condenser, and dropping funnel were added 200 ml. of benzene and 13.2 g. (0.07 mole) of 2-chloroethyl vinylphosphonochloridate. To the stirred solution were added over a period of 20 min., a solution of 6.7 g. (0.21 mole) of methanol and 7.1 g. (0.07 mole) of triethylamine in 50 ml. of benzene. The reaction was exothermic. The cooled mixture was freed of amine hydrochloride by suction filtration, the solid was washed with three 50-ml. portions of benzene, and the filtrate was shaken with solid sodium carbonate and again filtered. The solvent was removed by distillation at reduced pressure. The residue was fractionated in a 6-in. Vigreux column. The yield of liquid distilling at 82–85° (1 mm.) was 9.5 g. (74%).

Anal. Calcd. for $C_5H_{10}ClO_3P$: P, 16.8. Found: P, 16.6.

2-Chloroethyl N,N-dimethyl-P-vinylphosphonamidate. In a 1-l., three-necked flask fitted with a mechanical stirrer, reflux condenser, a calcium chloride drying tube, and dropping funnel were placed 94.5 g. (0.50 mole) of 2-chloroethyl vinylphosphonochloridate and 300 ml. of benzene. A solution of 22.5 g. (0.50 mole) of dimethylamine and 50.5 g. (0.50 mole) of triethylamine in 80 ml. of benzene was prepared by bubbling gaseous dimethylamine into a chilled mixture of the other two components. The solution of amines was added to the phosphonochloridate solution with cooling and stirring. The amine hydrochloride was removed by suction filtration, the solid being washed with benzene several times. The filtrate was stirred with solid sodium carbonate for 30 min., and then the mixture was refluxed 1 hr. After filtration, the solution was freed of solvent by distillation, first at atmospheric pressure and then under reduced pressure, keeping the pot temperature below 130°. The residue was fractionated in a 6-in. Vigreux column at 1 mm., giving 65 g. (66% yield) distilling at 107–110°, and 17 g. of residue. The product was redistilled at 118.5–119.5° (1.5 mm.).

Anal. Calcd. for $C_6H_{13}ClNO_2P$: N, 7.09; P, 15.7. Found: N, 7.04; P, 15.3.

Diethyl 1(and 2)-propynylphosphonate. Commercial grade diethyl phosphite and propargyl bromide were redistilled just prior to use. In a 200-ml., three necked flask fitted with a water bath, reflux condenser, dropping funnel, and thermometer were placed 20 ml. of tetrahydrofuran, which had been dried and redistilled over sodium, and 25 g. (0.21 mole) of propargyl bromide. In the funnel was placed a solution prepared from 4.6 g. (0.2 g.-atom) of sodium, 27.6 g. (0.2 mole) of diethyl phosphite and 26 ml. of tetrahydrofuran. The addition was carried out over a period of 20 min., the temperature of the stirred mixture rising to 40°. The suspension was refluxed 1 hr. It was then cooled, filtered under suction, the solid washed with acetone, and after 1 hr. the filtrate was refiltered. The crude dried sodium bromide weighed 15 g. (73% yield). A few crystals of hydroquinone were added to the filtrate, which was then freed of solvent by distillation at atmospheric pressure and finally at reduced pressure, keeping the pot temperature below 115°. The residue was fractionated in a 6-in. Vigreux column at 1 mm., giving 2.9 g. distilling at 45–88° and 12.7 g. (36% yield) at 99–115°. There was 13 g. of polymeric residue. Redistillation of the main fraction gave 7.9 g. coming off at 105.5–110.0° (1 mm.).

Anal. Calcd. for $C_7H_{13}O_3P$: C, 47.71; H, 7.43; P, 17.6. Found: C, 47.85; H, 7.49; P, 17.1.

The product gave a very deep wine-red color when treated with two volumes of a solution of 0.5 g. of 3,5-dinitrobenzoic acid in 10 ml. of 2% sodium hydroxide. This indicates the presence of an active hydrogen compound.[10] The material also gave a moderate quantity of a white precipitate when treated with 2–10 volumes of a half-saturated solution of mercuric cyanide in 2% sodium hydroxide. The precipitate was probably the mercury derivative of diethyl 2-propynylphosphonate. No precipitate was given by diethyl phosphite or diethyl ethylphosphonate. Previously reported constants of diethyl 1-propynylphosphonate are[12]: b.p. 108–110° (2.1 mm.) and 98–1003° (2 mm.); n_D^{25} 1.4449.

Absorption spectra. Measurements on methyl 2-chloroethyl vinylphosphonate and 2-chloroethyl *N,N*-dimethyl-*P*-vinylphosphonamidate were made with a Beckman model IR-4 spectrophotometer. With diethyl propynylphosphonate, a Perkin-Elmer Model 21 instrument was used. All data were obtained on the compounds in chloroform solution.

Acknowledgment. Our thanks go to Harold P. Pastor, James A. Harris, Julian F. Jurgens, and (Mrs.) Marian Willis who performed the phosphorus and nitrogen analyses, to Frank C. Magne and Idas W. Lohmann for density and refractive index measurements, and to Elizabeth R. McCall and (Mrs.) Elsie F. DuPré for infrared spectral measurements. The advice of Robert T. O'Connor in interpeting the spectra is greatly appreciated.

NEW ORLEANS, LA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Aromatic Cyclodehydration. XLVII.[1] Pyrido[2,1-*b*]benz[*f*][1,3]oxazepinium Salts

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Received February 2, 1961

Through the cyclization of 1-acetonyl-2-(3-alkoxyphenoxy)pyridines the first derivatives of the new pyrido[2,1-*b*]benz[*f*][1,3]oxazepinium system have been prepared. The difficulty encountered in the cyclization may be explained in terms of izinium-oxonium resonance. Evidence for the existence of such resonance in the 1-methyl-2-phenoxypyridinium system has been presented.

The success met with in the cyclization of some benzylpyridinium salts (I) to the new morphanthridizinium system (II)[3] raised the question whether other groups or atoms might replace the methylene bridge connecting the aromatic rings. The 2-phenoxypyridinium salts were selected for the first study since the required 2-phenoxypyridines are readily prepared, and the final ring

(1) For the preceding communication of this series, see *J. Org. Chem.*, **26**, 2231 (1961).

A part of this work originally appeared as a letter to the Editor, *Chem. & Ind.*, 1126 (1959).

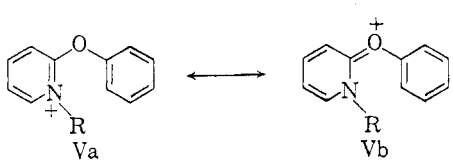
(2) Monsanto Chemical Co. Fellow, 1959–1960. This research was supported in part by a research grant (NSF-G6215) of the National Science Foundation.

(3) K. B. Moser and C. K. Bradsher, *J. Am. Chem. Soc.*, **81**, 2547 (1959).

I X=CH_2 II
III X=O IV

system (IV) would be a new one, likely to possess interesting properties.

It was found the 2-phenoxypyridine could be easily quaternized with iodoacetone, yielding the expected 1-acetonyl-2-phenoxypyridinium (III. R = CH_3) iodide. The iodide was converted to the chloride which (without purification) was refluxed with hydrochloric acid under conditions analogous to those found adequate for the cyclization of 1-acetonyl-2-benzylpyridinium chloride. None of the expected pyridobenzoxazepinium salt (IV) was obtained. While there was no evidence that the desired pyridobenzoxazepinium salt was not too unstable to exist under the conditions of the cyclization, it seemed more likely that the failure was due to a novel type of resonance to which we refer as izinium-oxonium resonance. The benzylpyridinium salt (I) is a diarylmethane derivative, while naively considered, the phenoxypyridinium system (III) belongs to the *usually* reactive class of diaryl ethers. A consideration of the possibility for resonance makes it clear why the phenyl group attached to the oxygen atom should actually be *less* reactive toward electrophilic attack than that connected to a methylene group. The resonance form expressed by formula Va is probably the most important, but some contribution to the hybrid must be made by form Vb.



Va ⟷ Vb

Izinium-Oxonium Resonance

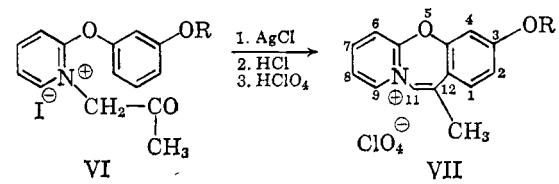
Clearly, even a partial positive charge on oxygen would deactivate the phenyl nucleus in a way that has no counterpart in the benzylpyridinium system.

The existence of this inhibition has been demonstrated in a model system. In acetic acid soution 2-phenoxypyridine reacted rapidly with bromine affording 2-(4-bromophenoxy)pyridine in 48% yield. Under conditions even more vigorous, the corresponding methiodide (V. R = CH_3), on treatment in acetic acid with an excess of bromine, appeared to be unreacted and titration showed that 98% of the bromine was still present. While this experiment demonstrated effectively the reality of the deactivation, it raised the interesting question whether if electrophilic substitution of the quaternary were forced, substitution would occur at the *meta* or the *ortho-para* positions.

Nitration of 1-methyl-2-phenoxypyridinium nitrate yielded a product which was demonstrated to be 1-methyl-2-(4-nitrophenoxy)pyridinium nitrate. The 1-alkyl-2-oxypyridinium group thus shares with the halogens the property of inhibiting substitution while at the same time being *ortho-para* directing. A number of aryloxypyridines were prepared in the course of this study.

If one accepts the hypothesis that deactivation of the phenyl ring is responsible for the failure of the original cyclization attempt, two methods are suggested by which this deactivation might be overcome. The first and more obvious of these two methods is the introduction of an alkoxyl group *para* to the position of expected cyclization. It had been observed[3] earlier in the benzylpyridinium (I) cyclizations that the presence of a methoxyl group *para* to the point of cyclization not only accelerates greatly the cyclization of 1-acetonyl-2-benzylpyridinium salts (I. R = CH_3), but also makes possible the cyclization of the 1-phenacyl analogs (I. R = C_6H_5) which do not undergo cyclization in the unactivated state.

Quaternization of 2-(3-methoxyphenoxy)pyridine with iodoacetone yielded 1-acetonyl-2-(3-methoxyphenoxy)pyridinium iodide (VI).



VI VII

Conversion of the iodide salt (VI) to the corresponding chloride, followed by refluxing in concentrated hydrochloric acid for twenty-four hours, yielded the desired 3-methoxy-12-methylpyrido[2,1-*b*]benz[*f*][1,3]oxazepinium (VII) salt (29%), isolated as the perchlorate. Evidence that cyclization has indeed occurred is afforded by infrared data showing the disappearance of the carbonyl absorption at 5.75 μ, and the disappearance of all but very weak absorption in 13.3–14.3 μ region, indicating a transition from 1,3-disubstitution to 1,2,4-trisubstitution in the phenyl nucleus.[4] The ultraviolet absorption spectrum (Fig. 1) affords evidence that there is a significant increase in conjugation, as would be expected when the aromatic rings are joined by a double bond. Hydrogenation of the new oxazepinium salt (VII) resulted in an uptake of slightly over five moles of hydrogen, but the product could not be crystallized and decomposed on attempted distillation.

The second method which was used (in conjunction with the first) to overcome the deactivating effect of the izinium-oxonium resonance was more novel. Methyl groups were introduced in the

(4) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Second Edition, John Wiley and Sons, Inc., New York, N.Y., 1959, p. 78.

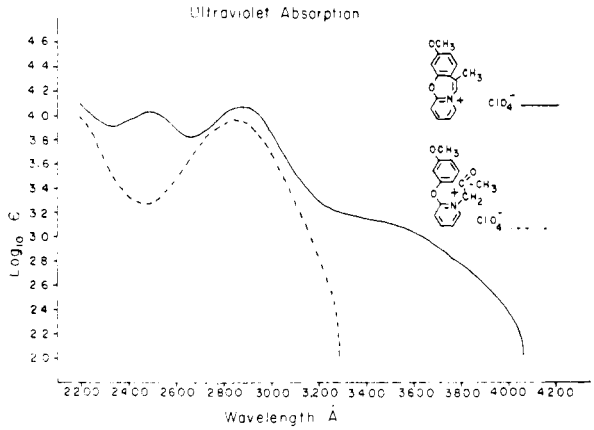
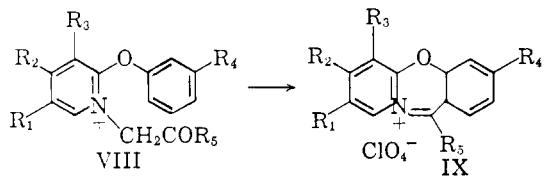


Figure 1

pyridinium moiety of the quaternary intermediates either *ortho* or *para* to the oxygen bridge. As can be seen from Table I the effect of these substituents was dramatic. The observed increase in yield is almost certainly due to the effect of the electron release from the methyl group in diminishing the partial positive charge on the oxygen bridge, for introduction of a methyl group *meta* to the oxygen atom is without beneficial effect.

TABLE I

PYRIDO[2,1-*b*]BENZ[*f*][1,3]OXAZEPINIUM PERCHLORATES

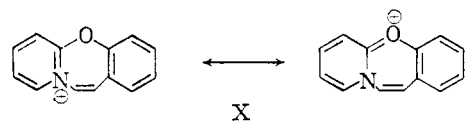


R_1	R_2	R_3	R_4	R_5	Quant. Yield, %	Cyclization Time, Hr.	Cyclization Yield, %
—	—	—	—	CH_3	73	228[a]	0
—	—	—	—	C_6H_5	39	96	0
—	—	—	OCH_3	CH_3	84	24[b]	29
—	—	—	OCH_3	C_6H_5	100	48[c]	0
—	—	—	OC_2H_5	CH_3	91	3	11
CH_3	—	—	OCH_3	CH_3	98	24	55
—	CH_3	—	OCH_3	CH_3	33	24	4
—	—	CH_3	OCH_3	CH_3	46	24	47

[a] Yield at 4 hr. was zero. [b] Four hr. 18%, 49 hr. 9%. [c] Failed also at 4, 8, 26 hr.

One additional observation from Table I is that phenacylpyridinium salts ($R_5 = C_6H_5$) could not be cyclized even when a methoxyl group was present in a position where it should bring about activation. This is in contrast to experience in the cyclization 1-phenacyl-2-benzylpyridinium salts (I. R = C_6H_5) in which introduction of a methoxyl group in the corresponding position made it possible for ring closure to occur. This is further evidence of the effectiveness of izinium-oxonium resonance in inhibiting electrophilic substitution reactions.

The major interest in the new heterocyclic system is that the central nucleus may achieve some degree of aromatic character through izinium-oxonium resonance (X).



X

While the Fisher-Hirschfelder models of the new system indicate a somewhat warped ring structure the approach to planarity is evidently close enough to permit the central nucleus to serve effectively in conjugating the terminal nuclei (Fig. 1).

As the preparation of the required phenoxypyridines is easily accomplished,[5] several members of the new series of pyrido[2,1-*b*]benz[*f*]oxazepinium salts can be regarded as readily available compounds.

EXPERIMENTAL[6]

2-Aryloxypyridines.[5b] A mixture containing 2 molar equivalents of the phenol and 1 each of the 2-bromopyridine and anhydrous potassium carbonate in a round-bottom flask, equipped with a reflux condenser, was heated in a Wood's metal bath for 3 hr. at 200–210°. At the end of the reaction period the mixture was diluted with water and made strongly alkaline by the addition of potassium hydroxide. The mixture was extracted with ether and the ethereal extract dried with magnesium sulfate. The ethereal solution was concentrated and the residue purified by vacuum distillation. The results of these experiments are summarized in Table II.

Quaternization of 2-aryloxypyridines by reaction with iodoacetone or phenacyl bromide. The aryloxypyridine was mixed with a 5–10% excess of the halide and allowed to stand in a stoppered flask in the refrigerator. When the halide was phenacyl bromide, the reactants were first heated on the steam bath until the solid halide had melted. After the indicated reaction period (Table III), ethyl acetate was added and the insoluble salt, if not already crystalline, was induced to crystallize by stirring, and scratching the walls of the flask. The product was usually recrystallized from methanol or methanol–ethyl acetate. Except as noted all melting points were taken on the Fisher-Johns block. The reported melting points (Table III) are for the analytical sample, but the product obtained in the reported yield melted in no case more than 7° (average 3°) below the analytical sample.

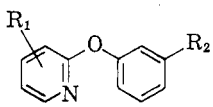
3-Methoxy-12-methylpyrido[2,1-b]benz[f][1,3]oxazepinium perchlorate (IX. $R_4 = OCH_3$, $R_5 = CH_3$). To a solution containing 7.7 g. of 1-acetonyl-2-(3-methoxyphenoxy)pyridinium iodide in 190 ml. of water, 10 ml. of concd. hydrochloric acid was added and the acidic solution stirred for 5.5 hr. with thoroughly washed silver chloride, freshly prepared from 9 g. of silver nitrate. After removal of the silver halides by filtration, the filtrate was concentrated under reduced pressure. The yellow residue was dissolved in 40 ml. of concd. hydro-

(5) (a) R. R. Renshaw and R. C. Conn, *J. Am. Chem. Soc.*, **59**, 297 (1937); (b) A. J. Hill and W. S. McGraw, *J. Org. Chem.*, **14**, 783 (1949).

(6) Except as noted all analyses were by Dr. A. Schoeller, Kronach, Germany. Ultraviolet spectra were taken in 95% ethanol using 1 cm. matched quartz cells in the Warren Spectracord (W) or the Cary Spectrophotometer (C). All boiling and melting points are uncorrected. Melting points were determined by use of the Fisher-Johns block (FJ) or the Mel-Temp Capillary apparatus (MT).

TABLE II

2-ARYLOXYPYRIDINES



R_1	R_2	Yield, %	B.P.	Mm.	Formula	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
—	OC_2H_5	65	107–109	0.3	$C_{13}H_{13}NO_2$	72.54	72.31	6.09	6.10	6.51	6.73
3-CH_3	OCH_3	76[a]	109–134	1.1–1.3	$C_{13}H_{13}NO_2$	72.54	72.12[b]	6.09	6.22	6.51	6.51
4-CH_3	OCH_3	69[a]	173–174	7	$C_{13}H_{13}NO_2$	72.54	72.19[b]	6.09	5.88	6.51	6.60
5-CH_3	OCH_3	79[a]	174–175	6.3	$C_{13}H_{13}NO_2$	72.54	72.24[b]	6.09	6.25	6.51	6.56
6-CH_3	OCH_3	71[a]	131–132	1	$C_{13}H_{13}NO_2$	72.54	72.13[b]	6.09	6.25	6.51	6.43
—	Br	67	144–146	4[c]	$C_{11}H_8BrNO$	52.82	53.01	3.22	3.36	5.60	5.59

[a] Yield allowing for 22–33% recovery of halide. The required methyl-2-bromopyridines were prepared by the general method of F. H. Case, *J. Am. Chem. Soc.*, **68**, 2574 (1946). [b] Ref. 7. [c] The analytical sample crystallized from methanol, m.p. 57–58°.

chloric acid and the mixture allowed to reflux for 24 hr.[9] The acid was removed under reduced pressure and the brown residue taken up in methanol. The perchlorate was precipitated by addition of 72% perchloric acid as olive crystals, m.p. 245–250°. The analytical sample crystallized from methanol as irregular olive-colored clusters, m.p. (FJ) 262–263°. λ_{max} (log ϵ): 248(4.05), 288(4.08). λ_{min}: 233(3.95) 266 mμ (3.83).

Anal. Calcd. for $C_{15}H_{14}ClNO_6$: C, 53.03; H, 4.15; N, 4.12. Found: C, 53.26; H, 4.01; N, 4.17.

The product was found to take up 5.35 moles of hydrogen in the presence of Adams catalyst. An attempt to purify the product (as the free base) by vacuum distillation resulted in almost complete decomposition.

3-Ethoxy-12-methylpyrido[2,1-b]benz[f][1,3]oxazepinium perchlorate (IX, $R_4 = OC_2H_5$, $R_5 = CH_3$). The chloride obtained by the silver chloride method from 8 g. of 1-acetonyl-2-(3-methoxyphenoxy)pyridinium iodide was cyclized by refluxing it for 3 hr. in 40 ml. of concd. hydrochloric acid. The product which was isolated as the perchlorate, consisted of small yellow crystals, m.p. 185–187°, yield 0.8 g. (11%). The analytical sample crystallized from methanol as yellow-green platelets, m.p. (FJ) 191–193°, λ_{max} (log ϵ) 288(4.03), shoulder at 245. λ_{min} 266 mμ (3.85) shoulder at 235[10] mμ.

Anal. Calcd. for $C_{16}H_{16}ClNO_6$: C, 54.32; H, 4.56; N, 3.96. Found: C, 54.57; H, 4.79; N, 4.05.

3-Methoxy-6,12-dimethylpyrido[2,1-b]benz[f][1,3]oxazepinium perchlorate (IX, $R_3 = R_5 = CH_3$, $R_5 = OCH_3$). The cyclization of the chloride salt obtained from 8.0 g. of 1-acetonyl-2-(3-methoxyphenoxy)-3-methylpyridinium iodide was carried out by refluxing it for 24 hr. in concd. hydrochloric acid. The perchlorate (3.95 g.) was precipitated as a yellow solid. One gram recrystallized, yielded 0.85 g. (47%) of yellow material, m.p. 234–238°. The analytical sample was obtained from methanol as tiny light-yellow needles, m.p. (MT) 238.5–240.5°. λ_{max} (log ϵ): 248(4.03), 286(3.91), 343(3.34). λ_{min} 231(3.88), 271(3.84), 322 mμ (3.26).

Anal. Calcd. for $C_{16}H_{16}ClNO_6$: C, 54.32; H, 4.56; N, 3.96. Found: C, 54.29; H, 4.52; N, 3.97.

3-Methoxy-7,12-dimethylpyrido[2,1-b]benz[f][1,3]oxazepinium perchlorate (IX, $R_2 = R_5 = CH_3$, $R_4 = OCH_3$). Starting with 7.0 g. of 1-acetonyl-2-(3-methoxyphenoxy)-4-methylpyridinium iodide and using the exact procedure used in making the 6,12-dimethyl analog (IX, $R_3 = R_5 = CH_3$, $R_4 = OCH_3$), 1.4 g. (23%) of an olive-colored powder, m.p. 197–207°, was formed. Twice recrystallized from methanol it afforded 0.25 g. (4%) which was not improved on further recrystallization. The analytical sample consisted of feathery buff-colored needles, m.p. 241–241.5°. λ_{max} (log ϵ): 244(3.99), 286(3.96). λ_{min}: 234(396), 267 mμ (3.80).

Anal. Calcd. for $C_{16}H_{16}ClNO_6 \cdot {}^1/_4CH_3OH$; C, 53.95; H, 4.74; N, 3.87. Found: C, 53.74; H, 4.49; N, 3.64.

3-Methoxy-8,12-dimethylpyrido[2,1-b]benz[f][1,3]oxazepinium perchlorate (IX. $R_1 = R_5 = CH_3$, $R_4 = OCH_3$). From 8 g. of 1-acetonyl-2-(3-methoxyphenoxy)-5-methylpyridinium iodide following the general procedure, 5.7 g. of greenish brown powder was obtained. Recrystallization of 4.5 g. of this material from methanol gave 3.1 g. (55%), m.p. 180–183°. The analytical sample was obtained as irregular amber needles, m.p. (MT) 198–200°. λ_{max} (log ϵ): 223(4.02), 246(3.93), 292(3.93). λ_{min} 235(3.91), 267 mμ (3.67).

Anal. Calcd. for $C_{16}H_{16}ClNO_6$: C, 54.32; H, 4.56; N, 3.96. Found: C, 54.31; H, 4.84; N, 3.82.

Bromination of 2-phenoxypyridine. A solution of 2.0 g. of 2-phenoxypyridine in 25 ml. of glacial acetic acid was cooled at −5 to −10° while 2.4 g. of bromine was added dropwise. Stirring was maintained during the addition and afterward until a period of 1 hr. had elapsed. The solution was neutralized with alkali, diluted, and extracted with ether. The extract was dried over magnesium sulfate, concentrated and the residue distilled. The product, 1.4 g. (48%), was a colorless liquid, b.p. 116–118° (0.9 mm.), lit.,[5b] 122–123° (1 mm.) and gave an infrared spectrum identical with that of 2-(4-bromophenoxy)pyridine prepared from 2-bromopyridine and phenol.[5b]

For further confirmation the bromophenoxypyridine was converted to the methiodide. The analytical sample of *1-methyl-2-(4-bromophenoxy)pyridinium iodide* consisted of light orange crystals, m.p. (FJ) 207–208°. The methiodides obtained from the bromination product and from an authentic sample of 2-(4-bromophenoxy)pyridine[5b] showed no significant melting point depression.

Anal. Calcd. for $C_{12}H_{11}BrINO$: C, 36.73; H, 2.84; N, 3.57. Found: C, 36.84; H, 2.75; N, 3.57.

1-Methyl-2-(3-bromophenoxy)pyridinium iodide was obtained by reaction of methyl iodide with 2-(3-bromophenoxy)pyridine as cream-colored crystals, m.p. (FJ) 148–150°.

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

(8) Analysis by Drs. Weiler and Strauss, Oxford, England.

(9) Cyclization experiments identical in every respect except that the refluxing periods were 5 hr. or 48 hr., yielded 18% and 9%, respectively.

(10) The spectral data reported earlier (ref. 1) for this substance are erroneous.

TABLE III

QUATERNARY SALTS DERIVED FROM 2-ARYLOXYPYRIDINES

R_1	R_2	R_3	X	Time, Days	Yield, %	M.P.	Formula	C		H		N	
								Calcd.	Found	Calcd.	Found	Calcd.	Found
—	CH_3	—	I	7[a]	73[b]	163–165	$C_{14}H_{14}INO_2$	47.32	47.36	3.94	4.19	3.94	3.92
—	C_6H_5	—	Br	2	39	162–164	$C_{19}H_{16}BrNO_2$	61.62	61.48[c]	4.32	4.58	3.78	3.58
—	CH_3	OCH_3	I	10[d]	84[e]	153–154	$C_{15}H_{16}INO_3$	46.75	46.98	4.16	4.30	3.64	3.52
—	CH_3	OCH_3	ClO_4	—	—[f]	150–151[g]	$C_{15}H_{16}ClNO_7$	50.36	50.63[h]	4.51	4.69	3.92	4.15
—	C_6H_5	OCH_3	Br	5	100[i]	181–183	$C_{20}H_{18}BrNO_3$	60.00	60.23	4.50	4.68	3.50	3.42
—	CH_3	OC_2H_5	I	12	91[j]	153–155	$C_{16}H_{18}INO_3$	48.13	48.19	4.54	4.76	3.51	3.47
3-CH_3	CH_3	OCH_3	I	15	46[k]	139.5–141.5[g]	$C_{16}H_{18}INO_3$	48.13	48.37	4.54	4.65	3.51	3.24
4-CH_3	CH_3	OCH_3	I	13	33[l]	117.5–119.5[g]	$C_{16}H_{18}INO_3$	48.13	48.25	4.54	4.96	3.51	3.42
5-CH_3	CH_3	OCH_3	I	14	98[m]	180–181.5[g]	$C_{16}H_{18}INO_3$	48.13	48.28	4.54	4.55	3.51	3.43
6-CH_3	CH_3	OCH_3	I	15	0[n]								

[a] A few drops of dimethylformamide was added to the reaction. [b] Irregular white needles. [c] Ref. 8. [d] A few drops of formamide was added to the reaction. [e] Irregular hexagonal plates. [f] Obtained by addition of perchloric acid to a solution of iodide, colorless needle clusters. [g] Mel-Temp melting point apparatus used. [h] Ref. 7. [i] Tiny irregular colorless crystals. [j] Clusters of yellow needles. [k] Clusters of cream-colored tetragons. Crystallization of the crude product was induced by refluxing it overnight with a mixture of ether and ethyl acetate. [l] Irregular cream-colored clusters. [m] Colorless irregular clusters. [n] No salt having the expected properties could be isolated.

Anal. Calcd. for $C_{12}H_{11}BrINO$: C, 36.73; H, 2.84; N, 3.57. Found: C, 36.77; H, 2.89; N, 3.69.

Attempted bromination of 1-methyl-2-phenoxypyridinium iodide. Exactly 500 mg. of 1-methyl-2-phenoxypyridinium iodide was dissolved in 30 ml. of glacial acetic acid at 5–16°. The solution was stirred while 12.8 ml. of a bromine–glacial acetic acid solution was added and the temperature was maintained at the same level for 1 hr. After addition of 3 ml. of starch solution and 12 g. of potassium iodide in 100 ml. of water titration with standardized thiosulfate solution revealed the presence of the equivalent of 0.381 g. (98%) of the 0.387 g. (.0024 mole) of bromine originally introduced. If complete monobromination had occurred the titration would have indicated 0.129 g. (.0008 mole) of apparent "bromine" due to the liberation of free iodine from the anion by the first half of a molecular equivalent of bromine added.

1-Methyl-2-(4-nitrophenoxy)pyridinium iodide was prepared in 46% yield by refluxing 2-(4-nitrophenoxy)pyridine[11] with a 1:2 mixture of methyl iodide and ether. The analytical sample formed golden platelets from methanol, m.p. (MT) 235–237°.

Anal. Calcd. for $C_{12}H_{11}INO_3$: C, 40.24; H, 3.10; N, 7.82. Found: C, 40.55; H, 3.29; N, 8.04.

1-Methyl-2-(4-nitrophenoxy)pyridinium nitrate was prepared by passing a water solution of the iodide through Amberlite IRA-401 ion-exchange resin saturated with nitrate ions. The analytical sample formed long light-yellow needles from ethanol, m.p. (MT) 174–174.5°.

Anal. Calcd. for $C_{12}H_{11}N_3O_6$: C, 49.15; H, 3.75; N, 14.33. Found[7]: C, 49.00; H, 3.79; N, 14.21.

1-Methyl-2-(3-nitrophenoxy)pyridinium iodide was prepared (69% yield) by refluxing 2-(3-nitrophenoxy)pyridine[11] for only 2 days with a mixture of methanol and methyl iodide. Recrystallization from methanol-ether gave dark yellow needles, m.p. (FJ) 221–222.5°.

Anal. Calcd. for $C_{12}H_{11}IN_2O_3$: C, 40.24; H, 3.10; N, 7.82. Found: C, 40.59; H, 3.29; N, 7.75.

1-Methyl-2-phenoxypyridinium nitrate. To a solution of 1-methyl-2-phenoxypyridinium iodide[5a] in water, a silver nitrate solution was added dropwise until there was no further turbidity. The silver iodide was removed by filtration and the crude 1-methyl-2-phenoxy pyridinium nitrate recovered by vacuum-evaporation of the water. Crude nitrate, m.p. 116–118°, was used for the nitration experiments but material of analytical purity was obtained by recrystallization from ethanol–ethyl acetate (or ether) as colorless crystals, m.p. 127–129° (FJ).

Anal. Calcd. for $C_{12}H_{12}N_2O_4$: C, 58.06; N, 4.87; N, 11.29. Found: C, 58.38; H, 4.97; N, 11.12.

Nitration of 1-methyl-2-phenoxypyridinium nitrate. Two grams of crude 1-methyl-2-phenoxypyridinium nitrate in 20 ml. of concd. nitric acid (sp. gr. = 1.5) containing 5 drops of concd. sulfuric acid was refluxed for 20 hr. The nitric acid was removed under reduced pressure and the residue crystallized from ethanol-ethyl acetate yielding 2.69 g. of white crystals, m.p. 165–167°. A small amount of hydrochloric acid was added and the excess acid removed by vacuum evaporation. The salt was dissolved in water and passed through Amberlite IRA-401 resin loaded with nitrate ion. Concentration of the solution under reduced pressure yielded a colorless residue which when crystallized from ethanol melted at 173.5–174.5° (MT). This product gave no depression of melting point when mixed with an authentic sample of 1-methyl-2-(4-nitrophenoxy)pyridinium nitrate. Infrared spectra showed the two materials to be identical.

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(11) T. Takahashi and J. Shibasaki, *J. Pharm. Soc. Japan*, **72**, 1137 (1952).