Aromatic Cyclodehydration.[1] XLIV. The Benz[b]Acridizinium System[2]
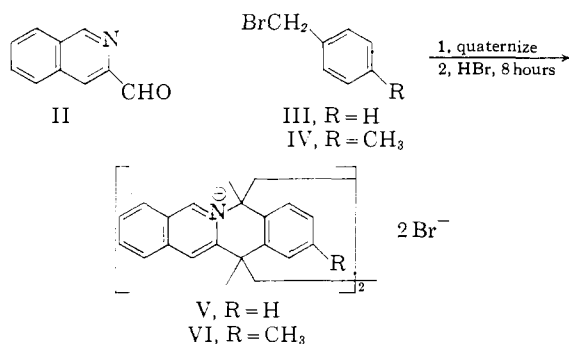
BY C. K. BRADSHER AND T. W. G. SOLOMONS[3]

The usual hydrobromic acid cyclization of the crude quaternary salts formed by the reaction of isoquinoline-3-carboxaldehyde with either benzyl bromide or α-bromo-p-xylene did not lead to the expected benz[b]acridizinium salts IX and X, but gave instead what are believed to be the dimers V and VI. The oxime derivatives VII and VIII were found to cyclize more rapidly and thus allowed isolation of the benz[b]acridizinium salts before appreciable dimerization had occurred. The benz[b]acridizinium bromides were found to be dimerized by boiling hydrobromic acid or by light.

In earlier communications[4] it was demonstrated that acridizinium salts (I) could be obtained by the hydrobromic acid-catalyzed cyclization of the crude quaternary salts formed from pyridine-2-carboxaldehyde and various benzyl halides. It seemed likely, therefore, that the pyridine-2-carbox-

I
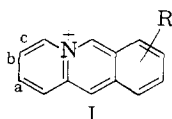
aldehyde could be replaced by isoquinoline-3-carboxaldehyde in the same general scheme and thus provide a route to benz[b]acridizinium salts. Although partially hydrogenated derivatives of the benz[b]acridizinium system have been known for some time,[5,6] the fully aromatic system has not, until now, been synthesized.

The aldehyde II was prepared readily by the selenium dioxide oxidation of 3-methylisoquinoline[7]

II   III, R = H
IV, R = CH₃

2 Br⁻

V, R = H
VI, R = CH₃

and in separate experiments was quaternized with either benzyl bromide (III) or α-bromo-p-xylene (IV). Treatment of these crude salts with boiling hydrobromic acid for eight hours gave faintly orange solids which on recrystallization yielded colorless nonfluorescent products, obviously not the highly conjugated benz[b]acridizinium salts. On

the basis of spectral evidence and certain analogies with the acridizinium photodimer,[8] they are believed to be the dimers V and VI.

Although no dimerization such as this had been observed in the synthesis of other acridizinium salts, it had been shown that acridizinium salts photodimerize under the influence of ultraviolet light. That light was not necessary for the formation of V was indicated by the fact that a similar cyclization carried out in total darkness also gave the dimerized product. It appeared, therefore, that the benz[b]acridizinium system was formed, but was so reactive that it dimerized under the usual cyclization conditions. This consideration led to the search for an intermediate that would cyclize more rapidly and thus allow isolation of the benz[b]acridizinium salts.

It was gratifying to find that the quaternary salts VII and VIII, obtained by the reaction of isoquinoline-3-aldoxime[7] with either III or IV, met this requirement.[9] The cyclization of VII in boiling hydrobromic acid for only ten minutes[10] gave a 23% yield of benz[b]acridizinium bromide (IX) accompanied by a 35% yield of the dimer V. In a similar way, cyclization of VIII for four minutes gave a 71% yield of 2-methylbenz[b]acridizinium bromide (X). The salts IX and X are red-orange crystalline solids and in solution show a yellow-green fluorescence.

VII, R = H   IX, R = H
VIII, R = CH₃   X, R = CH₃
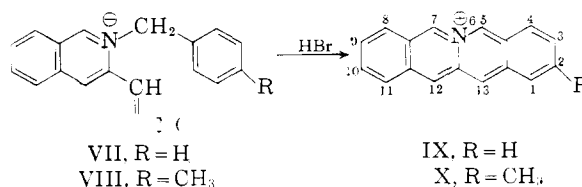
When hydrobromic acid solutions of either of the two benz[b]acridizinium salts, IX and X, were refluxed for one or two hours the corresponding dimers V and VI were isolated in good yield. The salts IX and X resembled acridizinium bromide in undergoing photodimerization. The photodimers obtained were identical with the dimers formed by the action of hydrobromic acid.

The ultraviolet absorption spectra (Fig. 1) of benz[b]acridizinium bromide (IX) and its dimer V are quite different in that V does not absorb at the

(1) For the preceding communication of this series see C. K. Bradsher and N. L. Dutta, THIS JOURNAL, 82, 1145 (1960).

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(3) Abstracted from part of a dissertation submitted by T. W. G. Solomons in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Duke University.

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(9) For further examples of the cyclization of oximes to form acridizinium derivatives, see C. K. Bradsher, T. W. G. Solomons and F. R. Vaughan, ibid., 24, in press (1959).

(10) In this regard it should be stated that cyclization of the quaternary salt formed by the reaction of II with benzyl bromide for a similar period gave only a very low yield of IX.

longer wave lengths. This makes it clear that the dimerization has destroyed the conjugation characteristic of the benz[b]acridizinium system. The similarity of the spectrum of V to that of 2-(2-methylbenzyl)-3-methylisoquinolinium bromide indicates that the absorbing groups in the dimer are isolated benzene and isoquinolinium structures. This is apparently due to dimerization involving an inner rather than a terminal ring.

It had been shown previously[8] that the acridizinium bromide photodimer dissociates readily when refluxed in alcohol. When a similar experiment was carried out with V, spectral measurements did indicate some dissociation of IX, but because the dissociation appeared to be complicated by the existence of a secondary reaction, it was not studied quantitatively. Dissociation of the dimers in hot glacial acetic acid was likewise observed.

Dimerization of either IX or X through the *meso* positions could theoretically produce a number of isomers. On the basis of our present knowledge, it is impossible to write exact stereochemical formulas for the products.

Experimental[11]

Spectroscopy.—All visible and ultraviolet spectra were determined in 95% ethanol solution using the Warren Spectracord recording spectrophotometer and 1-cm. matched silica cells. The infrared data were determined by the potassium bromide plate method using the Perkin–Elmer Infracord spectrophotometer.

Benz[b]acridizinium Bromide Dimer (V).—Isoquinoline-3-carboxaldehyde (3.14 g.) was quaternized by benzyl bromide (5.00 g.) by refluxing the mixture in absolute methanol for 4 hours. Most of the methanol was evaporated on a steam-bath and the yellow oil which remained washed thoroughly with ether. Concentrated hydrobromic acid (50 ml.) was added to this oil and the resulting solution refluxed for 8 hours to give a pale orange suspension. This suspension was diluted with 40 ml. of water and cooled in ice. The product was collected and dried in a vacuum desiccator; yield 3.75 g. (56%), m.p. 287–297° dec. (s. t. inserted at 250°). The visible spectrum of this material indicated that it contained less than 15% of benz[b]acridizinium bromide. The analytical sample crystallized from methanol as colorless prisms, m.p. 320–322° dec. (s. t. inserted at 300°).

Anal. Calcd. for $C_{34}H_{24}Br_2N_2 \cdot 3H_2O$: C, 60.55; H, 4.48; N, 4.16. Found: C, 60.76; H, 4.48; N, 4.06.

The **picrate** was prepared from methanol as yellow microcrystalline prisms, m.p. 288–289° dec. (s. t.).

Anal. Calcd. for $C_{46}H_{28}N_8O_{14} \cdot \frac{1}{2}H_2O$: C, 59.69; H, 3.16; N, 12.11. Found: C, 59.35; H, 3.33; N, 12.46.

The **perchlorate** was prepared by passing a methanolic solution of the bromide over an ion-exchange column of Amberlite IRA-410 resin loaded with perchlorate ion. This compound explodes when heated to 323°.

Anal. Calcd. for $C_{34}H_{24}Cl_2N_2O_8 \cdot CH_4O$: C, 60.79; H, 4.08; N, 4.05. Found: C, 60.68; H, 4.21; N, 3.88.

2-Methylbenz[b]acridizinium Bromide Dimer VI.—The quaternization of 1.57 g. of isoquinoline-3-carboxaldehyde with 2.50 g. of α-bromo-p-xylene was carried out essentially as described in the preparation of V. Cyclization of the salt afforded 1.50 g. (44%) of a pale orange solid, m.p. 286–290° dec. (s. t. inserted at 250°). The analytical sample crystallized from ethanol–ether as a colorless powder which appeared to be hydrated, m.p. 297–299° dec. (s. t. inserted at 250°); λ_{max} (log ε): 250 (4.90), 352 (4.18); λ_{min} 225 (4.65), 318 mμ (4.06).

(11) All melting points were determined in a heated block and are not corrected. The abbreviation "s.t." has been used to indicate that the melting point was taken in a sealed capillary tube and in most cases the tube was inserted into a preheated block to minimize preliminary decomposition. Except as noted the analyses were done by Drs. Weiler and Strauss, Oxford, England.
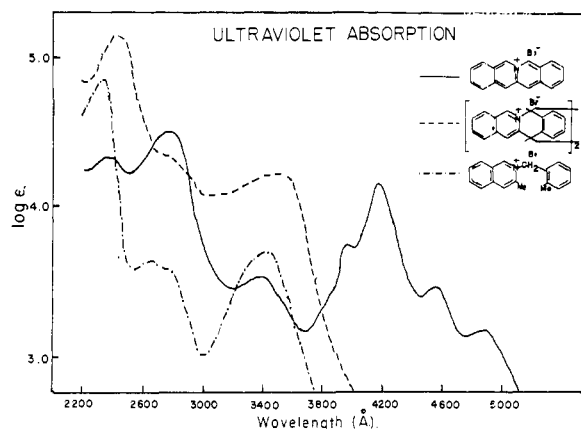

FIG. 1.

Anal. Calcd. for $C_{36}H_{28}N_2Br_2 \cdot 7H_2O$: C, 55.82; H, 5.45; N, 3.62. Found[12]: C, 56.10; H, 5.47; N, 3.63.

The **picrate** was prepared from ethanol as a bright yellow powder, m.p. 269–271° dec. (s. t. inserted at 200°).

Anal. Calcd. for $C_{48}H_{32}N_8O_{14}$: C, 61.02; H, 3.41; N, 11.86. Found: C, 61.22; H, 3.29; N, 11.90.

2-Benzyl-3-aldoximinoisoquinolinium Bromide (VII).—A solution of isoquinoline-3-aldoxime[7] (8.6 g.) and benzyl bromide (11.0 g.) in dimethylformamide (25 ml.) was formed by gentle warming on a steam-bath and then set aside at room temperature for 5 days. The mixture which resulted was triturated with ethyl acetate (150 ml.) and the product collected. The yield was 15.85 g. (92%) of a cream-colored powder, m.p. 191–195° dec. (s. t.). The analytical sample formed colorless irregular crystals from ethanol, m.p. 206–207° dec. (s. t.).

Anal. Calcd. for $C_{17}H_{15}BrN_2O$: C, 59.38; H, 4.42; N, 8.16. Found: C, 59.44; H, 4.47; N, 8.35.

Benz[b]acridizinium Bromide (IX).—Crude 2-benzyl-3-aldoximinoisoquinolium bromide (12 g.) was placed in a 100-ml. flask equipped with a magnetic stirrer and reflux condenser. Concentrated hydrobromic acid (50 ml.) was added, the stirrer started, and the solution heated to reflux temperature rapidly. Refluxing was carried out for 10 minutes during which time the solution turned deep red and became cloudy. The hydrobromic acid was removed *in vacuo* (20 mm.)[13] and the deep red solid which remained treated with 100 ml. of boiling methanol. Filtering this hot solution gave 3.97 g. (35%) of the dimer V as a yellow powder, m.p. 318–319° dec. (s. t. inserted at 250°). On cooling, the filtrate deposited 2.57 g. (23%) of benz[b]acridizinium bromide as small red prisms, m.p. 289–290° dec. (s. t. inserted at 250°). The analytical sample was prepared from acetonitrile, m.p. 290–291° dec. (s. t. inserted at 250°).

Anal. Calcd. for $C_{17}H_{12}BrN \cdot 3/2H_2O$: C, 60.55; H, 4.48. Found: C, 60.74; H, 4.40.

The **picrate** was prepared from a methanolic solution of the bromide and crystallized from acetonitrile as tiny red prisms, m.p. 259–260° (s. t. inserted at 240°).

Anal. Calcd. for $C_{23}H_{14}N_4O_7$: C, 60.27; H, 3.08. Found: C, 60.34; H, 2.96.

The **perchlorate** was prepared as a red-orange micro-crystalline powder, m.p. 280–282° dec. (s. t. inserted at 250°) by the addition of a 20% aqueous solution of perchloric acid to a methanolic solution of the bromide.

Anal. Calcd. for $C_{17}H_{12}ClNO_4$: C, 61.92; H, 3.67; N, 4.24. Found: C, 61.68; H, 3.84; N, 4.47.

Dimerization of Benz[b]acridizinium Bromide (IX). (a) By the Action of Boiling Hydrobromic Acid.—A solution of benz[b]acridizinium bromide (100 mg.) in 48% hydrobromic acid (4 ml.) was refluxed for one hour. The mixture was diluted with 10 ml. of water and cooled in ice. The product was collected and washed with water, cold ethanol, and ether

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

(13) It seems essential that this process be carried out rapidly and at a low temperature; otherwise considerable dimerization occurs.

in that order. The yield was 80 mg. (80%) of a faintly yellow powder, m.p. 309–310° dec. (s. t. inserted at 300°). The infrared spectrum of this material was identical with that of V isolated in the cyclization experiments.

(b) By Light.—One hundred milligrams of benz[b]acridizinium bromide was placed in a covered petri dish and irradiated for 48 hours with the light from a 150 watt General Electric frosted bulb. During the course of the irradiation the color of the solid changed from red to yellow. The weight was essentially unchanged, m.p. 320–321° dec. (s. t. inserted at 300°). This product was shown to be identical with that of V isolated in the cyclization experiments by mixed melting point and infrared spectra.

2-(4-Methylbenzyl)-3-aldoximinoisoquinolinium Bromide (VIII).—The quaternization of 5.23 g. of isoquinoline-3-aldoxime by 10 g. of α-bromo-p-xylene in 20 ml. of dimethylformamide was carried out for 4 days at room temperature. Trituration of the reaction mixture with 60 ml. of ethyl acetate gave 9.60 g. (8i%) of colorless irregular plates, m.p. 210–211° dec. (s. t.). The analytical sample was prepared from ethanol, m.p. 211–212° dec. (s. t.).

Anal. Calcd. for $C_{18}H_{17}BrN_2O$: C, 59.51; H, 4.91; N, 7.72. Found: C, 59.53; H, 4.92; N, 7.43.

2-Methylbenz[b]acridizinium Bromide (X).—A solution of 8.0 g. of the crude bromide VIII in 40 ml. of hydrobromic acid was refluxed for 4 minutes. The acid was removed in vacuo and the residue taken up in 50 ml. of hot methanol. On cooling, this solution deposited 5.44 g. (71%) of orange-red irregular plates, m.p. 242–243° dec. (s. t. inserted at 240°). The melting point of the analytical sample, taken in the same way, was 243–244° dec.; λ_{max} (logϵ): 240 (4.12), 257 (4.06), 280 (4.28), 340 (3.59), 398 (3.43), 420 (3.81), 458 (3.16), 487 (3.55); λ_{min} 252 (4.05), 262 (4.04), 317 (3.57), 368 (2.88), 404 (3.40), 448 (3.11), 478 mμ (2.45).

Anal. Calcd. for $C_{18}H_{14}BrN \cdot H_2O$: C, 63.17; H, 4.72; N, 4.10. Found: C, 63.01; H, 4.47; N,[12] 4.24.

The picrate was prepared from ethanol as orange-red rectangular plates, m.p. 267–268° dec. (s. t. inserted at 250°).

Anal. Calcd. for $C_{24}H_{16}N_4O_7$: C, 61.01; H, 3.41; N, 11.85. Found[11,12]: C, 60.50, 61.51; H, 3.27, 3.53; N, 11.75, 11.55.

Dimerization of 2-Methylbenz[b]acridizinium Bromide (X). (a) By the Action of Boiling Hydrobromic Acid.—A solution of 500 mg. of X in 15 ml. of 48% hydrobromic acid was refluxed for 2 hours. The reaction mixture was cooled, diluted with water, and the product separated. After washing with water, cold ethanol, and ether, a colorless powder remained; yield 300 mg. (60%), m.p. 297–299° dec. (s. t. inserted at 250°). The melting point of a mixture of this material and that of VI isolated in the cyclization experiment was undepressed.

(b) By Light.—One hundred milligrams of X was irradiated for 48 hours to produce a yellow powder, m.p. 298–299° dec. (s. t. inserted at 250°). The weight was essentially unchanged. A mixture of this material and that isolated in the cyclization experiment also showed no melting point depression.

2-(2-Methylbenzyl)-3-methylisoquinolinium Bromide.—The quaternization of 3-methylisoquinoline (1.43 g.) by α-bromo-o-xylene (1.85 g.) in 1 ml. of dimethylformamide was carried out at room temperature for 20 hours. The reaction mixture was triturated with ethyl acetate and the product collected. The yield was quantitative, m.p. 198–202°. The analytical sample crystallized from ethanol-ether as colorless irregular plates, m.p. 203–207°.

Anal. Calcd. for $C_{18}H_{18}BrN \cdot 1/2H_2O$: C, 64.10; H, 5.68; N, 4.15. Found[12]: C, 64.47; H, 5.67; N, 4.44.

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Studies in Stereochemistry. XXXII. Mechanism of Elimination of Sulfoxides[1]

BY CHARLES A. KINGSBURY[2] AND DONALD J. CRAM

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The preparation and properties of the four diastereomeric 1,2-diphenyl-1-propyl phenyl sulfoxides are described. When heated to 80°, these diastereomers undergo elimination reactions to give the isomeric α-methylstilbenes. These reactions are predominantly stereospecific, and the product of cis elimination dominates over the product of trans elimination by factors that vary between 3 and 16. The stereospecificity of the reaction varies little with the configurations about either of the two asymmetric carbon atoms or about asymmetric sulfur. The pyrolysis reactions display good first-order kinetics in dioxane, dimethylformamide, and 50% dioxane–50% methanol as solvents. The reaction rates and the stereospecificity of the transformations vary little as solvent is changed from dioxane to 50% dioxane–50% methanol, to pyridine, to dimethylformamide. In pure methanol, the reaction rate is dramatically depressed, but the stereospecificity is not changed. At higher temperatures (e.g., 120°), the stereospecificity of the reaction is lost. The values of $\Delta H^{\pm}$ are not constant with temperature over a 40° range, and therefore two primary processes are operative. At lower temperatures the classical, cyclic, concerted mechanism appears to apply. At higher temperatures, a second process predominates, which may assume either a cis or trans steric course. In the preferred mechanism for this process, a radical pair is produced in a first stage, which disproportionates by a hydrogen atom transfer in a second stage. The steric direction of this latter reaction is controlled by the relative rates of hydrogen abstraction and of configurational adjustments of the radical pair within the solvent cage.

Pyrolysis of esters,[3] xanthates,[4] carbonates,[5] halides[6] and amine oxides[7] have been observed to

result in cis elimination reactions to give olefins. Evidence has been presented that the minor product of the Hoffman elimination reaction may proceed through an ylid intermediate which undergoes a cis elimination reaction.[8] Other base-catalyzed reactions have also been observed to assume a cis steric course,[9] but probably mechanisms apply which are different from those observed in the pyrolytic reactions.

Sulfoxides have been postulated to have a dipolar sulfur–oxygen bond[10] analogous to the

(1) This research was supported in part by the Office of Ordnance Research, U. S. Army.

(2) U. S. Rubber Co. Fellow, 1958–1959.

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