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Preliminary Note

Reactions of polyhalogenopyridines with methyl fluorosulphonate

E. AGER AND H. SUSCHITZKY

Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, Lancashire (Great Britain)

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The basicity of polyhalogenopyridines is considerably reduced by the strong inductive effect of the halogen atoms and *N*-alkylation is usually not very successful. For instance, we find that reaction of pentachloropyridine with triethyloxonium fluoroborate produces only a low yield (12%) of the *N*-ethyl pyridinium salt. Methyl fluorosulphonate, however, can be made to react with pentachloropyridine, tetrachloro-2-fluoropyridine, 3,5-dichlorotrifluoropyridine and pentabromopyridine in the absence of a solvent to give good yields of the corresponding *N*-methylated pyridinium fluorosulphonates (Table 1). The products are high melting solids which, on exposure to atmospheric moisture, give the corresponding *N*-methyl 2-pyridones and also react with other nucleophiles usually at ambient temperature (*cf.* Table 2).

TABLE 1

REACTION OF POLYHALOGENOPYRIDINES WITH AN EXCESS OF METHYL FLUOROSULPHONATE AT 90°

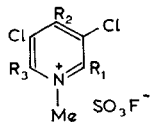
Compound	Time (h)	Product (%)*	M.p. (°C)
3,5-Dichlorotrifluoropyridine	2.0	*N*-Methyl 3,5-dichlorotrifluoropyridinium fluorosulphonate (67)	136–138
Tetrachloro-2-fluoropyridine	1.0	*N*-Methyl tetrachloro-2-fluoropyridinium fluorosulphonate (80)	146–149
Pentachloropyridine	0.5	*N*-Methyl pentachloropyridinium fluorosulphonate (83)	224–225
Pentabromopyridine	24.0	*N*-Methyl pentabromopyridinium fluorosulphonate (80)	150° (dec.)

* All products had the correct analyses and expected spectral data (IR, NMR and mass spectra).

The strong inductive effect of the positively charged nitrogen atom thus activates the 2 (6) positions to nucleophilic substitution to an even greater extent than the analogous pentachloropyridine-1-oxide[3].

TABLE 2

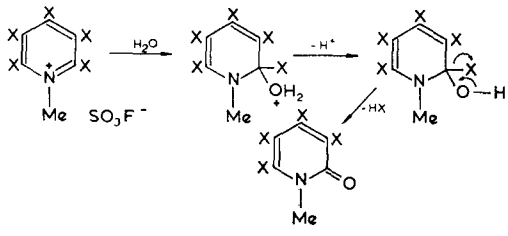
REACTIONS OF *N*-METHYL POLYHALOGENOPYRIDINIUM FLUOROSULPHONATES WITH NUCLEOPHILES



Compound R_1 R_2 R_3	Nucleophile	Time/Temp. (°C)	Product (%)*	M.p. (°C)
F F F	H_2O	10 min/25	*N*-Methyl-3,5-dichlorodi-fluoro-2-pyridone[1] (80)	81–82
F Cl Cl	H_2O	1 h/25	*N*-Methyltetrachloro-2-pyridone[2] (89)	149.5–150.5
Cl Cl Cl	H_2O	24 h/25	*N*-Methyltetrachloro-2-pyridone[2] (80)	
F F F	NaN_3/H_2O	30 min/50	*N*-Methyl-4,6-diazido-dichloro-2-pyridone (86)	115 (dec.)
Cl Cl Cl	NaN_3/H_2O	30 min/50	*N*-Methyl-4,6-diazido-dichloro-2-pyridone (80)	
Cl Cl Cl	NH_3/H_2O	30 min/25	*N*-Methyltetrachloro-2-pyridimine (89)	173–175 (dec.)
Cl Cl Cl	$NaSH/H_2O$	1 h/25	*N*-Methyltetrachloro-2-pyridthione (42)	221–222
Cl Cl Cl	$MeNH_2/H_2O$	5 min/0	*N,N'*-Dimethyl-tetrachloro-2-pyridimine (85)	86–88
Cl Cl Cl	Me_2NH/H_2O	5 min/25	*N*-Methyl-2,4,6-tris-(dimethylamino)dichloro-pyridinium fluorosulphonate (63)	158–160
N-Methyl penta-bromopyridinium fluorosulphonate	H_2O	24 h/100	*N*-Methyl tetrabromo-2-pyridone (80)	183–184.5

* All products had the correct analyses and expected spectral data (IR, NMR and mass spectra).

The reaction of water with pyridinium salts appears to proceed *via* the following mechanism, involving HX elimination:



This pathway will apply to any nucleophile which can lose a proton at the final stage to give the neutral molecule (*i.e.* –SH or –NHR) thus deactivating the molecule to further nucleophilic substitution under mild conditions. Where such deactivation is not possible (*e.g.* X = N_3, secondary amines) further substitution takes place in the 4 and 6 positions. For instance, the reaction with aqueous sodium azide gives *N*-methyl 4,6-diazidodichloro-2-pyridone which is probably formed by reaction of water with the initially produced *N*-methyl 2,4,6-triazido-dichloropyridinium salt. The reaction of *N*-methyl pentachloropyridinium fluorosulphonate with dimethylamine gives *N*-methyl 2,4,6-tris(dimethylamino)dichloropyridinium fluorosulphonate which is rapidly hydrolysed with cold aqueous sodium hydroxide to give *N*-methyl 4,6-bis(dimethylamino)dichloro-2-pyridone (60%, m.p. 114°).

Pentafluoropyridine gave a liquid product under continued reflux with an excess of methyl fluorosulphonate. Addition of water to the reaction mixture gave *N*-methyl tetrafluoro-2-pyridone (shown by mass spectrometry) together with *N*-methyl 3,5-difluoro-2,4-dihydroxy-6-pyridone. Since polyhalogeno-*N*-heterocycles with fluorine next to the *N*-hetero atom do not form *N*-oxides[4], the successful *N*-methylations of the fluoropyridines described is significant as it can be synthetically utilised by analogy with the polyhalogeno-*N*-oxides[3].

Pentachloropyridine-1-oxide reacted readily with methyl fluorosulphonate in methylene chloride at room temperature to give *N*-methoxy pentachloropyridinium fluorosulphonate (90%, m.p. 203–205°). This compound reacted with cold water to give *N*-methoxy tetrachloro-2-pyridone (88%, m.p. 124–125°) and with an excess of aqueous sodium azide to give 2,4,6-triazido-dichloropyridine (82%, m.p. 80–81° (dec.)) by loss of the methoxy group. It appears that the initially formed triazido-*N*-methoxy compound follows the normal reaction of *N*-methoxy heterocyclic salts with water to give the heterocycle together with formaldehyde[5].

Experimental details of this work and of reactions of other *N*-polyhalogeno-heterocycles will be reported in full.

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