

Fluorocyano-benzenes and -pyridines

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THE KF exchange reaction¹⁻³ has been extended to the synthesis of fluorocyano-benzenes and -pyridines from the corresponding chloro-compounds. By these syntheses we have demonstrated the activating effect of the cyano-group on the halide-fluoride exchange reaction in the halogenated benzenes and pyridines. We are reporting also a fluorocyanobenzene synthesis by a dual halogen exchange with a CuCN-KF mixture. The fluorocycano-compounds were identified by chemical analyses, infrared spectra, and by hydrolysis to the known corresponding acids except 6-fluoronicotinonitrile. As the hydrolyses were easy, the KF exchange reaction provides a convenient route to the fluorobenzoic and fluoropyridinecarboxylic

acids. The detailed results will be published in a forthcoming paper.

Procedure: The chlorocyano-benzene or -pyridine compound was reacted with anhydrous potassium fluoride by heating and stirring in dimethyl sulphone (DMSO)₂⁴ as a solvent in the usual manner. Dimethylformamide (DMF) was used in several experiments. Additional experimental conditions are given in the Table and yields are based on the initial amount of organic reactants.

The KF exchange reaction on 2,4-dichlorobenzonitrile gave, in addition to the difluoroderivative, a 36% yield of an approximately 1:1 mixture of 2-chloro-4-fluoro- and 4-chloro-2-fluoro-benzonitrile.

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² G. C. Finger and L. D. Starr, *J. Amer. Chem. Soc.*, 1959, **81**, 2674.

³ G. C. Finger, L. D. Starr, D. R. Dickerson, H. S. Gutowski, and J. Hamer, *J. Org. Chem.*, 1963, **28**, 1666.

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3-Cyano-4-fluorobenzotrifluoride, b.p. 99° (27 mm.) was prepared in a 57% yield in a single operation from 3-bromo-4-chlorobenzotrifluoride.

A 43% yield of the intermediate 4-chloro-3-cyanobenzotrifluoride, m.p. 39—40°, was obtained also. The increased lability of an α -chlorine atom to

TABLE: *Synthesis of fluorocyano-benzenes and -pyridines with KF in DMSO₂*

Reactant	Time	Reaction		Product		Yield (%)
		Temp.	Compound	M.p.	B.p.	
(A) Cyanobenzene Derivatives						
2-Chloro-	40 hrs.	200°	2-Fluoro-	—	103°/35 mm.	66.5
4-Chloro-	96 "	200°	4-Fluoro-	38°	—	59
2,4-Dichloro-	30 "	160°	2,4-Difluoro-	46—47°	—	48
2,6-Dichloro-	7 "	200°	2,6-Difluoro-	—	99°/20 mm.	77
2-Chloro-5-trifluoromethyl-	3 "	160°	2-Fluoro-5-trifluoromethyl-	—	99°/27 mm.	83
2-Chloro-3-cyano-	120 min.	140°	2-Fluoro-3-cyano-	30—30.5°	90°/6 mm.	88*
2-Chloro-4-cyano-	90 "	180°	2-Fluoro-4-cyano-	33—34°	76°/3 mm.	56
2-Chloro-5-cyano-	10 "	180°	2-Fluoro-5-cyano-	51—52°	—	78
2-Chloro-6-cyano-	80 "	180°	2-Fluoro-6-cyano-	34°	—	54

* DMF as solvent.

To the bromochloro-compound in warmed DMF was added an excess of cuprous cyanide and anhydrous potassium fluoride, and the resulting mixture heated with stirring at 145° for 42 hours.

the exchange reaction by a cyano-group on the pyridine ring is noteworthy. By comparison with a nitro-group² or chlorine³ atom, the cyano-group is a very effective activator.

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