Photochemistry of Heterocyclic Compounds. VII. The Photochemical Behavior of Phthalazine and Quinoxaline in Acidified Alcohols

Shigeo Wake, Yuichi Takayama, Yoshio Otsuji, and Eiji Imoto
Department of Applied Chemistry, College of Engineering, University of Osaka Prefecture, Sakai-shi, Osaka 591

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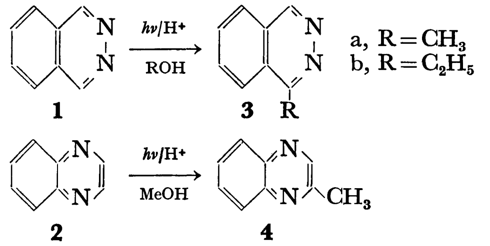
Irradiation of phthalazine (**1**) and quinoxaline (**2**) in acidified methanol yielded 1-methylphthalazine (**3a**) and 2-methylquinoxaline (**4**), respectively. The quantum yields for the formation of 1-alkylphthalazines, which were obtained upon irradiation of **1** in acidified alcohols, varied with the sort of alcohols used and decreased in the order of methanol>ethanol≫2-propanol. When a mixture of **1** and 2,6-di-*t*-butylphenol (**6**) was irradiated in benzene containing trifluoroacetic acid under evacuated conditions, the oxidation of **6** occurred to form 3,5,3′,5′-tetra-*t*-butyldiphenoquinone (**7**) without destruction of **1**. Detailed mechanistic studies suggest that the photoalkylations of **1** and **2** in acidified alcohols proceed through an electron-transfer from solvents to an excited state of the protonated diazines.

In the previous communication,[1)] we have reported that phenazine undergoes an ionic solvent-addition reaction to form 1-hydroxy- or 1-alkoxyphenazines upon irradiation in water or alcohols in the presence of protic acids. However, other studies on the photoreactions of nitrogen heteroaromatic compounds in acidified alcohols have indicated that the photoalkylation, rather than the solvent-addition, appears to be a general reaction for this class of compounds.[2—3)] These two distinct observations led us to study the photochemical behaviors of phthalazine and quinoxaline, both of which belong to the class of diazine similar to phenazine.

In contrast to phenazine, phthalazine and quinoxaline underwent the photoalkylation reaction upon irradiation in acidified alcohols. Detailed mechanistic studies on the photoreaction of phthalazine suggested that the photoalkylation proceeded through the pathway involving an electron-transfer from alcohols to the excited protonated phthalazine. The details are presented in this paper.

Results

Photo-products. Irradiation of dilute solutions of phthalazine (**1**) in methanol and ethanol containing HCl with a low-pressure Hg lamp under nitrogen atmosphere afforded 1-methyl and 1-ethylphthalazines (**3a** and **3b**), respectively. Irradiation of quinoxaline (**2**) in acidified methanol under similar conditions gave 2-methylquinoxaline (**4**). The results are summarized in Table 1. *p*-Toluenesulfonic acid was also effective as an acid-catalyst for these photoalkylations. On the other hand, when a 0.01 M solution of **1** in methanol was irradiated for 3 hr in the absence of acid, **3a** was not obtained. However, treatment of the resulting reaction mixture with HCl gave **3a** in an 11% yield.

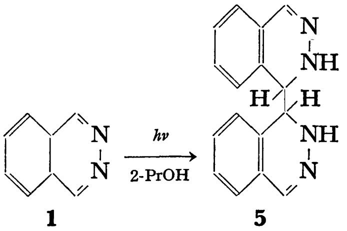


1 **3** **2** **4**

Reaction temperature influenced remarkably on the yields of the products, *i.e.*, irradiation of the solutions of **1** and **2** in acidified methanol at their reflux temperatures raised the yields of the products as shown in Table 1. No reactions took place upon irradiation of aqueous solutions of **1** and **2** both in the presence and absence of acids.

In contrast to the above photoreactions, irradiation of **1** in 2-propanol containing *p*-toluenesulfonic acid gave only a small amount of tarry material. Vpc analysis of the reaction mixture did not show any indication for the presence of the photoalkylation products. Vpc analysis also showed that the rate of disappearance of **1** was faster in methanol than in 2-propanol. Thus, irradiation of **1** in 2-propanol containing 0.1 M *p*-toluenesulfonic acid for 3 hr resulted in a 77% recovery of **1**, while a similar irradiation of **1** in methanol resulted in a 51% recovery of the starting material (see Table 1).

Irradiation of **1** in 2-propanol without added acid afforded a reductive dimerization product (**5**). The structure of **5** was established by a combination of the elemental analysis and spectral data (see Experimental section). The dimer was not obtained by the irradiation in methanol.



1 **5**

*Photoreaction of 2,6-Di-*t*-butylphenol (6) in the Presence of 1 in an Acidic Medium.* When irradiation of an equimolar mixture of **1** and **6** in benzene containing trifluoroacetic acid was carried out under evacuated conditions, 3,5,3′,5′-tetra-*t*-butyldiphenoquinone (**7**) was obtained together with a small amount of unidentified tarry material. The yield of **7** increased with increase of irradiation time, and in every case **1** was recovered

TABLE 1. PHOTOREACTIONS OF **1** AND **2**

Compd.[a]	Solvent	Irrad. conditions		Recovered starting material, %	Product	
		Temp., °C	Time, hr		Compd.	Yield[b] %
1	MeOH 0.08 M HCl	20	3	28	**3a**	30
1	EtOH 0.08 M HCl	20	3	74	**3b**	5
1	MeOH 0.08 M HCl	reflux	3	9	**3a**	50
1	MeOH 0.1 M TsOH[c]	20	3	51	**3a**	32
1	2-PrOH	20	3	83	**5**	8
1	2-PrOH 0.1 M TsOH[c]	20	3	77	—	—
2	MeOH 0.08 M HCl	20	1	64	**4**	trace
2	MeOH 0.08 M HCl	reflux	1	54	**4**	10

a) The 0.01 M solutions of **1** and **2** were irradiated under nitrogen atmosphere. b) The yields are based on the amount of the starting material used. c) TsOH represents *p*-toluenesulfonic acid.

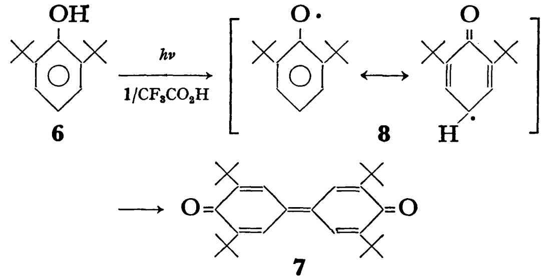
TABLE 2. IRRADIATION OF A MIXTURE OF **1** AND **6** IN AN ACIDIC MEDIUM[a]

Irrad. time, hr	Recovered starting materials, %		Yield of **7**,[b] %
	1	**6**	
12	88	83	9
24	80	71	11
50	74	47	18

a) A mixture of 0.5 mmol of **1** and 0.5 mmol of **6** in 50 ml of benzene containing trifluoroacetic acid (0.1 M) was irradiated under evacuated conditions.

b) The yields of **7** were calculated on the basis of the amount of **6** used.

in a high yield. The results are shown in Table 2. However, **7** could not be detected in the reaction mixture when the irradiation was conducted without added acid or in the absence of **1**. In these cases, the starting materials were recovered unchanged. No reaction also took place without irradiation.



Quantum Yields. The quantum yields for the formation of alkylated products obtained by irradiation of **1** in various acidified alcohols were measured. The results are shown in Table 3. The quantum yields decreased in the order of methylation$>$ethylation$\gg$propylation.

TABLE 3. THE QUANTUM YIELDS FOR THE FORMATION OF 1-ALKYLPHTHALAZINES[a]

Solvent	Product	Φ
MeOH, 0.1 M HCl	**3a**	0.026
EtOH, 0.1 M HCl	**3b**	0.0055
2-PrOH, 0.1 M HCl	—[b]	0

a) The 0.01 M solutions of **1** in acidified alcohols were irradiated for 4 hr, and then the products were analyzed to determine the quantum yields.

b) No alkylated product was detected in the reaction mixture.

The quantum yields for the formation of **3a** from **1** were also determined in the presence of various amounts of HCl. The results are depicted in Fig. 1. The

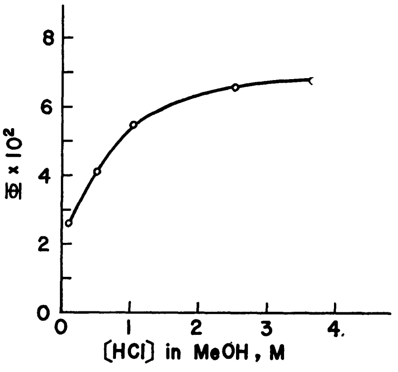


Fig. 1. Effect of HCl concentrations on the quantum yields for the formation of **3** upon irradiation of **1** in acidified methanol. A 0.01 M solution of **1** was irradiated.

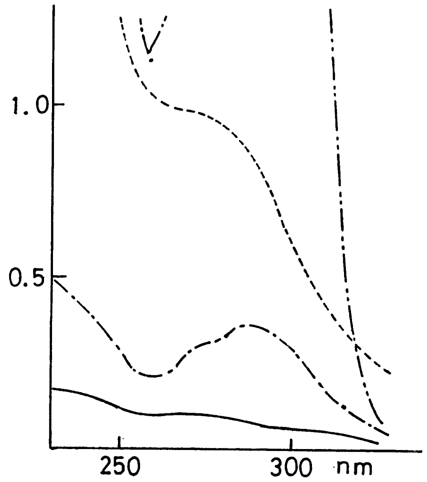


Fig. 2. UV spectra of acidified alcohols: ——, methanol containing of 1 M HCl; ------, methanol containing 5 M HCl; -·-·-, ethanol containing 1 M HCl; —·—, ethanol containing 5 M HCl.

quantum yields increased with increase of the concentration of the acid present. However, when the irradiation was carried out in the presence of 7.2 M HCl, it was found that the quantum yield for the formation of **3a** decreased to a half of the value that was obtained upon irradiation in the presence of 3.6 M HCl. However, spectral examination (Fig. 2) demonstrated that in the presence of higher concentrations of acids, methanol itself absorbed much of the light at 245 nm which was also a main effective light for the photoreaction. Therefore, decrease in the quantum yield for the formation of **3a** in the presence of 7.2 M HCl does not necessarily mean that the quantum efficiency for the reaction decreases at higher concentrations of the acid, but it may merely due to the decrease in number of quanta absorbed by **1**.

To evaluate effects of air on the quantum efficiency of the photoreaction, irradiation of **1** in 0.1 M HCl–MeOH was carried out under evacuated conditions. Quenching experiment employing 1,2-dibromoethane as a quencher was also performed. The results are summarized in Table 4.

TABLE 4. IRRADIATION OF **1** IN ACIDIFIED METHANOL[a)]

Quencher	Quantum yield for disappearance of **1**	Quantum yield for the formation of **3a**
None	0.102	0.080
Air	0.072	0.026
1,2-DBE,[b)] 0.19 M	0.121	0.073

a) A 0.01 M solution of 1 in methanol containing 0.1 M HCl was irradiated. b) 1, 2-DBE represents 1,2-dibromoethane.

Absorption Spectra. The absorption spectra of **1** and *N*-methylphthalazinium iodide were studied. The absorption spectra of **1** in MeOH, EtOH, and 2-PrOH were essentially identical. A red shift was observed upon an addition of acid. The spectra of **1** in methanol containing 0.1—1.0 M HCl were very similar in shape to the spectrum of *N*-methylphthalazinium iodide in methanol as shown in Fig. 3.

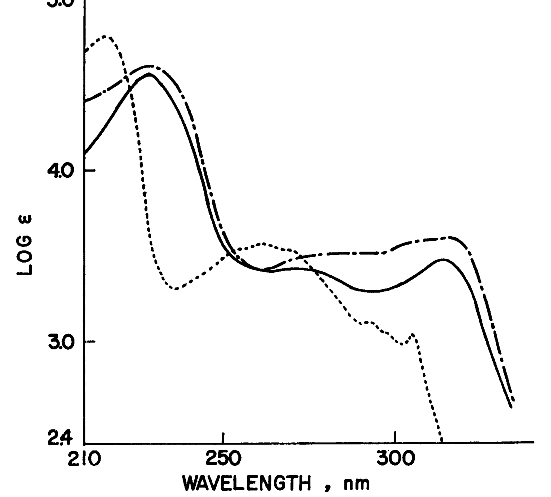
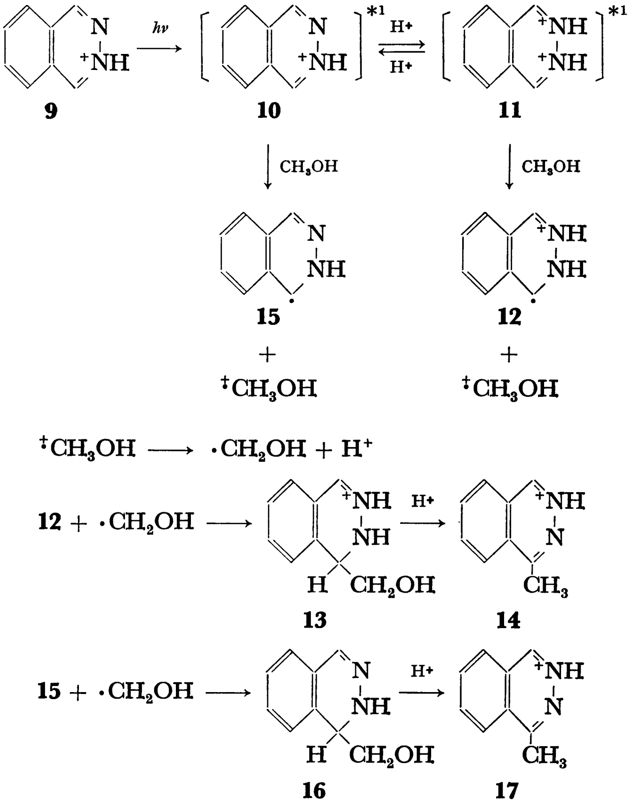


Fig. 3. UV spectra of **1** and *N*-methylphthalazinium iodide: ------, **1** in methanol; ——, **1** in methanol containing 1.0 M HCl; -·-·-, *N*-methylphthalazinium iodide in methanol.

Discussion

A proposed mechanism for the photoalkylation of azaaromatic compounds is illustrated in Scheme 1 taking an example of the photomethylation of **1** in acidified methanol.

Absorption spectra shown in Fig. 3 strongly suggest that **1** exists at its ground state predominantly in the



Scheme 1.

form of monoprotonated phthalazinium cation (**9**) in methanol containing 0.1—1.0 M HCl. However, at the excited state **1** may exist either in the excited monoprotonated form (**10**) or in the excited diprotonated form (**11**) in acidified methanol.[4)]

The excited diprotonated species **11** picks up an electron from methanol to form the cation radical **12** and the cation radical of methanol, $^{+}\cdot CH_3OH$, which is converted to hydroxymethyl radical. A coupling of **12** with hydroxymethyl radical produces the intermediate **13**. The reaction of **13** with a proton affords the monoprotonated 1-methylphthalazinium cation (**14**).

The result of Fig. 1 can be explained by assuming that the reactive species is **11**, since the proportion of **11** in the reaction mixture would increase with increase of the acid concentrations.[5)]

A striking feature of the proposed mechanism is the electron transfer from alcohols to the excited protonated azines. This mechanism was derived from the following considerations. Firstly, the electron affinity of **11** is supposed to be high enough to take up an electron from alcohols. An increased electron affinity of the dication of diazines has been recognized by Curphey,[6)] who observed that *N,N′*-diethylpyradinium difluoroborate is reduced to the corresponding cation radical upon dissolving it in ethanol even in the dark. Secondly, the solvent effects on the photoreaction of **1** are consistent with the electron transfer mechanism. We observed that the quantum yields of the photoalkylations of **1** in acidified alcohols varied with the sort of alcohols used and decreased in the order of methanol>ethanol≫2-propanol (Table 1). Furthermore, the results of Table 1 indicate that the rate of disapperance of **1** decreases also in the above order. If the photoreaction is initiated *via* a hydrogen abstraction from alcohols by **10** or **11**, the reversed solvent effects must be observed. Absorption spectra shown in Fig. 2 suggest that alcohols may be transformed to their oxonium ions in the presence of higher concentrations of HCl (HCl and alcohols themselves have no absorptions at 220—250 nm where the acidified alcohols exhibited strong absorptions). If this is the case, it is reasonable to assume that the formation of oxonium ions in acidified alcohols would become favorable in more basic 2-propanol than in more acidic ethanol or methanol. An electron abstraction from the oxonium ions would be more difficult than from the free alcohols. Thus, it is supposed that the photoreactivity varies in the observed order, if the photoreaction is initiated *via* the electron transfer from acidified alcohols to **11**. Thirdly, an evidence supporting the electron transfer mechansim was provided by the result that the irradiation of a mixture of **1** and **6** in benzene in the presence of acid brought about the oxidation of **6** to **7** without destruction of **1**. This photooxidation can be best explained in terms of the mechanism involving the electron transfer from **6** to **11** to form the phenoxy radical **8**.[7)] Finally, further supporting data for the mechanism were found in the literature. 1) Ochiai and co-workers[8)] have found that the photomethylation of pyrimidine derivatives in acidified methanol is favored by the electron-withdrawing substituents attached to the pyrimidine ring, and they have also observed the $\cdot CH_2OH$ radical. 2) Castellano and co-workers[9)] have recently detected the cation radicals of **2**, pyrazine, and phenazine in the reaction mixtures by ESR spectroscopy upon irradiation of their acidified methanolic solutions. These results are in accordance with the mechanism shown in Scheme 1.

It must be noted here that the photoreactions of azaaromatic compounds in the absence of acids may proceed through a hydrogen abstraction from alcohols by the excited azaaromatics.[3)]

1,2-Dibromoethane caused essentially no quenching effect on the quantum yield for the formation of **3a**. This result suggest that the photoreaction of **1** proceeds from a singlet excited state. A decrease in the quantum yield of the photoalkylation of **1** in the presence of air is explainable on the basis of the assumption that oxygen reacts with the intermediate radical species (**12** or hydroxymethyl radical, or both) to quench further reactions. The effect of temperature on the yields of **3a** and **4** in the photolyses of **1** and **2** may be attributed to the acid-catalyzed dehydration reaction of the type **13**→**14** in the dark. However, a more work has to be done before the final conclusion can be reached.

Experimental

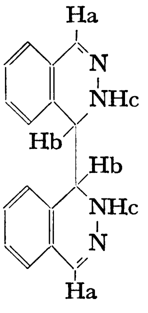
Melting points are uncorrected. UV spectra were recorded with a Hitachi EPS-3T recording spectrophotometer. IR spectra were obtained with a Hitachi model 215 infrared spectrophotometer. NMR spectra were obtained with a Hitachi H-60 high resolution NMR spectrometer, using TMS as an internal standard. Microanalyses were performed with a Yanagimoto MT-1 CHN corder. Mass spectra were obtained with a Hitachi RMU-6E mass spectrometer. Vpc analyses were performed with a Hitachi K-23 gas chromatograph, using a column packed with 30% Silicone grease on Celite 545. Unless otherwise noted, irradiations were carried out with a Taika 15 W low-pressure mercury lamp in an immersion-type apparatus.

Materials. Phthalazine (**1**) was prepared by the method of Gabriel and Muller[10)] and purified by recrystallization from ether, mp 89—91 °C. Quinoxaline (**2**) was prepared by the method of Jones and McLaughlin[11)] and purified by distillation, bp 109.5—111 °C/15 mmHg. All other chemicals were of commercial origin and were usually used after purification by distillation or recrystallization.

Preparation of the Authentic Samples. 1-Methylphthalazine (**3**) was prepared by the method of Popp and Wefer;[12)] NMR (CCl_4) δ 2.87 (3H, s, $-CH_3$), 7.55—8.00 (4H, m, benzoaromatic H), and 9.12 ppm (1H, s, -CH=N-); picrate, mp 201—203 °C (lit,[13)] mp 205 °C). 2-Methylquinoxaline (**4**) was prepared by the method of Bottcher,[14)] bp 121—125 °C/19 mmHg; NMR (CCl_4) δ 2.66 (3H, s, $-CH_3$), 7.25—7.95 (4H, m, benzoaromatic H), and 8.49 ppm (1H, s, -N=CH-). 3,5,3′,5′-Tetra-*t*-butyldiphenoquinone (**7**) was prepared by the method of Cook, English, and Wilson,[7)] mp 232—234 °C.

Photoreaction of 1. (A) Irradiation in Acidified Methanol: A solution of 130 mg (1 mmol) of **1** in 100 ml of an anhydrous methanol containing 0.08 M dry HCl or 0.1 M *p*-toluensulfonic acid was placed in a cylindrical quartz vessel and nitrogen was passed into the solution for 20 min. Irradiation was then carried out at room temperature or at refluxing temperature of the solvent. After irradiation for an appropriate period of time, the irradiated solution was evaporated to dryness under reduced pressure. The residue was neutralized with 10% aqueous Na_2CO_3, and the aqueous mixture was extracted with benzene by means of a liquid extractor. The benzene extract was dried over Na_2SO_4 and then evaporated. The NMR, IR and vpc examinations showed that the residue consisted of a mixture of **1** and **3**. The quantitative analysis of the residue was performed by vpc, employing quinaldine as an internal standard.

(B) Irradiation in Methanol without Added Acid: A solution of 130 mg (1 mmol) of **1** in 100 ml of an anhydrous methanol was irradiated at room temperature as described above. A concentrated HCl (1 ml) was then added to the reaction mixture, and the resulting mixture was refluxed for 1 hr. The mixture was then worked up as described above.



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(C) Irradiation in 2-Propanol. A solution of 130 mg (1 mmol) of **1** in 100 ml of an anhydrous 2-propanol was irradiated for 3 hr as described above. The solution was concentrated to 5 ml under reduced pressure. The crystals precipitated were collected by filtration and washed with 2-propanol, then with ether. The crystals (10 mg, 8%) were recrystallized from ethanol to give an analytical sample, mp 225—227 °C (decomp.), which was identified as the dimer **5**; NMR (CF_3COOH) δ 5.15 (2H, s, Hb), 7.09—7.21 (2H, broad m, Hc), 7.68—8.08 (8H, m, benzoaromatic H), and 8.6 ppm (2H, s, Ha); MS (50 eV) *m/e* 262 (M^+), 236, 230, 131, and 130. UV (EtOH) λ_{max} 245 (ε 2.56×10^4) and 345 nm (ε 5.63×10^3); IR (KBr) 3300, 3050, 1490 and 1420 cm^{-1}.

Found: C, 73.02; H, 5.59, N, 21.13%. Calcd for $C_{10}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36%.

The filtrate and washings obtained above were evaporated under reduced pressure and the residue was subjected to vpc analysis. The analysis indicated that the starting material was recovered in an 83% yield.

Photoreaction of **2**. A solution of 130 mg (1 mmol) of **2** in 100 ml of an anhydrous methanol containing 0.08 M dry HCl was irradiated at room temperature or at refluxing temperature of the solvent, in the same manner as previously described for the photolysis of **1**. After irradiation, the irradiated solution was evaporated to dryness under reduced pressure. The residue was neutralized with 10% aqueous Na_2CO_3, and the neutralized solution was extracted with benzene by means of a liquid extractor. The benzene extract was dried over Na_2SO_4 and then evaporated. Examinations of the residue by NMR, IR and vpc revealed that the residue consisted of a mixture of **2** and **4**. The quantitative analysis was performed by vpc with diphenyl ether as an internal standard.

Photoreaction of a Mixture of **1** *and* **6**. A mixture of 65 mg (0.5 mmol) of **1** and 103 mg (0.5 mmol) of **6** in a dry benzene containing 0.1 M trifluoroacetic acid was placed in a cylindrical quartz vessel and degassed by four or five freeze-pump-thaw cycles. Irradiation was then carried out from the outside of the reaction vessel at room temperature for 12 hr. The irradiated solution was extracted with 1 M HCl. The benzene layer was dried over Na_2SO_4 and then evaporated under reduced pressure. The residue was separated by preparative tlc on silica using CCl_4 as an eluent. Extraction of the first spot (R_f 0.3) with $CHCl_3$ and evaporation of the solvent gave 85 mg (83%) of unreacted **6**. Extraction of the second spot (R_f 0.5) with $CHCl_3$ and evaporation of the solvent gave 9 mg (9%) of **7** which melted at 231—233 °C after recrystallization from ethanol and was identical with the authentic sample in every respect. There were other few spots, from which 8 mg of unidentified materials were obtained.

On the other hand, the aqueous acid solution was made to pH 8 with Na_2CO_3 and filtered. The filtrate was extracted with benzene by means of a liquid extractor. The benzene extract was dried over Na_2SO_4 and then evaporated to give 57 mg (88%) of **1**.

Quantum Yield Determinations. A reactant solution (20 ml) in a quartz vessel was irradiated after degassing by four freeze-thaw cycles or under air with a Taika 15 W low-pressure mercury lamp. Although filter was not employed, the spectral examination of the radiation showed that the light source radiated the light with the following wavelength distribution: 74% 2537 Å, 4% 3130 Å, 4% 3660 Å, 4% 4055 Å, and 14% 4358 Å. All studies were made at room temperature. Potassium ferrioxalate actinometer[15] was used for measuring the light intensity. Reproducible output rates of 3.4×10^{18} quanta min^{-1} were recorded. After irradiation for 4 hr, the solution was neutralized with Na_2CO_3 and evaporated to dryness under reduced pressure. The residue was extracted with benzene, and the benzene extract was subjected to vpc analysis.

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4) It is well known that pK_a's in the lowest excited singlet state of azaaromatic compounds are much higher than the corresponding ground state pK_a's. (E. V. Donckt, "Progress in Reaction Kinetics," ed. by G. Porter, Pergamon Press, Oxford, Vol. 5 (1970), p. 273.)

5) The possibility remaines that the excited monoprotonated phthalazinium cation (**10**) may also pick up an electron from methanol to form the radical **15** and $^{+}CH_3OH$. However, it is reasonable to assume that the diprotonated species (**11**) more effectively picks up an electron than does **10**.

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