extracted with warm pentane. The pentane-insoluble solid (0.15 g) was recrystallized from pentane–chloroform, mp 134–135°.

Anal. Calcd for $C_9H_{10}F_2N_2O$: C, 53.99; H, 5.04; N, 14.00; F, 18.98. Found: C, 53.27; H, 5.30; N, 13.75; F, 17.97.

Reductions with Titanous Chloride. 2-Methyl-2-difluoraminopropane.[6]—To 0.61 g of the difluoramine in 10 ml of glacial acetic acid was added 1.5 ml of 20% titanous chloride reagent at 60°. The solution was heated 80° for an hour and then allowed to stir overnight. The clear solution was divided into two portions. One portion was treated with 2,4-dinitrophenylhydrazine reagent to yield a yellow solid, mp 125°, identical by mixture melting point and infrared spectrum with an authensample of acetone 2,4-dinitrophenylhydrazone.

The other portion was made alkaline and steam distilled. The distillate was treated with phenyl isothiocyanate to yield a white solid, mp 115°, identical with an authentic sample of N-methyl-N′-phenylthiourea.

α-Difluoramino-α-methylphenylacetonitrile.—To a solution 3.68 g (0.02 mole) of the difluoramine was added 60 ml of 20% titanous chloride reagent at 60°. The solution was heated at 75° for 2 hr at which point decolorization had been effected. The mixture was poured into water and extracted with methylene chloride. Concentration of these extracts yielded 0.36 g of unreacted difluoramine.

The aqueous solution was made basic and extracted with CH_2Cl_2. Concentration of these extracts yielded 2.4 g of a mixture of acetophenone (15%) and aniline (85%) identified by their infrared spectra and glpc retention times on a 5° silicone column at 148°.

Alkylations of Heterocyclic Ambident Anions. II. Alkylation of 2-Pyridone Salts[1a]

GEORGE C. HOPKINS, JAMES P. JONAK,[1b] HARRY J. MINNEMEYER, AND HOWARD TIECKELMANN

Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214

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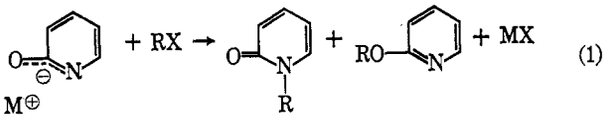
Alkali metal and silver salts of 2-pyridone were treated with simple alkyl halides and tosylates in a variety of solvents, and the ratios of nitrogen to oxygen alkylation were quantitatively assayed. By variation of the solvent and metal ion, virtually exclusive nitrogen or oxygen alkylation could be obtained in methylations, ethylations, and benzylations. Oxygen alkylation predominated in reactions with isopropyl compounds presumably owing to steric factors. A kinetic study in dimethylformamide demonstrated that reactions of ethyl and isopropyl iodides with the sodium salt were second order. Solvent had the largest effect on silver salt alkylations where alkoxypyridine formation was favored in poor ion-solvating media. Alkali metal salts were less solvent sensitive, but a moderate increase in oxygen alkylation was observed in dimethylformamide compared to protic and nonpolar solvents. The preference of the silver salt to alkylate on oxygen in nonpolar media is proposed to result from heterogeneous reaction.

The studies described in this paper are a continuation of our investigations of alkylation reactions of ambident anions derived from heterocyclic compounds.[2] A general method for alkylating 2-pyridones consists of reacting their metal salts, usually in a solvent, with alkyl halides.[3] It is well-known that this reaction can give both nitrogen and oxygen alkylation. Nitrogen *vs.* oxygen alkylation in the 2-pyridone system has been discussed by several authors,[3,4] but a reliable assessment of the factors which govern product distribution was limited by the absence of a sufficient body of comparable data. Thus, while it is commonly accepted that silver salts of 2-pyridones favor oxygen alkylation, and that the corresponding alkali metal salts favor nitrogen alkylation,[3] silver and alkali metal salts of 2-pyridone have not been alkylated in a common solvent under comparable reaction conditions. The solvent is currently recognized as an important consideration in ambident anion alkylations,[5] but its influence on alkylations of 2-pyridone salts has not been evaluated. It has been noted also that steric factors are significant in determining the alkylation site of 2-pyridones,[3] but only two examples of this influence were found in the literature. Both examples illustrated that oxygen alkylation was favored when a methyl group occupied the 6 position of 2-pyridone and bulky alkylating agents were employed.[6]



(1)

The present paper reports a systematic study of the sensitivity of the alkylation site of metal salts of 2-pyridone toward a number of factors known to have influence in other ambident anion systems.[4,5,7,8] Alkali metal and silver salts of 2-pyridone were treated with simple alkyl and benzyl halides or tosylates. Factors such as the cation, solvent, leaving group, and alkyl halide structure were systematically varied. Product ratios were quantitatively determined by vapor phase chromatography. Calibrations were made with characterized or known samples of the nitrogen and oxygen alkylated pyridines and 2-pyridone. Kinetic studies of alkali metal salt alkylations are described in the Experimental Section.

Results and Discussion

Table I summarizes data which show the influence of cation and alkylating agent in determining the reaction site in 2-pyridone. All reactions listed in this table were conducted in dimethylformamide under comparable reaction conditions. Influences due to variation of solvent are illustrated by Tables II and

(1) (a) This investigation was supported by the U. S. Public Health Service Grant No. GM-12112 from the National Institute of General Medical Sciences; (b) Allied Chemical Corp. Fellow, 1964–1965.

(2) G. C. Hopkins, J. P. Jonak, H. Tieckelmann, and H. J. Minnemeyer, *J. Org. Chem.*, **31**, 3969 (1966).

(3) H. Meislich, "Pyridine and Its Derivatives," Part III, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1962, pp 631–640.

(4) N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Am. Chem. Soc.*, **77**, 6269 (1955).

(5) (a) N. Kornblum, P. J. Berrigan, and W. J. LeNoble, *ibid.*, **85**, 1141 (1963); (b) N. Kornblum, R. Seltzer, and P. Haberfield, *ibid.*, **85**, 1148 (1963).

(6) (a) F. Ramirez and A. P. Paul, *J. Org. Chem.*, **19**, 183 (1954); (b) N. J. Leonard and S. H. Boyer, *J. Am. Chem. Soc.*, **72**, 2980 (1950).

(7) A. Brändstrom, *Arkiv Kemi*, **6**, 155 (1953).

(8) (a) N. Kornblum and A. P. Laurie, *J. Am. Chem. Soc.*, **81**, 2705 (1959); (b) N. Kornblum and R. Seltzer, *ibid.*, **83**, 3668 (1961).

TABLE I
EFFECT OF ALKYLATING AGENT AND CATION ON THE ALKYLATION SITE OF 2-PYRIDONE[a]

Alkylating agent[b]	Salt	% yield[c]	Product compn, % N-Alkyl	O-Alkyl	2-Pyridone
MeI	Na	93	95	5	...
MeI	K	83	92	8	...
MeI	Ag	81	74	12	21
EtBr	Na	94	77	23	...
EtBr	K	94	66	34	...
EtBr	Ag	80	20	38	42
EtI	Na	87	69	31	...
EtOTos	Na	89	61	39	...
i-PrBr	Na	84	29	68	3
i-PrBr	K	81	27	71	2
i-PrBr	Ag	No alkylation; only 2-pyridone was formed			
i-PrI	Na	90	30	61	9
i-PrOTos	Na	87	30	63	7
$PhCH_2Cl$	Na	100	94	6	...
$PhCH_2Br$	Na	95	97	3	...
$PhCH_2Br$	Ag	85	54	46	...
$PhCH_2I$	Na	99	98	2	...

[a] All reactions were conducted at room temperature in dimethylformamide. Reactions were homogeneous with the alkali metal salts, but heterogeneous conditions prevailed in all silver salt alkylations. Alkylations were complete within 24 hr in all cases. [b] Alkylating agents were in 5% excess. [c] Determined by quantitative vpc.

TABLE II
ALKYLATION OF THE SILVER SALT OF 2-PYRIDONE IN SELECTED SOLVENTS[a]

Alkyl halide[b]	Solvent	% yield[c]	Product compn, % N-Alkyl	O-Alkyl	2-Pyridone
MeI	DMF	81	74	12	14
MeI	Ether	81	37	42	21
MeI[d]	Benzene	99	3	97	...
MeI[d]	Hexane	94	3	97	...
EtBr	DMF	80	20	38	42
EtI	DME[e]	90	27	54	19
EtI	Ethanol	91	1	80	19
EtI	Ether	93	1	96	3
EtI	Benzene	93	...	100	...
EtI[d]	Benzene	100	...	100	...
$PhCH_2Br$	DMF	85	54	46	...
$PhCH_2Br$[d]	Benzene	100	...	100	...
$PhCH_2Br$[d]	Pentane	100	...	100	...
i-PrBr	DMF	No alkylation; only 2-pyridone was formed			
i-PrI[d]	Benzene	100	...	100	...
i-PrI[d]	Hexane	100	...	100	...

[a] All reactions were conducted at room temperature. [b] Alkyl halide varied from 5 to 400% excess, but had no effect on product ratios. [c] Determined by quantitative vpc. [d] These reactions were conducted by *in situ* generation of the silver salt with silver carbonate. [e] 1,2-Dimethoxyethane.

III for the silver and alkali metal salt alkylations, respectively.

As suggested in the literature,[3,4] the silver salt of 2-pyridone gave more oxygen alkylation when compared with its alkali metal salts. In dimethylformamide oxygen alkylation of the silver salt increased as the alkyl halides were varied from methyl to ethyl or benzyl halides, while isopropylation of the silver salt produced only 2-pyridone suggesting the incursion of an elimination reaction. These results are completely consistent with Kornblum's proposal that the silver ion enhances unimolecular character in the silver salt reactions, thereby favoring alkylation at the more electronegative oxygen atom.[4] However, the following studies, especially those related to the influence of solvent, led us to prefer an alternate explanation for the increased oxygen alkylation from the silver salt.

TABLE III
SOLVENT EFFECTS ON ALKYLATIONS OF THE SODIUM SALT OF 2-PYRIDONE[a]

Alkyl halide[b]	Solvent	% yield[c]	Product compn, % N-Alkyl	O-Alkyl	2-Pyridone
EtBr	DMF	94	77	23	...
EtBr	MeOH	80	66	5	29
EtBr	DME[d]	88	87	6	7
i-PrI	DMF	90	30	61	9
i-PrI	MeOH	100	14	30	56
i-PrI	EtOH	86	27	54	19
i-PrI	DME	*e*	44	50	6

[a] All reactions were conducted at room temperature. Reaction mixtures in DME were heterogeneous, while all other were homogeneous. [b] Alkyl halides were 5% in excess except reactions with isopropyl iodide in alcohols and DME where 400% excess iodide was employed to enhance reaction rates. [c] Yields were established by quantitative vpc and are total volatile pyridines. [d] 1,2-Dimethoxyethane. [e] Reaction was 32% complete after 11 days, the time at which these product ratios were established.

It was found (Table II) that the silver salt alkylations were highly solvent sensitive. Only oxygen alkylation was observed in ethylations, isopropylations, and benzylations of the silver salt in nonpolar solvents such as benzene, hexane, and pentane. Under these conditions methylations led to only minor amounts of N-methyl-2-pyridone. Nitrogen alkylation increased in better ion-solvating media such as dimethylformamide, 1,2-dimethoxyethane, diethyl ether, and ethanol. This effect was maximum in methylations and benzylations where elimination reactions were not competitive in ion-solvating media. Solvent influence, as well as the theoretical yields of alkoxypyridines from ethylations and isopropylations in nonpolar solvents,[9] is not in the expected direction if it is assumed that in the silver salt the major fraction of charge resides on oxygen[10-12] and that oxygen alkylation is favored according to the ability of the solvent to enhance unimolecular character.

We propose that here oxygen alkylation is a result of heterogeneous reaction specific to the silver salt.[13] Thus, as the ion-solvating ability of the media increases, more reaction occurs in solution and oxygen alkylation is decreased while elimination reactions, where possible, become competitive due to enhanced unimolecular character in the alkylation transition state.

Alkylations of 2-pyridone in the presence of silver carbonate were conducted in benzene, *n*-hexane, and *n*-pentane and gave results similar to those obtained with the isolated silver salt. Some examples are included in Table II. This procedure eliminates the task of preparing the silver salt and retains the selective oxygen alkylation. These reactions with methyl iodide, ethyl iodide, isopropyl iodide, and benzyl bro-

(9) If a high degree of unimolecular character prevailed in these reactions, appreciable elimination reaction, with loss in yield of alkoxypyridine, would be expected.

(10) At present, the distribution of charge in the 2-pyridone anion is not understood,[11,12] but the most recent report[12] suggests that it is on oxygen.

(11) E. Spinner, *J. Chem. Soc.*, 1232 (1966).

(12) E. Spinner and J. C. B. White, *ibid.*, 966 (1966).

(13) All alkylations of the silver salt were run under heterogeneous conditions.

mide proceeded at least as rapidly as those of the isolated silver salt and were complete in 24 hr at room temperature. Yields of the oxygen-alkylated pyridines were near theoretical (vpc). Bench-scale preparations of 2-methoxy-, 2-isopropyloxy-, and 2-benzyloxypyridine by this procedure are described in the Experimental Section. The procedure is simple and may constitute a convenient synthesis for certain 2-alkoxypyridines.

The rates of silver salt alkylations were generally slow in nonpolar media when a stoichiometric quantity of the reactants was employed. A fourfold excess of the alkyl halide had no apparent effect on product ratios or yield, but the reaction rate was considerably increased. In ether with 5% excess alkylating agent, methyl and ethyl iodides reacted at approximately the same rates and were 57–60% complete after 4 days at room temperature. Under the same conditions, but with a fourfold excess of ethyl iodide, ethylation was 93% complete in 3 days.

In view of the relatively large solvent effects on the alkylation site of the silver salt of 2-pyridone, the generalization that electron-withdrawing substituents significantly alter ratios of nitrogen to oxygen alkylation from 2-pyridone silver salts needs to be reexamined.[3,14] It was proposed[3] that electron-withdrawing substituents *ortho* and *para* to the 2-oxo group favored alkylation at nitrogen. This conclusion, however, was based on alkylations conducted in different solvents. Alkylations of the substituted 2-pyridone silver salts had been run in alcohol,[15,16] whereas alkylation of the silver salt of 2-pyridone had been run in ether.[17]

Some results of the solvent study with the sodium salt of 2-pyridone are shown in Table III. Although methanol and ethanol have been the "traditional" solvents employed in 2-pyridone alkylations, they appear to be relatively poor solvents for ethylations and isopropylations.[18]

Solvent effects on product distributions from the sodium salt of 2-pyridone were relatively moderate and in the same direction as those observed in other comparable ambident anion systems.[2] Oxygen alkylation was increased in dimethylformamide compared to less polar aprotic and protic solvents. This is expected if the protic solvents show a greater tendency to hydrogen bond at oxygen[5a] and aprotic solvents of low dielectric constant favor the transition state leading to nitrogen alkylation where charge separation is minimum.[19]

Alkylations of the sodium salt were run in selected nonpolar solvents other than shown in Table III, but rates were generally too slow for study at ambient temperatures. In general, rates were rapid in dimethylformamide, intermediate in alcohols, and slow, or alkylation did not proceed at all, in poor ion-solvating media. Quantitative rate data for alkylations in dimethylformamide are illustrated in the Experimental Section.

From the data in Table I, it is observed that the alkyl halide structure is also a significant factor in determining the alkylation site of metal salts of 2-pyridone.[2] This effect was most pronounced in the alkali metal salt alkylations where a progressive increase in oxygen alkylation occurred when the halides were varied from benzyl or methyl to ethyl to isopropyl. In fact, isopropylation gave predominant oxygen alkylation.[20,21] Effects due to variation of leaving groups from chloride to bromide to iodide to tosylate were relatively minor.

The higher amount of nitrogen alkylation obtained in methylations of the alkali metal salts did not result from thermodynamic control since 2-methoxypyridine did not rearrange under the reaction or analysis conditions.[22] Kinetic studies, as illustrated in Figure 1, indicate that isopropylation proceeds by bimolecular nucleophilic substitution. The order of reactivity isopropylation < ethylation < methylation also suggests a bimolecular mechanism. The change in product ratios with alkylating agent is attributed to changes in the relative rates of alkylation at nitrogen and oxygen resulting from greater steric requirements for nitrogen alkylation.[23]

An interesting and practical result of these studies is that control of the alkylation site of 2-pyridone salts can be effected by manipulation of a few simple variables. This is illustrated in Table IV by rearranged data from the preceding tables. The control of product distributions was minimized in alkylations with isopropyl halides where steric factors enter.

TABLE IV
SELECTIVITY IN ALKYLATIONS OF 2-PYRIDONE[a]

Alkyl halide	Salt	Solvent	Product compn, % N-Alkyl	O-Alkyl	2-Pyridone
MeI	Na	DMF	95	5	...
MeI	Ag	Benzene	3	97	...
EtBr	Na	DME[b]	87	6	7
EtI	Ag	Benzene	...	100	...
$PhCH_2Br$	Na	DMF	97	3	...
$PhCH_2Br$	Ag	Benzene	...	100	...

[a] Data from Tables I–III. [b] 1,2-Dimethoxyethane.

In summary, the relationships between and magnitudes of the influence of solvents and alkyl halides on the alkylation site of silver and alkali metal salts of 2-pyridone have been compared under similar reaction conditions. The alkylation site of 2-pyridone salts

(14) We are currently examining several ring-substituted 2-pyridones and will report our results in a subsequent paper.

(15) C. Rath, *Ann.*, **484**, 52 (1930).

(16) W. Gruber, *Can. J. Chem.*, **31**, 1181 (1953).

(17) H. Pechmann and O. Baltzer, *Ber.*, **24**, 3144 (1891).

(18) In these alkylations, considerable amounts of 2-pyridone are generated from its salts. Dehydrohalogenation of the alkyl halides is apparently more favored in the alcohols than in dimethylformamide.

(19) This explanation is based on rationale due to Kornblum who assumed that in the alkylation of sodium β-naphthoxide the reaction in aprotic solvents of low dielectric constant was essentially one involving ion pairs. The transition state leading to carbon alkylation was assumed to possess the better geometry for the formation of a sodium bromide ion pair.[5b]

(20) Rath[21] had alkylated the potassium salt of 2-pyridone with methyl, ethyl, and isopropyl iodides in protic solvents, but did not report alkoxypyridine formation. He was primarily interested in preparing the nitrogen alkylated pyridines and obtained the N-isopropyl derivatives in 30% yield which is consistent with our data.

(21) C. Rath, *Ann.*, **489**, 107 (1931).

(22) 2-Methoxypyridine was dissolved in dimethylformamide and stoichiometric quantities of methyl iodide and potassium iodide were added. After 2 days under the reaction conditions, no rearrangement was detected. Control experiments also ruled out thermal isomerizations at the vpc injection port.

(23) Models suggest that 2-pyridones and similar 2-oxo heterocycles have greater steric requirements for nitrogen compared to oxygen alkylation.[2] The source of the apparent steric interactions arises from interference between the oxygen atom and the alkylating agent and is more subtle than previously observed in other ambident anion alkylation studies showing the significance of steric factors in governing product distributions.[6,8]

was far more sensitive to changes in solvent and cation than the 2-pyrimidone salts previously examined.[2] Both systems, however, were highly sensitive to steric factors resulting from changes in the alkyl halide structure. The over-all greater sensitivity of the 2-pyridone system can be related to the fact that this heterocycle contains only a single nitrogen atom. In the 2-pyrimidone system, the combined electron-withdrawing effect exerted by the two ring nitrogens reduces the negative charge on oxygen and renders this site less competitive toward alkylation. Nitrogen alkylation is also favored in 2-pyrimidones by a statistical factor.

The large solvent effects on alkylations of the silver salt of 2-pyridone may be unique, but this deserves further study in other systems. The mechanism which leads to oxygen alkylation of the silver salts of 2-pyridones also needs further examination and may be more related to heterogeneous reaction than to the ability of the silver ion to promote unimolecular reaction as previously suggested. Our current studies are mainly directed at examining the alkylation reactions of other pyrimidone and pyridone systems in order to formulate some general principles regarding the factors which determine the sensitivity of the alkylation site of heterocyclic ambident anions toward factors such as those examined here.

Experimental Section[24]

Materials.—All solvents and alkylating agents were reagent or spectroscopic grade and were stored over Linde Molecular Sieves (Type 13X) to remove or prevent the absorption of water. Additional purification was carried out by standard procedures when the need was indicated. 2-Pyridone, 2-methoxypyridine, and 2-ethoxypyridine were obtained from the Aldrich Chemical Co. Purification of 2-pyridone was effected by recrystallization twice from benzene. The alkoxypyridines were used without purification since vpc indicated these materials were of high purity. 2-Benzyloxypyridine,[25] 1-alkyl-2-pyridones,[21] and the potassium[21] and silver[26] salts were prepared by known procedures.

Vapor Phase Chromatography.—Vpc analyses were determined on an F & M Model 720 gas chromatograph. The column support consisted of 60–80 mesh Chromosorb W which had been washed with 10% sodium hydroxide solution, 4 *N* hydrochloric acid, and, finally, with water. After drying at 110° for 16 hr, the support was treated with hexamethyldisilizane[27] and coated with 20% by weight of XF-1150. Two-foot stainless steel columns (0.25 in. o.d.) containing this packing were used in analyses of the methyl, ethyl, and isopropyl derivatives. The helium flow was 60 cc/min, and temperature was programmed at 10°/min from 80 to 220°. The benzyl alkylation products were analyzed on 2-ft columns of the above substrate coated with 10% by weight of silicon gum rubber (SE-30). The helium flow was 60 cc/min and the temperature was programmed from 100 to 300° at 15°/min. All quantitative analyses were by standard procedures employing weighed samples calibrated against peak areas.

Alkylation Procedures.—The pyridine (0.500–1.00 mmole) was weighed into a small glass vial and 2.0–4.0 ml of solvent was added. The alkylating agent was added below the solvent surface with a calibrated, 50-μl syringe and the stoppered vial was placed on a shaker. After suitable times 10–40-μl samples were withdrawn for vpc analyses.

Sodium Salt of 2-Pyridone.—Sodium (5.75 g, 0.250 g-atom) dissolved in 160 ml of absolute ethanol was added to a solution of 2-pyridone (23.8 g, 0.250 mole) in 100 ml of absolute ethanol and the solution was allowed to stand overnight with stirring. The solvent was removed under reduced pressure and the residue was poured into anhydrous ether. The sodium salt (27.5 g, 94%) was collected by filtration and dried *in vacuo*. The composition of this salt was demonstrated by its conversion to alkylated derivatives.

2-Isopropyloxypyridine.—Sodium (2.3 g, 0.10 g-atom) dissolved in 250 ml of 2-propanol, was added to a solution of 2-bromopyridine (15.8 g, 0.10 mole) in 250 ml of 2-propanol.

TABLE V
SUMMARY OF KINETIC STUDIES IN DIMETHYLFORMAMIDE AT VARIOUS TEMPERATURES[a]

Alkyl halide	Rate constant[b] or qualitative description 0°	Acetone bath[c]	25°
MeI	Complete <20 min		Complete <5 min
EtI	0.259		Complete <60 min
i-PrI	Too slow to obtain data	1.01×10^{-2} (12°) 1.57×10^{-2} (16.6°)	
$PhCH_2I$	82% complete in 2 min		

[a] The sodium salt of 2-pyridone and an equivalent amount of alkyl halide (0.50 mmole) were reacted in 2.0 ml of dimethylformamide. [b] Rate constants are in l. mole^{-1} min^{-1}. [c] Surface evaporation was used to control the system temperature.

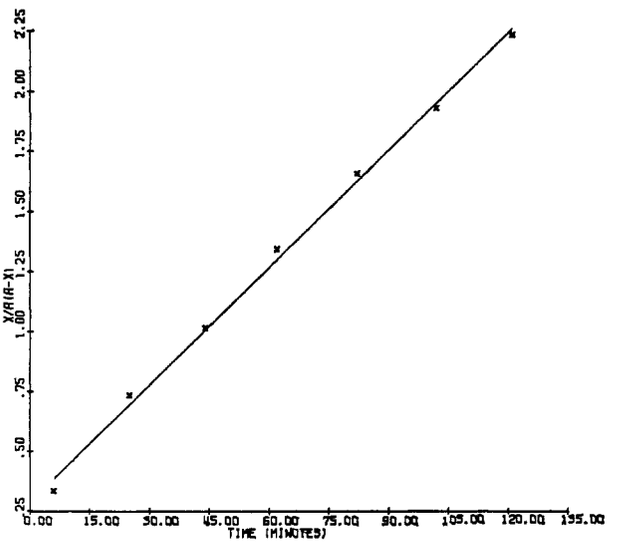


Figure 1.—Second-order plot for reaction of isopropyl iodide and the sodium salt of 2-pyridone in dimethylformamide at 16.8°; $k = 1.52 \times 10^{-2}$ mole l.$^{-1}$ min^{-1}. Rate data were obtained as described in the Experimental Section.

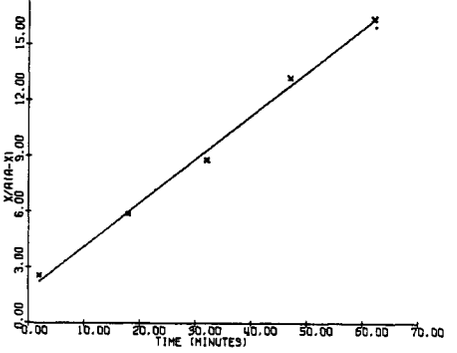


Figure 2.—Second-order plot for reaction of ethyl iodide and the sodium salt of 2-pyridone at 0°; $k = 2.59 \times 10^{-1}$ mole l.$^{-1}$ min^{-1}. Rate data were obtained as described in the Experimental Section.

(24) Ultraviolet spectra were determined on a Beckman DK-2 instrument and infrared spectra on a Beckman IR-5A spectrophotometer. Microanalyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford, England.

(25) E. N. Shaw, U. S. Patent No. 2,540,218 (Feb 6, 1951).

(26) J. P. Scannell and F. W. Allen, *J. Org. Chem.*, **25**, 2143 (1960).

(27) J. Bohemen, S. H. Langer, R. H. Perrett, and J. H. Purnell, *J. Chem. Soc.*, 2444 (1960).

The solution was refluxed for 3 days, but the reaction was not complete on the basis of a qualitative examination by ultraviolet spectroscopy. Additional sodium (6.9 g, 0.30 g-atom) in 200 ml of 2-propanol was added and reflux was continued another 4 days. The reaction was cooled to room temperature and filtered, and the filtrate was concentrated to a small volume. Water (200 ml) and ether (200 ml) were added and the mixture was neutralized with dilute hydrochloric acid. The ether layer was separated, washed with water, dried over magnesium sulfate, and distilled to give 3.7 g (27%) of product; bp 92–97° (75–78 mm); λ_{max} at 272 mμ in 95% ethanol.

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.85; H, 8.04; N, 10.40.

2-Alkoxypyridines by Alkylation of 2-Pyridone. 2-Isopropyloxypyridine.—2-Pyridone (5.1 g, 0.053 mole), silver carbonate (7.5 g, 0.027 mole), and isopropyl iodide (8.8 g, 0.052 mole) were stirred for 24 hr in 60 ml of pentane at 42° in the dark. The mixture was cooled in an ice bath for 0.5 hr and filtered from silver salts.

The filtrate was washed with 50 ml of 1% sodium bicarbonate solution and then twice with 25-ml portions of water. The pentane was removed at atmospheric pressure, except for the last traces which were removed under vacuum. The remaining pale yellow liquid (5.4 g, 76%) was 95% (area) 2-isopropyloxypyridine by vpc. Chromatographically pure product was obtained by distillation, bp 90–92° (155 mm).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.02; H, 8.07; N, 10.27.

This procedure was also used to prepare **2-methoxy-** and **2-benzyloxypyridine** in 57 and 78% yield, respectively, after distillation. All three products were chromatographically pure and were identified by comparison with authentic samples (infrared and ultraviolet spectra, boiling points, and vpc retention times were compared).

Rate Studies.—Reactions were run in dimethylformamide dried over Linde Molecular Sieves (Type 13X) and products were analyzed by vpc as noted previously. Table V summarizes the results of this study. Figures 1 and 2 show the second-order rate plots for ethylation and isopropylation. Methylation and benzylation were too rapid for study by this technique. Isopropylation was followed only to 30–36% completion, but corresponding first-order plots were curved lines.

Notes

Organic Fluoronitrogens. VIII.[1] Hydrolytic Reactions of Tetrafluoroformamidine and Pentafluoroguanidine

R. L. REBERTUS AND B. W. NIPPOLDT

Central Research Laboratories, Minnesota Mining and Manufacturing Company, St. Paul, Minnesota 55101

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Recently the synthesis and properties of tetrafluoroformamidine and the closely related compound, pentafluoroguanidine, were disclosed.[1,2] Unlike many saturated fluoronitrogens, these materials are quite sensitive to moisture and therefore we have surveyed their reactions with water, aqueous base, and strong acids.

The reactions of both tetrafluoroformamidine and pentafluoroguanidine with alkali are rapid and exothermic. Frequent explosions occurred during the contacting of excess gaseous pentafluoroguanidine with 5 *N* or more concentrated solutions of sodium hydroxide. However, this reaction can be controlled by gradually exposing the gaseous fluoronitrogen to a well-stirred solution of excess alkali. Tetrafluoroformamidine yields mostly nitrogen as a gaseous product from 5 *N* or more concentrated alkali (eq 1). On

$$F_2NCF{=}NF + 6OH^- \rightarrow CO_3^{2-} + 4F^- + 3H_2O + N_2 \quad (1)$$

the other hand, the major gaseous products from pentafluoroguanidine include nitrogen, nitrous oxide, and the two isomers of difluorodiazine. The difluoramino anion[3] is a probable intermediate (eq 2–4).

$$(F_2N)_2C{=}NF + 6OH^- \rightarrow CO_3^{2-} + 3F^- + 3H_2O + N_2 + [NF_2^-] \quad (2)$$

$$2[NF_2^-] \rightarrow N_2F_2 + 2F^- \quad (3)$$

$$2[NF_2^-] + 2OH^- \rightarrow N_2O + H_2O + 4F^- \quad (4)$$

The reactions of tetrafluoroformamidine and pentafluoroguanidine with concentrated sulfuric acid are relatively slow (eq 5 and 6). Under our experimental conditions, a period of about 2 days is required for a complete reaction. The oxidation numbers of the nitrogen atoms in the difluoramino and fluorimino groups are preserved in the hydrolysis products, difluoramine and hydroxylammonium ion. The hydrofluoric acid produced reacts with the glass reaction vessel and appears in the gas phase as silicon tetrafluoride. In view of the over-all dehydrating conditions, it is quite possible that the hydroxylammonium species is originally present as hydroxylamine O-sulfonic acid. Thus, the diluted solution purged free of difluoramine oxidizes iodide as would be expected of this derivative. However, after boiling the diluted solution and removing the excess sulfuric acid by chloride anion exchange, hydroxylammonium chloride is the isolated product.

$$F_2NCF{=}NF + 3H_2O + H_2SO_4 \rightarrow HNF_2 + CO_2 + 2HF + HONH_3^+ + HSO_4^- \quad (5)$$

$$(F_2N)_2C{=}NF + 3H_2O + H_2SO_4 \rightarrow 2HNF_2 + CO_2 + HF + HONH_3^+ + HSO_4^- \quad (6)$$

In water tetrafluoroformamidine and pentafluoroguanidine hydrolyze completely within a few hours. The distribution of the hydrolysis products from tetrafluoroformamidine is shown in Table I. The carbon is converted entirely to carbon dioxide. Difluoramine and hydroxylammonium ion (or its precursor) are produced in equimolar amounts originally, but much of the latter disproportionates to ammonium ion and nitrogen. Difluoramine and hydroxylammonium ion can also react to form nitrogen gas (eq 7); this reaction was demonstrated independently by combining the two reactants in aqueous solution at room temperature. The addition of sulfuric acid to a final concentration of 1 *N* reduces the yield of nitrogen from

$$HNF_2 + HONH_3^+ \rightarrow N_2 + 2HF + H^+ + H_2O \quad (7)$$

(1) Previous paper in this series: R. J. Koshar, D. R. Husted, and C. D. Wright, *J. Org. Chem.*, **32**, 3859 (1967).

(2) R. A. Davis, J. L. Kroon, and D. A. Rausch, *ibid.*, **32**, 1662 (1967).

(3) The existence of the difluoramino anion and its scheme of hydrolysis have been reported: K. J. Martin, *J. Am. Chem. Soc.*, **87**, 394 (1965).