Preliminary Note

Tetraphenylphosphonium bromide-catalyzed 'Halex' fluorination of chloroaryl sulfonyl chlorides

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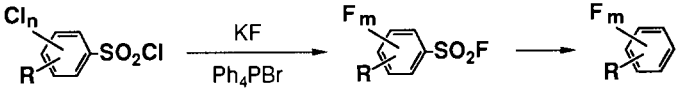
(Received August 10, 1991; accepted October 22, 1991)

Abstract

Halogen-exchange of chloroaryl sulfonylchloride derivatives with spray-dried potassium fluoride was found to proceed efficiently by employing tetraphenylphosphonium bromide as a catalyst. Subsequent desulfonylation of the fluoroaryl sulfonyl derivatives readily afforded fluoroaromatics under acidic condition.

Recent studies in our laboratory have been directed towards the development of methodologies suitable for the preparation of aryl fluorides via the 'Halex' reaction [1]. Halex fluorination of aryl chlorides is well documented and can generally be a high-yielding process if there are strong electron-withdrawing groups situated *ortho* and/or *para* to the chlorine substituents of the aryl chlorides.

A very limited number of examples, however, are found in the literature for the reaction of chloro-substituted aryl sulfonyl chlorides (1) with potassium fluoride (KF). The only reported methods for the Halex fluorination of 1 are (a) a reaction in an autoclave at 275–290 °C without solvent [2] and (b) a reaction in the presence of tris(3,6,9-trioxadecyl)amine in an aprotic solvent [3].



1 2

These reactions seem not to be applicable to the large-scale preparation of fluoroaryl sulfonyl fluoride (2) due to the rather low yield (40–60%) and/or the use of tedious reaction conditions.

We and others have recently reported that tetraphenylphosphonium bromide (Ph_4PBr) is a superior catalyst for Halex fluorinations [1, 4, 5].

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0022-1139/91/$3.50

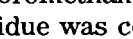
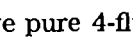
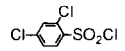
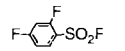
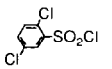
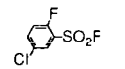
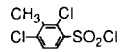
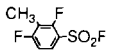
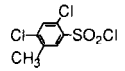
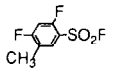
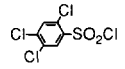
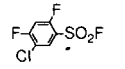
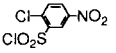
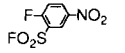
During the course of these studies, we became interested in the Halex fluorination of **1** catalyzed by Ph_4PBr, because this reaction followed by desulfonylation would seem to be a new route to fluoroaromatics.

In a typical experiment, a mixture of 4-chlorobenzene sulfonyl chloride (105 g, 0.5 mol), spray-dried KF (116 g, 2 mol), Ph_4PBr (21 g, 0.05 mol) and anhydrous sulfolane (30 g) was stirred for 2 h at 215 °C after azeotropic dehydration by toluene. After cooling, the mixture was diluted with dichloromethane (0.5 l) and then filtered to remove inorganic matter. The residue was concentrated and distilled to give pure 4-fluorobenzene sulfonyl fluoride (78 g, 88%) having a boiling point of 63–64 °C/4 mmHg and ^1H NMR, IR and mass spectra identical with those of an authentic sample. The preparation of several varieties of **2** are listed in Table 1. Simple work-up of the reaction mixture gave virtually pure product.

Next, transformation of **2** to fluoroaromatics through desulfonylation was examined. Thus, 2,4-difluorobenzene sulfonyl fluoride was hydrolyzed

TABLE 1

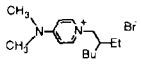
Preparation of fluoroaryl sulfonyl fluoride derivatives

Run	1[a]	KF (equiv)	Catalyst (equiv)	Solvent	Temp. °C	Time h	2	(GC Yield/%) [Isolated yield/%][b]	B.P.
1		4.0	Ph_4PBr (0.1)	Sulfolane	215	2		(93) [88]	63-64°C/4mmHg
2	〃	4.0	-	〃	215	2	〃	(29)[c]	
3	〃	3.0	DMAPBr[d] (0.1)	〃	210	5	〃	(74)	
4	〃	4.0	Ph_4PBr (0.1)	3,4-Dichloro-toluene	reflux	7	〃	(59)	
5		4.0	Ph_4PBr (0.1)	Sulfolane	180	4		[74]	58-59°C/4mmHg
6		4.0	Ph_4PBr (0.1)	〃	180	5		[62]	96-97°C/7mmHg
7		4.0	Ph_4PBr (0.1)	〃	200	1.5		[74]	110°C/10mmHg
8	〃	4.0	Ph_4PBr (0.1)	1,3-Dimethyl-imidazolidinone	200	1.5	〃	[66]	
9		4.0	Ph_4PBr (0.1)	Sulfolane	180	4		[77]	103-105°C /4mmHg
10		4.0	Ph_4PBr (0.1)	Sulfolane	180	4		[32][e]	69-70°C/2mmHg
11		2.5	Ph_4PBr (0.05)	〃	130	16		[90]	115°C/0.3mmHg

[a] Starting substrates were prepared from the corresponding aryl chlorides and chlorosulfonic acid.

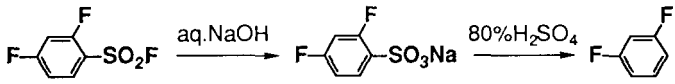
[b] All products gave satisfactory NMR, IR, and MS spectra.

[c] 70% of chlorobenzene sulfonyl fluoride was given.

[d] 

[e] Reaction is not optimized.

to form sodium 2,4-difluorosulfonate, which was treated in 80% sulfuric acid at 200 °C. 1,3-Difluorobenzene, having a low boiling point (82 °C), was readily collected, as it distilled from the reaction mixture during the reaction



(62% yield) and was identified by GC–MS analysis. Similarly, 2,6-difluorotoluene was produced from 2,4-difluoro-3-methylbenzene sulfonyl fluoride in 79% yield.

As described above, we have succeeded in developing a novel catalyzed reaction which is useful in the synthesis of fluoroaryl sulfonyl fluoride derivatives. The method may offer a new synthetic route to some fluoroaromatics.

References

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2 (a) G. G. Yakobson, V. M. Vlasov and N. N. Voroshtsov, Jr., *Zh. Vses. Khim. Ova.*, *10* (1965) 466 [*Chem. Abstr.*, *63* (1965) 14 740e]; (b) *idem*, *Zh. Obshch. Khim.*, *37* (1967) 163 [*Chem. Abstr.*, *66* (1967) 94 741e].
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