

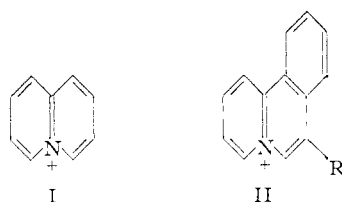
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Aromatic Cyclodehydration. XXX. Acridizinium Salts¹BY C. K. BRADSHER AND LEO E. BEAVERS^{2,3}

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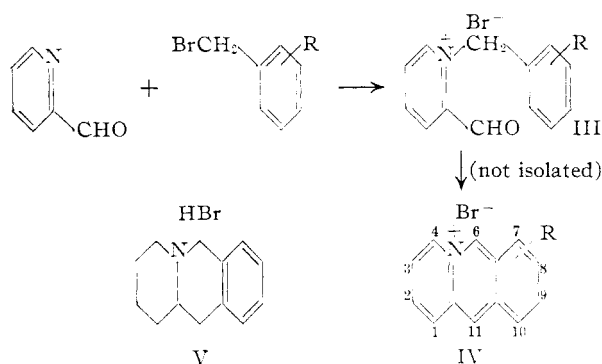
Through aromatic cyclodehydration of the crude salts obtained by reaction of benzyl bromide with pyridine-2-carboxaldehyde, the hitherto unknown benzo[b]quinolizinium salts have been obtained. Similarly *o*-methylbenzyl bromide and *p*-methylbenzyl bromide yielded the 7-methyl- and 9-methylbenzo[b]quinolizinium salts. The name acridizinium has been proposed for the benzo[b]quinolizinium ion.

Of the aromatic heterocyclic nuclei, the quinolizinium ion I is the most recently synthesized.⁴ In the preceding communication of this series⁵ it was shown that the principle of aromatic cyclodehydration can be conveniently adapted to the synthesis of the hitherto unknown aromatic benzo[a]quinolizinium salts (II). The method used was closely related



to that used earlier⁶ for the synthesis of phenanthrene derivatives.

It appeared likely that the unknown linear benzo-log of I might be prepared by a synthesis analogous to that developed for the synthesis of anthracenes.⁷ It has been found that this interesting new aromatic compound (IV, R = H) can be prepared from commercially available starting materials in two steps. The crude quaternary salt obtained by the



reaction of pyridine-2-carboxaldehyde⁸ and benzyl bromide was cyclized in 60% yield (over-all) by refluxing it for 15 hours in hydrobromic acid solution. The cyclization product for which the name

acridizinium⁹ bromide is proposed, gives an intense blue-violet fluorescence to an ethanol solution from which it crystallizes as large yellow prisms. The ultraviolet absorption spectrum indicates a high degree of conjugation and absorption extends further into the visible range than in the case of anthracene.

The structure of the acridizinium salt was demonstrated in two ways. On catalytic hydrogenation, four moles of hydrogen was absorbed yielding the hydrobromide of benzo[c]azabicyclo[4.4.0]decane (V). The picrate prepared from this proved identical with an authentic sample.¹⁰ Oxidation of the acridizinium bromide with permanganate afforded phthalic acid in 81% yield.

The new acridizinium synthesis has been applied to the synthesis of two homologs. From α -bromo-1,4-dimethylbenzene the 9-methylacridizinium bromide (IV, R = 9-CH₃) was obtained while α -bromo-1,2-dimethylbenzene yielded the 7-methyl derivative (IV, R = 7-CH₃).

Experimental

Acridizinium Bromide (IV, R = H).—One gram of pyridine-2-aldehyde was mixed with 1.6 g. of benzyl bromide and allowed to stand at room temperature for two weeks. At the end of this time a dark red glass had formed leaving a little supernatant liquid. The crude product was washed with ether, dissolved by warming gently in 10 ml. of 48% hydrobromic acid, and transferred with the aid of 5 ml. of 48% hydrobromic acid to a 25-ml. flask equipped with a ground glass condenser. A stream of nitrogen was directed onto the surface of the hot liquid until approximately 1 ml. of the acid had been evaporated. After 15 hours of refluxing under a nitrogen atmosphere, the very dark liquid was rinsed into a 125-ml. flask equipped with a bubbler and a spray trap and evaporated under reduced pressure until only a dark residue remained. This was dissolved in 30 ml. of hot water (Norite), filtered and again concentrated under vacuum until a volume of approximately 10 ml. remained. This was placed in an ice-bath until crystallization occurred, and the yellow solid was filtered off, rinsed with a few drops of ice-water and dried over calcium chloride in a vacuum desiccator. The crude yield was 1.57 g. (60.4%) of the monohydrate as yellow platelets, m.p. 236–239° dec. Recrystallization from ethanol-ether mixture gave 1.51 g., m.p. 238–240° dec. From pure alcohol, large yellow prisms were obtained of the same melting point. The analytical sample melted at 239–240° dec.

*Anal.*¹¹ Calcd. for C₁₃H₁₀NBr·H₂O: C, 56.13; H, 4.35. Found: C, 56.70; H, 4.50.

The perchlorate was obtained from an aqueous solution of the bromide by addition of 3 M perchloric acid. It

(9) The name acridizinium for the benzo[b]quinolizinium ion offers the advantage of simplicity in the naming of derivatives and benzologs of IV. It is proposed that the *Chemical Abstracts* numbering_s for this system be retained.

(10) N. J. Leonard, S. Swann, Jr., and G. Fuller, *THIS JOURNAL*, **76**, 3193 (1954). We are indebted to Dr. Leonard for supplying this sample.

(11) Except as noted, all analyses were by Micro-Tech Laboratories Skokie, Illinois.

(1) A preliminary report of this work appeared as a letter to the Editor, *Chemistry and Industry*, 1394 (1954).

(2) Public Health Service Fellow of the National Institutes of Health (1952–1954).

(3) Taken in part from a thesis submitted by Leo E. Beavers in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1955.

(4) V. Boekelheide and W. G. Gall, *THIS JOURNAL*, **76**, 1322 (1954).

(5) C. K. Bradsher and L. E. Beavers, *ibid.*, **77**, 453 (1955).

(6) C. K. Bradsher and W. J. Jackson, Jr., *ibid.*, **76**, 734 (1954).

(7) C. K. Bradsher, *ibid.*, **62**, 486 (1940). Cf. E. Bergmann, *J. Org. Chem.*, **4**, 1 (1939).

(8) Dr. F. Raschig, G. M. B. H., Ludwigshaven am Rhein, Germany.

gave light yellow prisms from acetone; m.p. 205–206.2°; ultraviolet absorption (95% ethanol) maxima (and log extinction coefficients) 242 (4.68), 361 (3.99), 379.5 (4.01) and 399 m μ (3.93); minima 311 (3.15), 369.5 (3.88) and 389.5 m μ (3.81).

Anal. Calcd. for $C_{13}H_{10}NClO_4$: C, 55.82; H, 3.61; N, 5.09. Found: C, 55.87; H, 3.61; N, 5.29.

The picrate was obtained from an alcoholic solution of the bromide by addition of alcoholic picric acid. It formed sparingly soluble yellow fibrous needles from acetone, m.p. 216–218°.

*Anal.*¹² Calcd. for $C_{19}H_{12}N_4O_7 \cdot C_3H_5O$: C, 56.65; H, 3.89. Found: C, 56.38; H, 3.66.

Benzo[c]azabicyclo[4.4.0]decane Hydrobromide (V).—Platinum oxide (0.020 g.) was introduced into a solution of 0.20 g. of benzo[b]quinolizinium bromide monohydrate in 25 ml. of 95% ethanol and reduced in a micro-hydrogenation apparatus until no more hydrogen was taken up. The gas absorbed was 98.9% of that calculated for 4 moles of hydrogen. The catalyst was filtered off, 10 ml. of benzene added, and the solution concentrated, ether added and crystallization allowed to proceed overnight; 0.166 g. (86%) of fine white needles was obtained by filtration, m.p. 236–238°. The analytical sample melted at 241.5–243.2° dec.

Anal. Calcd. for $C_{13}H_{18}NBr$: C, 58.21; H, 6.76. Found: C, 58.51; H, 6.51.

The picrate was obtained from an alcoholic solution of the hydrobromide by addition of alcoholic picric acid; yellow prisms from alcohol, m.p. 163–164°. The analytical sample melted at 163.8–165° (lit.¹⁰ 161–162°).

Anal. Calcd. for $C_{19}H_{20}N_4O_7$: C, 54.80; H, 4.85; N, 13.46. Found: C, 54.54; H, 4.89; N, 13.42.

Oxidation of Acridizinium Bromide.—Benzo[b]quinolizinium bromide monohydrate (0.260 g.) was dissolved in 10 ml. of water and stirred while the temperature was maintained at 80°. Ten milliliters of a solution of 1.9 g. of potassium permanganate in 60 ml. of water was added, the solution being decolorized immediately. Two milliliters of 25% sodium hydroxide solution was then added, followed by the remainder of the permanganate solution in portions of about 10 ml. each over a period of two hours. Complete decolorization of the permanganate occurred after 42 hours. The solution was then acidified while hot with dilute sulfuric acid and the manganese dioxide filtered off and washed with hot water. The combined washings and filtrate were reduced in volume to about 40 ml., placed in a continuous liquid–liquid extractor and extracted with ether for 8 hours. Evaporation of the wet ether extracts gave 0.127 g. (81.8%) of somewhat sticky crude phthalic acid, m.p. 190–195°. A thrice sublimed sample melted at 131.5° and was unde-

pressed when mixed with an authentic sample of phthalic anhydride. Both the crude and the sublimed products gave a very strong fluorescein test.

9-Methylacridizinium Bromide (IV, R = 9-CH₃).—One gram of pyridine-2-aldehyde was mixed with 1.8 g. of α -bromo-1,4-dimethylbenzene, heated until a homogeneous solution resulted and then allowed to stand for three weeks. The resultant dark glassy material was washed with ether, dissolved in 15 ml. of 48% hydrobromic acid, refluxed and worked up as before except that the water used as solvent was replaced by ethanol to facilitate crystallization. A total of 1.08 g. of brown crystals was collected, m.p. 185–189°. This was dissolved in alcohol, treated with Norite to give a greenish solution which became orange-yellow while being concentrated. A complete work-up gave 1.00 g. (39.1%) of yellow prisms, m.p. 191–193° dec. To the mother liquors of the first crystallization an alcoholic solution of picric acid was added, the solution concentrated and allowed to crystallize yielding 0.66 g. of a dark picrate. The picrate was crystallized from acetone (Norite) to give 0.64 g. (16.2%) of thin yellow leaves, m.p. 252–253° dec. The total yield of acridizinium derivatives was 55.3%.

Anal. Calcd. for $C_{20}H_{14}O_7N_4$: C, 56.87; H, 3.34. Found: C, 56.80; H, 3.53.

The perchlorate was obtained from aqueous solution of the bromide by addition of 3 *M* perchloric acid. It was crystallized from acetone–alcohol as pale yellow ragged flakes, m.p. 203–205°; ultraviolet absorption (95% ethanol) maxima (and log extinction coefficients) 244.5 (4.71, 379 (4.09), 398 (3.93); minima 314 (3.08) and 392 m μ (3.90).

*Anal.*¹² Calcd. for $C_{14}H_{12}NO_4Cl$: C, 57.25; H, 4.12; N, 4.77. Found: C, 57.38; H, 4.43; N, 4.69.

7-Methylacridizinium Bromide (IV, R = 7-CH₃).—One gram of pyridine-2-aldehyde was mixed with 2.0 g. of α -bromo-1,2-dimethylbenzene and allowed to stand for three weeks. The resultant red glass was washed with ether, dissolved in 15 ml. of 48% hydrobromic acid, cyclized and worked up as in the case of the isomer. Thrice crystallized from absolute ethanol, it afforded 1.17 g. (45.7%) of small yellow prisms, m.p. 270–275° dec. Further recrystallizations did not give a sharper melting point.

*Anal.*¹² Calcd. for $(C_{14}H_{12}NBr)_2 \cdot H_2O$: C, 59.37; H, 4.63; N, 4.95. Found: C, 59.32; H, 4.59; N, 4.97.

The perchlorate was obtained from an aqueous solution of the bromide by addition of perchloric acid. It crystallized as yellow needles from acetone, m.p. 232.9–233.2° dec. Ultraviolet absorption (95% ethanol), maxima (and log extinction coefficients) 250 (4.78), 366 (3.99), 388.5 (4.00) and 408.5 m μ (3.95); minima 316.5 (3.21), 377.5 (3.89) and 399.5 m μ (3.88).

Anal. Calcd. for $C_{14}H_{12}NO_4Cl$: C, 57.25; H, 4.12; N, 4.77. Found: C, 57.34; H, 4.12; N, 4.70.

DURHAM, N. C.

(12) Analysis by Galbraith Laboratories, Knoxville, Tennessee.