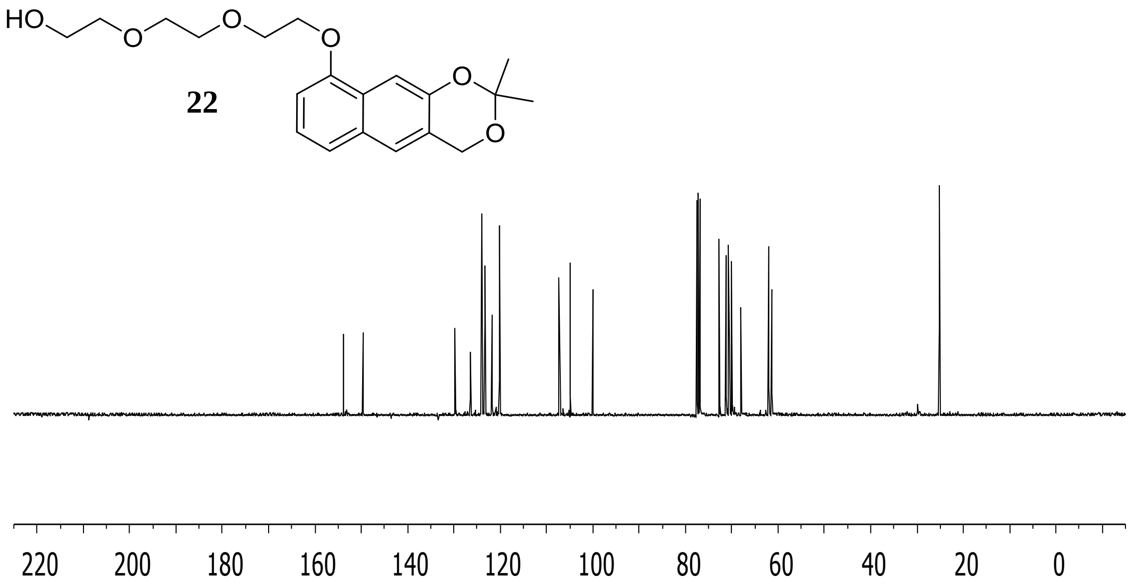

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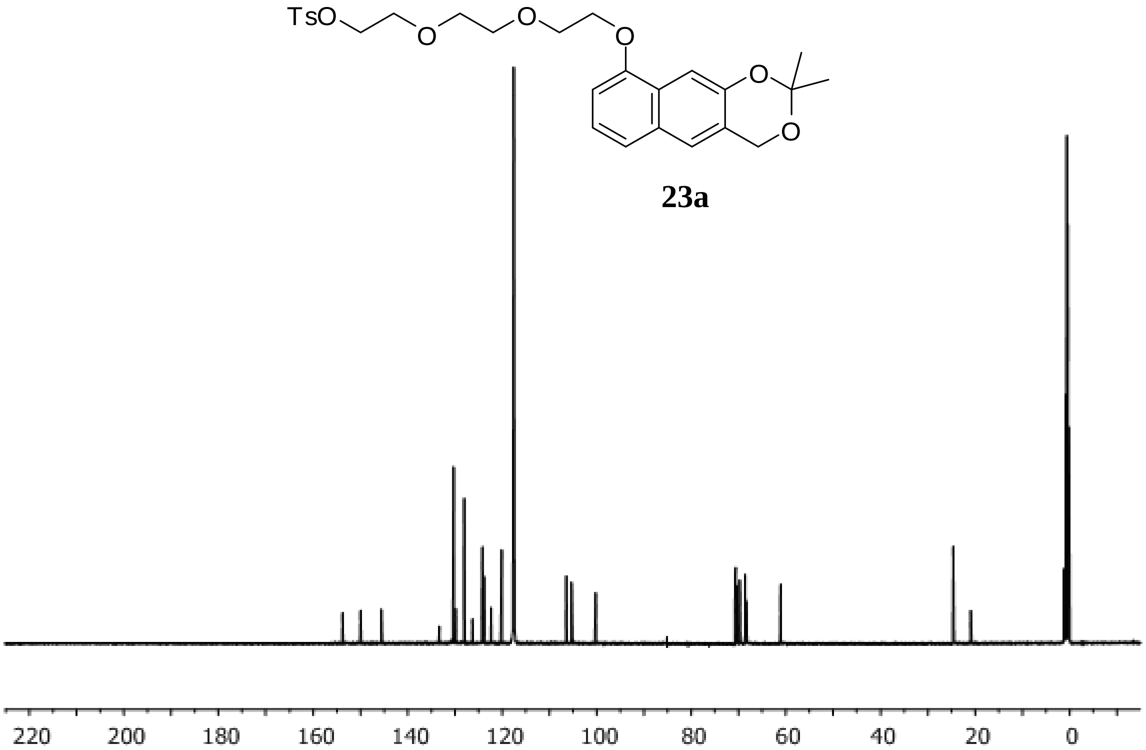

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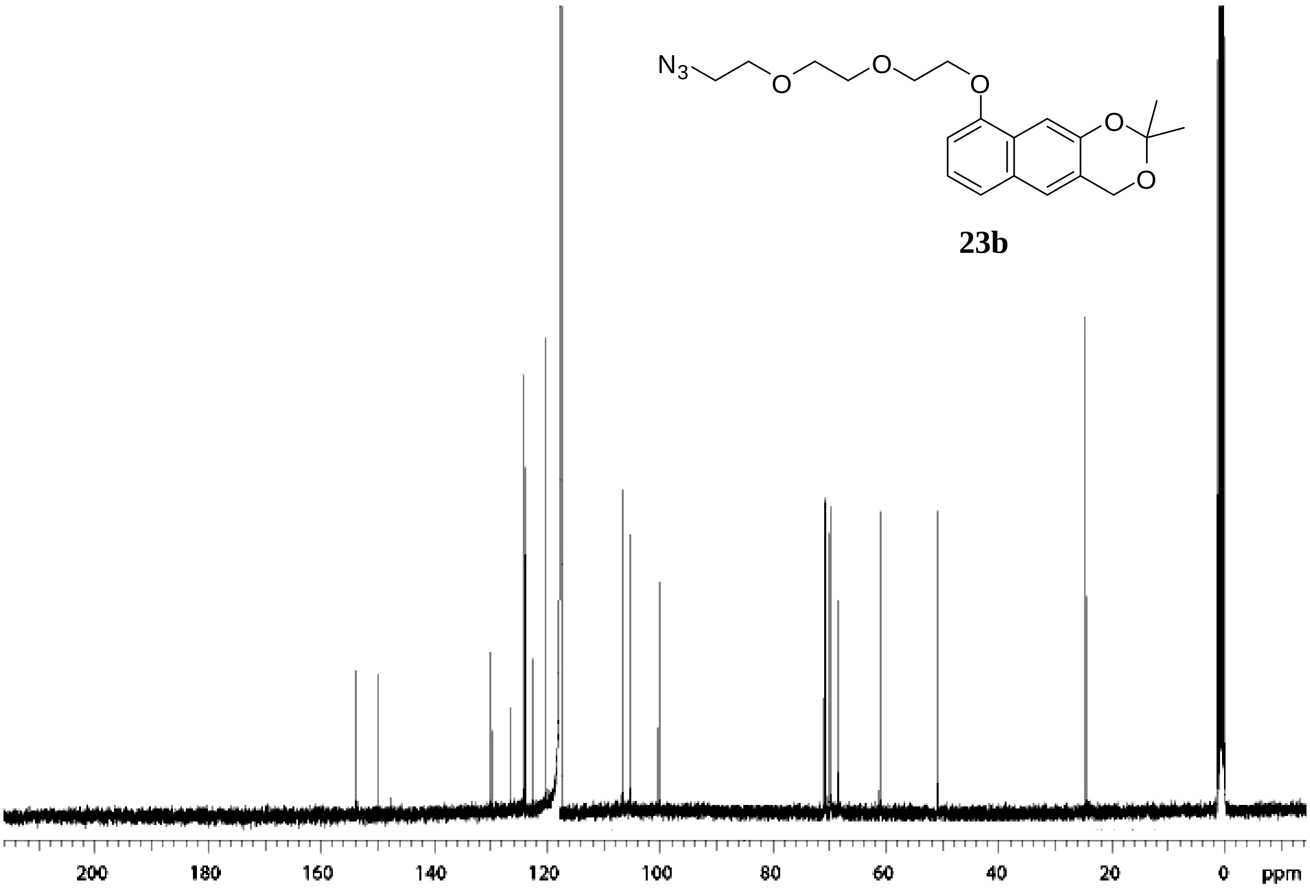

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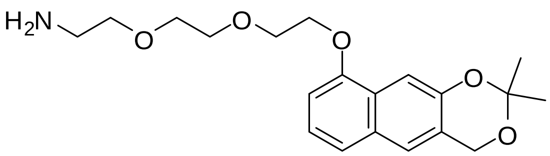

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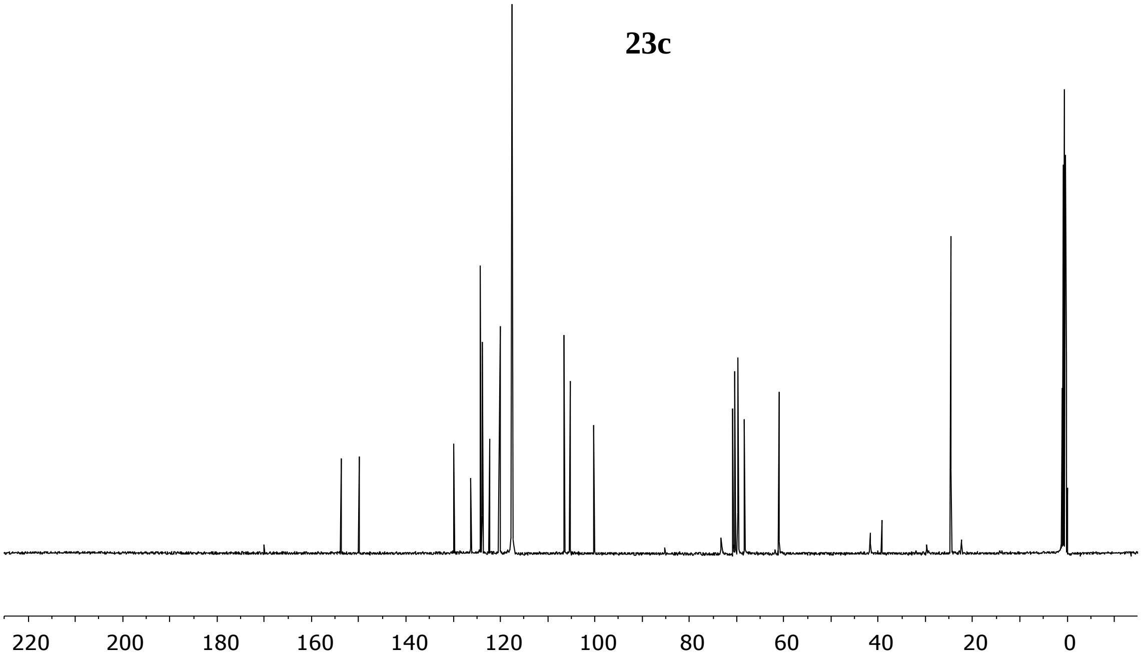

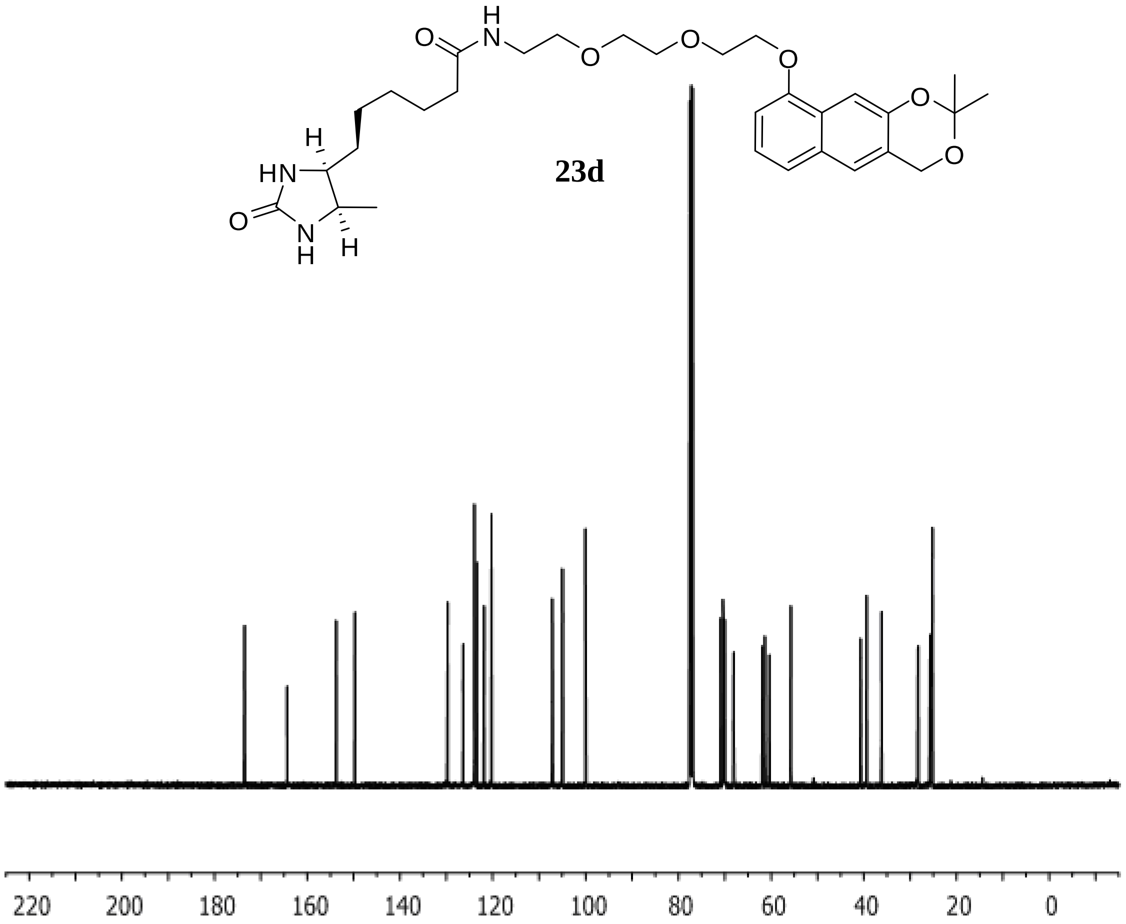

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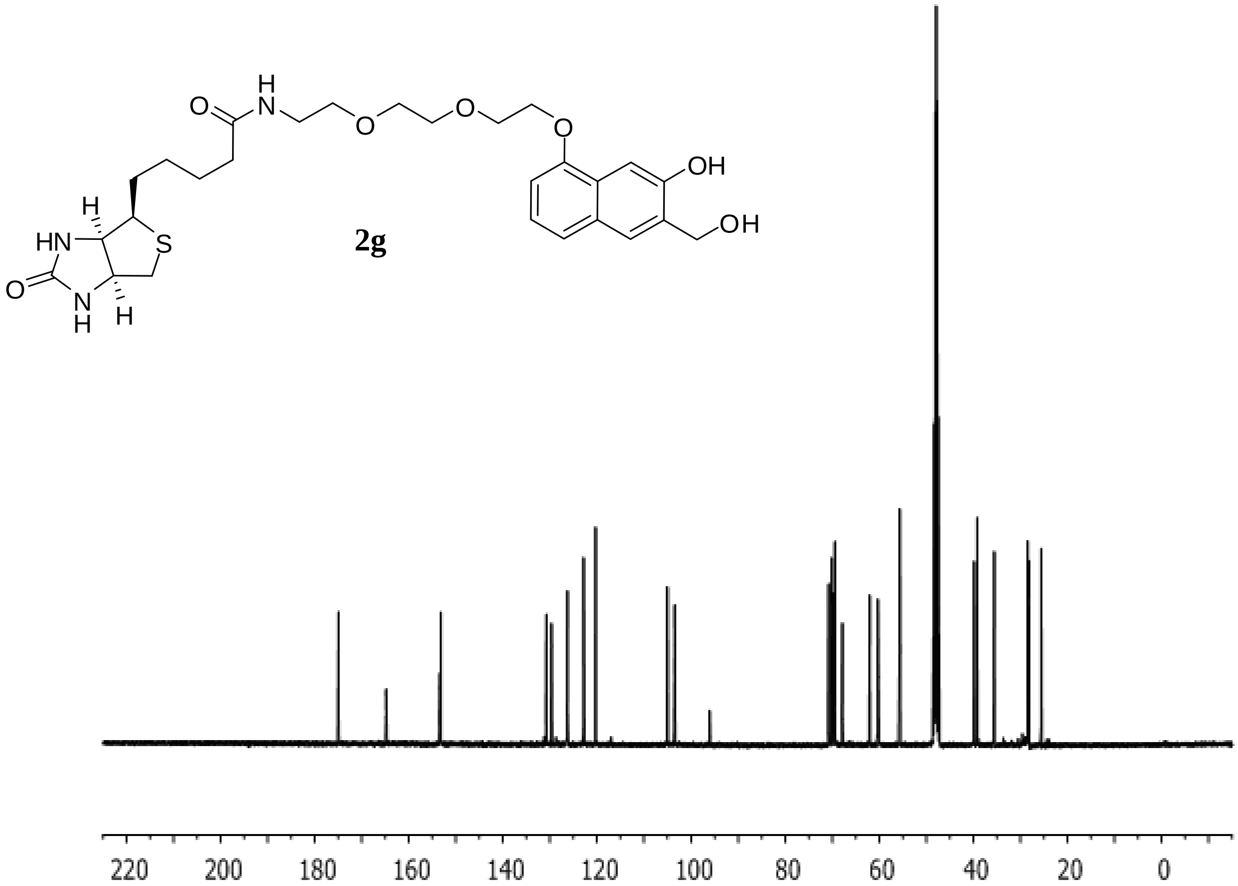

2g

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