Solvent Effect on the Excited State Dynamics of Indazole

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Abstract

The dynamics of the excited state of indazole in various protic solvents has been studied by fluorescence and phosphorescence measurements and picosecond spectroscopy. It is shown that the fluorescenct properties of indazole are remarkably dependent on the nature of the solvent. In a nonacidic solvent only fluorescence of 1H indazole is observed. In a carboxylic acid with pKa $\simeq$4.5 such as acetic acid, 1H is converted into 2H indazole in the excited state by double proton transfer. The rate of conversion and its activation energy are determined. In an acid with a smaller pKa value indazole is protonated in the ground state and provides a broad Stokes-shifted fluorescence spectrum. It is shown that a structural change takes place in the excited singlet state of the protonated species in the time period of 10$\sim$100 ps depending on the solvent. It is suggested that indazole is protonated in a benzoic acid host and the triplet states of both 1H and 2H indazoles are produced from the excited state of protonated indazole.

Introduction

The excited-state tautomerism associated with proton transfer in a topic of current interest and various systems involving both intra- and intermolecular proton transfer have been investigated actively by spectroscopic methods[1-10]. In the course of my investigation of the lowest excited triplet (T_1) state of indazole in a benzoic acid host, I have found that the T_1 state of indazole exists in two tautomeric forms, 1H- and 2H- indazole (abbreviated as 1H and 2H, respectively) [11].

Since indazole in the ground state is considered to exist only in the 1H form, it was thought that proton transfer in the excited singlet (S_1) state might be involved in the formation of 2H in the T_1 state. To examine the occurrence of such proton transfer I have investigated the fluorescence properties of 1H- indazole in a variety of solvents by means of ordinary fluorescence measurement as well as picosecond spectroscopy[12].

In a preliminary report[12] it was shown that 1H in acetic acid is converted into 2H with a rate constant of 2.7×10^9 s^{-1} at 20°C. Since the same proton transfer does not take place in other polar protic solvents such as alcohols, it was thought that the double proton switching in a hydrogen bonded indazole-acetic acid complex might be responsible for the tautomerization. However, there remained a number of questions to be answered concerning the proton transfer in acids as well as the mechanism to produce 2H in benzoic acid. First, it is important to know whether or not this type of proton transfer

takes place generally in carboxylic acids. It is also interesting to know how the transfer process is affected by the nature of the solvent. Secondly, the temperature and deuteration effects on the transfer rate should be investigated in order to further understand the mechanism of the transfer. Thirdly, the detailed mechanism of the double proton transfer has not been established yet, though a concerted mechanism in an acetic acid-indazole complex was proposed. Fourthly, the connection between the proton transfer observed in acetic acid and the tautomerization found in a benzoic acid host has not been clarified. In order to answer these questions I have studied the absorption and fluorescence spectra and fluorescence decay rate constants of indazole in various solvents. The solvents used here include ordinary polar and nonpolar solvents, carboxylic acids with different pKa values and acidic ethanol (ethanol containing $HClO_4$).

It was found that the fluorescent properties are remarkably different depending on the nature of the solvent. In an ordinary polar solvent such as alcohol, only fluorescence of 1H is observed. In a carboxylic acid with pKa $\simeq$4.5 such as acetic acid, excited state proton transfer from 1H to 2H takes place generally. However, in a carboxylic acid with a smaller pKa value indazole shows a completely different fluorescence spectrum. Here I discuss possible processes which give rise to these different fluorescence properties. On the basis of the present results I propose a scheme which explains the formation of the triplet states of two tautomers of indazole in a benzoic acid host.

Experimental

Indazole (Aldrich) was purified by repeated recrystalization from water and vacuum sublimation. 1-Methylindazole and 2-methylindazole were synthesized according to the procedures given by Auwers[13] and Shad[14], respectively. The carboxylic acids used in this work are acetic acid (AA; 4.757), isobutyric acid (IBA; 4.85), isovaleric acid (IVA; 4.78), formic acid (FA; 3.75), methoxyacetic acid (MA; 3.57), dichloroacetic acid (DCA; 1.29), trifluoroacetic acid (FAA, $<$0.1), and benzoic acid (BA; 4.21). The symbols and numbers in the parentheses are the abbreviations for the acids and their pKa values, respectively. Ethanol, cyclohexane (Wako spectrosol), $HClO_4$ (Wako special grade) and commercially obtained above liquid acids were used without further purification. Concentrations of indazole were $2x10^{-4}$M. Benzoic acid was purified by extensive zone refining after recrystalization. Mixed crystals containing small amounts of indazole were grown by the standard Bridgman method. Absorption spectra were recorded with a Shimadzu U-125MU spectrometer. Fluorescence emission and excitation spectra were taken with a Hitachi MPF -2A spectrometer. NMR spectra were taken with a JEOL JNM-PS-100 NMR spectrometer.

The phosphorescence excitation spectrum of the benzoic acid mixed crystal was obtained at 4.2° K by monitoring the phosphorescence at either 420 nm (0-0 of 1H phosphorescence) or 480 nm (0-0 of 2H phosphorescence). The exciting light was provided by the light from a 900 W xenon arc monochromatized by a Spec 1702 spectrometer. These apparatus belong to Kyoto University.

The fluorescence rise and decay curves were recorded with a picosecond spectrospcopic

system consisting of a mode-locked Nd:YAG laser with a fourth harmonic generator (266 nm, ~10 ps), a Hamamatsu C979 streak camera, and a microcomputer system (Hamamatsu C1000) to process transient signals[15]. In order to study the wavelength dependence of the rise and decay curves, the desired portions of the emission spectra were selected with a band-pass or cut-off filter. This apparatus belongs to Institute for Molecular Science, Okazaki.

Results and Discussion

1. Absorption spectra and ground state structures

Indazole in acetone and water (pH7) was assigned to be in the 1H form from the NMR measurements[16,17]. The absorption spectra of indazole in cyclohexane, acetone, ethanol and water (pH7) are all similar, indicating that indazole exists in the 1H form in these solvents[18]. A typical spectrum is shown in Fig. 1-a. The absorption spectra in AA, IBA and IVA are also similar, showing partially resolved structures, though the spectra are broader than in cyclohexane (Fig. 1-a). They are similar to that of 1-methylindazole, but are rather different from that of 2- methylindazole. (Fig. 1-b) These observations seem to suggest that indazole in these acids are all in the 1H form. This assignment is also supported by the NMR spectrum of indazole in AA which is similar to that taken in acetone. (Fig. 2) On the other hand, the absorption spectra of indazole in carboxylic acids with smaller pKa values (FA, MA, and DCA) are quite different as shown in Fig. 1-c. The spectra are red-shifted and are less structured. 1-Methylindazole and 2-methylindazole in FA also give very similar spectra. (Fig. 1-c) Therefore, indazole as well as methylindazoles have different ground state structures in these acids.

These absorption spectra are similar to that of indazole in acidic ethanol in which indazole is considered to be protonated[19]. (Fig. 1-c) Therefore indazole is likely to be protonated in carboxylic acids with smaller pKa values. The NMR spectrum of indazole in FA is also different from those in AA and non acidic solvents, showing that a drastic structural change in the ground state has taken place on going from AA to FA. In fact the NMR spectrum in FA is more close to that taken in acidic alcohol, further supporting the above assignment of the protonated indazole. (Fig. 2-c, d)

Fig. 1

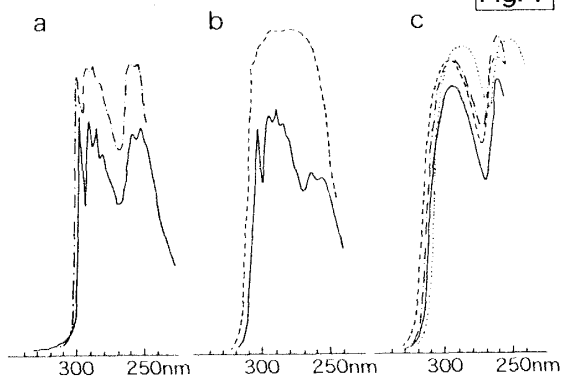

Figure 1. Absorption spectra of indazoles at room temperature;
a) Absorption spectra of indazole in cyclohexane (——) and acetic acid (- -).
b) Absorption spectra of 1-methylindazole (——) and 2-methylindazole (·····) in cyclohexane.
c) Absorption spectra of indaozle (——), 1-methylindazole (·····) and 2-methylindazole (- - -) in formic acid and of indazole in $HClO_4$-ethanol (——).

Fig. 2

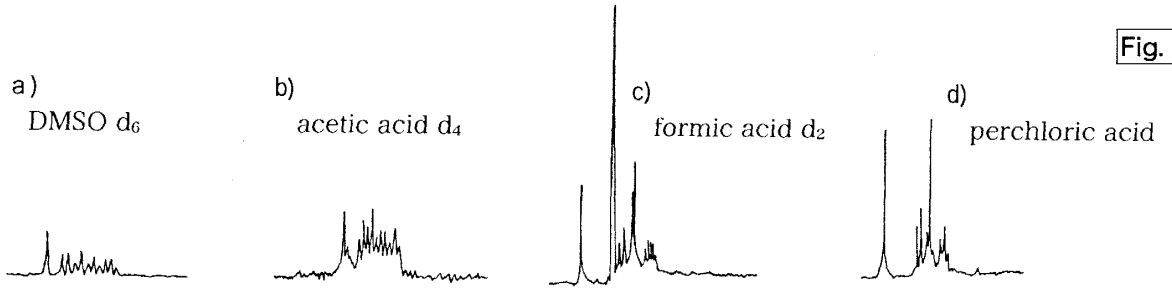

Figure 2. NMR spectra of indazole in some solvents.

Fig. 3

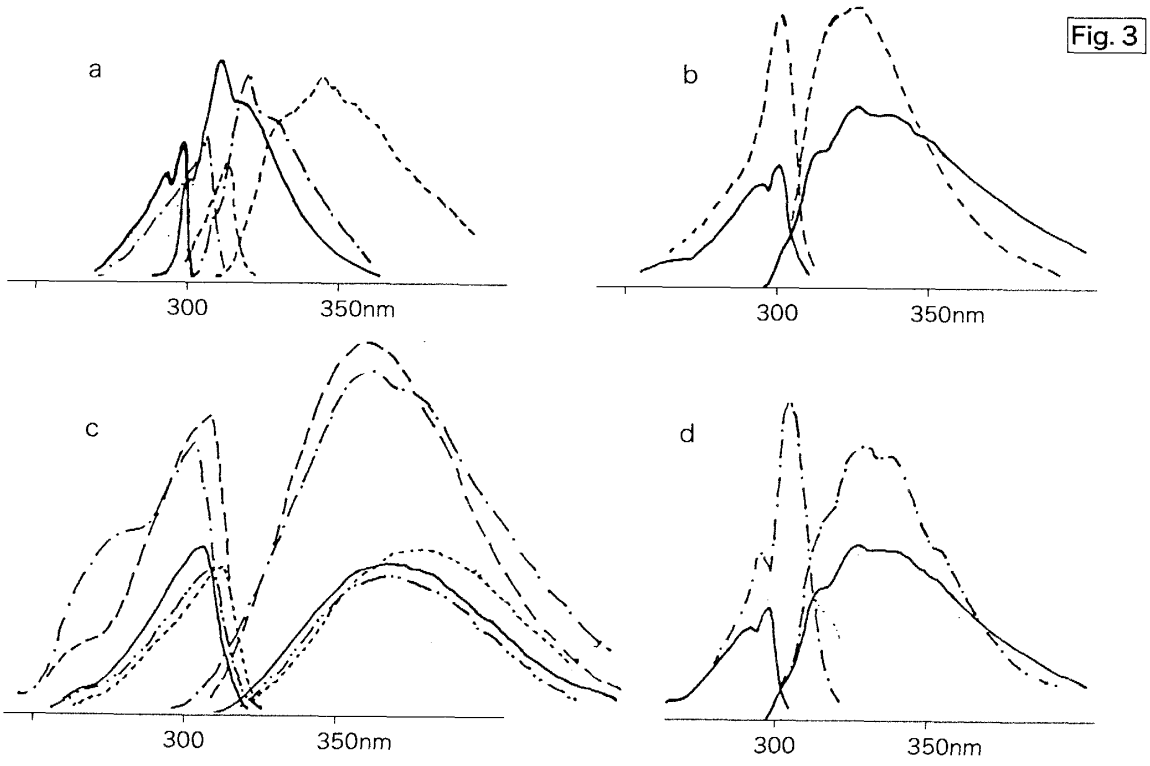

Figure 3. Fluorescence and fluorescence excitation spectra of indazoles in several solvents. Intensities are arbitrary.

a) Indaole in cyclohexane (——), 1-methylindazole in cyclohexane (– – –) and 2-methylindazole in cyclohexane (·····) at room temperature.

b) Indazole in acetic acid (——) and indazole in isobutyric acid (·····) at room temperature.

c) Indazole in formic acid (——), $HClO_4$-ehtanol (– –), and methoxyacetic acid (– – –), 1-methylindazole in formic acid (·····) and 2-methylindazole in formic acid (– – –) at room temperature.

d) Indazole in formic acid at 77 K (– – –) and indazole in acetic acid at room temperature (——).

2. Fluorescence spectra

The fluorescence excitation and emission spectra of indazole in various solvents are shown in Fig. 3. The spectra taken in many nonpolar (e. g. cyclohexane, diethylether) and polar (ethanol, H_2O) solvents are all similar. A typical example is shown in Fig. 3-a. The fluorescence spectra in carboxylic acids are very different from those in other solvents, but remarkably depend on the acidity of solvents. In AA and other acids with

similar pKa values the fluorescence spectrum is structured, but is red shifted with tails in the longer wavelength region compared with those in nonacidic solvents. The fluorescence excitation spectra are similar to those in other nonacidic solvents. To assign the species responsible for these spectra I compare them with those of 1- and 2-methylindazoles given in Fig. 3-a. As already stated in the preliminary report the spectrum in AA is closer to that of 2-methylindazole rather than that of 1-methylindazole, but the spectra can only be well reconstructed by the superposition of the spectra of 1- and 2-methylindazoles. This situation is also true in the cases of IBA and IVA, although the spectra are less structured. These observations suggest the possiblilty that indazole in these acids emit from both 1H and 2H forms and that tautomerization from 1H to 2H takes place in the excited state.

On the other hand, the fluorescence spectra in FA, MA, DCA, FAA and acidic alcohol are very broad and structureless, being further red shifted with the maxima at ~370 nm. (Fig. 3-c) These spectra are considered to represent the fluorescence spectra of protonated indaozle. 1- and 1-methylindazoles in FA also show very broad spectra, indicating that both are also protonated in FA and have similar electronic structures. The fact that these spectra show large Stokes shifts indicates that the structures of the emitting states are rather different from those of the ground states. (Fig. 3-c)

3. Fluorescence and dynamics of the excited states.

As discussed in the previous section the fluorescence spectra of indazole are different depending on the solvent. In this section I discuss the respective dynamic processes

Fig. 4

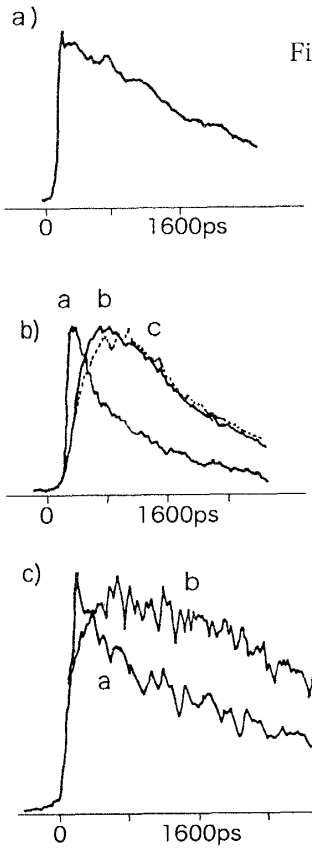

Figure 4. Fluorescence rise and decay curves at room temperature.
a) Fluorescence decay of indazole in ethanol.
b) Fluorescence rise and decay of indazole-h in acetic acid observed at 310 nm (a) and > 350 nm (b) and of indazole-d in acetic acid-d_4 observed at 350 nm (c) (------).
c) Fluorescence rise and decay of indazole in isobutyric acid observed at 310 nm (a) and 350 nm (b).

Fig. 5

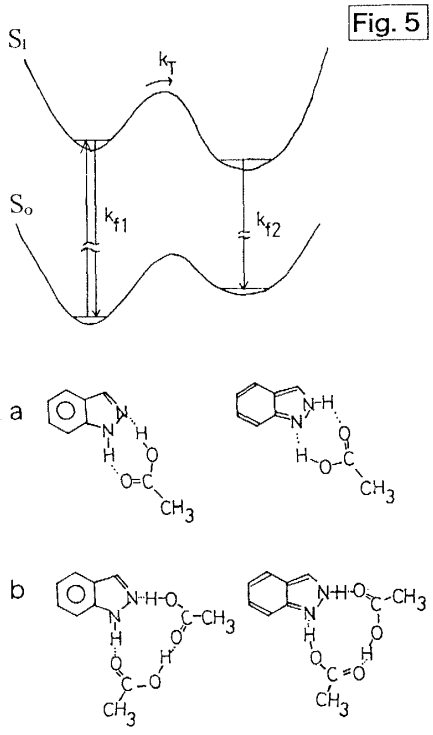

Figure 5. Proton transfer scheme of indazole in acetic acid.
a : structure of 1 : 1 complex of indazole and acetic acid, b : structure of 1 : 2 complex of indazole and acetic acid.

occurring in different solvent systems.

a) Nonacidic solvents

The fluorescence decays of 1H in nonacidic polar and nonpolar solvents are well described by single exponential curves as shown in Fig. 4-a, though the decay rate constants vary considerably depending on the solvent, being $3x10^8$ s^{-1} in ethanol and $1.0x\ 10^9$ s^{-1} in cyclohexane. No fluorescence rises were detected in these cases within the experimental time resolution (~10ps). Therefore, it can be safely concluded that fluorescence takes place from the excited state of 1H.

b) AA, IBA and IVA.

In AA, IBA and IVA the fluorescence rise and decay curves depend on the wavelength at which the fluorescence was monitored. In Fig. 4-b curve a was obtained by monitoring the emission in AA at 310 +10 nm where 1H gives the maximum emission. Curve b was obtained by collecting emissions with wavelength longer than 350 nm. It is seen that the 310 nm emission decays with a much larger decay rate constant than those found in the other polar and nonpolar solvents. The emission at longer wavelength rises first and then decays. Similar decay characteristics were observed in IBA and IVA. Therefore, it is considered that 2H is formed at the expense of 1H in these systems.

I now analyze the long wave length emission (2H) by the scheme shown in Fig. 5. Here k_{f1} and k_{f2} are the decay rate constants of the excited singlet states of 1H and 2H, respectively. k_T is the rate constant of tautomerization from 1H to 2H in the excited state. Solving the appropriate rate equation, I obtain the time dependence of the fluorescence intensity as,

$$I(t) \propto \int_0^t P_0(t)[\exp(k_{f2}-k_r)t-1]\exp(-k_{f2}t)dt$$

Where $k_r = k_{f1}+k_T$ and $P_0(t)$ is the intensity of the excitation pulse. From simulation to the observed curves, we obtained k_r and then estimated k_T by taking $k_f=3.6x\ 10^8$ s^{-1} obtained from the decay in ethanol. The estimated k_T at 20°C are $2.7x\ 10^9$ s^{-1} in AA, $3.5x10^9$ s^{-1} in IBA and $3.5x10^9$ s^{-1} in IVA.

The tautomerization from 1H to 2H involves double proton transfer. A simple scheme to account for this process seems to be the concerted double proton switching in a cyclic indazole-AA complex shown in Fig. 5-a, if AA and indazole form such a complex structure. However, the energy stabilization obtained by forming a cyclic complex may be small, because indazole is not structurally suited to form a six membered cyclic complex. The result of a preliminary ab initio calculation[20] supports this conjecture. Furthermore, no evidence for the formation of such a cyclic complex was found in my recent experiments on the indazole-carboxylic acid complexes in supersonic jet. Therefore, it seems more likely that in acid solutions indazole is hydrogen-bonded with two or more acid molecules as shown in Fig. 5-b. In such a case tautomerization would involve proton transfer with two or more acid molecules.

In order to gain further insight into the mechanism of the tautomerization I have studied the change of the fluorescence spectrum and fluorescence decay in mixed solvents of ethanol and AA. The intensity of the 2H type fluorescence decreases with the increase of the fraction of ethanol, indicating suppression of the tautomerization from 1H to 2H.

At the same time the rise of the fluorescence at 350 nm becomes slower with the increase of the fraction of ethanol. This observation can be rationalized by the sheme shown in Fig. 5-b. As the fraction of ethanol is increased, hydrogen bonded acid molecules are replaced by ethanol molecules, preventing the formation of the complex needed for the proton transfer to take place. The hydrogen-bonded acid and alcohol molecules are exchanged rapidly, but the rate of tautomerization would become slower, because the proton transfer can take place only when indazole forms a complex with acid molecules which has the correct geometry.

I have studied the temperature dependence of k_r to determine the activation energy for the tautomerization process. The result was obtained over the temperature range form 5°C to 66° C. It is seen that the temperature dependence of k_r follows the Arrhenius type equation well with an activation energy of 4.0 Kcal mol^{-1} (1390 cm^{-1}).

I have also studied the isotope effect on k_r by using indazole whose hydrogen at the N_1 position was replaced by deuterium and acetic acid -d_4. Though the fluorescence risetime k_r was found to be slightly slower in the deuterated system, the ration $k_r(h)/k_r(d)$ is rather small. This deuterium effect is in fact even smaller than in 7-azaindole (2.9) [21,22]. This observation indicates that the effect of proton tunneling is not important in the tautomerization process[23]. It is concluded that the tautomerization takes place by a thermally activated process with an activation energy of 4.0 Kcal mol^{-1}.

c) FA and stronger acids

The fluorescence of protonated indazole in FA and acidic ethanol shows detectable rises. The risetimes are 18ps is FA and 60 ps in acidic ethanol at room temperature. These risetimes are considered to correspond to the times needed for protonated indazole to undergo a structural change in the excited state which accompanies a large Stokes shift. The fact that the absorption and fluorescence spectra of protonated indazole, 1- and 2-methylindazoles are all similar suggests that the ground states of the protonated forms of these molecules are similar. Back proton transfer from protonated indazole to acid would take place producing excited neutral indazole. However, this possibility appears to be remote, because the Stokes shifted fluorescence spectra are rather different from those of 1H and 2H. Therefore, a more likely possibility is a structural change in the

Fig. 6

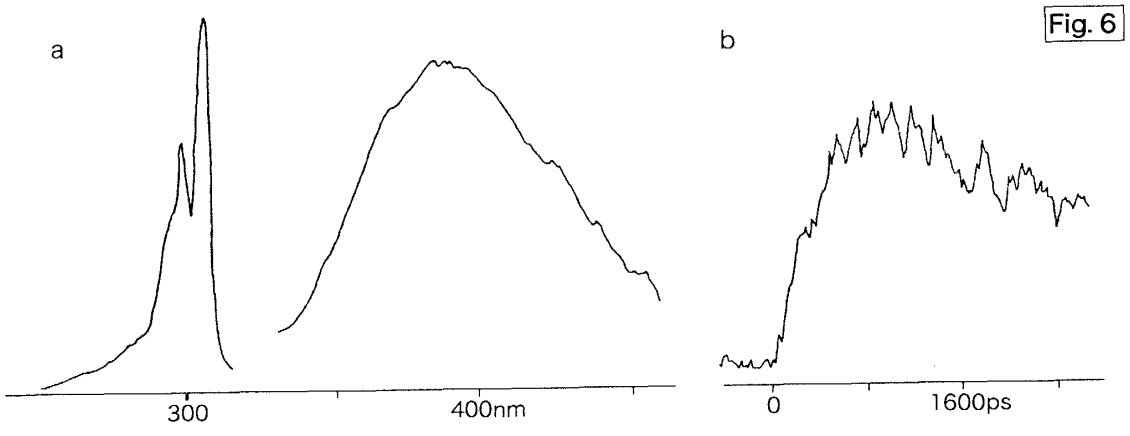

Figure 6. a : Fluorescence and fluorescence excitation spectra of indazole in benzoic acid at 77 K.
b ; Fluorescence rise and decay curves of indazole in benzoic acid at 77 k.

Fig. 7

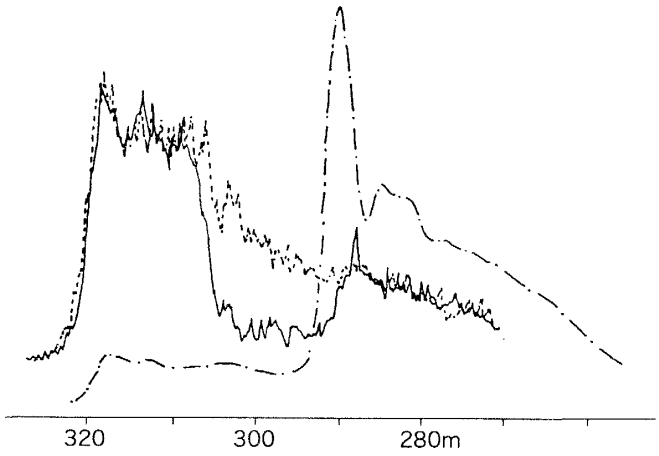

Figure 7. Phosphorescence excitation spectrum of indazole observed at 420 nm (——), indazole observed at 480 nm (------), and benzimidazole (–·–·–).

protonated species, for example, isomerization to a species protonated at a different position. At present I am unable to identify this structural change unambiguously. Though the fluorescence spectra are all similar with very broad structureless features, the observed risetimes are different depending on the system, 18 ps in FA, 30 ps in FA(2) +ethanol (1), mixture, 60 ps in acidic ethanol, indicating that this process is sensitive to the local environment of indazole.

It is considered that the main factor determining the fluorescence spectrum of indazole in acids is the pKa value. Since the difference in the pKa value between AA and FA is not large, I expect that the fluorescence spectrum in FA is sensitive to temperature. In fact the fluorescence spectrum in FA at 77 K is very similar to that in AA. (Fig. 3d)

d) Tautomerization in a benzoic acid host

On the basis of the results presented in this paper we now consider a possible mechanism to produce the triplet states of two tautomers of indazole in a benzoic acid (BA) reported in a previous pater[11]. The fluorescence emission and excitation spectra of indazole in BA at 77 K are shown in Fig. 6. The fluorescence spectrum is very similar to that in FA at room temperature, being very broad, structureless and Stokes-shifted. The excitation spectrum is located in the same region as that in FA, though it is better resolved. The fluorescence shows a considerably slow rise at 77 K. These results seem to show that indazole in BA is protonated, and a structural change in the excited singlet state is taking place.

As shown in Fig. 7 the phosphorescence excitation spectra of both 1H and 2H start at 318 nm which is considered to be the onset of the $S_0 \rightarrow T_2$ ($n\pi^*$) absorption of BA. This band exists in the phosphorescence excitation spectra of other quest molecules in BA as shown in the case of bezimidazole in BA must be due to the absorption of the BA crystal. Since the T_1 and S_1 states are located at 371 nm and 287 nm[24], respectively, the most likely candidate responsible for this absorption is the T_2 ($n\pi^*$) state of BA. The absorption by this band produces triplet excitation of BA which then produces the triplet state of protonated indazole by the energy transfer. The observation that the phosphorescence excitation spectra of both 1H and 2H are similar in this region implies that the triplet states

of both tautomers are produced from the triplet state of protonated indazole. On the other hand, when I compare the excitation spectra shown Fig. 7, I notice that the excitation spectrum of 2H has a much higher intensity in the region from 309 nm to 290 nm, which corresponds to the region of the fluorescence excitation spectrum of indazole in BA. This correspondence seems to show that excitation of protonated indazole to the S_1 state produces the triplet state of 2H favorably. Thus it is likely that the S_1 state of protonated indazole is converted into the S_1 state of 2H which produces the T_1 state of 2H via intersystem crossing.

Summary and conclusion

It is shown that the fluorescence behavior of indazole is remarkably different depending on the nature of the solvent used. In a nonacidic solvent only fluorescence of 1H is observed. In carboxylic acids with pKa $\simeq$4.5 indazole exists in the 1H form in the ground state, but is converted into 2H in the excited state by the double proton transfer. The rate constant of conversion and its activation energy were determined. In an acid with a small pKa value indazole is protonated in the ground state, and gives rise to very broad Stokes-shifted fluorescence. It was demonstrated that a structural change in the excited singlet state of protonated indazole takes place in the time period of 10$\sim$100 ps. However, further investigation is needed to identify the structural change. It is suggested that indazole is protonated in BA and the triplet states of both 1H and 2H are produced from the triplet state of protonated indazole, while the triplet state of 2H is produced preferentially from the excited singlet state of protonated indazole.

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