

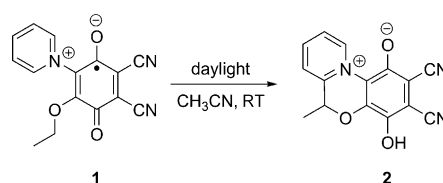
A Spectroscopic and Computational Study of a Photoinduced Cross-Dehydrogenative Coupling Reaction of a Stable Semiquinone Radical

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Light-induced promotion of molecules to electronically excited states may initiate photochemical processes resulting in the formation of photoproducts or intermediates that will further transform into products.^[1] Examples of photochemical reactions include the Barton^[2,3] and Norrish-type-II reactions.^[4,5] For Barton-type reactions, the characteristics of the primary photochemical processes are homolytic fission of the N–O bond of organic nitrites which results in transient alkoxy radicals, whereby through δ -hydrogen abstraction, alkoxy radicals (δ -hydroxy alkyl radicals) are generated. Through further transformations, this reaction provides a unique tool for preparing suitable δ -substituted derivatives in steroids. The Norrish-type-II reaction addresses the phototransformation of ketones that contain a hydrogen atom at the γ position. Both photoinduced processes have in common a 1,5-hydrogen migration from C(4) to the oxygen atom via a six-membered ring transition state, hence C–H bonds remote from the functional groups are activated. Thus, the 1,5-hydrogen transfer is initiated either from transient alkoxy radicals or from electronically excited carbonyl states.

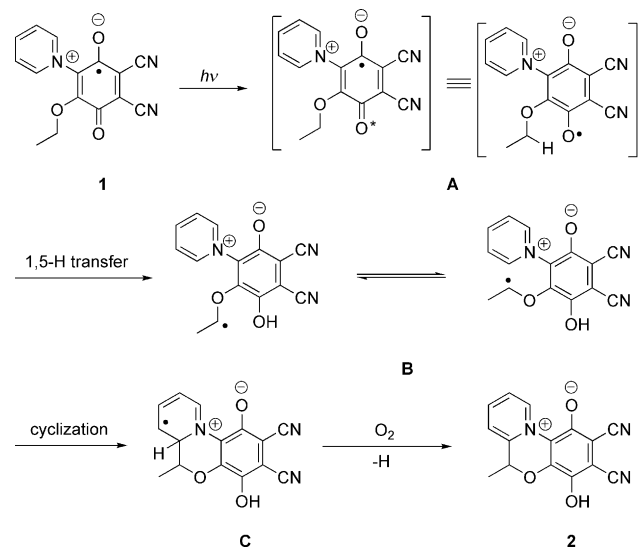
In a recent study we reported the synthesis of stable semiquinone radicals in a zwitterionic neutral form.^[6] It is well known that quinones and their reduced forms, semiquinones and dihydroquinones, represent prototypical examples of organic redox systems. Next, to shed light on the photochemistry of these new zwitterionic semiquinone radicals, we reported the occurrence of a photoinduced intramolecular de-

hydrogenative-coupling reaction (Scheme 1).^[7] This notable example involves aspects of a Norrish-type-II reaction, but remarkably, it is now based on a radical molecular platform



Scheme 1. Synthesis of **2** by a photoinduced cross-dehydrogenative coupling reaction of **1**.^[7]

(Scheme 2). As a result, the 1,5-hydrogen transfer does not lead to transient 1,4-diradicals but to 1-aryloxyalkyl radicals. In the sequence of the reaction, a cyclization and rearomatization process yields the formation of a new C–C bond, leading to [1,4]oxazinium derivatives. From this perspective, one may note that the newly formed C–C bond emerges from both a C(sp³)–H and a C(sp²)–H bond cleavage. Although there is no question that transition-metal-catalyzed C–H activation methods have been widely developed^[8] and consequently a large variety of hydrocarbon hydrogen atoms can be cleaved, alternative reaction methods based



Scheme 2. Proposed reaction mechanism for the photoinduced cross-dehydrogenative coupling reaction.^[7]

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on photoactivated compounds, for example, aldehydes or ketones, are also well documented.^[1–5] A more recent example has been given by Phillips et al., while unravelling the reaction mechanism for a fast photocyclization of 2-benzoylpyridine by time-resolved spectroscopy and density functional theory calculations showing that transient diradical species are involved.^[9] However, in stark contrast, the actual study presented herein breaks new ground while exploring a photochemical reaction starting from a stable radical compound, and is thereby bypassing the diradical transient species occurring in the systems reported so far. Up to now, various heterocycles of the herein studied zwitterionic radical-type have been probed,^[6,7] but otherwise to the best of our knowledge no analogous radical-based photochemical reaction has been reported.

In this paper, density functional theory (DFT) computations are performed to gain further insight into the reaction mechanism of this cross-dehydrogenative coupling reaction. Moreover, we provide spectroscopic characterization of the electronically excited state of the radical (**1**^{*}) and of the intermediates **B** and **C** along the mechanistic pathway which leads to the stable photoproduct **2**. We triggered the photochemical reaction by a laser pulse and monitored the course of the reaction by the absorption of the transient species involved. The combined theoretical and experimental study proves very useful in determining the sequential steps in the mechanism for the photoinduced cross-dehydrogenative coupling reaction of radical **1**.

DFT optimizations of the geometries (Figure S1 in the Supporting Information) determined in the crystal structures^[6,7] of **1** and **2** as respective starting and end points reveal that the calculated molecular structures are in good agreement with the experimental X-ray data. Selected structural parameters in acetonitrile are presented in Table S1 (in the Supporting Information). The frontier molecular orbitals of **1** are shown in Figure S2 (in the Supporting Information). The time-dependent (TD)-DFT calculation predicts the $D_1 \leftarrow D_0$ excitation of **1** to be dominated (97%) by a one-electron SOMO to LUMO promotion at 610 nm (2.03 eV). The steady-state electronic absorption spectra of **1** and **2** together with the calculated transitions are shown in Figure 1. Solutions of **1** are brownish owing to a series of broad absorption bands over almost the entire visible spectral region

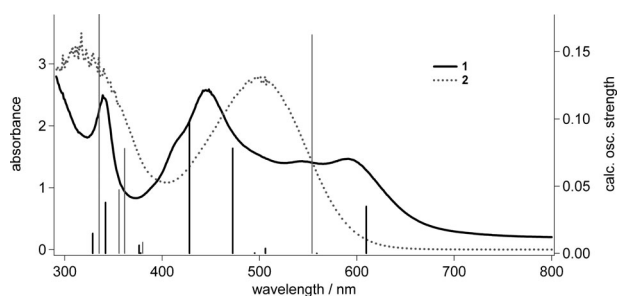


Figure 1. Steady-state electronic absorption spectra of **1** and **2** in CH₃CN, together with the TD-DFT (B3LYP/cc-pVTZ level) calculated transitions indicated by vertical lines.

and are non-fluorescent. In acetonitrile, there are absorption maxima at 592, 542, and 445 nm that are hardly shifted in DMF solution. Solutions of **2** have a red color and show a single broad absorption band in the visible peaking at 500 nm. No fluorescence could be observed from this compound as well. The successive change of the electronic absorption spectrum of **1** upon irradiation is shown in Figure S3 (in the Supporting Information).

To access the intermediates of the photochemical process (Scheme 2), transient absorption (TA) measurements with **1** in argon-saturated acetonitrile were performed. Spectra recorded at various time delays after 400 nm excitation are shown in Figure 2. The spectra show a rich structure with pronounced minima and maxima. At first, the entire TA signal undergoes a uniform decrease of amplitude at all wavelengths. Then, within a few picoseconds, most of the positive signal decays to small positive or negative value, whereas the bleach at 600 nm remains unaltered. Finally, a sharp excited-state absorption band with a maximum at 515 nm, rises on a much slower timescale. Target analysis of the TA data, assuming a reaction scheme with four successive first-order steps,^[10] yields the evolution-associated difference spectra (EADS) shown at the bottom of Figure 2 and the lifetimes listed in Table 1. The first EADS that consists of a broad positive band should be considered with caution since the associated lifetime is close to the instrument response function (IRF). Indeed, several non-linear processes, such as cross-phase modulation, can contribute to the TA signal when the pump and probe pulses overlap temporally.^[11] However, this spectrum might also reflect an optically populated state that decays within the IRF. As discussed elsewhere for the case of carotenoids,^[12] an unequivocal assignment is not possible and hence this component will be ignored in the further discussion.

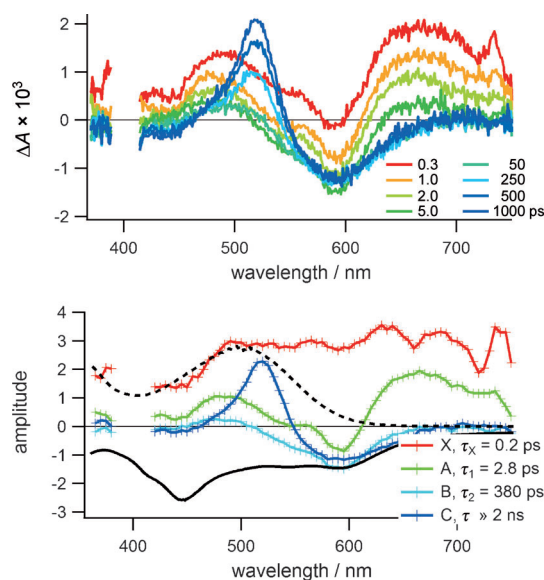


Figure 2. Top: TA spectra measured with **1** in CH₃CN at various time delays after 400 nm excitation. Bottom: EADS from the target analysis together with the steady-state absorption of **1** (black solid line, sign inverted) and **2** (dashed line).

Table 1. Time constants obtained from the target analysis of the TA spectra in solvents of different viscosity (η) and dielectric constant (ϵ) at 25 °C.

Solvent	η [cP]	ϵ	τ_x [ps]	τ_1 [ps]	τ_2 [ps]
CH ₃ CN	0.33	35.7	0.2	2.8	380
DMF	0.80	36.7	0.2	8.0	480
PhCN	1.4	25.2	— ^[a]	— ^[a]	400

[a] Not resolvable.

The three other species/states (**A**, **B**, and **C**) have lifetimes of 2.8, 380 ps, and ≥ 2 ns, respectively. Species/state **C** is too long-lived to exhibit any temporal evolution within the time window of the experiment.

Essentially identical transient spectra have been observed in DMF solution. In PhCN, the early transient spectra are strongly distorted by non-resonant contributions from the solvent but clearly the **B** \rightarrow **C** step is associated with a 400 ps time constant.

The absorption spectra of the intermediates can be estimated from the EADS. For this, the arbitrarily scaled steady-state absorption of **1** has been added to the EADS to give smooth spectra. The results are shown in Figure 3. The

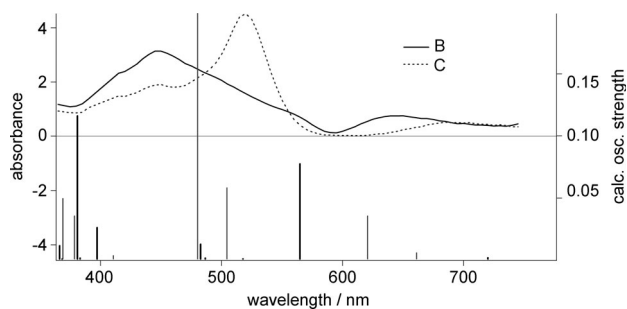
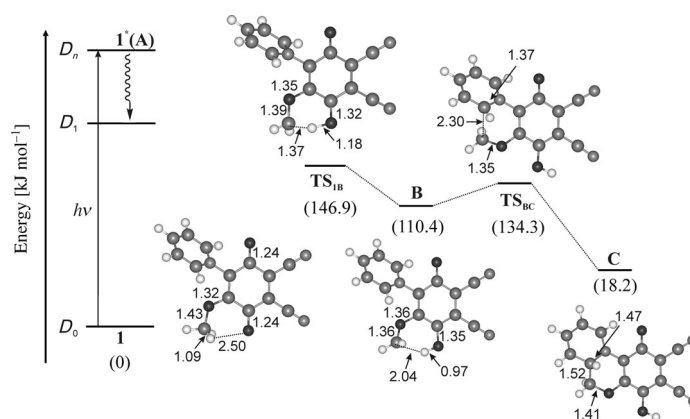


Figure 3. Estimated electronic absorption spectra of **B** and **C**, together with the TD-DFT (B3LYP/cc-pVTZ level) calculated transitions indicated by vertical lines.

intermediate with a lifetime of about 400 ps has absorption maxima around 450 and 650 nm, whereas absorption maxima around 450, 515, and 700 nm are characteristic for the intermediate with a ≥ 2 ns lifetime. It should be mentioned that our set-up suffers from some chromatic aberration and that the bands at the red edge appear most likely blueshifted from their actual position.^[13] Comparison of the estimated absorption spectra with those calculated for the two intermediates **B** and **C** points to reasonably good agreement (Figure 3). Notably, the calculated spectra appear at higher energy than the experimental estimates. The formation of **2** is not present in the TA data since this bimolecular process takes place on a much slower timescale in oxygen-poor solutions.

Scheme 3 depicts the Gibbs free energy reaction diagram for the photoinduced cross-dehydrogenative coupling reaction of **1** and Table S2 (in the Supporting Information) summarizes the selected structural parameters of the intermediates along the reaction path. After irradiation, the reaction



Scheme 3. Reaction path for the photoinduced cross-dehydrogenative coupling reaction of **1**. The Gibbs free energies (in kJ mol⁻¹) in acetonitrile solvent are given with respect to **1** in its ground state. Selected optimized bond lengths are given in Å.

starts by a 1,5-hydrogen transfer leading to 1-aryloxyalkyl radical **B** through a six-membered ring transition state, **TS_{1B}**. The computed barrier of 146.9 kJ mol⁻¹ (1.52 eV) corroborates the experimental findings that the reaction does not proceed thermally.^[7] The next step is a cyclization through a new C–C bond formation yielding an intermediate **C**, which is only 18.2 kJ mol⁻¹ (0.19 eV) higher in energy than **1**. It is reached through a transition state **TS_{BC}**, which has a barrier of 134.3 kJ mol⁻¹ (1.39 eV) with respect to the ground state of **1**, hence only 23.9 kJ mol⁻¹ (0.25 eV) above **B**. Finally, a rearomatization takes place, resulting in the formation of **2**.

According to our experiments, the **A** \rightarrow **B** reaction is associated with a rate constant of (2.8 ps)⁻¹ in CH₃CN. Frictional forces seem to play a determining role since the reaction is slowed down to (8 ps)⁻¹ in DMF, a solvent of very similar polarity. Intermediate **B** has a lifetime of 380 ps in CH₃CN (Table 1). The transition state that connects it with **C**, **TS_{BC}**, is found 23.9 kJ mol⁻¹ (0.25 eV) above **B**, which is considerably more than thermal energy at room temperature (0.013 eV). Since **B** is much longer lived than typical rate constants for vibrational cooling in CH₃CN, (20 ps)⁻¹, this reaction step cannot benefit from internal vibrational energy that stems from its fast formation in the first reaction step either. Contrary to the formation of **B**, no effect of friction is observed when changing the solvent indicating that this reaction step is kinetically controlled. Assuming a reaction barrier of 0.25 eV, the pre-exponential factor in an Arrhenius-type law should amount to 2×10^{13} s⁻¹ (or 670 cm⁻¹) to account for the experimental rate constant of (380 ps)⁻¹. This value is within the vibrational spectrum of **B**. However, given the exponential relationship between the barrier height and the rate constant, the error on the pre-exponential factor is too high to make a precise assignment to a given vibrational coordinate. In any case, this good agreement between experiment and calculations indicates that the reaction from **B** to **C** most probably takes place on the ground-state surface.

In summary, we have characterized by transient absorption spectroscopy and DFT calculations the dynamics and

energetics of a photoinduced cross-dehydrogenative coupling reaction involving a 1,5-hydrogen transfer followed by a cyclization step that forms a new C–C bond. The study makes a number of important contributions. Firstly, a Norrish-type-II photoreaction is examined that, as a novel aspect, specifically starts on a radical molecular platform. Secondly, a proposed reaction scheme could convincingly be verified by tracing experimentally and theoretically two intermediates (**B** and **C**) and the corresponding transition states of the overall reaction path. Thirdly, the molecules involved are stable semiquinone radicals, hence belonging to a class of compounds with profound chemical and biological interest.

Experimental Section

The transient absorption setup has been described elsewhere.^[14,15] Excitation pulses at 400 nm with 6 mJ cm⁻² were derived from the fundamental laser output by frequency doubling. The white light probe pulses were generated in a CaF₂ window and spectrally dispersed after the sample to record the transient spectrum from approximately 360 to 800 nm. The data has been corrected for the chirp of the probe pulse. The sample was flown through a cuvette with 1 mm pathlength and had an absorbance of about 0.2 at the excitation wavelength. Analytical grade acetonitrile (CH₃CN), *N,N*-dimethylformamide (DMF), and benzonitrile (PhCN), were purchased from Aldrich and saturated with argon by bubbling for 1 h to reduce the oxygen content prior to the experiments.

DFT calculations were performed at the PBE0^[16]/cc-pVTZ^[17] level using the Gaussian 09 program.^[18] The polarized continuum model (PCM)^[19] was employed to describe the solvent implicitly ($\epsilon=35.688$ of acetonitrile). The nature of all stationary points was verified by analytic computation of vibrational frequencies, which were also used for the computation of zero-point vibrational energies and molecular partition functions for use in computing 298 K thermal contributions to free energy employing the usual rigid-rotator harmonic oscillator approximation.^[20] TD-DFT^[21] computations at the B3LYP^[22]/cc-pVTZ level were performed to assess the excited states of the structures of interest. The hybrid B3LYP density functional was found to give the best agreement with the experimentally measured UV/Vis spectra.

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Keywords: density functional calculations • photochemistry • radicals • transient absorption • transition states

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