Mechanism of Photolysis of (9-Acridinylmethyl) Quaternary Ammonium Salts

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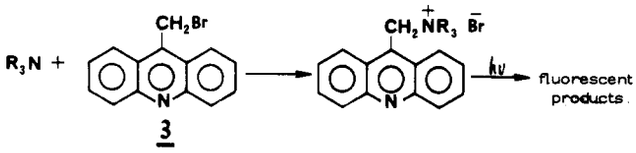
The products and mechanism of photolysis in deoxygenated methanol of (9-acridinylmethyl)trimethylammonium bromide (2) and (9-acridinylmethyl)-3-phenylpropylammonium bromide (3) have been investigated. The primary photoproducts are 9-methylacridine, 1,2-bis(9-acridinyl)ethane, trimethylamine hydrobromide (from 2), and *N,N*-dimethyl-3-phenylpropylamine hydrobromide (from 3). Only products resulting from homolytic cleavage of the C–N bond are observed. The rate of photolysis of 2 was found to be decreased by oxygen and by solvents of increasing hydrogen bonding ability. The effects of energy transfer agents on the photolysis reaction have been investigated and are discussed.

Tertiary amines react readily with 9-bromomethylacridine[1] (1) to yield quaternary ammonium compounds (Scheme I). Separation of the quaternary ammonium compounds from

Scheme I



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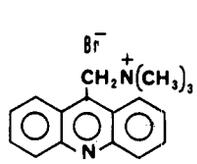
reactants and other products by TLC on silica gel, followed by irradiation of the TLC plates with UV light, yields fluorescent products whose magnitude of fluorescence depends upon the original concentration of amine. The procedure enables the assay of tertiary amine drugs in biological fluids at the picomole level.[2,3] Although the major products of the silica gel photolysis have been identified,[3] overall yields were low and little mechanistic information could be obtained. We report herein the results of our studies of the photolysis, in methanol solvent, of the quaternary ammonium salts, 2 and 3, produced by reacting 9-bromomethylacridine with trimethylamine and *N,N*-dimethyl-3-phenylpropylamine, respectively. It was hoped that photolysis under more controlled conditions would provide greater mechanistic insight into the course of this photolytic reaction. Also, it was of interest to compare the results of photolysis of (9-acridinylmethyl) quaternary ammonium salts with those of the related quaternary benzylammonium salts, which have been extensively studied.



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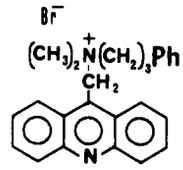

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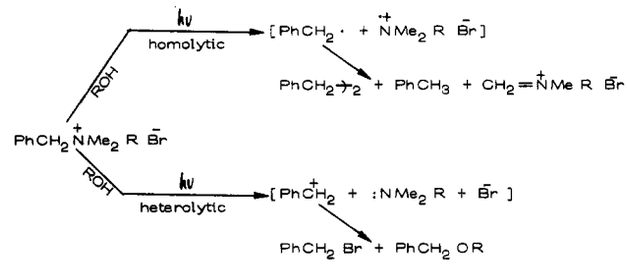
In those studies, benzyl quaternary ammonium salts have been shown to yield products formally derivable via heterolytic and homolytic photolytic pathways[4] (Scheme II). Toluene and bibenzyl were observed, and their formation was attributed to further reaction of the benzyl radical produced via the homolytic pathway. Solvent cage disproportionation of the radical pair produced by homolytic cleavage was suggested, owing to the production of demethylated amine, RNHMe, after acidic hydrolysis of the immonium ion. Similarly, ether and benzyl bromide products were attributed to a heterolytic cleavage process. While the relative contributions of the two pathways varied, depending upon the substrate

Scheme II

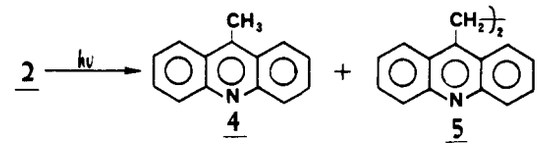


photolyzed and the solvent composition, both pathways were observed. The determination of the product composition in photolyses of 2 and 3 offered the possibility of determining the effect of substitution of a 9-substituted acridine ring for a phenyl ring upon the relative contribution of the two pathways.

Results

The quaternary ammonium salts, 2 and 3, were prepared, in good yield, by reaction of 9-bromomethylacridine with the appropriate tertiary amines at room temperature in acetonitrile. Initial studies of the photolysis of 2 in methanol solution which had been "degassed" by bubbling prepurified nitrogen through the solvent indicated that complex mixtures were produced. Further, the product distribution varied even though apparently identical reaction conditions were employed. The oxygenated nature of several of the products[5] suggested that incomplete and variable removal of oxygen was being achieved. Subsequently, all photolyses were effected in methanol that had been degassed by freeze–thaw procedures. Reproducible results were then obtained.

A preparative scale photolysis of 2 in degassed methanol yielded two major acridine nucleus containing products, 9-methylacridine[6] (4, 8% yield) and 1,2-bis(9-acridinyl)ethane



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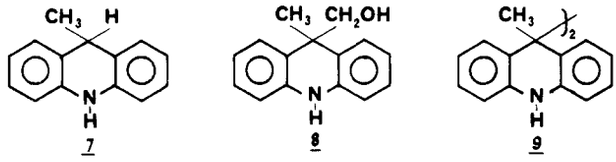
(5, 45% yield), which crystallized from the reaction mixture during the photolysis. The structure of the dimer was determined by spectral and microanalytical data whereas the structure of 4 was assigned on the basis of comparison of its NMR spectrum and TLC R_f value with that of independently synthesized 9-methylacridine.[6] Additionally, basification of the reaction mixture with sodium carbonate, followed by trapping of the volatile amine products, yielded trimethylamine as the sole volatile amine. No dimethylamine could be detected.

Time profiles for the disappearance of **2** and appearance of **4** and **5** were then obtained for photolyses of 10^{-2} and 10^{-3} M solutions of **2** in degassed methanol and are shown in Figure 1. Under these conditions, all products remained in solution. The concentration of the various components was determined by TLC separation of the products after photolysis, extraction of the components from the silica gel, and measurement of the intensity of their ultraviolet maxima relative to those of known quantities of the products processed in the same manner. At early reaction times, 9-methylacridine and the dimer, **5**, account for a large percentage of the acridine nucleus containing products. However, at later stages in the reaction, these two components account for a lesser percentage of products. This is attributed to further photolysis of **4** and **5** under reaction conditions. Secondary photolysis of those products was confirmed by irradiating 10^{-2} M degassed methanolic solutions of **4** and **5**. Thus, 9-methylacridine was found to yield a series of products identified as the acridans (**7–9**) which were isolated by column chromatography following a preparative scale photolysis. Their structures were assigned by comparison of their physical properties with those reported in a previous study of the photolysis of 9-methylacridine in degassed methanol.[7] When photolyzed, the dimer, **5**, was found to rapidly disappear from the reaction mixture and to yield 9-methylacridine and the same series of acridans, as judged by TLC examination of the product mixture. Thus, the decrease in concentration of **5** in Figure 1B can be attributed to its conversion to 9-methylacridine (**4**).



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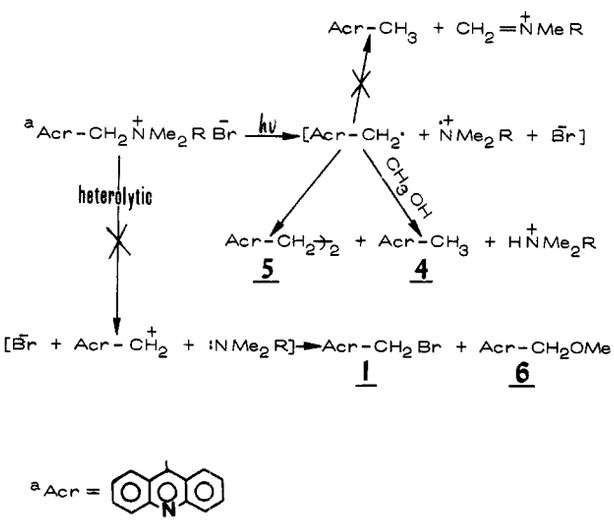
Similar results were obtained in the photolyses of 10^{-2} M degassed methanolic solutions of **3**. The dimer, **5**, and 9-methylacridine were observed as the only acridine nucleus containing products at early stages of the reaction. The fate of the amine fragment was investigated by photolyzing a 10^{-2} M solution of **3** to 90% completion, concentrating the reaction mixture, and treating the products under aqueous acidic conditions that would hydrolyze any immonium ion intermediates to secondary amines.[4] Examination of the amine fraction revealed the presence of *N,N*-dimethyl-3-phenylpropylamine as the only product, in 76% yield.

These results are consistent with the reaction pathway shown in Scheme III. Homolytic cleavage of the carbon–ni-

Scheme III



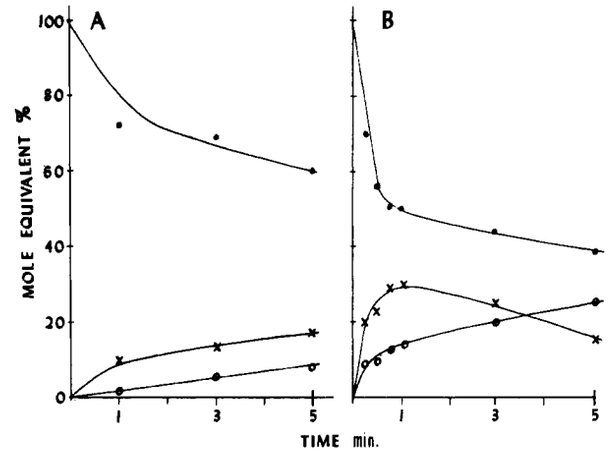


Figure 1. Time profiles for photolyses of 10^{-2} (A) and 10^{-3} M (B) solutions of **2** in degassed methanol. Compounds measured are **2**, ●–●–●; **5**, X–X–X; **4**, O–O–O.

trogen bond occurs to the apparent exclusion of heterolytic cleavage. Thus, 9-bromomethylacridine (**1**) and 9-(methoxymethyl)acridine (**6**), expected products of heterolytic cleavage, are not observed as products, while **4** and **5** are produced in good yield. Further, control photolyses of **6** and **1** revealed that they cannot be produced in significant yield in the reaction. Thus, 9-bromomethylacridine, when photolyzed in degassed methanol, was found to be converted in high yield to the ether, **6**. Minor amounts of other products believed to be acridans were also detected. No significant quantity of 9-methylacridine or of dimer, **5**, could be detected (<10%).

The ether, **6**, was independently prepared by the reaction of 9-bromomethylacridine with sodium methoxide in methanol, and was fully characterized by spectral and microanalytical means. Photolysis of **6** (a 10^{-2} M solution) in degassed methanol under the standard conditions of photolysis led to a slow conversion to products. No dimer, **5**, was detected and 9-methylacridine, if present, was a very minor component (<10%). The products were not investigated in detail, but appeared by NMR and TLC analysis to be the acridans expected to result from photoreduction of **6** with methanol. Further, these products had R_f values slightly different from those produced in prolonged photolyses of **2** and **3**. Solvent cage disproportionation of the radical pair resulting from homolysis does not occur in this system. The amine produced in the reaction is exclusively the tertiary amine. No secondary amine, which should be produced by hydrolysis of the immonium ion, could be observed. This mechanism proposes that the hydrogen atom abstracted by the 9-acridinylmethyl radical originates from the solvent. An attempt to obtain further confirmation of this pathway, by analysis of the deuterium content of the 9-methylacridine resulting from photolysis of **2** in methanol-d_4, was unsuccessful. Control experiments established that 9-methylacridine containing deuterium atoms in the methyl group suffered extensive deuterium loss during the isolation procedure.

The reaction pathway in Scheme III further proposes that the amine cation radical produced by homolysis escapes the solvent cage and abstracts a hydrogen atom from solvent. Hydrogen abstraction from solvent by aminium ions is well documented.[8] Support for the proposed fate of the aminium ion was provided by observing the NMR spectrum of the reaction mixture obtained by photolyzing **2** in methanol-d_4. A large singlet at δ 2.95, the same as that observed for the hydrochloride salt of trimethylamine, was observed prior to workup of the reaction mixture. The lack of solvent cage disproportionation in this system, as opposed to that observed in photolyses of benzyl quaternary ammonium salts, may re-

Table I. The Effect of Deuterated Methanol on the Photolysis of 2[a]

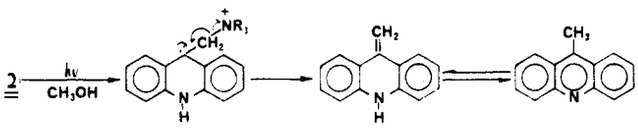
Solvent	Reactant consumed, %	Products produced, % 4	5
Methanol	67.8	7.7	39.7
90% methanol-d_4	64.7	1.3	36.2

[a] 2 (10^{-2} M) in anhydrous deoxygenated solvent; 3 min photolysis using broad band irradiation at 350 nm.

flect a greater stability of 9-acridinylmethyl radical vs. benzyl radical, which enables escape of the radical from the solvent cage prior to reaction.

The deuterium isotope effects on the rate of production of 4 and 5 in MeOH-d_4 vs. MeOH have been examined. The reduced yield of 4 obtained during photolysis in MeOH-d_4 relative to that obtained in MeOH (Table I) is consistent both with the proposed mechanism (Scheme III) and with an alternative mechanism for the production of 9-methylacridine via photoreduction (Scheme IV). However, the latter mech-

Scheme IV



anism is unlikely based upon results obtained during photolysis of 2 in the presence of 10^{-2} M benzophenone. Previous results[9,10] have established that a five- to sixfold increase in the rate of photoreduction of acridine occurs under these conditions, due to rapid hydrogen atom donation by the benzophenone ketyl radical. However, the yield of 4 produced from the photolysis of 2 is unchanged by the presence of 10^{-2} M benzophenone. Consequently, the photoreduction route to 4 is unlikely.

The proposed photolytic route in Scheme III leaves unspecified the multiplicity and nature of the reactive excited state. In order to gain insight into the excited state involved, several experiments were devised. The effect of reaction medium on the photolysis and fluorescence of 2 (Table III) makes the involvement of a $^1\pi,\pi^*$ state highly unlikely. Thus, as the hydrogen bonding ability of the solvent increases, fluorescence is enhanced, as expected,[11] but the rate of photolysis decreases. The effect is especially pronounced in the case of strongly acidic medium, wherein the acridine nitrogen is protonated. Further, the quantum yield of fluorescence is unaffected when the MeOH solution is saturated with O_2, although the rate of photolysis drops sharply under those conditions.

The effect of oxygen upon the rate of photolysis (Table II) enables the calculation of an approximate lifetime of the photoreactive state.[12] Assuming a Stern–Volmer relationship for the quenching, and quenching constants of 3.1×10^{10} and 3.4×10^9 M^{-1} s^{-1} for singlets[13] and triplets,[14] respectively, lifetimes of ≥215 ns are calculated for a triplet and ≥25 ns for a singlet. The effects of energy transfer agents on the photolysis reaction have been investigated (Table II), using concentrations dictated by the approximate lifetimes calculated. The lack of triplet sensitization requires that a triplet state, if involved, have $E_T \geq$ ca. 60 kcal/mol. Since acridine is reported[9] to have energy levels at ca. 45 kcal/mol for the $^3\pi,\pi^*$ state and in the range of 61–67 kcal/mol for the $^3n,\pi^*$ state, the involvement of the $^3\pi,\pi^*$ state is unlikely because of the large energy difference between it and the sensitizer. The involvement of the $^3n,\pi^*$ state is also unlikely, based upon the quenching data cited in Table II, since the lower energy quenchers do not retard the photolysis rate. Thus triplet states do not make a major contribution to the reaction.

The involvement of a $^1n,\pi^*$ excited state is a strong possibility. The lifetime calculated for the excited state in this reaction (≥25 ns) is somewhat longer than expected based upon the value (1–5 ns) reported by Whitten and Lee[15] for the proposed $^1n,\pi^*$ state involved in the photoreduction of acridine, but it is not unreasonable.[16] Since the energy of the $^1n,\pi^*$ state of 2 is difficult to estimate (75 ± 5 kcal/mol?),[18] and the concentrations of the lower energy singlet quenchers were limited because of their absorptivity to levels that are calculated to produce small effects on reaction rate, the data in Table II are equivocal with respect to the involvement of the $^1n,\pi^*$ state. Another possible excited state, involving charge transfer between the counterion (Br^-) and the acridine nucleus, is unlikely, since replacement of Br^- with BF_4^-[19] had no effect on the reaction rate. The $^1n,\pi^*$ state thus appears to be the most likely candidate for the photoreactive state.

Experimental Section

UV spectra were obtained on a Cary 14 spectrophotometer. Fluorescence spectra were obtained on either an Aminco Bowman or a Perkin-Elmer MPF3L spectrofluorometer. NMR spectra were obtained on a Varian XL-100 spectrometer. IR spectra were recorded on a Beckman IR-8. Intensities of absorption are referred to as strong (s), moderate (m), and weak (w). Melting points are uncorrected. Merck $PF_{254-366}$ silica gel was used for column and general thin layer chromatography (TLC) while 100 μ terephthalate backed silica gel plates without indicator, Eastman Kodak, were used for the quantitative analyses. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Anhydrous methanol refers to Nanograde methanol which was dried by distillation over $Mg(OMe)_2$.[20] Degassed methanol refers to methanol that was degassed by at least four freeze–thaw cycles under a vacuum of 0.05–0.01 Torr by alternating between liquid N_2 and dry ice–acetone baths.

Photolyses were effected with a Rayonet RPR-100 photochemical reactor. The photolysis results cited in Figure 1 and Tables I–III were obtained by the following procedure. To a 8 mm × 10 cm Pyrex tube sealed at one end was placed 0.5 mL of a 10^{-2} or 10^{-3} M solution of 2 or 3 in anhydrous methanol. The samples were degassed by the procedure cited above, flame sealed under vacuum, and photolyzed for periods of time from 10 s to 10 min in a Rayonet reactor equipped with eight 3500-Å lamps. Following photolysis, the tubes were opened and 10-μL aliquots were spotted on two silica gel TLC plates. One was developed with benzene–acetone (95:5) to isolate the dimer, 5, and methylacridine (6), and the other was developed in acetonitrile–water (9:1) to isolate the quaternary salts, 2 or 3. The products were visualized under UV light, and the spots were cut out with scissors and added to 50-mL centrifuge tubes. Products 5 and 6 were eluted from the silica gel with 5 mL of 95% ethanol and 2 and 3 were eluted with 5 mL of a 2 N ethanolic H_2SO_4 solution. The tubes were shaken for 15 min, then the solvent was decanted and analyzed spectrophotometrically at 252 (for 5 and 6) and 262 nm (for 2 and 3). Yields were determined by comparing the extinction coefficients of the products at the cited wavelengths with those of known quantities of 2, 3, 5, and 6 that were processed in the same manner.

In the oxygenation experiments, compressed air or 100% oxygen was bubbled through the sample for 10 min to obtain the desired concentrations.

Control photolyses of the dimer 5, 9-methylacridine (4), 9-bromomethylacridine (1), and ether 6 were also performed under the above conditions.

Preparation of (9-Acridinylmethyl)trimethylammonium Bromide (2). Into a saturated solution of 9-bromomethylacridine (200 mg, 0.735 mmol) in acetonitrile (ca. 20 mL) was bubbled approximately a fivefold molar excess of trimethylamine (generated from the hydrochloride salt by addition of 40% KOH). The reaction mixture was allowed to stand at room temperature for 24 h and deposited crystals of 2 (208 mg, 85% yield), which were recrystallized from a 9:1 mixture of acetonitrile–methanol as light yellow plates that decomposed upon heating above 175 °C without melting. The spectral data for 2 follow: NMR (CD_3OD, Me_4Si) δ 3.23 (9 H, s), 5.76 (2 H, s), 8.74–7.66 (8 H, m); UV (95% EtOH) λ_{max} (ϵ_{max}) 252 nm (1.25×10^5), 366 (7.2×10^3), 390 (3.1×10^3); IR (KBr) 3405 (m), 3340 (w), 3050 (w), 2995 (m), 2985 (m), 1660 (w), 1620 (m), 1540 (w), 1480 (s), 1470 (s),

Table II. The Effect of Various Energy Transfer Agents on the Photolysis of the Quaternary Salt 2

Agent	Concn, M	Energy levels of agents E_T	Energy levels of agents E_S	Results[a] P^0/P
Sensitizers				
Benzophenone[b]	10^{-2}	69		1.0
Michler's ketone[c,d]	10^{-2}	61		0.11
Quenchers[e]				
Oxygen	1.8×10^{-3}[f]		22.5, 36.6[g]	2.9
	8.9×10^{-3}[f]			≥ 7.5[h]
NaI	10^{-3}–10^{-1}			~1[i]
Benzophenone	10^{-3}–10^{-2}	69[j]	76[j]	1.0
Biphenyl	10^{-3}–10^{-2}	65[j]	116[j]	0.875–1.05
Naphthalene	10^{-3}	61[j]	90[j]	0.91
Biacetyl	10^{-2}	55[k]	68	0.89
Benzil	10^{-3}–10^{-2}	53[j]	73[l]	0.875–1.0
Benzoquinone	10^{-3}	50[j]	60[m]	1.02
Azobenzene	10^{-3}[n]	~40[j]	64[o]	1.03

[a] Ratios of 2 consumed under control conditions (P_0) to the amount consumed in the presence of the energy transfer agent (P). [b] 2 (5×10^{-3} M) in anhydrous methanol, 10 min photolysis at 280 ± 5 nm. [c] 4,4'-Bis(dimethylamino)benzophenone. [d] 2 (1×10^{-3} M) in anhydrous methanol, 3 min photolysis using broad irradiation at 350 nm; >95% of light absorbed by sensitizer. [e] 2 (5×10^{-3} M) in anhydrous methanol, 3 min photolysis time using broad irradiation with a maximum of 350 nm. [f] Gmelins "Handbuch der Anorganischen Chemie", 8th ed, Verlag Chemie, Weinheim/Bergstr., Germany, 1958. [g] O. J. Guzeman, F. Kaufman, and G. Porter, *J. Chem. Soc., Faraday Trans. 2*, **69**, 708 (1973). [h] Higher ratios were also observed but the values obtained are subject to wide variations because of the small value of the denominator. [i] High concentrations of NaI interfere somewhat with the analytical chromatography and UV analysis and the results at high concentration are approximate. [j] O. L. Chapman, "Organic Photochemistry", Vol. 2, Marcel Dekker, New York, N.Y., 1969, pp. 10–13. [k] N. J. Turro, "Molecular Photochemistry", W. A. Benjamin, New York, N.Y., 1967, p 132. [l] B. S. Ault and B. S. Pimentel, *J. Phys. Chem.*, **79**, 626 (1975). [m] P. E. Stevenson, *J. Mol. Spectrosc.*, **17**, 58 (1965). [n] Higher concentrations absorbed significant amounts of the incident light and were not investigated. [o] E. D. Bergman and B. Pullman, Ed., "The Jerusalem Symposia on Quantum Chemistry and Biochemistry", Vol. 2, "Quantum Aspects of Heterocyclic Compounds in Chemistry and Biochemistry", The Israel Academy of Science and Humanities, 1970, p 204.

1450 (S(= [44] (s), 1130 (m), 1025 (w), 960 (m), 930 (w), 865 (m), 840 (w), 760 (s), 725 cm^{-1} (s). Anal. Calcd for $C_{17}H_{19}N_2Br$: C, 61.64; H, 5.78; N, 8.45. Found: C, 61.50; H, 5.71; N, 8.47.

Preparation of (9-Acridinylmethyl)(3-phenylpropyl)dimethylammonium Bromide (3). *N,N*-Dimethyl-3-phenylpropylamine[21] (0.3 g, 1.83 mmol) was added to a solution of 1 (0.5 g, 1.8 mmol) in ca. 50 mL of CH_3CN. The reaction mixture was allowed to stand at room temperature for 72 h, the CH_3CN was removed under reduced pressure, and the solid residue was titurated with three 5-mL portions of acetone (417 mg, 87% yield) and then recrystallized twice from CH_3CN at −20 °C. The pale orangish-yellow plates of 3 melted with decomposition at 160–164 °C. Spectral data for 3 follow: NMR ($CDCl_3$, Me_4Si) δ 2.06 (2 H, m), 2.58 (2 H, t), 3.33 (6 H, s), 3.98 (2 H, m), 6.68 (2 H, s), 6.86–7.26 (5 H, m), 7.58–8.16 (8 H, m); UV (95% EtOH) λ_{max} (ϵ_{max}) 252 nm (1.14×10^5), 365 (8.4×10^3), 390 (3.4×10^3); IR (KBr) 3450 (s), 3410 (s), 3050 (m), 2980 (w), 1625 (w). 1600 (w), 1550 (w), 1515 (m), 1495 (m), 1450 (s), 1135 (w), 1120 (w), 1020 (w), 975 (w), 940 (w), 035 (m), 760 cm^{-1} (s). Anal. Calcd for $C_{25}H_{27}N_2Br$: C, 68.96; H, 6.25; N, 6.43. Found: C, 68.85; H, 6.28; N, 6.28.

Preparative Scale Photolysis of 2. A 50-mL pear-shaped Pyrex flask containing 2 (100 mg, 0.3 mmol) in 30 mL of anhydrous methanol was fitted with a vacuum stopcock and deoxygenated by freeze–thawing under a vacuum of 0.01 Torr. The mixture was photolyzed for 1 h in a Rayonet reactor using eight 3500-Å lamps. A straw-colored product 5 (26 mg, 45%) crystallized out of the reaction mixture. It was collected and recrystallized from $CHCl_3$ at −20 °C as clear, straw-colored needles that melted at 257–259 °C with decomposition when the melting point chamber was preheated to that temperature. Spectral data for 5 follow: NMR ($CDCl_3$, Me_4Si) δ 4.15 (4 H, s), 7.35–8.35 (16 H, m); UV (95% EtOH) λ_{max} (ϵ_{max}) 342 nm (1.26×10^4), 359 (1.94×10^4), and 393 (9.41×10^3); IR (KBr) 3480 (w-br), 3050 (m), 1620 (w), 1605 (w), 1548 (m), 1510 (w), 1485 (w), 1435 (w), 1405 (m), 732 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel abundance) 384 (M^+, 4), 192 (base peak). Anal. Calcd for $C_{28}H_{20}N_2 \cdot 2H_2O$: C, 79.98; H, 5.75; N, 6.66. Found: C, 80.23; H, 5.67; N, 6.69.

The filtrate was concentrated and analyzed by NMR, which indicated the presence of unreacted starting material, 4 (ca. 8%) and 5 (ca. 4%). The presence of 4 in the mixture was suggested by the presence of its characteristic methyl absorption (ca. δ 3.0,[22] s) and further confirmation was obtained by TLC comparison of the reaction mixture with authentic 4, using benzene–acetone (95:5) as the eluting solvent. AN ADDITIONAL NMR absorption (δ 2.95, s) was ascribed to trimethylammonium bromide. The assignment was confirmed in a subsequent experiment in which a deoxygenated 1.9×10^{-1} M methanol-d_4 solution of 2 was photolyzed for 90 min. The photolysis tube was opened while frozen in liquid N_2, solid K_2CO_3 was added, and the tube was resealed under vacuum with a NMR tube attached as a side arm. The mixture was allowed to warm to room temperature and the volatile components were transferred to the NMR tube by cooling it in liquid N_2. The only absorption observed was a singlet at δ 2.2, which is identical with the chemical shift of authentic trimethylamine in the same solvent. Also, acidification of the solution with HCl shifted the absorption to δ 2.95, the same absorption observed for authentic trimethylamine acidified with HCl.

Table III. The Effect of Reaction Medium on the Photolysis[a] and Fluorescence[b] of 2

Reaction medium	Photolysis P/P_0[c]	Fluorescence f/f_0[d]
Anhydrous methanol	1.0	0.1
Anhydrous methanol ($O_2 = 8.9 \times 10^{-3}$ M)	0.13[e]	0.1
33% aqueous methanol	0.49	0.2
66% aqueous methanol	0.33	0.5
90% aqueous methanol	*f*	1.0
0.5 N aqueous H_2SO_4	~0	*g*

[a] 2 (10^{-2} M) in stated solvent; 3 min photolysis using broad band irradiation at 350 nm. Deoxygenated reaction medium unless otherwise stated. [b] 2 (2×10^{-6} M) in stated solvent. Values obtained at peak height at excitation and emission maxima. [c] P_0 taken as the amount of 2 consumed in anhydrous deoxygenated methanol. [d] f_0 taken as the fluorescence intensity observed in 90% aqueous methanol. [e] See *h* in Table II. [f] The desired concentration[b] of 2 could not be attained because of solubility problems. [g] Under these conditions, the intense fluorescence of the dication is observed at a different emission maximum.

Preparation of 9-(Methoxymethyl)acridine (6). Sodium methoxide (6 mL, 0.4 M) in methanol was added dropwise over a 2-h period to a solution of 9-bromomethylacridine (273 mg, 1.0 mmol) in anhydrous methanol (5 mL). The reaction mixture was allowed to

stand at −20 °C for 12 h, then it was added to ether (ca. 100 mL) and the solution was washed with saturated aqueous $NaHCO_3$ (20 mL) once and with water (20 mL) three times. Removal of the ether layer and evaporation afforded the crude product (210 mg, 94%) as a straw-colored powder. It was recrystallized twice from ether at −20 °C and was further purified by column chromatography using TLC grade silica gel and CH_2Cl_2 and CH_2Cl_2–acetone (9:1) as eluting solvents. The **6** isolated in this manner was recrystallized twice from Et_2O to afford light straw-colored needles of mp 113.5–114 °C. Spectral data for **6** follow: NMR ($CDCl_3$, Me_4Si) δ 3.4 (3 H, s), 5.36 (2 H, s), 7.3–8.4 (8 H, m); UV (95% EtOH) λ_{max} (ϵ_{max}) 252 nm (1.47×10^5), 343 (6.8×10^3), 359 (1.0×10^4), 384 (3.9×10^3); IR (KBr) 3060 (w), 2990 (w), 2880 (w), 1620 (w), 1605 (w), 1550 (w), 1450 (w), 1090 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel abundance) 223 (M^+, base peak), 208 (18), 192 (86), 180 (47), 178 (10). Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87. Found: C, 80.49; H, 5.90.

Identification of the Amine Produced in Photolysis of 3. A 50-mL flask containing **3** (43.5 mg, 0.1 mmol) in 10 mL of anhydrous CH_3OH was deoxygenated and photolyzed for 30 min. An aliquot of the reaction mixture was removed and analyzed by TLC–UV, which indicated that the reaction was 92% complete. The remaining solution was concentrated to ca. 1 mL, and 0.2 N H_2SO_4 was added.[4] The solution was allowed to stand at room temperature for 30 min. The reaction mixture was neutralized with Na_2CO_3 and extracted with hexane. This procedure extracts the amine products relatively free of acridine products. The hexane extract was concentrated to 0.5 mL and was examined by GLC (6 ft × 0.125 in., 5% Apiezon L on 3% KOH-treated Chromosorb W 100/120, 175 °C). These conditions separate *N,N*-dimethyl-3-phenylpropylamine and *N*-methyl-3-phenylpropylamine. Only *N,N*-dimethyl-3-phenylpropylamine could be detected. Its yield was estimated at 76%, based upon comparison of peak areas resulting from three 1-μL injections of the hexane solution with three 1-μL injections of a standard hexane solution of the amine (11.7 mg/0.5 mL).

Photolyses of 9-Bromomethylacridine (1) and 9-(Methoxymethyl)acridine (6). Photolyses were effected under the conditions described for preparative scale photolysis of **2**. The reaction mixtures were analyzed by TLC and NMR. The NMR spectra of the mixtures produced in the photolyses of **1** and **6** were almost identical. In each instance, 9-(methoxymethyl)acridine was identified as the major constituent by its characteristic NMR absorptions at δ 3.40 (3 H, s) and 5.36 (2 H, s) and by its TLC R_f value of 0.51 in benzene–acetone (95:5). Furthermore, no absorption characteristic of the methyl group in 9-methylacridine (ca. δ 3.0)[22] was observed. Additionally, each mixture contained minor products tentatively identified as acridans derived from **6** by their characteristic TLC behavior, namely, their spots are initially nonfluorescent but, upon standing, exhibit the fluorescence characteristic of acridines.

Registry No.—**1**, 1556-34-9; **2**, 62509-60-8; **3**, 62509-61-9; **5**, 62509-62-0; **6**, 62509-63-1; *N,N*-dimethyl-3-phenylpropylamine, 1199-99-1.

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Synthesis of 4,5:11,12-Diepoxy-4,5,11,12-tetrahydrobenzo[*a*]pyrene and Related Compounds

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The synthesis of a new diepoxide of the carcinogen benzo[*a*]pyrene is described. This "K-region" diepoxide, 4,5:11,12-diepoxy-4,5:11,12-tetrahydrobenzo[*a*]pyrene (**7**), was obtained via the osmium tetroxide oxidation of the hydrocarbon. The syn and anti tetrols along with the substituted K-region isomer, i.e., 4,5,5a,6-tetrahydroxy-4,5,5a,6-tetrahydrobenzo[*a*]pyrene (**3**), obtained from this reaction were characterized. The syn and anti tetrols yielded the diepoxide using procedures described earlier. Compound **3** yielded an internal hemiacetal, **8**, upon oxidation with lead tetraacetate.

Benzo[*a*]pyrene (BaP) is a potent carcinogen and one of the most ubiquitous environmental pollutants.[1] It is now generally believed that aromatic hydrocarbon carcinogens such as BaP are metabolized to activated carcinogenic intermediates that subsequently bind to cellular constituents. In the metabolism of BaP the available evidence indicates that these intermediates are epoxides or related compounds.[2] The "K-region" [3] 4,5-epoxide of BaP has recently been shown to be the principal metabolite of BaP that covalently binds to microsomal proteins.[4] Recently it was reported that BaP-4,5-epoxide and BaP-11,12-epoxide were equally potent as mutagens in Chinese hamster V79 cells.[5] However, some studies have suggested that the intermediate which binds to DNA in vivo is the diol epoxide, 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene.[6]

Since polycyclic aromatic hydrocarbons may undergo me-