sodium hydroxide and 0.5 g. of acridizinium bromide was refluxed for 2 hours. The red solution was poured into 75 ml. of cold water and extracted with carbon tetrachloride. A solution of bromine in carbon tetrachloride was added until precipitation of the salt appeared complete. The mixture was evaporated under reduced pressure and the residue dissolved in ethanol and treated with picric acid solution. The red solid was collected, m.p. 120–130°, yield 0.37 g. (37%). Recrystallization from ethanol gave a reddish-tan powder, m.p. 130–133°. This compound shows infrared absorption at 1682 cm.$^{-1}$ (phenyl ketone) and at 2080 and 2660 cm.$^{-1}$ (amine salt).

*Anal.* Calcd. for $C_{27}H_{20}N_4O_8 \cdot {}^1/_2H_2O$: C, 60.40; H, 3.93; N, 10.42. Found: C, 60.56; H, 3.77; N, 10.59.

**Reaction of 9-Methylacridizinium Bromide with Acetophenone.**—A mixture containing 0.5 g. of acetophenone, 0.5 g. of 9-methylacridizinium bromide and 5 ml. of 1 *N* sodium hydroxide solution in 25 ml. of propyl alcohol was refluxed for 2 hours and then diluted with water. The red oil which first formed solidified and was collected. It was immediately dissolved in a small quantity of ethanol and enough hydrochloric acid added to make the solution acidic and ethanolic picric acid was added. The crude precipitate weighed 0.41 g. (43%), m.p. 160–178°. The analytical sample crystallized from ethanol as yellow granules, m.p. 195–196°. This compound showed infrared absorption at 1682 cm.$^{-1}$ (phenyl ketone) and at 2080 and 2660 cm.$^{-1}$ (amine salt). The analysis indicated that the reaction of two moles of acetophenone per mole of 9-methylacridizinium bromide had taken place.

*Anal.* Calcd. for $C_{36}H_{30}N_4O_8$: C, 65.30; H, 4.57; N, 8.46. Found: C, 65.18; H, 4.54; N, 8.69.

**Reaction of 8,9-Methylenedioxyacridizinium Bromide with Acetophenone.**—A solution containing 0.5 g. of 8,9-methylenedioxyacridizinium bromide, 3 ml. of 1 *N* sodium hydroxide and 2 ml. of acetophenone in 20 ml. of ethanol was refluxed for 16 hours, after which it was poured into water and extracted with methylene chloride. The methylene chloride was evaporated and the residue converted to a picrate in ethanol solution; yield 0.46 g. (40%), m.p. 172–180°. The analytical sample crystallized from acetone–ethanol as dark yellow prisms, m.p. 200–202°.

This compound exhibits infrared absorption at 1682 cm.$^{-1}$ (phenyl ketone) and 2080 and 2660 cm.$^{-1}$ (amine salt). The analysis indicated the reaction of two moles of acetophenone per mole of the acridizinium derivative.

*Anal.* Calcd. for $C_{36}H_{27}N_4O_{11}$: C, 62.55; H, 3.94; N, 8.10. Found: C, 62.79; H, 4.12; N, 8.09.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

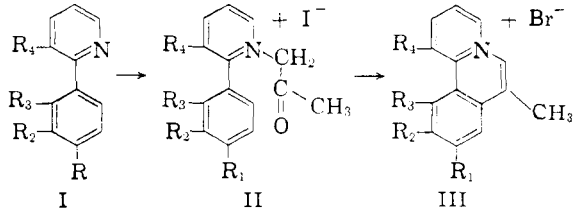
# Aromatic Cyclodehydration. XXXVIII.[1,2] Phenanthridizinium Derivatives with Substituents in the Terminal Rings

BY C. K. BRADSHER AND K. B. MOSER

RECEIVED OCTOBER 2, 1958

The method developed earlier for the synthesis of benzo[a]quinolizinium derivatives has been extended to the synthesis of fully aromatic benzo[a]quinolizinium salts having substituents in the terminal rings. The poor yield obtained in the cyclization of the 1-acetonyl-2-(2-tolyl)-pyridinium salt (XI) has been attributed to steric interference with the achievement of coplanarity. The name phenanthridizinium has been proposed for the benzo[a]quinolizinium ion.

In an earlier communication[3] it was shown that phenylpyridine (I) with iodoacetone yielded a quaternary cation (II) which, in the presence of boiling hydrobromic acid, afforded 7-methylphenanthridizinium salts[4] (III).



I II III

| | | | |
|---|---|---|---|
| $R_1 = CH_3$ | IV | V | VI |
| $R_2 = CH_3$ | VII | VIII | IX |
| $R_3 = CH_3$ | X | XI | XII |
| $R_2 = OCH_3$ | XIII | XIV | XV (picrate) |
| $R_4 = OH$ | XVI | XVII (bromide) | XVIII |

All R groups not otherwise specified are assumed to be hydrogen.

With the exception of the 1,2,3,4-tetracarbomethoxyphenanthridizinium salts prepared by O. Diels and J. A. Harms (*Ann.* **525,** 73 (1936)), the only fully aromatic phenanthridizinium compounds appear to be those described in reference 3.

It was the purpose of the present work to learn whether this method was sufficiently general to allow the preparation of phenanthridizinium salts with substituents in the terminal rings. Of particular interest was the question whether substituents ($R_3$ and $R_4$) which might impede the achievement of coplanarity in the uncyclized salt would noticeably retard or even prevent the cyclization.

TABLE I

PHENANTHRIDIZINIUM SALTS

| Substituent | Yield, % quaternization | Cyclization time, hr. | Yield, % cyclization |
|---|---|---|---|
| $R_1 = CH_3$ | 65 | 50.5 | 71 |
| $R_2 = CH_3$ | ..[a] | 66 | 64[b] |
| $R_3 = CH_3$ | 85 | 50.5 | 9 |
| $R_2 = OCH_3$ | 99 | 0.05 | 50 |
| $R_4 = OH$ | 62 | 50 | 85 |

[a] Yield not determined, but must be at least equal to over-all yield (64%). [b] Over-all yield from arylpyridine.

The salt XI formed by reaction of iodoacetone with 2-(2-tolyl)-pyridine (X) proved much more difficult to cyclize than did its isomers V and VIII. The 2-(2-tolyl)-pyridinium salt (XI) afforded only

(1) For the previous communication of this series, see *J. Org. Chem.*, **23,** 430 (1958).

(2) Abstracted from part of a dissertation to be presented by K. B. Moser in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Duke University. This research was supported by a grant (NSF-G2364) from the National Science Foundation.

(3) C. K. Bradsher and L. E. Beavers, THIS JOURNAL, **77,** 453 (1955).

(4) The name phenanthridizinium as a substitute for benzo[a]quinolizinium ion offers the advantage of simplicity in the naming of derivatives, and is consistent with those of the quinolizinium and acridizinium ions. The numbering used is that recommended by *Chemical Abstracts*.

a 9% yield of 7,11-dimethylphenanthridizinium bromide while under comparable conditions the salt V from 2-(4-tolyl)-pyridine gave a 71% yield of the 7,9-dimethyl analog VI. The Stuart–Hirschfelder model of 7,11-dimethylphenanthridizinium bromide is non-planar, and it is not surprizing that only small quantities of this product are formed under the usual cyclizing conditions. Cyclization *para* to a methoxyl group proved to be rapid, a 50% yield being obtained in only three minutes.[5]

The only one of our phenylpyridines substituted in the pyridine ring, 3-hydroxy-2-phenylpyridine (XVI), gave good yields in both the quaternization and cyclization reactions. It is interesting that the presence of a free hydroxyl group, even at one of the positions where it is most likely to impede achievement of coplanarity,[6] is without harmful effect.

## Experimental[7]

**2-(2-Tolyl)-pyridine (X).**—A lithium reagent was prepared from 214 g. of *o*-bromotoluene in ether and 200 g. of anhydrous pyridine in 200 ml. of ether was added cautiously, and the ethereal layer separated and dried over potassium hydroxide. The ether and all material boiling below 200° (atmospheric pressure) were evaporated, the residue refluxed for 2 hours with 0.5 g. of 10% palladium–charcoal and then distilled under reduced pressure. The product was 58.9 g. (28%) of a clear yellow liquid, b.p. 129–132° (6.5 mm.). A picrate prepared for analysis crystallized from ethanol as small irregular yellow needles, m.p. 141.5–143°.

*Anal.* Calcd. for $C_{18}H_{14}N_4O_7$: C, 54.27; H, 3.54; N, 14.07. Found: C, 54.57; H, 3.11; N, 14.02.

**1-Acetonyl-2-(2-tolyl)-pyridinium Iodide (XI).**—A mixture containing 2.12 g. of 2-(2-tolyl)-pyridine (X) and 3.0 g. of iodoacetone was kept in the refrigerator in a stoppered flask for 5 days. The reaction mixture turned to an orange crystalline mass. The solid was washed with peroxide-free ether and crystallized from ethanol–ether as light orange plates, m.p. 158.5–160°, yield 3.75 g., 85%. The analytical sample consisted of yellowish-tan plates, m.p. 161.5–163.5°.

*Anal.* Calcd. for $C_{15}H_{16}INO$: C, 51.00; H, 4.57; N, 3.97. Found: C, 51.16; H, 4.69; N, 4.08.

A picrate was prepared in ethanol solution and recrystallized from ethanol as yellow crystals, m.p. 183–184°.

*Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: N, 12.33. Found[8]: N, 12.69.

**7,11-Dimethylphenanthridizinium Bromide (XII).**—A solution containing 7 g. of 1-acetonyl-2-(2-tolyl)-pyridinium iodide (XI) was prepared in 75 ml. of water containing a few drops of hydrochloric acid, and the mixture stirred with pure freshly precipitated silver chloride (from 9 g. of silver nitrate) for 2.75 hours. The silver iodide–chloride mixture was removed by filtration and the filtrate evaporated under reduced pressure. The residue was taken up in 45 ml. of 48% hydrobromic acid and refluxed for 50.5 hours. The acid was removed under reduced pressure (aspirator), the residue taken up in water and treated with Norite. The water was evaporated, replaced by ethanol, which was evaporated in turn, and the residue crystallized from ethanol–ether. This afforded 0.63 g. (9%) of cream colored crystals, m.p. 284.5–289.5° dec. (cor.). The mother liquor on treatment with picric acid yielded only the picrate of the starting material. An analytical sample was prepared by recrystallization from ethanol–ether as fine white crystals, m.p. 290–292.5° dec. (cor.); $\lambda_{max}$ 239, 285, 332, 347 and 364 mμ; $\lambda_{min}$, 258, 323, 336 and 354 mμ.

*Anal.* Calcd. for $C_{15}H_{14}NBr$: C, 62.51; H, 4.90; N, 4.86. Found: C, 62.11; H, 4.94; N, 4.68.

The picrate was crystallized as fine yellow needles from acetic acid–ethanol, m.p. 205–206°.

*Anal.* Calcd. for $C_{21}H_{16}N_4O_7$: C, 57.80; H, 3.70; N, 12.84. Found: C, 58.07; H, 3.79; N, 12.78.

**1-Acetonyl-2-(4-tolyl)-pyridinium iodide (V)** was prepared as in the case of the 2-tolyl isomer XI, except that quaternization of 2-(4-tolylpyridine)[9] was allowed to proceed for 25 days and the salt crystallized from methanol–ethyl acetate as light yellow needles, m.p. 158.5–160.5°, yield 2.9 g. (65%). The analytical sample from ethanol–ether melted at 161–162.5°.

*Anal.* Calcd. for $C_{15}H_{16}INO$: C, 51.00; H, 4.57. Found[10]: C, 50.99; H, 4.55.

The picrate was obtained as yellow needles from ethanol, m.p. 112.5–115.5°.

*Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: C, 55.52; H, 3.99; N, 12.33. Found: C, 55.76; H, 4.23; N, 12.16.

**7,9-Dimethylphenanthridizinium bromide (VI)** was prepared by a procedure identical with that used in preparing the isomeric 7,11-isomer XII. The yield was 4.7 g. (71%) of product melting at 311–313 dec. (cor).). The analytical sample was prepared from ethanol–ether solution as colorless crystals, m.p. 314.5–316.5° dec. (cor.); $\lambda_{max}$ 227, 240, 273, 325, 341 and 357 mμ; $\lambda_{min}$ 232, 255.5, 317, 331 and 348 mμ.

*Anal.* Calcd. for $C_{15}H_{14}NBr.H_2O$: C, 58.83; H, 5.27; N, 4.57. Found: C, 59.18; H, 5.20; N, 4.77.

The picrate, fine yellow needles from ethanol and glacial acetic acid, melted at 224–226°.

*Anal.* Calcd. for $C_{21}H_{16}N_4O_7$: C, 57.80; H, 3.70. Found[10]: C, 57.92; H, 3.63.

**7,10(?)-Dimethylphenanthridizinium Bromide (IX).**—Quaternization of 2-(3-tolyl)-pyridine (VII)[9] was carried out as in case of the isomers IV and X. The water solution of the salt VIII was freed from starting materials by washing it with ether. Silver chloride was again used to convert the anion from iodide to chloride and the crude chloride corresponding to VIII was cyclized by refluxing it for 66 hours in 48% hydrobromic acid. The product believed to be IX, m.p. 324–331° dec., was obtained in an over-all yield of 64%, calculated from the free base. The analytical sample crystallized from ethanol as colorless needles, m.p. 342.5–345.5 dec.; $\lambda_{max}$ 225, 242, 285, 329, 345, and 363 mμ; $\lambda_{min}$, 229.5, 272, 322, 333 and 352 mμ.

*Anal.* Calcd. for $C_{15}H_{14}NBr$: C, 62.51; H, 4.90; N, 4.86. Found[10]: C, 62.32; H, 4.88; N, 4.85.

The picrate formed yellow needles from acetic acid–ethanol, m.p. 260–261°.

*Anal.* Calcd. for $C_{21}H_{16}N_4O_7$: C, 57.80; H, 3.70; N, 12.84. Found[10]: C, 57.77; H, 3.66; N, 12.63.

**1-Acetonyl-2-(3-tolyl)-pyridinium Iodide (VIII).**—Although the best over-all yield of 7,10-dimethylphenanthridizinium bromide (IX) could be obtained by omitting the crystallization of the crude quaternization product (VIII), it was found possible to isolate VIII in a crystalline condition. The crude glass obtained by purification of the quaternization product was triturated with ethyl acetate and the solid thus obtained was crystallized from ethanol–ether as large irregular amber colored crystals, m.p. 128–131°.

*Anal.* Calcd. for $C_{15}H_{16}INO$: C, 51.00; H, 4.57; N, 3.97. Found[10]: C, 50.70; H, 4.77; N, 3.80.

The picrate crystallized from ethanol as yellow needles, m.p. 156.5–158°.

*Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: C, 55.52; H, 3.99; N, 12.33. Found: C, 55.72; H, 4.13; N, 12.62.

**1-Acetonyl-3-hydroxy-2-phenylpyridinium Bromide (XVII).**—One gram of 3-hydroxy-2-phenylpyridine[11] (XVI) in 25 ml. of dry reagent grade acetone was refluxed for 23

(5) Unlike a comparable cyclization in the carbocyclic system [C. K. Bradsher, F. C. Brown and P. H. Leake, THIS JOURNAL, **79**, 1471 (1957)] the product gave no evidence of the formation of isomers.

(6) It is recognized that the hydroxyl group would offer less steric hindrance than methyl and that a planar model of the cyclization product XVIII can be constructed.

(7) Except as indicated all analyses were by Micro-Tech Laboratories, Skokie, Ill. A few of the melting points have been taken in sealed capillaries and the temperature corrected. These are indicated by the abbreviation (cor.).

(8) Sample used in carbon–hydrogen analysis exploded.

(9) J. S. Meek, R. T. Merrow and S. J. Cristol, THIS JOURNAL, **74**, 2667 (1952).

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

(11) H. Leditschke, *Chem. Ber.*, **85**, 202 (1952).

hours with 2 g. of bromoacetone. The crude quaternary salt XVI was precipitated by the addition of ether, the filtrate concentrated, and more product precipitated by addition of ethyl acetate. The quaternary salt XVII recrystallized from ethanol and ether yielded 0.8 g., m.p. 202–205°. By continuing the reflux period for an additional 46 hours it was possible to obtain another 0.35 g. of the salt XVII, making the total yield 1.15 g. (62%). The analytical sample was obtained from ethanol–ether as colorless plates, m.p. 204.5–207.5°.

*Anal.* Calcd. for $C_{14}H_{14}BrNO_2 \cdot {}^1/_2H_2O$: C, 53.01; H, 4.77; N, 4.42. Found[10]: C, 53.01; H, 4.77; N, 4.47.

**1-Hydroxy-7-methylphenanthridizinium Bromide (XVIII).**—A solution of 1.125 g. of 1-acetonyl-3-hydroxy-2-phenylpyridinium bromide (XVII) in 15 ml. of 48% hydrobromic acid was refluxed for 50 hours. Isolated in the usual way, 0.875 g. (85%) of light tan product, m.p. 306–313° dec. (cor.), was obtained. The analytical sample crystallized from ethanol as a cream-colored powder, m.p. 310–313° dec. (cor.); $\lambda_{max}$ 230, 283, 309, 342, 357 and 375 mμ; $\lambda_{min}$ 256, 304, 331, 345 and 365 mμ.

*Anal.* Calcd. for $C_{14}H_{12}NOBr$: C, 57.94; H, 4.17; N, 4.83. Found[10]: C, 57.58; H, 4.12; N, 4.52.

**The picrate** was obtained as yellow crystals from ethanol, m.p. 244–247.5°, which appeared to be solvated.

*Anal.* Calcd. for $C_{20}H_{14}N_4O_8 \cdot C_2H_6O$: C, 54.54; H, 4.16. Found[10]: C, 54.77; H, 3.99.

**10-Methoxy-7-methylphenanthridizinium Picrate (XV).**[12]—The quaternization of 2-(3-methoxyphenyl)-pyridine[13] with iodoacetone (III) was carried out at room temperature over a period of 10 days. The iodide XIV was converted to the chloride in the usual way and cyclization was effected by refluxing the salt for 3 minutes with 48% hydrobromic acid. The product which was recrystallized from alcohol and obtained in an over-all yield of 50% is believed to be 10-methoxy-7-methylphenanthridizinium bromide, m.p. 283° dec. The bromide was converted to the picrate XV which crystallized from acetone as very fine yellow needles, m.p. 232–234° dec.[14]

*Anal.* Calcd. for $C_{21}H_{16}N_4O_8$: C, 55.75; H, 3.57. Found: C, 55.58; H, 3.52.

**1-Acetonyl-2-(3-methoxyphenyl)-pyridinium Picrate (XV).**—A sample of the crude 1-acetonyl-2-(3-methoxyphenyl)-pyridinium iodide obtained in the previous experiment was converted to the **picrate XV** which formed feathery yellow needles, m.p. 150–150.5°[14] (with previous softening).

*Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: C, 53.62; H, 3.85. Found: C, 53.84; H, 3.79.

(12) This preparation as well as that following was carried out by Dr. Leo E. Beavers.

(13) J. W. Haworth, I. M. Heilbron and D. H. Hey, *J. Chem. Soc.*, 358 (1940).

(14) Capillary melting point (uncorrected).

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[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, UNION CARBIDE CHEMICALS COMPANY]

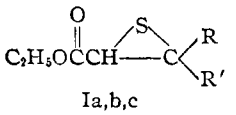
# The Reaction of Glycidic Esters with Thiourea in Aqueous Sulfuric Acid Solution

BY JOHN A. DURDEN, JR., HARRY A. STANSBURY, JR., AND WILLIAM H. CATLETTE

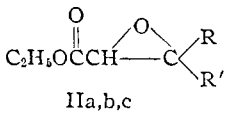
RECEIVED SEPTEMBER 27, 1958

The reaction of glycidic esters with thiourea has been studied in the presence of aqueous sulfuric acid. With ethyl 2,3-epoxy-3-methylvalerate the reaction proceeded to form ethyl 2,3-epithio-3-methylvalerate in low yield. This is apparently the first reported synthesis of an α,β-epithioester. The reaction proceeded with less substituted glycidic esters to produce either 2-amino-2-thiazolin-4-ones or the dihydroxyesters resulting from hydration of the epoxide. The probable mechanisms involved in the formation of these products are discussed.

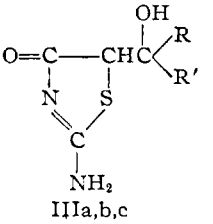
Recent work in this Laboratory has made the preparation of α,β-epithioesters (I) from the corresponding glycidic esters (II) of interest. Apparently no α,β-epithioester has been described, but



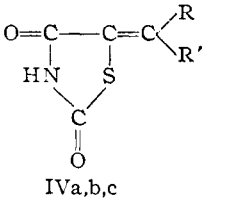
Ia,b,c



IIa,b,c



IIIa,b,c



IVa,b,c

a, R = $CH_3$, R′ = H; b, R = R′ = $CH_3$; c, R = $CH_3$, R′ = $C_2H_5$

several syntheses of episulfides from epoxides have been reported in the literature.[1–4]

Culvenor, *et al.*,[2] have reported the synthesis of episulfides by the reaction of epoxides with thiourea in either anhydrous or aqueous methanol. A group led by Culvenor[5] has also reported an attempted synthesis of Ib by action of thiourea on ethyl 2,3-epoxy-3-methylbutyrate (IIb). The product obtained in the reaction was shown by them to be 2-amino-5-(1-hydroxy-1-methylethyl)-2-thiazolin-4-one (IIIb).

Bordwell and Anderson[3] have shown that the use of mineral acid in the reaction of thiourea with epoxides followed by neutralization of the reaction mixture with base resulted in enhanced yields of episulfides.

## Discussion and Results

The application of the method of Bordwell and Anderson[3] to the preparation of α,β-epithioesters from glycidic esters has now been studied. Using the alkyl-substituted glycidic esters, ethyl 2,3 epoxybutyrate (IIa), ethyl 2,3-epoxy-3-methylbutyrate (IIb) and ethyl 2,3-epoxy-3-methylvalerate (IIc), three different types of products were formed.

When ethyl 2,3-epoxybutyrate (IIa) was treated with thiourea–sulfuric acid mixture there was obtained, as the only isolable product, a white solid which was shown to be 2-amino-5-ethylidene-2-thiazolin-4-one (Va). This compound was synthe-

(1) E. E. van Tamelen, THIS JOURNAL, **73**, 3444 (1951).

(2) C. C. J. Culvenor, W. Davies and W. E. Savige, *J. Chem. Soc.*, 4480 (1952).

(3) F. G. Bordwell and H. M. Anderson, THIS JOURNAL, **75**, 4959 (1953).

(4) C. C. J. Culvenor, W. Davies and K. H. Pausacker, *J. Chem. Soc.*, 1050 (1946).

(5) C. C. J. Culvenor, W. Davies, J. A. MacLaven, P. F. Nelson and W. E. Savige, *ibid.*, 2573 (1949).