Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Structural and Photodynamic Properties of the Anti-Cancer Drug Irinotecan in Aqueous Solutions of Different pHs

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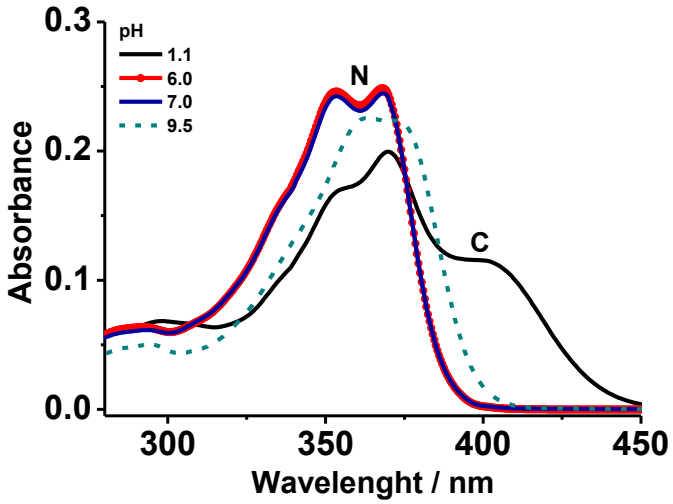


Figure S1. UV-visible absorption spectra of camptothecin (CPT) in aqueous solutions as a function of pH. The $S_0 \rightarrow S_1$ absorption bands of neutral and cationic species are marked as N and C, respectively. Data at pH = 1.1 and 6.0 are from Ref. 40.

Determination of pK_a^* (S_1):

The plot of the fluorescence intensities *vs* pH at 433 and 610 nm, where C1 or C2 – respectively – mainly emit, is presented in Figure S2.

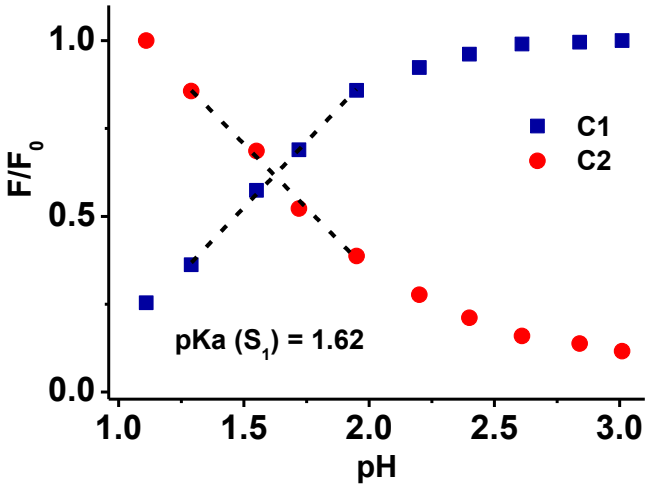


Figure S2. Fluorescence intensity changes of C1 (■, λ_{em} = 433 nm) and C2 (●, λ_{em} = 610 nm) structures with the pH of the medium.

The excited-state pK_a (pK_a^*) was obtained by determining the pH of the point of intersection between the two linear curves as shown in Figure S2 (black dashed lines). To determine this point, we solved the linear equations of the four points closest to the junction at each curve (S1):

$$0.74811x - 0.59666 = -0.72711x + 1.79605 \quad \text{(S1)}$$

Where

$$x = \frac{2.39271}{1.47522} \quad \text{(S2)}$$

Therefore,

$$pK_a^* = 1.62$$

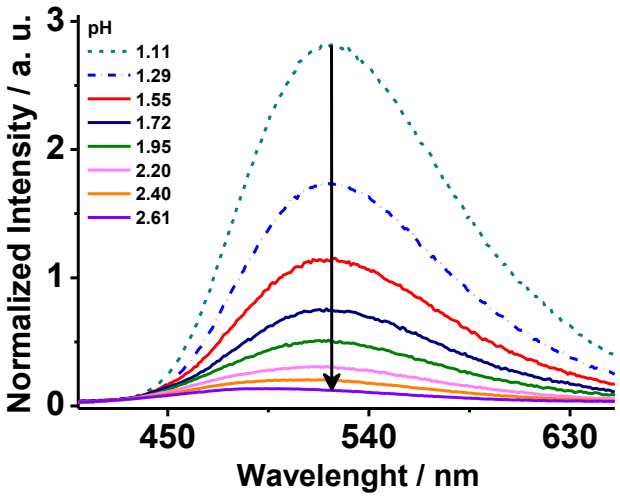


Figure S3. Emission spectra of IRT in acidic aqueous solutions (pH = 1.11–2.61). The excitation wavelength is at 400 nm.

Correction of the Emission Spectra in the 11–2.61 pH range:

At low concentrations (absorbance < 0.1), the fluorescence intensity approaches a linear expression:

$$F_\lambda = k' I_0 (\log \varepsilon l c) = K l c \quad \text{(S3)}$$

where F_λ is the fluorescence intensity at a given wavelength of excitation, k' is a rate constant that takes into account the fluorescence quantum yield, ε is the extinction coefficient at the excitation wavelength, l is the optical path, and c is the concentration of the fluorophore.

Taking into account Equation S3 for diluted aqueous IRT solutions, we corrected the emission spectra of the drug in the 1.11–2.61 pH range by Equation S4:

$$F_{\lambda}^{corr}(pH) = F_{\lambda} \times \left(A_{2.61}^{371} / A_{pH}^{371} \right) \quad \text{(S4)}$$

where $F_{\lambda}^{corr}(pH)$ is the corrected F_{λ} at a given pH, while $A_{2.61}^{371}$ and A_{pH}^{371} are the absorbance values at 371 nm at pH 2.61 and at the given pH, respectively. The corrected emission spectra in the 1.11–2.61 pH range are shown in Figure S4:

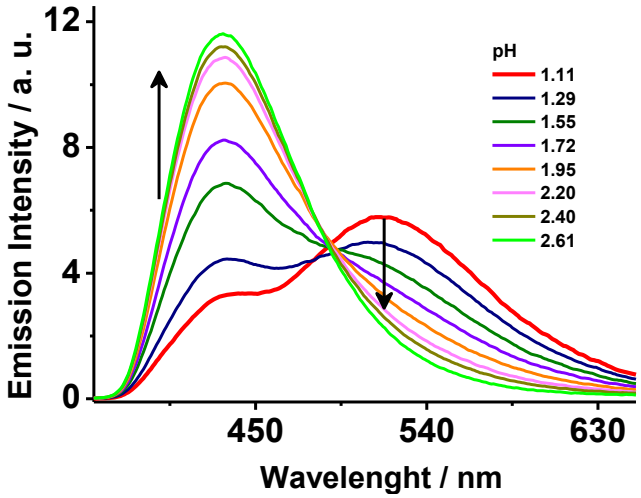
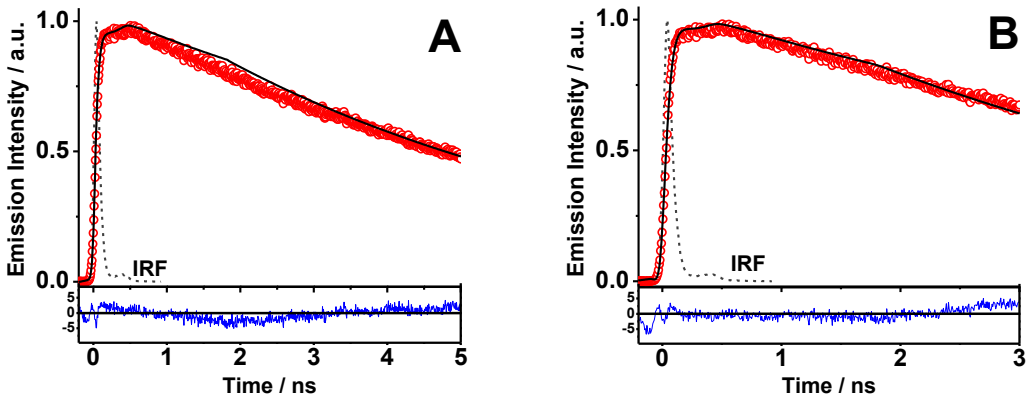


Figure S4. Corrected emission spectra of IRT in acidic aqueous solutions (pH = 1.11–2.61). The excitation wavelength is at 371 nm.

Picosecond to Nanosecond Time-Resolved Measurements



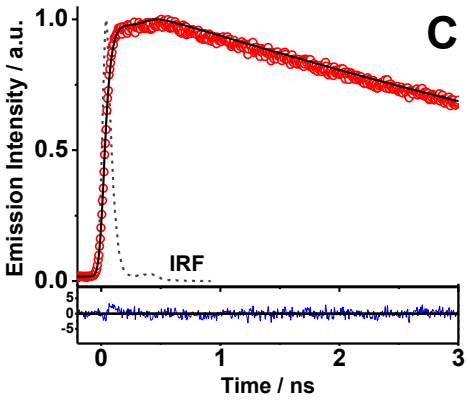


Figure S5. Normalized (to the maximum of intensity) magic-angle emission decay of IRT in aqueous solution at pH = 2.61observing at 630 nm and fitting to a mono-exponential (A) or bi-exponential function including a 100 ps- (B) or 3 ns- (C) rise time. The residual distribution is also shown for each fit. IRF is the instrumental response function (~70 ps). The excitation wavelength is at 371 nm.

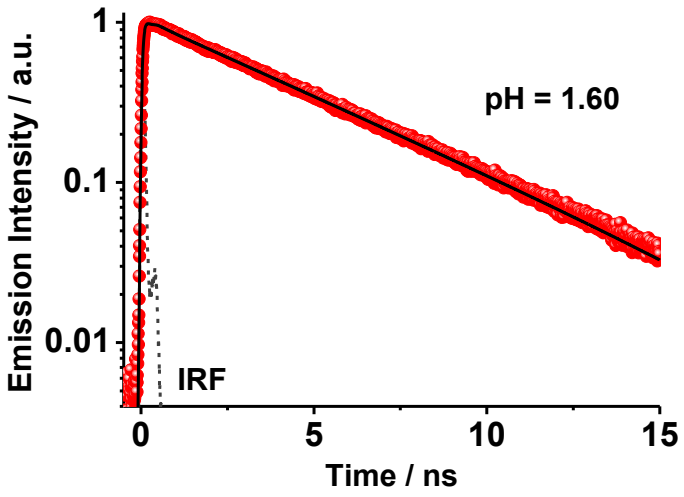


Figure S6. Normalized (to the maximum of intensity) magic-angle emission decay of IRT in aqueous solution at pH 1.60 observing at 600 nm. IRF is the instrumental response function (~70 ps). The excitation wavelength is at 433 nm.

Irinotecan in water at different pH values (Exc = 371 nm)

pH = 1.11				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	1.3	99.7	4.6	0.3
450		95		5
475		67		33
500		(-)5		95
550		(-)37		63
600		(-)40		60
630		(-)40		60

pH = 1.29				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	1.5	99.5	4.6	0.5
450		96		4
475		69		31
500		(-)1		99
550		(-)39		61
600		(-)42		58
630		(-)43		57

pH = 1.55				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	2.0	99	4.6	1
450		96		4
475		73		27
500		9		91
550		(-)40		60
600		(-)44		56
630		(-)45		55

pH = 1.72				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	2.3	98	4.7	2
450		95		5
475		77		23
500		22		78
550		(-)39		61
600		(-)44		56
630		(-)45		55

pH = 1.95				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	2.7	98	4.7	2
450		96		4
475		82		18
500		41		59
550		(-)36		64
600		(-)43		57
630		(-)44		56

pH = 2.20				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	2.9	96	4.7	4
450		95		5
475		86		14
500		57		43
550		(-)29		71
600		(-)41		59
630		(-)43		57

pH = 2.40				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	3.1	95	4.8	5
450		94		6
475		88		12
500		68		32
550		(-)15		85
600		(-)37		63
630		(-)40		60

pH = 2.61				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	3.2	93	4.8	7
450		93		7
475		89		11
500		78		22
550		28		72
600		(-)23		77
630		(-)29		71

pH = 2.84				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	3.2	92	4.9	8
450		92		8
475		90		10
500		83		17
550		57		43
600		18		82
630		0.4		99.6

pH = 3.01				
λ_{em}/nm	τ_1/ns	A_1/%	τ_2/ns	A_2/%
400	3.2	91	4.9	9
450		90		10
475		89		11
500		86		14
550		72		28
600		51		49
630		41		59

pH = 3.56				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.5	95	800	5
450		95		5
475		95		5
500		95		5
550		95		5
600		96		4
630		96		4

pH = 4.06				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.6	93	800	7
450		93		7
475		94		6
500		94		6
550		95		5
600		95		5
630		94		6

pH = 4.56				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.8	89	800	11
450		89		11
475		89		11
500		88		12
550		85		15
600		82		18
630		77		23

pH = 5.13				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.8	87	800	13
450		87		13
475		86		14
500		85		15
550		82		18
600		79		21
630		75		25

pH = 6.01				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.8	87	812	13
450		87		13
475		85		15
500		84		16
550		81		19
600		76		24
630		74		26

pH = 6.56				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.8	88	810	12
450		88		12
475		87		13
500		86		14
550		84		16
600		81		19
630		78		22

pH = 7.00				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.8	89	810	11
450		89		11
475		89		11
500		89		11
550		89		11
600		88		12
630		86		14

pH = 9.46				
λ_{em}/nm	τ_1/ns	A_1/%	τ_N/ps	A_2/%
400	3.9	85	813	15
450		85		15
475		84		16
500		82		18
550		79		21
600		76		24
630		74		26

Tables S1-S18. Values of fluorescence time constants (τ_i) and normalized (to 100) pre-exponential factors (A_i) of fitting decay functions for IRT in water solution (pH = 1.11–9.46) at different emission wavelengths (λ_{em}). The excitation wavelength is at 371 nm.

The Debye-Smoluchowski Model

Estimation of the Dielectric Constant

The dielectric constant of each acidic solution was obtained from literature data.[1]

Estimation of the Proton Diffusion Coefficient

The proton diffusion coefficient D_{H^+} is estimated using the Nernst equation:

$$D_{H^+} = RT\mu_{H^+} \Big/ F^2 \tag{S3}$$

where μ_{H^+} is the proton mobility, R is the ideal gas constant, and F is the Faraday constant.

Estimation of the Proton Mobility

The proton mobility was estimated from electrochemical data on equivalent conductance for HCl at several concentrations at 25 °C (concentration (eq dm^{-3}))[2] and number of transferred protons in water.[3-7]

Estimation of the Diffusion Constant for C1*

The diffusion constants of C1*, D_{C1^*}, was evaluated from the Stokes-Einstein relationship, Equation S4:

$$D = \frac{k_B T}{6\pi\eta R} \tag{S4}$$

where η is the viscosity of the solution. In pure water its value is 0.35×10^{-5} cm^2 s^{-1}. It was scaled to its value in HCl solutions (HCl-S) using the viscosity ratio $\eta_{H_2O} / \eta_{HCl-S}$ (the data on the viscosities of the HCl solutions were estimated from Ref. 8).

The kinetic Equations Extracted for the 1.11 ≤ pH ≤ 1.95 Regime

$$\frac{d[C1^*]}{dt} = -\left\{\frac{1}{\tau_{C1}} + k_q[H^+] + k_{DPT}^{C1^*}[H^+]\right\}[C1^*] \tag{S5}$$

$$\frac{d[C2^*]}{dt} = k_{DPT}^{C1^*}[H^+][C1^*] - \frac{1}{\tau_{C2}}[C2^*] \tag{S6}$$

where $1/\tau_{C1}$ and $1/\tau_{C2}$ are the rate constants for the no-quenched emission of C1* and C2*, respectively.

The variation of [C1*] and [C2*] with time is expressed as:

$$[C1^*] = [C1^*]_0 e^{-t/\tau_1} \quad \text{(S7)}$$

where τ_1 is the fluorescence lifetime from ps experiments.

$$[C2^*] = \frac{[C1^*]_0 k_{DPT}^{C1^*}[H^+]}{k_{DPT}^{C1^*}[H^+] + k_q[H^+] + \frac{1}{\tau_{C1}} - \frac{1}{\tau_{C2}}}[e^{-1/\tau_{C2}} - e^{-1/\tau_1}] \quad \text{(S8)}$$

From Equation (S8), $k_{DPT}^{C1^*}$ can be finally evaluated as:

$$k_{DPT}^{C1^*} = \left(\frac{1}{\tau_1} - \frac{1}{\tau_{C1}} - k_q[H^+]\right)[H^+]^{-1} \quad \text{(S9)}$$

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