The Photoreaction of Pyrazine Derivatives

Kazutoshi Yamada, Kiyoshi Katsuura, Hideaki Kasimura, and Hirotada Iida

Department of Synthetic Chemistry, Faculty of Engineering, Chiba University, Yayoi-cho, Chiba 280

(Received February 27, 1976)

The irradiation of the pyrazine derivative with an α-carbonyl substituent (**1**) under a nitrogen atmosphere gave hydroxypyrazine (**2**) and two solvent adducts (**3** and **4**). In the case of **1e**, the charge-transfer complex of pyrazine and dihydropyrazine, produced by the reduction of the pyrazine, was isolated. The mechanism of this photoreaction was similar to that of flavine. The attack of oxygen on dihydropyrazine produced **2**. Furthermore, the photoreduction with DTT occurred through the intermediate, which was similar to the case of flavine. The reaction rates of various pyrazines were measured. The quenching studies indicate that the photoreaction proceeds *via* the n-π* triplet state.

We have previously investigated the reactions of enaminoketone and have reported the relation between the conformation of the enaminoketone and its photoreaction. At that time, we planned also to study the photoreaction of the pyrazine derivative (**1**) as a model of enaminoketone with a fixed conformation.[1]

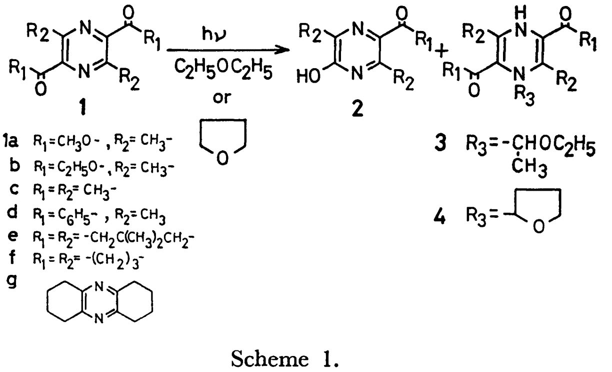
Several photoreactions of pyrazines have been studied, but the photoreaction of pyrazine with an α-carbonyl substituent is not known. Padwa and his co-workers prepared pyrazine by the photodimerization and the photoisomerization of azirine.[2] Chambers and his co-workers showed the rearrangement of pyridazine to pyrazine by irradiation.[3] Lahmani and Ivanoff irradiated pyrazine derivative and thus obtained the pyrimidine derivative.[4] Furthermore, in the case of phenazine, which had a pyrazine ring in a molecule, the photoreaction occurred in either an acidic or reducible condition, and 1-alkoxyphenazines were produced as photoproducts.[5]

We wish now to report the results on the photobehavior of the pyrazine derivative (**1**), which produced hydroxypyrazine (**2**) and two solvent adducts (**3** and **4**), and discuss the mechanism, which might be similar to that in the behavior of flavin. It was found that pyrazine exhibited photochromism and could be considered a model of the photoreaction of flavin.

Results and Discussion

Photolysis of Pyrazine Derivatives. The irradiation of the pyrazine derivative **1a** in diethyl ether with a 450-W high pressure mercury lamp (>330 nm) gave two significant photoproducts (**2a** and **3a**) (Scheme 1).

The structures of **2a** and **3a** were identified as methyl 3,6-dimethyl-5-hydroxypyrazine-2-carboxylate and a solvent adduct respectively on the basis of their physical data. The mass spectrum of **2a** gave a molecular ion at m/e 182 ($C_8H_{10}N_2O_3$). The UV spectrum showed absorptions at 236 (ε 13900) and 307 nm (ε 6650). The IR spectrum had a hydroxyl absorption at 3430 cm^{-1}. The NMR spectrum of **2a** in $CDCl_3$ showed three sharp singlets for the C(2), C(3), and C(6) methyl groups, and a broad singlet for the hydroxyl group. Moreover, the structure of **2a** was identified by the fact that the hydrolysis and further thermal degradation of **2a** gave 3,6-dimethyl-2-pyrazinol, identical with the independently prepared sample.[6] The mass spectrum of **3a** showed peaks at m/e 298 ($M^{+\cdot}$; $C_{14}H_{22}N_2O_5$) and 225 ($M^{+\cdot}-C_4H_9O$). The UV spectrum showed absorptions at 266 (ε 14000) and 322 nm (ε 5300). The NMR spectrum of **3a** in $CDCl_3$ showed three sharp singlets for the C(2), C(3), C(5), and C(6) methyl groups, and nine protons for the 1-ethoxyethyl group. The presence of a NH group was confirmed by the IR band at 3270 cm^{-1}. Thus, **3a** was identified as dimethyl 1,4-dihydro-3,6-dimethyl-1-(1-ethoxyethyl)-2,5-pyrazinedicarboxylate.



Scheme 1.

Using tetrahydrofuran as a solvent, **2a** and a solvent adduct (**4a**) were obtained. In each case of **1b**, **1c**, and **1d**, the corresponding hydroxyl compound (**2**) and a solvent adduct (**3** or **4**) were given. However, the physical data and yields of **3b**, **3d**, **4b**, and **4d** were hard to obtain, because the isolation of these compounds was difficult. The yields and physical data of **2**, **3**, and **4** are given in Table 1.

Spectrobehavior of Pyrazine Derivatives. The change in the absorption spectrum of **1a** during the photoreaction under an argon atomosphere was examined.

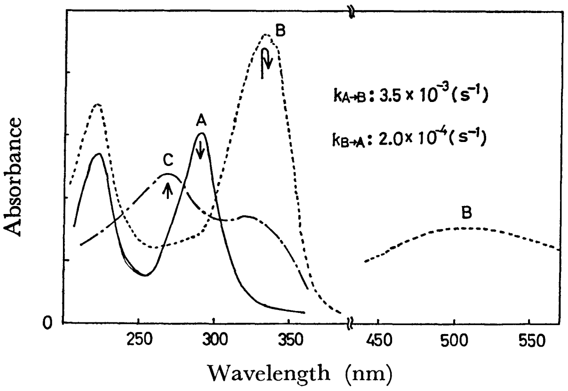


Fig. 1. Spectral change of **1a** in 2-propanol with irradiation.

TABLE 1. YIELDS AND PHYSICAL DATA FOR THE PHOTOPRODUCTS FROM **1a** TO **1d**

	Yield %	Mp °C	UV in EtOH λ(nm)	UV in EtOH ε	IR (cm^{-1})	Mass (m/e)	NMR (δ in $CDCl_3$)	Anal. Found (Calcd) C%	Anal. Found (Calcd) H%	Anal. Found (Calcd) N%
2a	23—54	230[a]	264 307	13900 6650	1716 3430	182[b] 150	2.49 (s, 3H), 2.73 (s, 3H), 3.94 (s, 3H), 12.93 (s, 1H)	52.80 (52.74)	5.58 (5.53)	15.24 (15.34)
2b	20	220.5 221.0	264 308	18800 4500	1703 3430	196[b] 151 123	1.40 (t, 3H), 2.48 (s, 3H), 2.72 (s, 3H), 4.42 (q, 2H), 12.93 (s, 1H)	55.09 (55.10)	6.25 (6.17)	14.55 (14.28)
2c	36	180[a]	285	13800	1689 3430	166[b] 151	2.45 (s, 3H), 2.58 (s, 3H), 2.69 (s, 3H), 12.80 (s, 1H)	57.60 (57.82)	6.09 (6.07)	16.56 (16.86)
2d	small amount		295			228[b]				
3a	27	152 154	266 322	14000 5300	1722 3270	298[b] 225 193 165	1.12 (t, 3H), 1.22 (d, 3H), 2.17 (s, 3H), 2.40 (s, 3H), 3.38 (q, 2H), 3.76 (s, 6H), 4.28 (q, 1H), 5.04 (bs, 1H)	56.40 (56.30)	7.46 (7.51)	9.45 (9.39)
3c	33	liquid	234 288	5400 8000	1698 3380	220 205 193				
4a	20	152 153.5	267 331	14000 3900	1733 3340	296[b] 226 193 165	2.00 (m, 4H), 2.20 (s, 3H), 2.40 (s, 3H), 3.77 (s, 6H), 3.85 (m, 1H), 4.60 (t, 2H), 5.00 (bs, 1H)	56.68 (56.74)	6.85 (6.80)	9.40 (9.45)
4c	35	liquid	234 289	9000 13900	1730 3375	220 177 164				

a) Decomposition. b) Molecular ion.

The results are shown in Fig. 1. Upon irradiation, the absorption (A) of **1a** at 289 nm rapidly decreased. At the same time, a new absorption (B) appeared at 330 and 505 nm and increased quickly. Then the color of the solution changed from colorless to red. If the irradiation was interrupted at the stage when the peak of (B) was at its maximum and the solution was then kept in the dark, the spectrum of the solution returned to **1a**. This indicates that the change of (A) to (B) is reversible. The first-order rate constant of the change of (A), measured from the decrease in the peak at 289 nm of **1a**, was $3.5\times10^{-3}\,s^{-1}$, while that of the regeneration of (A) from (B), measured from the decrease in the peak at 330 nm of (B), was $2.0\times10^{-4}\,s^{-1}$. Upon further irradiation, another new absorption (C) appeared at about 260 nm and increased with the decrease in (B). The formation of (C) was irreversible, so (C) did not return to (B) or (A) upon remaining in the dark.

In the case of **1a**—**d**, similar behavior was observed, and the same change occurred in tetrahydrofuran, diethyl ether, and 2-propanol. The peaks of the **1** absorption (A), (B), and (C) in 2-propanol are shown in Table 2. This spectrobehavior was similar to that of phenazine (which has a pyrazine ring in a molecule) upon irradiation.[7] To investigate the relationship between phenazine and pyrazine derivatives, three pyrazine derivatives, **1e**, **1f**, and **1g**, with structures similar to phenazine were synthesized, and the spectral change in them upon irradiation were studied. These results are also shown in Table 2. In the irradiation of **2g** (which does not have an α-carbonyl group), no spectral change similar to that of **1a**—**f** was shown. In the case of **1e**, the first-order rate constant of the change of (A) to (B), as measured from the decrease in the peak at 318 nm of **1e**, was $4.5\times10^{-2}\,s^{-1}$, while that of the regeneration of (A) from (B), as measured from the decrease in the peak at 374 nm of (B) was $6.7\times10^{-3}\,s^{-1}$.

TABLE 2. THE VARIATION IN THE ABSORPTION SPECTRA OF PYRAZINE DERIVATIVES IN 2-PROPANOL

Pyrazine **1**	(A) (nm)	(B) (nm)		(C) (nm)
1a	289	330	505	260
b	288	320	502	256
c	298	384	—	292
d	290	384	—	237
e	317	372	502	290
f	317	366	520	282
g	290	290		290

Colored Compound. The solution of **1c** in diethyl ether gave a violet-colored compound, **5c**, upon irradiation; in the case of **1e** a red-brown-colored compound, **5e**, was precipitated. Both **5c** and **5e** were unstable and turned to **1c** and **1e** respectively after a few weeks in the solid state. They were difficult to dissolve and turned to **1c** and **1e** as soon as they are dissolved. Therefore, the UV spectra were measured in acetic acid under an argon atmosphere, they agreed with the (B) absorption of **1c** and **1e** (**5c**: 384 nm;

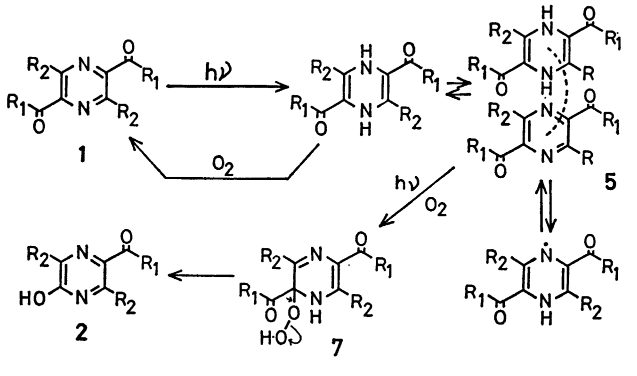
5e: 372 and 504 nm). The mass spectra of **5c** and **5e** showed peaks more than that of **1c** and **1e** by two (**5c**: *m/e* 194 ($M^{+\cdot}+2$) and 192 ($M^{+\cdot}$); **5e**: *m/e* 274 ($M^{+\cdot}+2$) and 272 ($M^{+\cdot}$)). The NMR spectrum of **5e** in CD_3COOD showed a signal of the NH proton at δ 2.15. By D–H exchange, the signal of the hydroxyl proton of acetic acid at δ 11.30 soon appeared and increased with a decrease in the signal at δ 2.15. The above facts indicate that these colored compounds surely have the structure of dihydropyrazine. Also, in the photoreaction of phenazine, a similar colored compound obtained; it was reported to be a dimer of phenazine and dihydrophenazine.[8]

Mechanism. We may conclude from the experiments described above that this reaction includes both a reduction process and an oxidation process. Therefore we investigated the oxidations and reductions of several compounds with heteroenone structures such as **1**. Beinert reported that the spectral behavior of reduced flavine upon oxidation was similar to that of **1** upon irradiation.[9] The redox mechanism of flavine can also well explain the initial process of this reaction. It appears that **1** is reduced by irradiation to produce dihydropyrazine because, first, the molecular complex **5** of pyrazine and dihydropyrazine is obtained as a colored precipitate, and second, a solution of dihydropyrazine hydrochloride, **6**, dissociated to show a (B) absorption identical with that of the molecular complex **5**. The peak near 500 nm of (B) of **1** is characteristic of the charge-transfer complex, and the peaks in the wavelength region of about 320 to 400 nm are due to the semiquinone radical produced by the dissociation of the complex. The complex and radical coexist at equilibrium to form the (B) absorption. In fact, the ESR spectrum of **5e** in acetic acid was obtained, but the hyperfine structure was not clear. The reversibility between the (A) and (B) absorptions may be based on the instability of the radical to the oxidation with oxygen.

The continuous irradiation of the solution showing the (B) absorption gave a mixture containing the solvent adduct and came to show the (C) absorption. The nature of the mixture is not clear, but the precursor of **2** is surely present in this mixture because the mixture reacted with oxygen upon irradiation to give **2**. The hydroxyl compound **2** was not detected in the solution showing the (C) absorption, nor was it obtained by the bubbling of oxygen into the solution showing the (C) absorption. The formation of **2** from the solution required both oxygen and light. Furthermore, the irradiation of the solvent adduct (**3** and **4**) did not yield **2**. These results indicate that the formation of **2** is different from the reaction which gave **3** or **4**.

From the above results and the mechanism of the photo-oxidation of tetrahydropteridine reported by Mager,[10] we presumed that **2** was formed through the intermediate, **7**, which was produced by the attack of oxygen on the dihydropyrazine derivative. Therefore the mechanism for this reaction may be illustrated as is shown in Scheme 2.

Photobehavior of Pyrazine Derivatives with 1,4-Dimercapto-2,3-butanediol. Flavin derivatives, *e.g.*, flavin adenine dinucleotide (FAD) and lipoic acid, are included in the cycle of the decarboxylation of α-ketoacid in a living organism.[11] In this cycle, FAD oxidizes dihydrolipoic acid to lipoic acid and is then itself reduced to dihydroflavin ($FADH_2$). This reaction of flavin presumably passes through the 4-adduct of flavin, with dihydrolipoic acid as an intermediate.[12] In order to confirm the mechanism of the photoreaction of **1**, we presumed **1** to be a model of flavin and 1,4-dimercapto-2,3-butanediol (DTT; **8**) to be a model of dihydrolipoic acid, and we studied reaction of **1** and DTT.



Scheme 2.

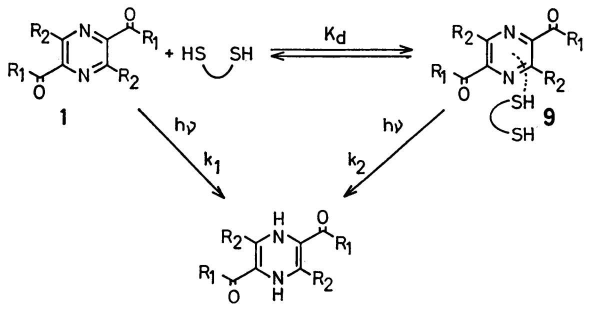
The change in the absorption spectrum during the photoreaction was examined. A solution of **1e** and DTT in 50% acetic acid in a quartz cell was irradiated under an argon atmosphere. All the original peaks diminished rapidly and were replaced by new peaks centered at 357 (ε 20900) and 500 nm (ε 1630), and the solution changed from colorless to red. The curves of the change in the absorption clearly defined two isosbestic points at 232 and 333 nm. The spectrum remained unchanged for at least several days in the dark. This suggests that there is no substantial dark side reaction and that the photoproduct is stable under these reaction conditions. After a four-hour irradiation the change in the spectrum almost entirely ceased. The resulting spectrum was identical in shape with that of the charge-transfer complex (**5e**). When the solution was then kept in the dark, the spectrum returned to the **1e** state upon air oxidation. The pseudo first-order rate constant of this reaction was measured from the decrease in the peak at 318 nm of **1e** and the increase in the peak at 357 nm (Table 3).

These results indicate that the photoreduction of **1** occurs in this system. We neglected the equilibrium between reactant and product and considered that **1** reacted with DTT to give a complex **9**, as is shown in Scheme 3. K_d was the dissociation constant of the equilibrium of the complex formation; k_1 and k_2 were

Table 3. REVERSIBILITY OF THE REACTION OF PYRAZINE DERIVATIVES IN 50% ACETIC ACID

λ_{max} (nm)	318	357
k_{photo}[a)] s^{-1}	4.7×10^{-4}	5.1×10^{-4}
k_{oxl}[b)] s^{-1}	6.5×10^{-5}	6.6×10^{-5}

a) The reaction rate of the photoreduction. b) The reaction rate of the oxidation reaction.



Scheme 3.

the rate constants for the reactions designated, and k_{obsd} was the observed rate constant. [DTT] was the concentration of DTT. When DTT existed in a larger quantity than **1e**, we obtained Eq. 1 (Lineweaver-Burk plots[13]):

$$(k_1-k_{\text{obsd}})^{-1} = (k_1-k_2)^{-1} + K_d(k_1-k_2)^{-1}[\text{DTT}]^{-1} \quad (1)$$

A series of measurements of the reaction rate with varying concentrations of DTT were carried out. A typical run was zero-order in the DTT and first-order in **1e**. The results, given in Fig. 2, were obtained by plotting 1/[DTT] *vs.* $1/(k_1-k_{\text{obsd}})$. From the good linearity of Fig. 2, we may conclude that the pyrazine derivatives, **1**, form the **9** complex with DTT such as do the flavin derivatives. From the intercept and slope of plotting, $K_d=5.1\times10^{-5}$ mol/l and $k_2=5.3\times10^{-5}$ s^{-1} were obtained. The DTT had a quenching effect, because k_2 was smaller than k_1 ($k_2/k_1 \simeq 10^{-3}$).

As the photoreaction of **1** was quenched by DTT, the quenching experiment was examined. The quantum yields were determined by using potassium tris(oxalato)ferrate(III) actinometry.[14] A Stern-Volmer plot of Φ against the concentration of DTT is given in Fig. 3, it shows good lineality, even in a large excess of DTT to **1** (DTT/**1**>10^2). Such examples are very few, but an instance has been shown in the photoreaction of pyridine; the quenching effect might be attributed to the reaction of pyridine and the quencher.[15] These data further indicate that the quenching effect of DTT occurs by the formation of a complex of pyrazine and DTT. The photoreaction of disulfide derivatives has been reported to produce dithiol derivatives ($\Phi=1$).[16] The low reactivity of the **9** complex on irradiation may be attributed to a difficulty on the formation of the disulfide derivative on irradiation.

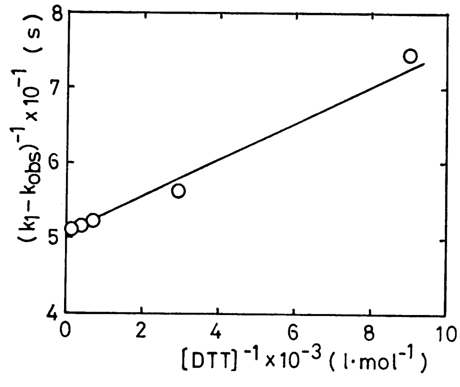


Fig. 2. Dependence of $1/(k_1-k_{\text{obs}})$ on the reciprocal of DTT. [**1e**]$=5\times10^{-5}$ mol/l.

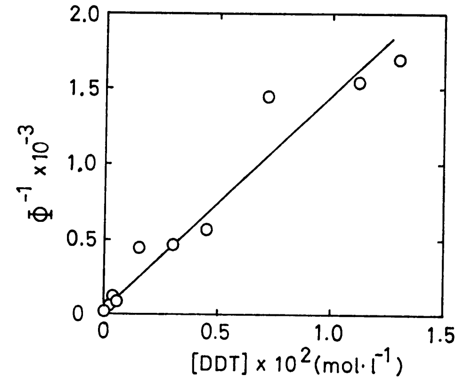


Fig. 3. Inverse quantum yields for photoreaction of **1e** (5×10^{-5} mol/l) against 1/[DTT].

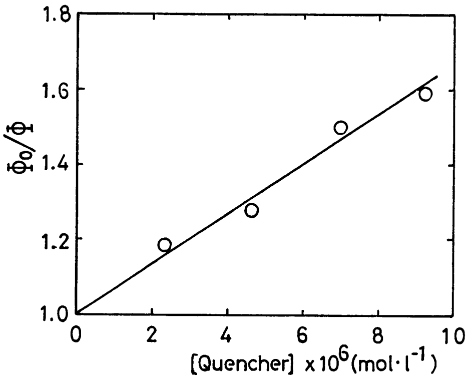


Fig. 4. Stern-Volmer plots of photoreduction of **1e** in 2-propanol solution (5×10^{-5} mol/l). The reaction was quanched by 9-fluorenone.

TABLE 4. SUBSTITUENT EFFECT ON THE PHOTOREACTION OF PYRAZINE DERIVATIVES WITH DTT IN 50% ACETIC ACID

Pyrazine	$k_1\times10^4$ s^{-1}	k_1/k_0
1a	5.22	1.0[a]
b	13.0	2.5
d	23.8	4.6
e	26.3	5.1
f	11.9	3.2

a) k_0.

The substituent effect of this reaction was studied, but no substituent effect was obtained, as is summarized in Table 4. This result indicates that the adduct of pyrazine with DTT as a **9** complex may have been formed.

Quenching Effects with 9-Fluorenone and Anthracene. In order to confirm the excited species, the quenching experiments were examined. The Stern-Volmer plots, which indicated a good linearity in the low-concentration areas of 9-fluorenone, are shown in Fig. 4. From the slope of Fig. 4, $k_q\tau=6.6\times10^4$ l/mol was obtained. Furthermore, from the quenching effect with anthracene, $k_q\tau=3.1\times10^4$ l/mol was obtained. As a result, a triplet state is proposed for this reaction, probably as a single excited species.

Experimental

All melting points were measured with a Yanagimoto micro melting point apparatus. The UV spectra were taken on a Hitachi ERS-3T or a Shimadzu UV-200 spectrometer. The IR spectra were measured using a Jasco IR-G spectrometer. The NMR spectra were measured with a Hitachi R-24 spectrometer using tetramethysilane as an internal standard. The mass spectra were recorded with a Hitachi RMU-6E mass spectrometer. The elementary analyses were performed at the Faculty of Pharmaceutical Sciences, Chiba University.

Materials. All materials, obtained from the Wako Pure Chemical Industries Ltd. and the Tokyo Kasei Co., were used without further purification. Dimethyl 3,6-dimethyl-2,5-pyrazinedicarboxylate (**1a**) and diethyl 3,6-dimethyl-2,5-pyrazinedicaboxylate (**1b**) were prepared by the method of Iida and his co-workers.[6]

2,5-Diacetyl-3,6-dimethylpyrazine (1c). To a solution of 200 g 2,4-pentanedione in 224 ml of acetic acid, a solution of 152 g of sodium nitrite in 270 ml of water was slowly added for 1 h below 7° C in ice bath. The solution was stirred for an hour at 30 °C and furthermore for two hours with 200 ml of water. The aqueous mixture was extracted with 200 ml of ether. The extracted liquor was neutralized, washed and dried with soldium sulfate. Romoval of the solvent gave 197 g (76 %) of white flaky crystals of 3-nitroso-2,4-pentanedione. A solution of 37.6 g of 3-nitroso-2,4-pentanedione in 120 ml of ethanol and 36 ml of acetic acid was reduced at room temperature using 4.0 g of 10% palladium charcoal as catalyst in 500 ml autoclave. The solution containing catalyst was filtered. The solvent of filtrate was removed and the residue was chromatographed on silica gel to give 14.2 g (16 %) of pale yellow needles of of **1c**, mp 99 °C, ν_{max} (KBr) 1699 cm^{-1}, λ_{max} (EtOH) 234 (ε 5200) and 298 nm (ε 8600), δ ($CDCl_3$) 2.67 (6H, s) and 2.79 (6H, s); *m/e* 192 ($M^{+\cdot}$). Found: C, 62.46; H, 6.63; N, 14.46%. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.63; N, 14.58%.

2,5-Dibenzoyl-3,6-dimethylpyrazine (1d). To a solution of 50 g of 1-phenyl-1,3-butanedione in 49 ml of acetic acid, a solution of 24 g of soldium nitrite in 47 ml of water was slowly added for about an hour below 25 °C in water bath. The solution was stirred for half an hour at 30 °C and was cooled to give white crystals of 1-phenyl-2-nitroso-1,3-butanedione. The solution containing the crystals was filtered and the filtrate was extracted with ether. The extracted liquor was concentrated and poured into a large quantity of water to give crystals of 57.5 g (97%) of 1-phenyl-2-nitroso-1,3-butanedione. The crystals were washed well. A solution of 17 g of 1-phenyl-2-nitroso-1,3-butanedione of 60 ml of ethanol and 20 ml of acetic acid was reduced at room temperature using 3.6 g of 10% palladium charcoal as catalyst in 500 ml autoclave. The solution containing catalyst was filtered. The solvent of filtrate was removed and the residue was dissolved in chloroform. The solution was neutralized, washed and dried with sodium sulfate. The chloroform was removed and the residue was dissolved in ethanol. Aeration of the solution for three hours gave 728 mg (2.6%) of white crystals of **1d**, mp 167—169 °C; λ_{max} (EtOH) 256 (ε 23300) and 290 nm (ε 21000); δ ($CDCl_3$) 2.59 (6H, s), 7.25—8.95 (10H, m); *m/e* 316 ($M^{+\cdot}$). Found: C, 75.97; H, 5.15; N, 8.79%. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86%.

1,2,3,4,6,7,8,9-Octahydro-3,3,8,8-tetramethyl-1,6-phenazinedion (1e). 5,5-Dimethyl-2-(hydroxyimino)-1,3-cyclohexanedione was prepared by the method of Hass.[17] A solution of 2 g of 5,5-dimethyl-2-(hydroxymino)-1,3-cyclohexanedione in 50 ml of ethanol was reduced using 0.2 g of 10% palladium charcoal as catalyst in 100 ml autoclave. The solution containing catalyst was filtered and the filtrate was aerated for three hours at 40—60 °C. After removal of the solvent, the separation of the reaction mixture by column chromatography gave 0.35 g (18%) of **1e**, mp 214—219 °C; λ_{max} (EtOH) 233 (ε 9400) and 317 nm (ε 9300); δ ($CDCl_3$) 1.17 (12H, s), 2.72 (4H, s), and 3.27 (4H, s); *m/e* 272 ($M^{+\cdot}$). Found: C, 70.17; H, 7.43; N, 10.11%. Calcd for $C_{16}H_{20}N_2O_2$: C, 70.17; H, 7.40; N, 10.29%.

Furthermore, **1e** was prepared by the following manner. Decahydro-3,3,8,8-tetramethyl-1,6-phenazinedione dihydrochloride (**6e**) in methanol was neutralized. The methanol was removed. The purification of the residue gave pale yellow crystals of **1e**.

1,2,3,4,6,7,8,9-Octahydro-1,6-phenazinedione (1f). Decahydro-1,6-phenazine dihydrochloride (**6f**) in methanol was neutralized. After the solvent was removed, the residue was chromatographed on silica gel to give **1f** (45%), mp 250—260 °C; λ_{max} (EtOH) 230 (ε 13700) and 317 nm (ε 15600); δ($CDCl_3$) 2.30 (4H, dt), 2.88 (4H, t), and 3.30 (4H, t); *m/e* 216 ($M^{+\cdot}$). Found: C, 66.38; H, 5.60; N, 12.75%. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96%

1,2,3,4,6,7,8,9-Octahydrophenazine (1g). 2-Chlorocyclohexanone was synthesized by the method of Organic Synthesis.[18] Ammonia was bubbled into a solution of 24 g of 2-chlorocyclohexanone in 350 ml of ethanol for about three hours below 7 °C in ice bath. The solution, which was added 40 ml of 3M-HCl, was extracted with four 80 ml portions of ether. Adjustment of the extracted liquor to pH 2 with sodium hydroxide gave white crystals in good yield. Upon recrystalization from acetone, **1g** was obtained as white plates, mp 108 °C; λ_{max} (EtOH) 290 nm (ε 10800), δ($CDCl_3$) 1.84 (8H, m) and 2.79 (8H, m); *m/e* 188 ($M^{+\cdot}$).

Decahydro-3,3,8,8-tetramethyl-1,6-phenazinedione Dihydrochloride (6e). 2-Amino-5,5-dimethyl-1,3-cyclohexanedion was prepared by the method of Regitz and Stadler.[19] A 10 g of 2-amino-5,5-dimethyl-1,3-cyclohexanedione was refluxed in 150 ml 15% HCl for few hours to obtain yellow crystals of **6f**. After filtration, same operation were repeated. **6f**, mp 177 °C; *m/e* 218 ($M^{+\cdot}-2HCl$). Found: C, 49.02; H, 5.48; N, 9.62; Cl, 23.94%. Calcd for $C_{12}H_{12}N_2O_2\cdot 2HCl$: C, 49.50; H, 5.54; N, 9.62; Cl, 24.35%.

Irradiation of Pyrazine Derivatives. A solution of 2.0 g of **1a**—**d** in 2 l of diethyl ether was irradiated with a Ushio UM-425 450-W high pressure mercury lamp for six hours. After irradiation, the solvent was removed ***in vacuo*** at room temperature and the oily residue was chromatographed on silica gel to give **2a**—**d** and the viscous liquid of solvent adducts **3a** and **3c**. **3a** was crystalized very slowly from hexane–benzene. Using tetrahydrofuran as a solvent, **4a** and **4c** were obtained. The yields and physical data of **2**, **3**, and **4** were shown in Table 1.

Determination of the Structure of 2. A solution of 200 mg of methyl 3,6-dimethyl-5-hydroxypyrazine-2-carboxylate (**2a**) in 5 ml of water containing 0.09 g of potassium hydroxide was stirred for an hour at room temperature and further for an hour at 40 °C. From the solution adjusted to pH 4—5 by dil. HCl, **2a** which had not reacted was removed by the extraction with ether. The residue was dried by repetition of azeotropy with benzene and extracted with ethanol in a Soxhlet extracter. Removal of the solvent gave 40 mg of residue. By thermolysis and sublimation of the mixture of this residue, a solid and a liquid were obtained. Solid, mp 202 °C; λ_{max} (EtOH) 267 nm. The solid compound was identical with 3,6-dimethyl-2-pyrazinol from its melting point (lit,[7] 207 °C).

Measurement of the Reaction Rate of Pyrazine Derivatives with DTT. Equivolume of distilled water and dried acetic acid were mixed as the solvent. **1e** (3.19 mg, 1.15×10^{-5} mol) was dissolved in 50 ml of the solvent using a volumetric flask DTT (20 mg, 1.3×10^{-4} mol) was transferred to a volumetric flask and diluted to 20 ml with the solvent. From solution of DTT, an appropriate aliquot was further dilute to yield 10^{-4}—10^{-2} mol/l solution for spectral analysis. One ml of a solution of **1e** and 0—3 ml of solution of DTT were mixed in a 1 ml quartz cell and diluted to 4 ml with the solvent.

After bubbling of argon gas for an hour, a quartz cell was sealed. Consecutive irradiations of short duration were carried out with a Ushio UM-103B 100-W high pressure mercury lamp in a sealed quartz cell which was transferred periodically to the UV spectrometer for spectral recording.

The reaction rate calculated from the decrease of the peak at 318 nm (ε 12000) of **1e** or the increase of the peak at 357 nm (ε 21800) of **5e**.

Substituent Effects on the Reaction of Pyrazines. Equivolume of distilled water and dried acetic acid were mixed as the solvent. Pyrazine derivatives **1** (1.1×10^{-5} mol) was dissolved in 50 ml of the solvent. DTT (1.37 mg, 8.88×10^{-6} mol) was dissolved in 20 ml of the solvent. 1 ml of each solutions were mixed and diluted to 4 ml of the solvent in a quartz cell.

After bubbling of argon gas for an hour, irradiations were carried out with a 100-W high pressure mercury lamp. Periodically UV spectra were recorded. And the reaction rates were calculated from the decrease of the peak of the pyrazine.

Quenching of the Photoreaction of Pyrazine Derivatives. Pyrazine **1e** (3.67 mg, 1.35×10^{-5} mol) was dissolved in 50 ml of dried 2-propanol. 9-Fluorenone (3.33 mg, 1.85×10^{-5} mol) was dissolved in 100 ml of dried 2-propanol. From a solution of 9-fluorenone, an appropriate aliquot was further diluted for spectral analysis. One ml of a solution of **1e** and 0—3 ml of a diluted solution of 9-fluorenone were mixed in a 1 ml quartz cell and diluted to 4 ml with dried 2-propanol. In analogy with measurement of substituent effects, the reaction rates were measured: a linear Stern-Volmer plots of $\Phi_0/\Phi(=k_0/k)$ *vs.* concentration of quencher was obtained with $k_q\tau = 6.6 \times 10^4$ l/mol.

From the quenching effect of **1e** (5.5×10^{-5} mol/l) with anthracene in dried acetic acid, $k_q\tau = 3.1 \times 10^4$ l/mol was obtained.

References

1) K. Yamada, T. Konakahara, S. Ishihara, T. Itoh, K. Kimura, and H. Iida, *Tetrahedron Lett.*, **1972**, 2513; K. Yamada, T. Konakahara, and H. Iida, *Bull. Chem. Soc. Jpn.*, **46**, 2504 (1973); K. Yamada, M. Kamei, Y. Nakano, H. Kasimura, and H. Iida, *Tetrahedron Lett.*, **1974**, 1741.

2) A. Padwa and E. Glazer, *J. Am. Chem. Soc.*, **94**, 7788 (1972); A. Padwa, M. Dharan, J. Smolanoff, and S. I. Wetmore, Jr., *J. Am. Chem. Soc.*, **95**, 1945 (1973); *ibid.*, **95**, 1954 (1973).

3) R. D. Chambars, J. R. Maslzkiewicz, and K. C. Srivastava, *J. Chem. Soc. Perkin. Trans. 1*, **1975**, 1130.

4) F. Lahmank and N. Ivanoff, *Tetrahedron Lett.*, **1967**, 3913.

5) C. Dufraisse, A. Etienne, and E. Toromanoff, *C. R. Acad. Sci.*, **235**, 759 (1952); E. Toromanoff, *Ann. Chem. (Paris)*, **1**, 115 (1956); T. Iwaoka, S. Niizima, and M. Koizumi, *Bull. Chem. Soc. Jpn.*, **43**, 2786 (1970); D. N. Bailey, D. K. Roi, and D. M. Herucles, *J. Am. Chem. Soc.*, **90**, 6291 (1968); S. Wake, Y. Otuji, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **47**, 1251 (1974).

6) H. Iida, K. Hayashida, M. Yamada, K. Takahashi, and K. Yamada, *Synth. Commun.*, **3**, 225 (1973).

7) W. Sparp and F. S. Spring, *J. Chem. Soc.*, **1948**, 1862.

8) S. M. Japar and E. W. Abrahamson, *J. Am. Chem. Soc.*, **93**, 4140 (1971).

9) H. Beinert, *J. Am. Chem. Soc.*, **78**, 5323 (1956); J. H. Swinehart, *ibid.*, **87**, 904 (1965); *ibid.*, **88**, 1056 (1966); Q. H. Gibson, V. Massey, and N. M. Atherton, *Biochem. J.*, **85**, 369 (1962); F. Muller, P. Hemmerrich, A. Ehrenberg, G. Palmer, and V. Massey, *Eur. J. Biochem.*, **14**, 185 (1970).

10) H. I. X. Mager and W. Berends, *Tetrahedron Lett.*, **1973**, 4051.

11) S. Shinkai, *Kagaku*, **30**, 39 (1975).

12) T. C. Bruice, L. Main, S. Smith, and P. Y. Bruice, *J. Am. Chem. Soc.*, **93**, 7327 (1971); E. L. Loecher and T. C. Hollocher, *ibid.*, **97**, 3235 (1975); I. M. Gascoigne and G. K. Radda, *Biochim. Biophys. Acta*, **131**, 498 (1967).

13) H. Lineweaver and D. Burk, *J. Am. Chem. Soc.*, **56**, 658 (1934).

14) C. G. Hatchard and C. A. Parke, *Proc. R. Soc. London, Ser. A*, **235**, 518 (1965).

15) T. J. van Berger and R. M. Kellogg, *J. Am. Chem. Soc.*, **94**, 8451 (1971).

16) C. C. Price, "Geometry of Molecule," McGraw-Hill, New York (1969).

17) P. Haas, *J. Chem. Soc.*, **91**, 1437 (1907).

18) M. S. Newman, M. D. Farbman, and H. Hipsher, *Org. Synth.*, Coll. Vol. III, 188 (1955).

19) M. Regitz and D. Stadler, *Justus Liebigs Ann. Chem.*, **687**, 214 (1965).