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Photochemical Reactions of Phthalazine in 2-Propanol

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Phthalazine undergoes dual photoreactions to simultaneously give two photoproducts, 1,2-dihydrophthalazine (**1**) and 1,1′,2,2′-tetrahydro-1,1′-biphthalazine (**2**), upon ultraviolet light irradiation in 2-propanol under nitrogen. There occurs neither photochemical nor thermal interconversion between **1** and **2**; these compounds are formed independently from a common intermediate through different reaction pathways. The results of quenching and sensitization experiments for both the reactions and the phosphorescence emission show that the lowest excited singlet and triplet states of phthalazine participate in the formation of **1** and **2**, respectively. The observed photochemical behaviors under various conditions lead us to propose a reaction mechanism: Phthalazine is photoreduced in the S_1 state to form 1,2-dihydro-1-phthalazinyl radical. The resulting radical in a solvent cage undergoes a subsequent hydrogen abstraction to form **1**. On the other hand, the same radical produced in the T_1 state escapes from the solvent cage to cause a dimerization which affords **2**.

The photochemical behavior of a variety of nitrogen heterocyclic compounds have been studied.[1,2] Especially, the photoreductions of acridine and phenazine have been extensively studied.[3–6] However, little is known concerning the photochemical behavior of ortho-diazines. Chen et al.[7] studied the photoreaction of 4-methylcinnoline in ethers, and showed that a 1,4-addition of the ethers occurred. Davis and Cohen[8] reported that benzo[*c*]cinnoline underwent a photoreduction to give 5,6-dihydrobenzo[*c*]cinnoline in a benzene solution containing triethylamine. In previous papers[9] we reported that the photoirradiation of benzo[*c*]cinnoline in acidified alcoholic solutions leads to the formation of 2,2′-diaminobiphenyl or carbazole as the final product, depending on the experimental conditions. It was found that 5,6-dihydrobenzo[*c*]cinnoline is formed through the lowest triplet state at the initial stage in both of these reactions.

As for phthalazine, there have not been many descriptions concerning its photochemical behavior. Previously, Wake et al.[10] reported that phthalazine undergoes photoalkylation in acidified alcohols. They also noted that a reductive dimerization product was obtained upon irradiation in 2-propanol without added acid. However, the mechanism of this reaction has not yet been ascertained.

In this paper, we describe photochemical reactions of phthalazine in 2-propanol. Analyses of the photoproducts are given, showing that two products were formed. The reactive excited states for each product which were determined are discussed along with the reaction mechanism in terms of the observed cage effects.

Experimental

Materials. Phthalazine was obtained from Aldrich Chem. Co. and was recrystallized from a mixture of benzene and hexane. 2,4-Hexadien-1-ol (Tokyo Kasei Kogyo) was purified by fractional crystallization, and 4,4′-bis(dimethylamino)benzophenone (Michler's ketone) was recrystallized from ethanol. Hexadecyltrimethylammonium chloride and bromide were obtained from Wako Pure Chemical Ind. and were recrystallized from a mixture of acetone and methanol.

Measurements. UV absorption spectra were measured with a Shimadzu UV-210A spectrophotometer. Phosphorescence spectra were recorded on a Shimadzu RF-500 spectrofluorimeter equipped with a cylindrical rotating sector at 77 K. IR spectra were obtained with a Hitachi EPI-G3 infrared spectrometer in a KBr disk. Proton NMR spectra were taken with a JEOL PS-100 100 MHz spectrometer in deuterated chloroform.

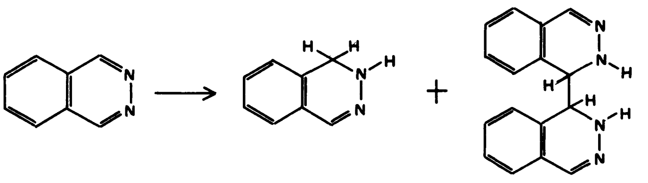
Light Source and Irradiation. In the preparative experiments, two light sources were employed using no filter: (I) a 400 W high-pressure mercury lamp (Rikagaku Sangyo UVL-400 HA) and (II) a 160 W low-pressure mercury lamp (Rikagaku Sangyo UVL-160 LA). For the 254-nm light irradiation, a 70 W low-pressure mercury lamp (Ushio UL1-7SQ) and a solution filter ($NiSO_4$ 500 g dm^{-3}) were used. For the 313-nm light irradiation, a 450 W high-pressure mercury lamp (Ushio UM-452) and a set of filters comprising a solution (1% K_2CO_3 containing 10^{-2} mol dm^{-3} K_2CrO_4) and a Corning glass (CS-7-54) were used. For the 366-nm light irradiation, a 450W high-pressure mercury lamp and Corning glass filters (CS-7-54 and CS-0-52) were used.

Unless otherwise noted, all irradiations were carried out in a 5×10^{-2} dm^3 quartz cylindrical vessel at room temperature. Solutions of phthalazine were flushed with nitrogen passed through a pyrogallol solution before and during irradiation.

Actinometry and Analysis of Products. For a determination of the quantum yields for photoreactions, the light intensities were measured using a potassium trioxalatoferrate(III) solution as an actinometer.[11] The amounts of photoproducts were spectrophotometrically determined using the molar extinction coefficients of the UV absorption bands of the products described in the text.

Isolation and Identification of the Photoproducts. A 3×10^{-3} mol dm^{-3} solution of phthalazine in 0.5 dm^3 of 2-propanol was irradiated for 5 h using light-source (I) under nitrogen. The irradiated solution was evaporated to dryness and the residue was subjected to TLC (silica gel, chloroform–methanol 30:1). The compound, thus obtained, showed the following properties: IR(KBr) 3250 (NH) and 1440 cm^{-1} (CH_2); ^1H NMR($CDCl_3$) δ=4.2(2H, s, CH_2), 5.3 (1H, m, NH) and 6.8—7.6(5H, m, aromatic H); mp 62.5—64.0 °C (decomp). The product **1** was identified as 1,2-dihydrophthalazine. Further supporting evidence for the identification of **1** was obtained from the benzoyl derivative of the isolated product. A treatment of the product with *p*-methylbenzoyl chloride gave a benzoyl derivative which was characterized by IR and elemental analyses.

A 1.5×10^{-2} mol dm^{-3} solution of phthalazine in 0.5 dm^3 of 2-propanol was irradiated for 8 h using light-source (II) under nitrogen. The irradiated solution was concentrated under reduced pressure. The precipitated crystals were collected by filtration and recrystallized twice from methanol. The physical properties of the crystals were identical with those of the dimerization product reported by Wake et al.[10] Product **2** was identified as 1,1′,2,2′-tetrahydro-1,1′-biphthalazine.



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Results and Discussion

Reaction Products. The absorption spectral change caused by the irradiation of a 2-propanol solution of phthalazine is shown in Fig. 1. During the initial stage of the reaction, an absorption band appeared around 335 nm. With successive irradiation the absorption maximum shifted progressively to shorter wavelengths accompanying an increase in intensity. These spectral features indicate that there are at least two main photoproducts. From the preparative experiments mentioned above, two photoproducts

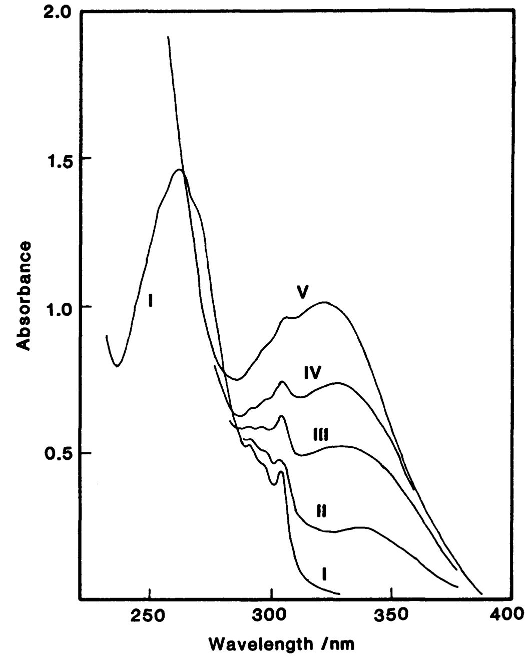


Fig. 1. Spectral change caused by the 254 nm light irradiation upon a 2-propanol solution of phthalazine (4.0×10^{-4} mol dm^{-3}).
Irradiation time (min); I: 0, II: 10, III: 40, IV: 80, V: 160.

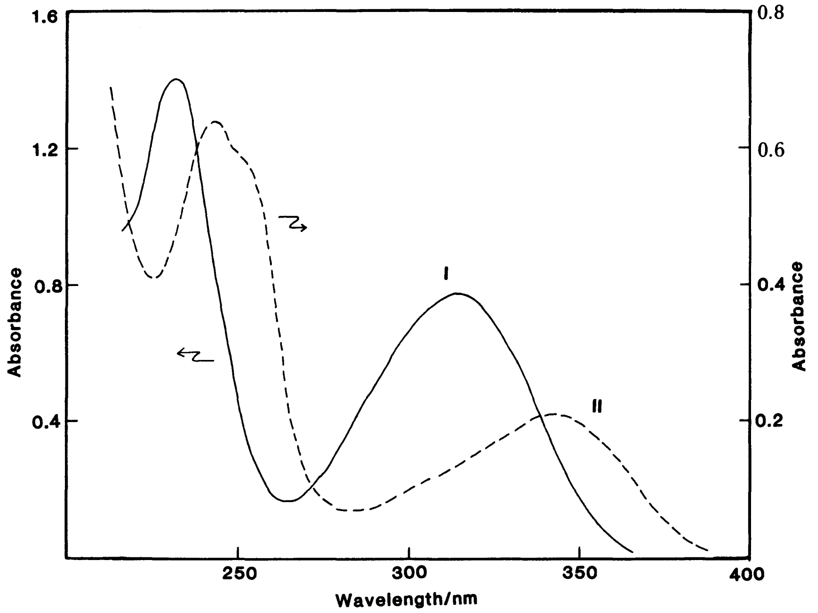


Fig. 2. Absorption spectra of the photoproducts in 2-propanol.
I: **1** (1.4×10^{-4} mol dm^{-3}), II: **2** (2.3×10^{-5} mol dm^{-3}).

were obtained: 1,2-dihydrophthalazine (**1**) and 1,1′,2,2′-tetrahydro-1,1′-biphthalazine (**2**). The absorption spectra of these compounds are presented in Fig. 2.

Changes in the concentrations of **1** and **2** during the course of the reactions were determined using the molar absorption coefficients of **1** and **2** (Fig. 3). It can be seen that the amount of **1** gradually increased with the irradiation time (37% yield based on the starting material at 140 min irradiation), whereas the amount of **2** reached a constant value after irradiation for an appropriate period (40% yield). However, **2** formed more rapidly than **1** during the initial stage of the reaction. These results could plausibly be interpreted as indicating that **2** was formed first, and then decomposed to give **1**. However, this is not the case (as indicated below).

In order to examine the possibilities of an interconversion between **1** and **2**, the photochemical behavior of **1** and **2** were studied using these compounds isolated in preparative experiments. Irradiation of 366-nm light for 50 min on a 2-propanol solution of **2** (3.6×10^{-5} mol dm^{-3}) resulted in the photodecomposition yielding phthalazine almost quantitatively.[12] Therefore, the saturation of the amount of **2** produced in the course of the photoreaction of phthalazine (curve II in Fig. 3) can be attributed to this backward photoreaction; the photostationary state could be established between phthalazine and **2** under the irradiation of light which could be absorbed by both compounds. On the other hand, the irradiation of 313-nm light on a solution of **1** did not cause a pronounced photoreaction. Consequently, it can be said that phthalazine undergoes photoreactions through two distinct pathways to afford **1** and **2** independently. A similar photochemical behavior has been found for acridine, which gives 9,10-dihydroacridine together with 9,9′,10,10′-tetrahydro-9,9′-biacridine.[13–16] Kira and Koizumi[17] reported that the photoproduct of 9,9′,10,10′-tetrahydro-9,9′-biacridine is acridine. This reaction is quite similar to the photoreaction of **2** (described above).

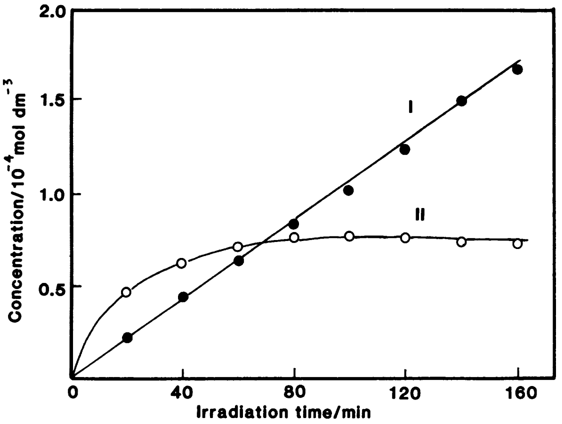


Fig. 3. Change in the concentrations of the products **1** (I) and **2** (II) with the 254 nm light irradiation of phthalazine (4.0×10^{-4} mol dm^{-3}) in 2-propanol.

Quenching and Sensitization. In order to elucidate the reactive excited states for the observed photoreactions, triplet quenching experiments were conducted employing 2,4-hexadien-1-ol having a lower triplet energy (E_T=249 kJ mol^{-1})[19] than that of phthalazine (E_T=256 kJ mol^{-1}). Quenching data are presented in Fig. 4. The value of ϕ_0 (quantum yield without quencher) for **1** and **2** are 0.013 and 0.041, respectively. As can be seen from Fig. 4, the formation of **2** is apparently quenched, while that of **1** is not influenced by the addition of the quencher (up to 1.0×10^{-3}mol dm^{-3}). In addition, quenching for the phosphorescence emission of phthalazine in a mixture of ethanol and methanol (1:1 v/v) at 77 K has also been observed in the presence of the same quencher (Fig. 5).

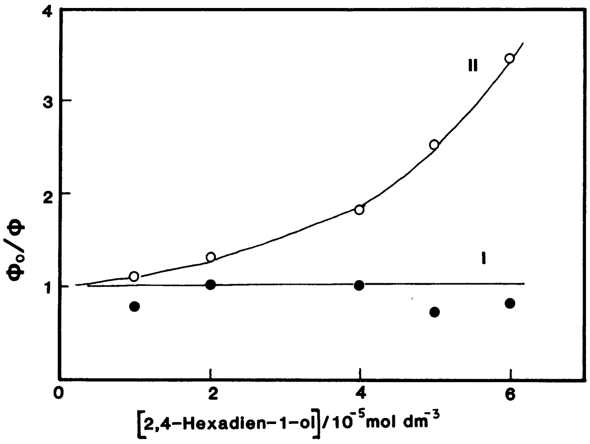


Fig. 4. Stern-Volmer quenching plots for the quantum yields of the formation of **1** (I) and **2** (II). [phthalazine]=2.0×10^{-4} mol dm^{-3}, excitation wavelength=313 nm.

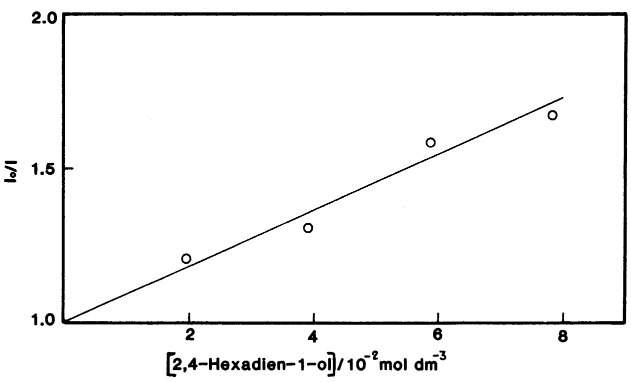


Fig. 5. Stern-Volmer quenching plots for the phosphorescence of phthalazine (480 nm) at 77 K. [phthalazine]=1.0×10^{-3} mol dm^{-3}, excitation wavelength=313 nm.

The feature of the reaction quenching plot (curve II in Fig. 4) differs from that of the phosphorescence. The observed upward curvature for the quenching plot at higher temperatures could be tentatively attributed to the quenching of two excited states, T_1 and T_2,[20] which are known to be located very close to each other;[21,22] thus, both states are in equilibrium at higher temperatures. However, further detailed studies need to be conducted before this subject can be solved.

Since the shapes of the absorption and the phosphorescence spectra of phthalazine have been confirmed to remain unaltered by the quencher, it may be considered that there are no specific interactions such as the ground-state complexing or an exciplex formation between the reactant and the quencher. In the present quenching system, a singlet-singlet energy transfer from the reactant to the quencher can evidently be ruled out as the quenching mechanism in view of the S_1 state energies of the compounds concerned.[23] Consequently, the quenching observed for the formation of **2** can be interpreted in terms of a triplet–triplet energy transfer. The obtained results suggest that the reactive excited states for the formations of **1** and **2** are the lowest excited singlet state and the lowest triplet state, respectively.

Supporting evidence for this suggestion has been provided by triplet sensitization studies. 4,4′-Bis(dimethylamino)benzophenone (Michler's ketone) was used as the triplet sensitizer under excitation with 366-nm light which was absorbed by only the sensitizer. This compound is photostable and has a triplet energy, E_T=259 kJ mol^{-1}.[24,25] A Stern–Volmer sensitization plot is shown in Fig. 6, in which a linear relationship is established between the reciprocal of the quantum yield and the reciprocal of the phthalazine concentration at a fixed concentration of the sensitizer (2.0×10^{-5} mol dm^{-3}). It can clearly be seen from Fig. 6 that the formation of **2** can be efficiently sensitized by Michler's ketone donor, while no sensitization is noted for the formation of **1**. In this connection, the occurrence of a triplet–triplet energy transfer from the ketone to the phthalazine acceptor can readily be recognized from the phosphorescence emission behavior illustrated in Fig. 7. A lack of the sensitization in the formation of **1** indicates that the S_1 mechanism is operative in the formation of **1** with a direct excitation of the substrate.

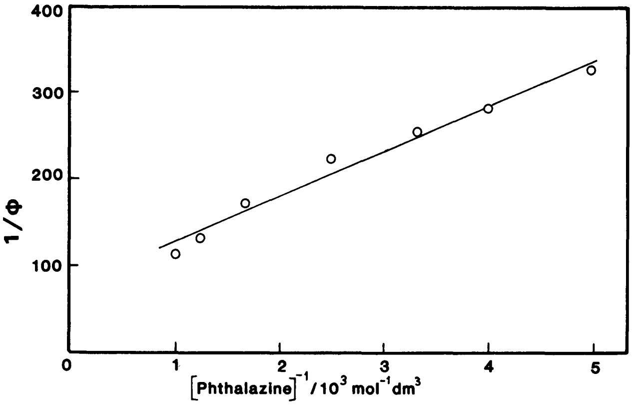
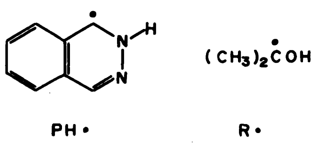


Fig. 6. Sensitization plots for the formation of **2**. [4,4′-bis(dimethylamino)benzophenone]=2.0×10^{-5} mol dm^{-3}, excitation wavelength=366 nm.

According to the present reaction mechanism, an S_1–T_1 intersystem crossing is required to take place appreciably in order to account for the formation of **2**. In this connection, the triplet quantum yield of phthalazine was recently reported to be 0.43 at room temperature[22] and 0.49 at 77 K.[26]

Effects of Surfactants. In view of the type of both reactions described above, it may be probable that during the primary step phthalazine (P), both in the S_1 and T_1 excited states, similarly undergoes hydrogen atom abstraction from 2-propanol (RH) to afford an 1,2-dihydro-1-phthalazinyl radical (PH·) and an alcohol radical (**R**·). In fact, Kanamaru et al.[27] reported the transient absorption spectrum of 1,2-dihydro-1-phthalazinyl radical generated in an alcoholic solution by flash photolysis method at room temperature. Castellano et al.[28] also obtained the same radical by UV irradiation at 115 K. It seems quite reasonable, therefore, that the production of **2** can be ascribed to the combination of 1,2-dihydro-1-



PH· R·

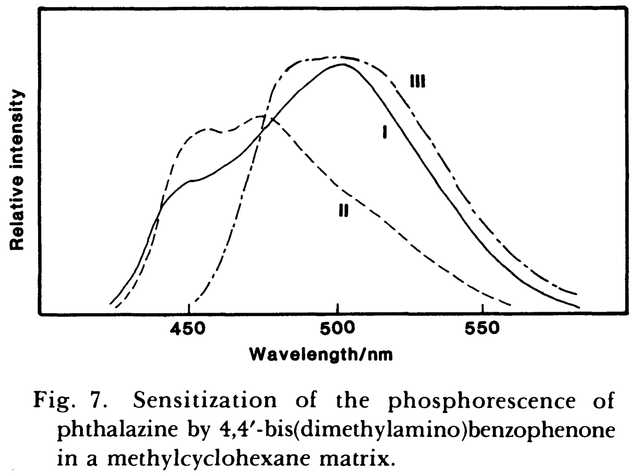


Fig. 7. Sensitization of the phosphorescence of phthalazine by 4,4′-bis(dimethylamino)benzophenone in a methylcyclohexane matrix.
I: [phthalazine]=6.0×10^{-4} mol dm^{-3}, [4,4′-bis(dimethylamino)benzophenone]=2.0×10^{-5} mol dm^{-3}, excitation wavelength=366 nm; II: [4,4′-bis(dimethylamino)benzophenone]=2.0×10^{-5} mol dm^{-3}, excitation wavelength=366 nm; III: [phthalazine]=6.0×10^{-4} mol dm^{-3}, excitation wavelength=305 nm.

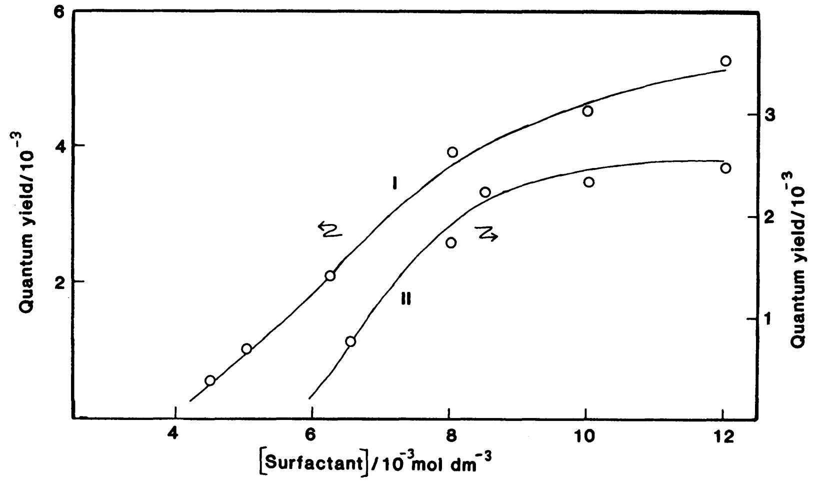
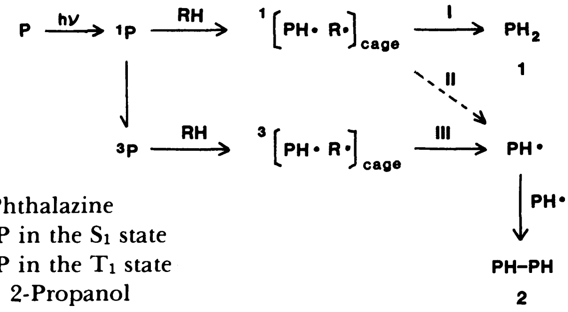


Fig. 8. Effects of the surfactants on the quantum yield of the formation of **1** in aqueous 2-propanol (0.3 mol dm^{-3}).
I: hexadecyltrimethylammonium chloride; II: hexadecyltrimethylammonium bromide, [phthalazine]=4.0×10^{-3} mol dm^{-3}, excitation wavelength=254 nm.

phthalazinyl radicals produced from the triplet precursor. A similar photoreductive dimerization was reported earlier for acridine.[13–16] Thus, the formation of 9,9′,10,10′-tetrahydro-9,9′-biacridine has been ascertained in the photoreduction of acridine in hydrogen-donating solvents; also, a semiquinone radical with an unpaired electron on 9-carbon atom is regarded as an intermediate in the dimerization.[17]

To obtain suggestive information concerning the mechanism for the formation of **1** as well as the origin of the different behavior between the 1,2-dihydro-1-phthalazinyl radical formed from the S_1 and that from the T_1 states of phthalazine, cage effects on the reactions were examined using surface-active agents. Micelles are known to become a good means for causing an efficient cage reaction of radical pair produced photochemically or thermally.[29–31] Figure 8 shows the results of the micellar effects on the photoreactions. The quantum yield for the production of **1** is significantly affected by the addition of the surfactants. The production of **1** is apparently observed above the cmc of surfactants.[32] On the other hand, **2** is formed to a very small extent, even at high concentrations of the surfactants. These results strongly indicate that **1** can be produced in micelles, but **2** cannot. Therefore, it is conceivable that for the photoreaction system in a 2-propanol solution, the 1,2-dihydro-1-phthalazinyl radical formed through the S_1 state and the alcohol radical are trapped as a radical pair in a solvent cage. This results in a further hydrogen abstraction, leading to product **1** and acetone. Although we cannot rule out the possibility of the participation of an alcohol molecule in the second hydrogen abstraction, at this time the hydrogen atom can be considered as coming from the alcohol radical, since the triplet sensitization reaction does not give product **1**. In any case, 2-propanol may be expected to give acetone; in fact, acetone has been detected in irradiated solutions by gas chromatography.

Here, it is particularly noteworthy that generally radical pairs produced from S_1 states undergo more effective cage reactions or micellar reactions than radical pairs from T_1 states.[30,33–35] Recently we have reported that some hydroxylamines undergo photorearrangements through a singlet-derived radical pair in a solvent cage as well as photofragmentation through a triplet-derived radical pair after escaping from a solvent cage.[36]



P: Phthalazine
^{1}P: P in the S_1 state
^{3}P: P in the T_1 state
RH: 2-Propanol
PH•: 1,2-Dihydro-1-phthalazinyl radical
R•: 1-Hydroxy-1-methylethyl radical
^{1}[ ]: Singlet state radical pair in solvent cage
^{3}[ ]: Triplet state radical pair in solvent cage

In conclusion, we propose a reaction mechanism for the dual photochemical reactions of phthalazine, as illustrated in the scheme. The pathway, denoted I, refers to the reaction of the 1,2-dihydro-1-phthalazinyl radical in the S_1 cage. Process II is a plausible escape route for radicals from the S_1 cage, taking place in competition with I. Although the extent of the contribution of this process to the formation of a free PH· radical is not clear, it cannot be ruled out only from the experimental results obtained here. Process III can be considered to result in a very efficient diffusion of the radical pair from the T_1 cage into solution. In a triplet cage, neither an intersystem crossing to the singlet radical pair nor a second hydrogen abstraction can take place sufficiently.

Accordingly, the results mentioned here are examples of photochemical reactions in which an excited molecule in the S_1 state abstracts hydrogen with an efficiency which is comparable to that of an intersystem crossing to the T_1 state. In this connection, the rate of the S_1–T_1 intersystem crossing (k_{ISC}) at room temperature has been reported to be about 1.5 ns^{-1}.[21,22]

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