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A Convenient Synthesis of Aromatic Fluoride by Thermal Stable Pyridinium Phase-transfer Catalyst

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Abstract: Using 4-Dialkylaminopyridinium salt as a thermal stable phase-transfer catalyst (PTC), the excellent results were obtained in the halogen-exchange fluorination.

Keywords: 4-Dialkylaminopyridinium salt, phase-transfer catalyst, fluorination.

Fluoroorganic compounds have been applied as useful intermediates in industry. Here, we use the PTC method for fluorination of aromatic halide by inorganic fluorides involving a halogen-exchange. This is a convenient and attractive synthetic way to obtain fluoro compounds, because inorganic fluorides such as potassium fluoride is safe to be handled and cheap[1]. However, owing to poor solubilities of inorganic fluorides in organic solvents, the halogen-exchange fluorination often requires elevated temperature in polar solvents. The tetraalkyl ammonium catalyst for the phase transfer reaction usually will discompose around 140°C and more thermal-stable PTC should be used in the fluorination. Here, we report a pyridinium PTC which is thermal-stable and the excellent results were obtained.

Experimental

Aromatic chloride and 4-dimethylaminopyridinium(DMAP) were purchased from Aldrich chemical Co.. Spray dried potassium fluoride was obtained from Dongyang Chemical Co.. Methane sulfonyl chloride, dimethyl sulfoxide(DMSO), sulfolane ($TMSO_2$) and toluene were distilled and kept over 3A molecular sieves. Yields of products were detected by a Shimadzu GC-9A FID with a Φ0.53mm×12m CBP1 capillary column and HP6890 GC-5973MSD. Pyridinium salt was systhesized according to references[2,3].

Synthesis of aromatic fluoride was carried out as follows **(Scheme 1)**: A mixture of aromatic chloride and solvent(DMSO or $TMSO_2$) was placed in a three-neck round-bottom flask equipped with a reflux condenser and a thermometer. The mixture was dried by azeotropic distillation with toluene. Then another mixture of potassium fluoride and the catalyst was added into the flask. The whole mixture was dried by azeotropic distil-

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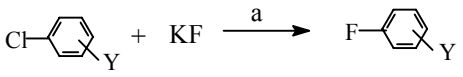
lation with toluene again and stirred at a certain temperature for a period of time.

Scheme 1



a: N-(2-ethylhexyl)-4-dimethylaminopyridium chloride

Results and Discussion

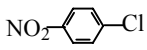
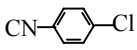
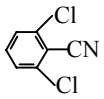
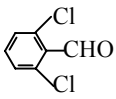
Fluorination with solid KF must be done under anhydrous conditions, because even a small amount of water affects strongly the reactivity of fluoride.

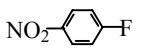
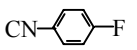
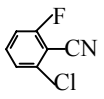
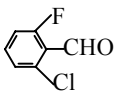
The results were shown in T**able 1**. Compared with entries 1-3, we can see that the PTC has excellent activity, allowing the reaction carried out at moderate temperature. The weaker the electrophilicity of electron-withdrawing group on the aromatic ring, the lower the yields obtained, even at elevated temperature, but the catalyst still showed great activity even at 210°C (entries7, 8). In a word, the thermal stable pyridinium PTC possesses very attractive potential industry use.

Table 1. Phase transfer catalyzed fluorination[a]

entry	Chloride[c]	Solvent	Temp.(°C)	Time(h)	Product[d](mp/°C)	Yield(%)
1	**1**	DMSO	170	3	**A**(liq)	33.78[b]
2	**1**	DMSO	189(reflux)	3	**A**	46.85[b]
3	**1**	DMSO	170	1.5	**A**	98.60
4	**2**	$TMSO_2$	190	2	**B**(35-37)	41.40
5	**2**	$TMSO_2$	200	2	**B**	78.60
6	**3**	$TMSO_2$	200	2	**C**(55-57)	54.32
7	**3**	$TMSO_2$	210	2	**C**	75.02
8	**4**	$TMSO_2$	210	2	**D**(34-36)	55.86

a: Reactions were carried out with chloride : KF : solvent : catalyst=1 : 1.5 : 6 : 0.1(mol)
b: The reaction was carried out without catalyst.

c: Chloride **1:**  **2:**  **3:**  **4:** 

d: Product **A:**  **B:**  **C:**  **D:** 

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