85 g. of bromobenzene, and 150 ml. of ether, was added, dropwise, and with stirring, to a solution of 20 g. of ethyl chloroacetate in 200 ml. of ether which was cooled by an ice bath. Ice water (200 ml.) was added. The ether layer was separated, washed with water, dried with magnesium sulfate, and fractionated. The fraction distilling at 140° (2 mm.) solidified in the receiver, and yielded 9.0 g. (24%) of white crystals, m.p. 63.4–65.0° (lit.[36] 64–65°), on recrystallization from hexane.

1,1-Diphenyl-2-chloroethylene. A mixture of 6.4 g. of 1,1-diphenyl-2-chloroethanol, 6.0 g. of phosphorus pentoxide, and 50 ml. of dry benzene was heated at reflux for 1 hr. Distillation yielded 4.3 g. (70%) of a colorless liquid, b.p. 138–139° (5 mm.) [(lit.[37] 189° (39 mm.)].

Anal. Calcd. for $C_{14}H_{11}Cl$: C, 78.32; H, 5.16. Found: C, 78.23; H, 5.25.

The product was unsaturated and yielded benzophenone (identified as the 2,4-dinitrophenylhydrazone) on cleavage with alkaline permanganate.[34]

Rate determinations. Solutions of sodium ethoxide in ethanol were prepared by adding sodium to absolute ethanol. The reaction solutions were prepared by diluting weighed samples of 1,1-diphenyl-2-haloethylene with ethanol containing sodium ethoxide in volumetric flasks at 25°. These solutions were heated at 99.75 ± 0.05° in ampoules, and the sodium ethoxide concentrations were determined periodically by titrating 5-ml. aliquots with standard hydrochloric acid, using phenolphthalein as the indicator.

1,1-Diphenyl-2-ethoxyethylene. A solution of 3.0 g. of 1,1-diphenyl-2-fluoroethylene in 70 ml. of absolute ethanol which was 0.64*M* in sodium ethoxide was heated at 99.75° for 118 hr. Water (500 ml.) was added, and the mixture was extracted with four 100-ml. portions of ether. The ether was removed, and distillation of the residue yielded a colorless liquid, b.p. 136–138° (2 mm.) [lit.[47] 178–182° (18 mm.)].

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 86.02; H, 7.09.

The product decolorized bromine and potassium permanganate solutions, and permanganate oxidation[34] gave benzophenone, identified as the 2,4-dinitrophenylhydrazone.

South Hadley, Mass.

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[36] H. Gilman and C. C. Wanser, *J. Am. Chem. Soc.*, **73**, 4030 (1951).

[37] W. T. Buttenberg, *Ann.*, **279**, 324 (1884).

[Contribution from the Department of Chemistry, Duke University]

Aromatic Cyclodehydration. XXXVII[1,2] Quinolizinium Derivatives Related to the Protoberberine Alkaloids

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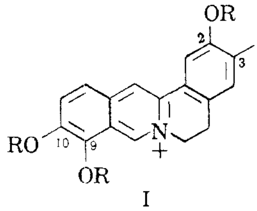
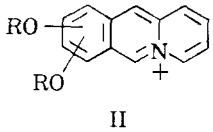
It has been found that isoquinoline-1-carboxaldehyde may be substituted for picolinic aldehyde in the acridizinium ion synthesis, affording a new method for the synthesis of the benz[*a*]acridizinium system (V). Salts of three new alkoxybenz[*a*]acridizinium ions have been synthesized.

In earlier model experiments[3] directed toward the synthesis of the protoberberine alkaloids (I), it was shown that salts produced by the reaction of alkoxybenzyl halides with picolinic aldehyde can be cyclized in the presence of hydrochloric acid to yield alkoxyacridizinium salts (II). It seemed likely that if 1-isoquinoline aldehyde (IV) were used instead of picolinic aldehyde a route to benzo[*a*]acridizinium salts (V) would be afforded.



I



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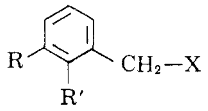
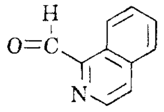
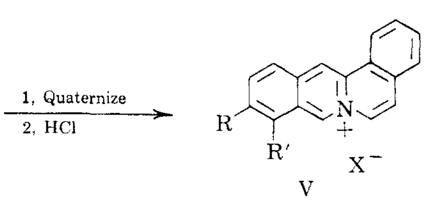


III



IV



V

The aldehyde (IV), available by the selenium dioxide oxidation of 1-methylisoquinoline,[4] was found to quaternize with benzyl bromide satisfactorily. Cyclization of the crude salt gave the expected benzo[*a*]acridizinium bromide (V, R = R′ = H; X = Br) in 52% yield. This new salt (V) might be regarded as the parent substance of all of the protoberberine alkaloids and could be referred to as a "dehydroprotoberberinium" salt. By the use of alkoxybenzyl halides several alkoxybenzo[*a*]acridizinium salts were produced (Table I).

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[1] For the previous communication of this series see *J. Am. Chem. Soc.*, **80**, 930 (1958).

[2] This investigation was supported by a research grant (H-2170) from the National Heart Institute of the National Institutes of Health. Abstracted in part from a dissertation to be submitted by James H. Jones in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Duke University.

[3] C. K. Bradsher and James H. Jones, *J. Am. Chem. Soc.*, **79**, 6033 (1957).

[4] R. S. Barrows and H. G. Lindwall, *J. Am. Chem. Soc.*, **64**, 2430 (1942).

TABLE I

BENZO[*a*]ACRIDIZINIUM SALTS (V)

R	R′	Yield, %	M.p., °C.[a] Bromide	Perchlorate	Picrate
H	H	52	257–258	234–235	277
CH_3O	H	78	235 dec.	276 dec.	283 dec.
CH_3O	CH_3O	53[b]		265–267	212
O—CH_2—O		66[c]		318–320	274–275

[a] The melting points reported are for analytical samples. [b] The product could not be isolated as the bromide. The yield reported is that of the perchlorate. [c] Crystallized from the cyclization mixture as the chloride, m.p. 309° dec.

While all of the salts described in Table I are new, they do not represent the first examples of fully aromatic benzo[*a*]-acridizinium salts. At least one earlier example is extant,[5,6] probably the earliest known instance of a compound having the aromatic quinolizinium[7] nucleus.

EXPERIMENTAL[8]

Benzo[a]acridizinium bromide (V, R=R′=H; X=Br). Two grams of isoquinoline-1-carboxaldehyde was refluxed with 2.05 g. of benzyl bromide and 3 ml. of methanol on the steam bath for 2 hr. Concentrated hydrochloric acid (60 ml.) was added and refluxing maintained for an additional 4 hr. The solvent was removed by vacuum evaporation and the residual oil washed with ether. Crystallization of the residue from propyl alcohol gave 2.0 g. (52%) of reddish-yellow crystals, m.p. about 250°. The analytical sample melted at 257–258°, λ max, 260, 270, 296, 309, 346, 364, 383, 403, 475, 507 mμ, min., 239, 265, 287, 304, 338, 355, 370, 391 mμ.

Anal. Calcd. for $C_{17}H_{12}BrN$: C, 62.21; H, 4.30; N, 4.27. Found: C, 61.85; H, 4.29; N, 4.22.

The *perchlorate* formed well-defined reddish crystals from ethanol, m.p. 234–235°.

Anal. Calcd. for $C_{17}H_{12}ClNO_4$: C, 61.92; H, 3.68; N, 4.25. Found: C, 61.76; H, 3.92; N, 4.59.

The *picrate*, m.p. 277°, was prepared in ethanol.

Anal. Calcd. for $C_{23}H_{14}N_4O_7$: C, 60.24; H, 3.08; N, 12.21. Found: C, 60.21; H, 3.04; N, 12.59.

10-Methoxybenzo[a]acridizinium bromide (V, R=OCH_3, R′=H, X=Br). Isoquinoline-1-aldehyde (3.0 g.), *m*-methoxybenzyl bromide[3,9] (3.8 g.) and methanol (4 ml.) were heated together on the steam bath for 2.5 hr., 90 ml. of concentrated hydrochloric acid added, and heating continued for 2 hr. The product, isolated in the usual way, afforded 5.1 g. (78%) of fine yellow crystals from ethanol, m.p. about 230°. The analytical sample consisted of clusters of microscopic yellow crystals, which melted at 235° dec., λ_{max} 270, 296, 309, 323, 345, 397, 417 mμ; min., 243, 286, 319, 370, 380, 405.

Anal. Calcd. for $C_{18}H_{14}BrNO$: N, 3.91. Found: N, 4.09.

The *perchlorate* was obtained from ethanol as fine yellow needles, m.p. 276° dec.

Anal. Calcd. for $C_{18}H_{14}ClNO_5 \cdot {}^1/_2H_2O$: C, 58.61; H, 4.06; N, 3.80. Found: C, 58.82; H, 3.86; N, 4.00.

The *picrate* was prepared in ethanol solution as a yellow solid, m.p. 283° dec.

Anal. Calcd. for $C_{24}H_{16}N_4O_8$: C, 57.72; H, 3.23; N, 11.22. Found: C, 57.99: H, 3.25; N, 11.56.

9,10-Dimethoxybenzo[a]acridizinium perchlorate (V, R=R′=OCH_3; X=ClO_4). The quaternary salt was formed from 2 g. of isoquinoline aldehyde, 2.94 g. of 2,3-dimethoxybenzyl bromide[3,10] and cyclized as in the case of the 10-methoxy analog. Since the oil which remained after removal of the hydrochloric acid could not be crystallized, it was treated with perchloric acid to give 2.5 g. (53%) of brown crystals, m.p. 265–267°. The analytical sample consisted of irregular clusters of orange-brown microscopic needles which melted at 265–267°; λ_{max} 259, 317, 332, 473, and 504 mμ; min., 245, 294, 400, 450, 482 mμ.

Anal. Calcd. for $C_{19}H_{16}ClNO_6$: C, 58.60; H, 4.14; N, 3.60. Found: C, 58.88; H, 4.26; N, 3.65.

The *picrate* separated from ethanol solution as yellowish brown crystals, m.p. 212°.

Anal. Calcd. for $C_{25}H_{18}N_4O_9$: N, 10.81. Found: N, 11.01.

9,10-Methylenedioxybenzo[a]acridizinium chloride (V, R—R′=OCH_2O, X=Cl). Quaternization of 2,3-methylenedioxybenzyl bromide[3,11] (2.74 g.) with 2.0 g. of isoquinoline aldehyde in the presence of methanol (2 ml.) was carried out as in the previous cases, but the cyclization was effected by refluxing the mixture with acid for only 0.5 hr. The product separated from the reaction mixture as fine red crystals which were recrystallized from ethanol as very small elongated rectangular plates, m.p. 304° dec.: yield 2.98 g. (66%). The analytical sample melted at 309° dec., λ_{max}, 229, 262, 284, 328, and 340 mμ, min., 244, 275, 300, 335 and 363 mμ.

Anal. Calcd. for $C_{18}H_{12}ClNO_2 \cdot {}^1/_2H_2O$: C, 67.81; H, 4.11; N, 4.40. Found: C, 67.75; H, 4.16; N, 4.79.

The *perchlorate* crystallized from ethanol as bright red crystals m.p. 318–320°.

Anal. Calcd. for $C_{18}H_{12}ClNO_6$: C, 57.84; H, 3.24; N, 3.75. Found: C, 57.81; H, 3.47; N, 3.85.

The *picrate*, prepared in ethanol solution, was bright red, m.p. 274–275°.

Anal. Calcd. for $C_{24}H_{14}N_4O_9$: C, 57.38; H, 2.81; N, 11.15. Found: C, 57.15; H, 2.83; N, 11.16.

DURHAM, N. C.

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[5] W. Schneider and K. Schroeter, *Ber.*, **53B**, 1459 (1920).

[6] W. Schneider and O. Böger, *Ber.*, **54B**, 2021 (1921).

[7] *Chemical Abstracts* nomenclature.

[8] All analyses were by Micro-Tech Laboratories, Skokie, Ill. All melting points were taken on the Fisher-Johns block and are uncorrected. The ultraviolet absorption spectra were measured in 95% ethanol solution using a Warren Spectracord spectrophotometer and 1-cm. quartz cells.

[9] E. Späth, *Monatsh*, **34**, 1965 (1913).

[10] R. D. Haworth and W. H. Perkin, Jr., *J. Chem. Soc.*, 127, 1434 (1925).

[11] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 105, 1456 (1914).