was evolved gradually and most of the solid dissolved. The filtered solution was concentrated and 30–60° petroleum ether was added to yield the methylchloropyridone as a white solid, m.p. 160–162° (9.0 g.). From the mother liquor was obtained a further 2.5 g. (total yield 11.5 g., 73%). Recrystallization from benzene gave long white needles, m.p. 162–163°.

Anal. Calcd. for C_6H_6ClNO: C, 50.02; H, 4.18; N, 9.77; Cl, 24.42. Found: C, 50.23; H, 4.13; N, 9.83; Cl, 24.37.

3,5-Dichloro-6-methyl-2-pyridone. Gaseous chlorine was passed through a cooled solution of 6-methyl-2-pyridone[15] (18.0 g.) in 2*N* sodium hydroxide (90 ml.). The precipitated solid was filtered, and the mother liquor chlorinated once more to obtain a second crop. The combined solids were dissolved in benzene, the solution dried (sodium sulfate), concentrated, and cooled. The crystalline precipitate (11.5 g., 40%: m.p. 215–218°) was filtered and dried. Recrystallization from benzene raised the melting point to 219–220°.

Anal. Calcd. for $C_6H_5Cl_2NO$: C, 40.50; H, 2.81; N, 7.86; Cl, 39.30. Found: C, 40.93; H, 2.87; N, 8.08; Cl, 38.99.

2-Pyridoxyacetic acids and derivatives. The procedures employed are exemplified by the following preparations in the 3,5-dichloro series: *Ethyl 3,5-dichloro-2-pyridoxyacetate* (XI). A 150 ml. 3-necked flask fitted with a reflux condenser, mechanical stirrer, and dropping funnel, and containing 3,5-dichloro-2-pyridone (8.0 g.), was heated in an oil bath (bath temperature 160–165°). Ethyl diazoacetate (10.0 ml.) was added dropwise to the stirred pyridone over a period of 3 hr. (bath temperature 155–165°). Heating was continued for 1 additional hr. and the hot dark sirup transferred to a Claisen flask. Distillation at 2 mm. yielded the desired ester XI (b.p. 110–120°; 9.0 g., 74%). On redistillation most of the ester boiled at 115–117° (2 mm.), and solidified on cooling. Crystallized from 30–60° petroleum ether, it formed needles, m.p. 40–41°. For analysis see Table I.

Distillation of the pot residue from the diazoacetic ester reaction gave a small amount of viscous liquid (b.p. 160–200° at 2 mm.), solidifying on standing to a semisolid mass. After several crystallizations from chloroform–petroleum ether, the pure *ethyl 3,5-dichloropyridone N-acetate* formed gleaming white flakes, m.p. 105–106°.

Anal. Calcd. for $C_9H_9Cl_2NO_3$: C, 43.20; H, 3.60; N, 5.06; Cl, 28.41. Found: C, 43.36; H, 3.62; N, 5.22; Cl, 28.20.

3,5-Dichloro-2-pyridoxyacetic acid (X). To a solution of the ethyl ester XI (3.0 g.) in ethanol (20 ml.) was added 1.023*N* sodium hydroxide (25 ml.), and the mixture was refluxed for 5.5 hr. The solvent was removed under vacuum and the residue dissolved in the minimal amount of water and neutralized by the addition of the theoretical quantity (22 ml.) of 1.162*N* sulfuric acid. The precipitated oxyacetic acid (2.45 g., 93%) was filtered, washed with a little cold water, and dried. Recrystallization from benzene gave small hard prisms, m.p. 170–171°. For analysis see Table I.

3,5-Dichloro-2-pyridoxyacetamide (XII). A solution of the ethyl ester XI (3.0 g.) in absolute ethanol (65 ml.) was cooled and saturated with gaseous ammonia. After several days in a refrigerator, the amide separated as long colorless needles, m.p. 167–168°, which were filtered and washed with cold ethanol. Concentration of the mother liquor yielded a second crop; the total yield was 2.2 g. (83%). The first crop of amide was directly analytically pure. For analysis see Table I.

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[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Pyridine Derivatives. III. The Rearrangement of Some Simple 3-Halopyridine-*N*-oxides[1]

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3-Chloropyridine, 3-bromopyridine, and 3-fluoropyridine were oxidized to the corresponding *N*-oxides, which were converted by hot acetic anhydride to haloacetoxypyridines. Hydrolysis of the latter yielded in all three cases the 3-halo-2-pyridones rather than the 5-halo isomers.

When pyridine-*N*-oxide is heated with acetic anhydride rearrangement of the oxygen function into the α-position of the ring occurs with the production of 2-acetoxypyridine.[2] The only simple β-substituted pyridine-*N*-oxide which has been subjected to this rearrangement is the 3-methyl derivative, which gives 3-methyl-2-acetoxypyridine, hydrolyzed by aqueous acid to 3-methyl-2-pyridone.[3] The object of the work reported here was to determine whether 3-halopyridine-*N*-oxides would rearrange in a similar manner to 3-halo-2-acetoxypyridines, or whether the rearrangement would occur para to the halogen atoms to give 5-halo-2-acetoxypyridines.

3-Fluoropyridine (I), 3-chloropyridine (II), and 3-bromopyridine (III) were converted to the corresponding *N*-oxides (IV, V, and VI) by oxidation with peracetic acid. Each *N*-oxide was rearranged by boiling acetic anhydride, and the substituted 2-acetoxypyridines (VII, VIII, and IX) which were formed were hydrolyzed to the corresponding 2-pyridones. In all cases only a single 2-pyridone was obtained, and this proved to be the 3-halo-derivative (X, XI, and XII). 3-Chloro-2-pyridone has been reported previously,[4] but 3-bromo-2-pyridone and 3-fluoro-2-pyridone are new compounds. However, 5-bromo-2-pyridone[5] and 5-

(1) Supported by a contract with the U. S. Army Chemical Corps, Fort Detrick, Frederick, Md.

(2) For a review of pyridine-*N*-oxide reactions, see: A. R. Katritzsky, *Quart. Revs.*, **10**, 395 (1956).

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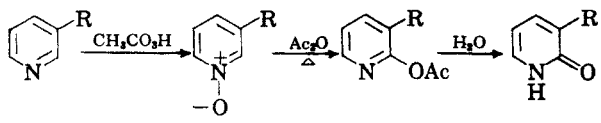
fluoro-2-pyridone[6] are known, and were shown to be different in melting point and infrared spectrum from the pyridones obtained *via* the *N*-oxide rearrangement.



I, R = F IV, R = F VII, R = F X, R = F
II, R = Cl V, R = Cl VIII, R = Cl XI, R = Cl
III, R = Br VI, R = Br IX, R = Br XII, R = Br

The effect of the 3-halo substituents on the ultraviolet spectrum of the 2-pyridone system is of some interest (Table I). 3-Fluoro-2-pyridone exhibits maxima almost identical to those of the parent 2-pyridone,[7] but 3-chloro-2-pyridone and 3-bromo-2-pyridone show appreciable bathochromic shifts.

TABLE I

ULTRAVIOLET MAXIMA OF 3-HALO-2-PYRIDONES (IN 95% ETHANOL)

3-Substituent	Mμ λ_{max} (E_{max})	Mμ λ_{max} (E_{max})
H[7]	227 (10,000)	297 (6310)
F	226 (5950)	296 (5510)
Cl	233 (5310)	306 (6060)
Br	234 (4350)	310 (6680)

EXPERIMENTAL[8]

3-Chloropyridine-N-oxide (V). A mixture of 3-chloropyridine (II, 2.50 g.), glacial acetic acid (45 ml.) and 30% aqueous hydrogen peroxide (10 ml.) was heated on a steam bath for 3 hr. An additional 5 ml. of 30% hydrogen peroxide was added and the solution was reheated for four days. The mixture was concentrated under reduced pressure to 20 ml., an equal volume of water was added, and the solution was concentrated to a sirup. Solid potassium carbonate (10.0 g.) was added and the residue was continuously extracted with chloroform overnight. The extract was concentrated under reduced pressure and the remaining liquid was distilled to give 1.00 g. (35%) of a colorless oil, b.p. 88–89° (1 mm.).

The hydrochloride of 3-chloropyridine-*N*-oxide was obtained from water as needles, m.p. 127.5–128.5°.

Anal. Calcd. for $C_5H_5Cl_2NO$: C, 36.17; H, 3.04; Cl, 42.71; N, 8.44. Found: C, 36.20; H, 2.99; Cl, 42.62; N, 8.61.

2-Acetoxy-3-chloropyridine (VIII). A solution of 3-chloropyridine-*N*-oxide (V, 0.90 g.) in acetic anhydride (15 ml.) was boiled under reflux for 4 hr. The reaction mixture was distilled directly to give 0.72 g. (61%) of a colorless liquid, b.p. 54–55° (1 mm.). The compound was not submitted to analysis since it hydrolyzed readily in air to the pyridone.

3-Chloro-2-pyridone (XI). A mixture of 2-acetoxy-3-chloropyridine (VIII, 0.68 g.) in 10% aqueous hydrochloric acid (10 ml.) was heated under reflux for 4 hr., then neutralized to the Congo Red endpoint with potassium hydroxide pellets and evaporated to dryness on a steam bath. The solid residue was broken up and was extracted several times with hot benzene. The combined extracts upon concentration and standing gave 0.40 g. (78%) of needles, m.p. 181.8–182.8°. An authentic sample[4] showed an identical infrared spectrum and gave no mixed melting point depression.

Anal. Calcd. for C_5H_4ClNO: C, 46.35; H, 3.11; Cl, 28.14; N, 10.90. Found: C, 46.70; H, 3.48; Cl, 27.75; N, 11.05.

3-Bromopyridine-N-oxide (VI). A mixture containing 3-bromopyridine (III, 10.00 g.), glacial acetic acid (50 ml.), and 30% aqueous hydrogen peroxide (10 ml.) was treated exactly as described for 3-chloropyridine. The residual liquid was distilled to give 5.07 g. (46%) of a viscous oil, b.p. 97–99° (0.5 mm.).

The hydrochloride of 3-bromopyridine-*N*-oxide was obtained from water as needles, m.p. 133.5–134.5° (dimorphism ?); reported, m.p. 181.5° and 181–182°.[9,10]

Anal. Calcd. for $C_5H_5BrClNO$: C, 28.53; H, 2.39; Br, 37.97; Cl, 16.85; N, 6.66. Found: C, 28.64; H, 2.30; Br, 37.92; Cl, 16.71; N, 6.74.

2-Acetoxy-3-bromopyridine (IX). A solution of 3-bromopyridine-*N*-oxide (VI, 2.50 g.) in acetic anhydride (15 ml.) was treated as described for 3-chloropyridine-*N*-oxide. Distillation gave 1.55 g. (50%) of a colorless liquid; b.p. 77–78° (0.5 mm.). The ready hydrolysis of the compound precluded an analysis.

3-Bromo-2-pyridone (XII). A mixture of 2-acetoxy-3-bromopyridine (IX, 1.08 g.) in 10% hydrochloric acid (10 ml.) was treated as described for 2-acetoxy-3-chloropyridine. The concentrated benzene extracts gave 0.69 g. (80%) of needles, m.p. 186.5–187.0°.

Anal. Calcd. for C_5H_4BrNO: C, 34.51; H, 2.31; Br, 45.93; N, 8.05. Found: C, 34.74; H, 1.97; Br, 46.13; N, 8.13.

3-Fluoropyridine-N-oxide (IV). A mixture containing 3-fluoropyridine (I, 7.63 g.), glacial acetic acid (50 ml.), and 30% aqueous hydrogen peroxide (10 ml.) was treated as described for 3-chloropyridine. The residual solid was sublimed under vacuum to give 2.12 g. (19%) of needles, m.p. 62.5–63.0°; on exposure to the atmosphere, the needles liquefied almost immediately.

The picrate of 3-fluoropyridine-*N*-oxide was obtained from benzene as needles, m.p. 107.0–108.0°.

Anal. Calcd. for $C_{11}H_7FN_4O_8$: C, 38.61; H, 2.06. Found: C, 38.77; H, 2.41.

2-Acetoxy-3-fluoropyridine (VII). A mixture containing 3-fluoropyridine-*N*-oxide (IV, 2.26 g.) in acetic anhydride (15 ml.) was treated as described for 3-chloropyridine-*N*-oxide. Distillation gave 2.22 g. (65%) of a colorless liquid; b.p. 82–83° (1 mm.). Ready hydrolysis of the compound prevented an analysis.

3-Fluoro-2-pyridone (X). A mixture of 2-acetoxy-3-fluoropyridine (VII, 0.51 g.) and 10% hydrochloric acid (10 ml.) was treated as described for 2-acetoxy-3-chloropyridine. The concentrated benzene extracts gave 0.27 g. (80%) of needles, m.p. 166.0–166.5°.

Anal. Calcd. for C_5H_4FNO: C, 53.10; H, 3.56; F, 16.80; N, 12.39. Found: C, 53.15; H, 3.61; F, 16.71; N, 12.37.

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