as a yellow solid: mp 269.5–270°; ir (mineral oil mull) 5.60 μ; nmr ($CDCl_3$) δ 8.1–7.4 (m, 6), 7.05 (s, 1, ArCH=C), 6.13 (s, 2, OCH_2O).

Anal. Calcd for $C_{16}H_9NO_6$: C, 61.74; H, 2.91. Found: C, 61.58; H, 2.83.

3-(Phenylimino)phthalide (5a).—To a solution of 4.15 g (0.010 mol) of **1a** and 1.07 g (0.010 mol) of nitrosobenzene in 30 ml of CH_2Cl_2 was added dropwise, during 3 min, 1.01 g (0.010 mol) of triethylamine with stirring at 25 ± 2° (ice-bath cooling required). The solution was stirred another 7 min at 10–25°, and then 20 ml of CH_2Cl_2 was added. The solution was extracted with three 25-ml portions of ice water, dried ($CaSO_4$), and concentrated under vacuum at 20° to 4.5 g of yellow solid. The solid was stirred with 15 ml of methanol, collected, and washed with 5 ml of methanol. The resultant 2.83 g of pasty solid was dissolved in 45 ml of CH_3CN, the solution was filtered, and 25 ml of ice water was added to the filtrate to give 1.63 g (73% yield) of yellow solid: mp 120–121.5° (lit.[10] mp 119–120°, lit.[14] mp 120–122°); ir (mineral oil mull) 5.60, 5.89 μ.

In preliminary experiments, crystallizations of the product from hot hexane gave solid of constant mp 114–115.5°. Examination of the ir spectrum of this material revealed weak extraneous absorptions at 7.26, 8.98, 11.33, and 13.89 μ due to small amounts of *N*-phenylphthalimide.

3-(*o*-Tolylimino)phthalide (5b).—To a solution of 8.30 g (0.020 mol) of **1a** and 2.42 g (0.020 mol) of 2-nitrosotoluene in 60 ml of CH_2Cl_2 was added dropwise, during 4 min, 2.02 g (0.020 mol) of triethylamine with stirring at 25–30° (ice-bath cooling). The solution was stirred for another 15 min at 5–15°, and then 40 ml of CH_2Cl_2 was added. The solution was extracted with three 50-ml portions of ice water, dried ($CaSO_4$), and concentrated under vacuum at 20° to a yellow solid. The solid was swirled with methanol and collected to give 3.90 g (82% yield) of yellow solid: mp 136–138° (lit.[15] mp 136–137°, lit.[16] mp 136°); ir (mineral oil mull) 5.51 (sh), 5.60, 5.88 μ. There was no trace of the isomeric phthalimide present as judged from the absence of absorptions at 11.65 and 13.89 μ, bands that are strong in the spectrum of *N*-(*o*-tolyl)phthalimide.

Reaction of 1a and 2,4-Dichlorobenzaldehyde Using Sodium Hydroxide as the Base.—A solution of 4.15 g (0.010 mol) of **1a** and 1.75 g (0.010 mol) of 2,4-dichlorobenzaldehyde in 60 ml of methylene chloride was extracted at 0–5° with two 20-ml portions of 0.5 *M* aqueous sodium hydroxide and 20 ml of water. The very pale, yellow-green methylene chloride solution was dried ($CaSO_4$) and analyzed by ir within 5 min; no residual aldehyde was present. Gc analysis of the solution indicated that **3a** and **4a** had formed in a 93:7 ratio in 94% total yield.

Registry No.—**1a**, 42116-85-8; **1b**, 42116-86-9; **3a**, 42086-67-9; **3b**, 42086-68-0; **3c**, 42086-69-1; **3d**, 42086-70-4; **3e**, 42086-71-5; **4a**, 42086-72-6; **4b**, 42086-73-7; **4c**, 42086-74-8; **4d**, 42086-75-9; **4e**, 42086-76-0; **5a**, 487-42-3; **5b**, 42116-88-1; 2-carboxybenzaldehyde, 119-67-5; tributylphosphine, 998-40-3; triphenylphosphine, 603-35-0; 2,4-dichlorobenzaldehyde, 874-42-0; 3-cyanobenzaldehyde, 24964-64-5; *o*-fluorobenzaldehyde, 446-52-6; piperonal, 120-57-0; 6-nitropiperonal, 712-97-0.

(14) S. Hoogewerff and W. A. van Dorp, *Recl. Trav. Chim. Pays-Bas*, **21**, 339 (1902).

(15) *Beilstein*, **17**, I 253.

(16) W. R. Roderick and P. L. Bhatia, *J. Org. Chem.*, **28**, 2018 (1963).

11-Aminoacridizinium Derivatives[1]

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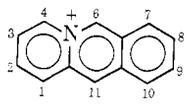
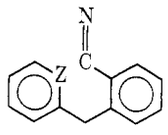
Acid-catalyzed cyclization of the 1-benzyl-2-cyanopyridinium ion and its congeners has provided a means for the synthesis of some 11-aminoacridizinium salts. Hydrolysis of the 11-aminoacridizinium ion afforded the 11-hydroxyacridizinium ion while diazotization effected ring opening and closing to form a 3-*v*-triazolo[1,5-*a*]pyridine derivative.

The relatively large number of acridizinium derivatives (**1**) which have been synthesized[2] includes only one amine, the 6-aminoacridizinium ion, obtained by the cyclization of *o*-(2-pyridylmethyl)benzonitrile (**2**).[3]



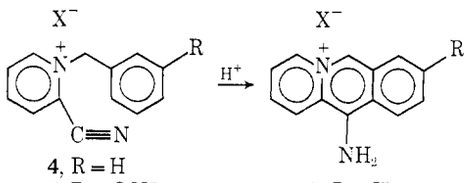
1



2, Z = N
3, Z = CH

This nitrile cyclization as well as the earlier cyclization[4] of *o*-benzylbenzonitrile (**3**) suggested that 11-aminoacridizinium salts (**6**) might be obtained by acid-catalyzed cyclization of 1-benzyl-2-cyanopyridinium salts (**4**).

While a variety of acidic cyclization reagents, including trifluoroacetic acid, polyphosphoric acid, fluorosulfonic acid, and hydrogen chloride in acetic acid,



4, R = H
5, R = OCH_3

7, R = H
6, R = OCH_3

were tried, under a variety of conditions, nothing appeared superior to concentrated sulfuric acid (at 100° for 15 min) and yields of **6** did not surpass 35%. An important side reaction was cleavage of the quaternary salt **4**; for example, the cyclization attempt using hydrogen chloride afforded a good yield of 2-picolinamide hydrochloride.

Since the cyclization reaction can be regarded as an internal Hoesch[5] reaction, it is not surprising that introduction of a methoxyl group para to the position of expected cyclization (**5**) resulted in an improved (70%) yield. Efforts to prepare benzologs of **6** by the cyclization of 1α- or 1β-naphthylmethyl-2-cyanopyridinium salts failed.

An alternate approach to the synthesis of benzologs of the 11-aminoacridizinium system **6** was through the

(1) This research was supported by Grant No. CA-05509 of the National Cancer Institute of the U. S. Public Health Service.

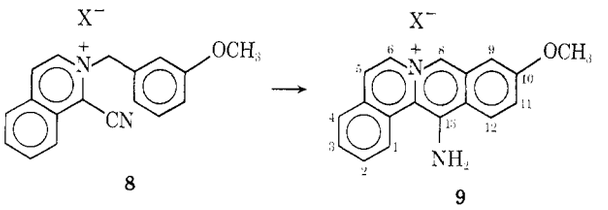
(2) C. K. Bradsher, *Accounts Chem. Res.*, **2**, 181 (1969). One aminophenol has been reported: D. L. Fields and J. B. Miller, *J. Heterocycl. Chem.*, **7**, 91 (1970).

(3) C. K. Bradsher and J. P. Sherer, *J. Org. Chem.*, **32**, 733 (1967).

(4) C. K. Bradsher and D. J. Beavers, *J. Org. Chem.*, **21**, 1067 (1956).

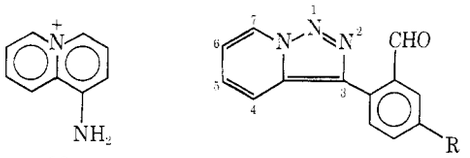
(5) P. E. Spoerri and A. S. DuBois, "Organic Reactions," Vol. 5, Wiley, New York, N. Y., 1949, p 387.

use of 1-cyanoisoquinoline,[6] which can be quaternized with *m*-methoxybenzyl bromide to yield **8**, X = Br. Cyclization of the tetrafluoroborate salt (**8**, X = BF_4) in 100% phosphoric acid at 130° gave an 88% yield of **9**.



8 **9**

As might be expected from the reported behavior[7] of the 1-aminoquinolizinium ion (**10**), the new 11-aminoacridizinium ion (**6**) shows very weak basicity, but can be acetylated. Diazotization of 11-aminoacridizinium perchlorate (**6**) brings about (in good yield) a complex ring opening and recyclization reaction leading to a neutral, nonionic species. From its physical and chemical properties and by analogy to the diazotization of 1-aminoquinolizinium[8] ion, the new compound was characterized as 2-(3-*v*-triazolo[1,5-*a*]-pyridyl)benzaldehyde (**11**). The 8-methoxy-11-aminoacridizinium ion behaved similarly on diazotization, affording **12**.

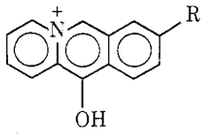


10

11, R = H
12, R = OCH_3

The amino group of 11-aminoacridizinium ion is too weakly basic to be alkylated by dimethyl sulfate or methyl iodide, nor would it form a Schiff base by reaction with 2,4-dinitrobenzaldehyde.

Hydrolysis of the amino group of **6** to afford the unknown 11-hydroxyacridizinium ion (**13**) is easily accomplished by heating **6** in dilute hydrochloric acid. The new hydroxy acridizinium salt **13** evidently exists as a betaine in neutral or alkaline solution, since on acidification there is a characteristic hypsochromic shift in the uv absorption spectrum. Similar behavior was noted for the 8-methoxy-11-hydroxyacridizinium salt **14** derived from **7**. The hydroxy group of **13**



13, R = H
14, R = OCH_3

could be acetylated, but it could not be replaced by chlorine using phosphorus oxychloride alone or admixed with phosphorus trichloride.

(6) J. J. Padbury and H. G. Lindwall, *J. Amer. Chem. Soc.*, **67**, 1268 (1945).
(7) A. R. Collicutt and G. Jones, *J. Chem. Soc.*, 4101 (1960).
(8) L. S. Davies and G. Jones, *J. Chem. Soc. C*, 688 (1970).

Experimental Section

Elemental analyses were carried out by the M-H-W Laboratories, Garden City, Mich. The melting points (uncorrected) determined in capillaries using a Hoover melting point apparatus. Spectra data were recorded as follows: uv, Beckman D. B. spectrometer; ir, Perkin-Elmer 137 or 237 spectrometer; nmr, Varian T-60 spectrometer. Chemical shifts, δ (parts per million) were determined using tetramethylsilane as an internal standard, except when D_2O was the solvent and when tetramethylsilane in carbon tetrachloride was used as an external standard. Mass spectra were recorded on an AE1 MS902 spectrometer through the cooperation of the Research Triangle Mass Spectrometry Center, which is sponsored by Grant No. FR-0330-02, National Institutes of Health.

1-Benzyl-2-cyanopyridinium Bromide[9] (**4**, **X = Br**).—A solution of 2-cyanopyridine (20 g, 0.19 mol) and benzyl bromide (35 g, 0.20 mol) in sulfolane (20 ml) was allowed to stand for 24 hr at 45°. The solid which formed was triturated with ethyl acetate and then recrystallized from methanol–ethyl acetate as colorless plates, mp 136–137°, yield 37.5 g (72%).

Anal. Calcd for $C_{13}H_{11}BrN_2$: C, 56.74; H, 4.03; N, 10.18. Found: C, 56.69; H, 4.19; N, 10.05.

The tetrafluoroborate salt, prepared by addition of a saturated solution of sodium tetrafluoroborate to an aqueous solution of **4** bromide, crystallized from water as needles, mp 95–97°.

Anal. Calcd for $C_{13}H_{11}BF_4N_2$: C, 55.36; H, 3.93; N, 9.93. Found: C, 55.48; H, 3.80; N, 9.54.

11-Aminoacridizinium Perchlorate (**6**, **X = ClO_4**).—The reaction flask (under nitrogen) containing 10 g of the bromide salt (**4**, X = Br) was cooled in an ice–water bath while 40 ml of concentrated sulfuric acid was added slowly. A vigorous stream of nitrogen was passed through the solution throughout in order to sweep out the hydrogen bromide and bromine formed. Fifteen minutes after addition was complete the mixture was heated for 15 min on a steam bath. The cooled solution was added to ice-cold anhydrous ether, precipitating a brown oil. The ether (containing the sulfuric acid) was decanted and the oil was taken up in 150 ml of water. The filtered aqueous solution was made basic with sodium bicarbonate and the resulting solution was washed several times with chloroform. To the aqueous solution an excess of saturated sodium perchlorate solution was added and the resulting yellow solid collected and dried in a vacuum desiccator, affording 3.8 g (35%). The analytical sample was crystallized from water as yellow needles: mp 247–250° dec; uv max (95% C_2H_5OH) 245 nm (log ϵ 4.90), 418 (4.71); nmr (CD_3CN) δ 6.1 (s, br, 1, NH_2), 7.3–8.1 (m, 7, aromatic), 8.3–8.5 (m, 1, H-4), 8.75 ppm (s, 1, H-6).

Anal. Calcd for $C_{13}H_{11}ClN_2O_4$: C, 52.99; H, 3.76; N, 9.51. Found: C, 53.09; H, 3.55; N, 9.86

1-(*m*-Methoxybenzyl)-2-cyanopyridinium Bromide (**5**, **X = Br**).—The reaction of *m*-methoxybenzyl bromide[10] with 2-cyanopyridine was carried out as in the preparation of **4** (84% yield). It was recrystallized from water as yellow needles, mp 151–152°

Anal Calcd for $C_{14}H_{13}N_2BrO$: C, 55.10; H, 4.29; N, 9.17. Found: C, 55.07; H, 4.23; N, 9.13.

The tetrafluoroborate of **5**, prepared as in the case of **4**, afforded a 93% yield of product which crystallized from water as needles, mp 116–118°.

Anal. Calcd for $C_{14}H_{13}BF_4N_2O$: C, 53.88; H, 4.20; N, 8.98. Found: C, 53.70; H, 4.15; N, 8.67.

11-Amino-8-methoxyacridizinium Bisulfate (**7**, **X = HSO_4**).—A solution of 5 g of the tetrafluoroborate salt (**5**, X = BF_4) in concentrated sulfuric acid (15 ml) was heated for 1 hr on a steam bath while a vigorous stream of nitrogen was passed through the solution, entraining a considerable quantity of hydrogen fluoride and boron trifluoride. The cooled solution was poured into 1 l. of anhydrous ether, the ether was decanted, and the yellow product was triturated with water (20 ml). The yellow solid was collected, dried, and suspended in methanol (150 ml). To the suspension enough triethylamine was added to make the solution basic, the resulting solution was filtered, and the filtrate was poured into 1 l. of anhydrous ether. The product was collected and washed with hot chloroform to remove any triethylamine

(9) This preparation was first described by J. D. Turner, Ph.D. Dissertation, Duke University, 1965, p 91.
(10) W. Q. Beard, D. N. Van Enam, and C. R. Hauser, *J. Org. Chem.*, **26**, 2310 (1961).

salt. The salt (5, X = HSO_4) crystallized from aqueous ethanol as yellow needles, mp 274–277° dec, yield 3.6 g (70%).

Anal. Calcd for $C_{14}H_{14}N_2O_5S$: C, 52.17; H, 4.38; N, 8.69. Found: C, 52.27; H, 4.69; N, 8.54.

The perchlorate (7, X = ClO_4) was prepared by addition of an aqueous solution of sodium perchlorate to an aqueous solution of the bisulfate (7, X = HSO_4) and crystallized from water as yellow prisms: mp 222–224° dec; uv max (95% C_2H_5OH) 250 nm (log ϵ 4.77), 266 (4.76), 305 sh, 342 sh, 420 (4.75); nmr (CF_3COOH) δ 4.20 (s, 3, CH_3), 7.4–9.2 ppm (m, 8, aromatic).

Anal. Calcd for $C_{14}H_{13}ClN_2O_5$: C, 51.79; H, 4.03; N, 8.63. Found: C, 51.69; H, 3.82; N, 8.38.

1-(2-Naphthylmethyl)-2-cyanopyridinium Tetrafluoroborate.—This salt was prepared from 2-bromomethylnaphthalene[11] in essentially the same way as was 4, X = BF_4. It crystallized from acetone–ethyl acetate as prisms: mp 147–148°; yield 81%; nmr (CF_3CO_2H) δ 6.20 (s, 1, CH_2), 7.3–8.9 (m, 10 aromatic), 9.10 ppm (d, 1, pyridyl 6-H).

Anal. Calcd for $C_{17}H_{13}BF_4N_2$: C, 61.48; H, 3.94; N, 8.44. Found: C, 61.75; H, 4.05; N, 8.25

1-(1-Naphthylmethyl)-2-cyanopyridinium Iodide.—A solution of 17.7 g (0.1 mol) of 1-chloromethylnapthalene and 15 g (0.1 mol) of sodium iodide in 150 ml of acetone was allowed to stand at room temperature for 5 hr. To the filtered solution 10.4 g (0.1 mol) of 2-cyanopyridine was added and the solvent was removed under reduced pressure. The residue was allowed to stand for 3 days at 45°. The iodide crystallized from water as red needles, mp 105–106°, yield 17.4 g (47%).

Anal. Calcd for $C_{17}H_{13}IN_2$: C, 54.84; H, 3.52; N, 7.55. Found: C, 54.74; H, 3.64; N, 7.42.

The tetrafluoroborate salt crystallized from water as orange plates, mp 159–160°.

Anal. Calcd for $C_{17}H_{13}BF_4N_2 \cdot H_2O$: C, 58.31; H, 4.32; N, 8.00. Found: C, 58.44; H, 3.86; N, 8.07

Although cyclization of both of the naphthylmethyl-2-cyanopyridinium tetrafluoroborates was attempted, using concentrated sulfuric acid or 100% phosphoric acid, only dequaternization and decomposition were observed.

1-Cyano-2-(*m*-methoxybenzyl)isoquinolinium Tetrafluoroborate (8, X = BF_4).—The quaternization of 9.6 g of 1-cyanoisoquinoline[5] with *m*-methoxybenzyl bromide was carried out in the usual way. The tetrafluoroborate salt (8, X = BF_4) crystallized from acetone as prisms, mp 181–182°, yield 40%.

Anal. Calcd for $C_{18}H_{15}BF_4N_2O$: C, 59.70; H, 4.17; N, 7.74. Found: C, 59.41; H, 4.12; N, 7.54.

10-Methoxy-13-aminobenz[*a*]acridizinium Tetrafluoroborate (9, X = BF_4).—To a 100% phosphoric acid solution, prepared by the addition of 14 g of phosphorus pentoxide to 31 g of 85% phosphoric acid, 5 g of 2-(*m*-methoxybenzyl)-1-cyanoisoquinolinium tetrafluoroborate was added and the mixture was heated at 130° for 1 hr. The red mixture was poured into ice water containing 5 ml of concentrated tetrafluoroboric acid. The resulting yellow solid was crystallized from aqueous acetone: yield 4.4 g (88%); mp 229–231° dec; uv max (95% C_2H_5OH) 237 nm (log ϵ 4.72), 281 sh, 290 (4.74), 320 (4.71), 330 (4.71) 390 sh, 420 sh, 440 (4.69); nmr (CF_3CO_2H) δ 4.15 (s, 3, CH_3), 7.6–8.6 (m, 9, aromatic), 9.25 ppm (s, 1, H-6).

Anal. Calcd for $C_{18}H_{13}BF_4N_2O$: C, 59.70; H, 4.18; N, 7.74. Found: C, 59.42; H, 4.43; N, 7.42.

11-Acetamidoacridizinium Perchlorate. A. By Use of Acetic Anhydride.—A solution of 11-aminoacridizinium perchlorate (6, X = ClO_4) in 25 ml of acetic acid and 10 ml of acetic anhydride was refluxed under nitrogen for 2 hr. Addition of ethyl acetate to the cooled solution precipitated the 11-acetamidoacridizinium perchlorate (0.43 g, 75%) which crystallized from water as yellow prisms: mp 263–265° dec; uv max (95% C_2H_5OH) 224 nm (log ϵ 4.80), 370 (4.76), 387 (4.76), 408 (4.76); ir (KBr) 1700 cm^{-1} (amide C=O); nmr (CF_3CO_2H) δ 2.2 (s, 3, CH_3), 7.2–8.0 (m, 7, aromatic), 8.5 (d, 1, H-4), 9.4 ppm (s, 1, H-6).

B. By Action of Acetic Acid–Hydrogen Chloride.—A solution of 6, X = ClO_4, in 30 ml of acetic acid was refluxed for 2 hr while hydrogen chloride was passed through the solution. The product, isolated and crystallized as before, afforded 0.35 g (61.3%).

Anal. Calcd for $C_{15}H_{13}ClN_2O_5$: C, 53.50; H, 3.90; N, 8.32. Found: C, 53.35; H, 3.93; N, 8.12.

2-(3-*v*-Triazolo[1,5-*a*]pyridyl)benzaldehyde (11).—A solution of 0.5 g of 11-aminoacridizinium perchlorate (6, X = ClO_4) in 50 ml of water at 5° was treated with an excess of a saturated aqueous sodium nitrite solution and then with 5 ml of 1 *N* hydrochloric acid. The solution was allowed to warm to room temperature (30 min) and the insoluble product was collected. The aldehyde 11 was obtained as a tan solid (0.3 g, 79%) which was crystallized from ethanol (charcoal) as needles: mp 191.5–192.5; uv max (95% C_2H_5OH) 246 nm (log ϵ 4.55), 288 (4.51), 318 (4.51); ir (KBr) 1680 cm^{-1} (CH=O); nmr ($CDCl_3$) δ 7.0–8.0 (m, 6, aromatic), 8.2 (d, 1, H-4), 8.9 (d, 1, H-7), 10.4 ppm (s, 1, CHO); mass spectrum *m/e* 223.0741 (M^+), 195, 167, 140, 139.

Anal. Calcd for $C_{13}H_9N_3O$ (223.0745): C, 69.95; H, 4.06; N, 18.82. Found: C, 69.98; H, 3.78; N, 18.69.

The 2,4-dinitrophenylhydrazone of 11 crystallized from xylene as a red solid, mp 269–270° dec.

Anal. Calcd for $C_{19}H_{13}N_7O_4$: C, 56.56; H, 3.25; N, 24.30. Found: C, 56.78; H, 3.50; N, 24.08.

2-(3-*v*-Triazolo[1,5-*a*]pyridyl)-5-methoxybenzaldehyde (12).—The addition of 1 ml of concentrated hydrochloric acid to a solution of 0.5 g (15.5 mmol) of 11-amino-8-methoxyacridizinium bisulfate (7, X = HSO_4) caused the formation of a precipitate. When the solution was cooled to 0° and treated dropwise with a solution containing 0.5 g (72 mmol) of sodium nitrite in 5 ml of water, the precipitate dissolved to give a deep red solution. The solution was stirred for an additional 30 min at 0–5° and then allowed to warm to room temperature. The solution was extracted with chloroform and the dried (Na_2SO_4) extract was evaporated to dryness under reduced pressure. The residue crystallized as needles from aqueous ethanol (0.33 g, 41%): mp 176–177°; uv max (95% C_2H_5OH) 241 nm (log ϵ 4.70), 293 (4.67), 333 (4.67); ir (KBr) 1675 cm^{-1} (CH=O); nmr ($CDCl_3$) δ 4.0 (s, 3, CH_3), 6.9–7.9 (m, 6, aromatic), 8.9 (d, 1, H-7), 10.3 ppm (s, 1, CHO).

Anal. Calcd for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.37; N, 16.59. Found: C, 66.51; H, 4.43; N, 16.50.

11-Hydroxyacridizinium Perchlorate (13, X = ClO_4).—A solution of 11-aminoacridizinium perchlorate (1 g) in 20 ml of 1 *N* hydrochloric acid was heated for 30 min on a steam bath. When the hot solution was filtered and allowed to cool, 11-hydroxyacridizinium perchlorate (13, X = ClO_4) crystallized as yellow needles: yield 0.85 g (85%); mp 110° (unchanged by recrystallization); nmr (CF_3CO_2H) δ 7.7–9.0 (m, 8, aromatic), 9.45 ppm (s, 1 H, H-6).

Anal. Calcd for $C_{13}H_{10}ClNO_5$: C, 52.81; H, 3.41; N, 4.74. Found: C, 52.70; H, 3.43; N, 4.81.

Betaine of 11-Hydroxyacridizinium Ion.—A solution of 1 g of 11-hydroxyacridizinium perchlorate in 25 ml of water was made basic by addition of solid sodium bicarbonate and the solution was extracted several times with chlororm. The combined extracts were dried (sodium sulfate) and concentrated and the red residue was recrystallized from methanol–ether to give the betaine as a yellow solid (0.32 g, 32%): mp 260–265° dec; uv max (95% C_2H_5OH) 243 nm (log ϵ 4.79), 418 (4.72); mass spectrum 195.0716 (M^+) (calcd for $C_{13}H_9NO$, 195.06841), 167, 139.

11-Acetoxyacridizinium Perchlorate.—A solution of 0.3 g of 13, X = ClO_4, in 20 ml of acetic anhydride was heated for 15 min on a steam bath. Addition of ether to the cooled solution precipitated the acetate as a yellow solid, 0.29 g (84%). The solid crystallized from aqueous acetone as yellow needles: mp 220–224° dec; uv max (95% C_2H_5OH) 250 nm (log ϵ 4.87), 371 (4.67), 388 (4.68), 411 (4.67); ir (KBr) 1775 cm^{-1} (ester C=O); nmr (CF_3CO_2H) δ 2.5 (s, 3, CH_3), 7.45–8.4 (m, 7, aromatic), 8.85 (d, 1, H-4).

11-Hydroxy-8-methoxyacridizinium Bisulfate (14, X = HSO_4).—The hydrolysis of 1 g of 7 bisulfate was carried out essentially as in the hydrolysis of 6: yield 70% of yellow needles; mp 146–148°; uv max (95% C_2H_5OH) 245 nm (log ϵ 4.82), 262 sh, 286 (4.79), 302 (4.78), 334 (4.76), 418 (4.80); nmr (D_2O) δ 3.5 (s, 3, CH_3), 6.0–8.3 ppm (m, 8, aromatic).

Biological Testing.—Screening tests carried out by agencies under contract to the Drug Research and Development branch of the National Cancer Institute have demonstrated that compound 9, X = BF_4, has reproducible minimal activity in the KB cell culture test.

Registry No.—4 (X = Br), 6318-97-4; 4 (X = BF_4), 42031-31-2; 5 (X = Br), 42031-32-3; 5 (X = BF_4), 42031-33-4; 6 (X = ClO_4), 42031-34-5; 7 (X = HSO_4), 42031-35-6; 7 (X = ClO_4), 42031-36-7; 8 (X = BF_4), 42031-37-8; 9 (X = BF_4),

(11) N. B. Chapman and J. F. A. Williams, *J. Chem. Soc.*, 5044 (1952).

42031-38-9; 11, 42031-39-0; 11 2,4-DNP, 42031-40-3; 12, 42031-41-4; 13 (X = ClO_4), 42031-42-5; 13 betaine, 42031-43-6; 14 (X = HSO_4), 42031-44-7; 1-(2-naphthylmethyl)-2-cyanopyridinium tetrafluoroborate, 42031-45-8; 1-(1-naphthylmethyl)-2-cyanopyridinium iodide, 42031-46-9; 1-(1-naphthylmethyl)-2-cyanopyridinium tetrafluoroborate, 42133-37-9; 11-acetamidoacridizinium perchlorate, 42031-47-0; 11-acetoxyacridizinium perchlorate, 42031-48-1.

Studies on the Synthesis of Benzo[*b*]quinolizinium Salts

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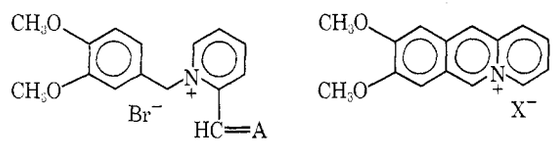
An improved procedure for the preparation of 8,9-dimethoxybenzo[*b*]quinolizinium bromide and a method for the preparation of selected 11-aminobenzo[*b*]quinolizinium bromides are described.

As a consequence of our work on derivatives of 1,3,4,6,11,11a-hexahydro-2*H*-benzo[*b*]quinolizine (**1**),[1] we became interested in the synthesis of derivatives of the parent aromatic system **2**.[2] These latter sub-

1 **2**

stances have been studied extensively by Bradsher and his coworkers,[3] but our findings differ significantly from those reported.

Bradsher and Dutta[4] reported that cyclization of the pyridinium salt **3a** in concentrated hydrochloric acid at 100°, followed by ion exchange, gave the quaternary chloride **4a**. However, in agreement with the report



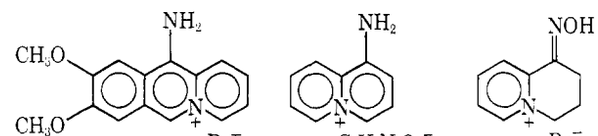
3a, A = O
b, A = NOH

4a, X = Cl
b, X = Br

of Kupchan, Flouret, and Matuszak,[5] we found that the cyclization reaction was accompanied by demethylation, and that we were unable to obtain a pure product.

We decided to modify the procedure of Bradsher and Dutta[4] by using hydrobromic acid to avoid the necessity for ion exchange. We found that cyclization could be effected in 5 min at 75° in the concentrated acid. Pouring the reaction mixture into tetrahydrofuran precipitated the product **4b** as a yellow solid which could be obtained analytically pure after one recrystallization.

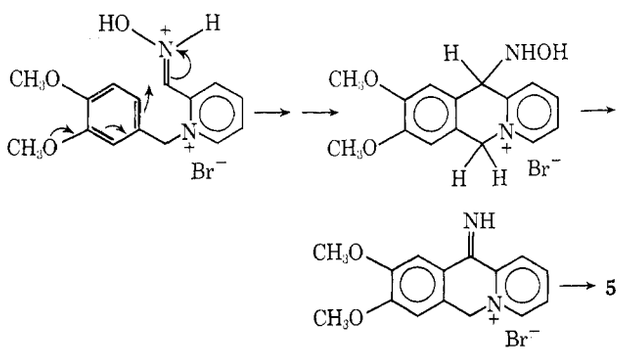
Bradsher has also advocated the preparation of benzo[*b*]quinolizinium salts by cyclization of the appropriate quaternary oxime,[6] and we attempted to prepare **4b** from **3b**. Conducting the reaction in hydrobromic acid as described above gave a product the nmr spectrum of which shows two equivalent exchangeable protons and only seven aromatic protons. Microanalysis indicated the presence of an additional nitrogen atom. These data suggested that the product is the 11-amino derivative **5**. This structure is analogous to that of the bicyclic primary amine picrate salt **6** prepared by Collicut and Jones[7] by treatment of the quaternary oxime **7** with acetic anhydride and con-



5 **6** **7**

centrated sulfuric acid, followed by hydrolysis of the acetamide of **6**.

It is tempting to suggest that the conversion of **3b** to **5** proceeds by way of the nitrile,[8] but dehydration of an aldoxime with aqueous acid is unprecedented. Normally an oxime would be hydrolyzed under these conditions. In this case we suggest that instead of being attacked by water, the protonated oxime cyclizes. The resulting intermediate then dehydrates to the imine, which is a tautomer of **5**. Presumably such a



dihydroaromatic hydroxylamine derivative is also involved in the acid-promoted conversion of 3,5-dimethylcyclohexenone oxime to 3,5-xylylamine,[9] and transformations similar to the above are involved in Semmler–Wolff aromatizations in general.[7,10]

The oximes **8a** and **8b** underwent cyclization to the 11-amino derivatives **9a** and **9b**, respectively. How-

(1) J. W. H. Watthey and K. J. Doebel, U. S. Patent 3,484,443 (1969) [*Chem. Abstr.*, **72**, 3396f (1970)].

(2) K. J. Doebel and J. W. H. Watthey, S. African Patent 6,707,635 [*Chem. Abstr.*, **70**, 96652h (1969)].

(3) For a review see C. K. Bradsher, *Accounts Chem. Res.*, **2**, 181 (1969).

(4) C. K. Bradsher and N. L. Dutta, *J. Amer. Chem. Soc.*, **82**, 1145 (1960).

(5) S. M. Kupchan, G. R. Flouret, and C. A. Matuszak, *J. Org. Chem.*, **31**, 1707 (1966).

(6) C. K. Bradsher, T. W. G. Solomons, and F. R. Vaughan, *J. Org. Chem.*, **25**, 757 (1960).

(7) A. R. Collicut and G. Jones, *J. Chem. Soc.*, 4101 (1960).

(8) Cyclization of analogous nitriles to 11-aminobenzo[*b*]quinolizinium salts is described in the accompanying paper: C. K. Bradsher and L. S. Davies, *J. Org. Chem.*, **38**, 4167 (1973).

(9) L. Wolff, *Justus Liebigs Ann. Chem.*, **322**, 351 (1902).

(10) M. V. Bhatt, *Experientia*, **13**, 70 (1957).