

Supporting Information

Synthesis and evaluation of radiolabeled porphyrin derivatives for cancer diagnoses and their nonradioactive counterparts for photodynamic therapy

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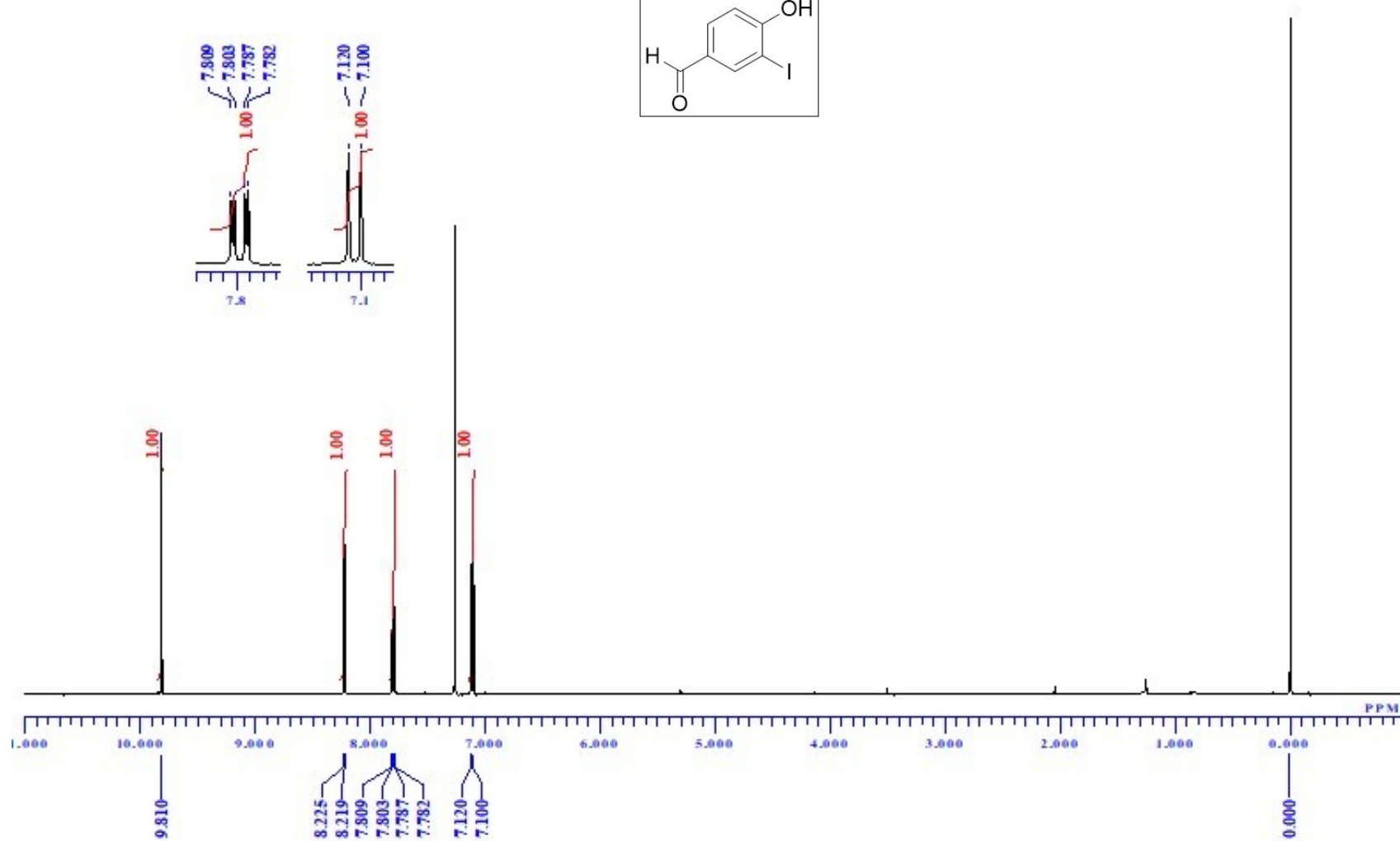
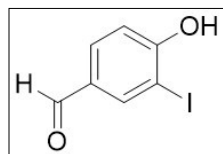
E-mail: kogawa@p.kanazawa-u.ac.jp

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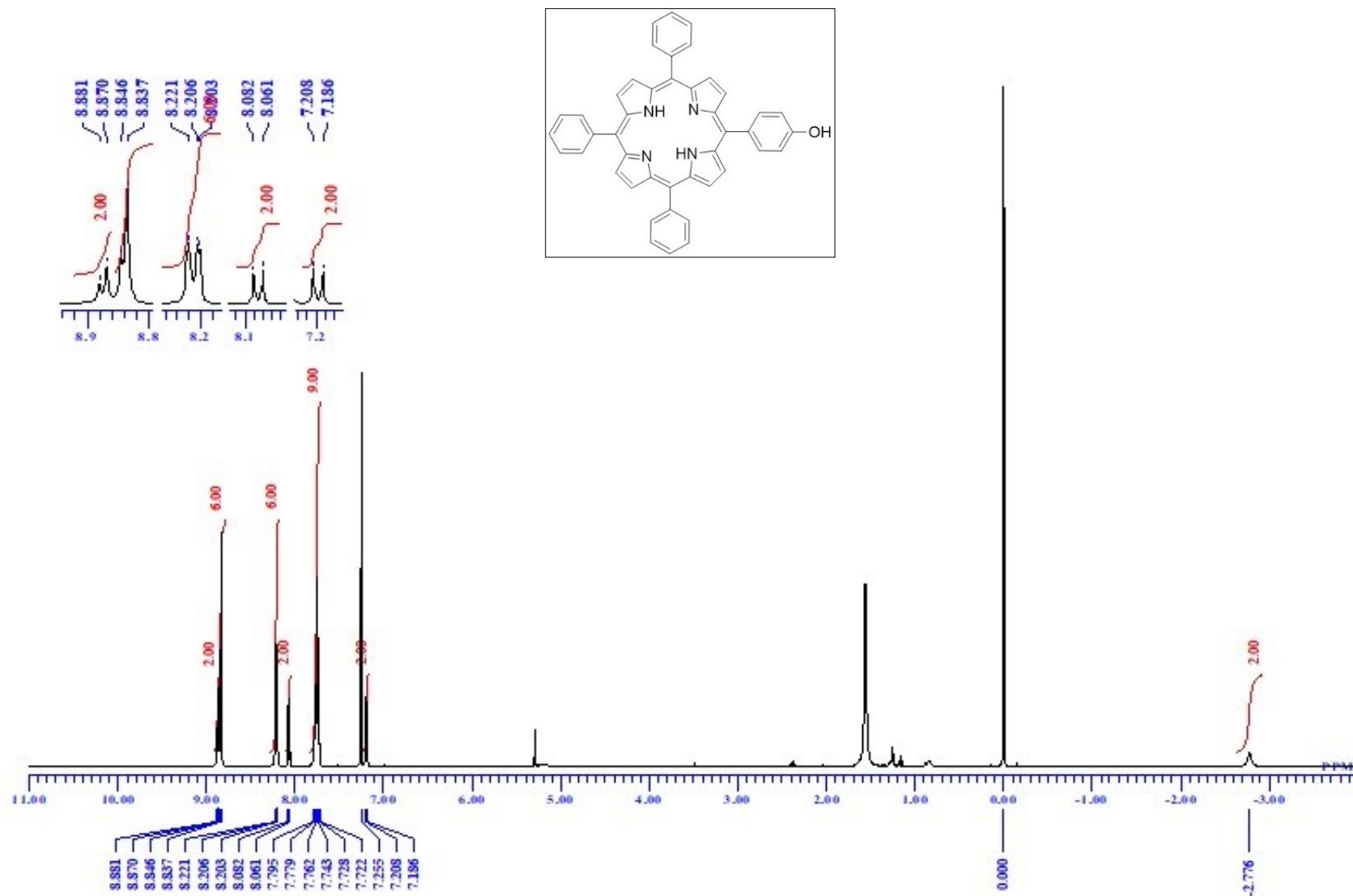
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1. NMR spectra

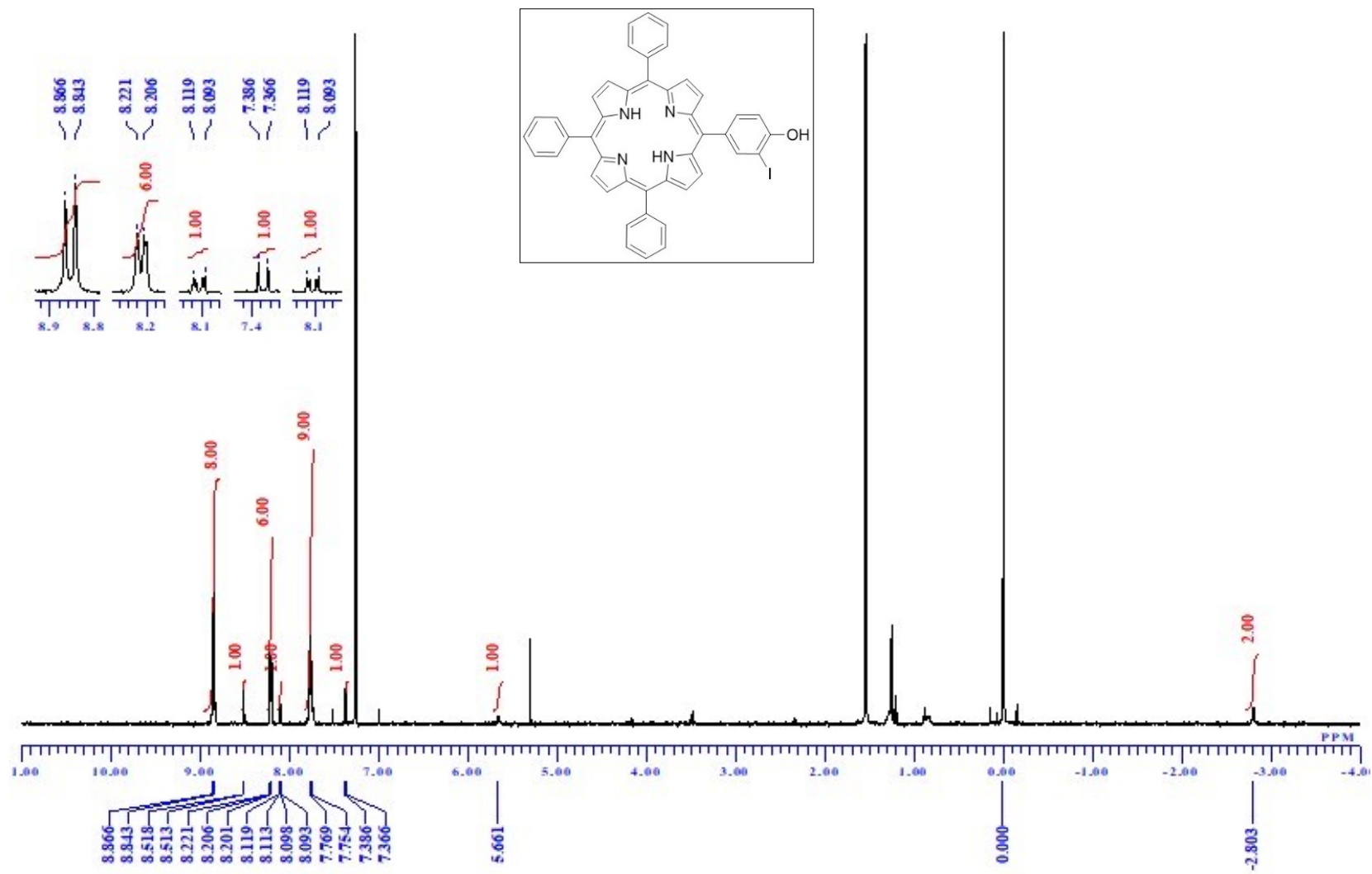
¹H NMR spectrum of **1** (400 MHz, CDCl₃)



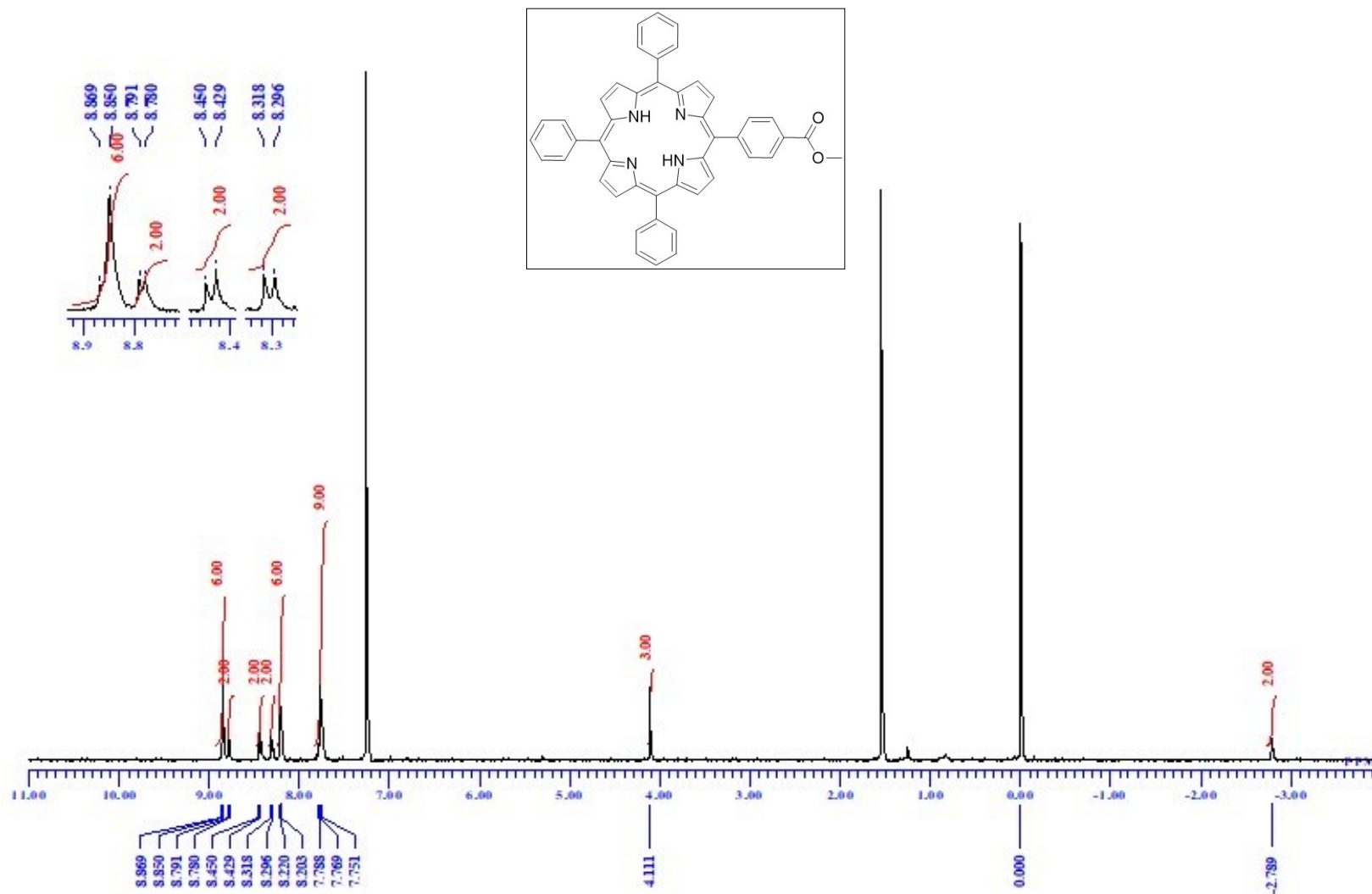
^1H NMR spectrum of **2** (400 MHz, CDCl_3)



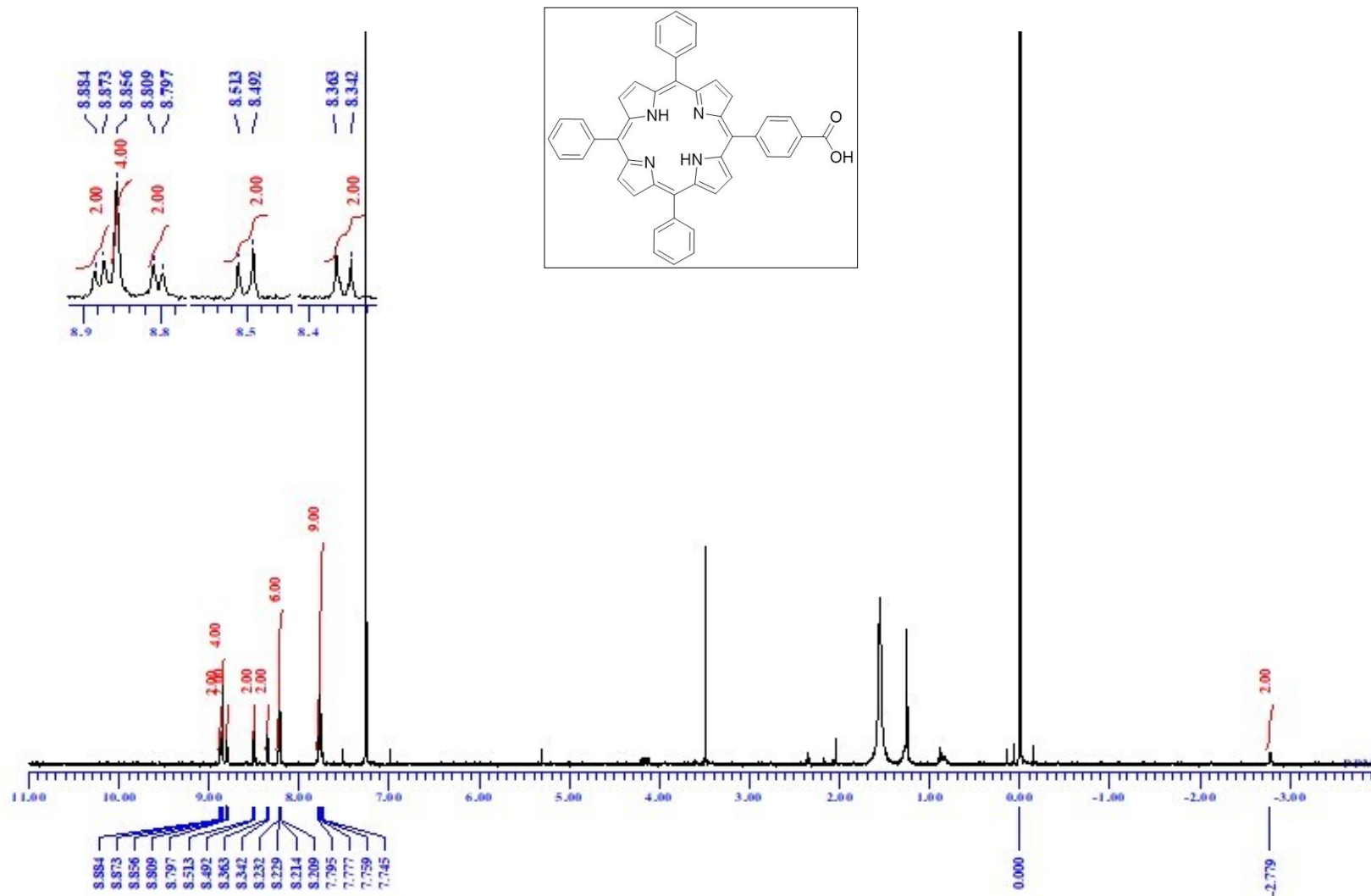
^1H NMR spectrum of **3** (400 MHz, CDCl_3)



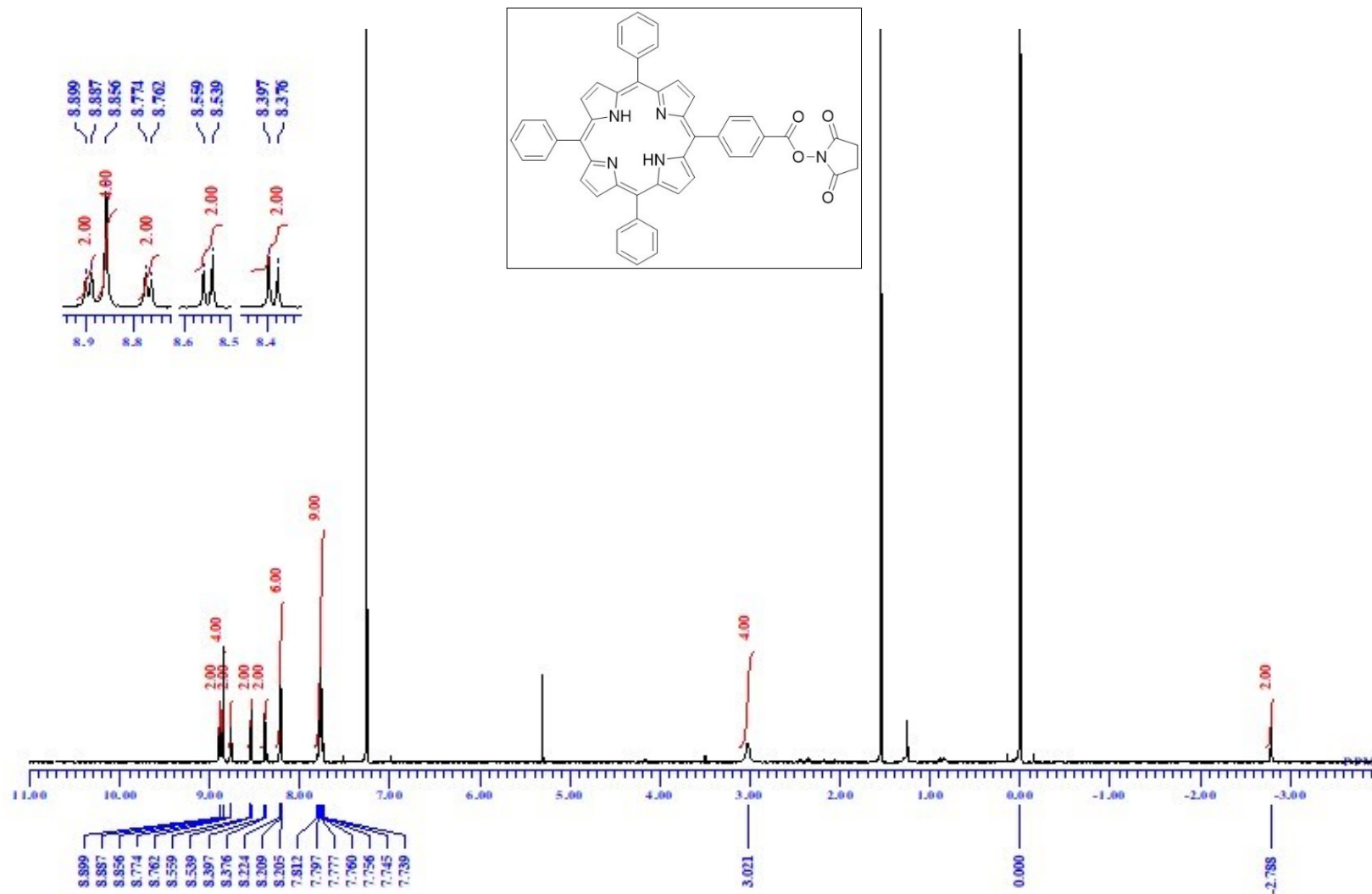
^1H NMR spectrum of **4** (400 MHz, CDCl_3)



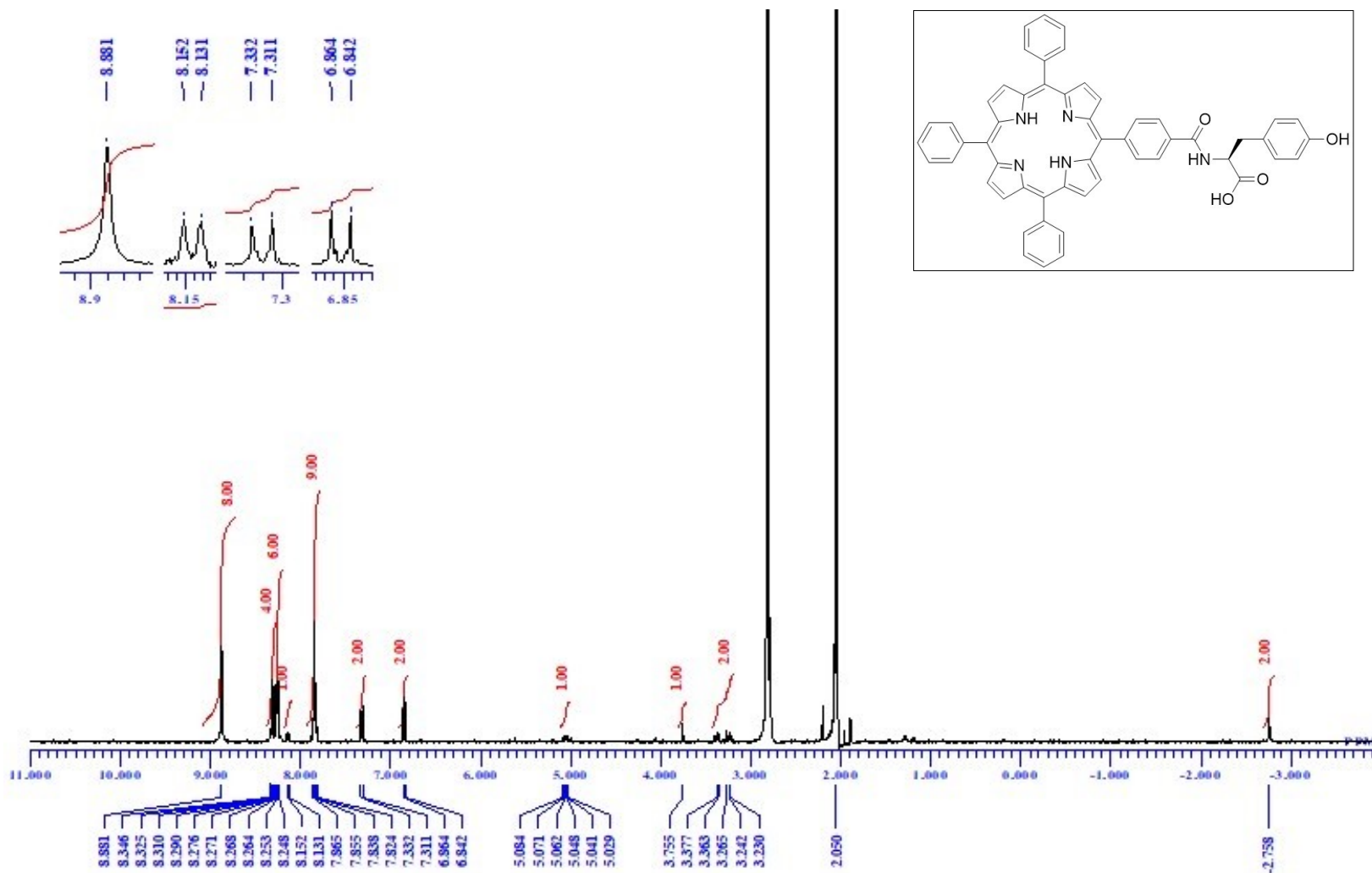
^1H NMR spectrum of **5** (400 MHz, CDCl_3)



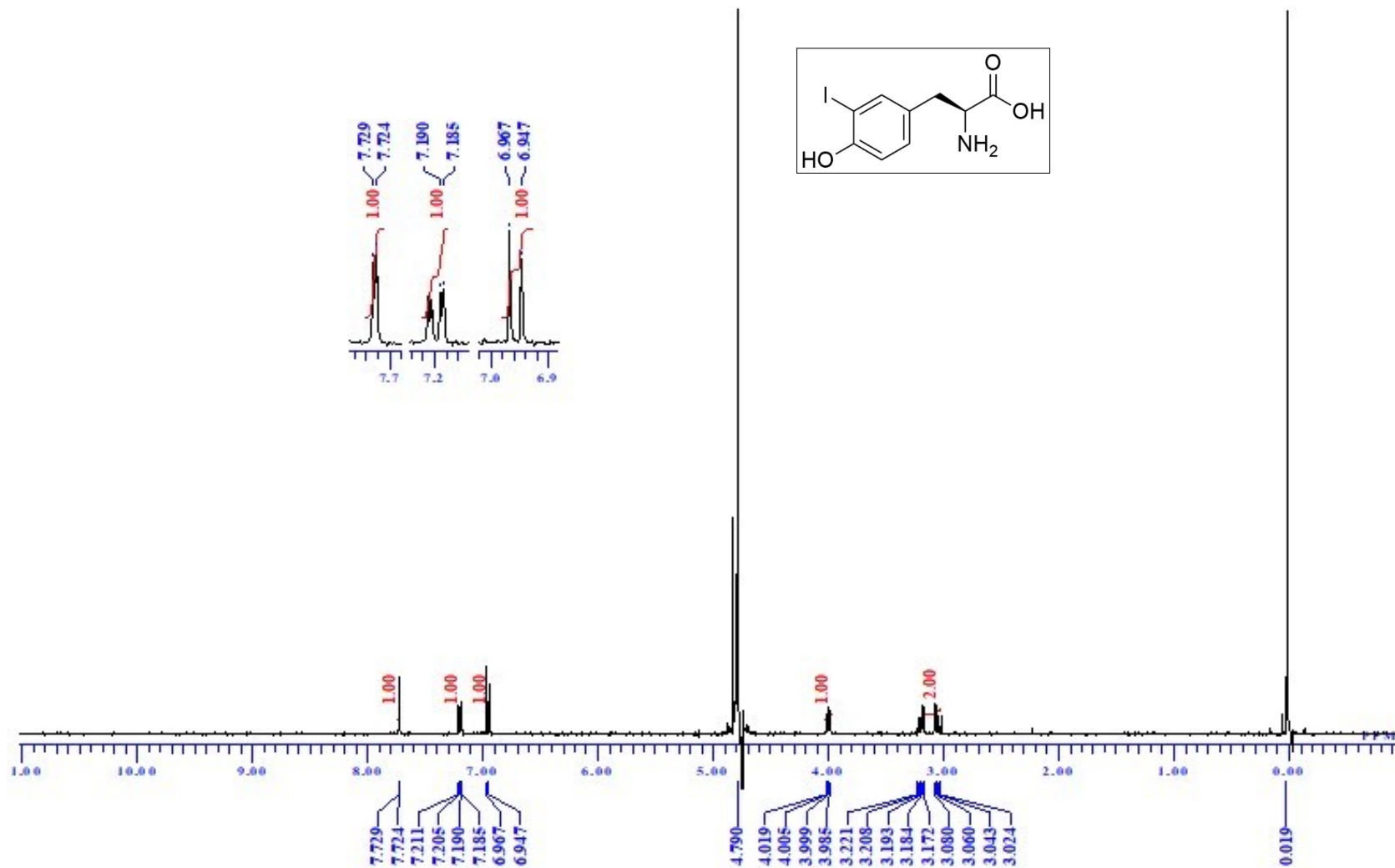
^1H NMR spectrum of **6** (400 MHz, CDCl_3)



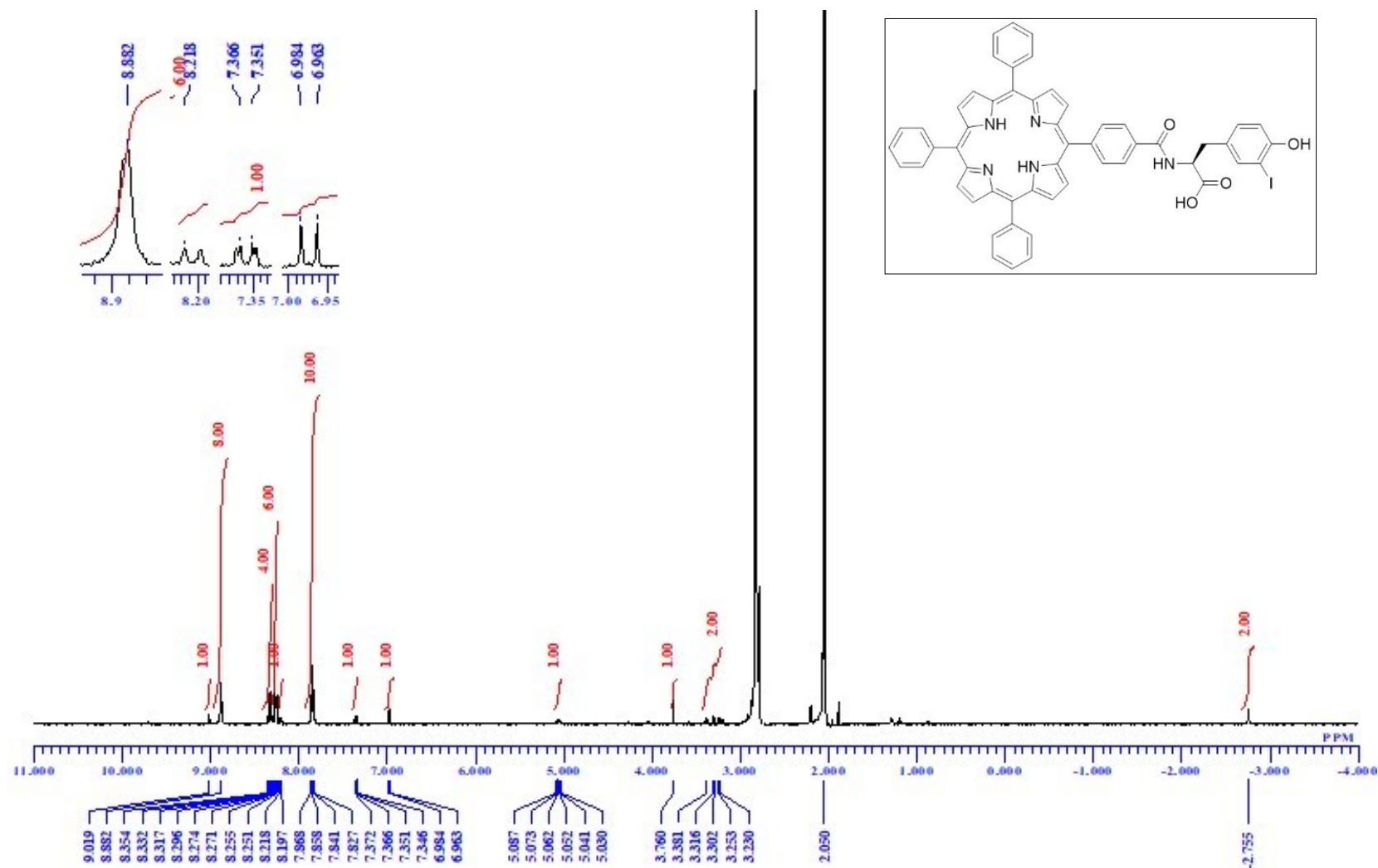
^1H NMR spectrum of 7 (400 MHz, acetone- d_6)



^1H NMR spectrum of **8** (400 MHz, D_2O)



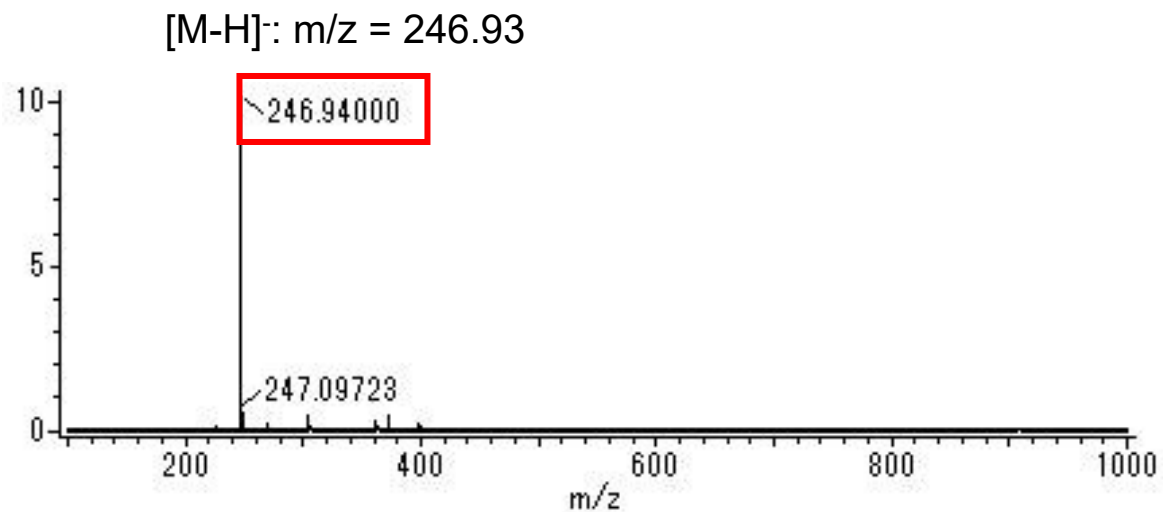
^1H NMR spectrum of **9** (400 MHz, acetone- d_6)



2. MS spectra

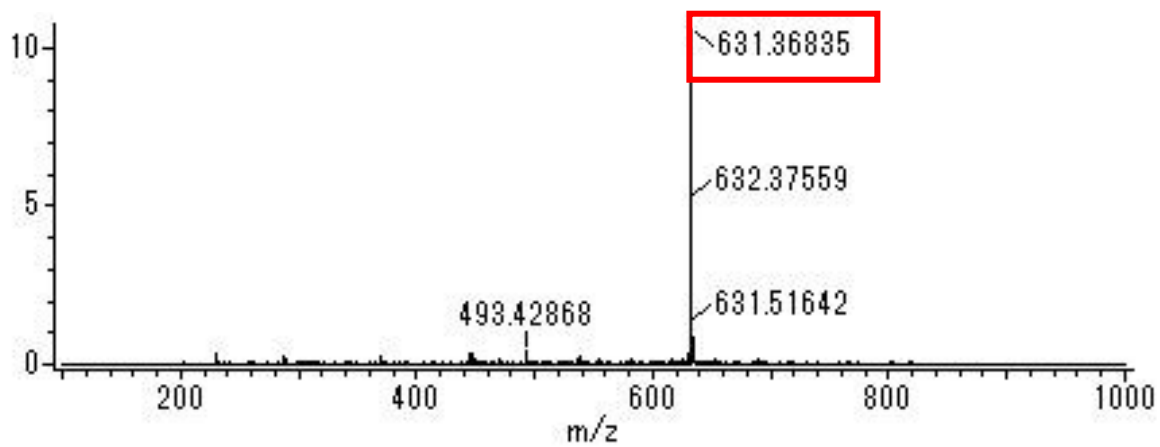
MS

(ESI-) spectrum of 1

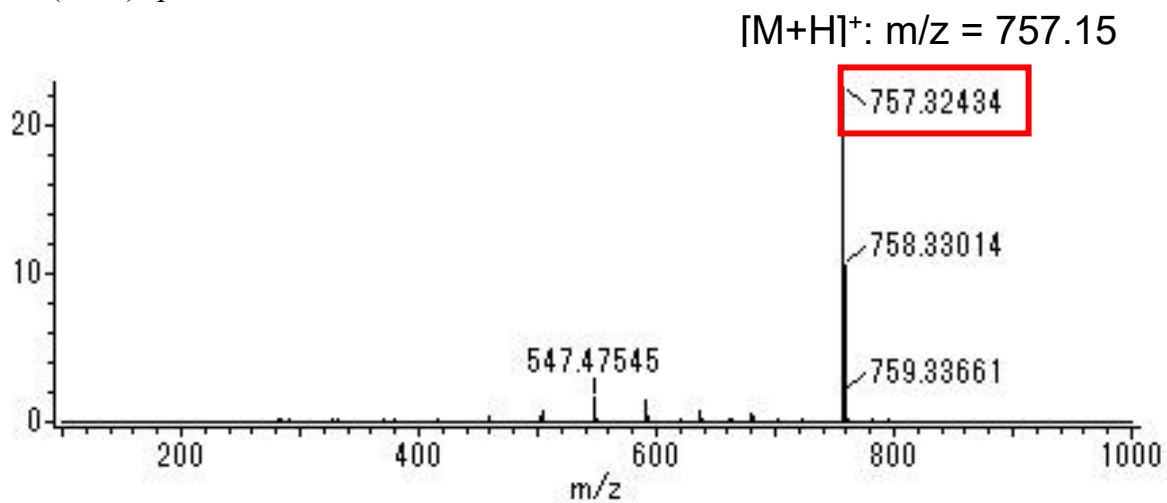


MS (ESI+) spectrum of 2

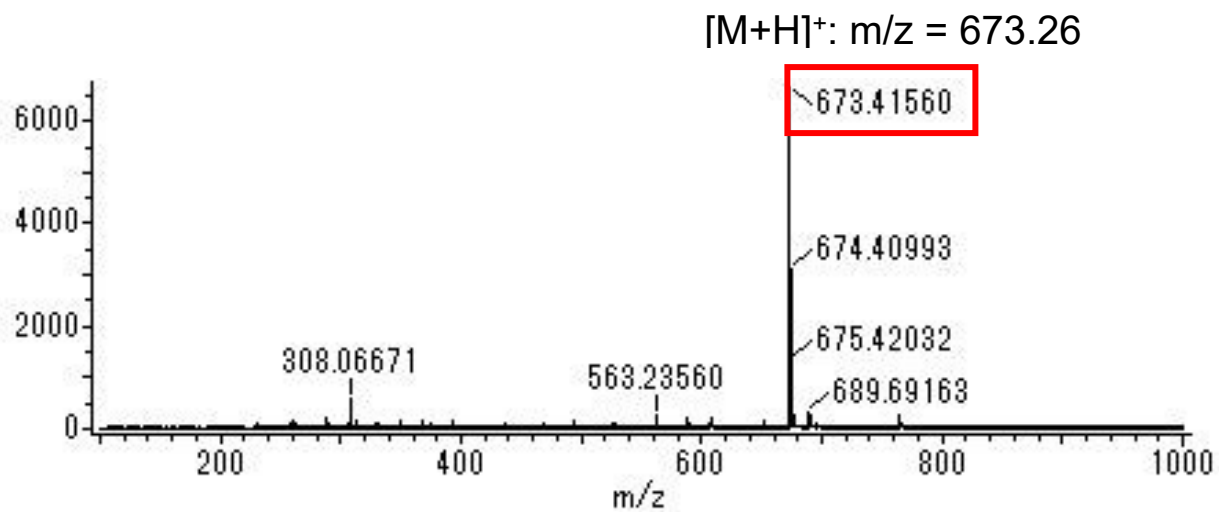
[M+H]⁺: m/z = 631.25



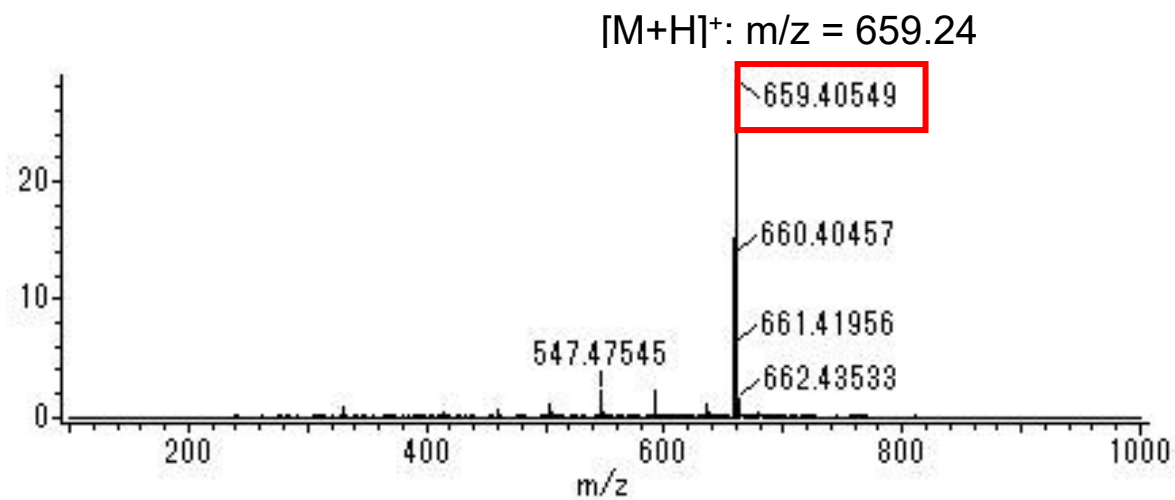
MS (ESI+) spectrum of 3



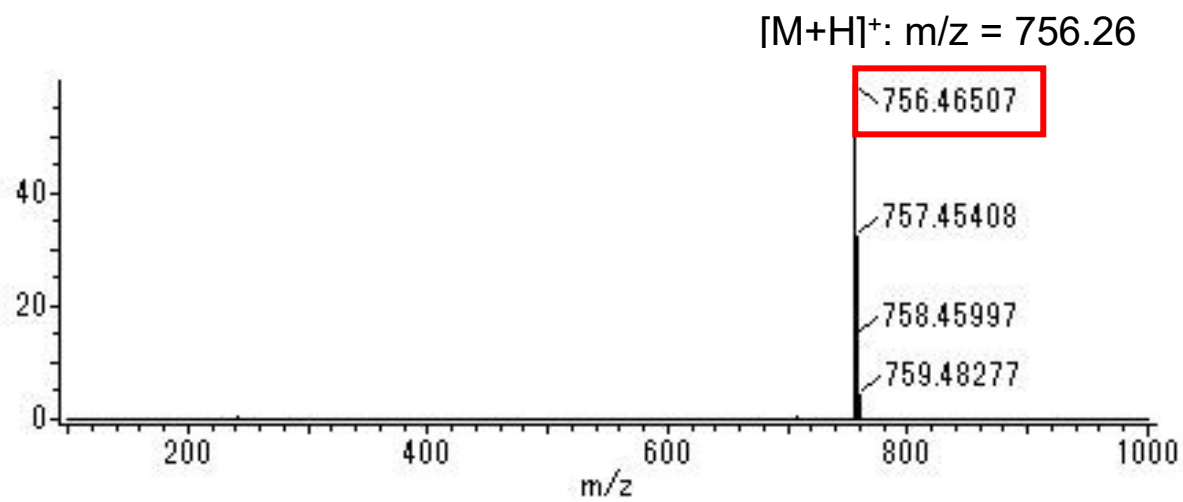
MS (ESI+) spectrum of 4



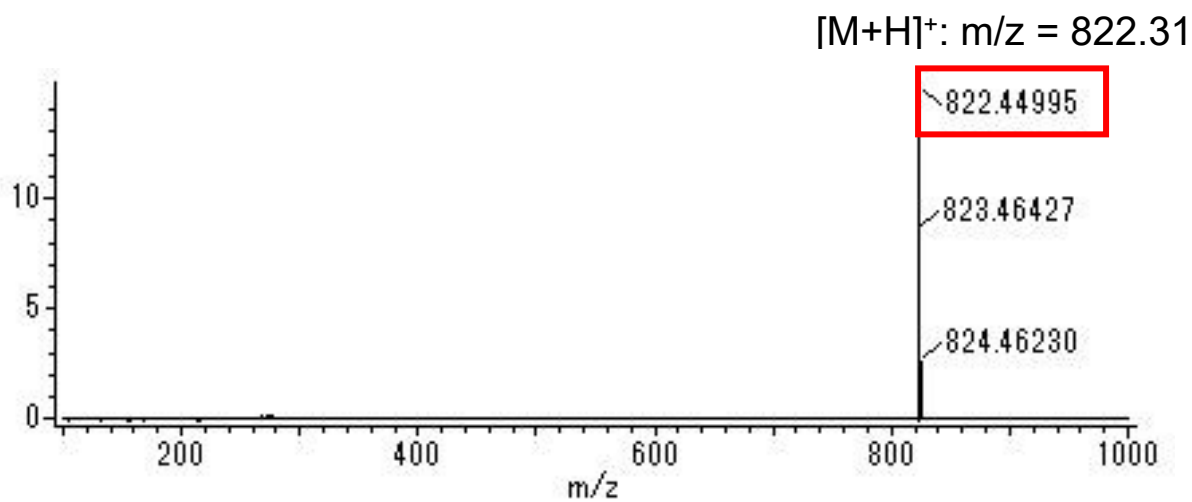
MS (ESI+) spectrum of **5**



MS (ESI+) spectrum of **6**

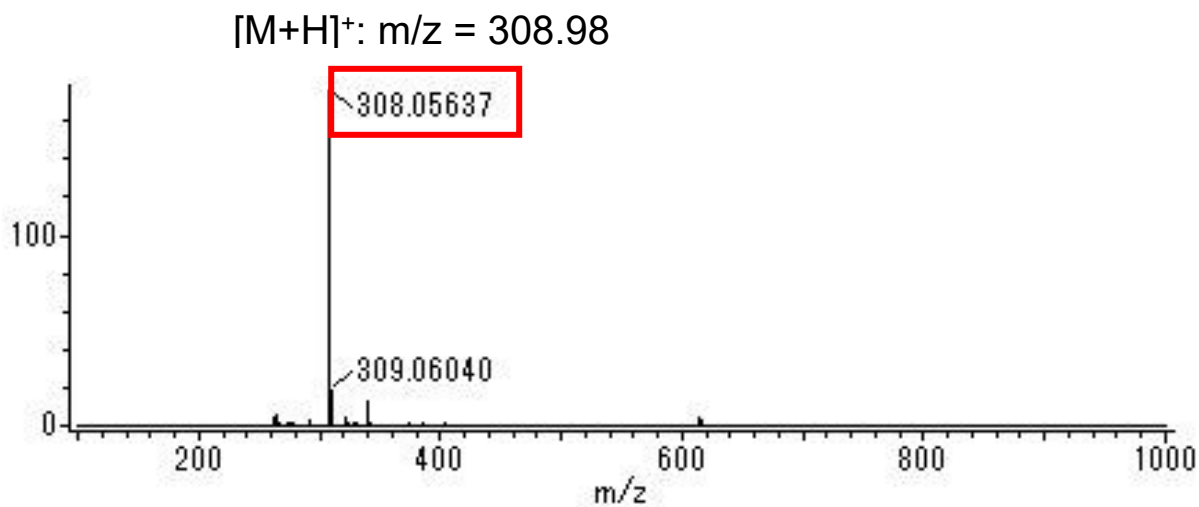


MS (ESI+) spectrum of **7**

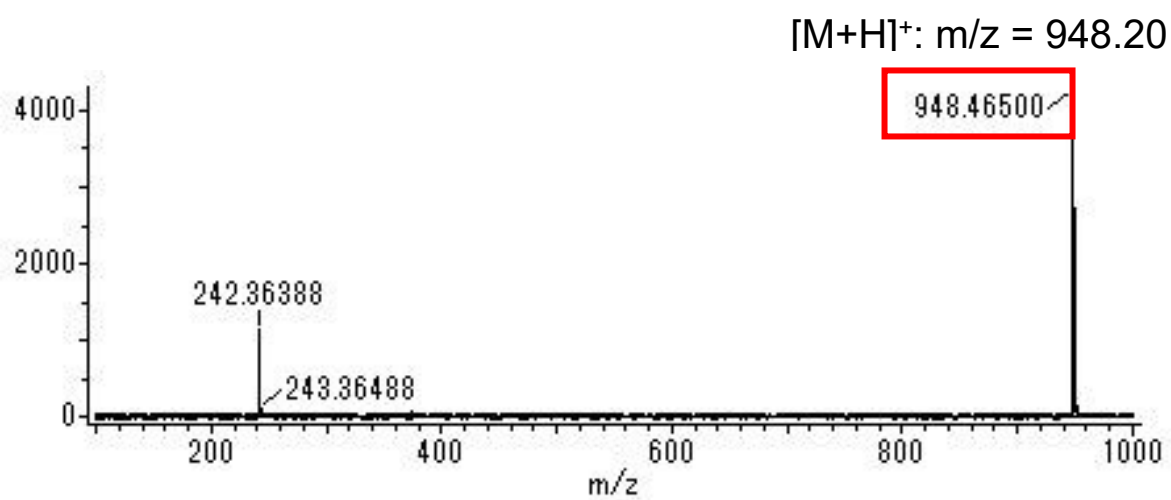


MS (ESI+)

spectrum of **8**



MS (ESI+) spectrum of **9**



3. Absorption spectra

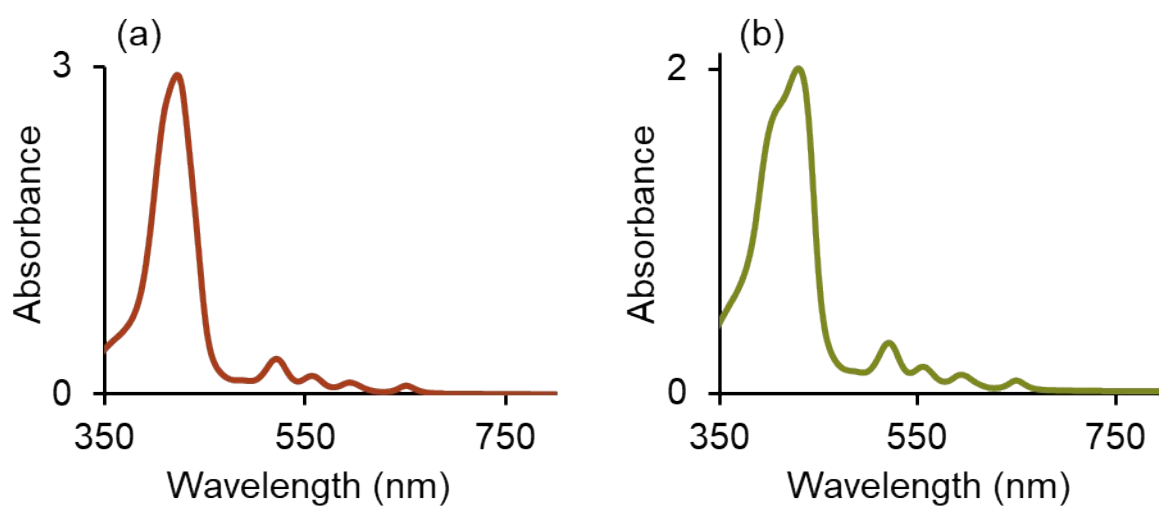


Figure S1. Absorption spectra of (a) I-TPP_{OH} (**3**) and (b) I-L-tyrosine-TPP (**9**) at 25 μ M (10% DMSO in H₂O).

4. HPLC analysis

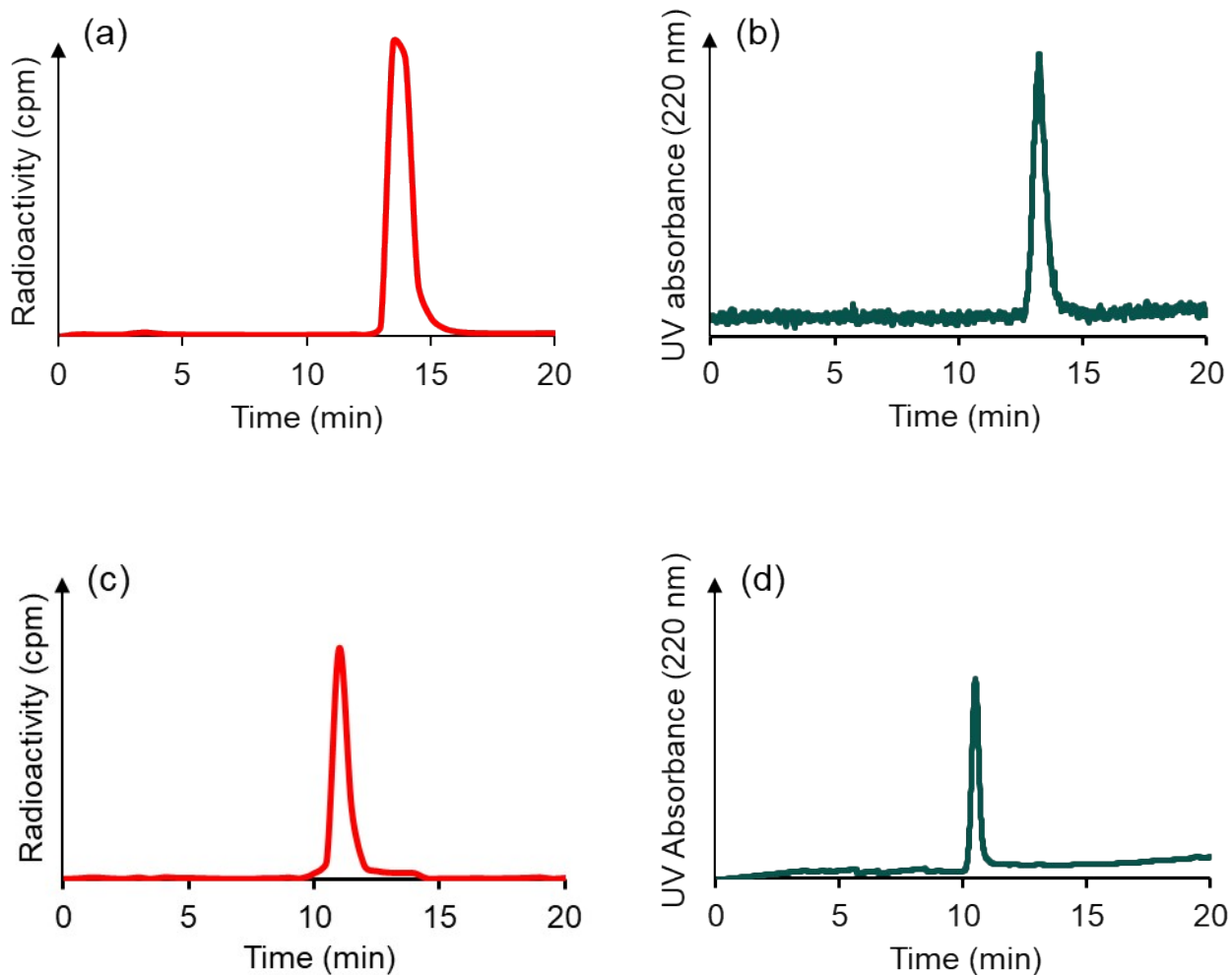


Figure S2. RP-HPLC chromatograms of (a) [^{125}I]I-TPP_{OH} ([^{125}I]3), (b) I-TPP_{OH} (3), (c) [^{125}I]I-L-tyrosine-TPP ([^{125}I]9), and (d) I-L-tyrosine-TPP (9) after purification. HPLC condition: a flow rate of 1 mL/min with a gradient mobile phase of 90 % methanol in water with 0.1% TFA to 100 % methanol in water with 0.1% TFA for 20 min.

5. Detailed biodistribution data

Table S1. Biodistribution of [¹²⁵I]I-TPP_{OH} ([¹²⁵I]**3**) and [¹²⁵I]I-L-tyrosine-TPP ([¹²⁵I]**9**) at 1, 24, 48, and 96 h after intravenous injection in Colon 26 tumor bearing mice

Tissues	Time after injection			
	1 h	24 h	48 h	96 h
[¹²⁵I]3				
Blood	47.40 (2.95)	10.52 (0.73)	3.19 (0.28)	1.15 (0.27)
Liver	12.94 (1.83)	20.59 (1.15)	19.62 (0.59)	17.23 (2.74)
Kidney	9.51 (1.42)	4.58 (0.38)	4.21 (0.50)	3.58 (0.42)
Small intestine	2.38 (0.20)	4.67 (0.39)	6.52 (0.20)	4.38 (0.93)
Large intestine	0.77 (0.09)	3.90 (0.46)	5.82 (0.84)	3.88 (1.30)
Spleen	6.03 (1.04)	9.94 (0.89)	11.82 (0.83)	8.28 (2.99)
Pancreas	1.87 (0.26)	1.90 (0.18)	2.10 (0.25)	1.80 (0.38)
Lung	24.41 (3.74)	8.14 (0.35)	6.00 (0.70)	3.79 (1.00)
Heart	7.81 (0.74)	4.49 (0.50)	4.29 (0.68)	3.85 (0.64)
Stomach [†]	0.36 (0.04)	0.79 (0.07)	0.76 (0.08)	0.71 (0.10)
Bone	3.59 (0.60)	3.58 (0.48)	3.54 (0.13)	2.77 (0.38)
Muscle	1.00 (0.18)	1.22 (0.31)	1.40 (0.29)	1.42 (0.42)
Brain	0.88 (0.16)	0.27 (0.04)	0.16 (0.01)	0.12 (0.02)
Colon 26	4.02 (0.92)	13.64 (1.91)	18.01 (2.13)	11.07 (2.42)
Tumor/blood	0.08 (0.02)	1.30 (0.16)	5.65 (0.49)	9.68 (1.14)
Tumor/muscle	4.06 (0.92)	11.66 (3.21)	13.29 (2.86)	7.96 (1.14)
[¹²⁵I]9				
Blood	42.71 (2.72)**	9.68 (1.32)*	3.48 (0.82)**	1.99 (0.35)**

Liver	11.36 (0.96)*	18.74 (2.76)	15.06 (1.94)**	11.53 (1.66)**
Kidney	8.26 (1.20)	4.84 (0.79)	2.82 (0.60)**	2.23 (0.19)**
Small intestine	2.49 (0.31)	4.05 (0.65)**	3.37 (0.45)**	2.27 (0.25)**
Large intestine	1.10 (0.28)	4.11 (0.38)	3.01 (0.40)**	2.36 (0.24)**
Spleen	5.09 (0.25)*	9.26 (1.29)	7.17 (2.11)*	6.41 (3.29)*
Pancreas	1.07 (0.19)*	1.99 (0.25)	1.97 (0.54)*	1.42 (0.24)*
Lung	20.31 (4.08)*	7.65 (1.21)	3.95 (0.69)**	3.17 (0.25)**
Heart	6.84 (1.01)	4.85 (0.47)	2.91 (0.42)*	2.36 (0.38)*
Stomach [†]	1.62 (0.11)**	0.70 (0.08)	0.50 (0.10)**	0.51 (0.03)**
Bone	4.03 (0.43)	3.68 (0.16)	2.63 (0.54)**	2.23 (0.28)**
Muscle	0.84 (0.22)**	1.30 (0.32)	0.70 (0.27)*	0.94 (0.29)*
Brain	0.86 (0.16)	0.34 (0.06)	0.19 (0.06)	0.13 (0.02)
Colon 26	2.81 (0.64)**	10.94 (2.16)*	8.70 (1.16)**	7.86 (0.47)**
Tumor/blood	0.07 (0.02)	1.13 (0.16)	2.57 (0.41)**	4.04 (0.70)**
Tumor/muscle	3.52 (1.21)	9.80 (0.50)	11.18 (1.10)*	9.06 (3.20)

Data are expressed as % injected dose per gram of tissue. Each value represents mean (SD) for four mice. Significance was determined using an unpaired Student's t-test (* $p < 0.05$, ** $p < 0.01$ vs. the corresponding data of [¹²⁵I]**3**). [†] Data are expressed as % injected dose.

6. Photodynamic therapy (PDT)

6.1 Detailed PDT data

Table S2. Relative tumor volume (V/V_0) of control groups, I-TPP_{OH} (**3**) and I-L-tyrosine-TPP (**9**) treated mice, with and without light irradiation in Colon 26 tumor bearing mice, monitored up to 7 days

Days post injection	Relative tumor volume (V/V_0)					
	Control		3		9	
	Light	Dark	Light	Dark	Light	Dark
1	1.73 (0.74)	1.86 (0.76)	1.66 (0.36)	1.53 (0.40)	1.66 (0.40)	1.61 (0.25) [#]
2	2.12 (0.73)	2.97 (0.59)	0.98 (0.36) ^{***, ###, †}	1.53 (0.24) ^{###}	0.90 (0.24) ^{***, ###, †††}	1.99 (0.42)
3	3.18 (1.34)	4.19 (1.76)	0.90 (0.53) ^{***, ###, †}	2.28 (0.31) [#]	0.88 (0.38) ^{***, ###, †}	2.51 (0.67) [#]
4	4.80 (1.82)	6.17 (1.98)	1.03 (0.55) ^{***, ###, †, ††}	3.07 (0.55) ^{###}	0.76 (0.24) ^{***, ###, †, ††}	3.13 (0.83) [#]
5	7.24 (3.48)	8.53 (2.42)	1.01 (0.62) ^{***, ###, †}	4.20 (0.89) ^{##}	1.17 (0.27) ^{***, ###, †}	4.01 (1.21) [#]
6	9.07 (4.34)	10.81 (4.59)	1.05 (0.85) ^{***, ###, †}	5.37 (1.23) [#]	1.15 (0.43) ^{***, ###}	4.83 (1.36) [#]
7	10.76 (3.72)	12.93(5.11)	1.43 (1.24) ^{***, ###, †, ††}	6.67 (2.33) [#]	1.34 (0.66) ^{***, ###, †}	6.25 (2.07)

Data were presented as relative values of tumor volume (V/V_0) where V_0 corresponds to the tumor volume on day 0. Each value represents mean (SD) for seven or eight mice. Significance was determined using one way analysis of variance (ANOVA) with Tukey's post hoc test (^{***} $p < 0.001$ vs. Control (Light), [#] $p < 0.05$, ^{##} $p < 0.01$, ^{###} $p < 0.001$ vs Control (Dark), [†] $p < 0.05$, ^{††} $p < 0.01$, vs. **3** (Dark), [†] $p < 0.05$, ^{††} $p < 0.01$, ^{†††} $p < 0.001$ vs. **9** (Dark)).

6.2 Tumor weight

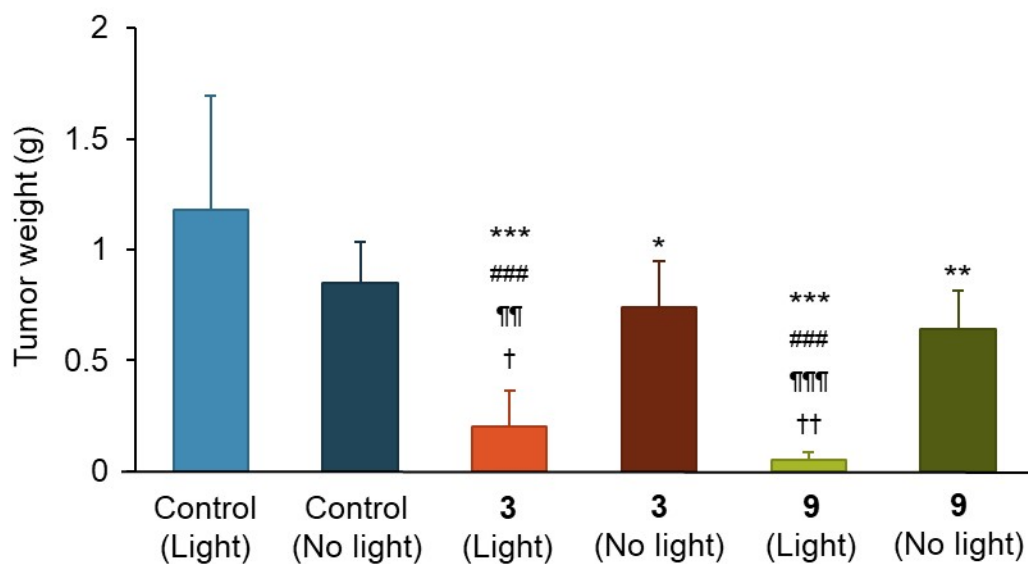


Figure S3. Tumor weight (g) on day 8 postinjection for control mice, I-TPP_{OH} (**3**) treated mice, and I-L-tyrosine-TPP (**9**) treated mice with or without light irradiation. Each value represents mean (SD) for seven or eight mice. Significance was determined using one way analysis of variance (ANOVA) with Tukey's post hoc test ($*p < 0.05$, $**p < 0.01$, $***p < 0.001$ vs. Control (Light), $###p < 0.001$ vs Control (No light), $†††p < 0.01$, $††††p < 0.001$, vs. **3** (No light), $†p < 0.05$, $††p < 0.01$ vs. **9** (No light)).

6.3 Body weight

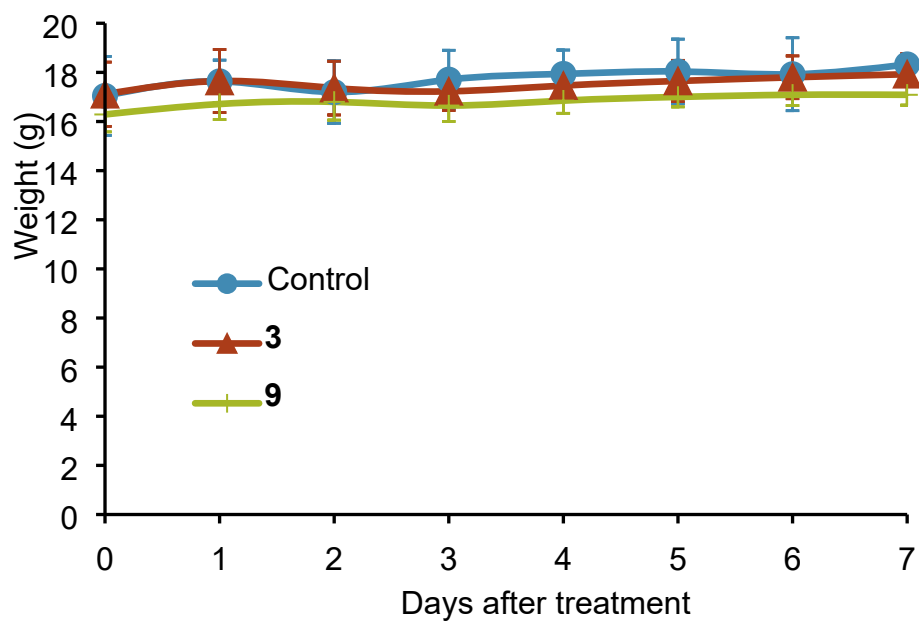


Figure S4. Body weight changes of control mice, I-TPP_{OH} (**3**) treated mice, and I-L-tyrosine-TPP (**9**) treated mice. Each value represents mean (SD) for seven or eight mice.