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Mechanistic approach to the cyclization reaction of a 2′-hydroxychalcone analogue with light and solvent

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A photochemical cyclization reaction of 1-(2′-hydroxy-1′-naphthyl)-3-(1-naphthyl)-2-propen-1-one (1,1-NHC) to give a flavanone derivative took place in benzene, but did not take place in methanol and the controlling factor of the reaction was discussed based on laser transient spectroscopy and product analysis.

Photoinduced hydrogen atom transfer reactions have received considerable attention in recent years.[1–9] They can occur either in an excited singlet state or in the triplet state. Among compounds undergoing adiabatic hydrogen atom transfer reactions in the excited state, we have reported hydrogen atom transfer reactions in ethenes having heteroaromatic rings such as pyrrole and pyridine rings at the ethylenic carbon.[8,9] Furthermore, we have been interested in intramolecularly hydrogen bonded compounds such as 2′-hydroxychalcone, where both *cis*- and *trans*-isomers form intramolecular hydrogen bonds and undergo adiabatic intramolecular hydrogen atom transfer both in the excited singlet and triplet states. The triplet state hydrogen atom transfer reaction and its role in the one-way *cis*⟶*trans* isomerization of 2′-hydroxychalcone has been particularly successful and was reported for the first time by Arai and co-workers.[1] 2′-Hydroxychalcones and related compounds are closely related to naturally occurring flavonoid dyes, and the whole picture as to the effect of substituent and substitution positions on their photochemical behaviour is essential for a better understanding of their properties. It is imperative to study the dynamic behaviour of the excited state as well as the ground state intermediate. Towards this point, we have prepared several analogues of 2′-hydroxychalcones and studied their photochemical behaviour. 1-(1′-Hydroxy-2′-naphthyl)-3-(1-naphthyl)-2-propen-1-one (1,2-NHC) underwent intramolecular hydrogen atom transfer in the excited triplet state as well as in the excited singlet state as revealed by the observation of the tautomer fluorescence and the T–T absorption spectra of the tautomer.[3]

To explore which kind of chalcone dyes are photochemically stable and to clarify the reason for these properties is important in understanding the photochemical behaviour of flavonoid compounds. Among the chalcone analogues, we have found that 1-(2′-hydroxy-1′-naphthyl)-3-(1-naphthyl)-2-propen-1-one (**1,1-NHC**) † is considerably photolabile. Thus, we have investigated the photochemical behaviour of **1,1-NHC** by transient spectroscopy as well as by product analysis. We wish to report here that **1,1-NHC** undergoes hydrogen atom transfer in the excited singlet state followed by facile deactivation to the ground state *trans*-keto tautomer, which may be the precursor for the production of the cyclization product.

Fig. 1a shows the absorption spectra of **1,1-NHC** in benzene and methanol. The absorption maximum appeared at 400 nm and 350 nm, respectively in benzene and methanol. The considerably large difference in absorption profile indicates the solvent effect on the conformation of **1,1-NHC** including the O–H : O intramolecular hydrogen bonding; the intramolecular hydrogen bonding should be present in benzene, while the methanol may interact to break any intramolecular hydrogen bonds. The dramatic change in the absorption spectrum depending on the non-polar solvent and polar protic solvent is unusual for 2′-hydroxychalcone and related compounds. The spectral profile changes with the molar ratio of benzene and methanol exhibiting an isosbestic point at 370 nm as shown in Fig. 1a. The absorption maximum of **1,1-NHC** is almost the same in methanol, ethanol, 2-propanol, and *tert*-butanol, but the small shoulder at 400 nm increases in this order. These facts indicate that the bathochromic shift of the absorption spectrum of **1,1-NHC** in benzene should be related to the intramolecular hydrogen bonding interaction.[10] Methanol breaks the intramolecular hydrogen bonds by forming intermolecular hydrogen bonds between **1,1-NHC** and methanol. The absorption spectrum of **1,1-NHC** shifts to a longer wavelength in methanol with added NaOH, indicating that the anionic form has longer wavelength absorption than the normal form in methanol.

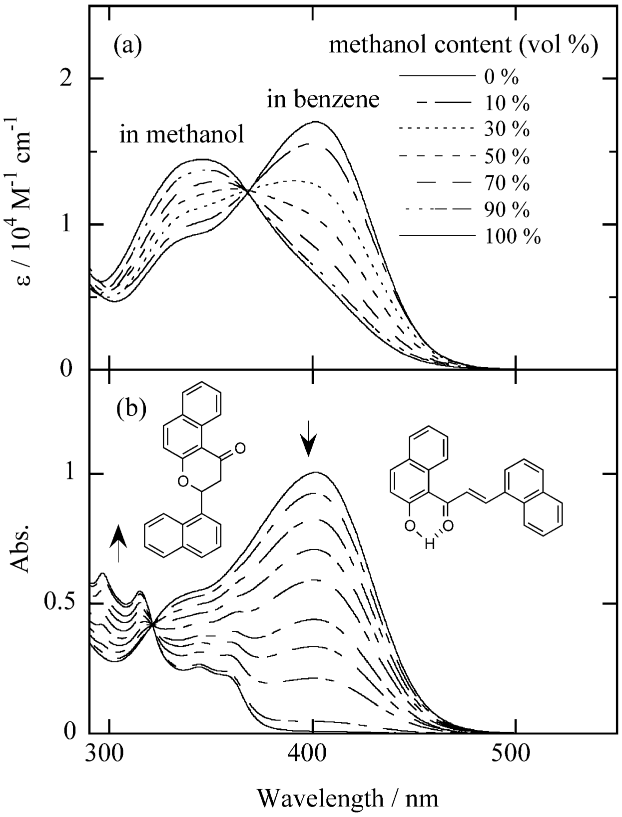

Fig. 1 (a) Absorption spectra of **1,1-NHC** in benzene, methanol, and a binary solution of benzene and methanol. (b) Change of the absorption spectrum of **1,1-NHC** (0.06 mM) on irradiation at 365 nm in benzene.

On photoirradiation, **1,1-NHC** undergoes a cyclization reaction as revealed from the spectral profile of the absorption spectra shown in Fig. 1b. The structure was confirmed by ^{1}H

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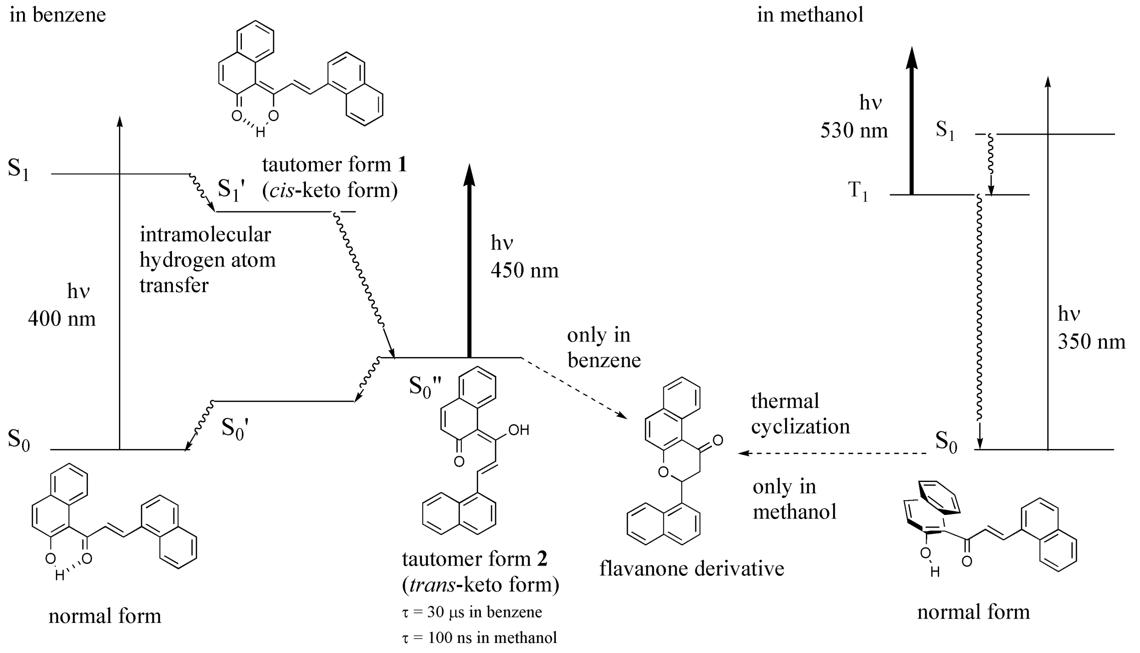

Scheme 1 Potential energy diagrams of photoinduced reaction of **1,1-NHC** in benzene and methanol.

NMR spectroscopy. The cyclization in 2′-hydroxychalcone and 1,2-NHC is very small with a quantum yield of 10^{-3} or less.[1,3,11] On the other hand, the quantum yield of the cyclization reaction of **1,1-NHC** to give flavanone derivatives is 0.013 under both an argon atmosphere and under air in benzene. However, in methanol, no detectable amounts of cyclization products were formed and the quantum yield can be estimated to be far less than 10^{-4} if it occurs. The considerable high efficiency of the cyclization reaction may be related to the facile deactivation from the excited state. It is also remarkable that 2′-hydroxychalcone undergoes the cyclization reaction both in benzene and methanol with almost the same quantum efficiency,[1] while the photochemical cyclization reaction only takes place in benzene for **1,1-NHC**.

The cyclization reaction also occured completely to give the same products when **1,1-NHC** was dissolved in methanol. The rate constant of the reaction was determined to be 4.5×10^{-4} s^{-1} and 8.3×10^{-6} s^{-1}, at 330 K and 295 K, respectively. The Arrhenius plot gave the activation energy and the frequency factor to be 93 kJ mol^{-1} and 2×10^{11} s^{-1}, respectively. The Eyring plot gave the activation enthalpy and activation entropy to be 91 kJ mol^{-1} and -36 J mol^{-1} K^{-1}, respectively. Very interestingly, the thermal cyclization did not take place in benzene. The result is very much in contrast with the photochemical cyclization taking place only in benzene solution.

Fig. 2 shows the transient absorption spectra observed on laser excitation of **1,1-NHC** in benzene and in methanol. In benzene the transient absorption maximum appeared at 450 nm. The lifetime of this transient was determined to be 30 μs, which was not affected by oxygen and was assigned to the ground state transient. Since **1,1-NHC** undergoes an efficient cyclization reaction to produce flavanone derivatives on photoirradiation, it should undergo an intramolecular hydrogen atom transfer reaction in the excited state followed by deactivation to give the *trans*-keto tautomer, which is the precursor of the cyclization product. In methanol, the transient absorption contains two components. One is the triplet state with the lifetime of 2 μs under an argon atmosphere and 140 ns under air and the other is the ground state tautomer with a lifetime of 100 ns under both argon and air. The quenching rate constant of the triplet state by oxygen can be estimated to be 3×10^9 M^{-1} s^{-1}, which is the usual value for quenching of the triplet state. The observation of both the ground state and the triplet state in methanol must be a compromise of the intramolecular and intermolecular hydrogen bonding in methanol solution. Some molecules of **1,1-NHC** with intramolecular hydrogen bonds may undergo photoinduced hydrogen atom transfer in the excited state followed by deactivation to the ground state *trans*-keto form giving the cyclization product, while other molecules having intermolecular hydrogen bonds with methanol break the intramolecular hydrogen bonds and may undergo intersystem crossing to give the triplet state in methanol.

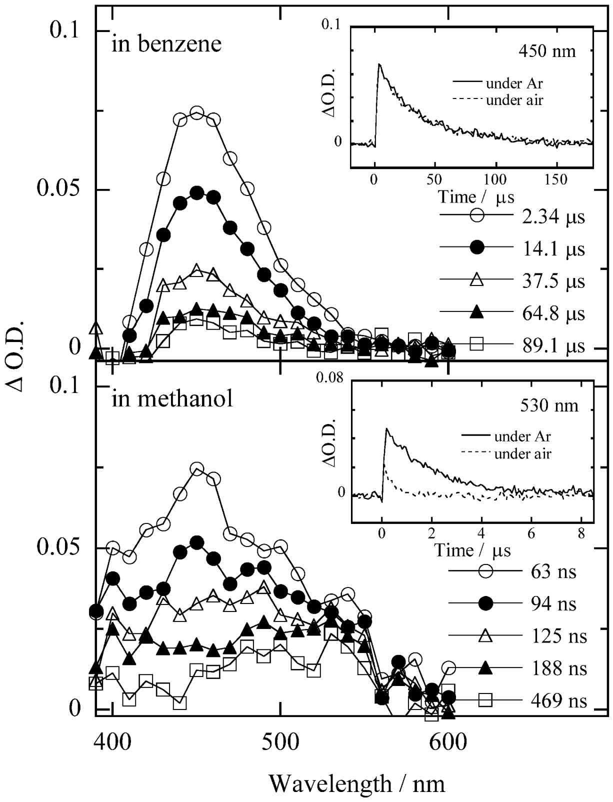

Fig. 2 Transient absorption spectra of **1,1-NHC** in benzene (0.1 mM) and in methanol (0.06 mM) under Ar.

The above results can be explained by the following discussion. The intermediate observed in benzene should be the tautomer **2** (*trans*-keto form) produced by intramolecular hydrogen atom transfer in the excited state followed by deactivation by isomerization around the quasi-double bond to the ground state. In methanol both the normal triplet state and the ground state tautomer **2** were produced. The tautomer **2** undergoes facile reversion to the ground state starting conformation due to the polar effect and/or protic effect of methanol. The absorption maximum of the ground state **1,1-NHC** appeared at 450 nm in methanol in the presence of NaOH, which was assigned to the anionic form of **1,1-NHC**. Therefore, another possibility is that in methanol, photochemical dissociation of the proton may take place to produce an anionic form of **1,1-NHC**, which cannot give any cyclization products.

The mechanism of the photoinduced reaction of **1,1-NHC** is summarized in Scheme 1. In benzene it should undergo intramolecular hydrogen atom transfer in the excited singlet state to produce tautomer form **1** followed by deactivation to the ground state tautomer form **2** (*trans*-keto form) and cyclization to a flavanone derivative. No intersystem crossing was observed in benzene, which is quite different from the photoexcited behaviour of 2′-hydroxychalcone and 1,2-NHC, where the T–T absorption spectrum of the tautomer was clearly detected. The structural factor affecting the above difference can be the steric effect present in **1,1-NHC**. Thus, the interaction of the hydrogen atom at the *peri*-position should facilitate the deactivation from the excited singlet state by rotation around the quasi double bond produced by the hydrogen atom transfer reaction before undergoing intersystem crossing to the triplet state.

In conclusion, we have succeeded in controlling the cyclization reaction of a 2′-hydroxychalcone analogue to produce a flavanone derivative by light irradiation and solvent. In addition, by the aid of laser flash photolysis and quantum yield determination of the cyclization reaction, we have studied the photochemical reaction dynamics of **1,1-NHC**, where the substitution position may strongly affect the photochemical reaction and the deactivation processes from the excited state. In addition, the solvent may affect the intramolecular hydrogen bonding giving only the ground state tautomer in benzene and both the ground state tautomer and the triplet state in methanol, which is, to the best of our knowledge, the first clear report of the solvent effect on photochemical behaviour in 2′-hydroxychalcone analogues.

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Notes and references

† **1-(2′-Hydroxy-1′-naphthyl)-3-(1-naphthyl)-2-propen-1-one (1,1-NHC)**: ^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.19 (1H, d, J = 9.2 Hz), 7.39 (1H, t, J = 7.6 Hz), 7.47–7.64 (5H, m), 7.80–7.85 (2H, m), 7.89–7.94 (3H, m), 8.10 (1H, d, J = 8.8 Hz), 8.32 (1H, d, J = 8.8 Hz), 8.76 (1H, d, J = 9.2 Hz), 12.7 (1H, s). Elemental analysis: found: C, 85.01; H, 5.08. Calc. for $C_{23}H_{16}O_2$: C, 85.16; H, 4.97%.

3-(1-Naphthyl)-2,3-dihydro-benzo[*f*]chromen-1-one (flavanone derivative): ^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 3.17 (1H, dd, J = 3.4 and 16.6 Hz), 3.39 (1H, dd, J = 13.4 and 16.6 Hz), 6.34 (1H, dd, J = 3.2 and 13.4 Hz), 7.43–8.10 (12H, m), 9.54 (1H, d, J = 8.8 Hz); Elemental analysis: found: C, 84.84; H, 5.00. Calc. for $C_{23}H_{16}O_2$: C, 85.16; H, 4.97%.

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