[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Aromatic Cyclodehydration. XLV.[1] Benz[*b*]acridizinium Derivatives[2]

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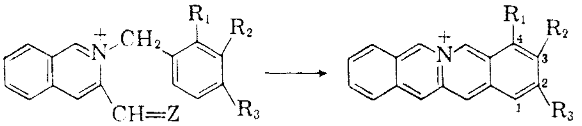
The method of aromatic cyclodehydration has been extended to the synthesis of alkoxybenz[*b*]acridizinium salts and to the synthesis of the dibenz[*b,h*] and dibenz[*b,j*]acridizinium systems.

Recently[1] the first synthesis of an interesting symmetrical cation, the benz[*b*]acridizinium ion (III) was described.



I. Z = NOH
II. Z = O

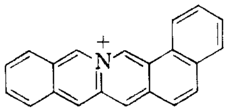
III
IV. $R_2 = OCH_3$
V. $R_1 = R_2 = OCH_3$
VI. $R_2 = R_3 = OCH_3$
VII. $R_2 = R_3 = OCH_2O$
(All group not otherwise indicated = H)

Our earliest attempts to synthesize this aromatic cation (III) were frustrated by the tendency of the ion to undergo dimerization under the conditions needed for the cyclization of 2-benzyl-3-formylisoquinolinium salts (II). While ultimately it was found[1] that 2-benzyl-3-aldoximinoisoquinolinium salts (I) cyclize fast enough to permit isolation of some of the desired benzacridizinium salt (III), it was observed that even 2-benzyl-3-formylisoquinolinium salts (II) may be cyclized if the benzyl group contains substituents which sufficiently enhance the rate of cyclization.

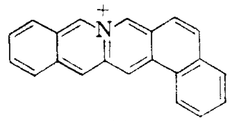
The present communication describes results obtained with alkoxybenzyl analogs[4] of II as well as with α- and β-naphthylmethyl bromides. Two of the quaternization reactions, one involving 3-methoxybenzyl bromide, and the other 3,4-dimethoxybenzyl bromide, yielded easily purified crystalline salts (II. $R_2 = OCH_3$ and $R_2 = R_3 = OCH_3$). This represents the first time that an aldehyde intermediate of this type has been obtained.

The 2-(3-methoxybenzyl)-3-formylisoquinolinium bromide salt (II. $R_2 = OCH_3$) was cyclized by allowing it to stand at room temperature for 2 hr. in concentrated hydrobromic acid, while the other quaternary intermediates were cyclized by heating in hydrochloric acid for 5–15 min. None of the cyclizations appeared to be accompanied by dimerization under these conditions. The alkoxybenz[*b*]acridizinium bromides are red-orange crystalline solids without well defined melting points, and are only sparingly soluble in water. Solution of these compounds are highly fluorescent.

By the use of 1-bromomethyl- and 2-bromomethylnaphthalene the previously unknown dibenz[*b,h*]- and dibenz[*b,j*]acridizinium ions [VIII and IX) were prepared in 43% and 66% over-all yields. These orange salts, possibly because of the operation of steric factors, show a remarkable resistance to thermal dimerization. No dimer formation was observed although refluxing periods as long as 6 hr. were used.



VIII



IX

EXPERIMENTAL[5]

Spectroscopy. All visible and ultraviolet spectra were determined in 95% ethanol solution, using the Warren Spectracord recording spectrophotometer and 1-cm. matched silica cells.

2-(3-Methoxybenzyl)-3-formylisoquinolinium bromide (II. $R_2 = OCH_3$). A solution of 0.78 g. of isoquinoline-3-carboxaldehyde[6] and 1.0 g. of *m*-methoxybenzyl bromide[7] in 1.0 ml. of dimethylformamide was allowed to stand at room temperature for 48 hr. The reaction mixture, containing a pale yellow solid, was triturated with ethyl acetate until crystallization was complete. The product, suitable for cyclization, was collected and dried *in vacuo*, yield 1.40 g. (78%), m.p. 140–145° dec. The analytical sample crystallized from acetonitrile as colorless microscopic plates, m.p. 165–166° dec.

Anal. Calcd. for $C_{18}H_{16}BrNO_2$: C, 60.33; H, 4.50; N, 3.91. Found: C, 60.44; H, 4.62; N, 3.59.

3-Methoxybenz[b]acridizinium bromide (IV). The cyclization of 750 mg. of the crude bromide (II. $R_2 = OCH_3$) in 6 ml. of 48% hydrobromic acid was carried out at room temperature for 2 hr. The reaction mixture was diluted with 20 ml. of water and cooled in ice. The product, consisting of

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(1) For the preceding communication of this series, see *J. Am. Chem. Soc.*, in press.

(2) This investigation was supported by research grants (NSF-G2364 and G6215) from the National Science Foundation.

(3) Taken from part of a thesis submitted by T. W. G. Solomons in partial fulfillment of the requirements for the Ph.D. Degree, Duke University, Du Pont Teaching Fellow, 1958–59.

(4) C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **79**, 6033 (1957).

(5) All melting points were taken in sealed capillary tubes and are not corrected. In most cases the capillary was inserted into a preheated block to minimize preliminary decomposition. Except where noted otherwise analyses were done by Dr. I. A. Schoeller, Kronach, West Germany.

(6) C. E. Teague and A. Roe, *J. Am. Chem. Soc.*, **73**, 689 (1951).

(7) E. Späth, *Monatsh.*, **34**, 1965 (1913).

orange-red clusters of blunt needles, was separated and dried, yield 540 mg. (76%). When this material, in a sealed capillary, was inserted into a block preheated to 200° it decomposed slowly from 235° with no defined melting point. Recrystallization from methanol–ethyl acetate did not change the melting behavior. λ_{max} (log ϵ): 264 (4.53), 285 (4.60), 338 (4.23), 400 (3.95), 423 (4.37) λ_{min}: 228 (4.15), 269 (4.48), 325 (4.19), 384 (3.50), 407 mμ (3.87).

Anal. Calcd. for $C_{18}H_{14}BrNO\cdot{}^1/_2H_2O$: C, 61.90; H, 4.33; N, 4.02. Found: C, 62.03; H, 4.40; N, 4.12.

The *picrate* was prepared from methanol as a red-orange powder, m.p. 271–272° dec.

Anal. Calcd. for $C_{24}H_{16}N_4O_8$: C, 59.02; H, 3.30; N, 11.5. Found:[8] C, 58.61; H, 3.61; N, 11.7.

3,4-Dimethoxybenz[b]acridizinium picrate (V). Isoquinoline-3-carboxaldehyde (0.78 g.) was quaternized by 2,3-dimethoxybenzyl bromide[9] (1.16 g.) by refluxing in absolute methanol (10 ml.) for 4 hr. Concentrated hydrochloric acid (10 ml.) was added and the solution refluxed 6 min. longer The acid and alcohol were removed *in vacuo* to leave a deep red oil which was taken up in alcohol and the picrate prepared, yield 0.90 g. (29%) of a red amorphous solid, m.p. 165–170°.

The analytical sample crystallized from acetonitrile as violet needles, m.p. 192–193°. λ_{max} (log ϵ): 280 (4.68), 355 (4.48), 413 (4.12), 436 (4.31); λ_{min}: 230 (4.45), 315 (4.34), 400 (4.07), 420 mμ (4.11).

Anal. Calcd. for $C_{25}H_{18}N_4O_9$: C, 57.91; H, 3.50; N, 10.81. Found: C, 57.85; H, 3.47; N, 10.97.

2-(3,4-Dimethoxybenzyl)-3-formylisoquinolinium bromide (II. $R_2 = R_3 = OCH_3$). A solution of 1.41 g. of isoquinoline-3-carboxaldehyde and 2.26 g. of 3,4-dimethoxybenzyl bromide[10] in 1.0 ml. of dimethylformamide was allowed to stand at room temperature for 22 hr., then worked up in essentially the same way as for II. $R_2 = OCH_3$, yield 3.47 g. (quant.) m.p. 156–158°.

Anal. Calcd. for $C_{19}H_{18}BrNO_3\cdot{}^3/_4H_2O$: C, 56.79; H, 4.86; N, 3.49. Found:[8] C, 56.79; H, 4.96; N, 3.35.

2,3-Dimethoxybenz[b]acridizinium chloride (VI). The cyclization of 1.5 g. of the crude bromide (II. $R_2 = R_3 = OCH_3$) was carried out by heating in 10 ml. of concentrated hydrochloric acid on a steam bath for 5 min. The reaction mixture was worked up in the same way as for IV, yield 1.0 g. (74%) of a solid which when heated in a sealed tube decomposed from 220° without a defined melting point.

To ensure anion consistency, a small sample of this material was dissolved in methanol and passed over a column of Amberlite IRA-410 ion exchange resin loaded with chloride ion. Evaporation of the methanol and crystallization from acetonitrile gave red needles with the same melting point behavior. λ_{max} (log ϵ): 257 (4.49), 304 (4.67), 400 (3.97), 423 (4.28), 456 (3.75), 485 (3.42). λ_{min}: 232 (4.15), 271 (4.32), 380 (3.59), 408 (3.94), 446 (3.72), 475 mμ (3.34).

Anal. Calcd. for $C_{19}H_{16}ClNO_2\cdot{}^3/_2H_2O$: C, 64.68; H, 5.42; N, 3.97. Found:[8] C, 64.68; H, 5.06; N, 4.35.

The *picrate* formed red-orange plates from methanol, m.p. 302–303° dec.

Anal. Calcd. for $C_{25}H_{18}N_4O_9$: C, 57.9; H, 3.50; N, 10.8. Found[8]: C, 58.2; H, 3.71; N, 11.3.

The *perchlorate* was obtained as an orange-red powder from dilute methanol, m.p. 282–284° dec.

Anal. Calcd. for $C_{19}H_{16}ClNO_6\cdot H_2O$: C, 55.96; H, 4.45. Found:[3] C, 55.99; H, 4.67.

2,3-Methylenedioxybenz[b]acridizinium chloride (VII). The quaternization of 1.57 g. of isoquinoline-3-carboxaldehyde by 2.16 g. of 3,4-methylenedioxybenzyl bromide[11] in 80% benzene-methanol solution (5 ml.) was effected by refluxing for 2.5 hr. The solvent was decanted from the crude salt that settled out and this material (presumed to be II, R_2, R_3 = OCH_2O) was cyclized in 25 ml. of concentrated hydrochloric acid by heating on a steam bath for 15 min. The reaction mixture was worked up in the same way as for VI to give 1.30 g. (39%) of an orange solid which decomposed gradually from 275° without a defined melting point. Passing a solution of this material over an ion exchange resin loaded with chloride ion gave on crystallization orange rectangular plates with the same melting point behavior. λ_{max} (log ϵ): 256 (4.52), 304 (4.62), 400 (3.84), 421 (4.13), 448 (3.71), 478 (3.42). λ_{min}: 270 (4.22), 378 (3.46), 407 (3.83), 440 (3.67), 465 mμ (3.31).

Anal. Calcd. for $C_{18}H_{12}ClNO_2\cdot{}^4/_3H_2O$: C, 64.77; H, 4.43; N, 4.20. Found:[8] C, 64.66; H, 4.48; N, 4.23.

The *picrate* was prepared from methanol and crystallized from dimethylformamide as red-orange needles, m.p. 289–289.5° dec.

Anal. Calcd. for $C_{24}H_{14}N_4O_9$: C, 57.37; H, 2.81; N, 11.15. Found:[8] C, 57.38; H, 2.62; N, 11.28.

Dibenz[b,h]acridizinium bromide (VIII). Isoquinoline-3-carboxaldehyde (1.57 g.) was quaternized by 1-bromomethylnaphthalene (2.21 g.) by refluxing in absolute methanol for 4 hr. Most of the methanol was evaporated and the yellow oil that remained was cyclized in 48% hydrobromic acid by refluxing for 6 hr. The reaction mixture was worked up by diluting with water (25 ml.) and cooling to give 1.60 g. (43%) of an orange solid, m.p. 266.5–268° dec.

The analytical sample crystallized from methanol–ethyl acetate as orange prisms, m.p. 278–280° dec. λ_{max} (log ϵ): 243 (4.56), 294 (4.68), 305 (4.85), 346 (4.27), 404 (4.11), 426 (4.30), 464 (3.59). λ_{min}: 223 (4.40), 269 (4.36), 297 (4.67), 337 (4.22), 376 (3.67), 408 (4.11), 457 mμ (3.54).

Anal. Calcd. for $C_{21}H_{14}BrN\cdot{}^2/_3H_2O$: C, 67.76; H, 4.06; N, 3.75. Found:[8] C, 67.50; H, 3.92; N, 3.83.

The *picrate* was prepared from ethanol as an orange powder, m.p. 289–289.2° dec.

Anal. Calcd. for $C_{27}H_{16}N_4O_7$: C, 63.78; H, 3.17; N, 11.02. Found:[8] C, 64.00; H, 3.53; N, 11.15.

Dibenz[b,j]acridizinium bromide (IX). Quaternization of isoquinoline-3-carboxaldehyde (1.57 g.) by 2-bromomethylnaphthalene (2.42 g.) in dimethylformamide (2 ml.) was carried out at room temperature for 45 hr. The bright yellow gum which formed was washed with ethyl acetate then taken up in 15 ml. of 48% hydrobromic acid. The resulting solution was refluxed for 3 hr., cooled, and diluted with water to given an orange solid. Recrystallization from ethanol gave 2.60 g. (66%) of broad orange spears m.p. 228–231°.

The melting point of the analytical sample was not changed. λ_{max} (log ϵ): 256 (4.70), 287 (4.65), 345 (4.48), 360 (4.53), 410 (4.23), 433 (4.40), 462 (3.67). λ_{min}: 228 (4.46), 267 (4.45), 326 (4.31), 352 (4.45), 378 (3.76), 420 (4.18), 456 mμ (3.81).

Anal. Calcd. for $C_{21}H_{14}BrN\cdot 2H_2O$: C, 63.64; H, 4.58; N, 3.53. Found:[8] C, 63.44; H, 4.44; N, 3.25.

The *picrate* was prepared from ethanol and crystallized from dimethylformamide as long orange needles, m.p. 309–309.1° dec.

Anal. Calcd. for $C_{27}H_{16}N_4O_7$: C, 63.78; H, 3.17; N, 11.07. Found:[8] C, 63.75; H, 3.54; N, 11.25.

The *perchlorate* was prepared from dilute methanol as an orange powder, m.p. 258–260° dec.

Anal. Calcd. for $C_{21}H_{14}ClNO_4\cdot{}^2/_3H_2O$: C, 64.38; H, 3.94; N, 3.58. Found:[8] C, 64.17; H, 3.95; N, 3.18.

DURHAM, N. C.

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(8) Analysis by Drs. Weiller & Strauss, Oxford, England.

(9) R. D. Haworth and W. H. Perkin, Jr., *J. Chem. Soc.*, 1434 (1925).

(10) R. D. Haworth, W. H. Perkin, Jr., and J. Rankin, *J. Chem. Soc.*, **127**, 1455 (1925).

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