isolated in 78% yield (14 mg.) by addition of water to the solution, treatment of the solution with ammonium hydroxide, extraction of the precipitate with ether, and recrystallization from pentane of the solid obtained from the ether extract. The oxime prepared from this sample of phenacylpyridine melted at 115–117°.

2-[β-Hydroxy-β-(*o*-boronophenyl)vinyl]pyridine was obtained by addition of sodium hydroxide in 50% alcohol–water to the hydrochloride salt (0.2940 g.), evaporation of the solution to dryness, extraction of the resulting solid with chloroform, and evaporation of the extract. For further purification, the sample was dissolved in methanol and the solution was filtered and taken to dryness. The resulting pale yellow solid charred and decomposed without melting when heated in the range of 230°. The analysis of the material dried at room temperature corresponded to a dihydrate of compound II.

Anal. Calcd. for $C_{13}H_{12}BNO_3 \cdot 2H_2O$: C, 56.3; H, 5.82; N, 5.06. Found: C, 55.9; H, 5.90; N, 4.92.

After the sample had been heated at 65° (1 mm.) for 24 hr., the analysis agreed with that for 2-[β-hydroxy-β-(*o*-boronophenyl)vinyl]pyridine .

Anal. Calcd. for $C_{13}H_{12}BNO_3$: C, 64.7; H, 5.02; N, 5.81. Found: C, 64.5; H, 5.33; N, 5.99.

A semicarbazone derivative was obtained by warming a solution of 86 mg. of compound II, 0.2 g. of semicarbazide hydrochloride, and 0.3 g. of sodium acetate in 4 ml. of ethanol and 2 ml. of water for 15 min. When the solution was cooled, 60 mg. of the yellow crystalline semicarbazone derivative of compound II was obtained, m.p. 169–172°. The analytical sample was dried at 65° (1 mm.) for 8 hr.

Anal. Calcd. for $C_{14}H_{15}BN_4O_3$: C, 56.4; H, 5.07; N, 18.80. Found: C, 56.5; H, 4.88; N, 18.78.

Notes

Reduction of 1-Methyl-3-acylindole Derivatives with Lithium Aluminum Hydride[1]

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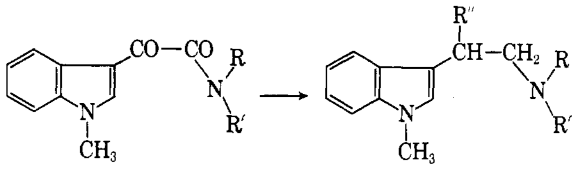
Department of Chemistry, University of Louisville, Louisville, Kentucky, and Department of Organic Chemistry, University of Adelaide, Adelaide, Australia

Received February 1, 1963

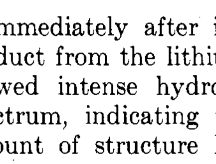
The application of lithium aluminum hydride to the reduction and cyclization of (2–3′-indolylethyl)- or (2–3′-indolyl-2-oxoethyl)pyridinum and isoquinolinium salts has been described in previous papers.[3] This note reports some results obtained in the *ind*-N-methyl series.[4]

The reduction of various 3-acylindoles with lithium aluminum hydride is a well authenticated[5] hydrogenolysis reaction, the 3-alkylindoles being readily obtained. With *ind*-N-methyl-3-acylindoles the reduction has been reported to stop at the intermediate alcohol stage and does not appear to be analogous to the reduction of a disubstituted vinylogous amide. Thus 1,N-dimethyl-3-indoleglyoxamide (I, R = CH_3; R′ = H) and lithium aluminum hydride gave the alcohol[6] II (R = CH_3; R′ = H; R″ = OH). However, conflicting reports have appeared, *e.g.*, the reduction of I (R = R′ = $-CH_2Ph$) with lithium aluminum hydride to give the oxygen-free product[7] II (R = R′ = $-CH_2Ph$; R″ = H); on the other hand, 1-methyl-3-indolylaldehydes have been shown[8] to undergo reduction to 1-methyl-3-hydroxymethyl indoles, in agreement with the former reaction. In attempts to effect the reductive cyclization of 1-[2-(1′-methyl-3′-indolyl)-2-oxoethyl]pyridinium derivatives, no clear-cut results could be obtained and it was decided to investigate the reduction of 1-methyl-3-acetylindole.

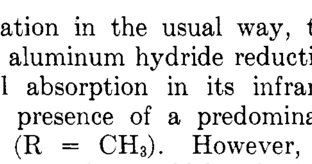


I II

Immediately after isolation in the usual way, the product from the lithium aluminum hydride reduction showed intense hydroxyl absorption in its infrared spectrum, indicating the presence of a predominant amount of structure III (R = CH_3). However, no derivative of the alcoholic function could be obtained and, on standing, the crude product developed an odor of acetaldehyde. This was of interest in view of the reported[8] decomposition of 1-methyl-3-hydroxymethylindole (III, R = H) to formaldehyde and the diindolylmethane IV (R = H). However, this decomposition pathway was not followed in the case of our 1-(1′-methyl-3′-indolyl)ethanol. On distillation or on boiling with water it underwent ready dehydration to 1-methyl-3-vinylindole, which immediately polymerized to poly-(1-methyl-3-vinylindole). There was no evidence of the formation of an appreciable amount of 1,1-di(1′-methyl-3′-indolyl)ethane (IV, R = CH_3), authentic



III



IV

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[1] Regarded as Part IV in the series: Synthetic Experiments Related to the Indole Alkaloids.

[2] Recipient of a C.S.I.R.O. Senior Postgraduate Studentship, 1961–1962.

[3] Part III: K. T. Potts and D. R. Liljegren, *J. Org. Chem.*, **28**, 3066 (1963).

[4] This work was supported in part by PHS Grant H-6475 from the National Heart Institute, Public Health Service.

[5] E. Leete and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

[6] M. E. Speeter, U. S. Patent 2,815,734; *Chem. Abstr.*, **52**, 12923*f* (1958).

[7] A. Buzas, C. Hoffman, and G. Regnier, *Bull. soc. chim. France*, 643 (1950).

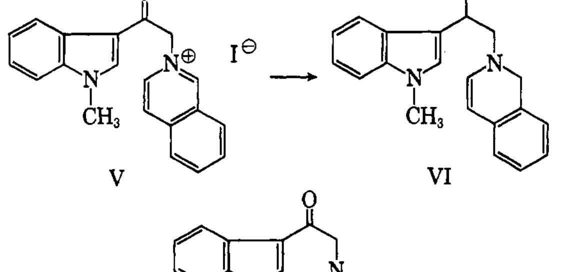
[8] E. Leete, *J. Am. Chem. Soc.*, **81**, 6023 (1959).

samples of which were prepared by (1) methylation of 1,1-di(3'-indolyl)ethane, and (2) from 1-methylindole, paraldehyde, and zinc chloride. The poly(1-methyl-3-vinyl)indole structure was assigned on the basis of the following evidence. Analytical data established the empirical formula $(C_{11}H_{11}N)_n$, supported by complete absence of hydroxyl absorption in the infrared spectrum. The ultraviolet spectrum showed, in addition to the peak characteristic of 1-methylindole, a broad shoulder at 2670 Å.; 1-methyl-3-vinylindoles have been found[9] to exhibit maxima in the region of 2650 Å. The isolation of a small amount of acetaldehyde can be most simply attributed to a retroaldol type reaction, probably catalyzed by the alkali of the glass though we were unable to establish the conditions under which this was the major decomposition pathway.

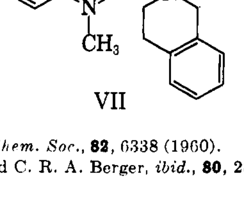
The conjugate base of the indole system must assist in the hydrogenolysis of the coordinated oxygen atom of the 3-ketone function and, as no conjugate base can be formed in the case of the 1-methylindole products, the reduction was next carried out in a system in which the carbon–oxygen bond was weakened by coordination with a stronger Lewis acid such as aluminum chloride. 1-Methyl-3-acetylindole was accordingly reduced with lithium aluminum hydride–aluminum chloride mixture and, as expected, 1-methyl-3-ethylindole was isolated in excellent yield.

Parallel results were also obtained with similar arylmethyl ketones such as 3,4-dimethoxyacetophenone. Reduction with lithium aluminum hydride gave 1-(3,4-dimethoxyphenyl)ethanol, which readily lost water on distillation forming 3,4-dimethoxystyrene, characterized as the dibromide. With lithium aluminum hydride and aluminum chloride, the course of the reaction was altered to yield 3,4-dimethoxyethylbenzene. This is analogous to the hydrogenolysis[10] of benzophenone to diphenylmethane, and acetophenone to ethylbenzene.

With this more definite knowledge of the behavior of 1-methyl-3-acetylindole toward lithium aluminum hydride, a series of reductions of the salt 2-[2-(1'-methyl-3'-indolyl)-2-oxoethyl]isoquinolinium iodide (V) was carried out. Despite repeated attempts using lithum aluminum hydride alone or mixed with aluminum chloride, no pure products could be isolated when tetrahydrofuran was used as the solvent. Spectral evidence indicated that in the majority of fractions at least partial reduction had occurred and it is likely that the large number of fractions formed is due to the many ways in which a highly reactive intermediate such as VI can undergo further reaction. The use of dioxane as solvent gave an intermediate reaction complex that was almost insoluble so that at no stage was the reaction mixture homogeneous. It is interesting that the main product isolated from this system was 2-[2-(1'-methyl-3'-indolyl)-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline (VII), besides unidentified oily fractions similar to those already mentioned. The identity of this product was indicated by analytical and spectral data. The infrared spectrum showed main absorption bands at 3100, 3020, 2911, 2805, and 1620 cm.$^{-1}$, and the ultraviolet spectrum showed the presence of a 1-methyl-3-acylindole chromophore[11] (λ_{max} 248, 306 mμ). The n.m.r. spectrum[12] was not complex, showing main peaks at 7.1 τ (N–CH_3), 6.26 and 6.23 τ (–CH_2– peaks), and aromatic protons. These results indicated that the 3-acylindole group had not undergone hydrogenolysis and that the pyridine ring system had been reduced to the tetrahydro stage. Confirmation was obtained by the synthesis of VII from the chloride of the salt V by reduction with Adam's catalyst in acetic acid solution. The failure of the 3-acylindole function to undergo hydrogenolysis in this reaction can be attributed to a large extent to the heterogeneous reaction medium.



V VI



VII

The results obtained with these 1-methylindole compounds indicate the desirability of working with the unmethylated series. The cyclized products may then be readily converted into the methyl-substituted series with sodamide and methyl iodide in liquid ammonia.[13,14]

Experimental[15]

Reduction of 1-Methyl-3-acetylindole with Lithium Aluminum Hydride. Poly(1-methyl-3-vinylindole).—1-Methyl-3-acetylindole[16] (6.0 g., 0.03 mole) and a solution of lithium aluminum hydride (4.0 g., 0.11 mole) in dry tetrahydrofuran (300 ml.) were heated together under reflux for 4.5 hr. After decomposition of the reaction complex with water, the reaction mixture was extracted with ether and the ether solution dried (sodium sulfate). Removal of the solvent left a pale yellow oil (6 g.), ν_{OH} 3400 cm.$^{-1}$ (broad, very intense). Extraction of the crude product, which had an odor of acetaldehyde, with cold water and treatment of the aqueous extract with Brady's reagent gave a yellow precipitate of acetaldehyde 2,4-dinitrophenylhydrazone, m.p. 168°, alone and when mixed with an authentic sample.[17] The infrared spectra of the two samples were superimposable.

The residue from the water extraction was divided into two portions. The first was boiled with water for 24 hr. and on cooling a brown solid, m.p. 70–80° was deposited. It showed no hydroxyl group absorption and was purified by dissolution in benzene and filtration through a column of neutral alumina.

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(9) E. Leete, *J. Am. Chem. Soc.*, **82**, 6338 (1960).

(10) R. F. Nystron and C. R. A. Berger, *ibid.*, **80**, 2896 (1958).

(11) J. A. Ballantine, C. B. Barrett, R. J. S. Beer, B. G. Boggiano, S. Eardley, B. E. Jennings, and A. Robertson, *J. Chem. Soc.*, 2227 (1957).

(12) The spectra were recorded from a Varian V-4302 dual purpose 60-Mc. n.m.r. spectrometer and chemical shift values are reported in τ units using tetramethylsilane (τ 10) as internal standard. We are indebted to Dr. T. Spotswood for his assistance in determining this spectrum.

(13) K. T. Potts and J. E. Saxton, *Org. Syn.*, **40**, 68 (1960).

(14) E. Wenkert, R. A. Massy-Westropp, and R. G. Lewis, *J. Am. Chem. Soc.*, **84**, 3732 (1962).

(15) Evaporations were carried out under reduced pressure on the water bath and melting points were determined in capillaries. Ultraviolet spectra were recorded in ethanol solution, and petroleum ether refers to the fraction, b.p. 60–80°. Microanalyses are by the C.S.I.R.O. Microanalytical Service, Melbourne.

(16) Y. A. Baskakov and M. N. Melnikov, *Sb. Statei Obshchei Khim. Akad. Nauk SSSR*, **1**, 712 (1953); *Chem. Abstr.*, **49**, 1006d (1955).

(17) Prepared from an aqueous solution of acetaldehyde and Brady's reagent in the standard way.

Evaporation of the solvent gave a colorless glass which did not crystallize.

An attempt was made to distil the second portion under high vacuum. As the sample appeared to be reaching the boiling point, polymerization occurred with the formation of a brown glass. Purification was effected by filtration in benzene solution through a column of neutral alumina and the product finally isolated had an infrared spectrum identical with that of the product obtained by boiling with water for 24 hr. Poly(1-methyl-3-vinylindole) distilled (distillation bulb, free flame, 0.001 mm.) as a colorless glass.

Anal. Calcd. for $(C_{11}H_{11}N)_n$: C, 84.0; H, 7.1; N, 8.9. Found: C, 84.0; H, 6.9; N, 8.8.

Light absorption: λ_{max} 2290, 2670 (broad sh), 2930 Å. (log ϵ 4.76, 4.07, 4.18); λ_{min} 2530 Å. (log ϵ 3.92).

The infrared spectrum was similar to but not identical with that of 1,1-di-1'-methyl-3'-indolylethane.

1,1-Di(1'-methyl-3'-indolyl)ethane. A.—Sodium (46 mg.) was added to liquid ammonia (30 ml.) containing a crystal of ferric nitrate. To the stirred reaction mixture, 1,1-di-3'-indolylethane[18] (470 mg.) was added, followed 5 min. later by the dropwise addition of methyl iodide (300 mg.). After the ammonia had evaporated at room temperature, the product (520 mg., quantitative) was isolated as a pale yellow oil by the addition of water and extracted with three 50-ml. portions of ether. Purification was effected by passage in benzene through a small column of Woelm neutral alumina (activity I). The product, obtained as a colorless glass soluble in petroleum ether, could not be induced to crystallize. It had an infrared spectrum identical with that of the product prepared as in method B.

B.—1-Methylindole (6.0 g.), paraldehyde (1.2 g.), and zinc chloride (1.5 g.) were heated together on a steam bath for 4 hr. The resultant black tar was extracted with hot benzene (charcoal), and the solvent removed to yield the diindolylethane as a pale yellow glass (5.8 g., 87%). After purification as in method A, the product distilled (distillation bulb, free flame, 0.001 mm.) as a colorless glass.

Anal. Calcd. for $C_{20}H_{20}N_2$: C, 83.3; H, 7.0; N, 9.7. Found: C, 83.1; H, 6.9; N, 9.9.

Light absorption: λ_{max} 2290, 2940 Å. (log ϵ 4.70, 3.98); λ_{min} 2560 Å. (log ϵ 3.64).

Reduction of 1-Methyl-3-acetylindole with a Mixture of Lithium Aluminum Hydride and Aluminum Chloride.—A solution of 1-methyl-3-acetylindole (1.7 g., 0.01 mole) and aluminum chloride (2.68 g., 0.02 mole) in dry tetrahydrofuran (100 ml.) was added over 30 min. to a stirred solution of lithium aluminum hydride (0.4 g., 0.01 mole) and aluminum chloride (1.0 g., 0.0075 mole) in tetrahydrofuran (50 ml.). An immediate blue fluorescence was produced and the mixture was heated under gentle reflux for 4 hr. The complex was decomposed by treating the cooled solution with hydrated sodium sulfate, and then with water. The filtered solution was extracted with ether and dried (sodium sulfate). Evaporation of the solvent yielded 1.4 g. of a fluorescent liquid, showing no hydroxyl group absorption in its infrared spectrum. The oil (1.2 g.) was distilled and 1-methyl-3-ethylindole (1.0 g., 74%) was collected, b.p. 74–76° (0.3–0.4 mm.); $n^{20}D$ 1.5808 [lit.[19] b.p. 95–96° (0.6 mm.); $n^{20}D$ 1.5806, fluorescent oil]. The picrate, formed in ethanol, crystallized from a small volume of ethanol as long, red needles, m.p. 97–98° (lit.[19] m.p. 96–97°).

Reduction of 2-[2-(1'-Methyl-3'-indolyl)-2-oxoethyl]isoquinolinium Iodide with a Mixture of Lithium Aluminum Hydride and Aluminum Chloride in Dioxane Solution.—A suspension of the iodide (3.87 g., 0.009 mole) and aluminum chloride (2.4 g., 0.018 mole) in dioxane (100 ml.) was added over a period of 30 min. to a stirred solution of lithium aluminum hydride (0.8 g., 0.021 mole) and aluminum chloride (1.62 g., 0.012 mole) in dioxane (200 ml.). As stirring was continued for 5 hr. at 60–65° under nitrogen a yellow-brown gummy precipitate was formed. After reaction work-up as essentially previously described, the residual orange-brown, glassy residue was absorbed onto Woelm neutral alumina (activity IV, 90 g.). Elution with petroleum ether gave 440 mg. of a pale yellow oil which decomposed to a brown mass on exposure to air. The sample was not obtained crystalline nor could satisfactory derivatives be obtained. Its behavior was similar to that of the oils obtained when tetrahydrofuran was used as solvent. Development of the column with a 1:1 mixture of benzene–petroleum ether yielded 2-[2-(1'-methyl-3'-indolyl)-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline (0.73 g., 27%) which crystallized from benzene as fine, colorless needles, m.p. 162–164°. This product did not depress the melting point and had an infrared spectrum identical with that of an authentic specimen prepared in the next section.

Further elution with a 4:1 mixture of benzene–ether gave a brown oil (480 mg.) which could not be characterized.

Increasing the reaction time to 18 hr. did not alter the results appreciably from those obtained in the foregoing procedure.

Reduction of the isoquinoline salt in tetrahydrofuran solution with lithium aluminum hydride alone, or mixed with aluminum chloride, gave an unstable oily product which, even after exhaustive chromatography on alumina, could not be resolved into recognizable entities.

2-[2-(1'-Methyl-3'-indolyl)-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline.—2-[2-(1'-Methyl-3'-indolyl)-2-oxoethyl]isoquinoliniumiodide (500 mg.) dissolved in a mixture of ethanol (350 ml.) and water (180 ml.) was heated under reflux with silver chloride (*ca.* 4 g.) for 18 hr. The cooled solution was filtered and the solvent removed from the filtrate under reduced pressure. The residue was dissolved in a small volume of methanol (charcoal) and on addition of ether the chloride separated as clusters of cream needles, m.p. 277–281° dec. Platinum oxide (19 mg.) was suspended in acetic acid (10 ml.) and reduced with hydrogen. The chloride (27.1 mg.) was introduced and hydrogen (4.07 ml.) was absorbed over 30 min. (calculated absorption for the reduction of two double bonds, 3.90 ml./774 mm./17°). The catalyst was removed and, after evaporation to dryness, water was added to dissolve the residue whose solution was basified wth ammonium hydroxide and extracted with ether. 2-[2-(1'-Methyl-3'-indolyl)-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline crystallized from benzene as small colorless needles, m.p. 162–164°.

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.9; H, 6.6; N, 9.2. Found: C, 78.8; H, 6.6; N, 9.1.

Light absorption: λ_{max} 2470, 3030 Å. (log ϵ 4.29, 4.26); λ_{min} 2330, 2750 Å. (log ϵ 3.99, 4.04).

Reduction of 3,4-Dimethoxyacetophenone. A. With Lithium Aluminum Hydride.—The ketone (7.2 g., 0.04 mole) was added in small portions to a suspension of lithium aluminum hydride (2.5 g., 0.06 mole) in dry tetrahydrofuran (150 ml.) with marked effervescence occurring. After a 4-hr. reaction period, the reaction mixture was worked up as in the previous reductions. The crude product was a colorless liquid (6.6 g.) exhibiting strong hydroxyl absorption in its infrared spectrum and distilled at 118–120° (0.5 mm.). During the distillation dehydration occurred, as evidenced by a decrease in the hydroxyl group absorption intensity and the appearance of absorption bands at 1625 (s), 1440 (s), 987 (s), 1305 (m), and 1830 (w) cm.$^{-1}$ usually associated with a conjugated vinyl group. The distillate, consisting mainly of 3,4-dimethoxyvinylbenzene was treated with bromine and carbon tetrachloride and gave 3,4-dimethoxy-1-(1,2-dibromoethyl)benzene as clusters of colorless needles, m.p. 97–98°, on crystallization from petroleum ether (lit.[20] m.p. 98°). 3,4-Dimethoxyvinylbenzene polymerized to a colorless rubbery mass on standing in air.

B. With a Mixture of Lithium Aluminum Hydride and Aluminum Chloride.—A solution of 3,4-dimethoxyacetophenone (3.6 g., 0.02 mole) and aluminum chloride (5.4 g., 0.04 mole) in dry tetrahydrofuran (100 ml.) was added over 30 min. to a stirred solution of lithium aluminum hydride (0.8 g., 0.02 mole) and aluminum chloride (2.0 g., 0.015 mole) in tetrahydrofuran (50 ml.). After a 4-hr. reaction period, the reaction mixture was worked up as previously described and gave 3.2 g. of a colorless oil. The infrared spectrum indicated the presence of a small amount of hydroxyl-containing product. Distillation of 3 g. of the oil yielded 3,4-dimethoxyethylbenzene (2.6 g., 87%), b.p. 122–124° (15 mm.), containing a trace of 1-(3,4-dimethoxyphenyl)-1-hydroxyethane. Distillation from sodium produced a pure sample of the hydrocarbon, b.p. 122–124° (15 mm.) [lit.[21] b.p. 110–112° (9 mm.)].

Anal. Calcd. for $C_{10}H_{14}N_2O$: C, 72.3; H, 8.5; O, 19.3. Found: C, 72.3; H, 8.7; O, 19.1.

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(18) J. E. Saxton, *J. Chem. Soc.*, 3592 (1952).

(19) H. R. Snyder, E. Eliel, and R. E. Carnahan, *J. Am. Chem. Soc.*, **73**, 970 (1951).

(20) R. Quelet and Calcagni, *Compt. rend.*, 222 (1946).

(21) G. Barger and R. Silberschmidt, *J. Chem. Soc.*, 2919 (1928).

Acknowledgment.—The authors wish to express their thanks to Professor G. M. Badger for his interest and encouragement throughout this work.

Aromatic Cyclodehydration. LV.[1] Quaternizations with Chloroacetaldoxime

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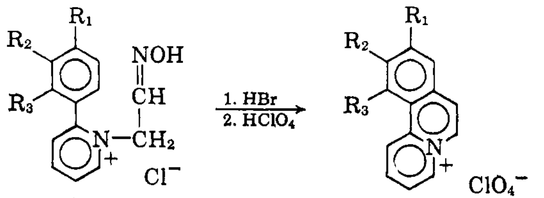
Department of Chemistry, Duke University, Durham, North Carolina

Received April 22, 1963

Previous attempts to obtain unsubstituted benzo[*a*]quinolizinium salts[3] by the cyclodehydration method have been unsuccessful. It was found that chloro-, bromo-, and iodoacetals would not form quaternary salts with 2-phenylpyridine, while bromopyruvic acid afforded only the hydrobromide of the starting material.[4]

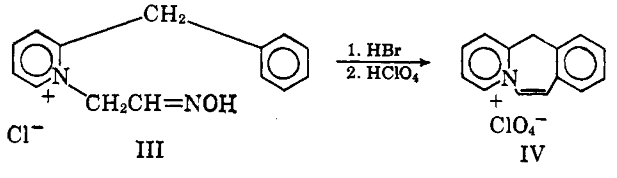
As the α-haloacetaldehydes exist predominantly as trimers or polymers, and therefore display low reactivity to quaternization, it was felt that an α-haloacetaldoxime might prove more reactive. The presence of a double bond in chloroacetaldoxime should activate the α-methylene group in the same manner as the olefin in allyl bromide or the carbonyl in bromoacetone. This activation by the carbon–nitrogen double bond in the oxime should facilitate the displacement of a halogen on the α-methylene group and permit quaternization with a tertiary amine. Our results confirm this hypothesis.

Quaternization of 2-phenylpyridine proceeded readily with chloroacetaldoxime in tetramethylene sulfone.



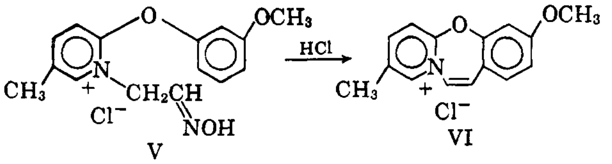
I (not isolated)

II



III

IV



V

VI

Cyclization with hydrobromic acid gave a mixed salt which on addition of perchloric acid was converted to benzo[*a*]quinolizinium perchlorate (II).[5] Similar procedures carried out with the three 2-tolylpyridines gave the expected methylbenzo[*a*]quinolizinium perchlorates (II, $R_1 = CH_3$; II, $R_2 = CH_3$; and II, $R_3 = CH_3$). Confirmation of cyclization in each case was given by the ultraviolet absorption spectrum of the product.

The low yield of 11-methylbenzo[*a*]quinolizinium perchlorate (12%) is apparently due to steric inhibition and is comparable to that of the 7,11-dimethyl analog (9%) reported previously.[6]

This method was successfully extended to include the preparation of the unsubstituted morphanthridizinium perchlorate[7] (IV) and a benz[*f*][1,3]oxazepinium chloride[8] (VI) having no substituent on the central nucleus.

Experimental

All analyses were carried out by Dr. Ing. A. Schoeller, Kronach, Germany. The melting points were determined in capillary tubes in a Mel Temp apparatus and are uncorrected. Ultraviolet absorption spectra were measured in 95% ethanol using 1-cm. quartz cells with a Cary Model 14 spectrophotometer. The asterisk (*) is used to denote a shoulder.

Chloroacetaldoxime.—To 40 g. of chloroacetaldehyde diethyl acetal (or the dimethyl acetal) was added a solution of 96 g. of hydroxylamine hydrochloride in 100 ml. of water and the mixture was stirred at room temperature for 72 hr. The resultant single phase solution was extracted continuously with ether in an ether extractor for 3 days. The ether extract was washed three times with water and dried over anhydrous calcium chloride. The ether was removed under vacuum (aspirator) at room temperature with slight warming to remove the final traces of solvent. The colorless oil which solidified in the refrigerator was sufficiently pure for the quaternization reactions; yield, 20 g. (85%). A sample on distillation had b.p. 64.5° (20 mm.), lit.[9] b.p. 61° (20 mm.).

Benzo[*a*]quinolizinium Perchlorate (II).—A solution containing 1 g. (0.0064 mole) of 2-phenylpyridine and 1 g. (0.011 mole) of chloroacetaldoxime in 3 ml. of dry tetramethylene sulfone was allowed to stand for 12 days in a stoppered flask at room temperature. The resultant dark viscous oil was triturated with ethyl acetate but could not be crystallized, nor could a solid perchlorate be formed by the addition of perchloric acid to a portion of it. The crude product was dissolved in 20 ml. of 48% hydrobromic acid and heated under reflux for 24 hr. The acid was removed under vacuum (aspirator) and the resultant mixed salt, isolated as a dark gum, was dissolved in 5 ml. of water. Addition of perchloric acid gave the perchlorate; yield 0.6 g. (35%), m.p. 195–196°. Crystallization from methanol (charcoal) afforded the pure product as colorless needles, m.p. 196–197° (lit.[3] m.p. 197°); λ_{max} (log ε), 217 (4.29), 222 (4.32), 237 (4.28), 256* (4.08), 269 (4.23), 278 (4.28), 323 (3.70), 337 (4.01), 354 mμ (4.14).

Anal. Calcd. for $C_{13}H_{10}ClNO_4$: C, 55.82; H, 3.79; N, 5.27. Found: C, 56.05; H, 3.72; N, 5.02.

Quaternization of 2-phenylpyridine with chloroacetaldoxime in refluxing acetone proved less satisfactory due to the greater decomposition encountered.

9-Methylbenzo[*a*]quinolizinium Perchlorate (II, $R_1 = CH_3$).—The quaternization of 2 g. of 2-(4-tolyl)pyridine by reaction with 2 g. of chloroacetaldoxime in dry tetramethylene sulfone was carried out over 6 days. Trituration with ethyl acetate, as previously described, gave a gum which was heated for 24 hr. under reflux with 20 ml. of hydrobromic acid. The perchlorate prepared as for II was crystallized (charcoal) from methanol; yield, 1.5 g. (45%); m.p. 227–229°. The analytical sample

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[1] For the preceding communication of this series, see *J. Org. Chem.*, **28**, 3070 (1963).

[2] This research was supported by a research grant (CA-05509) of the National Cancer Institute of the National Institutes of Health.

[3] E. E. Glover and G. Jones [*J. Chem. Soc.*, 3021 (1958)] have reported the synthesis of benzo[*a*]quinolizinium perchlorate from 1-cyanoisoquinoline by a 4-step route. The present 2-step procedure, however, offers considerable advantage in its simplicity.

[4] L. E. Beavers, Ph.D. dissertation, Duke University, 1955.

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

[6] C. K. Bradsher and K. B. Moser, *J. Am. Chem. Soc.*, **81**, 1941 (1959).

[7] K. B. Moser and C. K. Bradsher, *ibid.*, **81**, 2547 (1959).

[8] C. K. Bradsher, L. D. Quin, and R. E. LeBleu, *J. Org. Chem.*, **26**, 3273 (1961).

[9] H. Brintzinger and R. Titzmann, *Ber.*, **85**, 344 (1952).