

Electronic Supplementary Information

Photocaged histone deacetylase inhibitors as prodrugs in targeted cancer therapy

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1. Supplemental Figures

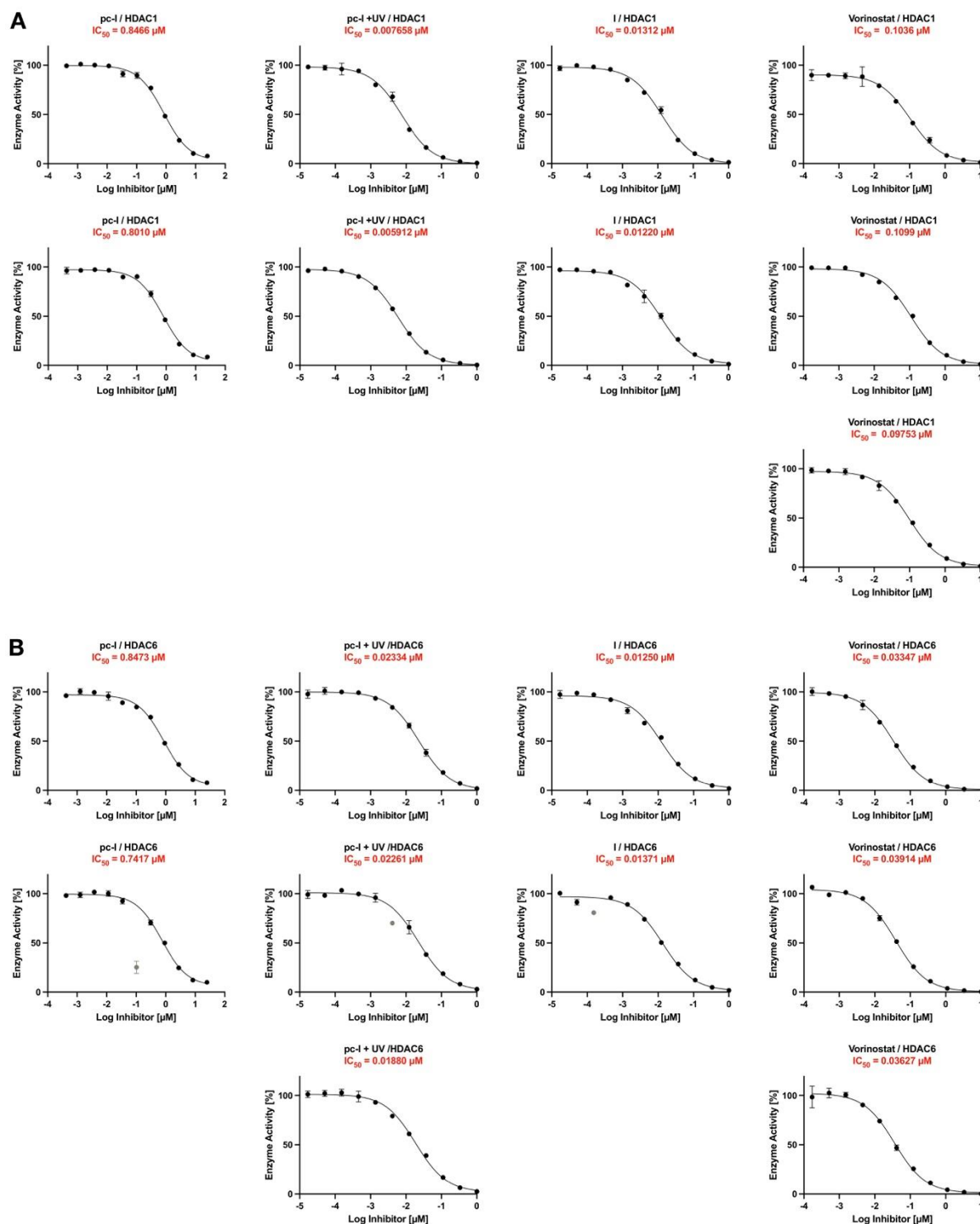


Figure S1. Normalized dose-response curves of the *in vitro* HDAC inhibition assays against HDAC1 (A) and HDAC6 (B). Data points which were used to calculate the IC_{50} values are depicted as black dots including the respective error bars (standard deviation). Excluded data points are depicted in grey. In some cases, more than two experiments were performed. Additionally, depending on the plate layout and the quantity of the investigated compounds, not all compounds were investigated in one assay run. Vorinostat was included in every assay run as a control compound.

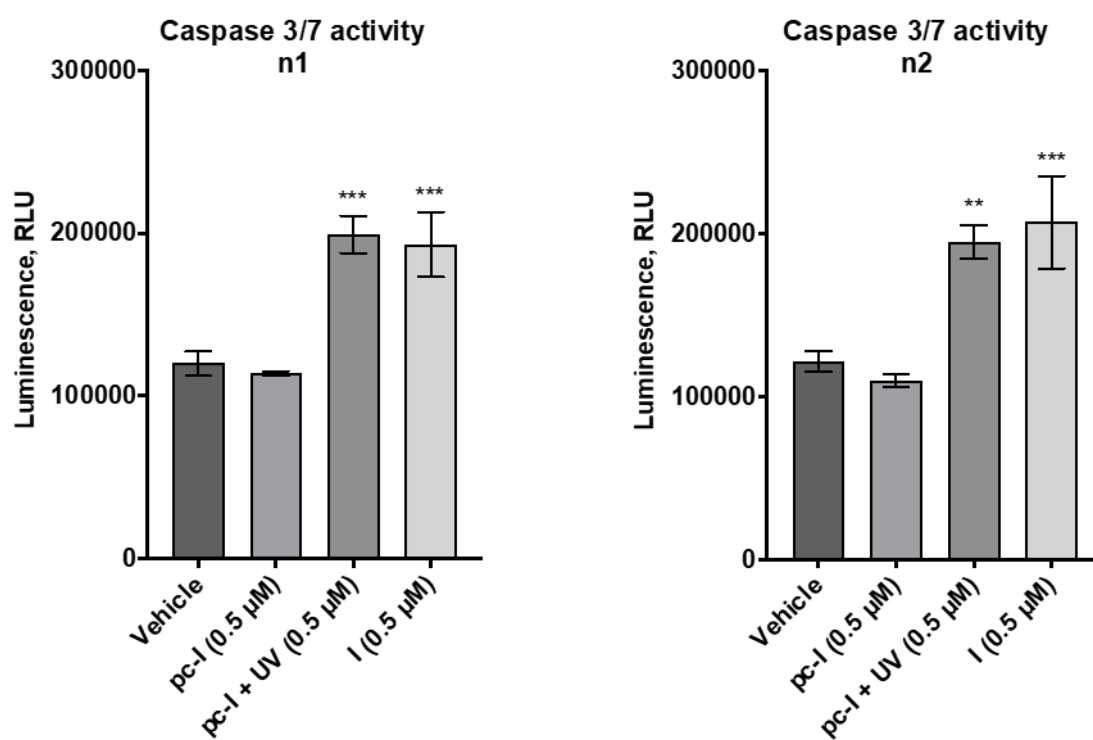


Figure S2. A2780 cells were treated with the indicated concentrations of pc-I, pc-I + UV, I and vehicle (DMSO) for 24h. Afterwards cells were incubated with Caspase-Glo 3/7 substrate and luminescence was determined. The assay was performed in two independent experiments (n1 and n2). Statistical analysis was calculated by one-way ANOVA (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

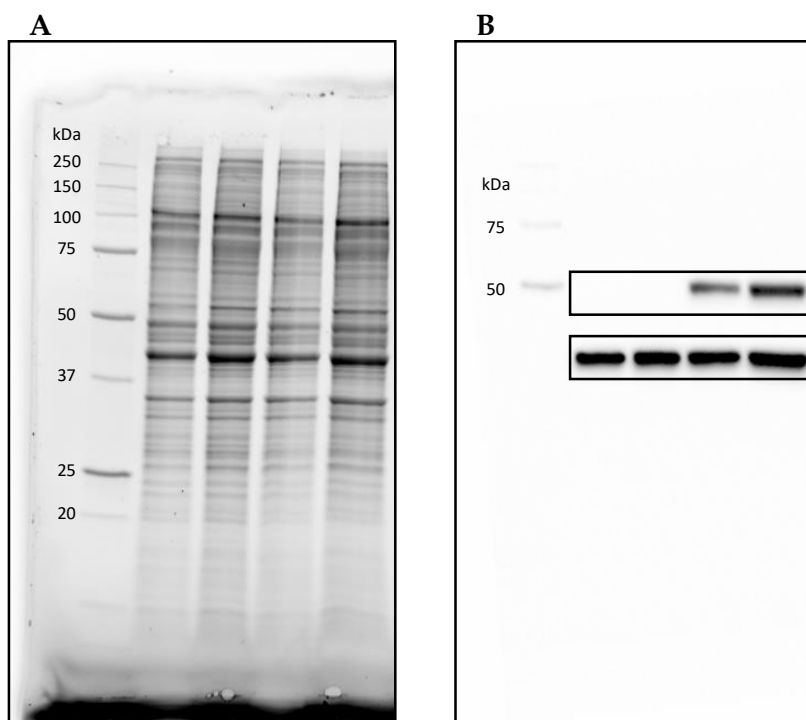


Figure S3. Original images of acetylated α -tubulin immunoblots. **A** shows the stain free detection image of the gel. **B** shows the image of the visualization of the selected acetylated α -tubulin and GAPDH bands.

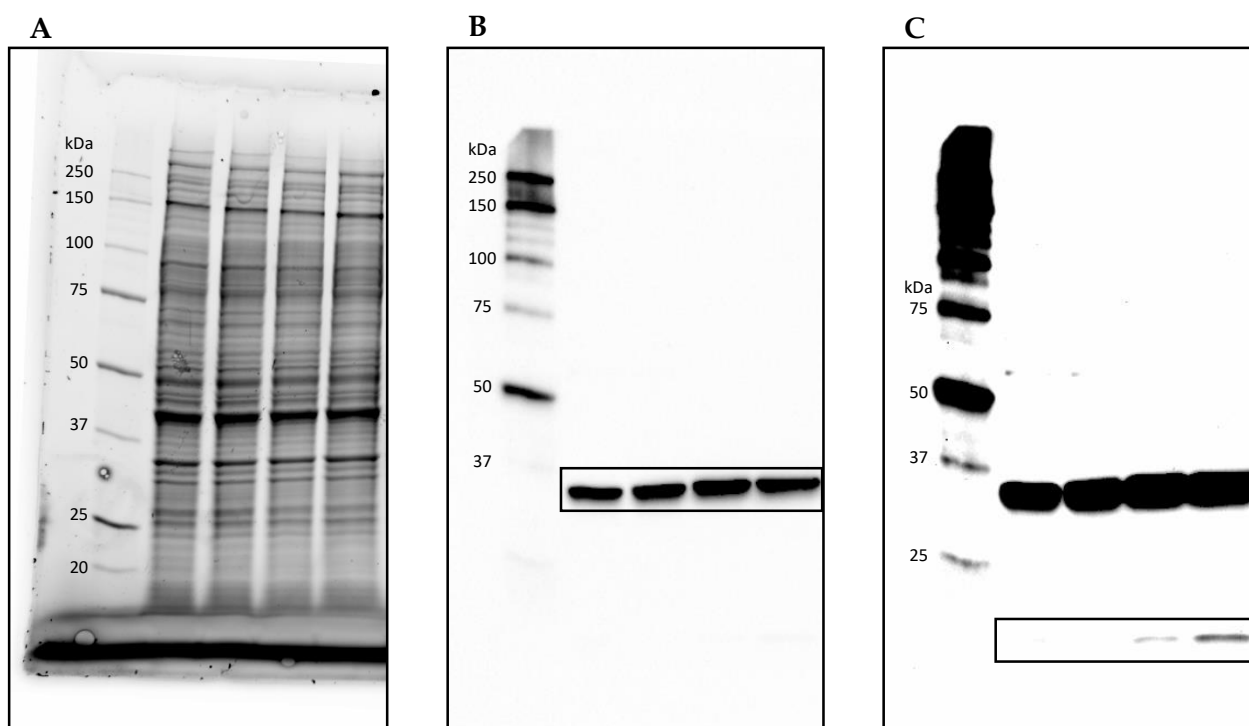


Figure S4. Original images of acetylated histone H3 immunoblots. **A** shows the stain free detection image of the gel. **B** shows the image of the visualization of the GAPDH band. **C** shows the image of the selected acetylated histone H3 band after longer visualization time.

2. Photouncaging Experiments

Photolysis (photouncaging) of photocaged HDACi prodrugs was performed at room temperature using an UVP CL-1000 Crosslinker (Analytik Jena GmbH, Jena, Germany) equipped with five UV-A tubes (F8T5/BL368; $\lambda_{\text{max}} = 365 \text{ nm}$; Analytik Jena GmbH, Jena, Germany). Hereafter, this entire experimental set-up will be referred to as the "UV-reactor".

For the deprotection experiments 10 μL of a 1.0 mM DMSO-solution of the respective compound were irradiated for 10 min using the UV-reactor described above. Subsequently, 90 μL acetonitrile were added and the samples were analyzed via HPLC. The amount of photo-cleaved HDACi was determined by comparison with a five-point calibration curve of the respective parent inhibitor using HPLC/UV detection at an appropriate wavelength (area under the curve; area $\text{mAu} \cdot \text{min}$).

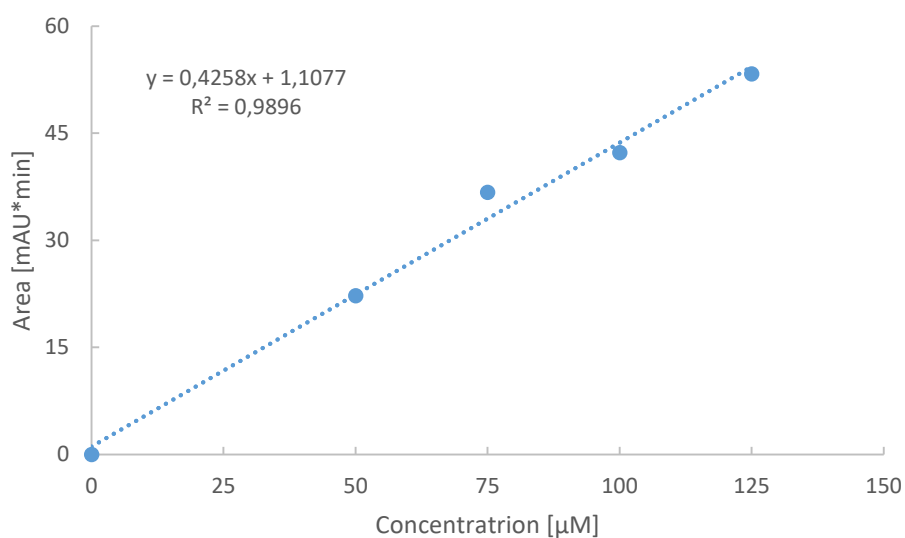


Figure S5. Calibration curve of DDK-137 (I).

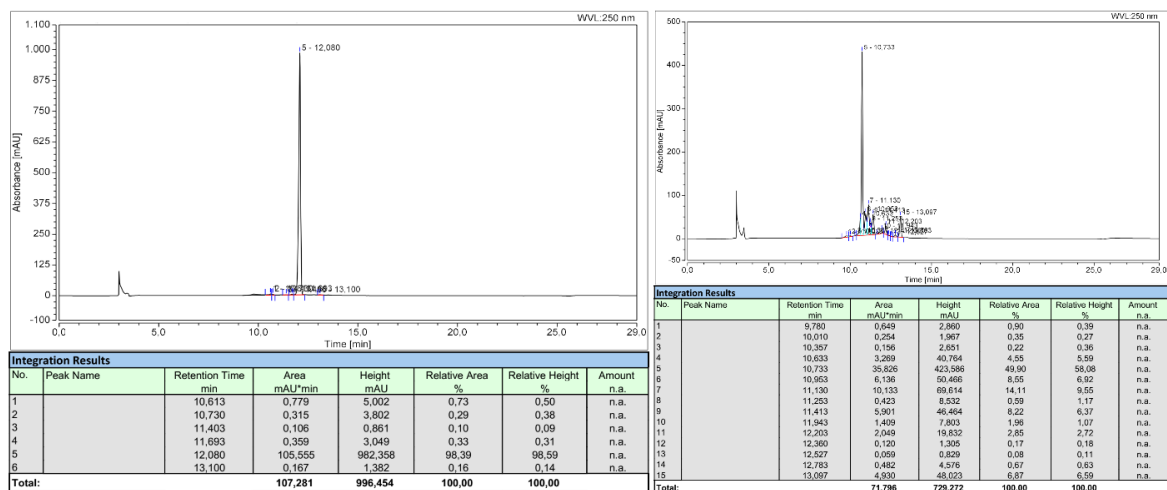


Figure S5. Representative chromatograms of **pc-I** before irradiation (left) and after 10 min of irradiation (right) with light at 365 nm. Initial concentration of **pc-I**: 100 μ M. Concentration of photo-released **I** (t_R = 10.73 min) after irradiation: 81.5 μ M (82%).

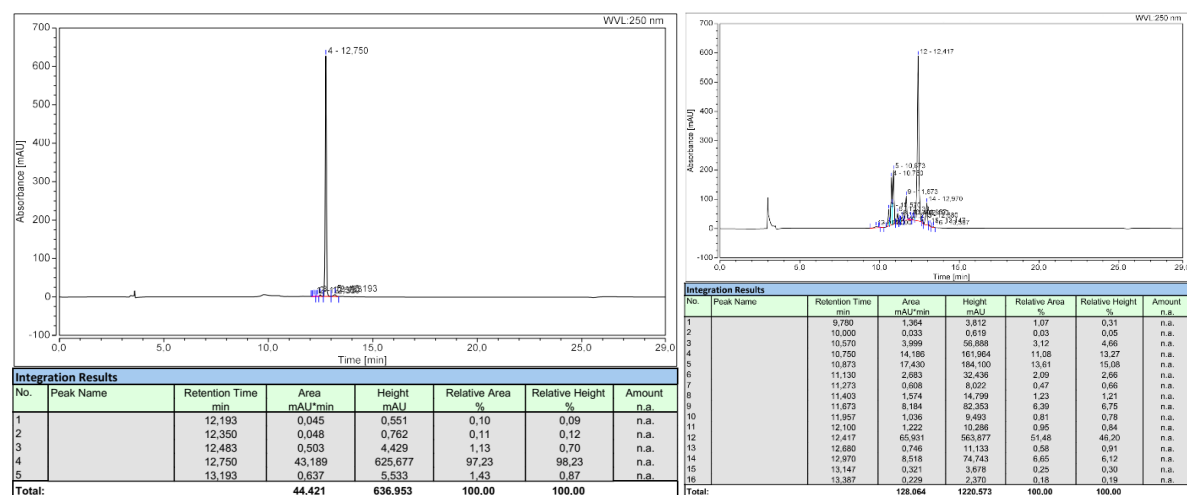
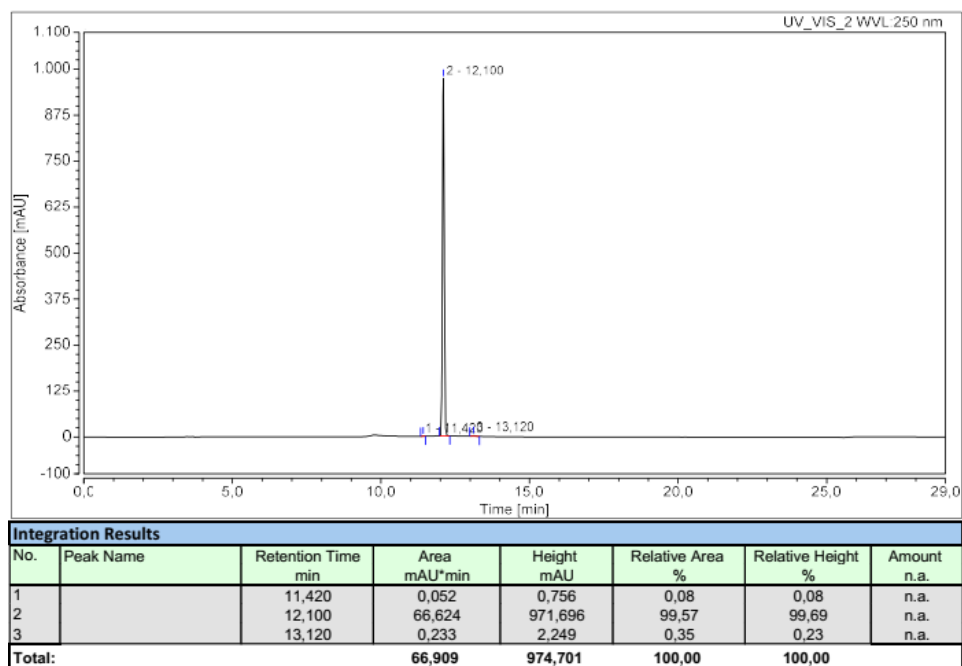


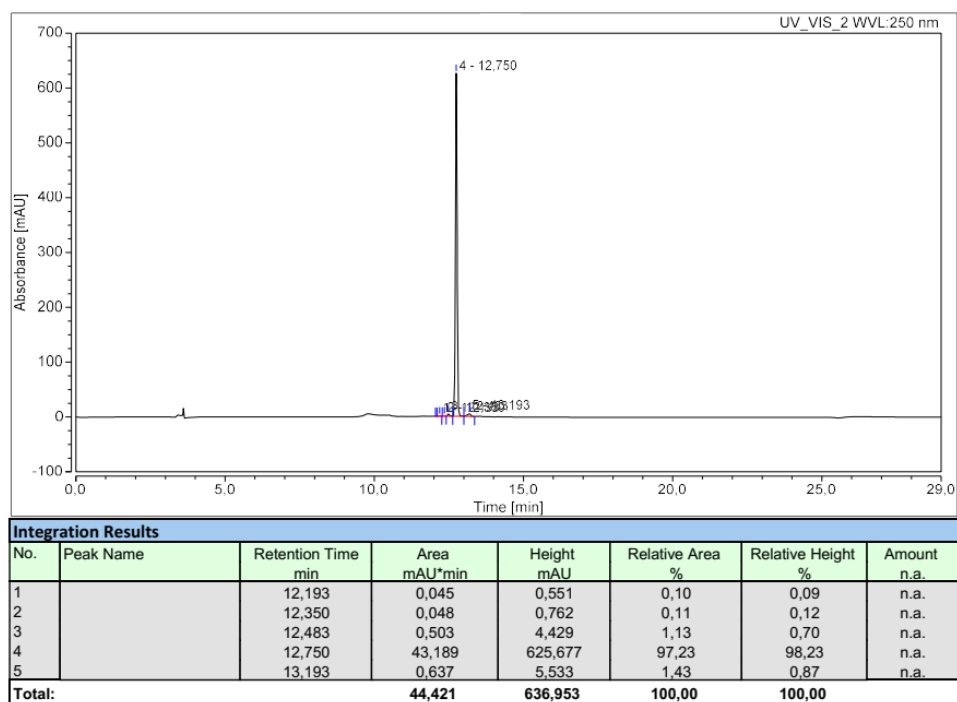
Figure S6. Representative chromatograms of **pc-II** before irradiation (left) and after 10 min of irradiation (right) with light at 365 nm. Initial concentration of **pc-II**: 100 μ M. Concentration of photo-released **II** (t_R = 10.89 min) after irradiation: not detected.

3. HPLC Chromatograms

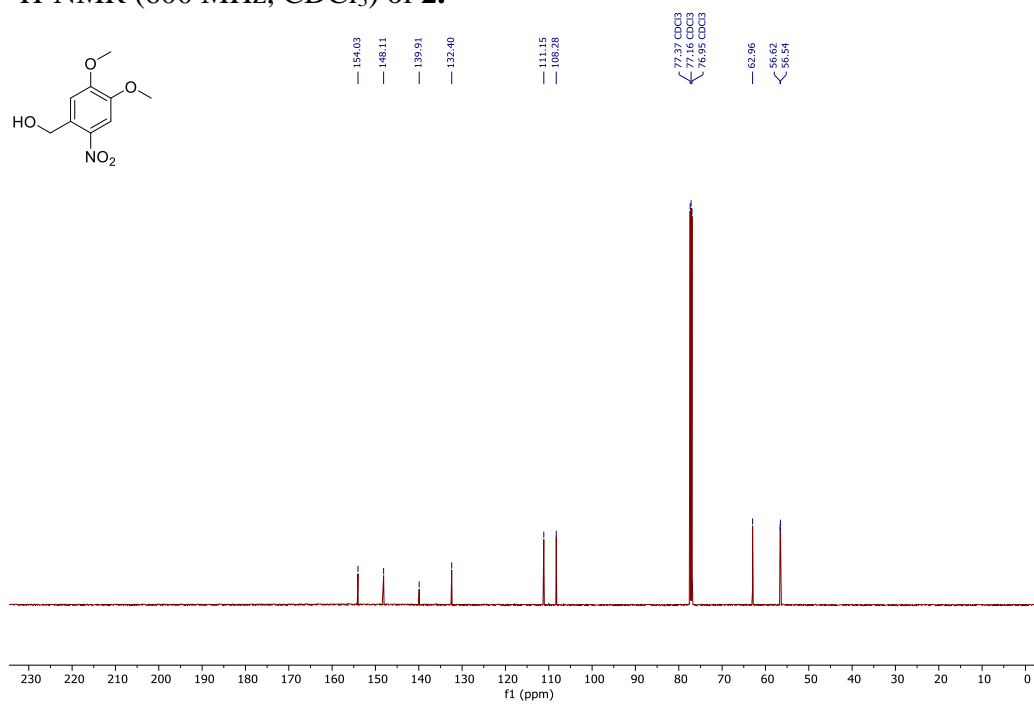
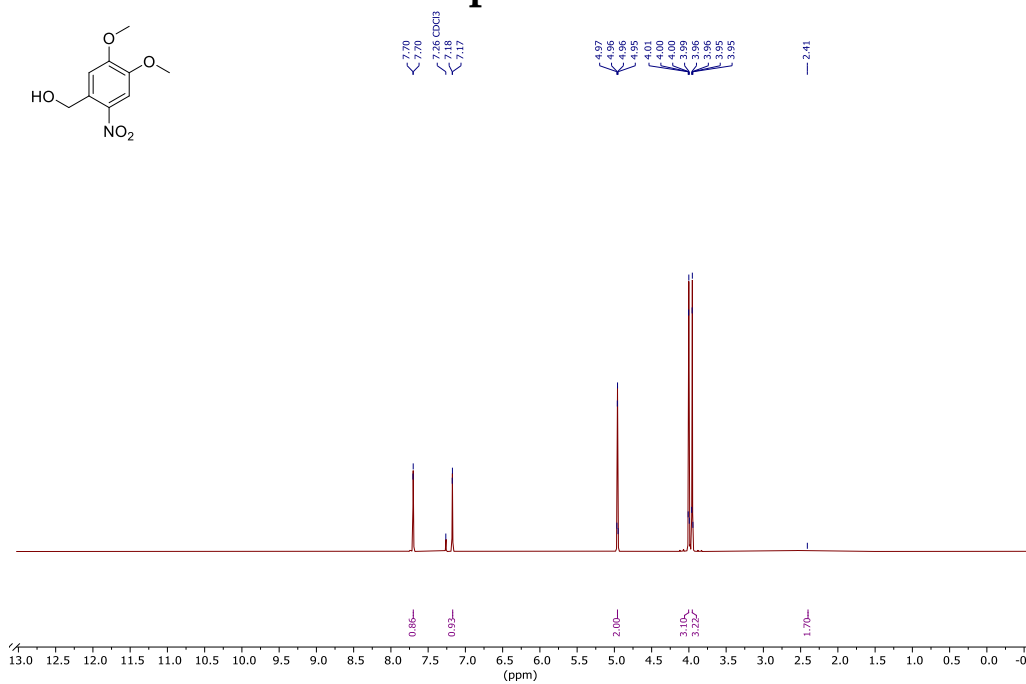
HPLC chromatogram of **pc-I** (purity: 99.6 %)

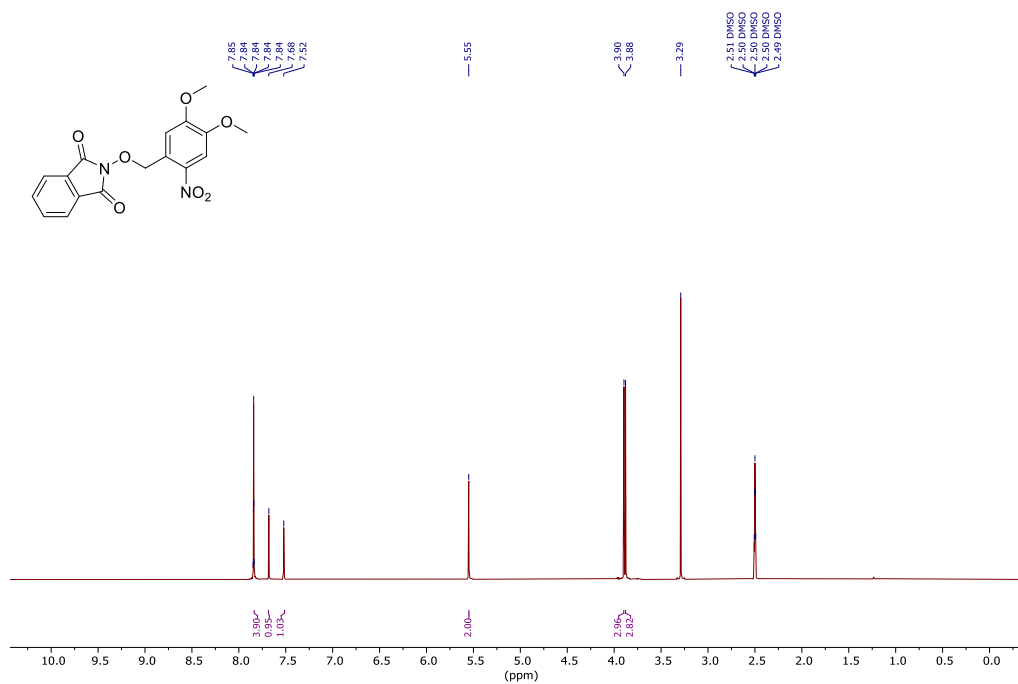


HPLC chromatogram of **pc-II** (purity: 97.2 %).

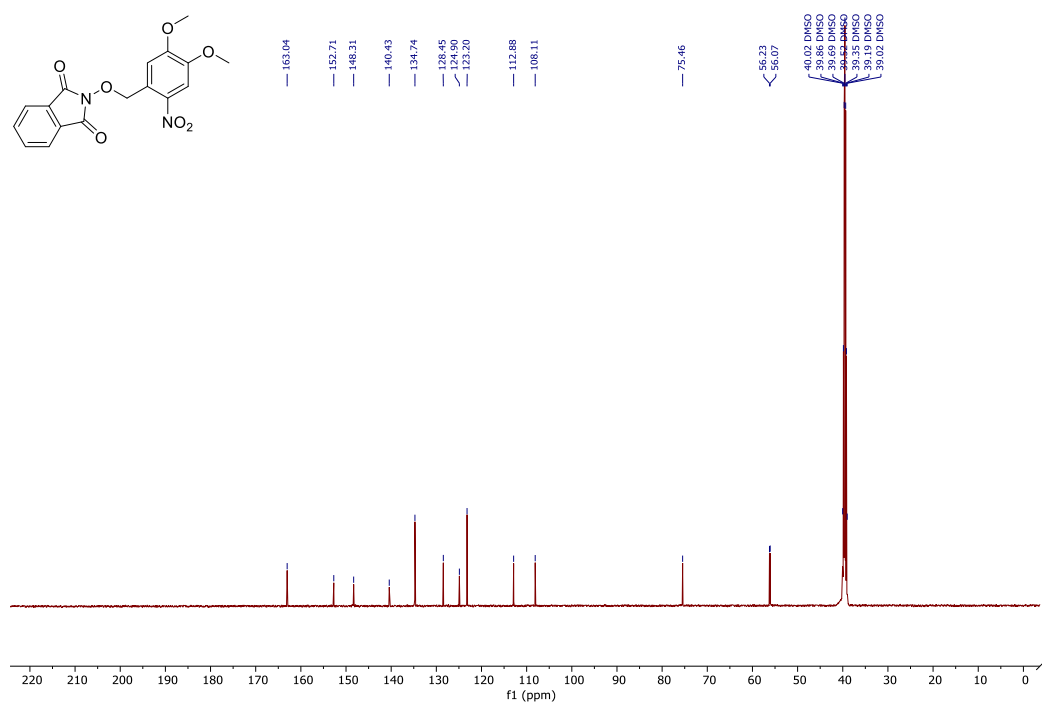


4. ^1H and ^{13}C NMR Spectra

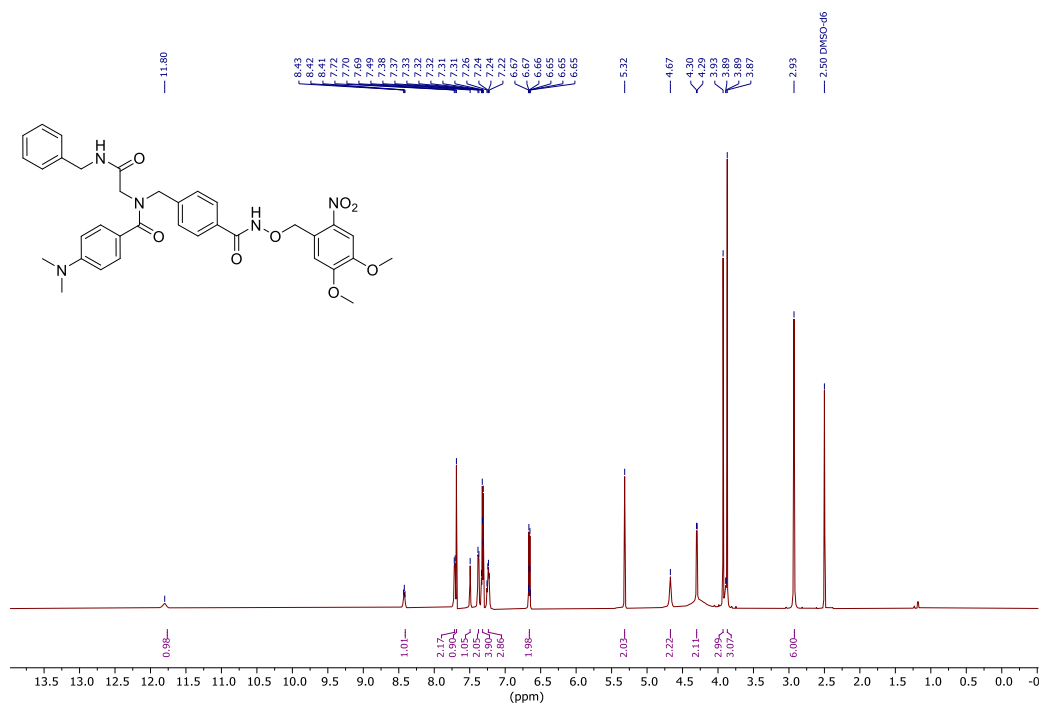




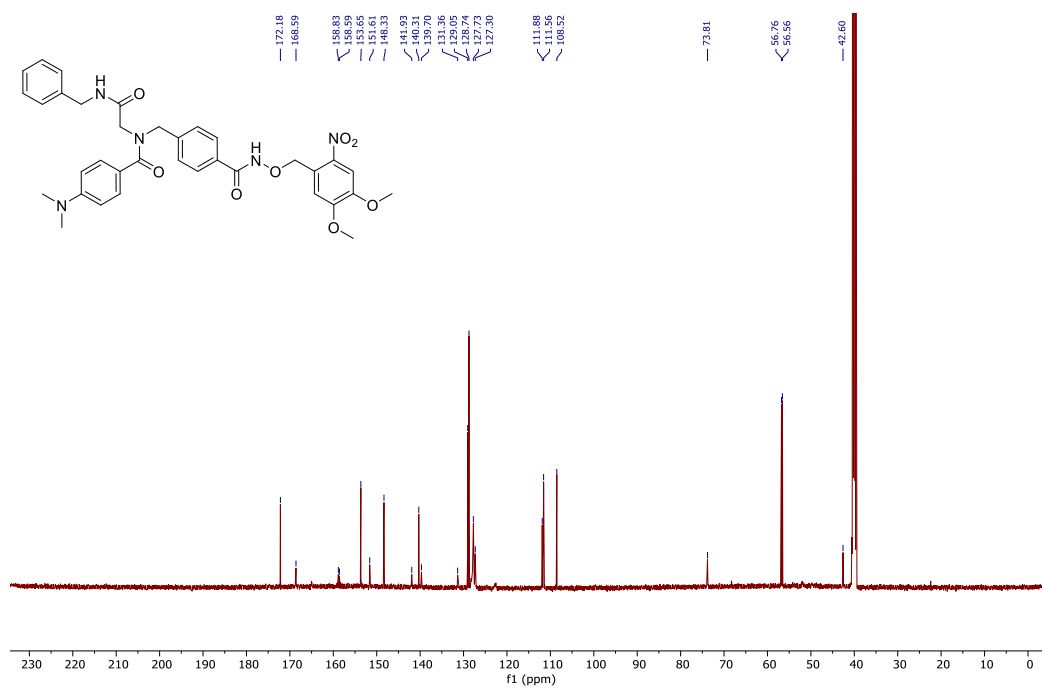
¹H-NMR (500 MHz, DMSO-*d*₆) of **4**.



¹³C-NMR (126 MHz, DMSO-*d*₆) of **4**.



¹H-NMR (500 MHz, DMSO-*d*₆) of pc-I.



¹³C-NMR (151 MHz, DMSO-*d*₆) of pc-I.

