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Chemiluminescence of photolyzed or radiolyzed acridine

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Abstract

The exposure of acridine in *N,N*-dialkylamides to sunlight or ^{60}Co γ-radiation gives 9-substituted aminomethylacridan derivatives in high yields. The mechanism of the aminomethylation reactions is discussed. The addition of strong bases such as hydrides, or alkoxides in the presence of atmospheric oxygen to the reaction mixtures results in very efficient chemiluminescence. Quantum yields are in the order of 0.3 mol einstein^{-1} for the photolysis and are as high as 7×10^{-3} einstein mol^{-1} for the chemiluminescence. Both the radiolysis and the radiolysis/chemiluminescence reactions constitute prospective radiation dosemeters.

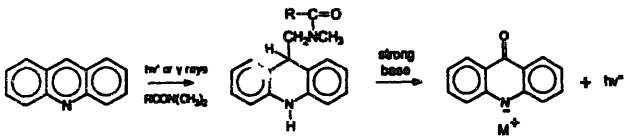
Keywords: Aminomethylation; Acridine; Chemiluminescence; Photolysis; Radiolysis

1. Introduction

We have recently observed that the exposure of deaerated acridine **1** (see Scheme 1) in *N,N*-dialkylated amides even to the diffuse light of the laboratory or to γ-irradiation results in photolysis or radiolysis, while the addition of strong bases to the above spent mixtures gives rise to very efficient chemiluminescence (CL).

It is known that several nitrogen heteroaromatic compounds undergo addition, reduction, and substitution reactions upon photolysis in the presence of suitable hydrogen atom donors (for a review see Ref. [1]). An aza-aromatic compound whose photochemistry has been particularly well studied is acridine [2–5]. However, much to our surprise, no photochemical or radiochemical reaction of this compound in amides has so far been reported.

In the present work, we report the novel reaction of acridine with *N,N*-dimethylformamide (DMF) and *N,N*-dimethylacetamide (DMA) via radiolysis or photolysis, which results in the formation of the 9-substituted (*N*-formyl-*N*-alkylaminomethyl) acridans **2**, together with chemiluminescence following the addition of strong bases to the photolyzed or radiolyzed spent mixtures or isolated products. It should be noted here that although reactions of acridine derivatives with oxidants such as singlet oxygen, ozone, hydrogen peroxide and persulphates or perchlorates are strongly chemiluminescent [6–12], reactions of acridan derivatives only with oxygen and strong bases, as far as we know, have seldom [13] been reported. We also wish to report the prospects of the forementioned reactions as γ-radiation dosemeters.



1 2 3

2a R = H
2b R = CH_3

Scheme 1. Photolysis–radiolysis of acridine in *N,N*-dimethylamides and chemiluminescence of the spent mixtures upon the addition of strong base.

2. Experimental techniques

2.1. Reagents

Acridine was purchased from Aldrich and was recrystallized from acetonitrile. The purity of the acridine was checked by NMR spectrometry. *N,N*-dimethylformamide and *N,N*-dimethylacetamide were purified and dried by the standard procedure [14]. Sodium hydride was purchased from Aldrich as the powder and was used without further purification. Sodium methoxide and potassium *tert*-butoxide were purchased from Merck AG, Germany and used without further pyrification. All solvents were distilled prior to use. Working

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solutions (deaerated for photolysis or radiolysis, aerated for chemiluminescence) were always freshly made (daily).

2.2. Gamma-radiolysis

Gamma-radiolysis experiments were performed in a ^{60}Co, 6500 Ci, gamma chamber (4000 A, Isotope Group, Bhaba Atomic Research Centre, Trombay, India). The dose rate was determined with use of Fricke's dosemeter [15] and was found to be equal to 48.3 Gy min^{-1}. Doses were calculated from Dose = $n \times 7.8 + 48.3 \times$ time (min) Gy, where n is the number of consecutive irradiations.

2.3. Quantum yield determinations

2.3.1. Photolysis

A standard actinometer (potassium ferrioxalate) was used for the quantum yield determination of the photochemical reactions of acridine with DMF and DMA [16,17]. A square quartz cuvette, which contained a DMF or DMA deaerated solution of acridine (2 ml; 10^{-4} M) was irradiated with monochromatic light (357 nm) from a 1000 W xenon source (Oriel, xenon lamp; monochromator, Oriel Corporation, model 77200). Under the conditions of the actinometry experiments, both the actinometer and acridine absorbed essentially all the incident light of $\lambda = 357$ nm. The light intensity of the monochromatic beam of $\lambda = 357$ nm was determined to be 3.5×10^{-6} einstein dm^{-3} s^{-1} with a slit width of 20 nm. The photochemical reaction was monitored using a Hitachi U-2000 UV spectrophotometer. The quantum yields were determined from the decrease in acridine absorbance ($\lambda = 357$ nm). All measurements were made at 25°C. The quantum yields were about 0.30 mol einstein^{-1} for both amides, and are in good agreement with those of the literature [18] for acridine in hydrocarbons and alcohols.

2.3.2. Chemiluminescence measurements

The chemiluminescence reactions were performed in an LKB 1250 Bio-Orbit luminometer with the timer circuitry disconnected. The cell jacket was thermostatically controlled with the aid of a constant temperature bath circulator, and the temperature was maintained at 25.0±0.1°C. The light reactions were started by adding about 50 mg of hydride or alcoholate to an aerated solution of the photolyzed or radiolyzed acridine solution (1.0 ml; 10^{-4} M). It should be noted here that concentrations other than those above resulted in less efficient CL. It should also be noted that during the first 5 min, the solution is very turbid (NaH). The insoluble hydride is then precipitated and the mixture becomes more transparent, the transmittance being 65% after 15 min. Such an effect is not observed to that extent with other bases. The light intensity–time integrals thus obtained were compared with the luminol standard [19] which served as an absolute photon source under the same geometry. The quantum yields based on the acridine **1** employed were in the order of 2×10^{-3} einstein mol^{-1} for DMF and DMA, while those based on the isolated acridan **2** are shown in Table 1. CL integrals as a function of γ-dose from the ^{60}Co source were obtained with DMF or DMA solutions of acridine **1** (1.0 ml; 10^{-4} M), photolyzed or radiolyzed on the addition of 50 mg of sodium hydride.

Table 1
CL quantum yields ($\varphi_{CL} \times 10^3$ einstein mol^{-1}) of isolated acridan **2a** with strong bases in polar aprotic solvents [a]

Solvent	NaH	*t*-BuOK	MeONa
DMF	3.73	2.53	3.18
DEF	5.95	3.78	–[b]
DMA	6.36	3.36	2.82
DMSO	2.13	1.44	1.34
AN	0.69	0.60	–[b]

[a] Concentration, 10^{-4} M.
[b] Very opaque reaction mixture.

2.4. Typical product isolation and identification

2.4.1. Radiolysis–photolysis

A deaerated solution of acridine in DMF (179 mg; 100 ml) was allowed to stand in the ^{60}Co source for 20 h. The solvent was evaporated to dryness in vacuo to leave a yellow solid. After washing with ether/petroleum ether, a pure white precipitate (158 mg; 63%) was obtained and identified as 9-(*N*-formyl-*N*-methylaminomethyl)-9,10-dihydroacridine (**2a**), by means of ^{1}H and ^{13}C NMR spectrometry, IR spectrophotometry, mass spectrometry (MS) and elemental analysis. The compound characteristics were m.p., 176–178°C; UV (DMF) $\lambda_{max} = 287$ nm ($\epsilon = 11\,000$); fluorescence $\lambda_{max} = 369$ nm ($\lambda_{exc} = 287$ nm); analysis: calculated for $C_{16}H_{16}N_2O$: C 76.16, H 6.39, N 11.10; found: C 75.59, H 6.42, N 11.18; ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.45 and 2.84 (2s, 3H, NCH_3, syn/anti, 1:3), 3.27 and 3.30 (2d, 2H, J = 7.6/7.2 Hz, NCH_2, anti/syn, 3:1), 4.16 and 4.43 (2t, 1H, J = 7 Hz, CH, anti/syn, 3:1), 6.4 (s, 1H, NH), 6.78 (d, J = 7.8 Hz, 2H), 6.93 (m, 2H), 7.07 (dd, J = 7.5/1.5 Hz, 2H), 7.16 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 30.9 (C-9), 40.2 and 41.1 (NCH_2, syn/anti, 1:3), 51.1 and 56.4 (NCH_3, syn/anti, 1:3), 113.5, 113.6, 119.9, 120.8, 127.4, 127.8, 128.6, 128.7, 139.6, 162.8 and 163.0 (CHO, syn/anti, 1:3); MS (70 eV): m/z (%) 252 (M^+, 8), 193 (7), 181 (16), 180 (100, acridan), 179 (15), 85 (14), 72 (13), 59 (8), 44 (12); IR (KBr): 3310 (NH), 3020, 2940, 2870, 1660, 1640, 1610, 1580, 1480, 1390, 1310, 1060, 1030, 980, 880, 810, 735.

Photolysis, on the other hand, in the set-up described above, lasted about 50 min (54 mg; 30 ml) under stirring in a specially constructed quartz cell, receiving the full spectrum of the xenon lamp. The same procedure was employed for the isolation and identification of the photoproduct, showing that with the exception of the syn/anti ratios, both photolysis and γ-radiolysis give the same products. It should be noted that the same product was isolated from a 10^{-2} M acridine

solution in a Pyrex vessel positioned near the laboratory's window for 2 days, not exposed to direct sunlight.

2.4.2. Chemiluminescence

An acridine (1) solution in DMF was radiolyzed (179 mg; 100 ml) or photolyzed (54 mg; 30 ml) as above. The solution was then aerated, sodium hydride (200 mg) was added, and the resulting mixtures were left in the dark for 5 h. Aliquots (1 ml) of methyl iodide were added, and the mixtures were left in the dark overnight. The solvents were then removed and the residues were carefully extracted with chloroform. After drying and removal of the solvent, *N*-methylacridone was obtained in overall yields from 36% (75 mg; radiolysis) to 42% (25 mg; photolysis). Product identification was performed by comparison of the ^{1}H and ^{13}C NMR spectra with those of an authentic *N*-methylacridone sample, indicating that the deprotonated acridone 3 is the CL product.

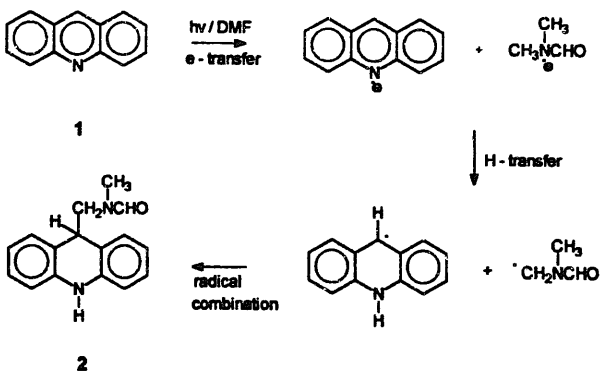
2.5. Equipment

The absorption spectra were obtained on JASCO V-560 and Hitachi U-2000 spectrophotometers. The fluorescence spectra were recorded on a JASCO FP-777 spectrofluorimeter (scan speed, 200 nm min^{-1}; emission band, 3 nm); the excitation λ_{max} was 357 nm for acridine 1 and 287 nm for the acridans 2. The ^{1}H and ^{13}C NMR spectra were measured on a Brucker AC 250 spectrometer. The IR spectra were recorded with the aid of a Perkin-Elmer model 283 spectrophotometer. The mass spectra were determined on a Finigan Mat Vg 250 TS instrument. Microanalyses were performed on a Perkin-Elmer CHN elemental analyzer, while melting points were measured on an electrothermal apparatus (Gallenkamp) and are uncorrected. Finally, the CL spectra were obtained using the JASCO FP-777 spectrofuorimeter with the excitation source off, employing wide slits (20 nm) and a scanning rate of 1000 nm min^{-1} (with 2.5 ml of acridan 2 (10^{-4} M) and about 100 mg of sodium hydride).

3. Results and discussion

3.1. Photolysis, radiolysis

Studies of the photoreduction of acridine have been extensively reported, but most of them have dealt with photoreduction in alcohols or hydrocarbons, where both radical and molecular mechanisms have been suggested [20]. In amide solvents, in analogy with the photoreduction of acridine in alcohols, the C-acridanyl radical may be produced from acridine through hydrogen transfer from an *N*-methyl group of DMF or DMA. As it is also well known that amines are particularly good electron donors to photoexcited molecules [21], it is reasonable to assume that following the electron transfer, reductive aminomethylation proceeds via proton transfer in the contact radical ion pair, followed by radical combination as shown in Scheme 2. This interpretation is also



Scheme 2. Mechanism of the reductive aminomethylation of acridine via electron and proton transfer from *N,N*-dimethylformamide.

supported by the type of hydrogen abstraction in the radiolysis of DMF in which the DMF radical seems to be the principal intermediate [22]. A differentiation is, however, expected between radiolysis and photolysis. In the former case, it is the amide radical that reacts with acridine, whereas in photolysis it is the excited acridine that reacts with the solvent–reagent. In any case, the steps following proton transfer should be the same. The main reaction may then be written as shown in Scheme 2, and it is interesting to note that no dimer formation from acridine was observed in all the cases studied here, most probably due to the high solvent-to-solute proportions employed, 2 being produced with a photochemical quantum yield of 0.3 mol $einstein^{-1}$.

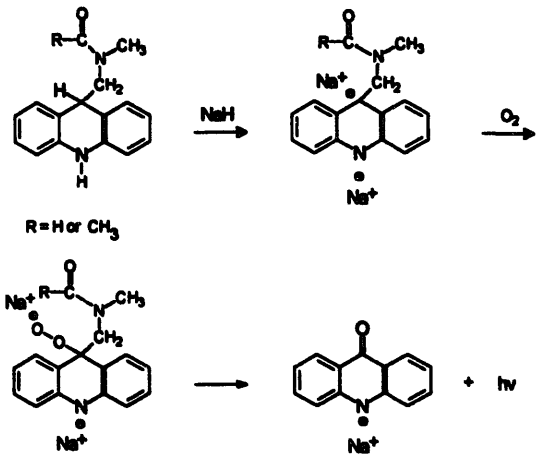
Products 2 exist in two syn/anti geometric isomers as expected for amides [23]. It should be noted that the syn/anti isomer ratio of the acridans 2 produced is not the same for photolysis and radiolysis. With the former method, the syn/anti ratio is 1:3, while for the latter method, the ratio is 1:5. The ratios above were determined with the aid of the ^{1}H and ^{13}C NMR spectra.

Spectroscopic monitoring of the reactions showed that in common with that occurring in DMF and DMA solutions, photochemical or radiochemical reactions of acridine in *N,N*-diethylformamide (DEF) and *N,N*-diethylacetamide (DEA) proceeded the same way (similar UV and fluorescence spectra), yet isolation of the latter products proved difficult. Conversely, the photolysis of acridine in aprotic solvents such as acetone, diethyl ether, dimethyl sulphoxide (DMSO) and chloroform did not lead to analogous products.

3.2. Chemiluminescence

The CL of acridine 1 after radiolysis or photolysis on the addition of strong bases required the presence of atmospheric oxygen, while it was affected by the concentration of the solutions in the sense that higher acridine concentrations resulted in quantum yields lower by up to a factor of three. Unlike solvents such as DMF and DMA, in DMSO the CL quantum yields were unaffected by the presence of atmospheric oxygen, radiolysis or photolysis. Here we are dealing with an entirely different reaction which warrants further investigation. The best concentration for optimum CL was

10^{-4} M. The influence of the solvent or the basicity of the bases on the CL quantum yields of acridan **2a** is shown in Table 1. It is interesting to note that CL is far more efficient in amides (DMF, DEF, DMA) than in acetonitrile (AN) or DMSO. It is possible that the nitrogen lone pair of electrons of the solvent facilitates the peroxide decomposition. The peroxide (Scheme 3) can result in deprotonation at position 9 by the strong base followed by oxygen attack as advocated by McCapra [13]. The duration of light emission as reflected in CL intensity–time diagrams (not shown) depends on the basicity of the strong base and the solvent. It ranges from about 3 h (sodium hydride, DMF) up to 30 h (sodium methoxide, DMA); these durations can, however, be shortened by employing lower concentrations, in which case quantum yields are also somewhat increased. In closing this section it should be noted that the possible action of sodium hydride as a reducing agent is seldom observed in such reactions [24], and in any case, no acridan was observed in the spent reaction mixture.



Scheme 3. Proposed CL reaction mechanism of acridan **2a** with sodium hydride.

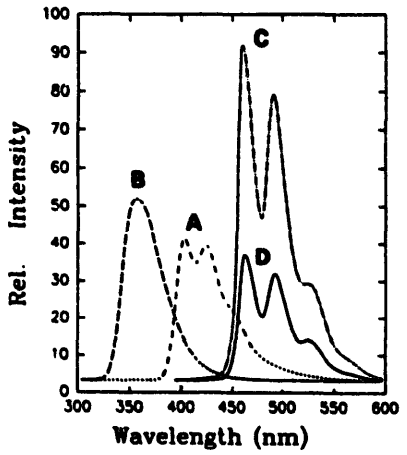


Fig. 1. Emission spectra in DMF. Spectrum A, fluorescence of acridine before photolysis or radiolysis; spectrum B, fluorescence of the reaction mixture after photolysis or radiolysis; spectrum C, fluorescence of sodium acridonyl; spectrum D, CL spectrum of photolyzed or radiolyzed acridine or **2a** on the addition of sodium hydride. The fluorescence spectrum of the CL spent reaction mixture was identical to spectra C and D.

The CL spectrum of **2a** is that of the deprotonated acridone **3** fluorescence (Fig. 1). The fluorescence spectrum of the CL spent reaction mixture was identical to that of an authentic sample of sodium acridonyl (λ_{max} = 472, 498 and 531 nm). It was difficult, however, to isolate the deprotonated acridone, and the structure of this product was identified after derivatization to *N*-methylacridone (^{1}H and ^{13}C NMR).

As mentioned above, the acridan **2a** of the present work is soluble and stable in many polar aprotic solvents. Furthermore, it is readily obtained from acridine on exposure to light or γ-rays, and its reaction with strong bases is chemiluminescent with an efficiency comparable to those of luminol and lucigenin.

3.3. Prospects for novel radiation dosemeters.

It is possible that both the radiolysis and radiolysis/CL reactions herein described can be employed as radiation dosemeters. Indeed, as shown in Fig. 2, radiolysis causes a decline in the absorption peak of acridine at 357 nm and an increase in the region around 287 nm with an isosbestic point at 326 nm. After 40 min, the absorption of acridine was virtually zero and that of the radiochemical product **2b** showed ϵ_{max} = 15 900 (10^{-4} M in DMA); similar but much faster changes occur in photolysis. In Fig. 3, the absorption of products **2a** and **2b** is plotted vs. irradiation dose. Acridine is transformed to the acridans **2a** and **2b**, and as the γ-irradiation

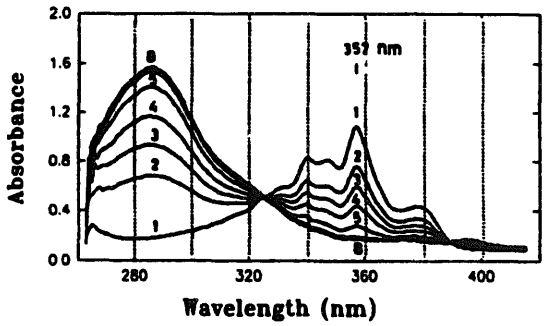


Fig. 2. Absorption spectra of acridine on radiolysis in degassed DMA. Spectrum 1, before radiolysis; spectrum 8, after radiolysis for 34 min (concentration, 10^{-4} M).

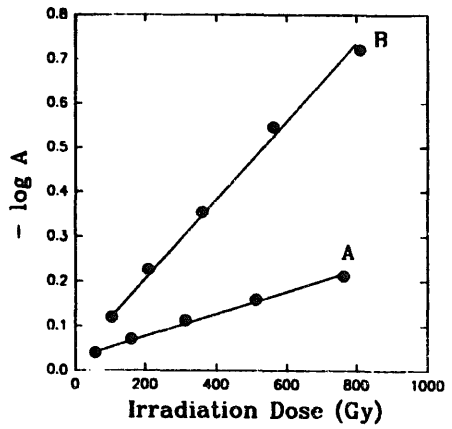


Fig. 3. Plots of the absorption of acridine in (A) DMF and (B) DMA versus absorbed dose from the ^{60}Co source (concentration, 10^{-4} M).

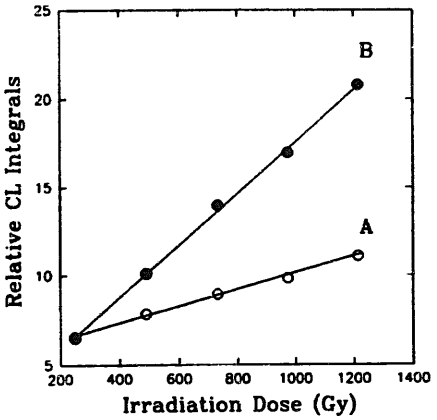


Fig. 4. CL light integrals of acridine in (A) DMF and (B) DMA plotted versus absorbed γ-ray dose.

dose increases, higher absorption values due to increased acridan concentration are obtained. This type of plot has the prospect of becoming a γ-radiation dosemeter and possibly a dosemeter for the internal irradiation of solutions by radioactive isotopes in amide solvents in the region 100–800 Gy. Furthermore, acridans **2** in the γ-radiolysis spent mixture, on reaction with sodium hydride and other strong bases, give rise to CL whose intensity–time integrals are, as expected, a function of the radiation absorbed. The light integrals thus obtained are directly proportional to the dose absorbed and this is shown in Fig. 4, where the dose absorbed was determined with the aid of Fricke's actinometer [15] as described in Section 2.3.1. Although under our conditions, linearity exists only for the first 20 min of irradiation, this plot shows that this reaction can serve as a γ-radiation dosemeter and most probably also for other ionizing radiations capable of radiolyzing the present solvents (internal dosemeters), in the region 100–800 Gy.

4. Conclusions

In conclusion, the photolysis or γ-radiolysis of acridine in amide solvents results in novel acridan derivatives in yields giving a synthetic value to this method, and it should be noted that such bialkylated aminoalkylacridans are known to have psychotropic properties [25]. The above derivatives are strongly chemiluminescent with quantum yields comparable to the classical CL systems (luminol, lucigenin, etc.). The novel CL reactions require only the presence of a strong base and could be of use in specialized analytical applications. Finally, it was hopefully shown that the reactions can be employed as radiation dosemeters even without the isolation of the radioproducts.

Acknowledgements

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