Supporting information for

Photo-controlled delivery of a potent analogue of doxorubicin

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Sections

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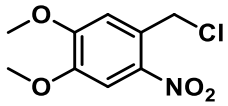
1. General methods

MCF-7 cells were obtained from ATCC, and A2780 and A2780ADR cells were obtained from Sigma-Aldrich. The CellTiter-Blue reagent was purchased from Promega (Catalogue number: G8081). CellTiter-Blue assay readings were taken with a BioTek Synergy H1 hybrid 96-well plate reader. Fluorescence activated cell sorting (FACS) data was obtained by running samples on Canto - BD FACSCanto™ II Analyzer instrument, equipped with BD FACS carousel loader and 2 lasers (blue: 488 nm, red: 633 nm). Post-experiment data analysis was performed with FACSDIVA and FCSExpress 5 flow software. Confocal microscopic images were captured using LSM710 Zeiss instrument (63X magnification using oil-immersion objective) and processed with Zen and ImageJ software. All reagents were purchased from Sigma-Aldrich, Fisher Scientific or TCI America unless otherwise specified and were used as received.

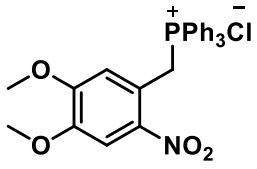
2. Experimental Procedures Synthesis.



Synthesis of 4,5-Dimethoxy-2-nitrobenzyl chloride. 4,5- Dimethoxy-2-nitrobenzyl alcohol (**2**) (3.0 g, 14.0 mmol) was treated with $SOCl_2$ neat (10mL, 138.8 mmol) and allowed to stir at RT for 30 min. The $SOCl_2$ was removed under reduced pressure and the remaining $SOCl_2$ was quenched with addition of water (100 mL), the aq. layer was extracted (3 X 50 mL) with DCM, dried over magnesium sulfate and evaporated under reduced pressure to give a solid residue, which was passed over silica gel column (eluted with ethyl acetate/hexane 1:1) to isolate the title compound (2.95 g, 98%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.69 (s, 1 H) 7.11 (s, 1 H) 5.01 (s, 2 H) 4.01 (s, 6 H) 3.94 (s, 3 H) *NMR matches previously reported compound[S2]

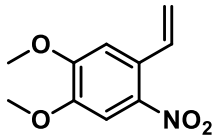
HRMS (ESI): $C_9H_{10}ClNO_4$; calculated. $(M+H)^+$ 332.0371, found = 332.0369



Synthesis of (4,5-dimethoxy-2-nitrobenzyl)triphenylphosphonium chloride (3): 4,5-Dimethoxy-2-nitrobenzyl chloride (6.0 g, 25.8 mmol) in toluene (30 mL) was added triphenyl phosphine (5.54 g, 21.1 mmol) and the reaction mixture was then heated to reflux and allowed to stir overnight. The reaction mixture was cooled on ice and cold hexane (30 mL) was added which caused a precipitate to form. The reaction mixture was filtered to afford the title compound (5.84 g, 98%) as a brown solid.

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm - 7.93 (d, *J*=2.26 Hz, 1 H) 7.70 - 7.84 (m, 8 H) 7.61 - 7.68 (m, 5 H) 7.42 - 7.59 (m, 1 H) 6.12 (s, 1 H) 6.09 (s, 1 H) 3.91 (d, *J*=2.01 Hz, 6 H)

HRMS (ESI): $C_{27}H_{25}ClNO_4P$; calculated. $(M-Cl)^+$ 458.1515, found = 458.1507

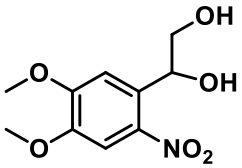


Synthesis of 1,2-dimethoxy-4-nitro-5-vinylbenzene. Phosphonium salt **3** (0.5 g, 1.01) mmol) was suspended in a 37% formaldehyde solution (4 mL, aqueous). The mixture was stirred for 15 min, and then an aqueous solution of 15% Na_2CO_3 (0.5 mL) was added intermittently via syringe. Each subsequent addition was made after the purple color of the phosphorane had dissipated. When the addition of the base was complete, the mixture was stirred at room temperature for 2 h, and then extracted with DCM (3×20 mL). The 3 combined organic extracts were dried over anhydrous magnesium sulfate and evaporated. The crude product was purified by flash chromatography through silica gel with DCM as eluent to afford the title compound as a yellow solid (0.200 g, 95%).

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.58 (s, 1 H) 7.28 - 7.35 (m, 1 H) 6.97 (s, 1 H) 5.64 (d, *J*=17.36 Hz, 1 H) 5.43 (d, *J*=11.00 Hz, 1 H) 3.93 - 4.02 (m, 6 H)

^{13}C NMR (CDCl3, 100 MHz): δ = 153.7, 145.9, 139.9, 133.6, 129.9, 117.8, 110.3, 110.2, 57.0, 56.4. *NMR matches previously reported compoud[S3]

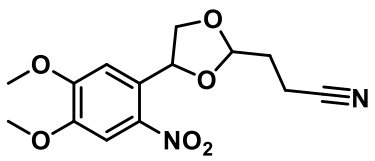
HRMS (ESI): $C_{10}H_{11}NO_4$; calculated. $(M+H)^+$ 210.0760, found = 210.0762



Synthesis of 1-(4,5-dimethoxy-2-nitrophenyl)ethane-1,2-diol (4): To a mixture of 1,2-dimethoxy-4-nitro-5-vinylbenzene (150 mg, 0.516 mmol) in dichloromethane (4 mL), N-methyl morpholine oxide (NMO) (50 mg, 0.5 mmol) in water (0.5 mL), OsO_4 (0.1 mL, 0.02 mmol, 4% in water) was added. The reaction mixture was vigorously stirred at RT for 48 h. The reaction mixture was quenched with Na_2SO_3 (0.45 g in 4.5 ml water) and stirred for an additional 24 h. The dichloromethane layer was separated and the aqueous phase was extracted with ethyl acetate (100 mL). The combined organic layers were dried over sodium sulfate and evaporated under vacuum. The resulting solid was purified by silica gel column (eluted with hexane/ethyl acetate, 1:1) to isolate the title compound (0.119 g, 95%) as a white solid.

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.49 (s, 1 H) 5.47 (br dd, *J*=7.46, 2.32 Hz, 1 H) 3.96 - 4.08 (m, 1 H) 3.88 - 3.94 (m, 4 H) 3.85 (s, 3 H) 3.45 - 3.50 (m, 1 H)

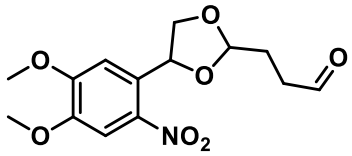
HRMS (ESI): $C_{10}H_{13}NO_6$; calculated. $(M+H)^+$ 244.0815, found = 244.0819



Synthesis of 3-(4-(4,5-dimethoxy-2-nitrophenyl)-1,3-dioxolan-2-yl)propanenitrile. A solution of **4** (0.100 g, .411 mmol), 4,4-dimethoxybutanenitrile (**5**, 0.126 mL, 0.126 mmol), and pyridinium p-toluenesulfonate (0.05g, 0.12 mmol) in dry benzene (50 mL) was refluxed in Dean-Stark apparatus (protected from light). Progress of the reaction was monitored by TLC (1:1 hexanes: EthOAc) and benzene was replenished as it was distilled. After completion the reaction, as indicated by absence of diol on TLC, the reaction mixture was diluted with ether (100 mL), and washed with saturated $NaHCO_3$ solution and brine prior to drying with sodium sulfate. The ethereal layer was evaporated to obtain a residue, which was purified further by rinsing with cold ether (3 X 20 mL) to obtain acetal **1.20** as a light brown solid (0.120 g, 95%).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ ppm 7.70 (d, *J*=2.45 Hz, 2 H) 7.22 - 7.31 (m, 2 H) 5.50 - 5.66 (m, 1 H) 5.12 (t, *J*=4.40 Hz, 1 H) 4.61 - 4.64 (m, 1 H) 4.39 (t, *J*=7.95 Hz, 1 H) 3.87 (s, 3H) 3.93(s, 3H) 3.75 - 3.80 (m, 1 H) 3.61 - 3.68 (m, 1 H) 2.62 - 2.65 (m, 2 H) 2.13-2.19 (m, 2H) 2.01 - 2.07 (m, 2 H)

HRMS (ESI): $C_{14}H_{16}N_2O_6$; calculated. $(M+Na)^+$ 331.0906, found = 331.0913

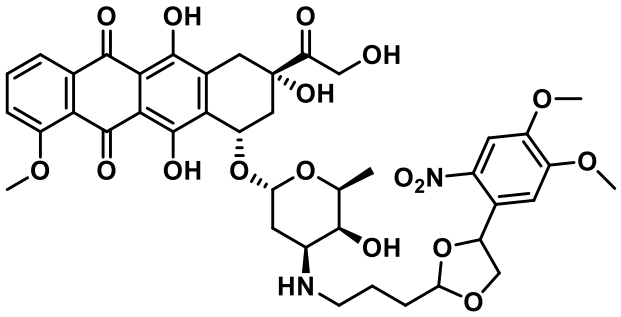


Synthesis of 3-(4-(4,5-dimethoxy-2-nitrophenyl)-1,3-dioxolan-2-yl)propanal (6): A solution of nitrile **1.20** (0.100 g, .324 mmol) in DCM (25 mL) was cooled to -78 °C and treated dropwise with Dibal-H (.324 mL of 1 M in hexanes, .324 mmol) within 10 min. The reaction mixture was allowed to warm to room temperature during 4 h after which was diluted with DCM (50 mL) and saturated sodium potassium tartrate solution (75 mL). The separated organic layer was washed with water and brine then dried with magnesium sulfate. The crude organic material was evaporated to leave a brown residue that was purified by flash chromatography on silica gel. Elution with 50% ethyl acetate in hexanes furnished **6** as a white solid (0.086 g, 86%).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ ppm 9.72 (s, 1 H) 9.69 (s, 0.3 H) 7.27 (s, 1 H) 7.20 (s, 0.3 H) 5.53 - 5.58 (m, 1 H) 5.09 (t, *J*=4.52 Hz, 1 H) 4.56 – 4.60 (m, 0.3 H) 4.34 (t, *J*=8.07 Hz, 1 H) 3.87 – 3.93 (m, 8 H) 3.73 – 3.76 (m, 1 H) 2.65 – 2.68 (s, 2 H) 2.58 – 2.61 (m, 0.6 H) 2.10 - 2.17 (m, 2 H) 1.99 - 2.03 (m, 0.6 H)

^{13}C NMR (CDCl3, 100 MHz):δ = 203.1, 203.0, 153.9, 148.1, 139.1, 132.8, 108.5, 103.8, 73.9, 72.1, 56.6, 38.0, 37.9, 25.9.

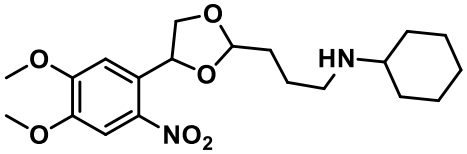
HRMS (ESI): $C_{14}H_{17}NO_7$; calculated. $(M+Na)^+$ 334.0902, found = 334.0894



Synthesis of compound 1. A stirred solution of doxorubicin hydrochloride (0.051 g, 0.085 mmol) and aldehyde **1.21** (0.025 g, 0.080 mmol) in CH_3CN-50mM NaOAc pH 5.0 (2:1) (10 mL) was treated with $NaBH_3CN$ (0.015 g, 0.24 mmol). The mixture was stirred under inert atmosphere at room temperature in the dark for 1 h. The reaction was monitored by TLC (1:10 DCM:MeOH). After completion, the reaction mixture was diluted with H_2O (8 mL) and then extracted repeatedly (10 × 10 mL) with $CHCl_3$-MeOH (5:1). The combined extracts were dried and evaporated to give a red film which was purified by preparative TLC using $CHCl_3$- MeOH (10:1.4) as eluent. The solution was dried under high vacuum to afford **1.24** (0.030 g, 45%) as a red film.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.32 (s, 1 H) 7.40 - 7.59 (m, 1 H) 6.99 - 7.17 (m, 1 H) 5.30 - 5.48 (m, 1 H) 5.17 - 5.28 (m, 1 H) 4.83 - 5.06 (m, 1 H) 4.58 (s, 1 H) 4.50 (ddd, *J*=8.60, 6.84, 3.64 Hz, 1 H) 4.15 - 4.43 (m, 1 H) 4.01 - 4.15 (m, 1 H) 3.83 - 4.00 (m, 2 H) 3.63 - 3.81 (m, 6 H) 3.35 - 3.53 (m, 1 H) 2.91 (br d, *J*=16.81 Hz, 1 H) 2.72 (br d, *J*=4.52 Hz, 1 H) 2.60 - 2.69 (m, 1 H) 2.01 - 2.26 (m, 2 H) 1.89 (s, 1 H) 1.56 - 1.84 (m, 5 H) 1.04 - 1.33 (m, 4 H)

MS (ESI): $C_{41}H_{47}N_2O_{17}$; calculated. $(M+H)^+$ 839.28, found = 839.20



***N*-(3-(4-(4,5-dimethoxy-2-nitrophenyl)-1,3-dioxolan-2-yl)propyl)cyclohexanamine (7).** A stirred solution of cyclohexylmine (0.011 mL, 0.091 mmol) and compound **6** (0.030 g, 0.096 mmol) in CH_3CN/50mM aq. NaOAc pH 5.0 (2:1) (10 mL) was treated with $NaBH_3CN$ (0.004 g, 0.06 mmol). The mixture was stirred under inert atmosphere at room temperature in the dark for 1 h. The reaction was monitored by TLC (1:10 CH_2Cl_2:MeOH). After completion, the reaction mixture was diluted with H2O (8 mL) and then extracted (3 × 10 mL) with CH_2Cl_2:MeOH (5:1). The combined extracts were dried and evaporated to give a colorless oil which was purified by column chromatography Hexanes- EtOAc (2:1) as eluent. The solution was dried under high vacuum to afford the title compound as a white solid (0.026 g, 69%).

^{1}H NMR (400 MHz, DMSO-d_6) ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.57 - 7.72 (m, 1 H) 7.14 - 7.32 (m, 2 H) 5.49 - 5.76 (m, 1 H) 4.95 - 5.18 (m, 1 H) 4.43 (dd, *J*=8.80, 7.83 Hz, 1 H) 3.81 -

4.00 (m, 5 H) 3.65 - 3.78 (m, 2 H) 3.44 - 3.63 (m, 1 H) 3.15 - 3.39 (m, 1 H) 2.06 - 2.18 (m, 1 H) 1.91 - 1.99 (m, 1 H) 1.61 - 1.89 (m, 5 H) 1.13 - 1.37 (m, 6 H) 1.00 - 1.10 (m, 1 H) 0.73 - 1.00 (m, 2 H) 0.44 - 0.73 (m, 1 H)

MS (ESI): $C_{20}H_{30}N_2O_6$; calculated. $(M+H)^+$ 395.2176, found = 395.2172

Cell viability assay: The cell viability was determined using CellTiter-Blue assay, a homogeneous, fluorometric method. The assay is principled on the ability of living cells to convert resazurin to a fluorescent product resorufin.[S1] Thus, the fluorescent intensity directly correlate to the number of living cells. Cytotoxicity tests were carried out in the following cell lines (passage number not exceeding 15): MCF-7 (human breast carcinoma), A2780 (human ovarian carcinoma) and A2780ADR (doxorubicin resistant human ovarian carcinoma). Approximately 5000 cells were seeded in 96 well tissue-culture plates in Dulbecco's Modified Eagle Medium (DMEM) containing 10% Fetal Bovine Serum (FBS) and were incubated for 24 h at 37 °C and 5% CO_2. Cells were treated with various concentrations of **1**, doxorubicin, 2P-dox and linker in 0.1% DMSO-DMEM for 2 h in absence of light. One such plate was exposed to light (380 nm, 9.0 $mW.cm^{-2}$) for 30 min in phenol-red free DMEM (kept on ice to prevent local overheating) while another identical plate was kept unexposed in similar conditions. The plates were then incubated for 72 h in dark, after which CellTiter-Blue reagent (20 μl) was added and further incubated for 3-4 h at 37 °C. Emission intensities were recorded at 590 nm. Cells treated with 0.1 % DMSO-DMEM did not show any significant cell death as compared to cells alone in both dark and light conditions. The inhibitory concentration (IC_{50}) values were determined by nonlinear regression analysis using GraphPad Prism5 and obtained from two independent set of experiments, each of which was performed in triplicate for each concentration.

FACS assay for cellular uptake: MCF-7 cells (~ 10^6) were plated in six well plates and allowed to attach for 24 h at 37 °C and 5% CO_2. Cells were then treated with **1** or doxorubicin (10 μM in 0.1% DMSO-DMEM) for 2 h, after which the media was aspirated. Cell were washed with PBS, trypsinized and collected by centrifugation. The pellets were taken in 500 μL PBS and homogenized to form single cell suspensions. Flow cytometric analysis of these samples was measured using excitation (488 nm) and emission (585 nm) channels in the red region along with proper controls. All the experiments were performed in duplicate to ascertain the results.

Confocal microscopy: Confocal microscopic images (63X) were captured using oil immersion lens of LSM710 Zeiss instrument. MCF-7 cells (~ 10^5) were allowed to adhere to cover slips in a 12-well tissue culture plate for 24 h. They were treated with compounds **1** or doxorubicin (10 μM in 0.1% DMSO-DMEM) for 2 h in light-protected conditions. After treatment, the media was aspirated, cells were washed with PBS and stained with 4,6-diamidino-2-phenylindole, dihydrochloride (DAPI, nuclear stain, 300 nM in PBS) for 5 min at room temperature. Cells were thoroughly washed to remove the excess dye. The cover slips were transferred carefully to slides containing AntifadeGold reagent (1 μl). They were fixed by coating the sides with quick-dry transparent nail-enamel. Cells treated with only 0.1% of DMSO were also stained with DAPI and used as controls to eliminate cellular auto-fluorescence and background signals. Experiments were

performed in duplicate and multiple images were recorded from each cover slip to confirm the results.

References:

S1. A. Walzl, C. Unger, N. Kramer, D. Unterleuthner, M. Scherzer, M. Hengstschläger, D. Schwanzer-Pfeiffer and H. Dolznig. The Resazurin Reduction Assay Can Distinguish Cytotoxic from Cytostatic Compounds in Spheroid Screening Assays. *SLAS DISCOVERY: Advancing Life Sciences R&D*, 2014, **19**, 1047 – 1059.

S2. Kantevari, S., Narasimhaji, C. V. & Mereyala, H. B. Bis(4,5-dimethoxy-2-nitrophenyl)ethylene glycol: a new and efficient photolabile protecting group for aldehydes and ketones. Tetrahedron 61, 5849–5854 (2005).

S3. Chiara Marinzi, John Offer, Renato Longhi, P. E. D. An o-nitrobenzyl scaffold for peptide ligation: synthesis and applications. Bioorg. Med. Chem. 12, 2749–2757 (2004).

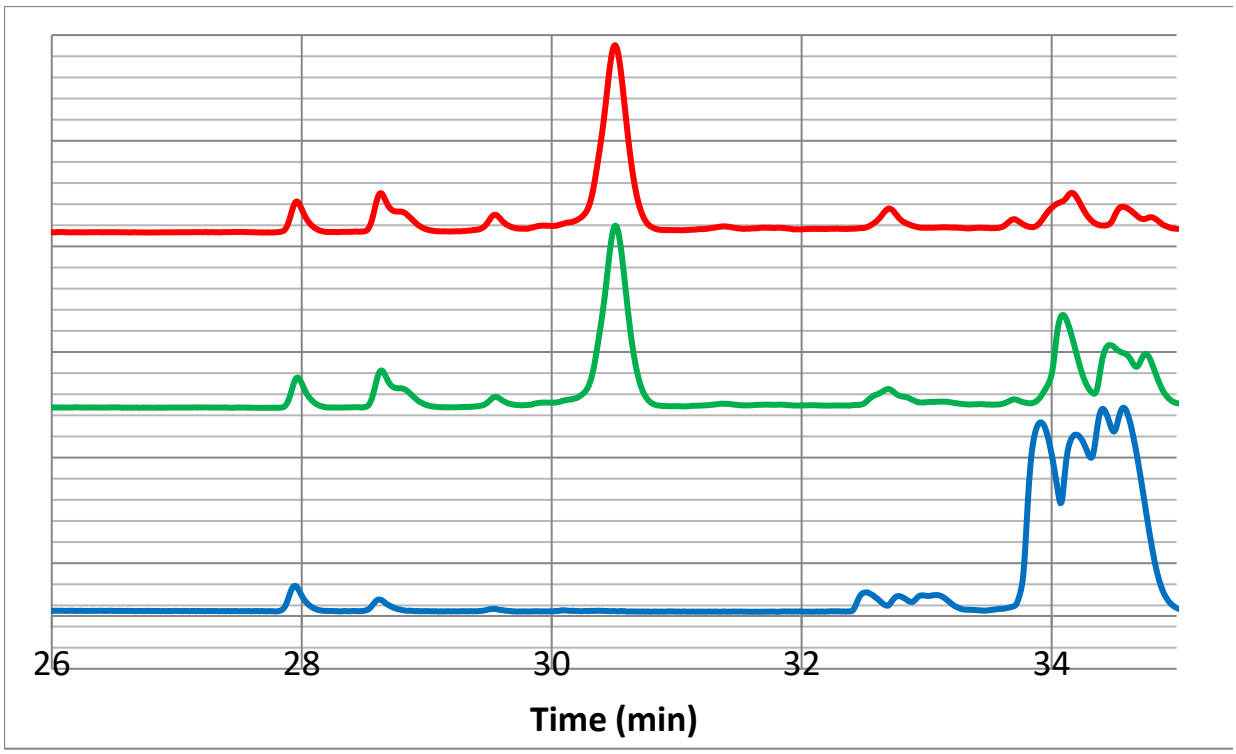


Fig. S1. Compound 1, a mixture of 4 diastereomers, but leads to a single major Dox-containing product as observed by HPLC. A 20 mM solution of compound **1** in PBS buffer was irradiated under 360 nm light (9.0 mW/cm^2) and aliquots were removed at various time points (0 min, blue; 20 min, green, and 60 min, red.). These aliquots were analyzed by RP-HPLC at λ = 480 nm.

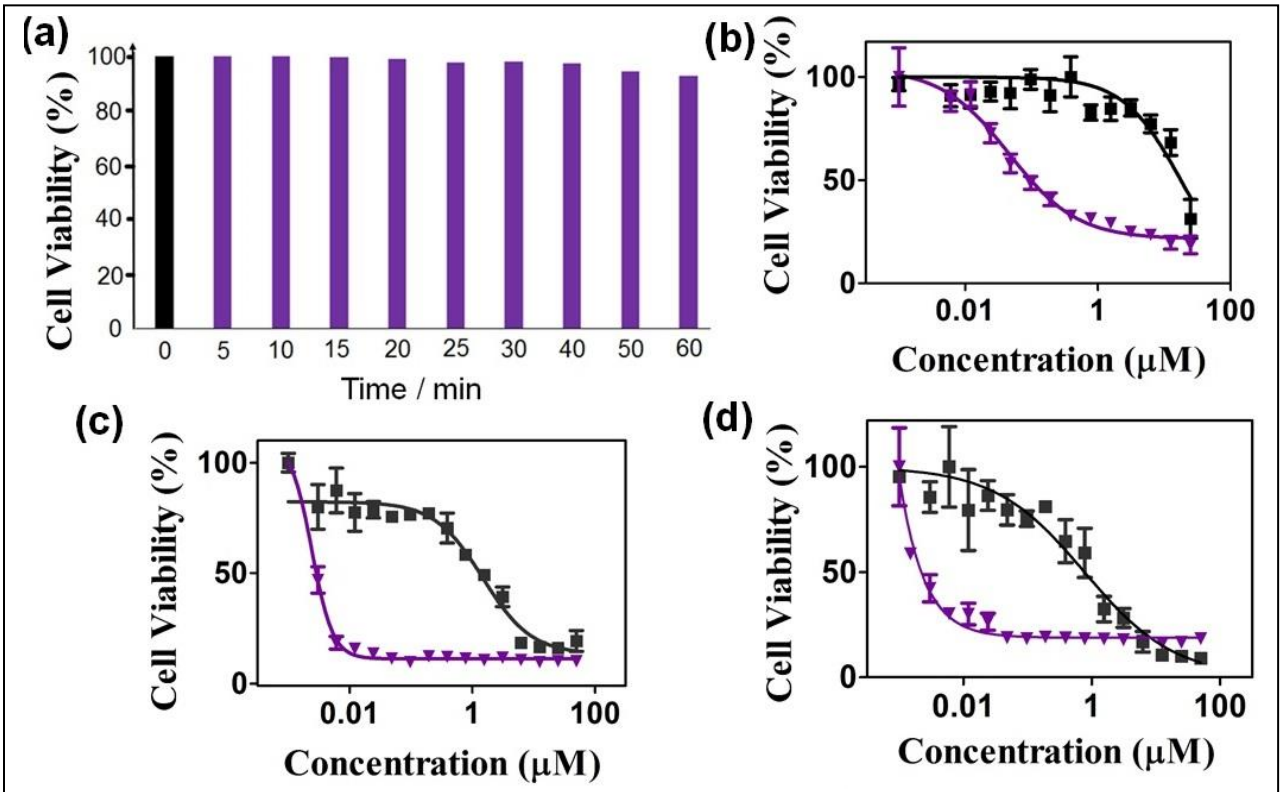


Fig. S2 (a) Bar diagram showing of MCF-7 cells kept in media containing 0.1% DMSO and exposed to different light dosages (380 nm, 9.0 $mW.cm^{-2}$) by varying the time of exposure as indicated in the figure. There was no significant reduction in viability of cells for 30 mins of exposure. Cellular viability curves as obtained from CellTiter-Blue assay in (b) MCF-7, (c) A2780 and (d) A2780ADR cell lines treated with compound **1** for 2 h followed by either light exposure (purple triangles, 380 nm, 9.0 mW/cm^2, 30 min) or kept unexposed (black squares).

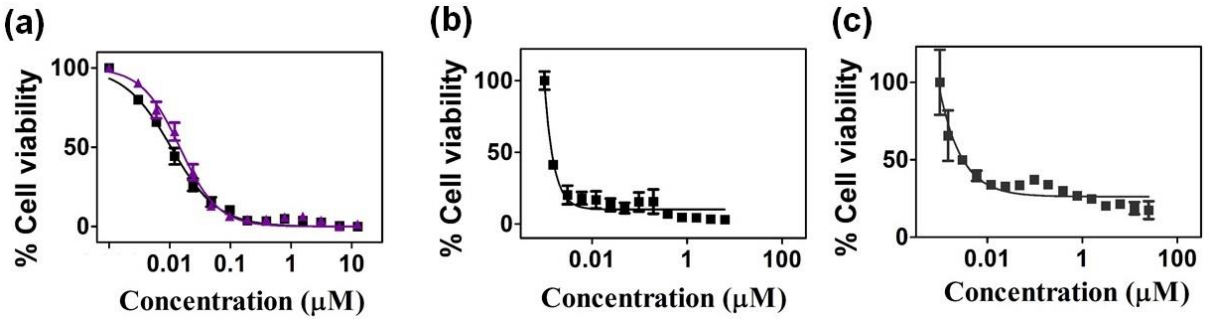


Fig. S3. Cellular viability curves as obtained from CellTiter-Blue assay in (b) MCF-7, (c) A2780 and (d) A2780ADR cell lines treated with **2P-Dox** for 2 h followed by either light exposure (purple triangles, 380 nm, 9.0 mW/cm^2, 30 min) or kept unexposed (black squares).

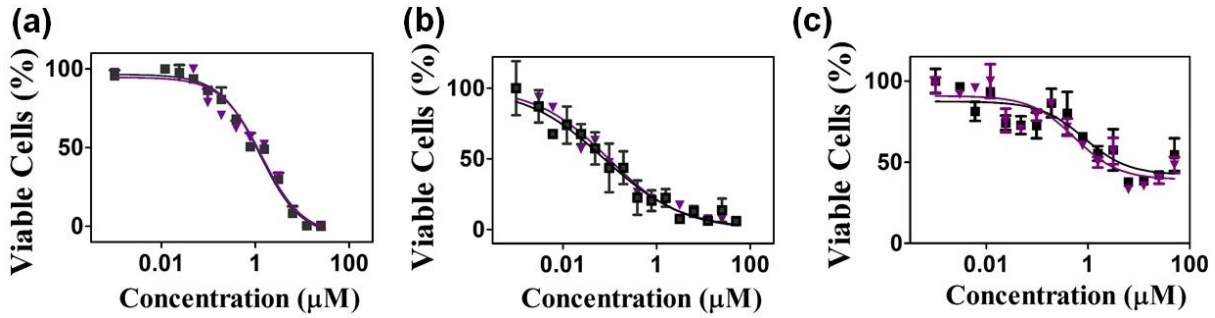


Fig. S4. Cellular viability curves as obtained from CellTiter-Blue assay in (a) MCF-7, (b) A2780 and (c) A2780ADR cell lines treated with doxorubicin for 2 h followed by either light exposure (purple triangles, 380 nm, 9.0 mW/cm^2, 30 min) or kept unexposed (black squares).

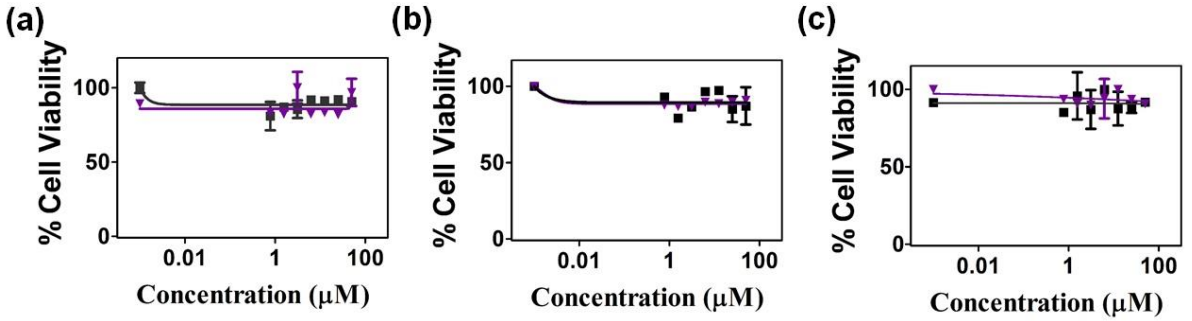


Fig. S5. Cellular viability curves as obtained from CellTiter-Blue assay in (a) MCF-7, (b) A2780 and (c) A2780ADR cell lines treated with control compound **7** for 2 h followed by either light exposure (purple triangles, 380 nm, 9.0 mW/cm^2, 30 min) or kept unexposed (black squares).

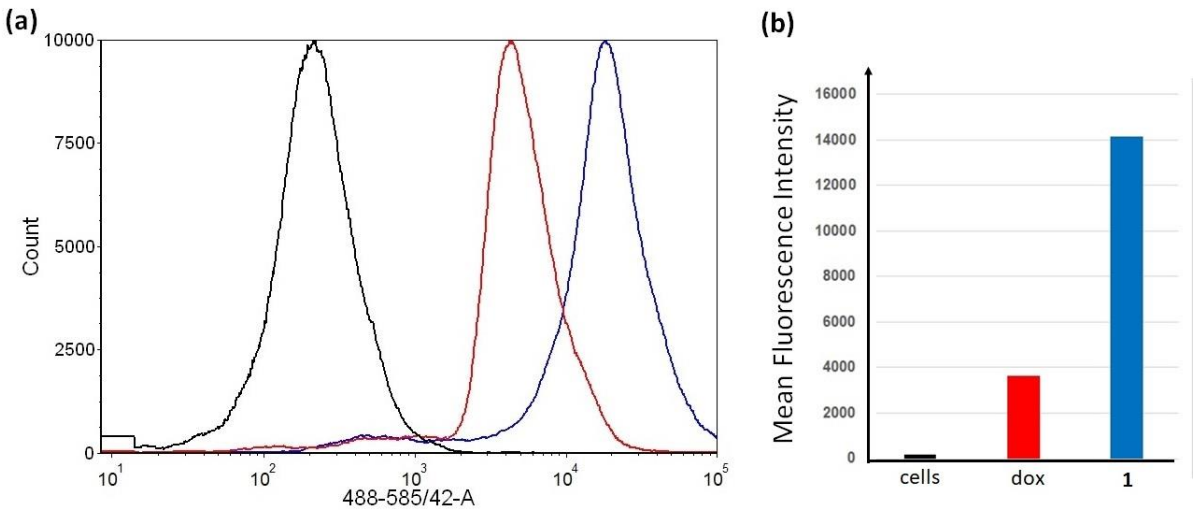
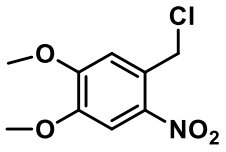
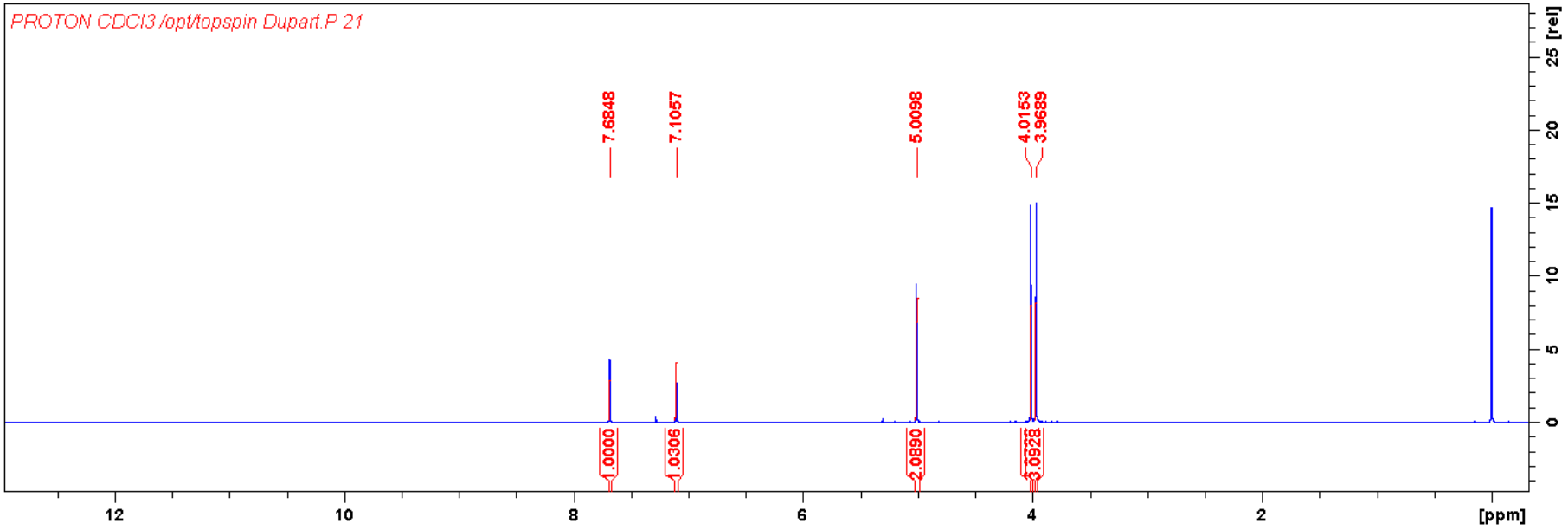


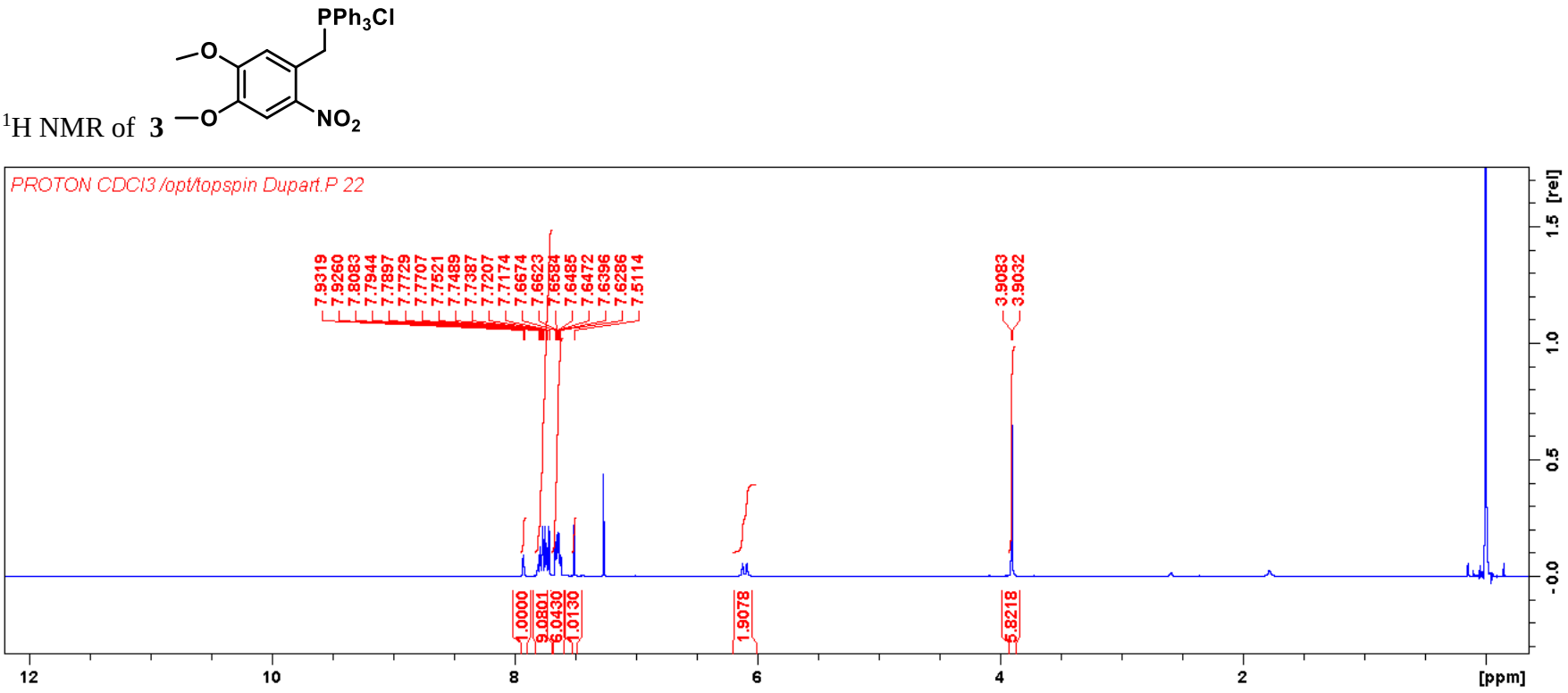
Fig. S6. Histograms depicting cellular uptake of compound **1** (blue) and doxorubicin (red) in MCF-7 cells after 2 h of treatment as obtained from flow cytometric analysis. A shift of the band to the right denotes higher mean fluorescence intensity and hence higher cellular uptake of the compounds. Cells alone (black) was taken as a control. (b) Bar diagram obtained from the same experiment showing mean fluorescence intensity for cells alone (black), doxorubicin (red) and compound **1** (blue) in MCF-7 cells.

NMR figures

^{1}HNMR of 



^{1}H NMR of **3**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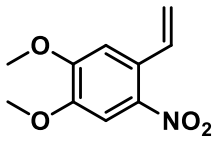
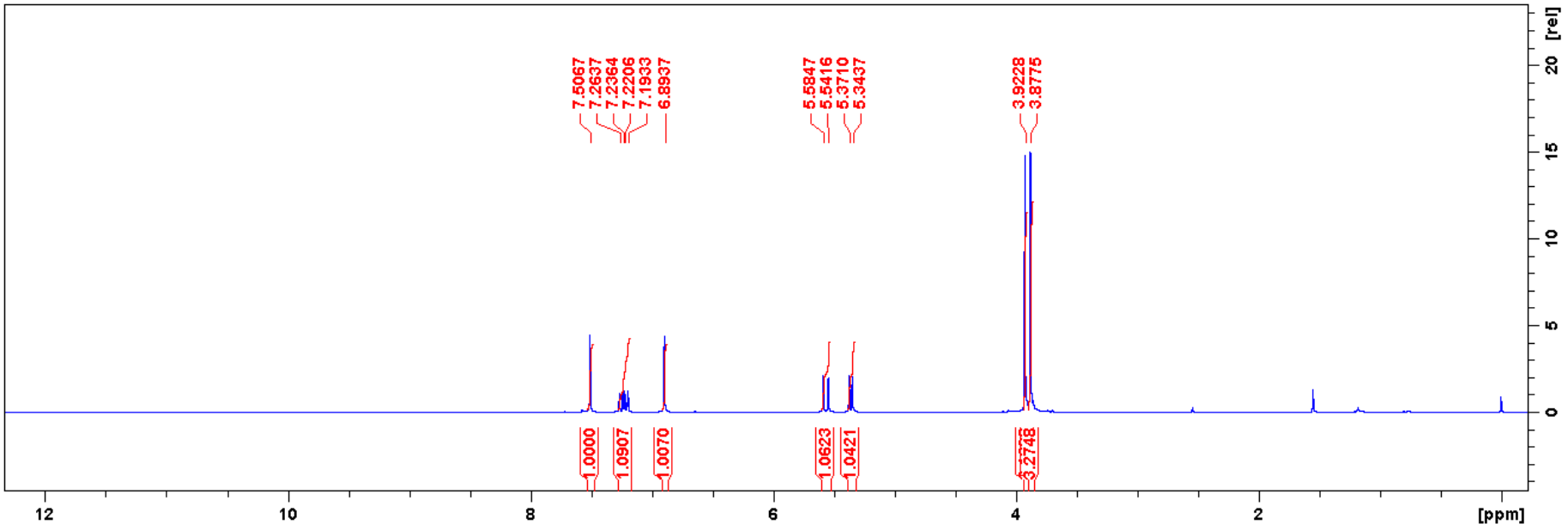
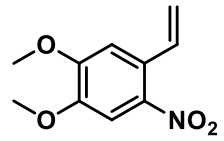
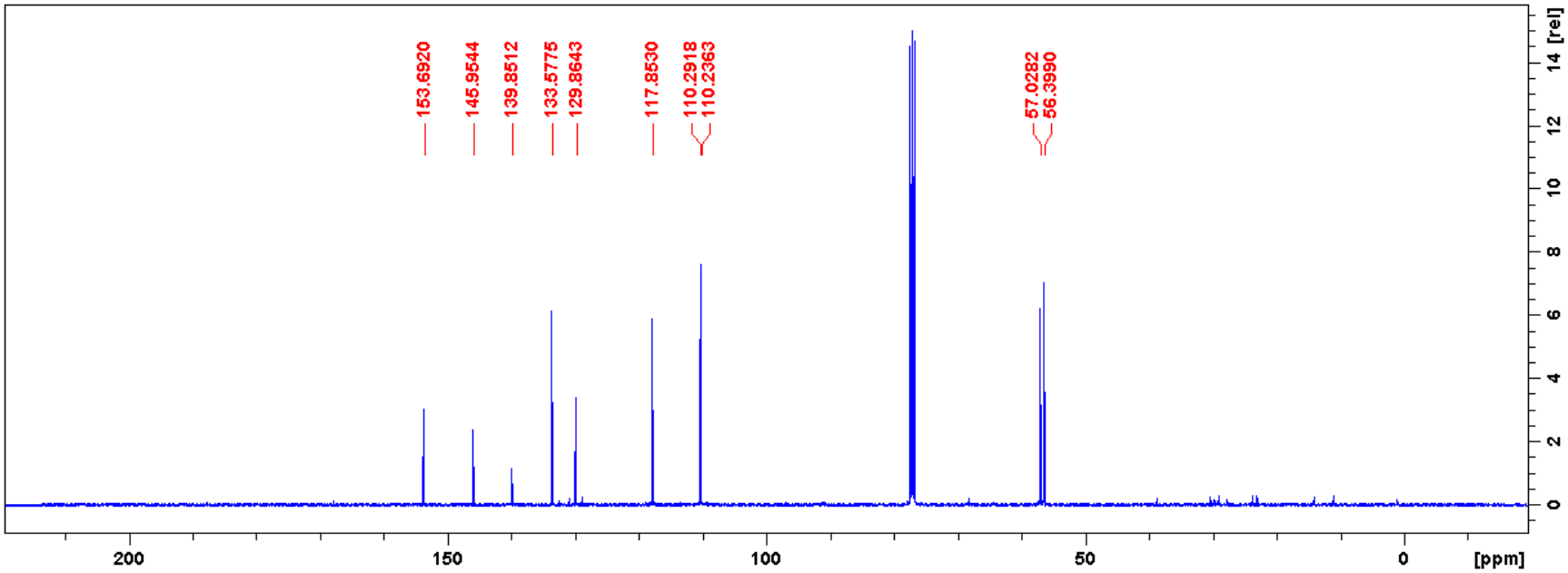
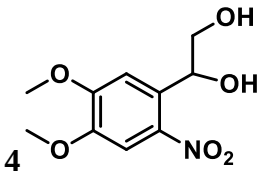
^{1}H NMR of 
O
O
NO2

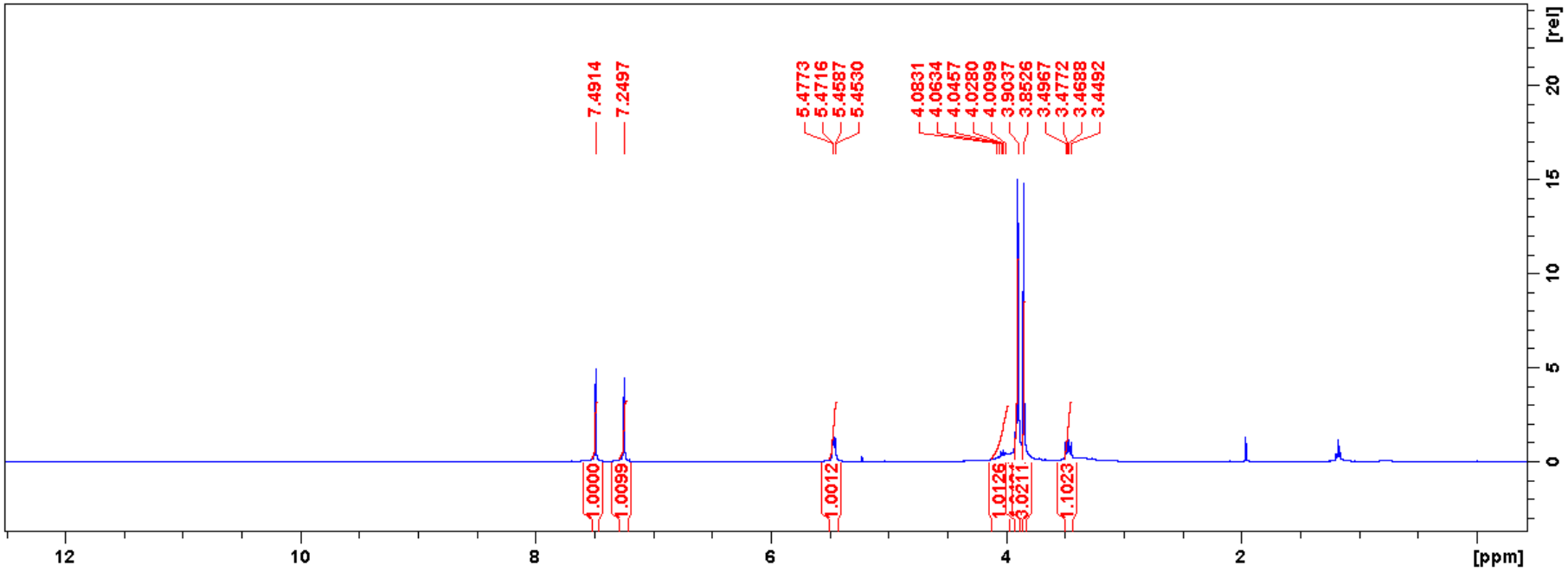

7.5067
7.2637
7.2364
7.2206
7.1933
6.8937
5.5847
5.5416
5.3710
5.3437
3.9228
3.8775
1.0000
1.0907
1.0070
1.0623
1.0421
3.2748
[rel]
20
15
10
5
0
12
10
8
6
4
2
[ppm]

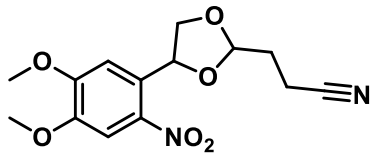
^{13}C NMR of 
O
O
NO2

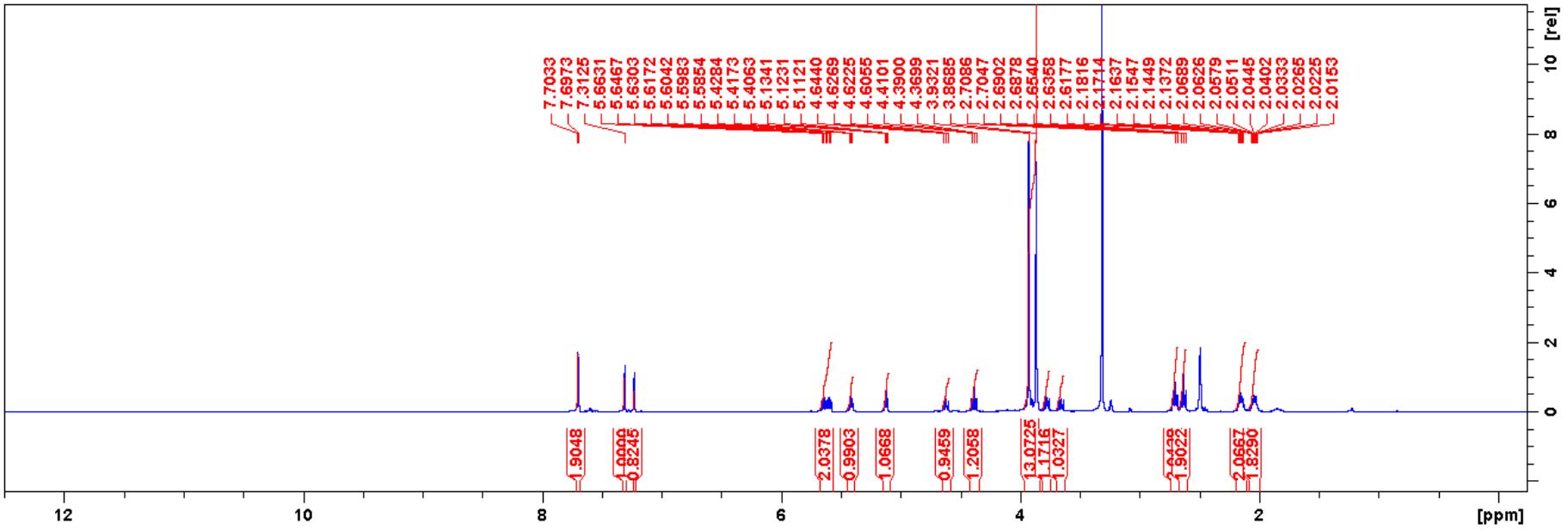

153.6920
145.9544
139.8512
133.5775
129.8643
117.8530
110.2918
110.2363
57.0282
56.3990
200
150
100
50
0
[ppm]
0
2
4
6
8
10
12
14 [rel]

^{1}H NMR of **4**

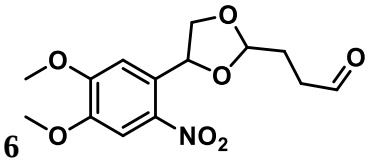

OH
OH
O
O
NO2

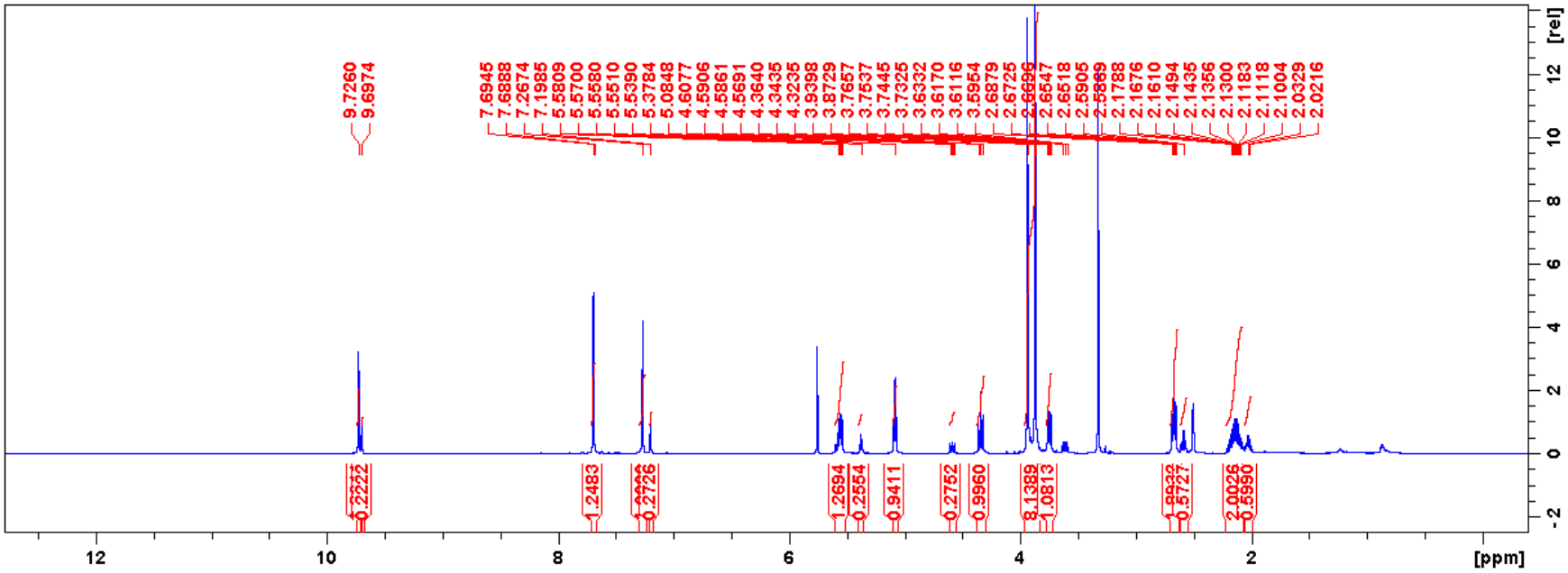

7.4914
7.2497
5.4773
5.4716
5.4587
5.4530
4.0831
4.0634
4.0457
4.0280
4.0099
3.9037
3.8526
3.4967
3.4772
3.4688
3.4492
1.0000
1.0099
1.0012
1.0126
4.0211
1.1023
12
10
8
6
4
2
[ppm]
[rel]
0
5
10
15
20

^{1}H NMR of 

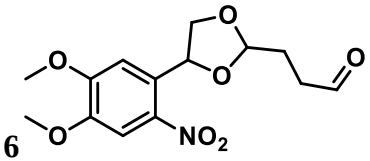

7.7033
7.6973
7.3125
5.6631
5.6467
5.6303
5.6172
5.6042
5.5983
5.5854
5.4284
5.4173
5.4063
5.1341
5.1231
5.1121
4.6440
4.6269
4.6225
4.6055
4.4101
4.3900
4.3699
3.9321
3.8685
2.7086
2.7047
2.6902
2.6878
2.6540
2.6358
2.6177
2.1816
2.1714
2.1637
2.1547
2.1449
2.1372
2.0689
2.0626
2.0579
2.0511
2.0445
2.0402
2.0333
2.0265
2.0225
2.0153
1.9048
1.0000
0.8245
2.0378
0.9903
1.0668
0.9459
1.2058
13.0725
1.1716
1.0327
2.0439
1.9022
2.0667
1.8290
12
10
8
6
4
2
[ppm]
10
8
6
4
2
0
[rel]

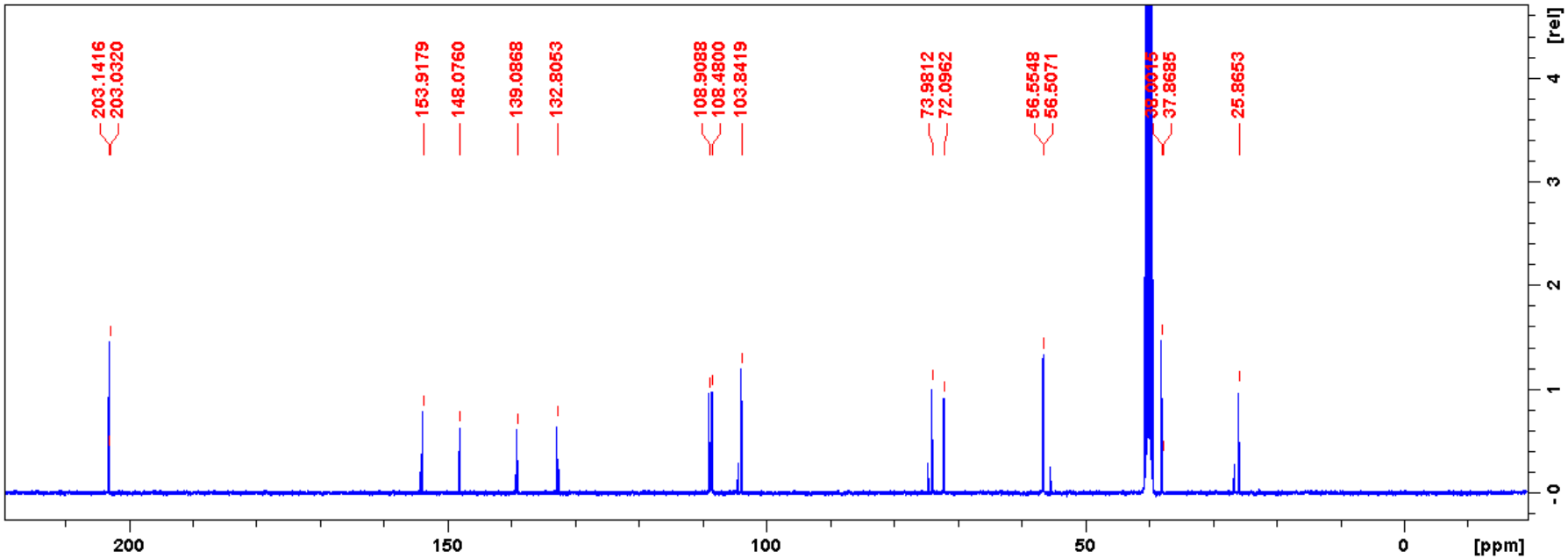
^{1}H NMR of **6**

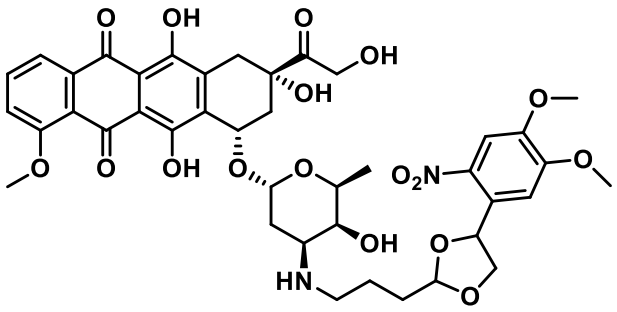

O
O
O
O
O
NO2


9.7260
9.6974
7.6945
7.6888
7.2674
7.1985
5.5809
5.5700
5.5580
5.5510
5.5390
5.3784
5.0848
4.6077
4.5906
4.5861
4.5691
4.3640
4.3435
4.3235
3.9398
3.8729
3.7657
3.7537
3.7445
3.7325
3.6332
3.6170
3.6116
3.5954
2.6879
2.6725
2.6547
2.6518
2.5905
2.5869
2.1788
2.1676
2.1610
2.1494
2.1435
2.1356
2.1300
2.1183
2.1118
2.1004
2.0329
2.0216
1.2483
1.2694
0.2554
0.9411
0.2752
0.9960
1.0813
0.5727
2.0025
0.5990
12
10
8
6
4
2
[ppm]
[rel]

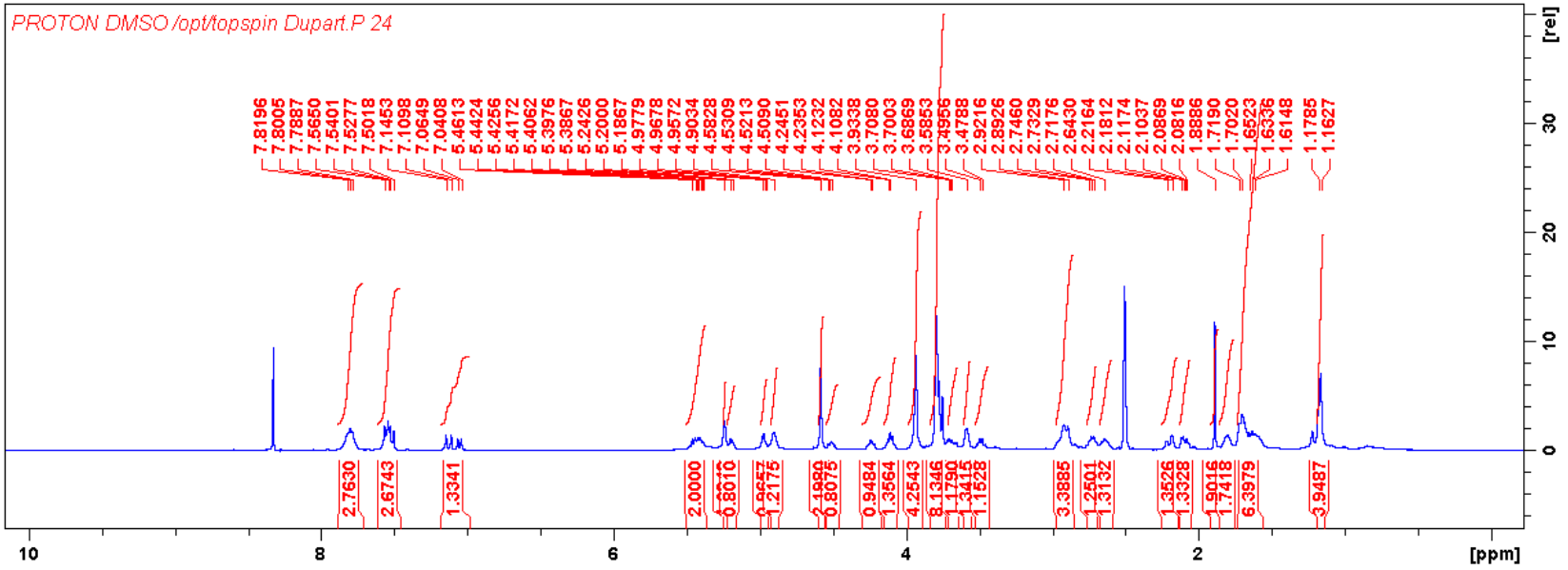
^{13}C NMR of **6**

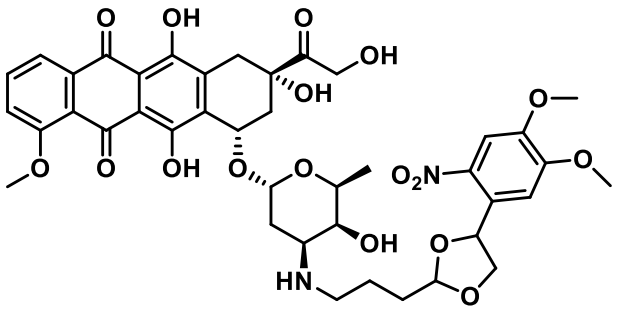

O
O
O
O
O
NO2


203.1416
203.0320
153.9179
148.0760
139.0868
132.8053
108.9088
108.4800
103.8419
73.9812
72.0962
56.5548
56.5071
37.8685
25.8653
200
150
100
50
0
[ppm]
[rel]

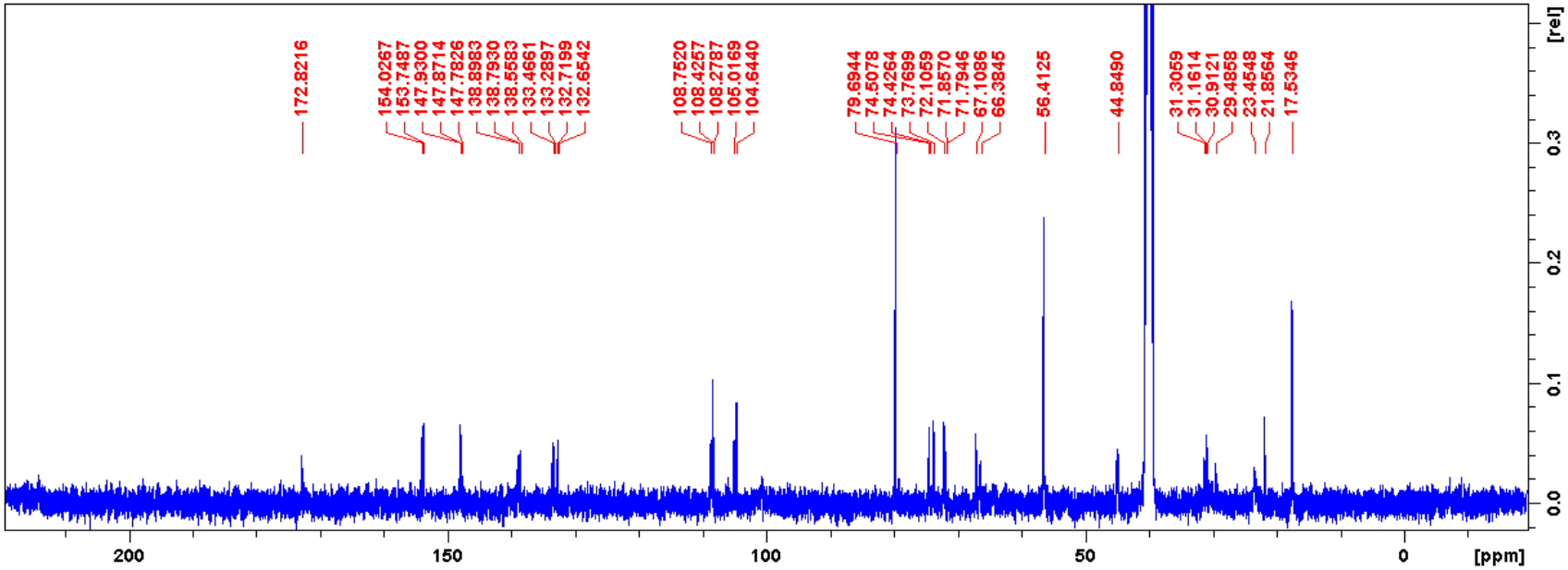

O
OH
O
OH
OH
O
O
OH
O
O
O
O
O2N
O
OH
HN
O
O

^{1}HNMR of **1**

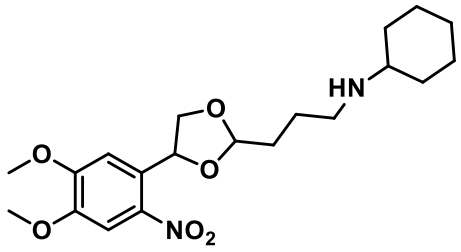

PROTON DMSO /opt/topspin Dupart.P 24
7.8196
7.8005
7.7887
7.5650
7.5401
7.5277
7.5018
7.1453
7.1098
7.0649
7.0408
5.4613
5.4424
5.4256
5.4172
5.4062
5.3976
5.3867
5.2426
5.2000
5.1867
4.9779
4.9678
4.9572
4.9034
4.5828
4.5309
4.5213
4.5090
4.2451
4.2353
4.1232
4.1082
3.9338
3.7080
3.7003
3.6869
3.5853
3.4956
3.4788
2.9216
2.8926
2.7460
2.7329
2.7176
2.6430
2.2164
2.1812
2.1174
2.1037
2.0869
2.0816
1.8886
1.7190
1.7020
1.6523
1.6336
1.6148
1.1785
1.1627
2.7630
2.6743
1.3341
2.0000
0.8010
0.9657
1.2175
2.1880
0.8075
0.9484
1.3564
4.2543
8.1346
1.1790
1.1415
1.1528
3.3885
1.2501
1.3132
1.3526
1.3328
1.9016
1.7418
6.3979
3.9487
10
8
6
4
2
[ppm]
[rel]
0
10
20
30

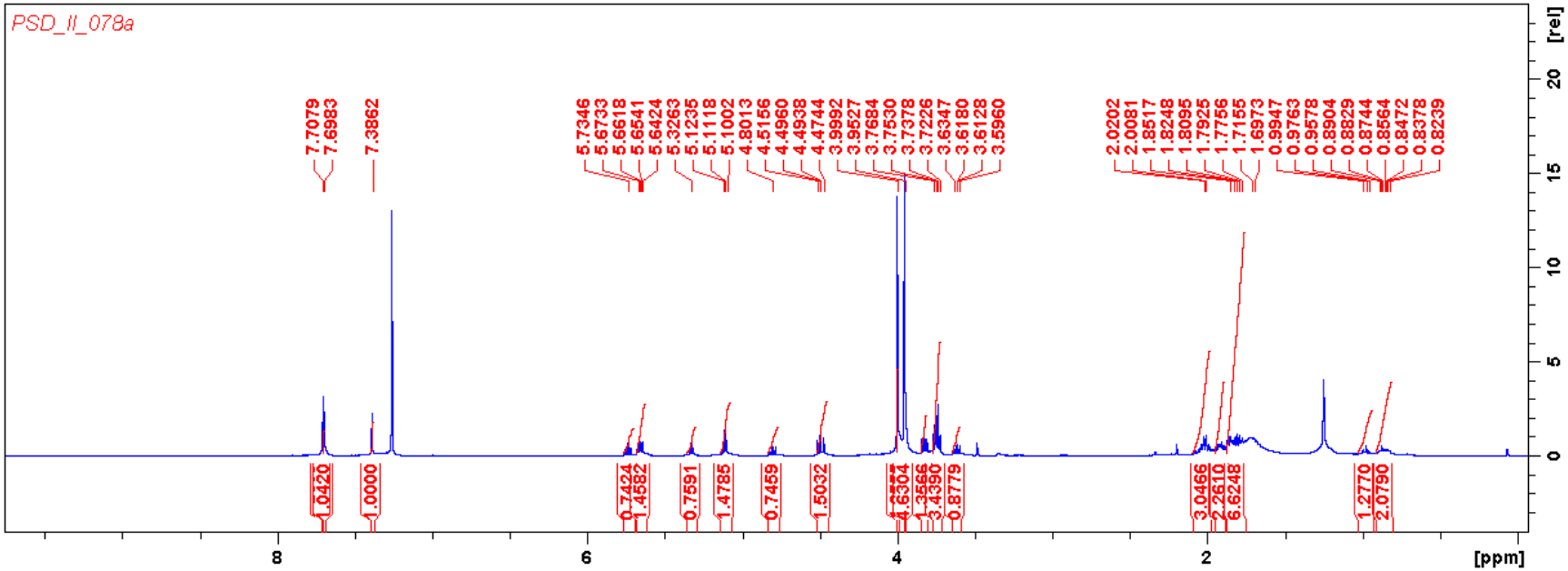


^{13}C NMR of **1**


172.8216
154.0267
153.7487
147.9300
147.8714
147.7826
138.8983
138.7930
138.5583
133.4661
133.2897
132.7199
132.6542
108.7520
108.4257
108.2787
105.0169
104.6440
79.6944
74.5078
74.4264
73.7699
72.1059
71.8570
71.7946
67.1086
66.3845
56.4125
44.8490
31.3059
31.1614
30.9121
29.4858
23.4548
21.8564
17.5346
[rel]
0.0
0.1
0.2
0.3
200
150
100
50
0
[ppm]

^{1}HNMR of **7**


HN
O
O
O
O
NO2


PSD_II_078a
7.7079
7.6983
7.3862
5.7346
5.6733
5.6618
5.6541
5.6424
5.3263
5.1235
5.1118
5.1002
4.8013
4.5156
4.4960
4.4938
4.4744
3.9992
3.9527
3.7684
3.7530
3.7378
3.7226
3.6347
3.6180
3.6128
3.5960
2.0202
2.0081
1.8517
1.8248
1.8095
1.7925
1.7756
1.7155
1.6973
0.9947
0.9763
0.9578
0.8904
0.8829
0.8744
0.8564
0.8472
0.8378
0.8239
1.0420
1.0000
0.7424
1.4582
0.7591
1.4785
0.7459
1.5032
4.6304
1.3566
3.4390
0.8779
3.0466
2.2610
6.6248
1.2770
2.0790
8
6
4
2
[ppm]
[rel]
0
5
10
15
20