Iridium(III) Polypyridine Complexes with a Disulfide Linker as Biological Sensors and Cytotoxic Agents

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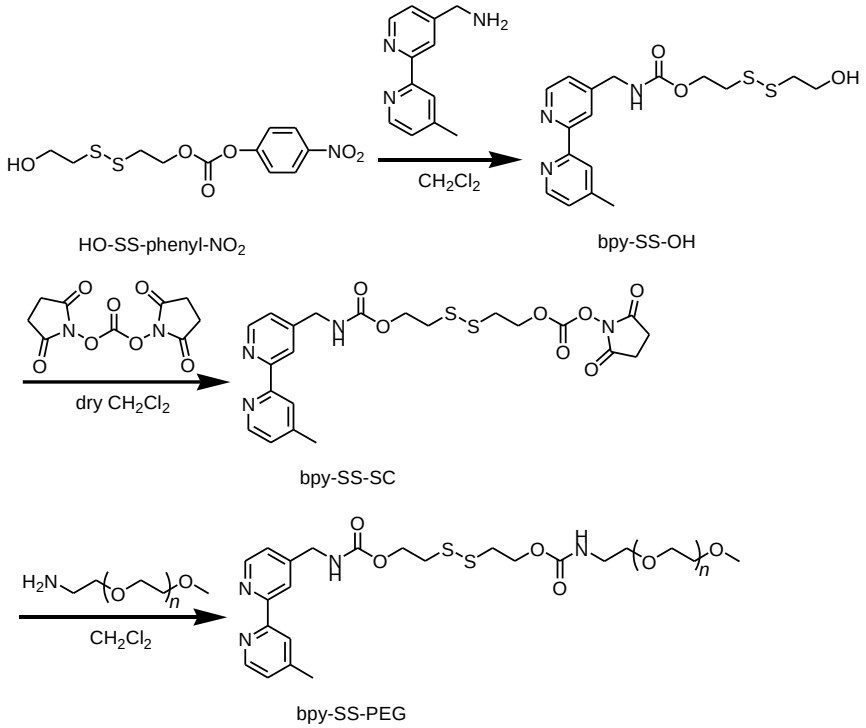
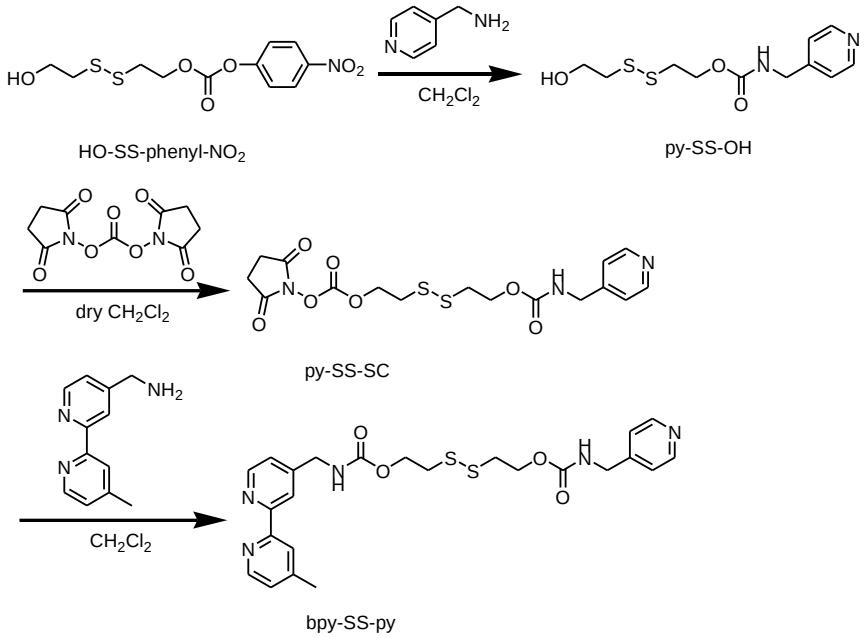
Electronic Supplementary Information (ESI)

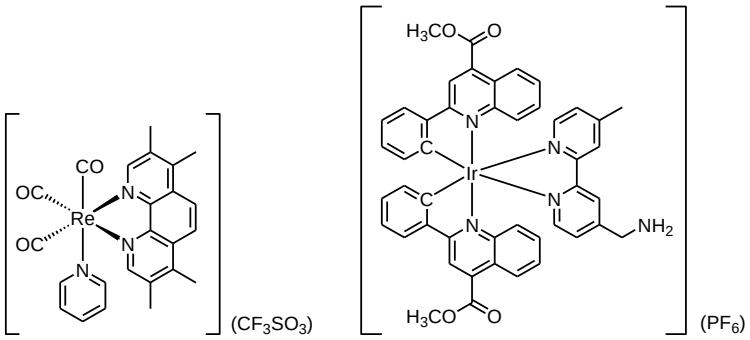
Scheme S1 Synthetic route of bpy-SS-PEG



Scheme S2 Synthetic route of bpy-SS-py.



Scheme S3 Structures of complexes **3-Re** and **3-Ir**.



3-Re **3-Ir**

Scheme S4 Corresponding sulfhydryl complexes formed after disulfide cleavage of all the complexes with GSH

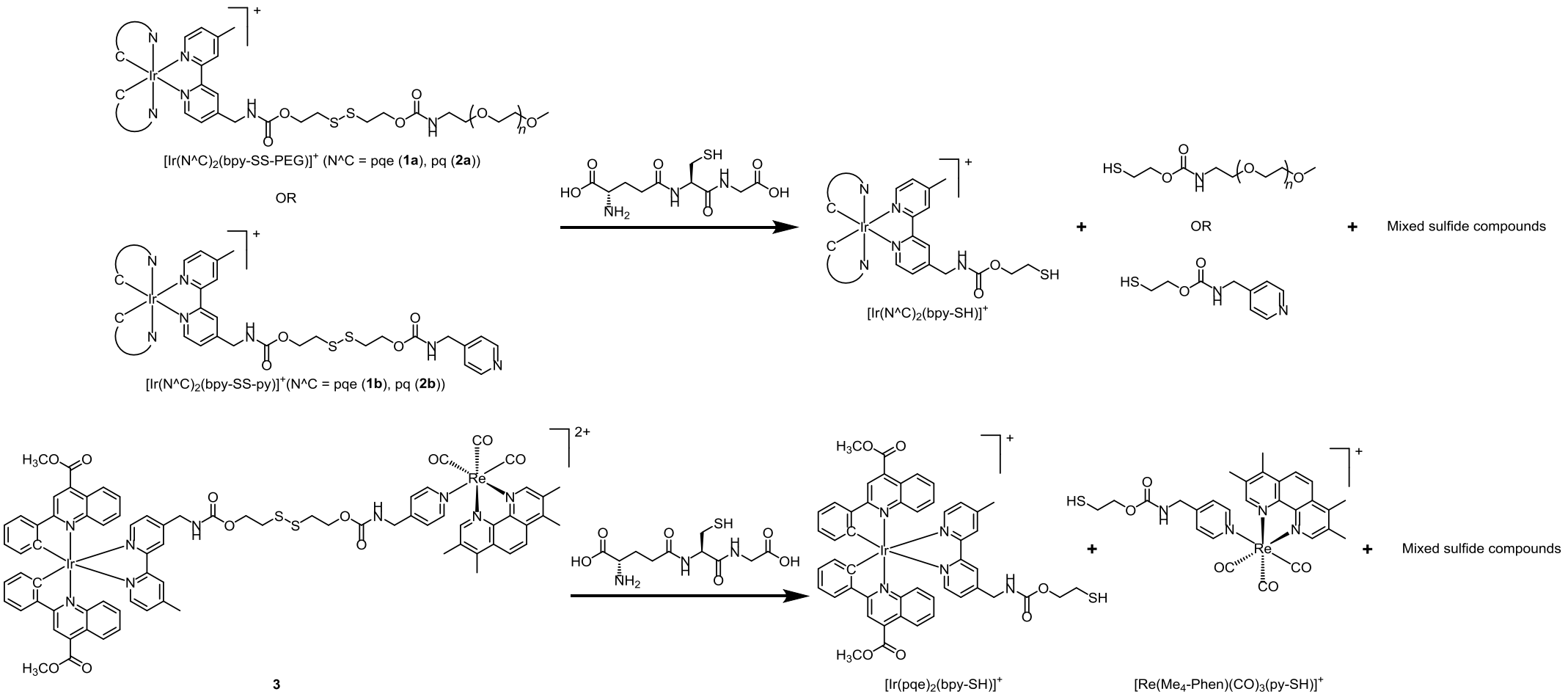


Table S1 Electronic absorption spectral data of complexes **1a–c**, **2a–c**, **3**, the donor complex **3-Re**, and the acceptor complex **3-Ir** in CH_3CN at 298 K.

complex	λ_{abs}/nm (ε/dm^3 mol^{-1} cm^{-1})
1a	266 (52,455), 290 (47,715), 350 (26,330), 369 sh (23,220), 480 (4,260)
1b	265 (56,545), 290 (50,805), 350 (27,745), 364 (26,320), 477 (4,475)
1c	263 (32,230), 290 (29,705), 319 sh (14,845), 353 sh (16,485), 435 (3,430)
2a	272 (51,575), 337 (21,875), 352 sh (18,285), 442 sh (4,775)
2b	265 (55,960), 282 sh (31,590), 307 sh (27,075), 336 (24,865), 351 sh (21,315), 435 (6,200)
2c	263 (50,090), 284 (45,235), 314 sh (24,405) 336 sh (23,125), 435 (6,595)
3	270 (46,785), 280 (48,080), 345 (19,180), 366 sh (17,245), 470 (2,905)
3-Re	250 (32,945), 281 (37,275), 370 sh (3,655)
3-Ir	267 (48,210), 291 (44,170), 349 (24,100), 368 sh (21,640), 472 sh (4,065)

Table S2 Photophysical data of complexes **1a–c**, **2a–c**, **3**, the donor complex **3-Re**, and the acceptor complex **3-Ir** in degassed CH_3CN at 298 K and in alcohol glass at 77 K.

complex	medium (T/K)	λ_{em}/nm	τ_o[a]/μs	Φ_{em}
1a	CH_3CN (298)	642	0.60	0.097
	glass[b] (77)	597, 643 sh		
1b	CH_3CN (298)	641	0.63	0.082
	glass[b] (77)	596, 647 sh		
1c	CH_3CN (298)	641	0.73	0.10
	glass[b] (77)	599, 648 sh		
2a	CH_3CN (298)	556, 596 sh	2.77	0.51
	glass[b] (77)	544 (max), 584		
2b	CH_3CN (298)	556, 594 sh	2.69	0.48
	glass[b] (77)	541 (max), 582, 634 sh		
2c	CH_3CN (298)	559, 596 sh	0.84	0.16
	glass[b] (77)	538 (max), 580, 631 sh		
3	CH_3CN (298)	517 sh, 640	0.60	0.054[c]
	glass[b] (77)	466, 498, 598 (max), 646		
3-Re	CH_3CN (298)	515	7.56	0.69[c]
	glass[b] (77)	464 (max), 496, 533 sh		
3-Ir	CH_3CN (298)	641	0.55	0.040[c]
	glass[b] (77)	597 (max), 644		
$[Ir(ppy)_2(bpy)](PF_6)$[d]	CH_3CN (298)	583	0.269	0.071

[a] The lifetimes were measured at the emission maxima.

[b] EtOH/MeOH (4:1, *v*/*v*).

[c] The emission quantum yields were determined using [Re(phen)$(CO)_3$(pyridine)](CF_3SO_3) (Φ_{em} = 0.18 in degassed CH_3CN, λ_{ex} = 355 nm) as a reference.

[d] Data taken from: M. S. Lowry, W. R. Hudson, R. A. Pascal and S. Bernhard, *J. Am. Chem. Soc*., 2009, **126**, 14129.

Table S3 ESI-MS data for complexes **1a**,**b** and **2a**,**b** (10 μM) upon incubation with GSH (500 μM) in PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K for 120 min.

complex	formulae $[Ir(N^C)_2(bpy\text{-}SH)]^+$	mass calculated	mass found
1a	$IrC_{49}H_{42}N_5O_6S$	1020.2	1020.6
1b	$IrC_{49}H_{42}N_5O_6S$	1020.2	1019.9
2a	$IrC_{45}H_{38}N_5O_2S$	904.2	904.6
2b	$IrC_{45}H_{38}N_5O_2S$	904.2	904.5

Table S4 Emission wavelengths, I_{517}/I_{655} ratios, and emission lifetimes of solutions containing complex **3** (10 μM) alone, complex **3** (10 μM) and GSH (200 μM), and **3-Re** (10 μM) and **3-Ir** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*), incubated at 298 K for 120 min. λ_{ex} = 355 nm.

	λ_{em}/nm	I_{517}/I_{655}	τ (517 nm)/μs	τ (655 nm)/μs
3	517, 655 (max)	0.21	n.d.[a]	0.042
3 + GSH	517, 655 sh	3.56	0.82	0.034
3-Re + 3-Ir	516, 655 sh	5.60	0.92	0.025

[a] The emission was too weak for accurate lifetime measurement.

Table S5 ESI-MS data for complex **3** (10 μM) upon incubation with GSH (200 μM) in PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K for 120 min.

suggested fragment	formulae	*m*/*z* calculated	*m*/*z* found
$[Re(Me_4\text{-}Phen)(CO)_3]^+$	$ReC_{19}H_{16}N_2O_3$	507.1	507.3
$[Re(Me_4\text{-}Phen)(CO)_4]^+$	$ReC_{20}H_{16}N_2O_4$	535.1	535.3
$[Re(Me_4\text{-}Phen)(CO)_3(py\text{-}SH)]^+$	$ReC_{28}H_{28}N_4O_5S$	719.1	717.9
$[Ir(pqe)_2(bpy\text{-}SS\text{-}py)Re(Me_4\text{-}phen)(CO)_3]^{2+}$	$IrReC_{77}H_{67}N_9O_{11}S_2$	868.9	869.2
$[Ir(pqe)_2(bpy\text{-}SH)]^+$	$IrC_{49}H_{41}N_5O_6S$	1020.2	1020.5
$[Ir(pqe)_2(bpy\text{-}SS\text{-}py)]^+$	$IrC_{58}H_{51}N_7O_8S_2$	1230.3	1231.4

Table S6 The k_{obs} values for complex **3** (10 μM) upon reaction with various concentrations of GSH (200, 600, 700, and 800 μM) in PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K.

concentration of GSH/μM	k_{obs}/ms^{-1}
200	0.102 ± 0.009
600	0.141 ± 0.009
700	0.151 ± 0.010
800	0.159 ± 0.004

Figure S1 Emission spectra of complex **1a** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

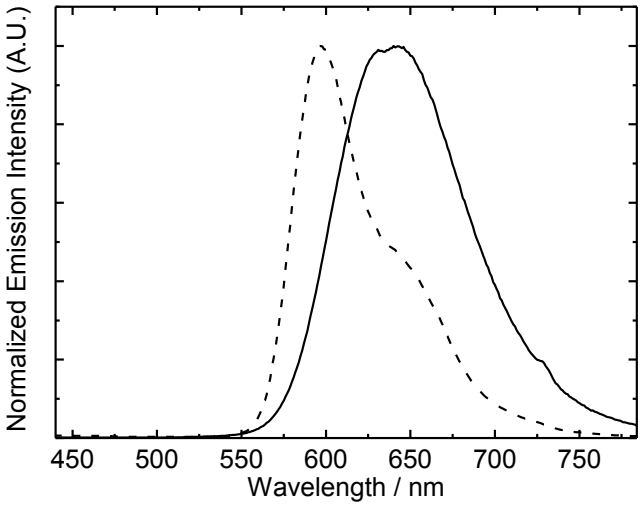


Figure S2 Emission spectra of complex **1b** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

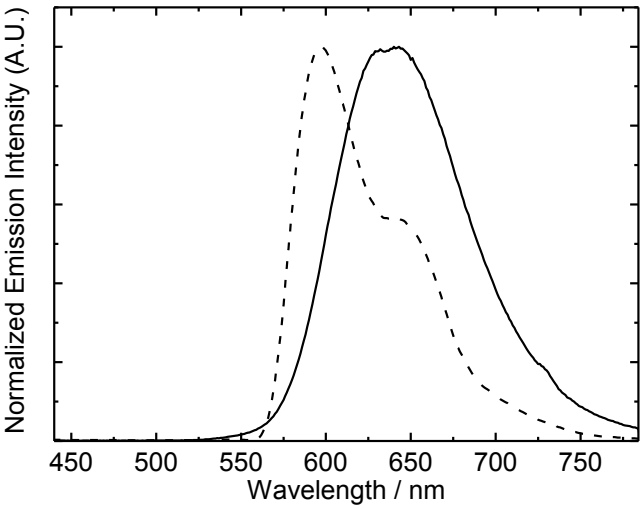


Figure S3 Emission spectra of complex **1c** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

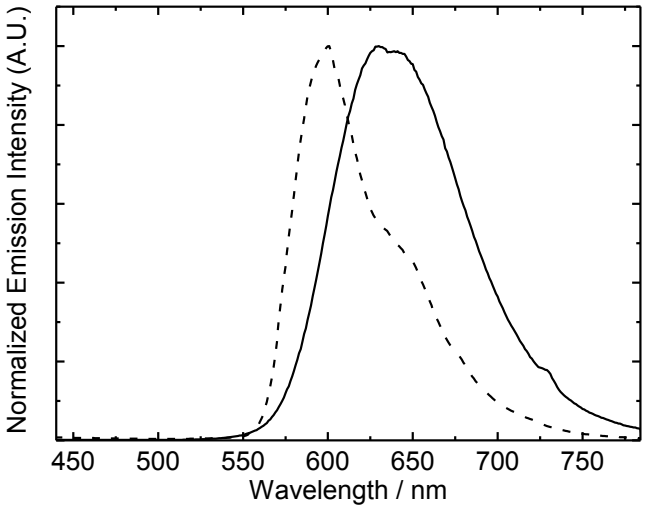


Figure 4 Emission spectra of complex **2a** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

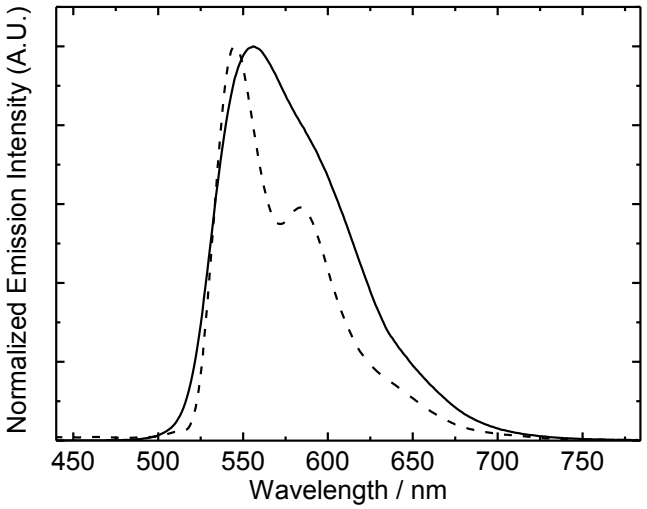


Figure S5 Emission spectra of complex **2b** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

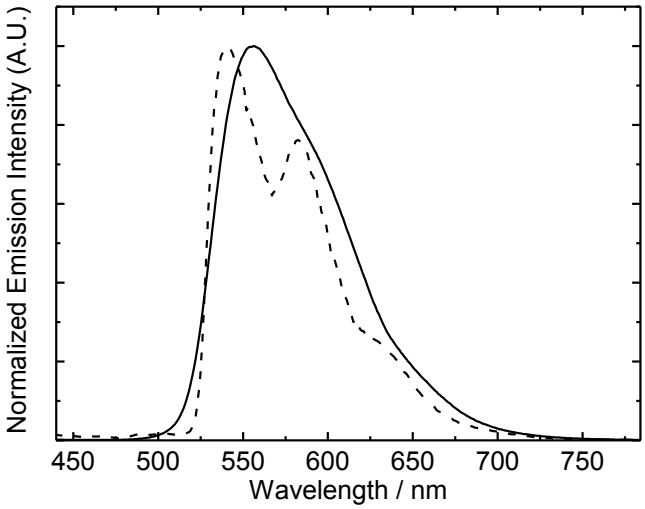


Figure S6 Emission spectra of complex **2c** in CH_3CN (solid) at 298 K and low-temperature glass (dashed) at 77 K.

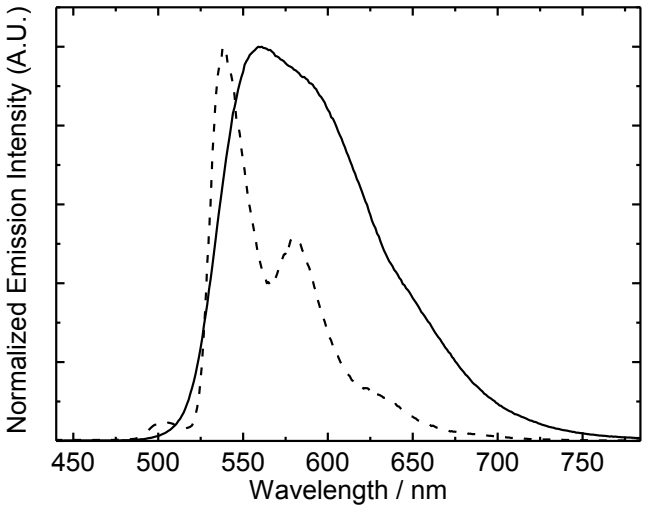
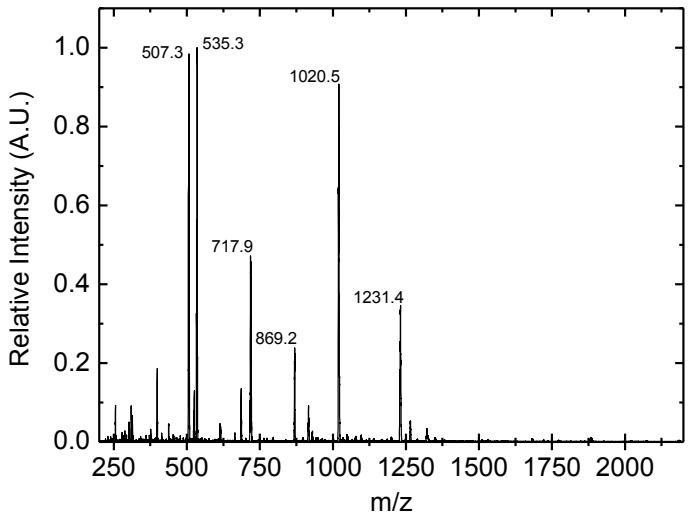


Figure **S7** ESI-mass spectra of complex **3** (10 μM) (**a**) incubated with or (**b**) without GSH (200 μM) in PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K for 120 min.

(**a**)



(**b**)

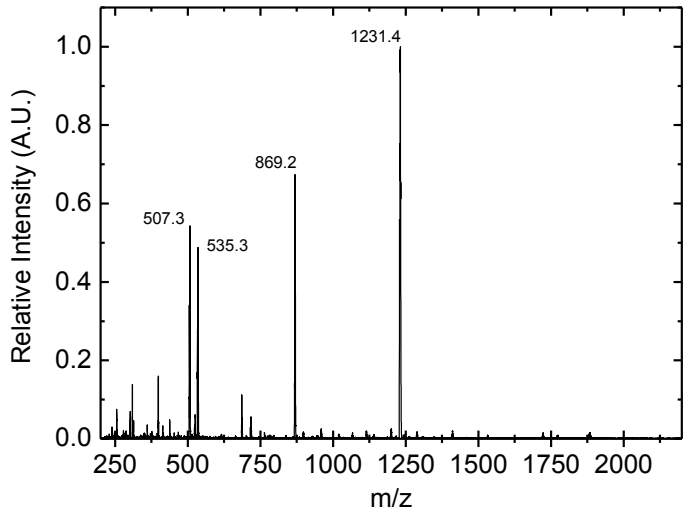


Figure S8 Emission spectral traces of complex **3** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K in the presence of 1250 μM GSH. The solution was allowed to incubate for 1 (solid), 20 (dashed), and 90 (dotted) min before an emission measurement. Excitation wavelength = 355 nm.

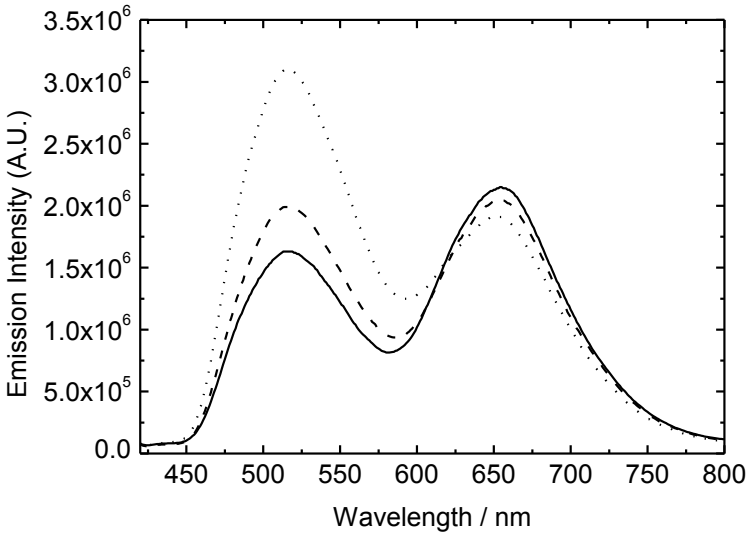


Figure S9 Time-dependent emission spectral traces (0 – 90 min) of complex **3** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K in the presence of 200 μM GSH.

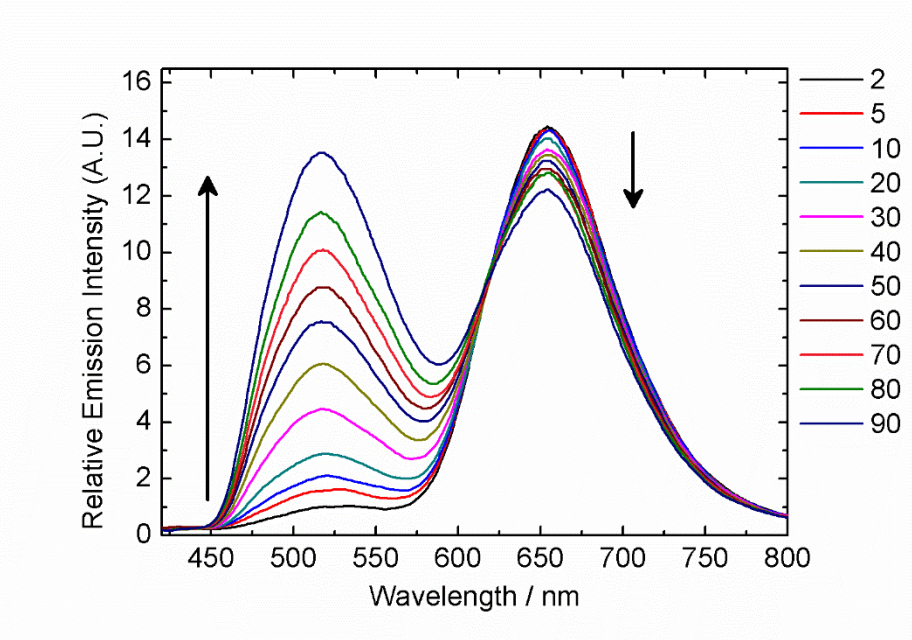


Figure S10 Time-dependent emission spectral traces (0 – 90 min) of complex **3** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K in the presence of 600 μM GSH.

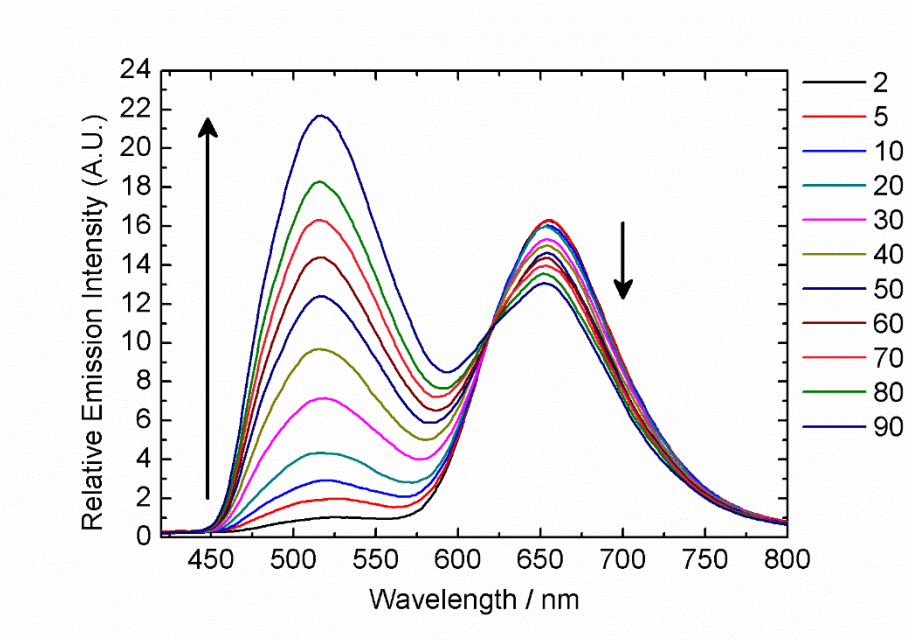


Figure S11 Time-dependent emission spectral traces (0 – 90 min) of complex **3** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K in the presence of 700 μM GSH.

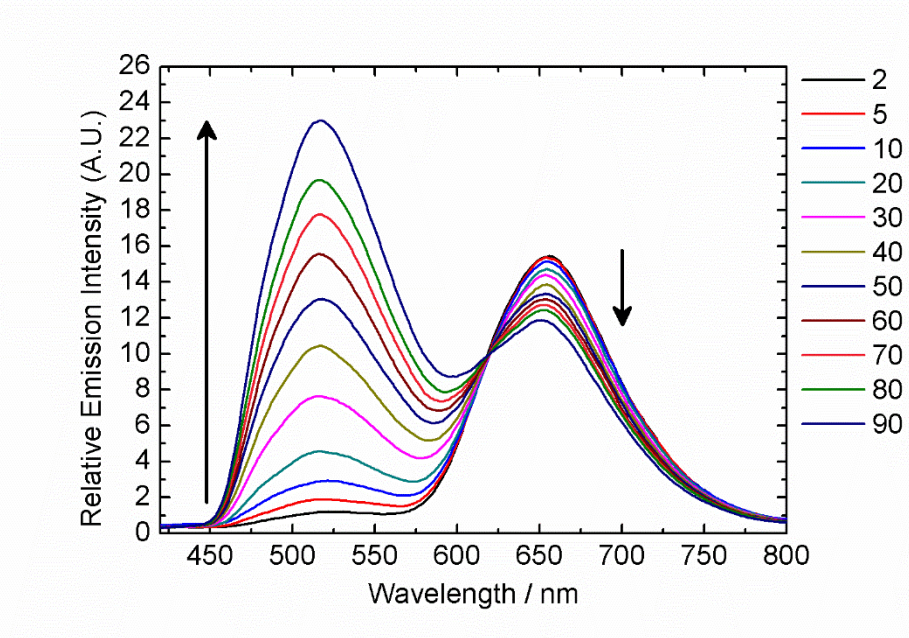


Figure S12 Time-dependent emission spectral traces (0 – 60 min) of complex **3** (10 μM) in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K in the presence of 800 μM GSH.

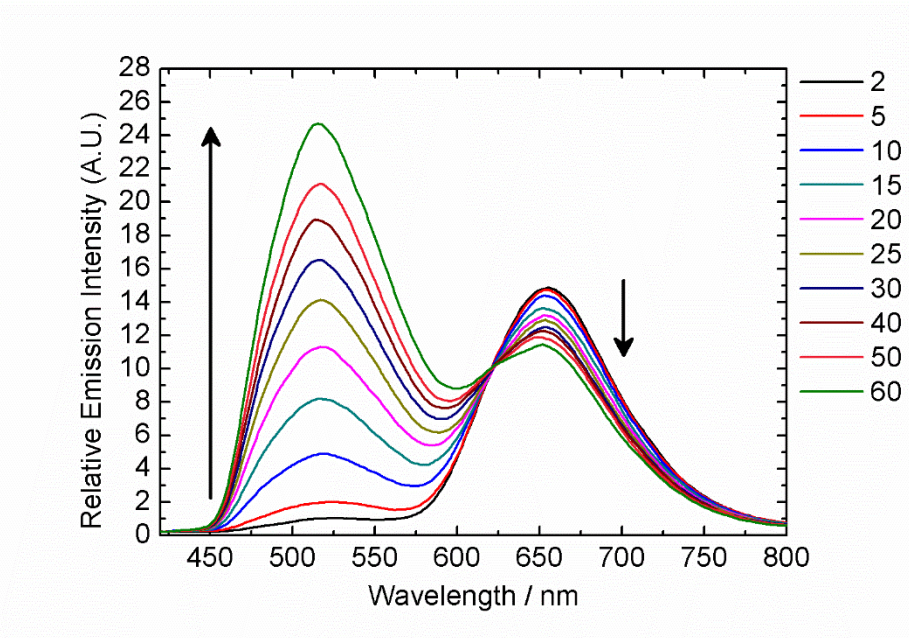


Figure S13 *Pseudo* first-order kinetics for the reactions of complex **3** with different concentrations of GSH in aerated PBS (pH = 7.2)/MeOH (7:3, *v*/*v*) at 298 K. The slope of the plot corresponds to the k_2 of the reaction (R^2 = 0.999).

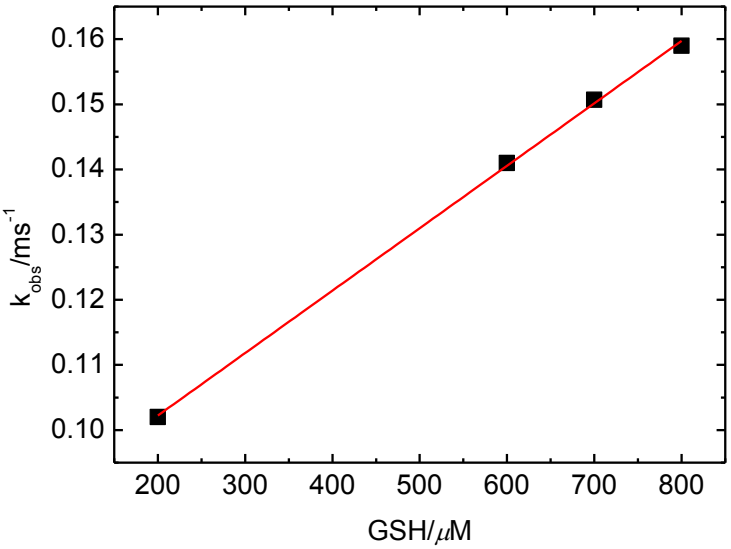


Figure S14 Cytotoxicity of complexes **1a** (a), **1b** (b), and **1c** (c) toward GSH-pretreated (5 mM, 37°C, 2 h, red) and untreated (black) HeLa cells upon incubation at 37°C for 16 h.