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Photochemical Reaction of 9-Cl-Acridine in Aerated and Deaerated Ethanol. I

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It was established that upon irradiation, the degassed ethanol solution of 9-chloroacridine is quickly converted into 9,9′-biacridyl by the reaction $2(\text{9-Cl-acridine}) \xrightarrow[(h\nu)]{+2H} \text{9,9′-biacridyl} + 2HCl$ and that 9,9′-biacridyl produced is then reduced photochemically to 9,9′-biacriden as the main product. The reaction scheme completely denies the scheme previously proposed (V. Zanker and W. Flügel, *Z. Naturforsch.*, **19(b)**, 376 (1964)) in which the primary photoproduct is a charge transfer complex between 9-Cl-acridine and its reduced form. 9,9′-biacridyl is photoreduced to an acridan-like compound even in the aerated solution perhaps *via* molecular mechanism in contrast to 9-Cl-acridine which yields acridone under similar conditions. ESR spectrum with hfs was detected in the acidic solution (degassed) containing 9,9′-biacriden produced photochemically. The mechanism of its production was discussed. Similar reactions using various solvents (aerated and deaerated) were examined and the general feature of the primary processes was described.

Photoreduction of acridine in various H-containing solvents has been studied extensively by the authors[1-3] and others.[4-7] Reactive sites on the acridine molecule are always 9C– and 10N– positions, the latter usually being hydrogenated preferentially in the primary act; the final products are acridans or biacridan according to experimental conditions.

Concerning the effect of substitution at 9-position, Zanker and Flügel studied the photoreaction of 9-halogen-acridine under various conditions[8] and reported that 9-Cl-acridine (9-Cl-A) in the aerated ethanol yields acridone while in the atmosphere of nitrogen, a photoproduct of quite a different type having an absorption peak at 430 nm (for the sake of convenience will refer to it as X-species) is produced which by prolonged irradiation is gradually transformed into another different species (Y-species) with a peak at 530 nm. Although they gave no suggestions as to the structure of Y-species, they proposed that X-species may be a charge transfer type molecular complex between the starting substance and the phtoproduct, perhaps 9-Cl-acridan. No work has been reported on these interesting reactions since then.

1) M. Koizumi, Y. Ikeda, and T. Iwaoka, *J. Chem. Phys.*, **48**, 1869 (1968); M. Koizumi, Y. Ikeda, and H. Yamashita, This Bulletin, **41**, 1056 (1968).

2) A. Kira and M. Koizumi, This Bulletin, **42**, 625 (1969).

3) Y. Miyashita, S. Niizuma, and M. Koizumi, *ibid.*, **43**, 3435 (1970).

4) V. Zanker, E. Erhardt, F. Mader, and J. Thies, *Z. Naturforsch.*, **21b**, 102 (1966); V. Zanker, E. Erhardt, and H. Mantsch, *Z. physik. Chem. N. F.*, **58**, 1 (1968); V. Zanker and E. Erhardt, *Ber. Bunsenges. phys. Chem.*, **72**, 267 (1968); V. Zanker and G. Prell, *ibid.*, **73**, 791 (1969).

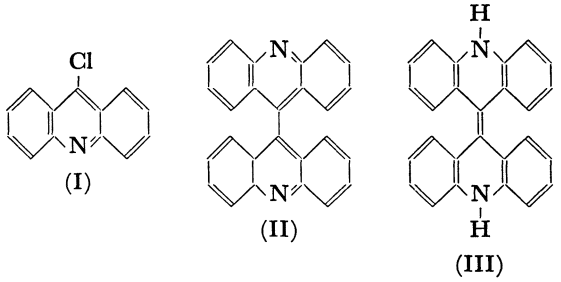
5) A. Kellmann and J. T. Dubois, *J. Chem. Phys.*, **42**, 2518 (1965).

6) E. Vander Donkt and G. Porter, *ibid.*, **46**, 1173 (1967).

7) F. Wilkinson and J. T. Dubois, *ibid.*, **48**, 2651 (1968).

8) V. Zanker and W. Flügel, *Z. Naturforsch.*, **19(b)**, 376 (1964).

We found a CT type complex somewhat analogous to that stated by Zanker and Flügel in a solution containing acridine and acridan or phenazine and dihydrophenazine.[9] The latter system has also been investigated by Bailey *et al.*[10] It was also found that these systems give ESR signals under suitable conditions. We were interested in the complex formation between oxidized and reduced forms and investigated the reaction of 9-Cl-A (I), studying in particular the reaction scheme up to the formation of X-species in detail. Careful reinvestigation of the overall reaction has revealed, however, that the fomation of X-species is preceded by another quite rapid process which yields 9,9′-biacridyl (II), and that X-species is 9,9′-biacriden (III) instead of a C-T complex.



Another interesting finding is that the photoproduct at the stage of X-species fomation, gives an ESR spectrum in acidic medium. Zanker and Flügel's observation of acridone formation in the aerated solution has been reconfirmed but we strongly suggest quite a different mechanism. Solvent effect on the reactions both in aerated and deaerated solutions has been examined.

Experimental

Materials. 9-Cl-acridine was prepared and purified according to the method of Albert and Ritchie (*Organic Synthesis*, **22**, 5 (1942)). Since 9-Cl-acridine in ethanol easily undergoes thermal transformation into acridone, the solution was always prepared immediately before the experiment. The concentration was 1×10^{-4}M unless otherwise stated. Ethanol was dried according to the method of Lund and Bjerrum.[11] Methyltetrahydrofuran was dehydrated with Na-K alloy in vacuo repeating freeze-pump-thaw 7—8 times.

Apparatus and Procedures. The apparatus for reaction was a similar one to that employed in our laboratory. The light source is a 100 W high pressure mercury lamp. 365 nm monochromatic light was taken out through a filter system consisting of a glass plate and U-2 filter. Fluorescence spectrum was measured with a Hitachi MPF-2 spectrofluorometer, and ESR spectrum with a JEOL P-10 type ESR spectrometer.

Results and Discussion

Reaction in the Deaerated Ethanol Solution. Figure 1 shows the change in the absorption spectrum caused by irradiation.

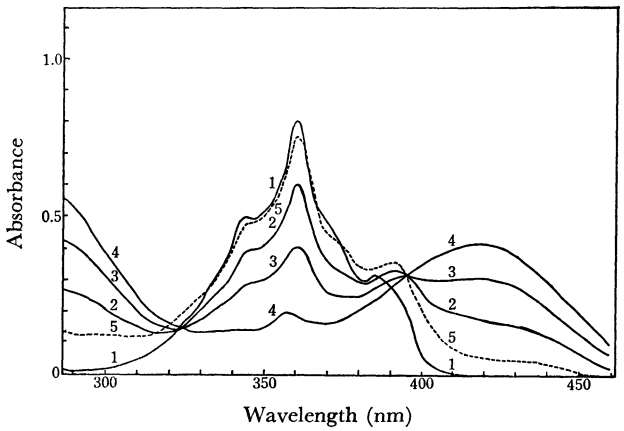


Fig. 1. Change of absorption spectra when the degassed ethanol solution of 9-Cl-A was irradiated by 365 nm (25°C).
1) 9-Cl-A
2) 1 min and 10 sec irradiation
3) 3 min and 20 sec irradiation
4) 7 min irradiation
5) air is introduced to 4),
for about 40 sec irradiation of 9-Cl-A, essentially the same spectrum as 5).

About 40 seconds after starting irradiation, the main peak shifted slightly to the shorter wavelength accompanied with a complicated change in the 385 nm region. This stage was then followed by a second extensive change *i.e.* a large decline of the main peak and a rise of a new broad maximum around 420 nm (X-species). Prolonged irradiation caused a gradual replacement of this band with a new band near 530 nm (Y-species). The two last changes are in complete agreement with Zanker and Flügel's observation but the first one escaped their notice. In Fig. 2, curve a) is the plot of $\ln(e^{\alpha cd}-1)$ (α, absorption coefficient at 365 nm; c, concentration of 9-Cl-A) against time for the reaction of 9-Cl-A. It is evident that a certain type of induction period exists corresponding to the spectral change in the earliest stage.

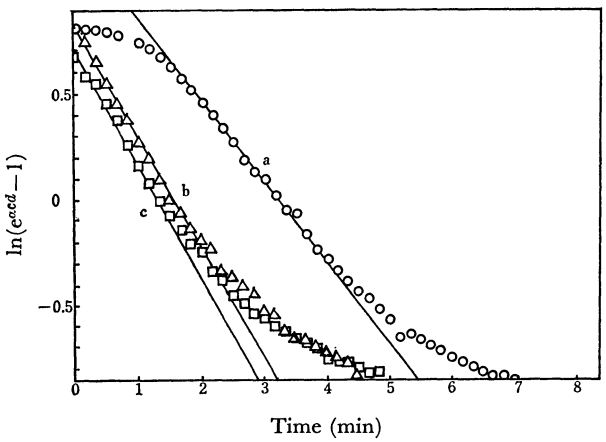


Fig. 2. Plot of $\ln(e^{\alpha cd}-1)$ *vs.* t for the degassed ethanol solution of 9-Cl-A (1×10^{-4}M) and of Z-species (see Text).
(excitation at 365 nm; temp., 25°C)
a) —○—○— first run (for 9-Cl-A)
b) -△-△- second run (for Z-species)
c) -□-□- third run (for Z-species)

9) T. Iwaoka, S. Niizuma, and M. Koizumi, This Bulletin, **43**, 2786 (1970).
10) D. N. Bailey, D. K. Roe, and D. M. Hercules, *J. Amer. Chem. Soc.*, **90**, 6291 (1968).
11) H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

Concerning the behavior of X-species, Zanker and Flügel only mentioned that it is gradually reconverted into the initial substance in the dark. We have found in addition to this recovery of absorption spectrum (but not of the initial substance), that the introduction of air quickly converts X-species into a compound with a spectrum resembling that of 9-Cl-A, as shown in Fig. 1. We concluded, however, by close examination that the spectrum agrees almost completely with that of the species produced during the first 40 second irradiation. This solution when irradiated again after having been degassed, turned into X-species. We found no induction period in this case, and the spectrum changed with a clear isosbestic point at 393 nm from the beginning. Quantum yield for X formation was almost the same as the value for 9-Cl-A obtained from the run after the induction period. The chemical behavior of this compound was found to be quite different from that of 9-Cl-A. Thus the latter is transformed into acridone when the aerated ethanol solution is irradiated as observed by Zanker and Flügel and as confirmed by us, whereas the former gives acridan-like product instead of acridone. This is shown in Fig. 3.

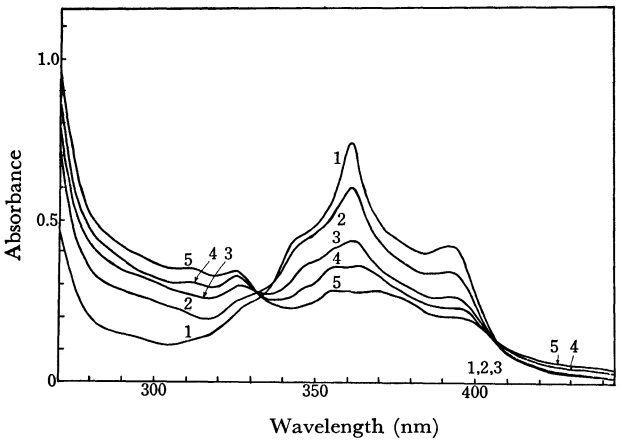


Fig. 3. Spectral change of Z-species in the aerated ethanol solution upon irradiation at 365 nm (25°C). Time of irradiation,
1) 0
2) 2 min and 30 sec
3) 9 min and 30 sec
4) 22 min
5) 127 min

These findings strongly suggest that 9-Cl-A is quickly transformed photochemically into a different substance which we denote tentatively by Z-species. The Z-species (oxidized form) is reduced to X which is reoxidized by oxygen to Z. It was confirmed that the reactions

$$Z \xrightarrow[h\nu]{\text{in ethanol}} X \qquad X \xrightarrow{O_2} Z \qquad (1)$$

can be repeated as shown by curves b) and c) in Fig. 2. Thus the identification of Z-species prior to that of X-species is required.

Identification of Z-species. It is well known that 9-Cl-A is susceptible to dechlorination and dimerization and yields 9,9′-biacridyl under reductive conditions such as with Raney nickel in methanol, with hydrogen and palladium on barium sulphate and with zinc dust in hydrochloric acid.[12] This leads to the expectation that Z-species in the present system is 9,9′-biacridyl. If a chlorine atom remains in the molecule, the molecular weight is ~214, while the molecular weight of 9,9′-biacridyl is 356. Hence a mass spectrometric determination of molecular weight was undertaken. To do this, preparation of Z-species was carried out on a large scale using a Riko-Kagaku K.K.'s irradiation apparatus. 1—1.5 *l* of the ethanol solution of 9-Cl-A 1—2 × 10^{-4}M, was irradiated by 365 nm in the atomsphere of argon. It was confirmed that the product gives the same spectrum as that for Z-species obtained by small-scale reaction. The crystal obtained by distilling off the solvent was subjected to thin layer chromatography and Z-species was separated by using the mixture of benzene (10) and ethylacetate (1) as a developer. It was established that the material thus separated undergoes essentially the same reactions as those for Z-species.

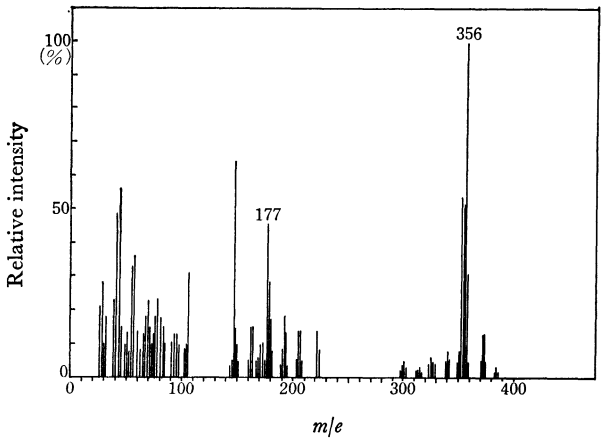


Fig. 4. Mass spectrum of Z-species prepared on a large scale and purified by thin layer chromatography. Relative intensity in reference to that for *m/e*=356 (100%). Temperature measured, 160°C.

Results of mass spectrometry are shown in Fig. 4. It is seen that a principal peak lies at 356 and there is no peak near 214. All the physical properties observed support the view that Z-species is 9,9′-biacridyl. Thus we have the results:

1) melting point, 379°C (literature value, 382°C[13])
2) Scarecely soluble in nearly all the solvents
3) The absorption spectrum agrees with that reported by Levshin.[14]
4) pH dependence of the absorption indicates the presence of two nitrogen atoms in a molecule as shown in Fig. 5.

It was confirmed that the solution, after 9-Cl-A has been converted into X-species, contains chlorine anion and is acidic and that the spectrum of Z-species in the solution (aerated) agrees very well with that for 10^{-4}M HCl given in Fig. 5.

12) R. M. Acheson, "Acridines," Interscience Pub., New York (1956), p. 277.
13) H. Decker and W. Petsch, *J. prak. Chem.*, **143**, 211 (1935).
14) L. V. Levshin, *Zh. Eksp. i Theor. Fiz.*, **28**, 213 (1955).

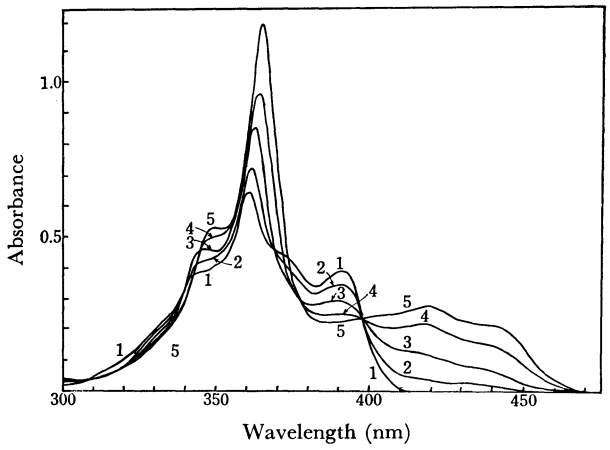


Fig. 5. Effect of the addition of HCl on the absorption spectra of the ethanol solution of Z-species (purified by thin layer chromatography).
Concentration of HCl,
1) 0
2) 1×10^{-4}M
3) 5×10^{-4}M
4) 5×10^{-3}M
5) 0.1M

We can now conclude that Z-species is 9,9′-biacridyl which is produced by reaction

$$2(9\text{-Cl-A}) \xrightarrow[(h\nu)]{2H} \text{biacridyl} + 2HCl \qquad (2)$$

X-Species and ESR Spectrum of the Photoproduct. Now that Z-species, a precursor of X-species, has been identified to be 9,9′-biacridyl, it is highly probable that X-species is a compound obtained by the photochemical reduction of 9,9′-biacridyl. 9,9′-biacriden is considered most likely to be such a compound. This compound was prepared by Decker and Petsch for the first time. According to their results, *N,N′*-dimethyl derivative is stable in the air, but not *N*-monomethyl derivative. These compounds emit green fluorescence as X-species does. Figure 6 shows the fluorescence spectrum of X-species together with those of 9-Cl-A and of Y. The absorption and fluorescence spectra of *N,N′*-dimethyl

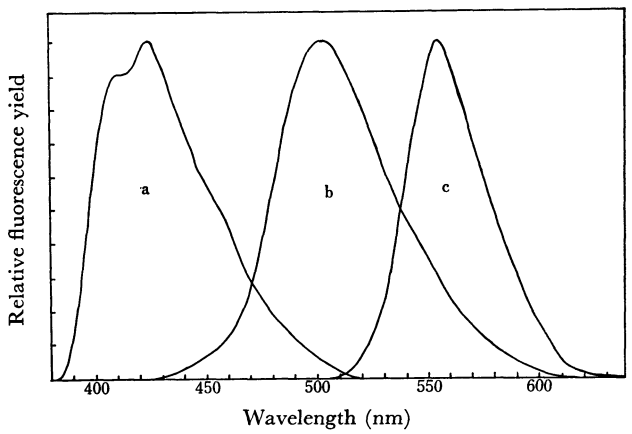


Fig. 6. Fluorescence spectra of 9-Cl-A, X, and Y in ethanol.
a : 9-Cl-A
b : X (obtained by 10 minutes irradiation of the degassed solution of 9-Cl-A)
c : Y (obtained by 33 hours irradiation of the degassed solution of 9-Cl-A)

derivative reported recently by Legg and Hercules[15] essentially agree with those of X-species. Thus we can conclude that X-species is biacriden.

The photoproduct involving X-species has been found to give ESR spectrum with well separated hfs, the analysis of which has not yet been completed. At present it is interesting to note that the general feature of the spectrum strongly suggests the existence of the two equivalent NH groups which supports the view that the radical is originated from biacriden. Another important fact is that the ethanol solution of 9,9′-biacridyl separated by thin layer chromatography exhibits no ESR spectrum upon irradiation, although on the basis of quite a similar spectral change the photochemical reaction is thought to proceed essentially in the same way, as shown in Fig. 7. In view of scheme (2) for the photochemical formation of biacriden from

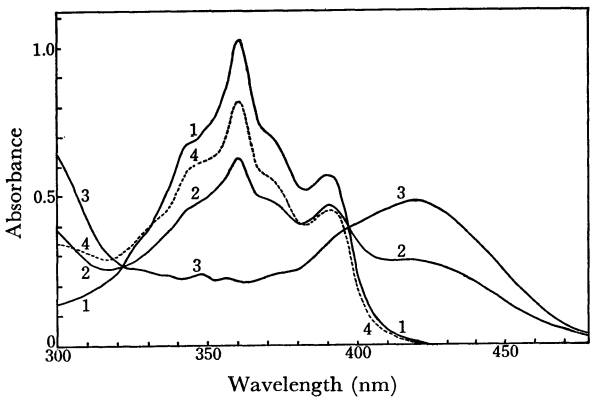


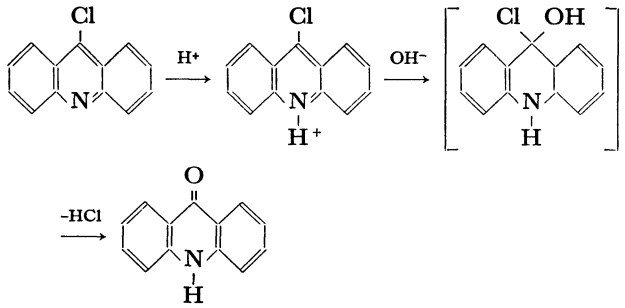
Fig. 7. Change of absorption spectra of Z (obtained on a large scale and purified by thin layer chromatography) in the degassed ethanol solution upon irradiation.
Time of irradiation,
1) 0
2) 1 min and 10 sec
3) 6 min
4) air introduced to 3)
T, 25°C; λ excitation, 365 nm

9-Cl-A, it was suspected that the acidic medium is necessary for the appearance of ESR. In fact we could confirm that the irradiated solution of the separated 9,9′-biacridyl in ethanol gives a similar ESR spectrum when a small quantity of HCl was added to the solution in a degassed condition. It should be added that 9,9′-biacridyl dissolved in acetic acid does not undergo photoreduction. This may be due to the non-reactivity of the double protonated species.

Reaction in the Aerated Ethanol Solution. Zanker and Flügel's observation that acridone is the main photoproduct in the aerated ethanol solution was reconfirmed. The solvent they used was 96% aqueous ethanol. They proposed the following mechanism for the photochemical reactions as well as for the thermal reaction.

About 100 times increase of the rate in the photochemical reaction as compared with that in the thermal one was attributed to the increased basicity of the

15) K. D. Legg and M. Hercules, *J. Amer. Chem. Soc.*, **91**, 1902 (1969).



excited state.

Our results on the effect of oxygen concentration and of the addition of water are shown in Figs. 8 and 9. It is evident from Fig. 8 that the existence of oxygen above 5×10^{-4}M is necessary for the occurrence of photochemical formation of acridone. Figure 9 shows that the addition of a large quantity of water does not induce the formation of acridone in the absence of oxygen. The results indicate that oxygen instead of water plays a dominant role in the reaction. In order to confirm definitely the none-participation of water in the reaction we carried out an experiment using a carefully dehydrated ethanol (aerated). It was found that the formation of acridone proceeds at essentially the same rate. A similar experiment was repeated using carefully dehydrated methyltetrahydrofuran. Formation of acridone was confirmed, though acridan-type compound was produced at the same time. Thus,

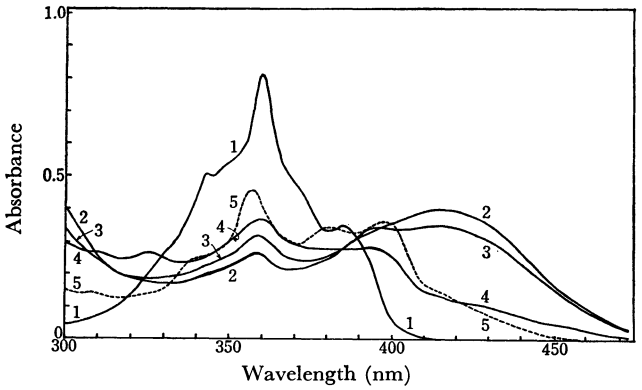


Fig. 8. Absorption spectra of irradiated ethanol solutions of 9-Cl-A dissolving various concentrations of oxygen. (Time of irradiation, 8—9 min at 365 nm, temp., 25°C)
1) 9-Cl-A
Concentration of oxygen of the irradiated solutions,
2) 1.6×10^{-6}M
3) 1.4×10^{-5}M
4) 7.4×10^{-5}M
5) 5.1×10^{-4}M

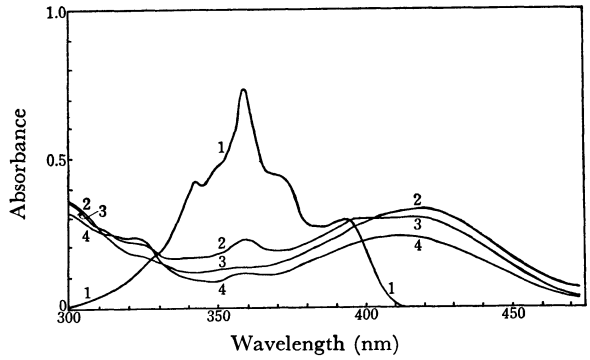


Fig. 9. Absorption spectra of irradiated solutions of 9-Cl-A in the mixed solvents of water and ethanol of various composition (time of irradiation, 9 min at 365 nm).
1) 9-Cl-A in the mixture of ethanol (3) and water (1). The ratio of ethanol to water (in vol) in the irradiated solution,
2) 3:1
3) 1:1
4) 1:2

TABLE 1. TYPES OF REACTION IN VARIOUS SOLVENTS (Φ,[c] Quantum yield)

	Solvent	Aerated	Deaerated
A)	Methanol	Acridone ($\Phi=0.016$)	Biacriden ($\Phi=0.0011$)
	Ethanol	Acridone ($\Phi=0.033$)	Biacriden ($\Phi=0.011$)
	Isopropanol	Acridone ($\Phi=0.012$)	Biacriden ($\Phi=0.012$)
	n-Butanol	Acridone	Biacriden
	n-Amyl alcohol	Acridone ($\Phi=0.0026$)	Biacriden
	s-Amyl alcohol	Acridone ($\Phi=0.0045$)	Biacriden
	t-Amyl alcohol	Acridone ($\Phi=0.0026$)	Biacriden
	Ethyleneglycol	Acridone ($\Phi=0.013$)	Biacriden
	Benzyl alcohol	Acridone+biacriden	Biacriden ($\Phi=0.033$)
	Cyclohexanol	Acridone ($\Phi=0.0062$)	Acridone
	Toluene	Acridone ($\Phi=0.0024$)[a]	Biacriden
B)	β-Phenetyl alcohol	Acridone ($\Phi=0.0076$)	Acridan type
	Tetrahydrofulfuryl alcohol	Acridone ($\Phi=0.026$)	Acridan type ($\Phi=0.041$)
	Tetrahydrofuran	Acridone ($\Phi=0.0041$)[a]	Acridan type ($\Phi=0.035$)
	Cyclohexane	Acridone ($\Phi=0.0076$)[a]	
	Dioxane: H_2O[b]=1:1 in vol	Acridone ($\Phi=0.011$)	Acridan type ($\Phi=0.048$)
	Trichloroethylene	Acridone ($\Phi=8.5\times10^{-4}$)[a]	
	n-Heptane	Acridone ($\Phi=0.0056$)[a]	
C)	Benzene	no reaction	no reaction
	CCl_4[b]	no reaction	no reaction

a) acridan-type compound may be produced simultaneously.
b) agrees with Zanker's result.
c) Quantum yields are the preliminary values obtained simply from the decrease of the optical density.

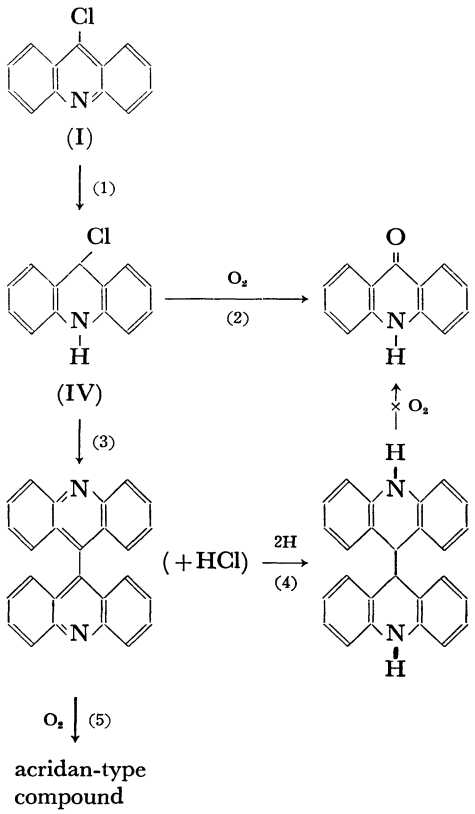
there is no room to doubt that the formation of acridone proceeds in a different mechanism from Zanker and Flügel's, in which oxygen instead of water plays an essential role.

Investigations on the Solvent Effect on the Reactions in Aerated and Deaerated Conditions. Table 1 gives preliminary results on the type of reaction and their quantum yields for various solvents aerated and deaerated.

A survey of the results leads us to the following conclusion. In an aerated condition, formation of acridone proceeds in all the solvents except for benzene and carbon tetrachloride which have no easily detachable hydrogen atoms. This suggests that the primary process for the production of acridone is the formation of semiquinone of 9-Cl-acridine with H-atom attached on N-atom, (C-radical). A larger quantum yield of acridone formation in ethanol than in methanol is also in line with this view. The effect of the addition of water to the aerated ethanol on the acridone formation quantum yield, also supports this view (Table 2).

Table 2. Quantum yield (Φ) of acridone formation in the aerated ethanol-water mixture

$EtOH:H_2O$ (in vol%)	100:0	95:5	90:10	75:25	50:50	33.3:66.7
Φ	0.033	0.027	0.020	0.016	0.009_3	0.005_1



Oxygen may perhaps oxidize the semiquinone and the resulting HO_2 or H_2O_2 may lead to acridone formation. A slight increase of the rate of acridone formation by the addition of H_2O_2 seems to support this mechanism. There is scarcely any sign of the formation of acridan-type compound in the solvents of A group. In the deaerated solution, two types of reaction occur, the formation of acridan-type compound and the formation of biacriden. However, it is not known whether the formation of acridan-type compound occurs *via* biacridine or directly from 9-Cl-acridine in the solvents of B group. Whether biacridan- or 9-(9-acridanyl)-acridine-type compound is produced in the former case is also unknown. One exception is cyclohexanol in which acridone is formed even in the absence of oxygen. Benzyl alcohol is of particular interest for its high reactivity and for the result that biacriden is likely to be produced even in the presence of oxygen.

Conclusion

A general feature of the photochemical reaction of 9-Cl-acridine may be summarized as follows.

Process (1) may occur both in the presence and in the absence of oxygen. One conceivable scheme for Process (2) is the formation of HO_2 and H_2O_2 and their attack on (IV). Process (3) is suppressed when the oxygen concentration is larger than $\sim 10^{-4}$M. It is not known whether the detachment of HCl preceeds or succeeds the dimerization. It is most likely that molecular mechanism does not occur at all or is negligible for 9-Cl-acridine in alcohols. Process (5) occurs most likely *via* molecular mechanism; primary product may perhaps be 9-(9-acridanyl)-acridine compound. In the deaerated alcohols, the reaction yielding biacriden is predominant, but formation of acridan-type compound can also occur *via* molecular mechanism. The relative magnitudes of the two type reactions depend on the nature of the solvent.

The formation of radical species (most likely radical ion) might be due to some kind of reaction between two substances, for instance, electron transfer between biacriden and 9,9′-biacridyl or between biacriden and 9-(9-acridanyl)-acridine. This is likely because the concentration of radical species is very small compared with that of biacriden. That the acidic medium is necessary for the appearance of ESR[16] suggests an analogous mechanism to that for the system of phenazine (ϕ) and dihydrophenazine (ϕH_2), in which radical cation is produced by the interaction of ϕ and ϕH_2 in a strong acidic medium[10] or by acidifying the ethanol solution containing an associated complex between ϕ and ϕH_2.

16) According to Maeda and Hayashi, lucigenine (10,10′-dimethyl 9,9′-biacridinium dinitrate) exhibits ESR in the solid state while 10,10′-dimethylbiacriden does not. These observations might have some relation with the present result. K. Maeda and T. Hayashi, This Bulletin, **40**, 169 (1967).