Supporting Information

Excited State Proton Transfer Dynamics of Topotecan inside Bio-mimicking Nano-cavity

Raj Kumar Koninti, Krishna Gavvala, Abhigyan Sengupta, and Partha Hazra*

Department of Chemistry, Indian Institute of Science Education and Research (IISER), Pune (411008), Maharashtra, India

*Corresponding author E-mail: p.hazra@iiserpune.ac.in.

Tel.: +91-20-2590-8077; Fax: +91-20-2589 9790.

Table S1. Fluorescence decay parameters of TPT in H_2O reverse micelles (λ_{ex} = 375 nm and λ_{col} = 520 nm).

w_0	τ_1 (ns)	τ_2 (ns)	τ_3 (ns)	R_1	R_2	R_3	$\tau_{avg}^{\#}$ (ns)	χ^2
$w_0 = 6$	0.65	3.30	5.05	-0.10	0.28	0.62	4.10	0.98
$w_0 = 10$	0.62	3.07	5.16	-0.17	0.29	0.54	3.78	1.01
$w_0 = 25$	0.49	3.04	5.37	-0.19	0.22	0.59	3.94	1.00
$w_0 = 50$	0.32	2.42	5.47	-0.16	0.19	0.65	4.08	1.02

$^{\#}\tau_{avg} = R_1\tau_1 + R_2\tau_2 + R_3\tau_3$

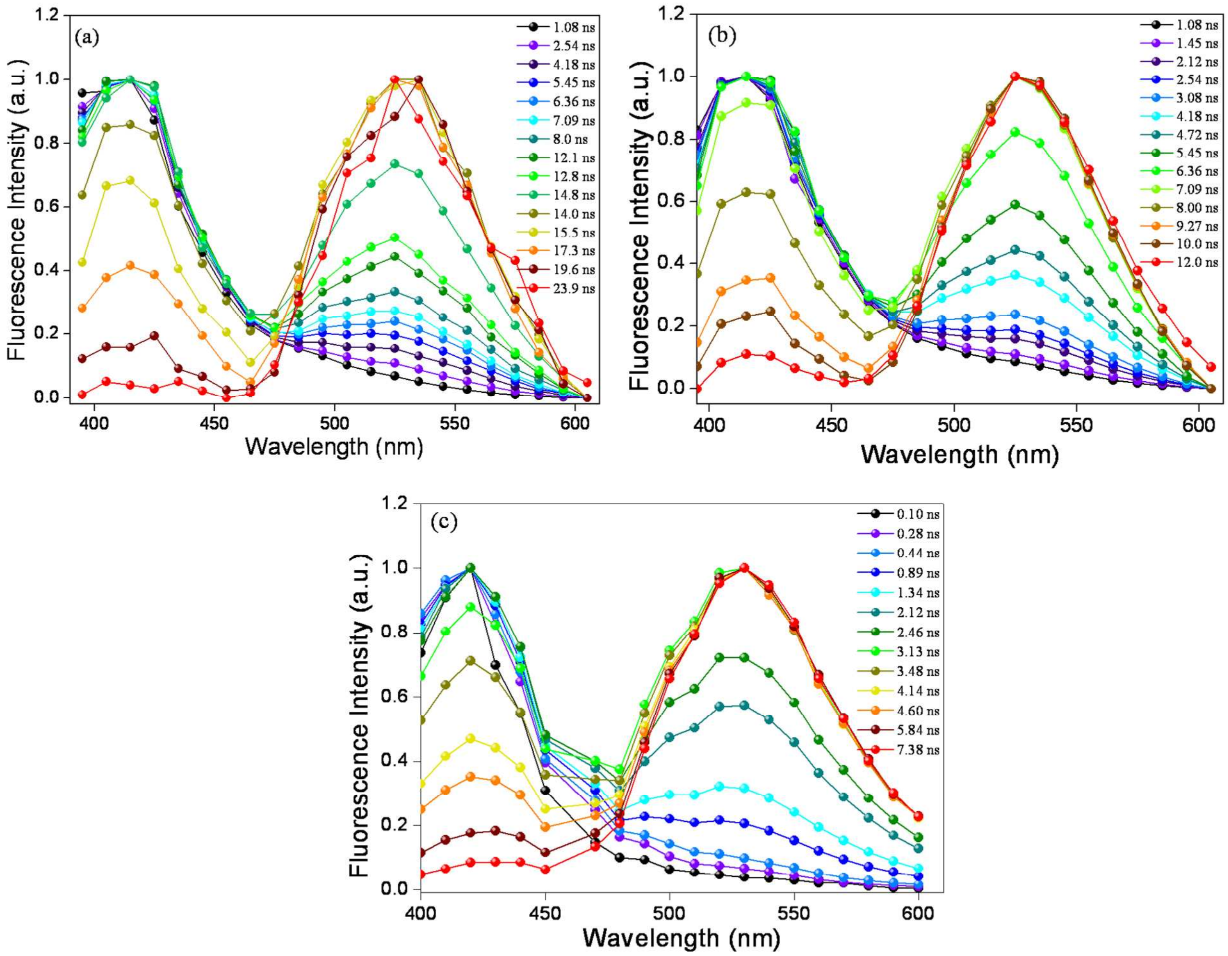

Figure S1. Time-resolved emission spectra (TRES) of TPT in reverse micelle (λ_{ex} = 375 nm) at (a) w_0 = 4, (b) w_0 = 10, and (c) w_0 = 50.

Table S2. Fluorescence decay parameters of TPT in D_2O reverse micelles (λ_{ex} = 375 nm).

w_0	$\lambda_{collection}$	τ_1 (ns)	τ_2 (ns)	R_1	R_2	$\tau_{avg}^{\#}$ (ns)	χ^2
w_0 = 15	570 nm	0.86	5.40	-0.37	0.63	3.74	1.15
w_0 = 25	570 nm	0.72	5.54	-0.35	0.65	3.84	1.07
w_0 = 50	570 nm	0.55	5.60	-0.35	0.65	3.86	1.18

$^{\#}\tau_{avg} = R_1\tau_1 + R_2\tau_2$

Note S1:

Rate of proton transfer ($k_{PT} = 1/\ \tau_1$) is measured from the rise lifetime component (τ_1 in Table 1 and Table S1).

Kinetic isotopic effect (KIE) is obtained by ratio of rate of proton transfer rate in D_2O and water, i.e., KIE = $k_{PT}(H_2O)/k_{PT}(D_2O)$

For example, at w_0 = 15,

Rate of proton transfer in H_2O-RM (w_0 = 15) is $k_{PT}(H_2O) = 1/(0.49\ \text{ns}) = 2.04 \times 10^9\ s^{-1}$

Rate of proton transfer in D_2O-RM is $k_{PT}(D_2O) = 1/(0.86\ \text{ns}) = 1.16 \times 10^9\ s^{-1}$

Therefore, KIE = $k_{PT}(H_2O)/k_{PT}(D_2O) = (2.04 \times 10^9\ s^{-1})/(\ 1.16 \times 10^9\ s^{-1}) = 1.75$

<u>Note S2</u>:

Wobbling-in-a-Cone Model: The fluorescence anisotropy decay of TPT in the reverse micellar media is biexponential in nature. The biexponential behavior of anisotropy decay can be explained with the help of wobbling-in-a-cone model.[1-3] Using wobbling-in-a-cone model, the decay of anisotropy can be described by the following equation:[1-3]

$$r(t) = r_0 \left[S^2 \exp\left(\frac{-\mathrm{t}}{\tau_{\mathrm{slow}}}\right) + (1 - \mathrm{S}^2) \exp\left(\frac{-\mathrm{t}}{\tau_{\mathrm{fast}}}\right) \right] \quad (1)$$

where S^2 is the order parameter, which can be used for understanding the location of the probe inside the reverse micelle. τ_{slow} and τ_{fast} are slow and fast rotational relaxation of the probe molecule inside the reverse micelle respectively, and r_0 is the limiting anisotropy. The order parameter describes the equilibrium orientational distribution of the probe inside the reverse micelle and follows the relation:

$$0 \leq S^2 \leq 1$$

where S = 0 indicates the motion is completely free and S = 1 corresponds to the completely restricted environment.

We have also calculated the wobbling semicone angle θ° for the drug to execute the wobbling in cone motion, and the semicone angle θ° can be defined by the following equation

$$\theta^\circ = Cos^{-1}\left[\frac{1}{2}\left(\left(\sqrt{(1+8S)}\right) - 1\right)\right] \quad (2)$$

The estimated cone angles (θ°) calculated using eqn. 2 are 28.05°, 26.98°, and 27.52° for w_0 = 4, 25, and 50 respectively.

References:

(1) Moilanen, D. E.; Fenn, E. E.; Wong, D.; Fayer, M. D. Water Dynamics at the Interface in AOT Reverse Micelles. *J. Phys. Chem. B* **2009,** *113*, 8560-8568.

(2) Patra, A.; Luong, T. Q.; Mitra, R. K.; Havenith, M. The Influence of Charge on the Structure and Dynamics of Water Encapsulated in Reverse Micelles. *Phys. Chem. Chem. Phys.* **2014,** *16*, 12875-12883.

(3) Douhal, A.; Angulo, G.; Gil, M.; Organero, J. Á.; Sanz, M.; Tormo, L. Observation of Three Behaviors in Confined Liquid Water within a Nanopool Hosting Proton-Transfer Reactions. *J. Phys. Chem. B* **2007,** *111*, 5487-5493.