Chlorate analyses were done by the following procedure. An aliquot (20 ml.) was transferred to a beaker containing excess (50 ml.) 0.1 *N* ferrous ammonium sulfate. The mixture was heated to boiling in an atmosphere of carbon dioxide. On cooling, the mixture was titrated with 0.1 *N* permanganate. The end point was determined electrometrically using a Beckman portable pH meter with a silver indicator electrode.

After 4 hr. of illumination, only 5% of the available chloric acid had been consumed. The original concentration of chloric acid (2 equiv./A.G.U.) was considerably greater than the chloric acid concentration that would be generated by comparable illumination of chlorine water (only 0.0034 mole of chloric acid was produced when 3.0 l. of 0.103 *N* chlorine water was illuminated for 5 hr. at pH 1.5 and 10°). These observations indicate that chloric acid is not a significant intermediate in the light-catalyzed chlorine–starch oxidation.

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Acridizinium Ion Chemistry. IV.[1] Oxidation with Nitric Acid

CHARLES K. BRADSHER AND MARVIN W. BARKER[2]

Department of Chemistry, Duke University, Durham, North Carolina

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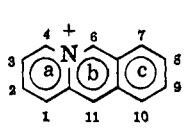
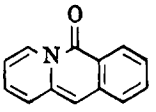
Oxidation of the acridizinium nucleus by nitric acid results in attack at ring b when no strong activating groups are present, yielding 2-(2-carboxy-4-nitrobenzoyl)pyridines. Oxidation with nitric acid of an acridizinium salt containing one or more hydroxyl or methoxyl groups in ring c, results in degradation of ring c, and the formation of a betaine of 2,3-dicarboxyquinolizinium hydroxide.

Although the acridizinium, or benzo[*b*]quinolizinium ion (I) has been known since 1954,[3] little is known about its behavior on oxidation. It has been stated[3] that oxidation of the ion (I) in alkaline permanganate yielded phthalic acid, while more recently Paquette[4] has shown that alkaline ferricyanide solution can convert the



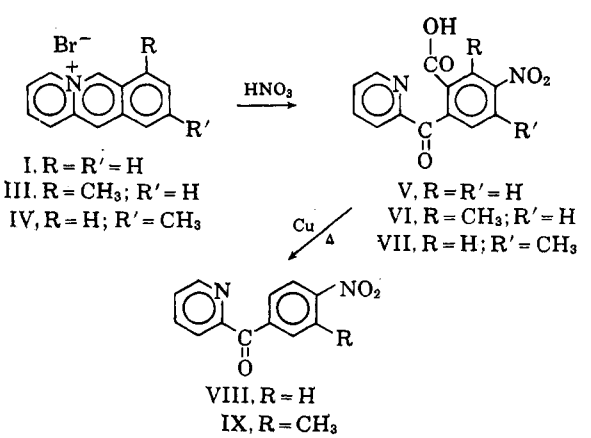
I



II

acridizinium ion to an amide (II). Since it is known[1,5] that the acridizinium ion in alkaline solution exists almost entirely as the pseudobase, both of the previous oxidation attempts could probably best be described as oxidation of the pseudobase.

It was felt that oxidations carried out in an *acidic* medium might lead to new and interesting results, and in this paper are described our experiments using nitric acid. When acridizinium bromide (I) was heated for 3 hr. at 100° with 12 *M* nitric acid, the product was an acid, the composition of which suggested that nitration as well as oxidation had occurred. Decarboxylation of the acid gave the known 2-(4-nitrobenzoyl)pyridine (VIII) and established the structure of the acid as V.

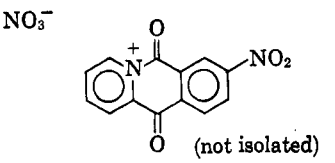


I, R = R′ = H
III, R = CH_3; R′ = H
IV, R = H; R′ = CH_3

V, R = R′ = H
VI, R = CH_3; R′ = H
VII, R = H; R′ = CH_3

VIII, R = H
IX, R = CH_3

The oxidation may be considered to be similar to that of the attack of nitric acid on anthracene to yield anthraquinone. The intermediate acylammonium salt (X) would be expected to hydrolyze rapidly to the keto acid V. The same nitroketo acid was obtained (25% yield) with even quite dilute (3 *M*) nitric acid. It is not certain whether nitration precedes oxidation, but it is perhaps significant that nitration has occurred in what corresponds to position 8, theoretically one of the least electron-deficient of the acridizinium nucleus.[6]



X

The oxidation of the 7-methyl- (III) and 9-methylacridizinium (IV) salts[3] likewise afforded nitroketo acids which by analogy were assigned structures VI and VII. That the assumption concerning the location of the nitro group was correct was shown by the fact that both acids afforded the same nitro ketone (IX) on decarboxylation.

This demonstration of the vulnerability of ring b to nitric acid oxidation made it of interest to try similar experiments in which ring c would be highly activated, and, hence, more likely to be oxidized. When 7,10-dimethoxyacridizinium picrate[7] (XI) was oxidized with 8 *M* nitric acid a very insoluble product was formed. This new substance had a composition indicating the loss of four carbon atoms, and a neutral equivalent cor-

(1) For the preceding communication of this series, see C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **81**, 1938 (1959).

(2) This research was supported by a research grant NSF-G19901 of the National Science Foundation.

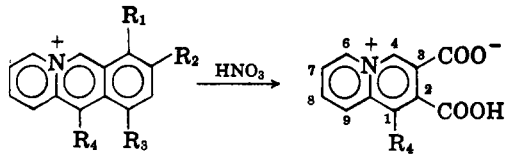
(3) C. K. Bradsher and L. E. Beavers, *Chem. Ind.* (London), 1394 (1954); C. K. Bradsher and L. E. Beavers, *J. Am. Chem. Soc.*, **77**, 4812 (1955).

(4) L. A. Paquette, *Chem. Ind.* (London), 1292 (1962).

(5) J. H. Saylor and J. G. Frost, unpublished spectrographic data.

(6) Position 8 is remote from the charged nitrogen atom and, unlike neighboring positions 7 and 9, cannot (by charge delocalization) become the site of a positive charge.

(7) C. K. Bradsher and M. W. Barker, *J. Org. Chem.*, **29**, 61 (1964).



XI, $R_1 = R_3 = OCH_3$; $R_2 = R_4 = H$
XII, $R_1 = R_2 = OCH_3$; $R_3 = R_4 = H$
XIII, $R_2 = OH$; $R_2 = R_3 = R_4 = H$
XIV, $R_1 = R_3 = OCH_3$; $R_2 = H$; $R_4 = C_6H_5$
XV, $R_4 = H$
XVI, $R_4 = C_6H_5$

responding to one acidic hydrogen. The ultraviolet absorption spectrum is remarkably like that reported for quinolizinium salts[8] and gives one every reason to believe that the new product is the betaine (XV)[9] of 2,3-dicarboxyquinolizinium hydroxide. The same product XV was obtained by oxidation of 7,8-dimethoxyacridizinium (XII) picrate[10] and 8-hydroxyacridizinium (XIII) bromide.[8]

Although the new betaine (XV) melted with gas evolution, no conditions were found for decarboxylation under conditions leading to the isolation of a product. It was found that 48% hydrobromic acid afforded a salt believed to be 2,3-dicarboxyquinolizinium bromide. The salt obtained by action of concentrated sulfuric acid gave a neutral equivalent indicating that it was 2,3-dicarboxyquinolizinium bisulfate, but was hydrolyzed in solution to yield the betaine (XV).

In order to afford further analytical evidence concerning the terminal ring oxidation, 7,10-dimethoxy-11-phenylacridizinium (XIV) perchlorate was synthesized by extension of a previously described[11] method. The oxidation product had the properties expected for the betaine (XVI) of 1-phenyl-2,3-dicarboxyquinolizinium hydroxide. The oxidation of these activated systems is important in that it has provided the first example of the transformation of an acridizinium derivative into a quinolizinium derivative.

Experimental

All analyses were by Dr. Ing. A. Schoeller, Mikoranalytisches Laboratorium, Kronach, West Germany. Melting points were determined using a Laboratory Devices Mel-Temp block and are uncorrected. Infrared spectra were measured in potassium bromide pellets using the Perkin-Elmer Model 21 spectrophotometer. The ultraviolet absorption spectra were recorded using a Cary Model 14 recording spectrophotometer with methanol as the solvent. Wave lengths are recorded in mμ and shoulders are indicated by an asterisk (*).

2-(2-Carboxy-4-nitrobenzoyl)pyridine (V).—To 4 g. of acridizinium bromide (I),[12] 40 ml. of 12 *M* nitric acid was added in one portion. After the vigorous reaction (red-brown fumes) had subsided, the mixture was heated on the steam bath for 3 hr. The acid was removed under reduced pressure (aspirator) leaving a yellow residue which was crystallized from acetic acid–water, 1.76 g. (43%), m.p. 218.5–221° dec. Recrystallization afforded colorless needles, m.p. 225–227° dec. The infrared spectrum showed a band in the carbonyl region at 5.95 μ.

Anal. Calcd. for $C_{13}H_8N_2O_5$: C, 57.36; H, 2.96; N, 10.29; neut. equiv., 272. Found: C, 56.93; H, 2.96; N, 10.02; neut. equiv., 266.

Oxidation of 4 g. of acridizinium bromide (I) with 40 ml. of 3 *M* nitric acid gave the same acid (V) in 25% yield.

2-(4-Nitrobenzoyl)pyridine (VIII).—A mixture of the acid (0.5 g.) and copper powder (0.5 g.) was heated for 2 hr. at 220°. The residue was vacuum distilled and the distillate crystallized from ethanol, 0.16 g. (35%), m.p. 96–98°. Recrystallization gave the pure product as colorless needles, m.p. 99–99.5° (lit.[13] m.p. 99–100°).

Anal. Calcd. for $C_{12}H_8N_2O_3$: C, 63.15; H, 3.53. Found: C, 63.14; H, 3.59.

The phenylhydrazone was prepared according to the method of Koenigs, Mensching, and Kirsch[13] as short red needles, m.p. 170–172° (lit.[13] m.p. 171°).

2-(2-Carboxy-3-methyl-4-nitrobenzoyl)pyridine (VI).—The oxidation of 4 g. of 7-methylacridizinium bromide (III)[3] was carried out as in the case of the lower homolog (I) except that the crude product was taken up in ether and the ethereal solution extracted with 3% sodium hydroxide in three portions. The basic solution was acidified to pH 6 with hydrochloric acid. The acidified solution was then extracted with ether and the ethereal solution washed with water and dried. Concentration of the ether solution gave 1.2 g. (29%) of solid, m.p. 176–180°. Recrystallization of the product from ether gave colorless needles, m.p. 190.5–192°.

Anal. Calcd. for $C_{14}H_{10}N_2O_5$: C, 58.74; H, 3.52; N, 9.79. Found: C, 58.94; H, 3.50; N, 9.57.

Phenylhydrazone of 2-(3-Methyl-4-nitrobenzoyl)pyridine (IX).—Acid VI (0.4 g.) was heated for 3.5 hr. at 185° with an equal weight of copper powder. On vacuum distillation of the residue too little of ketone IX was obtained for satisfactory isolation as such, and the crude product in acetic acid was converted to the phenylhydrazone. Recrystallization of the phenylhydrazone from ethanol gave yellow needles, m.p. 149–151°, with loss of solvent at 130°.

Anal. Calcd. for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86. Found: C, 68.46; H, 4.80; N, 16.51.

2-(2-Carboxy-4-nitro-5-methylbenzoyl)pyridine (VII).—The oxidation of 4 g. of 9-methylacridizinium bromide (IV)[3] was carried out exactly as in the case of the lower homolog (I). A colorless powder, 2 g. (46%), was obtained, m.p. 203–206° dec. Recrystallization of the product from dilute acetic acid afforded colorless needles, m.p. 220.5–221° dec.

Anal. Calcd. for $C_{14}H_{10}N_2O_5$: C, 58.74; H, 3.52; neut. equiv., 286. Found: C, 58.53; H, 3.53; neut. equiv., 283.

2-(3-Methyl-4-nitrobenzoyl)pyridine (IX).—The decarboxylation of acid VII (0.5 g.) was carried out as in the previous cases and the distillate crystallized from ethanol as colorless needles, 0.06 g. (15%), m.p. 89–90°.

Anal. Calcd. for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.57. Found: C, 64.65; H, 4.11; N, 11.67.

The phenylhydrazone was identical with that obtained from the decarboxylation product of VI (mixture melting point).

Betaine (XV) of 2,3-Dicarboxyquinolizinium Hydroxide. A. By Oxidation of 7,10-Dimethoxyacridizinium (XI) Picrate.[7]—To 8.7 g. of 7,10-dimethoxyacridizinium picrate, 120 ml. of 8 *M* nitric acid was added in one portion. After the initial reaction had subsided (about 1 min.), the solution was heated on the steam bath for 3 hr. The nitric acid was removed under reduced pressure (aspirator), and the residue crystallized from a large volume of acetic acid, 2.86 g. (71%), 260° dec. (gas evolution).

B. Oxidation of 7,8-Dimethoxyacridizinium (XII) Picrate.—Oxidation of 0.45 g. of 7,8-dimethoxyacridizinium picrate as described in A yielded 0.1 g. (50%) of product, 260.5° dec. (with gas evolution). The infrared spectrum was identical with that of the product XV obtained from XI.

C. By Oxidation of 8-Hydroxyacridizinium (XIII) Bromide.—The oxidation of 6 g. of 8-hydroxyacridizinium bromide was carried out as in A and B except that 12 *M* nitric acid was used, 0.58 g. (12%), 261° dec. (gas evolution). The infrared absorption spectrum was identical with spectra obtained for products from A and B. The analytical sample was a colorless microcrystalline powder, λ_{max} 327* mμ (log ε 4.04) and 337 (4.15) (trifluoroacetic acid).

Anal. Calcd. for $C_{11}H_7NO_4 \cdot 0.25\ H_2O$: C, 59.60; H, 3.41; N, 6.32; neut. equiv., 221.5. Found: C, 59.72; H, 3.58; N, 6.04; neut. equiv., 208.

2,3-Dicarboxyquinolizinium Bromide.—In an attempted decarboxylation, a sample of the betaine (XV) was refluxed for 24

(8) R. M. Acheson and G A. Taylor, *J. Chem. Soc.*, 1691 (1960).

(9) The formulation of the betaine as XV, with the 3-carboxyl rather than the 2-carboxyl ionized, is based upon minimum charge separation, but is not supported by experimental evidence.

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

(11) C. K. Bradsher and T. W. G. Solomons, *ibid.*, **81**, 2550 (1959).

(12) C. K. Bradsher, T. W. G. Solomons, and F. R. Vaughan, *J. Org. Chem.*, **25**, 757 (1960).

(13) E. Koenigs, H. Mensching, and P. Kirsch, *Ber.*, **59**, 1717 (1926).

hr. with 48% hydrobromic acid. At the end of this period the acid was removed and the residue digested with ethanol. Filtration of the suspension removed some unchanged starting material, but concentration of the filtrate afforded a small amount of a new compound, m.p. 300° dec. Recrystallization of this substance from ethanol–ethyl acetate afforded a colorless microcrystalline powder, m.p. 301.5° dec.

Anal. Calcd. for $C_{11}H_8BrNO_4 \cdot 0.5\ H_2O$: C, 43.01; H, 2.95; N, 4.59. Found: C, 42.73; H, 3.09; N, 4.62.

2,3-Dicarboxyquinolizinium Bisulfate.—A solution of the betaine (XV, 0.1 g.) in concentrated sulfuric acid (6 ml.) was heated for 1 hr. at 170°. The solution was cooled and slowly added to 30 ml. of cold ether. Collection of the colorless precipitate gave 0.1 g. (71%) of a very hygroscopic material, m.p. 234–235° dec.

Anal. Calcd. for $C_{11}H_9NSO_8$: neut. equiv., 105. Found: neut. equiv., 104.

When the bisulfate was washed with water or barium chloride solution (colorless precipitate), the betaine (XV) was recovered.

7,10-Dimethoxy-11-phenylacridizinium (XIV) Perchlorate.—A solution of 2,5-dimethoxybenzyl bromide[14] (15 g.) and 2-benzoylpyridine (12.8 g.) in dimethylformamide (15 ml.) was allowed to stand for 5 days at room temperature. When ether was added an oil separated. The ether was decanted and the oil transferred to a round bottom flask by use of methanol. After evaporation of the methanol, 90 g. of polyphosphoric acid was added, and the mixture stirred and heated at 90–100° for an hour. The acid was cooled and hydrolyzed by addition of ice. To the filtered phosphoric acid solution, an excess of 35% perchloric acid was added. The precipitate was collected and recrystallized from ethanol as orange needles, 9.6 g. (36%), m.p. 254–255° dec.; λ_{max} 250 mμ (log ε 5.08), 323* (3.31), 409 (4.02), and 455* (3.84).

Anal. Calcd. for $C_{21}H_{18}ClNO_6$: C, 60.65; H, 4.36; N, 3.37 Found: C, 60.64; H, 4.45; N, 3.51.

The **picrate** crystallized from ethanol as orange needles, m.p. 197–198° dec.

Anal. Calcd. for $C_{27}H_{20}N_4O_9$: C, 59.55; H, 3.73; N, 10.29. Found: C, 59.60; H, 3.64; N, 10.29.

Betaine (XVI) of 1-Phenyl-2,3-dicarboxyquinolizinium Hydroxide.—Five grams of 7,10-dimethoxy-11-phenylquinolizinium (XIV) perchlorate was oxidized in the usual way with 8 *M* nitric acid. The residue left by removal of most of the nitric acid was taken up in 50 ml. of water and the water evaporated *in vacuo*. After repetition of the process several times the product was allowed to crystallize from about 20 ml. of water, 1.78 g. (51%), 203° dec. (with gas evolution). Recrystallization of the product from methanol gave colorless needles, 210.5° dec. (gas evolution); λ_{max} 227 mμ (log ε 4.26), 255 (4.22), 332* (3.96), and 342 (4.12).

Anal. Calcd. for $C_{17}H_{11}NO_4$: C, 69.61; H, 3.78; N, 4.78. Found: C, 69.72; H, 3.86; N, 5.10.

(14) A. T. Shulgin and E. M. Gal, *J. Chem. Soc.*, 1316 (1953).

Hexofuranosyl Nucleosides from Sugar Dithioacetals[1]

M. L. WOLFROM, P. MCWAIN,[2] R. PAGNUCCO,[3] AND A. THOMPSON

Department of Chemistry, The Ohio State University, Columbus 10, Ohio

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Improved procedures were found for the partial hydrolysis of the diethyl dithioacetals of D-glucose and D-galactose (I) to their tetra-*O*-acetyl-1-thio-α-D-glycofuranosides (IIa and II). The acetylated thioglycoside of D-glucofuranose (IIa) was converted with bromine to tetra-*O*-acetyl-D-glucofuranosyl bromide (sirup) which was condensed with the chloromercuri derivative of 2,6-diacetamidopurine (IV) to give the acetylated nucleoside and this on partial deacetylation yielded 2-acetamido-9-β-D-glucofuranosyladenine (VIa). Tetra-*O*-acetyl-β-D-galactofuranosyl chloride (III), similarly prepared from the dithioacetal (I), was transformed to 9-β-D-galactofuranosyladenine (VIII, dimorphous), 2-acetamido-9-β-D-galactofuranosyladenine (VI), and 2,6-diamino-9-β-D-galactofuranosylpurine (VII).

In the pentose series, a sugar may be forced into its furanose form by suitable blocking of the terminal position. This procedure is not applicable in the hexose series and special methods are required to obtain furanoside derivatives. Haworth[4] and associates utilized carbonate esters in several successful syntheses of hexofuranosides. In the galactose structure, a furanose pentaacetate is obtainable by direct acetylation of the sugar and is separable from the pyranose pentaacetate by laborious fractional crystallization methods.[5] Todd and co-workers[6] have reported a crude picrate of 9-β-D-galactofuranosyl-2-methylthioadenine, prepared by using tetra-*O*-acetyl-β-D-galactofuranose derived from such an acetylation of D-galactose.

In the glucose series, the isopropylidene cyclic acetals (1,2 and 1,2:5,6)[7] possess a furanose ring and have been utilized in the synthesis of 9-β-D-glucofuranosyladenine[8] as well as 6-deoxy-D-glucofuranosyl[9] and 6-deoxy-6-iodo-L-iodofuranosyl[10] nucleosides. The nucleosides of L-rhamnofuranose,[11] 6-deoxy-D-allofuranose,[12] and 6-deoxy-L-talofuranose[13] were likewise synthesized utilizing 2,3-*O*-isopropylidene-L-rhamnofuranose[14] as the initial source of the hexofuranose.

Most aldose dithioacetals undergo partial demercaptalation under suitable conditions to form thioglycofuranosides.[15] Ethyl 1-thio-α-D-glucofuranoside has been obtained in 63% yield[16] from D-glucose diethyl dithioacetal by partial demercaptalation with aqueous mercuric chloride and mercuric oxide and it undergoes

(1) Preliminary communication, Abstracts, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962, p. 7D.

(2) Supported by Grant CY3232 (C3), Department of Health, Education, and Welfare, U. S. Public Health Service, National Institutes of Health, Bethesda 14, Md. (Ohio State University Research Foundation Projects 759C and E).

(3) Fellow under support of the National Science Foundation Grant NSF-G14629 (Ohio State University Research Foundation Project 1178).

(4) W. N. Haworth, "The Constitution of Sugars," Longmans Green and Co., New York, N. Y., 1929, p. 52.

(5) C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, **38**, 1223 (1916); H. H. Schlubach and V. Prochownick, *Ber.*, **63**, 2298 (1930); R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *J. Am. Chem. Soc.*, **73**, 3742 (1951).

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(9) E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1753 (1958).

(10) E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1757 (1958).

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(13) E. J. Reist, L. Goodman, and B. R. Baker, *ibid.*, **80**, 5775 (1958).

(14) P. A. Levene and I. E. Muskat, *J. Biol. Chem.*, **106**, 761 (1934).

(15) W. Schneider and J. Sepp, *Ber.*, **49**, 2054 (1916); W. Schneider, J. Sepp, and O. Stiehler, *ibid.*, **51**, 220 (1918); J. W. Green and E. Pacsu, *J. Am. Chem. Soc.*, **59**, 1205 (1937); M. L. Wolfrom, S. W. Waisbrot, D. I. Weisblat, and A. Thompson, *ibid.* **66**, 2063 (1944).

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