Studies of the Photocyclization of Some 1-(Haloarylmethyl)pyridinium Salts

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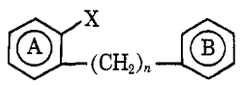
A series of 1-(2-halo-3-quinolylmethyl)- and 1-(2-chlorobenzyl)pyridinium salts were synthesized and photolyzed to investigate electronic factors governing photocyclodehydrohalogenation in π-deficient heteroaromatics and the orientation of the cyclization in unsymmetrically substituted rings. While the latter series gave photocyclization, the former did not. These results suggest that photocyclodehydrohalogenations between aromatic rings are not successful when both rings are electron-deficient heterocycles. Cyclization was favored at a position adjacent to a methyl substituent.

The photodehydrohalogenation reaction has been shown to be a highly successful synthetic method for forming polycyclic, aromatic heterocycles such as those found in alkaloids.[2] These reactions require a system (**1**) having a halogen attached to an aromatic



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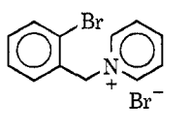
ring (A) connected by a chain to a second aromatic ring (B), the cyclization terminus. Although a large number of systems have been subjected to photolysis,[3] very little was known about the limitation of the electronic nature of the halogen-bearing ring (A), the cyclization terminus (B), the regioselectivity[4] relative to an unsymmetrical ring (B), or the generality of having a single methylene as the chain connecting A and B.

The lack of correlation of the structure of **1** with the success of cyclization can be illustrated. A system with a nitrogen's free pair of electrons unprotected failed to undergo cyclization; however, the corresponding proton salt underwent photocyclodehydrohalogenation.[2a] Similarly, cyclization into the electron-deficient pyridinium ring of 1-(*o*-bromobenzyl)-pyridinium bromide (**2**) has been reported. 2-Bromo-1-(2,5-dichlorobenzyl)pyridinium bromide (**3**), which



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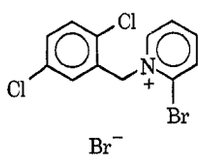

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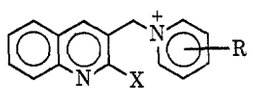
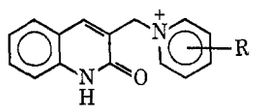
could give photocyclization to either ring, undergoes rupture of the pyridyl bromine bond with bond formation at the benzene ring.[5]

These results would suggest that successful cyclizations can be accomplished with a halogen-bearing ring A that is very electron deficient and cyclization to an electron-rich or poor aromatic ring (B) can occur equally well.

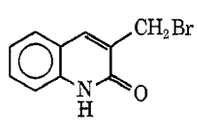
To test this generality a series of 1-(2-halo-3-quinolylmethyl)pyridinium salts (**4**) were prepared and subjected



4a, X = Cl; R = 3-CH_3
b, X = Br; R = 4-CH_3
c, X = Br; R = 3-CH_3
d, X = Br; R = 4-C(O)C_2H_5O



5a, R = 4-CH_3
b, R = 3-CH_3



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to photolysis (Table I). The uv absorption spectra of these salts showed maxima at ~267, 295, 308, and 322 nm. Photolysis using a Vycor filter should lead to excitation of those absorption bands due to both the quinoline and pyridinium chromophores (Figure 1). **4a** gave no reaction after 24 hr as evidenced by lack of change in the uv spectrum and isolation of the starting material from the photolysis mixture. **4b** in hydrobromic acid gave a change in the long-wavelength region of the spectrum after 26 hr of irradiation. Isolation of the product gave a solid with elemental analysis consistent with the formula $C_{16}H_{15}BrNO$. The spectral properties of the product showed it to be the quinolone **5a** (R = 4-CH_3) resulting from displacement of halogen by hydroxyl. An authentic sample of **5a** was prepared by reaction of 3-bromomethyl-2-quinolone (**6**) with 4-picoline, and this quinolone **5a** was identical with the photochemical product.

The formation of the quinolone **5a** was a photochemical process and not a simple hydrolysis, for stirring a solution of **4b** for 26 hr in the absence of irradiation caused no change in the uv spectrum. To gain some information about the manner in which the excited state of **4b** underwent reaction with solvent the photolytic reaction was carried out in acetic acid. No reaction occurred until benzophenone was added as a sensitizer. The uv absorption spectrum then began to change, indicating the formation of the quinolone (**5a**). The direct formation of the quinolone **5a** instead of the 2-acetoxy derivative strongly suggests that the solvent adds to form a 1,2-dihydroquinoline which

(1) This research was abstracted in part from the Ph.D. theses of M. J. K. and J. A. B. submitted to the Graduate School of the University of New Hampshire in partial fulfillment of the degree requirements.

(2) (a) S. M. Kupchan, J. L. Moniot, R. M. Kanojia, and J. B. O'Brien, *J. Org. Chem.*, **36**, 2413 (1971); (b) R. J. Spangler and D. C. Boop, *Tetrahedron Lett.*, 4851 (1971); (c) M. P. Cava, M. J. Mitchell, S. C. Havlicek, A. Lindert, and R. J. Spangler, *J. Org. Chem.*, **35**, 175 (1970); (d) J. L. Neumeyer, K. H. Oh, K. K. Weinhardt, and B. R. Neustadt, *ibid.*, **34**, 3786 (1969); (e) S. M. Kupchan and R. M. Kanojia, *Tetrahedron Lett.*, 5353 (1966); (f) K. Wiesner, I. Jirkovsky, M. Fishman, and C. A. J. Williams, *ibid.*, 1523 (1967).

(3) T. Kametani and K. Fukumoto, *Accounts Chem. Res.*, **5**, 212 (1972).

(4) A. Hassner [*J. Org. Chem.*, **33**, 2684 (1968)] did not propose specifically that regiospecificity might apply to orientation in aromatic substitution reactions; however, this type of reaction falls within the scope of the definition of this term.

(5) C. K. Bradsher and C. F. Voigt, *J. Org. Chem.*, **36**, 1603 (1971).

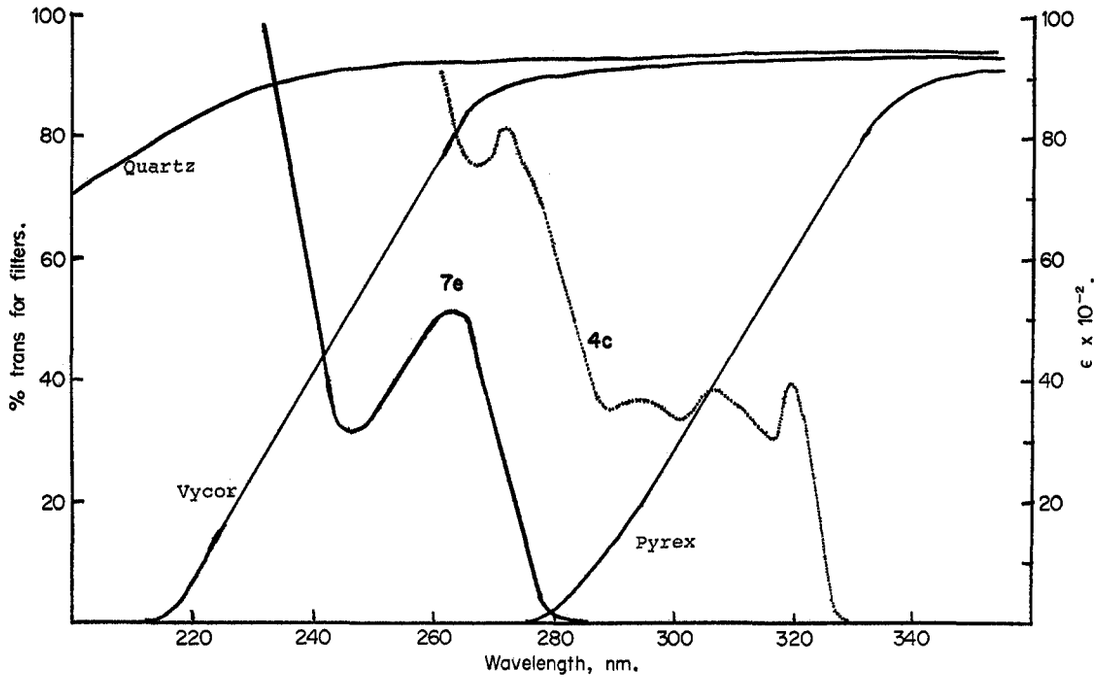


Figure 1.—A comparison of the uv absorption spectra of **4c** (· · · · ·) and **7e** (——) with the Pyrex and Vycor filters.

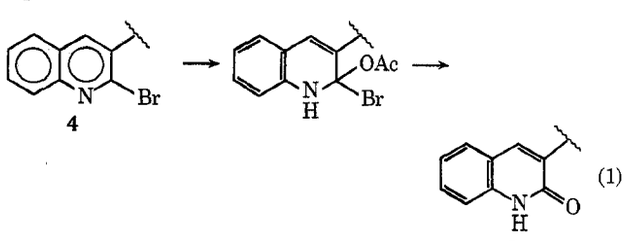
TABLE I

PHOTOLYSES OF 1-(2-HALO-3-QUINOLYLMETHYL)PYRIDINIUM BROMIDES (4)

Compd	X	R	$h\nu$ time, hr[a,b]	Solvent	Product	% yield
4a	Cl	3-CH_3	24	H_2O	s.m.[c]	25
4b	Br	4-CH_3	26	H_2O (HBr)	**5a**	47
4c	Br	3-CH_3	48	HOAc (Ac_2O)[d]	**5b**	43
4d	Br	4-(2-Ethyl-1,3-dioxolan-2-yl)	28	H_2O (HBr)[e]	s.m.	60
4e	Br	4-$COCH_3$	20[f]	H_2O	s.m.	*g*
4f	I	4-CH_3	17.5	H_2O	**5a**	50
4g	Cl	3,4-$(CH_3)_2$	140	22 *N* H_2SO_4	s.m.	*g*
4h	Cl	2-Br	24	H_2O	s.m.	*g*

[a] All photolyses were carried out with a Vycor filter unless otherwise specified. [b] See Experimental Section for the concentration of each solution. [c] Starting material was recovered. [d] The reaction was sensitized with benzophenone after 22 hr. [e] The reaction was sensitized with benzene after 22 hr. [f] The photolysis was carried out with the Srinivasan-type apparatus. [g] The uv absorption spectrum did not change during the photolysis indicating that no reaction had occurred.

then undergoes elimination to form **5a** as shown in eq 1.[6] Reaction of the solvent with an intermediate



(1)

radical formed by homolysis at the C–Br bond could not give 2-quinolone directly. Such *photohydration* of heterocycles has been observed previously.[7] The salts **4** listed in Table I gave either no reaction or photochemical hydration to the corresponding quinolone **5**, identified by spectral data and comparison with authentic samples. These results suggest that photodehydrohalogenation cyclizations are not successful when both aromatic rings are electron-deficient heterocycles.

Photolysis using a Pyrex filter should lead to excitation of only those maxima at ~295, 308, and 322 nm, and thus to selective excitation of the quinolone chromophore in the presence of the pyridinium ring. After 24 hr **4d** and **4e** showed spectral changes indicative of quinolone formation, but no bands at higher wavelength, expected for the cyclized product, were observed.

A number of cyclizations have been reported in which the cyclization terminus, B, is unsymmetrically substituted. In these cases the regiospecificity is biased by blocking one of the two favored positions with a substituent or by having a free phenolic substituent which leads to ortho or para regiospecificity regardless of ring size or presence of blocking group.[2,3] To study the effect of alkyl groups on the regioselectivity of this reaction the 1-(2-chlorobenzyl)pyridinium chlorides (**7**) were prepared and photolyzed, Table II.

(6) One referee proposed that the 2-acetoxyquinoline could be formed and undergo photolysis to the quinolone.

(7) (a) S. T. Reid, *Advan. Heterocycl. Chem.*, **11**, 1 (1970); (b) D. A. Nelson and D. W. Rowe, Abstracts of the First Rocky Mountain Regional Meeting of the American Chemical Society, Fort Collins, Colo., June 30, 1972, paper 4, p 32; (c) D. G. Crosby, *et al.*, in "Environmental Toxicology of Pesticides," F. Matsumura, G. M. Boush, and T. Misato, Ed., Academic Press, New York, N. Y., 1972, p 426.

TABLE II
PHOTOCYCLODEHYDROHALOGENATIONS OF 1-(*o*-CHLOROBENZYL)PYRIDINIUM CHLORIDES (7)

$$7 \xrightarrow[H_2O]{h\nu} 8$$

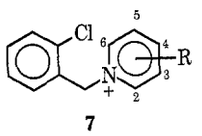
Compd	R	$h\nu$ time, hr	Product	R	% yield
7a	4-CH_3	19[a]	**8a**	3-CH_3	20
7b	3,5-$(CH_3)_2$	35[a]	**8b**	2,4-$(CH_3)_2$	30
7c	2,4-$(CH_3)_2$	7[b]	**8c**	1,3-$(CH_3)_2$	47
7d	3-CH_3	23[a]	**8d**	4-CH_3	33
7e	3,4-$(CH_3)_2$	78[a]	**8e** (33%)[c]	2,3-$(CH_3)_2$	20
			8f (67%)[c]	3,4-$(CH_3)_2$	

[a] Photolyzed in a 0.0224 *M* solution. [b] Photolyzed in a 0.0161 *M* solution. [c] Mixture.

The salts **7a** and **7b**, having a symmetrical ring B, were cyclized to give models for spectral identification, and **7c**, having one α position blocked, was used to check the blocking effect of a substituent on the reaction. The unsymmetrical systems **7d** and **7e** were studied to detect any regioselectivity.

The compounds **7** all gave uv absorption maxima below 280 nm which indicated that irradiation using a Pyrex filter, opaque below 280 nm, would prevent reaction. This was found to be true experimentally. Using a Vycor filter, opaque below 240 nm, or using a "Srinivasan" apparatus with 16 8-W lamps emitting 253.7-nm light gave cyclizations in both water and acetic acid. The reactions were considered to be complete when no further change in uv absorption occurred on further irradiation. The isolated yields of the cyclic compounds were low; however, there were no differences in the spectral properties of the crude reaction solutions and the purified products. The cyclic salts were all sensitive to basic reagents making isolation difficult.

The photolysis of **7d** gave only **8d** in which cyclization occurred adjacent to the methyl substituent. The



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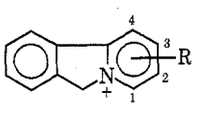

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photodehydrohalogenation of **7e** gave a cyclization product which appeared to be a mixture of **8e** and **8f**. The methyl group at lower field, 2.71 ppm, probably is deshielded by the adjacent aromtic ring and belongs to **8f**. The quantitative analysis of the mixture by nmr thus shows the photocyclization is regioselective to the extent of 67%, favoring reaction ortho to the methyl substituent in ring B as was observed with **7d**. The regioselectivity in these reactions compares with that observed for the Pschorr cyclization and may reflect similar controlling factors.[8]

Experimental Section

1-(2-Chloro-3-quinolylmethyl)-3-methylpyridinium Bromide (4a).—A mixture of 2.56 g (0.010 mol) of 2-chloro-3-bromomethylquinoline[9] and 0.93 g (0.010 mol) of β-picoline in 30 ml of sulfolane was stirred at room temperature for 4 days. After this time the mixture was diluted with ether, and the solid was separated by filtration and dried. Recrystallization of the solid from a 4:1 mixture of ethyl acetate–absolute ethanol gave 2.57 g (74%) of **4a** as tan crystals: mp 208–209°; pmr (CF_3COOH)[10] δ 9.16 (s, 1 H, het), 8.56 (br s, 2 H, het), 8.16–7.48 (m, 6 H, het), 6.00 (s, 2 H, CH_2), 2.36 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 267 nm (ϵ 6916), 293 (2957), 307 (3173), 321 (3287).

Anal. Calcd for $C_{16}H_{14}BrClN_2$: C, 54.95; H, 4.04; N, 8.01. Found: C, 55.29; H, 4.01; N, 7.99.

1-(2-Bromo-3-quinolylmethyl)-4-methylpyridinium Bromide (4b).—When the procedure above was used, 5.00 g (0.0166 mol) of 2-bromo-3-bromomethylquinoline[9] and 1.54 g (0.0166 mol) of γ-picoline in 40 ml of sulfolane gave, after 18 hr, 6.44 g (98%) of **4b**: mp 205–207°; pmr (CF_3COOH) δ 9.32 (s, 1 H, het), 8.90 (d, 2 H, het), 8.56–7.88 (m, 6 H, het), 6.00 (s, 2 H, CH_2), 2.88 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 240 nm (ϵ 67,213), 295 (4070), 308 (4486), 322 (4661).

Anal. Calcd for $C_{16}H_{14}Br_2N_2$: C, 48.75; H, 3.58; N, 7.07. Found: C, 48.86; H, 3.58; N, 7.06.

1-(2-Bromo-3-quinolylmethyl)-3-methylpyridinium Bromide (4c).—When the procedure to obtain **4a** was used, 5.00 g (0.0166 mol) of 2-bromo-3-bromomethylquinoline and 1.54 g (0.0166 mol) of β-picoline in 40 ml of sulfolane gave, after 18 hr, 5.58 g (84%) of **4c**: mp 204–206°; pmr (CF_3CO_2H) δ 8.81–7.43 (m, 6 H, Ar H), 5.93 (s, 2 H, CH_2), 2.25 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 267 nm (ϵ 7812), 295 (3448), 308 (3782), 322 (3900).

Anal. Calcd for $C_{16}H_{14}Br_2N_2$: C, 48.75; H, 3.59; N, 7.11. Found: C, 49.07; H, 3.50; N, 7.17.

1-(2-Bromo-3-quinolylmethyl)-4-(2-ethyl-1,3-dioxolan-2-yl)pyridinium Bromide (4d).—When the procedure to obtain **4a** was used, 5.00 g (0.0166 mol) of 2-bromo-3-bromomethylquinoline[9] and 2.98 g (0.0166 mol) of 4-(2-ethyl-1,3-dioxolan-2-yl)pyridine in 40 ml of sulfolane gave, after 3 days, 3.73 g (47%) of **4d**: mp 227–228°; pmr (CF_3COOH) δ 8.98 (s, 1 H, het), 8.64 (d, 2 H, het), 8.00–7.55 (m, 6 H, het), 6.01 (s, 2 H, CH_2N), 3.91–3.48 (m, 4 H, CH_2O), 1.68 (q, 2 H, CH_2C), 0.64 ppm (t, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 239 nm (ϵ 22,360), 295 (3616), 308 (3920), 322 (3960).

Anal. Calcd for $C_{20}H_{20}Br_2N_2O_2$: C, 50.01; H, 4.21; N, 5.84. Found: C, 50.06; H, 4.13; N, 5.82.

1-(2-Bromo-3-quinolylmethyl)-4-acetylpyridinium Bromide (4e).—When the procedure to obtain **4a** was used, 5.00 g (0.0166 mol) of 2-bromo-3-bromomethylquinoline[9] and 2.01 g (0.0166 mol) of 4-acetylpyridine in 40 ml of sulfolane gave, after 3 days, 6.84 g (98%) of **4e**: mp 204–205°; pmr (CF_3COOH) δ 9.10 (m, 3 H, het), 8.32 (d, 2 H, het), 8.18–7.72 (m, 4 H, het), 6.24 (s, 2 H, CH_2), 2.55 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 240 nm (ϵ 16,086), 275 (7609), 308 (4293), 322 (4130).

Anal. Calcd for $C_{17}H_{14}Br_2N_2O$: C, 48.36; H, 3.35; N, 6.64. Found: C, 48.20; H, 3.32; N, 6.67.

1-(2-Iodo-3-quinolylmethyl)-4-methylpyridinium Bromide (4f).—When the procedure to obtain **4a** was used, 2.00 g (0.0058 mol) of 2-iodo-3-bromomethylquinoline[9] and (0.0535 mol) of γ-picoline in 10 ml of sulfolane gave, after 24 hr, 1.90 g (75%) of **4f**: mp 221–223°; pmr (CF_3COOH) δ 8.60 (s, 1 H, het), 8.36 (d, 2 H, het), 8.00–7.32 (m, 6 H, het), 5.80 (s, 2 H, CH_2), 2.24 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 234 nm (ϵ 52,100), 311 (4980), 325 nm (5350).

Anal. Calcd for $C_{16}H_{14}BrIN_2$: C, 43.57; H, 3.20; N, 6.35. Found: C, 43.75; H, 3.22; N, 6.16.

1-(2-Oxo-1,2-dihydro-3-quinolylmethyl)-4-methylpyridinium Bromide (5a).—When the procedure to obtain **4a** was used, 2.00 g (0.0084 mol) of 3-bromomethyl-2-quinolone (**6**) and 0.78 g (0.0084 mol) of γ-picoline in 30 ml of sulfolane gave, after 0.5 hr, 2.60 g (94%) of **5a**: mp 255–258°; pmr (CF_3COOH) δ 8.86–8.66 (m, 2 H, het), 8.17–7.49 (m, 6 H, het), 5.95 (s, 2 H, CH_2), 2.69 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 225 nm (ϵ 33,500), 247 (11,140), 263 (8320), 275 (8400), 331 (6680).

(8) A. Lewis and T. Cohen, *J. Org. Chem.*, **32**, 3844 (1967).

(9) R. E. Lyle, D. E. Portlock, M. J. Kane, and J. A. Bristol, *J. Org. Chem.*, **37**, 3967 (1972).

(10) Chemical shifts are relative to TMS as an external standard except where otherwise indicated: het, heterocyclic.

Anal. Calcd for $C_{16}H_{15}BrN_2O$: C, 58.01; H, 4.57; N, 8.46. Found: C, 58.13; H, 4.56; N, 8.58.

1-(2-Oxo-1,2-dihydro-3-quinolymethyl)-3-methylpyridinium Bromide (5b).—When the procedure to obtain **4a** was used, 1.00 g (0.0042 mol) of 3-bromomethyl-2-quinolone (**6**) and 0.39 g (0.0042 mol) of β-picoline in 10 ml of sulfolane gave, after 2 days, 1.30 g (93%) of **5b**: mp 242–243°; pmr (CF_3COOH) δ 8.56–7.14 (m, 9 H, het), 5.56 (s, 2 H, CH_2), 2.28 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 223 nm (ε 32,320), 247 (10,911), 270 (12,486), 332 (7575).

Anal. Calcd for $C_{16}H_{15}BrN_2O$: C, 58.01; H, 4.57; N, 8.46. Found: C, 57.94; H, 4.43; N, 8.60.

1-(2-Chloro-3-quinolylmethyl)-3,4-dimethylpyridinium Bromide (4g).—When the procedure to obtain **4a** was used, 1.12 g (0.00437 mol) of 2-chloro-3-bromomethylquinoline[9] and 0.47 g (0.00437 mol) of 3,4-lutidine in 10 ml of sulfolane gave, after 8 hr, 1.53 g (96%) of **4g**: mp 243–244°; pmr (CF_3COOH) δ 9.06 (s, 1 H, het), 8.40 (s, 2 H, het), 8.10–7.43 (m, 5 H, het), 5.93 (s, 2 H, CH_2), 2.27 (s, 3 H, CH_3), 2.12 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 237 nm (ε 56,373), 262 (7779), 294 (3468), 307 (3740), 321 (3831).

Anal. Calcd for $C_{17}H_{16}BrClN_2$: C, 56.13; H, 4.44; N, 7.70. Found: C, 55.87; H, 4.28; N, 7.69.

1-(2-Chloro-3-quinolylmethyl)-2-bromopyridinium Bromide (4h).—When the procedure to obtain **4a** was used, 1.12 g (0.00437 mol) of 2-chloro-3-bromomethylquinoline and 0.69 g (0.00437 mol) of 2-bromopyridine in 10 ml of sulfolane gave, after 7 days and dilution with dry ether, 0.68 g (37%) of **4h**: mp 149–150°; pmr (CF_3COOH) δ 8.94 (d, 1 H, het), 8.66 (s, 1 H, het), 8.30–7.50 (m, 7 H, het), 6.21 ppm (s, 2 H, CH_2); $\lambda_{max}^{H_2O}$ 237 nm (ε 56,282), 274 (12,220), 307 (3770), 321 (3690).

Anal. Calcd for $C_{15}H_{11}Br_2ClN_2$: C, 43.45; H, 2.68; N, 6.76. Found: C, 43.13; H, 2.73; N, 6.66.

Photolysis Reactions.—The photolysis reactions were run in an Ace quartz apparatus using a 450-W, water-cooled high-pressure Hanovia lamp. The reactions were followed by monitoring changes in the uv absorption spectrum of aliquots withdrawn periodically from the reaction vessel. The solvent was water unless otherwise stated and the reactions were stirred and deoxygenated by passing a steady stream of nitrogen through the reaction mixture.

Photolysis of 4a.—A solution of 2.00 g (0.0057 mol) of **4a** in 650 ml of water was irradiated for 24 hr during which time the uv spectrum remained constant. Evaporation of the mixture and crystallization of the residue gave only recovered **4a**, identified by ir, pmr, uv, and melting points, in 25% yield.

Photolysis of 4b.—Hydrogen bromide gas was bubbled through a solution of 2.00 g (0.0051 mol) of **4b** in 100 ml of water until the pH ≃ 2. This solution was then diluted to 650 ml and photolyzed for 26 hr. After work-up, 766 mg of a tan crystalline solid, mp 252–253°, was obtained. The ir, pmr, and electronic spectra were all identical with those of an authentic sample of 1-(2-oxo-1,2-dihydro-3-quinolylmethyl)-4-methylpyridinium bromide (**5a**) described above. A mixture melting point was not depressed. This constitutes a 47% conversion to **5a**.

Attempted Hydrolysis of 4b.—Hydrogen bromide gas was bubbled into a solution of 0.33 g (0.00084 mol) of **4b** in 75 ml of water until the pH ≃ 2. The solution was then diluted to a volume of 110 ml and stirred at room temperature for 26 hr. No change in the uv absorption spectrum was observed during this time.

Photolysis of 4c.—A solution of 2.00 g (0.0051 mol) of **4c** in acetic acid containing a few drops of anhydride was photolyzed for 22 hr. No change in the uv spectrum was observed. Benzophenone (126 mg) was added and photolysis was continued for another 26 hr. The solution was concentrated under reduced pressure to give a brown oil which was dissolved in 300 ml of MeOH. The solution was treated with Norit and after standing for 3 hr was filtered through Celite. The clear filtrate was concentrated under reduced pressure to give a tan oil which crystallized on addition of EtOH and acetone. The solid, mp 227–230°, 730 mg (43%), gave identical uv and ir spectra with those of an authentic sample of 1-(2-oxo-1,2-dihydro-3-quinolylmethyl)-3-methylpyridinium bromide (**5b**). A mixture melting point with a crystallized (isopropyl alcohol) sample, mp 240–242°, of photolysis product was not depressed.

Photolysis of 4d, 4e, 4f, 4g, and 4h.—The photolyses were run as described for **4a** and **4b** with the solvents and results given in Table I.

1-(o-Chlorobenzyl)-4-methylpyridinium Chloride (7a).—A solution of 17.5 g (0.10 mol) of *o*-chlorobenzyl chloride and 9.3 g (0.10 mol) of γ-picoline in 20 ml of sulfolane was stirred at room temperature for 3 days. The mixture was diluted with ether, and the solid which separated was isolated by filtration and dried. Recrystallization of the solid from acetonitrile ether gave 21.2 g (84%) of **7a**: mp 208–209.5°; pmr (CF_3COOH) δ 7.93 (d, 2 H, α-pyr), 7.20 (d, 2 H, β-pyr), 6.88 (m, 4 H, Ar H), 5.27 (s, 2 H, CH_2), 2.25 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 256 nm (ε 3832), 275 sh (569).

Anal. Calcd for $C_{13}H_{13}Cl_2N$: C, 61.42; H, 5.16; N, 5.51. Found: C, 61.60; H, 5.15; N, 5.52.

1-(o-Chlorobenzyl)-3,5-dimethylpyridinium Chloride (7b).—When the procedure to obtain **7a** was used, 2.68 g (0.025 mol) of 3,5-lutidine and 4.40 g (0.025 mol) of *o*-chlorobenzyl chloride in 10 ml of sulfolane gave 6.30 g (94%) of **7b**: mp 233–234°; pmr (CF_3COOH) δ 7.84 (s, 2 H, α-pyr), 7.62 (s, 1 H, γ-pyr), 7.00 (s, 4 H, Ar H), 5.36 (s, 2 H, CH_2), 2.19 ppm (s, 6 H, CH_3); $\lambda_{max}^{H_2O}$ 273 nm (ε 6340).

Anal. Calcd for $C_{14}H_{15}Cl_2N$: C, 62.29; H, 5.65; N, 5.22. Found: C, 62.58; H, 5.44; N, 5.20.

1-(o-Chlorobenzyl)-2,4-dimethylpyridinium Chloride (7c).—When the procedure to obtain **7a** was used, 8.75 g (0.05 mol) of *o*-chlorobenzyl chloride and 5.36 g (0.05 mol) of 2,4-lutidine in 10 ml of sulfolane gave 10.80 g (81%) of **7c**: mp 210–211°; pmr (CF_3COOH) δ 7.98 (d, 1 H, α-pyr), 7.47–6.58 (m, 6 H, Ar H), 5.42 (s, 2 H, CH_2), 2.50 (s, 3 H, CH_3), 2.30 ppm (s, γ-CH_3); $\lambda_{max}^{H_2O}$ 262 nm (ε 5505).

Anal. Calcd for $C_{14}H_{15}Cl_2N$: C, 62.69; H, 5.64; N, 5.22. Found: C, 62.67; H, 5.62; N, 5.10.

1-(o-Chlorobenzyl)-3-methylpyridinium Chloride (7d).—When the procedure for the synthesis of **7a** was followed, 17.5 g (0.10 mol) of *o*-chlorobenzyl chloride and 9.3 g (0.10 mol) of β-picoline in 20 ml of sulfolane gave 18.0 g (71%) of **7d**: mp 128–130°; pmr (CF_3COOH) δ 8.18–7.83 (m, 3 H, α- and γ-pyr), 7.68–7.36 (m, 1 H, β-pyr), 7.10 (s, 4 H, Ar H), 5.47 (s, 2 H, CH_2), 2.18 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 267 nm (ε 4451), 275 sh (3336).

Anal. Calcd for $C_{13}H_{13}Cl_2N$: C, 61.42; H, 5.16; N, 5.51. Found: C, 61.24; H, 5.41; N, 5.43.

1-(o-Chlorobenzyl)-3,4-dimethylpyridinium Chloride (7e).—When the procedure to obtain **7a** was used, 2.68 g (0.025 mol) of 3,4-lutidine and 4.40 g (0.025 mol) of *o*-chlorobenzyl chloride in 10 ml of sulfolane gave 6.31 g (94%) of **7e**: mp 200–201°; pmr (CF_3COOH) δ 8.01–7.85 (m, 2 H, α-pyr), 7.31 (d, 1 H, β-pyr), 7.04 (s, 4 H, Ar H), 5.39 (s, 2 H, CH_2), 2.30 (s, 3 H, CH_3), 2.18 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 262 nm (ε 4722).

Anal. Calcd for $C_{14}H_{15}Cl_2N \cdot {}^1/_2H_2O$: C, 60.65; H, 5.83; N, 5.05. Found: C, 60.74; H, 5.55; N, 5.05.

Photolysis of 1-(o-Chlorobenzyl)-4-methylpyridinium Chloride (7a).—A solution of 3.71 g (0.0146 mol) of **7a** in 650 ml of water was photolyzed for 19 hr using a Vycor sleeve as a filter. The solution was concentrated under reduced pressure leaving a brown syrup which was dissolved in 10 ml of methanol. Acetone (125 ml) was added, the flocculent precipitate was removed by filtration, and 300 ml of ethyl acetate was added. The precipitate was removed and recrystallized from ethyl acetate–absolute ethanol to give 0.62 g (20%) of **8a** as tan needles: mp 244° dec; pmr (CF_3COOH)[11] δ 8.74 (d, 1 H, α-pyr), 8.08–7.86 (m, 2 H, β-pyr), 7.69–7.44 (m, 4 H, Ar H), 5.64 (s, 2 H, CH_2), 2.63 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 223 nm (sh, ε 14,464), 250 (10,893), 257 (11,607), 308 (10,625).

Anal. Calcd for $C_{13}H_{12}ClN$: C, 71.71; H, 5.56; N, 6.43. Found: C, 71.54; H, 5.73; N, 6.19.

Photolysis of 7b.—According to the procedure for the photolysis of **7a**, 3.92 g (0.0146 mol) of **7b** was photolyzed in 650 ml of water for 35 hr. Recrystallization of the residue from ethyl acetate–absolute ethanol gave 1.02 g (30%) of **8b**: mp 206–210° dec; pmr (CF_3COOH) δ 8.50 (s, 1 H, α-pyr), 7.97 (s, 2 H, Ar H), 7.58 (m, 3 H, Ar H), 5.64 (s, 2 H, CH_2), 2.73 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3).

Anal. Calcd for $C_{14}H_{14}ClN \cdot {}^1/_2H_2O$: C, 69.84; H, 6.29; N, 5.81. Found: C, 69.55; H, 6.08; N, 5.65.

Photolysis of 7c.—According to the procedure for the photolysis of **7a**, 2.80 g (0.0105 mol) of **7c** was photolyzed in 650 ml of water for 7 hr. Recrystallization of the residue from ethyl acetate–absolute ethanol gave 1.15 g (47%) of **8c**: mp 290° dec; pmr (CF_3COOH) δ 8.15–7.45 (m, 6 H, Ar H), 5.68 (s, 2 H, CH_2), 2.90 (s, 3 H, CH_3), 2.76 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 253 nm (ε 10,867), 257 (11,907), 310 (14,104).

(11) The chemical shifts are reported relative to the ring CH_2 which was assumed to be 5.64 ppm downfield from TMS.

Anal. Calcd for $C_{14}H_{14}ClN$: C, 72.55; H, 6.10; N, 6.04. Found: C, 72.71; H, 6.06; N, 5.70.

Photolysis of 7d.—A solution of 3.71 g (0.0146 mol) of **7d** in 650 ml of water was photolyzed according to the procedure for the photolysis of **7a**, using a Vycor sleeve as filter to give 1.05 g (33%) of **8d**: mp 235° dec; pmr (CF_3COOH) δ 8.49 (d, 1 H, α-pyr), 8.11–7.82 (m, 2 H, β- and γ-pyr), 7.56–7.29 (m, 4 H, Ar H), 5.64 (s, 2 H, CH_2), 2.83 ppm (s, 3 H, CH_3); $\lambda_{max}^{H_2O}$ 250 nm (sh, ϵ 1200), 254 (13,304), 317 nm (12,152).

Anal. Calcd for $C_{13}H_{12}ClN$: C, 71.71; H, 5.56; N, 6.43. Found: C, 71.30; H, 5.57; N, 6.15.

Photolysis of 7e.—According to the procedure for the photolysis of **7a**, 3.92 g (0.0146 mol) of **7e** was photolyzed in 650 ml of water for 78 hr. Recrystallization of the residue from ethyl acetate–absolute ethanol gave 0.67 g (20%) of a mixture of **8e** and **8f**, mp 268° dec. The mixture was not separated. However, analysis of the mixture showed ~67% **8f** and 33% **8e** to be present: pmr (CF_3COOH) δ 8.40–7.18 (m, 6 H, Ar H), 5.64 (s, 2 H, CH_2), 2.71 (s, 2 H, $^2/_3CH_3$), 2.51 (m, 3 H, CH_3), 2.37 ppm (s, 1 H, $^1/_3CH_3$); $\lambda_{max}^{H_2O}$ 225 nm (ϵ 14,900), 252 (12,190), 260 (11,700), 311 (10,290).

Anal. Calcd for $C_{14}H_{14}ClN \cdot {}^1/_2H_2O$: C, 70.72; H, 6.22; N, 5.89. Found: C, 70.58; H, 5.99; N, 6.08.

Registry No.—**4a**, 39727-35-0; **4b**, 39727-36-1; **4c**, 39727-37-2; **4d**, 39838-38-5; **4e**, 39727-38-3; **4f**, 39727-39-4; **4g**, 39727-40-7; **4h**, 39727-41-8; **5a**, 39727-42-9; **5b**, 39727-43-0; **6**, 35740-85-3; **7a**, 39727-54-3; **7b**, 39727-55-4; **7c**, 39727-56-5; **7d**, 39727-57-6; **7e**, 39727-58-7; **8a**, 39727-59-8; **8b**, 39727-60-1; **8c**, 39727-61-2; **8d**, 39727-62-3; **8e**, 39727-63-4; **8f**, 39727-64-5; 2-chloro-3-bromomethylquinoline, 35740-82-0; β-picoline, 108-99-6; 2-bromo-3-bromomethylquinoline, 35740-83-1; γ-picoline, 108-89-4; 4-(2-ethyl-1,3-dioxolein-2-yl)pyridine, 39727-67-8; 4-acetylpyridine, 1122-54-9; 2-iodo-3-bromomethylquinoline, 35740-84-2. 3,4-lutidine, 583-58-4; 2-bromopyridine, 109-04-6; *o*-chlorobenzyl chloride, 611-19-8; 3,5-lutidine, 591-22-0; 2,4-lutidine, 108-47-4.

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Formation of Long-Lived Free Radicals from Acylpyridinium Salts with Alkali

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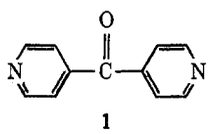
4-Acetylpyridinium methiodide reacted with concentrated aqueous alkali to yield a nonviologenic, stable, long-lived free radical whose esr spectrum indicated molecular symmetry. Several stable nonparamagnetic derivatives of the radical have been prepared and characterized. In contrast to the acetyl and valeryl derivatives, the bulkier alkyl analog 4,4-dimethylvalerylpyridinium salt reacted with hydroxide to yield dimethylviologen radical. On the other hand, di(4-pyridyl)methylcarbinol dimethiodide underwent a several-step transformation when dissolved in concentrated aqueous hydroxide to yield the same symmetrical stable radical as that obtained from 4-acetylpyridinium iodide. The reaction of the latter with sodium ethoxide in alcohol yielded still another radical which is different from that formed in hydroxide. The identity and esr spectra of the radicals and their derivatives and the overall mechanism of reaction are discussed.

We have recently reported[4–6] on the formation of several different long-lived free radicals from methiodide derivatives of di(4-pyridyl) ketone (**1**). The dimethiodide of **1**, in an unusual reaction, yielded rapidly the stable viologen cation radical **2** on simple mixing



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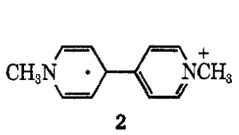

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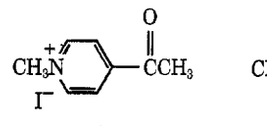
with concentrated aqueous hydroxide.[5] Since the long-lived pyridinyl radicals remain of high research interest because of their relevancy to basic chemical and biological reactions,[7–14] we have extended the study of N-heteroaromatic methiodides with bases to other acylpyridinium salts. In this paper, we report the formation of a nonviologen, stable, symmetrical radical from 4-acetylpyridinium methiodide **3** in aqueous alkali. Whereas the nonbranched homolog of **3**, 4-valerylpyridine methiodide (**4**), behaved analogous to **3**, its bulkier 4,4-dimethyl derivative **5** yielded dimethylviologen (**2**) with aqueous hydroxide in a manner resembling that of the dimethiodide of **1**. On the other hand, the same stable radical obtained



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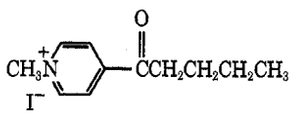

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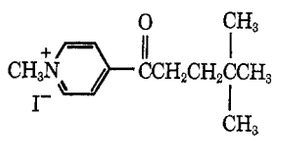

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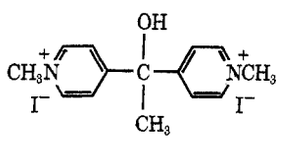

6

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