methanol, and then with five 10-ml. portions of distilled water. The combined filtrate was concentrated in vacuum at 40° and traces of water removed from the residue by repeated evaporation *in vacuo* with small quantities of absolute ethanol. Paper chromatography using acetone–butanol–water (2:2:1) as mobile phase revealed the presence of a high concentration of D-ribose (R_f 0.41) as well as traces of two nonreducing components (R_f 0.33 and 0.73) which could be revealed by periodic acid–benzidine coloration. Confirmation of the identity of the main component as D-ribose was obtained by means of comparative paper chromatography employing various other mobile phases as well as by conversion of the crude oily product into D-ribose di-*n*-propyl dithioacetal[11] (m.p. 81–82°).

2,3,4,5-Tetra-O-acetyl-D-ribose Dibenzyl Acetal (II). (a).—2,3,4,5-Tetra-O-acetyl-D-ribose diethyl dithioacetal[12] (6.37 g., 15 mmoles) was demercaptalated in the presence of yellow mercuric oxide (9.72 g., 45 mmoles), anhydrous calcium sulfate (15 g.), and anhydrous benzyl alcohol (100 ml.) by the addition of a solution of mercuric chloride (10.2 g., 37.5 mmoles) in 200 ml. of benzyl alcohol as described previously. After removal of the chloroform an oily residue was obtained. Traces of benzyl alcohol were removed by repeatedly dissolving the product in 25 ml. of ethanol and precipitating the oil with 400 ml. of water at 40°. Finally the product was repeatedly evaporated to dryness with small quantities of absolute ethanol to remove traces of water. The oily product, dried at 50° and 0.5 mm. for 3 hr., was soluble in methanol, ethanol, chloroform, ether, etc., and insoluble in water and petroleum ether. $[\alpha]^{20}D$ + 11.2 (*c* 10, methanol); $\lambda_{max}^{CH_3OH}$ 258 mμ (a_m 346); λ_{max}^{film} 5.72, 8.20, 9.52 μ.

Anal. Calcd. for $C_{27}H_{32}O_{10}$: C, 62.78; H, 6.25. Found: C, 63.88; H, 6.32.

After unsuccessful attempts to purify the material by crystallization, the product was further characterized by conversion into the crystalline D-ribose dibenzyl acetal by deacetylation.

(b).—D-Ribose di-*n*-propyl dithioacetal[11] was acetylated as described by Zinner[12] for other D-ribose dithioacetals and 2,3,4,5-tetra-O-acetyl-D-ribose di-*n*-propyl dithioacetal obtained as an oil which could not be crystallized. Upon demercaptalation of the product in benzyl alcohol as described previyusly, 2,3,4,5-tetra-O-acetal-D-ribose dibenzyl acetal was obtained as an oil and was shown to be identical to the product obtained from 2,3,-4,5-tetra-O-acetyl-D-ribose diethyl dithioacetal (a), by infrared spectroscopy.

D-Ribose Dibenzyl Acetal (III).—2,3,4,5-Tetra-O-acetyl-D-ribose dibenzyl acetal (7 g.) was dissolved in 90 ml. of anhydrous methanol in a 250-ml. round-bottomed flask fitted with a reflux condenser and a calcium chloride drying tube. Barium methylate solution (3 ml., 1.7 *N*) in anhydrous methanol was added, the mixture shaken well, and heated under reflux on a water bath for 2 hr., cooled to room temperature, and carbon dioxide bubbled through. The precipitated barium carbonate was filtered off and the yellow filtrate decolorised with activated charcoal. The solution was taken to dryness *in vacuo* at 40° and the oily residue redissolved in 50 ml. of hot benzene. Upon concentration of the benzene solution the product crystallized. A seeding crystal was retained and the product recrystallized from benzene; yield 3.0 g. (96%); m.p. 91–92°; $[\alpha]^{20}D$ + 10.0 (*c* 10, methanol); $\lambda_{max}^{CH_3OH}$ 258 mμ (a_m 325); λ_{max}^{KBr} 2.94, 9.60 μ.

Anal. Calcd. for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.39; H, 7.12.

Hydrogenolysis of D-Ribose Dibenzyl Acetal.—D-Ribose dibenzyl acetal was hydrogenated in the presence of 2 g. of palladized charcoal in 60 ml. of methanol. After 4 hr. 32 ml. of hydrogen had been consumed (calcd. 32.18 ml.; press., 651.6 mm.; temp., 20°). The catalyst was filtered off and the filtrate taken to dryness *in vacuo*. The residue (77 mg., 90% as D-ribose) consisted of a viscous oil. The material was shown to be practically pure D-ribose by comparative paper chromatography using various mobile phases and by conversion into the crystalline D-ribose di-*n*-propyl dithioacetal (m.p. 81–82°).

Acknowledgment.—The authors are indebted to the African Explosives and Chemical Industries Ltd. for a research grant and to the South African Atomic Energy Board for financial Assistance.

(11) H. Zinner, *Ber.*, **83**, 275 (1950).
(12) H. Zinner, *ibid.*, **83**, 418 (1950).

The Halogenation of 8-Hydroxy- and 8-Methoxyacridizinium Salts[1]

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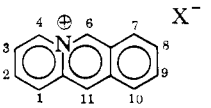
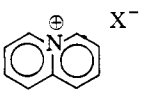
The aromatic nature of the acridizinium ion (I) results in an extensive delocalization of the positive charge. A consequence is that the system undergoes nucleophilic reactions,[2] but does not easily undergo electrophilic substitution. It has been reported[3] that the related quinolizinium iodides (II) react with bromine in acetic acid to yield dibromoiodides ($R^+IBr_2^-$) rather than substitution products.[4] The present communication describes the first examples of the electrophilic substitution of an acridizinium derivative, the halogenation of 8-hydroxy (III)- and 8-methoxyacridizinium (IV) salts.

The bromination of 8-hydroxyacridizinium bromide

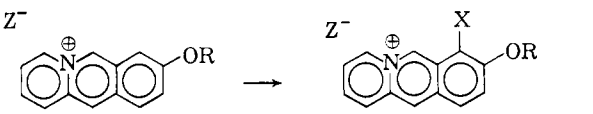


I

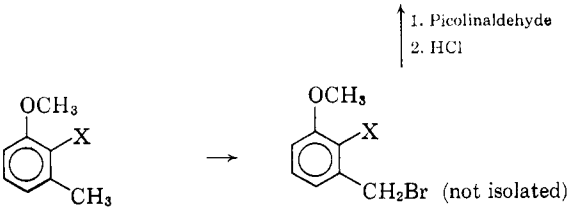


II

(III)[5] was carried out in refluxing acetic acid, using a onefold molar excess of bromine. The product (68% yield) had the composition of a monobromination product. Analogy suggested that bromination had occurred at the 7-position, and the synthesis of the 7-



III. R = H, Z = Br
IV. R = CH_3, Z = Cl
V. R = H, X = Br
VI. R = H, X = Br, Z = Pic



VII. X = Br
VIII. X = Cl
IX. X = Br
X. X = Cl

bromo-8-hydroxyacridizinium ion was undertaken. The bromination of 2-bromo-3-methoxytoluene[6] (VII) with N-bromosuccinimide gave crude 2-bromo-3-

(1) This research was supported by a research grant (H-2170) from the National Heart Institute, National Institutes of Health.
(2) C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **81**, 1983 (1959).
(3) A. Richards and T. S. Stevens, *J. Chem. Soc.*, 3067 (1958).
(4) G. Jones has succeeded in brominating hydroxyquinolizinium derivatives (private communication).
(5) C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **79**, 6033 (1957).
(6) H. H. Hodgson and H. G. Beard, *J. Chem. Soc.*, **127**, 498 (1925).

methoxybenzyl bromide (IX). The crude quaternary salt formed by reaction of the benzyl bromide (IX) with picolinaldehyde was cyclized by refluxing it for nine hours in hydrochloric acid solution. Since ether cleavage occurred during the long heating, the product was 7-bromo-8-hydroxyacridizinium bromide (V. Z = Br) rather than the corresponding methyl ether. This material was identical in melting point and infrared spectrum with that obtained by direct bromination of 8-hydroxyacridizinium bromide.

The chlorination of 8-methoxyacridizinium chloride[5] (IV) was carried out in dimethylformamide using sulfuryl chloride as the chlorinating agent. The monochlorination product, isolated in 60% yield as the picrate, was demonstrated to be 7-chloro-8-methoxyacridizinium picrate by synthesis from 2-chloro-3-methoxytoluene (VIII). The procedure used was analogous to that used in the synthesis of the 7-bromo-8-hydroxyacridizinium ion (V) except that the cyclization time was limited to three hours so that the 7-chloro-8-methoxyacridizinium ion (VI) was obtained with a minimum amount of ether cleavage.

Experimental

All melting points were taken on the Fisher Johns hot stage and are uncorrected. Except as noted, all analyses were by the Galbraith Laboratories, Knoxville, Tenn.

7-Bromo-8-hydroxyacridizinium Salts (V). (a) By Direct Bromination.—A solution containing 0.45 g. of 8-hydroxyacridizinium bromide[5] in 150 ml. of acetic acid was refluxed for 20 min. with 0.2 ml. of bromine. When the mixture cooled a yellow product was obtained, m.p. 280–295°. Recrystallization from ethanol afforded yellow needles of the **bromide**, m.p. 291–296°, yield, 0.39 g. (68%).

The **picrate**, m.p. 231–233° formed as long needles from ethanol.

(b) From 2-bromo-3-methoxytoluene (VII).—In a flask containing 4.5 g. of 2-bromo-3-methoxytoluene,[6] 3.91 g. of N-bromosuccinimide, and 50 ml. of dry carbon tetrachloride, 0.5 g. of dibenzoyl peroxide was added, and the resulting suspension refluxed for 1 hr. The solid was removed by filtration, and the filtrate concentrated under reduced pressure. A small quantity of benzene was added and removed under reduced pressure. The residual oil (5.33 g.), which consisted chiefly of 2-bromo-3-methoxybenzyl bromide, was dissolved in 20 ml. of methanol and refluxed for 3 hr. with 2.03 g. of picolinaldehyde. The solvent was evaporated under reduced pressure and the residual oil washed with ether. The ether was decanted and the oil taken up in 20 ml. of concentrated hydrochloric acid and the solution refluxed for 9 hr. Removal of the acid under vacuum and recrystallization of the residue from ethanol afforded 2.51 g. (39%) of the **bromide**, m.p. 293–296°. The preparations of the bromide obtained by methods a and b were shown to be identical by mixture melting point determinations and comparison of infrared spectra.

Anal. Calcd. for $C_{13}H_9Br_2NO \cdot H_2O$: C, 41.80; H, 2.95; N, 3.76. Found[7]: C, 42.12; H, 2.96; N, 3.94.

The **picrate** formed as needles from ethanol, m.p. 231–233°. By means of mixture melting point determinations and comparison of infrared spectra, it was shown that this picrate is identical with that obtained by procedure a.

Anal. Calcd. for $C_{19}H_{11}BrN_4O_8$: C, 45.34; H, 2.20; N, 11.14. Found: C, 45.45; H, 2.79; N, 11.52.

7-Chloro-8-methoxyacridizinium Picrate (VI). (a) By Chlorination.—To a solution containing 0.7 g. (0.0028 mole) of 8-methoxyacridizinium chloride in 15 ml. of dry dimethylformamide, in a flask protected by drying tubes, 0.4 g. (0.003 mole), of sulfuryl chloride was added and the solution was warmed for 20 min., after which an additional 0.1 g. of sulfuryl chloride was added, and heating continued for 0.5 hr. longer. After vacuum evaporation of the dimethylformamide the residue was converted to the picrate and crystallized from ethanol as very small yellow needles, m.p. 215–216°, yield 0.81 g. (60%).

(7) Analysis by Dr. Ing. A. Schoeller, Kronach, Germany.

(b) From 2-Chloro-3-methoxytoluene (VIII).—The bromination of 2-chloro-3-methoxytoluene[8] (1.85 g.) was carried out as in the case of the 2-bromo analog (VII). The crude 2-chloro-3-methoxybenzyl bromide (X) was allowed to react with 0.96 g. of picolinaldehyde in refluxing methanol. The crude quaternary salt was cyclized by refluxing it for 3 hr. in 20 ml. of concentrated hydrochloric acid. The crude salt was converted to the **picrate** for purification, m.p. 215–216°. This material was identical in melting point and infrared spectrum with the picrate obtained from the product of the chlorination reaction.

Anal. Calcd. for $C_{20}H_{13}ClN_4O_8$: C, 50.80; H, 2.77; N, 11.85. Found: C, 50.49; H, 2.51; N, 11.57.

(8) G. P. Gibson, *J. Chem. Soc.*, **123**, 1269 (1923).

The Preparation of N,N-Dimethyl- and N,N-Diethylenamines from Ketones

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Recent interest in enamine chemistry[1] prompts the reporting of a simple but useful modification of the Mannich–Davidsen[2] procedure for the preparation from ketones of N,N-dimethyl- and N,N-diethylenamines which previously could not be synthesized readily. The modification involves substituting granular calcium chloride for the normally employed potassium carbonate or calcium oxide to serve as catalyst and dehydrating agent. Although Mannich and Davidsen[2] report the formation of aminals which thermally decompose to the enamine in the reaction of cyclohexanone with piperidine, no evidence for such precursors has been observed in this work. Examination of the ether solution by infrared spectroscopy revealed the presence of the enamine double bond (1640 $cm.^{-1}$) prior to distillative work up. The enamines tabulated were prepared by the general procedure, given in detail for N,N-dimethylamino-1-cyclohexene, of treating the appropriate ketone with either dimethyl- or diethylamine. These enamines were found stable to storage at room temperature in the absence of moisture and oxygen. (See Table I, p. 1398.)

Experimental

Materials.—Commercially available cyclopentanone, cyclohexanone, dimethylamine, diethylamine, anhydrous diethyl ether, and anhydrous 12-mesh calcium chloride were used without further purification.

Dimethylamino-1-cyclohexene.—To a solution of dimethylamine (150 g., 3.4 moles) in anhydrous diethyl ether (400 ml.) was added cyclohexanone (196 g., 2 moles) and 12-mesh calcium chloride (150 g.). The mixture was vigorously stirred at room temperature under a nitrogen atmosphere for 64 hr. The slurry was filtered, and the residue washed with diethyl ether (200 ml.). Evaporation of the ether and fractionation of the residue afforded the desired enamine (108.3 g., 0.87 mole) as a colorless liquid, b.p. 81° (35 mm.). Ninety-four and a half grams (0.97 mole) of cyclohexanone was recovered.

(1) See, for example, the Abstracts from the 140th National Meeting of the American Chemical Society, Chicago, Ill., September 3–8, 1961, "Symposium on Enamine Chemistry," pp. 44Q–46Q, 53Q–56Q.

(2) C. Mannich and H. Davidsen, *Chem. Ber.*, **69**, 2106 (1936).