

Q and e were calculated.¹ The results are summarized in Table III.

Copolymerizations with methyl acrylate proceeded so vigorously and exothermically that no soluble polymers were produced.

Ultraviolet spectra were measured on a Beckmann DU spectrophotometer, as modified by Process and Instruments Co. The results are summarized in Table IV.

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[CONTRIBUTION FROM THE ILLINOIS STATE GEOLOGICAL SURVEY]

Aromatic Fluorine Compounds. IX. 2-Fluoropyridines^{1,2}

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The synthesis of 2-fluoro-3-nitropyridine, 2-fluoro-5-nitropyridine and 3-bromo-2-fluoro-5-nitropyridine from the corresponding chloropyridines in yields exceeding 50% has been accomplished in dimethylformamide by replacement of -Cl by -F using potassium fluoride. The 3-bromine as well as the 5-nitro group activates the 2-position as shown by the increased reaction velocity of the 2-chlorine in 3-bromo-2-chloro-5-nitropyridine as compared with 2-chloro-5-nitropyridine. With 2-chloro-4-nitropyridine both groups appear to be replaced, but no 2,4-difluoropyridine could be isolated. A fluoropyridine was not isolated by reaction of potassium fluoride with 2-bromopyridine, 2-bromopyridine-N-oxide, 2-chloropyridine or 2-chloropyridine hydrochloride.

Generally, 2-fluoropyridines are obtained in low yield from aminopyridines by diazotization in hydrofluoric acid^{3,4} or by the Schiemann reaction.⁵ The work reported here describes the synthesis of substituted 2-fluoropyridines in good yield using the previously reported potassium fluoride exchange technique.⁶

Using this method, 2-chloro-3-nitro- and 2-chloro-5-nitropyridine when heated with potassium fluoride in dimethylformamide (DMF) gave 2-fluoro-3-nitro- and 2-fluoro-5-nitropyridine in 76 and 78% yields, respectively. When 3-bromo-2-chloro-5-nitropyridine was heated with potassium fluoride for one hour at 100°, a 50% yield of 3-bromo-2-fluoro-5-nitropyridine was isolated as the sole product. That 2-chloro-3-fluoro-5-nitropyridine could not be isolated demonstrates preferential activation of the 2-position by the 5-nitro group in this substitution. Additional activation of the 2-position by the adjacent 3-bromine is demonstrated by comparing this example to 2-chloro-5-nitropyridine which, under similar conditions, afforded only a 26% yield of 2-fluoro-5-nitropyridine with a 38% recovery of starting material. Under these conditions no reaction could be detected with 2-chloro-3-nitropyridine.

Activation by the ring nitrogen alone is insufficient, for neither 2-chloro- nor 2-bromopyridine gave 2-fluoropyridine, although with potassium fluoride the latter example gave a good silver halide test⁷ in dimethyl sulfoxide (DMSO) with the evolution of dimethyl sulfide. This result alone cannot be accepted as evidence that replacement by fluorine did take place, for it has been shown that alkyl halides and DMSO may form

O- or S-alkylated adducts containing ionic halogen,^{8,9} and that DMSO can bring about an oxidative displacement of active halogen.¹⁰ Indeed, we have found that when 2-bromopyridine was heated in DMSO in the absence of potassium fluoride, dimethyl sulfide was evolved and, as before, a positive silver halide test was obtained. Attempts to increase the ease of replacement of the 2-halogen by employing 2-chloropyridine hydrochloride or 2-bromopyridine-N-oxide failed.

When 2-chloro-4-nitropyridine was heated with potassium fluoride in DMF, very little chlorine was displaced and some oxides of nitrogen were evolved. In DMSO at 160° the reaction was rapid, accompanied by the formation of chloride ion and evolution of oxides of nitrogen. One possible product arising from the replacement of both the chloro and nitro groups is 2,4-difluoropyridine which could not be isolated. In the absence of potassium fluoride no chlorine was displaced. This would indicate that the failure to isolate the 4-fluoropyridine probably was due to its instability, although again the observed results may have been caused by the action of the solvent (DMSO) in the presence of potassium fluoride.

Experimental^{11,12}

2-Fluoro-3-nitropyridine.¹³—To a solution of 12.3 g. of 2-chloro-3-nitropyridine¹⁴ and 30 ml. of DMF at 120° was added 9 g. of anhydrous potassium fluoride. After 6 hours at 150° the black mixture was cooled, poured onto crushed ice, saturated with salt and subjected to steam distillation. The distillate was extracted with ether, and the combined ether extracts after drying were evaporated. The remaining yellow oil was distilled to give 8.4 g. (76% yield) of 2-fluoro-3-nitropyridine, b.p. 109–109.5° (10 mm.), n_D^{25} 1.5278.

Anal. Calcd. for $C_5H_4FN_2O_2$: C, 42.26; H, 2.13. Found: C, 42.34; H, 2.00.

(8) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

(9) R. Kuhn, *Angew. Chem.*, **17**, 570 (1957); R. Kuhn and H. Grischmann, *Liebigs Ann.*, **611**, 117 (1958).

(10) Kornblum, *et al.*, *THIS JOURNAL*, **79**, 6562 (1957).

(11) All boiling points and melting points are uncorrected.

(12) Analyses by D. R. Dickerson, microanalyst for the Illinois State Geological Survey.

(13) This compound is a lachrymator and severe skin irritant.

(14) A. E. Chichibabin and I. G. Builinkin, *J. Russ. Phys.-Chem. Soc.*, **50**, 471 (1920).

(1) Published by permission of the Chief of the Illinois State Geological Survey.

(2) Presented before the Division of Organic Chemistry at the 134th Meeting of the American Chemical Society, Chicago, Ill., September 8, 1958.

(3) A. E. Chichibabin and J. G. Rjazancev, *J. Russ. Phys.-Chem. Soc.*, **47**, 1571 (1915).

(4) W. Gruber, *Can. J. Chem.*, **31**, 1020 (1953).

(5) A. Roe and G. F. Hawkins, *THIS JOURNAL*, **69**, 2443 (1947).

(6) G. C. Finger and C. W. Kruse, *ibid.*, **78**, 6034 (1956).

(7) The course of the reaction was conveniently followed by dissolving a small portion of the reaction mixture in water and adding dilute nitric acid and silver nitrate. The precipitated silver halide indicated halogen displacement.

2-Fluoro-5-nitropyridine.¹³—To a stirred solution of 300 ml. of DMF and 100 g. of 2-chloro-5-nitropyridine¹⁴ at 120° was added 73.3 g. of anhydrous potassium fluoride. After 8 hours at 120° the brown reaction mixture was cooled and processed as in the preceding preparation. The crude product was distilled to give 70.1 g. (78% yield) of 2-fluoro-5-nitropyridine, b.p. 86–87° (7 mm.), n_D^{25} 1.5243, whose infrared spectrum was identical with 2-fluoro-5-nitropyridine, n_D^{25} 1.5240, obtained from diazotized 2-amino-5-nitropyridine and hydrofluoric acid.⁴

3-Bromo-5-nitro-2-pyridone.—A solution of 28 g. of 2-amino-3-bromo-5-nitropyridine¹⁶ in 900 ml. of 25% aqueous sulfuric acid was cooled to 0° giving a slurry of the amine salt. To this was added dropwise with stirring at –2 to 0°, 13.3 g. of sodium nitrite in 65 ml. of water. This mixture then was heated to boiling, filtered and allowed to cool giving 3-bromo-5-nitro-2-pyridone as light tan needles which when collected, washed with water and air-dried amounted to 18.3 g. (72% yield), m.p. 206–209°. Decolorization and recrystallization from water gave the pure compound as pale yellow needles, m.p. 212° dec.

Anal. Calcd. for $C_5H_3BrN_2O_2$: C, 27.42; H, 1.38. Found: C, 27.29; H, 1.63.

3-Bromo-2-chloro-5-nitropyridine.—A stirred solution of 4.1 g. of 3-bromo-5-nitro-2-pyridone, 4 g. of phosphorus pentachloride and 1 ml. of phosphorus oxychloride was heated under reflux for 3 hours. The dark brown mixture was then concentrated *in vacuo*, and poured onto crushed ice. The product was collected, washed with water until the washings were neutral to litmus and air-dried, giving 4.2 g. (95% yield) of a tan solid, m.p. 65–66.5°. Vacuum sublimation at 60–70° (2 mm.) gave the pure compound as a white, highly crystalline solid, m.p. 67.3–68°.

Anal. Calcd. for $C_5H_3BrClN_2O_2$: C, 25.23; H, 0.85. Found: C, 25.47; H, 0.88.

3-Bromo-2-fluoro-5-nitropyridine.—A stirred mixture of 3.8 g. of 3-bromo-2-chloro-5-nitropyridine, 15 ml. of DMF and 1.8 g. of anhydrous potassium fluoride was heated for one hour at 100°. The mixture was cooled, poured onto ice, and subjected to steam distillation. After extraction of the distillate with ether, the combined ether extract was dried and evaporated to give 2.5 g. (69% yield) of crude product, m.p. 58–61°. Repeated vacuum sublimation gave 1.78 g. (50% yield) of pure 3-bromo-2-fluoro-5-nitropyridine as a light yellow crystalline solid, m.p. 60–61.5°. For analysis a sample was decolorized and recrystallized from ethanol with subsequent vacuum sublimation.

Anal. Calcd. for $C_5H_2BrFN_2O_2$: C, 27.17; H, 0.91; N, 12.68. Found: C, 27.36; H, 0.95; N, 12.43.

2-Chloropyridine-N-oxide.¹⁷—To a stirred solution of 50 g. of 2-chloropyridine and 66 ml. of glacial acetic acid was added dropwise 137 ml. of 40% peracetic acid at 45°. No heat of reaction was observed. After this addition, the mixture was heated at 50° for 5 hours and then at 70° for 17 hours. It was then concentrated *in vacuo* to 150 ml. on a steam-bath, poured onto crushed ice, made strongly alkaline with 40% aqueous sodium hydroxide and extracted with chloroform which was dried with magnesium sulfate to which was added a small amount of sodium carbonate. Evaporation of the solvent gave 47.6 g. of an oil which, after adding 10 ml. of anhydrous ether, gave 45.8 g. (80%

yield) of tan plates, m.p. 66–68°. Decolorization and recrystallization from an ether-ethanol mixture gave 2-chloropyridine-N-oxide as colorless plates, m.p. 69–69.5°.

Anal. Calcd. for C_5H_4ClNO : C, 46.35; H, 3.11; N, 10.81; Cl, 27.37. Found: C, 46.22; H, 3.04; N, 10.72; Cl, 27.50.

2-Chloro-4-nitropyridine-N-oxide.—To 15 ml. of concentrated sulfuric acid was added 10 g. of 2-chloropyridine-N-oxide at 0 to 5°. Then a mixture of 15 ml. of concentrated sulfuric acid and 27 ml. of fuming nitric acid (sp. gr. 1.5) was added dropwise with stirring at 1 to 2° over a 45-minute period. The mixture was heated slowly to 90° during one hour and then maintained at 90° with stirring for an additional hour after which the mixture was cooled to 10°, poured onto a stirred ice-water mixture, and neutralized with sodium carbonate. The yellow precipitate was collected, partially air-dried, and dissolved in 100 ml. of hot chloroform. The aqueous filtrate was extracted with chloroform. The combined chloroform solutions were dried and evaporated to give 11.4 g. of a tan solid, m.p. 144–151°, which when recrystallized from an ethanol-chloroform mixture gave 9.2 g. (69% yield) of 2-chloro-4-nitropyridine-N-oxide as yellow plates, m.p. 153–153.5°.

Anal. Calcd. for $C_5H_3ClN_2O_2$: C, 34.40; H, 1.73; N, 16.05; Cl, 20.31. Found: C, 34.51; H, 1.61; N, 16.04; Cl, 20.17.

2-Chloro-4-nitropyridine.—Following the procedure of Hamana,¹⁸ a mixture of 2 g. of 2-chloro-4-nitropyridine-N-oxide, 30 ml. of ethyl acetate and 2.9 ml. of phosphorus trichloride was heated with stirring at 70° for 10 minutes. The mixture was cooled, poured into an ice-water mixture, made alkaline to litmus with 10% aqueous sodium hydroxide and extracted with chloroform. After drying the combined chloroform extracts, the solvent was evaporated to give 1.65 g. (91% yield) of 2-chloro-4-nitropyridine as light yellow needles, m.p. 53.5–54°. Recrystallization from ethanol did not alter the melting point.

Anal. Calcd. for $C_5H_3ClN_2O_2$: C, 37.87; H, 1.91; Cl, 22.36. Found: C, 38.10; H, 2.02; Cl, 22.26.

2-Chloro-4-nitropyridine and Potassium Fluoride.—A stirred mixture of 5 g. of 2-chloro-4-nitropyridine, 3.7 g. of anhydrous potassium fluoride and 10 ml. of DMSO after one hour at 160° gave a good silver halide test.⁷ The mixture was cooled, poured onto crushed ice, saturated with sodium chloride and subjected to steam distillation. The distillate, 36 ml., was extracted repeatedly with chloroform and the combined extracts were dried. No residue remained upon evaporation of the chloroform. The pot residue from the steam distillation gave a small portion of unidentified solid, m.p. 96–101°, which when sublimed melted at 100.5–105°.

2-Chloro-4-nitropyridine and DMSO in the absence of potassium fluoride under similar conditions gave no evidence of reaction.

2-Chloropyridine Hydrochloride.—A slow stream of dry hydrogen chloride gas was passed for 2.25 hours into a stirred solution of 20 g. of 2-chloropyridine in 200 ml. of anhydrous ether. The ether was evaporated under reduced pressure leaving colorless, very hygroscopic needles, which were dried in a vacuum desiccator over calcium chloride. The 2-chloropyridine hydrochloride, 23.4 g. (89% yield), m.p. 101.5–102°, decomposes upon standing and darkened upon exposure to light.

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(17) The method of Adams and Reifschneider, *This Journal*, **79**, 2236 (1957), for the preparation of 2-bromo-6-methylpyridine-N-oxide was used to prepare 2-chloropyridine-N-oxide.