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A Genuine Intramolecular Proton Relay System Undergoing Excited-State Double Proton Transfer Reaction

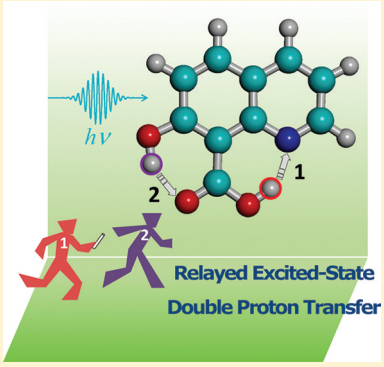
Kuo-Chun Tang,[†] Chyi-Lin Chen,[†] Hsiao-Han Chuang,[‡] Jien-Lian Chen,[‡] Yi-Ju Chen,[†] Yi-Chih Lin,[†] Jiun-Yi Shen,[†] Wei-Ping Hu,*[,‡] and Pi-Tai Chou*[,†]

[†]Department of Chemistry, National Taiwan University, Taipei, Taiwan

[‡]Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, Taiwan

Supporting Information

ABSTRACT: 7-Hydroxyquinoline-8-carboxylic acid (**1**), which possesses dual intramolecular hydrogen bonds, undergoes excited-state intramolecular double proton transfer, (ESIDPT) resulting in a quinolinone-like tautomer emission ($\lambda_{max} \sim 470$ nm). ESIDPT of **1** is cooperative, as evidenced by chemically blocking either proton donating site. While the overall rate of ESIDPT is higher than the system response limit, $(220\ fs)^{-1}$, the theoretical approach favors a concerted, asynchronous ESIDPT with a rather small or negligible barrier, demonstrating an intrinsic proton relay system that undergoes intramolecular double proton transfer in the electronic excited state.

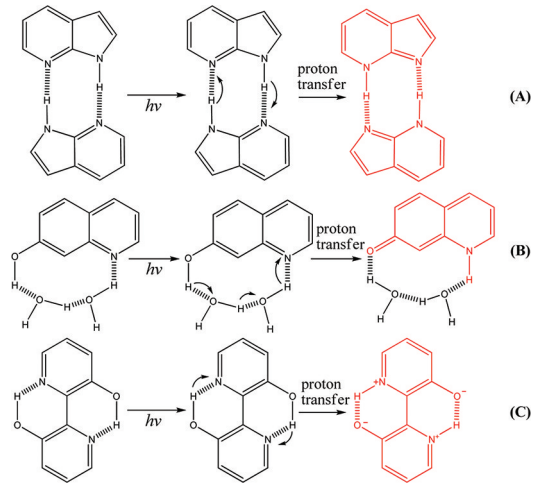


SECTION: Dynamics, Clusters, Excited States

During the past few decades, excited-state intramolecular proton transfer (ESIPT) has been an issue of fundamental importance.[1−10] Numerous molecules exhibiting such a phenomenon have been studied to shed light on the associated mechanisms. Most of the ESIPT reactions involve single proton (or hydrogen atom) transfer, giving rise to a proton-transfer tautomer in the excited state. Because of the significant alteration of the electronic structure, the tautomer possesses distinctly different photophysical properties from that of the original (normal) species, providing ample versatility in current cutting-edge applications, such as fluorescence probes,[11−13] molecular/ion probes,[14,15] and white organic light-emitting diodes.[16]

In yet another approach, excited-state proton transfer (ESPT) incorporating the transfer of two or more protons is of paramount interest. Such a phenomenon attracts more attention mainly due to its intrinsic property in mimicking proton relay in vital biosystems. Prototypes include ESPT of green fluorescence protein, which incorporates proton relay of specifically aligned H_2O and amino acid units,[17−25] and the possible photoinduced mutation of DNA A−T and G−C base pairs with double and triple hydrogen bonds.[26−29] Unlike the ubiquitous single-proton transfer cases, however, multiple proton-transfer systems are rare and usually involve molecular self-assembly or solvent assistance. One paradigm that should be credited to is the 7-azaindole dimer (see Scheme 1A). In the 7-azaindole monomer, the four-membered-ring configuration keeps the proton donor and acceptor sites far from forming an intramolecular hydrogen bond. Instead, upon forming the dual hydrogen-bonded dimer, excited-state double proton transfer (ESDPT) takes place, resulting in an imine-like dimer (Scheme 1A). Since two protons are involved, ESDPT brings

Scheme 1. Representative Excited-State Multiple Proton Transfer Systems: (A) 7-Azaindole Dimer, (B) 7-Hydroxyquinoline, and (C) [2,2′-Bipyridyl]-3,3′-diol[a]



[a]The arc circle arrows are for the direction of proton transfer.

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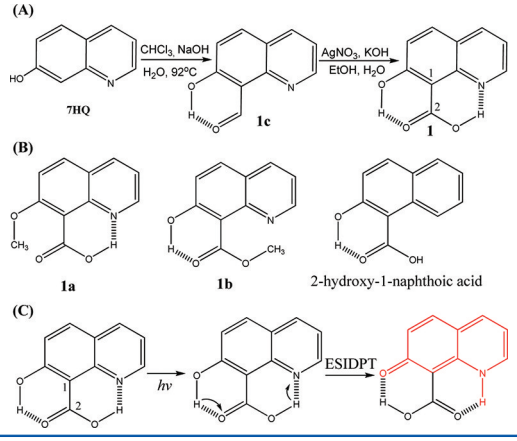
up a fundamental issue regarding stepwise versus concerted reaction pathways. The latter also refers to the definition of synchronous versus asynchronous patterns, especially when the two protons in the 7-azaindole dimer are symmetrically identical.[30−33] As for the excited-state triple proton transfer, a representative case should be ascribed to 7-hydroxyquinoline (7HQ, see Scheme 1B), in which the much farther separation between proton donor and acceptor sites requires two protic solvent (e.g., water) molecules to execute the proton transfer reaction in the excited state.[34−39] While the proton transfer in these two cases takes place via either self-assistance or solvent assistance, which is considered to be an intermolecular process, representative models for the excited-state intramolecular double proton transfer (ESIDPT) may be ascribed to [2,2′-bipyridyl]-3,3′-diol ($BP(OH)_2$, see Scheme 1C)[40] and benzoxazole derivatives.[41] $BP(OH)_2$ comprises a symmetric structure with two identical protons, so that ESIDPT occurs following photoexcitation via both concerted and/or stepwise proton transfer pathways.[42,43] A recent theoretical study by Lischka and co-workers, however, was keen on a sequential mechanism.[44]

Evidently, the first two classes shown in Scheme 1 (see A and B) require intermolecular interactions which are subject to perturbation from the "guest molecules". For the case of 7-azaindole hydrogen-bonded dimer, the double proton transfer dynamics may correlate with the time-dependent geometry variation induced by dual intermolecular hydrogen bonding.[45−54] As for the solvent-assisted multiple proton transfer (case B, Scheme 1), the dynamics of solvent perturbation may play even more determining roles. These make the fundamental approach regarding intrinsic multiple proton transfer intricate and even formidable. $BP(OH)_2$ (case C) possesses two identical hydrogen bonds residing in two equivalent chromophores, so that it could even execute single proton transfer for each independently, which makes the study of multiple proton transfer complicated. To our viewpoint, a case in point to probe, e.g., double proton transfer per se, lies in a system possessing a relay type of intramolecular dual hydrogen bonds, such that ESIDPT takes place free from the exterior perturbation. Herein, we report the strategic design and synthesis of a novel molecule 7-hydroxyquinoline-8-carboxylic acid (**1**, see Scheme 2) that possesses intramolecular dual hydrogen bonds per se. Using compound **1** and its analogues, we then demonstrated the relay-type intramolecular ESIDPT reaction via a combination of spectroscopy/dynamics, theoretical approach, and chemical modification.

Scheme 2. (A) Synthetic Route of 1; (B) Structures of Derivatives of 1a, 1b, and 2-Hydroxy-1-naphthoic Acid; (C) Proposed Mechanism of ESDPT of 1



The synthetic details of compound **1** are described in the Supporting Information. In brief, as depicted in Scheme 2A, the starting reagent 7-hydroxyquinoline was reacted with $CHCl_3$ in basic (NaOH) solution to form 7-hydroxyquinoline-8-carbaldehyde (**1c**), which was then oxidized by $AgNO_3$ in basic EtOH, giving compound **1** with a good yield (62%). Detailed characterization of **1** is provided in the Supporting Information. Notably, ^1H NMR spectra of **1** clearly reveal two downfield shifted protons located at 16.5 and 17.6 ppm in DMSO-d_6. For further firm assignment, compound **1a** (see Scheme 2B) was synthesized via methylating the quinolic O−H proton of **1** (see Supporting Information for details). As a result, **1a** reveals the disappearance of the quinolic O−H proton expected to be ∼14.0 ppm. In yet another approach, attempts to methylate the carboxylic −OH group, forming **1b**, unfortunately failed, perhaps due to the existence of a stronger intramolecular hydrogen bond that made it difficult to be methylated. Alternatively, the reaction intermediate **1c** (see Scheme 2A) was used as a model to represent the derivative of **1** without carboxylic proton. As a result, **1c** reveals a chemical shift of the quinolic O−H proton at ∼16.5 ppm (see Supporting Information). Combining the results, the proton peaks at 16.5 and 17.6 ppm for compound **1** are assigned to O−H and COOH protons, respectively. The significant downfield shifts of these two protons support the dual hydrogen-bonding formation in compound **1**, i.e., two six-membered-ring hydrogen bonds, one between the −COOH and the pyridyl nitrogen and the other between the −OH and the carbonyl oxygen (see Scheme 2).

Figure 1 depicts the steady-state absorption and emission spectra of compound **1** in cyclohexane at room temperature.

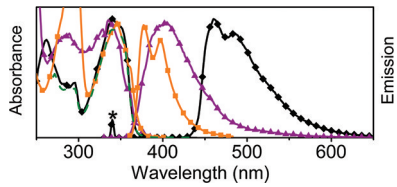


Figure 1. Absorption and emission spectra of **1** (black, ◆), **1a** (purple, ▲), and **1c** (orange, ■). Green dashed line, which overlaps well with the absorption spectrum of **1**, depicts the excitation spectrum of **1** monitored at 500 nm. The asterisk indicates excitation wavelength.

Compound **1** exhibits the lowest lying absorption band maximized at 340 nm, attributed to a $\pi\pi^*$ transition. From our theoretical calculation at the B3LYP/6-311+G(d,p) level, the HOMO and LUMO are evenly distributed throughout the molecule (see Figure S1 in the Supporting Information). Upon excitation, a large Stokes-shifted emission maximized at ∼465 nm is resolved ($\Phi \sim 0.3$) in cyclohexane. The identical excitation and absorption spectra (see Figure 1) conclude the same ground-state origin for the emission. The difference in peak frequency between absorption and emission is as large as 7910 cm^{-1}, which warrants the occurrence of proton transfer in the excited state, forming a proton-transfer tautomer.

In theory, since either proton in **1** may undergo ESIPT, the possibility of each single proton transfer must be taken into account. First, we probe this issue via chemical modification. The possibility of single proton transfer from carboxylic proton

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to quinolic nitrogen was examined using **1a** as a prototype, in which the quinolic O−H proton has been removed via methylation. As shown in Figure 1, **1a** reveals the absorption (λ_{max} = 335 nm) and emission (λ_{max} = 405 nm) that are mirror images, indicating a lack of single ESIPT from carboxylic proton to the quinolic nitrogen in **1a**. In yet another approach, **1c** shows a normal Stokes shifted emission (375 nm) versus the lowest lying absorption (335 nm, see Figure 1), and no large Stokes-shifted tautomer emission was observed. Also, it is noteworthy that, upon replacing the quinoline moiety in **1** by naphthalene, forming 2-hydroxy-1-naphthoic acid (see Scheme 2B), ESIPT from naphthol O−H to the carbonyl oxygen was prohibited.[55] As a result, the possibility of single ESIPT from quinolic O−H proton to carbonyl oxygen is discarded as well. Summarizing the steady-state spectroscopic approach of derivatives of **1**, we thus confidently concluded that the *intramolecular double proton transfer* takes place for **1** in the excited state, resulting in a *keto*-quinolinone-like tautomer depicted in Scheme 2C. The results of chemical derivations also implied that the sequential type of proton transfer in **1**, i.e., moving one proton with the other remaining unchanged, is not feasible.

We then made further attempts to resolve the dynamics of ESIDPT for **1** by using the femtosecond fluorescence up-conversion technique. The results shown in Figure 2 reveal that

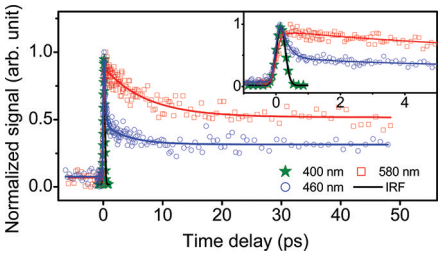

Figure 2. Time-resolved femtosecond fluorescence up-conversion of **1** monitored at 400 nm (green stars, ★), 460 nm, (blue open circles, ○), and 580 nm (red open squares, □). Solid lines depict the corresponding fitting curves (blue and red) and instrument response function. (black) Inset: the depiction of relaxation dynamics within 5 ps.

the tatuomer emission (monitored at 580 nm) consists of a rise time that is shorter than our system response (<220 fs), followed by a fast relaxation decay time of 5.1 ps (vide infra) and a much longer decay time that is further resolved to be 6.3 ns by time-correlated single photon counting measurement. Upon monitoring at e.g. near 400 nm, which is supposed to be in the normal emission region and is obscure in the steady-state measurement, the signal is almost identical to the instrument response function (IRF) which has been determined by monitoring the Raman scattering signal at ∼403 nm from neat cyclohexane. The concern that Raman scattering signal by 360 nm excitation pulse interfering the measurement around 400 nm cannot be ruled out. Unfortunately, it is not possible to tune the excitation wavelength bluer for current laser system free from the Raman scattering at 400 nm. On the other hand, attempts by monitoring at <400 nm emission are not successful due to the fact that the signal is weaker than the interference from scattering of non-phase-matching second harmonic generation of the probe pulse. When monitoring at 460 nm where both normal and tautomer emissions are possibly overlapped, a fast, irresolvable decay component (<220 fs) is acquired (see Figure 2 and the inset), which is assigned to the decay of the normal emission. Following the ultrafast decay, two decay components of 5.0 ps and 6.3 ns are reasonably ascribed to the relaxation dynamics of the proton transfer tautomer due to their identity with that monitored at 580 nm.

The above dynamics results, in combination with the information gathered from chemically modified derivatives, led us to conclude an ultrafast (<220 fs) ESIDPT for **1** in cyclohexane, forming a keto-like tautomer species depicted in Scheme 2C. Accordingly, 5.0 ps and 6.3 ns are assigned to be the vibrational coupled solvent relaxation and population decay time constants, respectively, for the keto-tautomer species. The former assignment is reasonable due to the highly exergonic ESIDPT reaction deduced via the computational approach (vide infra). Amid the vibrational relaxation, one might expect corresponding rise dynamics upon monitoring at longer wavelengths of the tautomer emission. However, the instant rise component at e.g. 580 nm (see inset of Figure 2) is indicative of the cancelation between decay and rise components at the tail of emission region. Upon deuterium substitution on both O−H and COOH sites, a similar system response limited rate constant of ESIDPT is observed (see Figure S2, Supporting Information), indicating that ESIDPT is either barrierless or perhaps triggered by low-frequency vibrational motions associated with hydrogen-bonding distances.[10] This viewpoint is further verified in the section of computational approach elaborated below.

More insight into the mechanism of ESIDPT for compound **1** was examined via computational approaches, in which we probed the energetics of ESIDPT along various proton transfer pathways. The ground-state potential energy surface calculated at the B3LYP/6-311+G(d,p) level is shown in Scheme S1 of the Supporting Information. The normal form was calculated to be the dominant ground-state species due to its lower energy than the keto-tautomer form by 4.4 kcal/mol. No intermediate can be located along the two pathways, in which path A begins with the transfer of the phenolic proton to the carbonyl oxygen followed by the transfer of the carboxylic proton to the quinolic nitrogen, while the order of proton transfer is reversed in pathway B. The calculated paths showed that after the small barrier was overcome during the first proton transfer, the second proton transfer, which was barrierless, followed immediately, i.e., a concerted type of reaction pattern. Our focus here, however, is primarily on the lowest excited-state potential energy surface (PES) in the singlet manifold, which was modeled with the various theoretical levels using the same basis set (see Supporting Information for details). Among the results, TD-B3LYP gave a vertical excitation energy of the normal form of 3.83 eV (323 nm), which is in good agreement with the absorption maximum (Figure 1). The calculated vertical emission energy of the tautomer was 2.46 eV (503 nm), which is also consistent with the emission spectral feature in Figure 1. At the TD-B3LYP/6-311+G(d,p) theoretical level, the tautomer was predicted to be 14 kcal/mol lower in energy than the normal form. As shown in Scheme 3, we also applied the CIS theory for comparison and located two distinct stepwise ESIPT pathways. These two pathways were similar to those located on the ground state (vide supra) but with an intermediate between two consecutive proton transfer processes. However, the single-point (SP) TD-B3LYP energy calculation on the stationary points located by the CIS theory resulted in a barrierless pathway B and a pathway A with only 2 kcal/mol of barrier. Neither pathway contained kinetically

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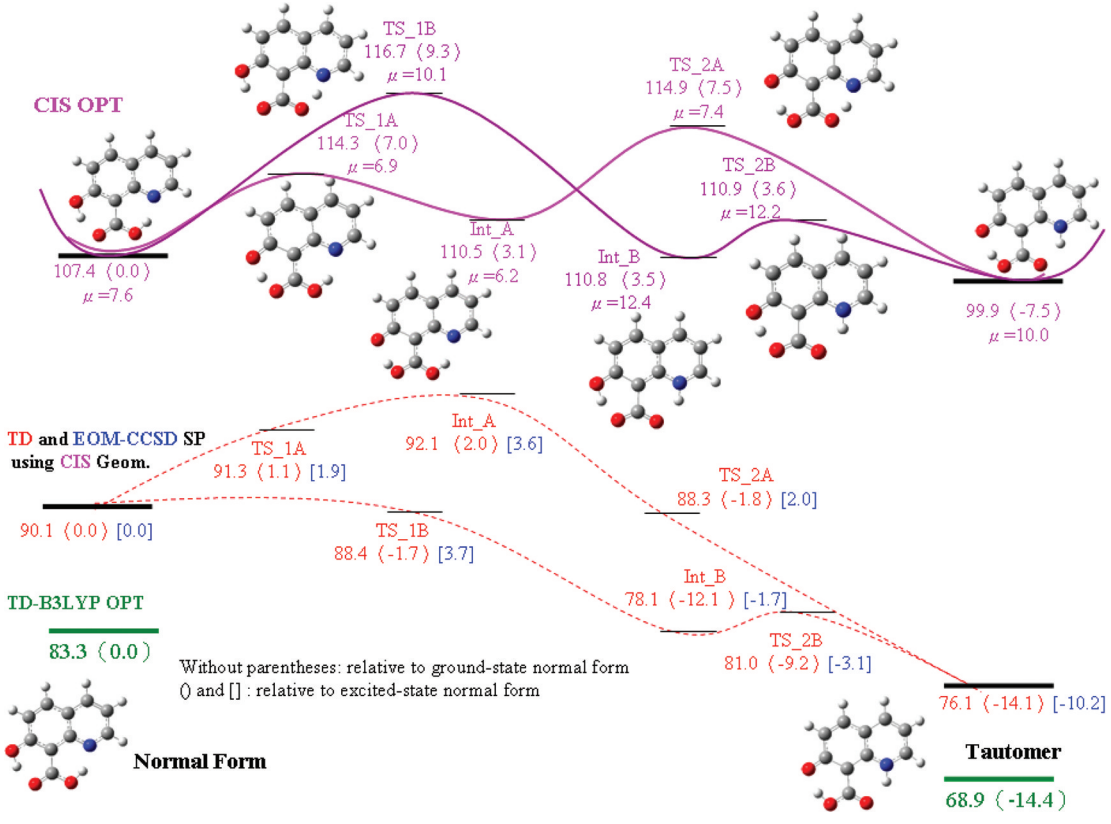
Scheme 3. Energy Diagram of ESIDPT Mechanism of Compound 1 in the Excited State by Means of Various Theoretical Approaches[a]



[a]The calculation is done in the gas phase. TS = transition state, Int = intermediate, OPT = geometry optimization, and SP = single point.

stable intermediates. We further calculated the relative energies on the first-excited states using the more sophisticated EOM-CCSD theory that has been shown to give more reliable energetics than the CIS and TD methods at the central regions of the reaction path.[56] As shown in Scheme 3, the EOM-CCSD calculation suggested that the tautomer is 10 kcal/mol lower in energy than the normal form, and both ESIPT paths predicted by the CIS theory had only one classical energy maximum with barriers of only 3.6 and 3.7 kcal/mol, respectively. If the vibrational zero-point energies of the transition states and the normal form (at CIS level) were included, the predicted barriers on paths A and B would be 0.7 and 0.4 kcal/mol, respectively. Thus, the highest level calculation also suggested that the ESIDPT would proceed concertedly along both reaction paths with very low barriers.

The combination of both experimental and theoretical approaches draws the conclusion that the ESIDPT in **1** would proceed very rapidly with a small or even negligible barrier, which may be fine-tuned by certain large-amplitude, structural motion associated with hydrogen bond, manifesting its lack of H/D effect in ESIDPT dynamics (vide supra). The experiment based on chemical modification concludes the prohibition of stepwise single proton transfer for either pathway A or B shown in Scheme 3. While ESIDPT in **1** favors a concerted type of reaction, at this stage, whether the reaction is synchronous or asynchronous is pending resolution mainly due to the very small barriers and hence system irresolvable reaction time scale. Nevertheless, owing to substantial difference in PES between A and B pathways and highly unsymmetrical dual hydrogen-bonding sites, the reaction is prone to an asynchronous process. The TD-B3LYP and, to a lesser extent, EOM-CCSD calculations predicted that the B path, in which the carboxylic proton is transferred before the quinolic proton, would be the preferred pathway.

In summary, having compound **1** with a relay of dual hydrogen bonds as a paradigm, we demonstrated a relayed intramolecular double proton transfer in the excited state. We can envisage that the use of carboxylic substituent in **1** as a bridge to "catalyze" the double proton transfer should not just be a unique case. Based on similar synthetic strategy, the design and synthesis of new systems with multiple hydrogen bonds are feasible, so that the study of a relay/networking type of proton transfer should attract a broad spectrum of interest from both fundamental and biomimicking aspects.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic and computational details, time-resolved spectroscopic result, and crystallographic data for **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chop@ntu.edu.tw (P.-T.C.), chewph@ccu.edu.tw (W.-P.H.).

■ ACKNOWLEDGMENTS

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