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Reaction of Acetyl Hypofluorite with Aromatic Mercury Compounds: a New Selective Fluorination Method

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Aromatic fluorine compounds are prepared in acetic acid from the corresponding mercury compounds and acetyl hypofluorite.

The methods used for the electrophilic introduction of fluorine into aromatic compounds (*i.e.* with F_2, $CsSO_4F$, CF_3OF, CF_3COOF, $FClO_3$, or XeF_2) often suffer from over-reactivity. For this reason, there are only a few practical methods available for the controlled, regiospecific introduction of fluorine into an aromatic compound. These are the Balz–Schiemann reaction and the nucleophilic displacement of activated halogen atoms or alkoxy- or nitro-groups.

Some information is available in the literature on the fluorination *via* organometallic compounds: Taylor *et al.*[1] reported the synthesis of fluoro compounds by the reaction of arylthallium(III) difluorides with BF_3 and Adam *et al.*[2] reported the synthesis of PhF from F_2 and $PhSnBu_3$. Controlled monofluorination of activated aromatic rings with MeCOOF[3] has been reported and hence we have investigated the displacement of the mercury group in arylmercury compounds with MeCOOF as a new approach to regiospecific fluorination.

The reaction of an arylmercury compound (30 μmol), dissolved in 1 ml of $MeCO_2H$, with 3—10 μmol of MeCOOF (or [^{18}F]MeCOOF) in 3 ml of $MeCO_2H$[4] at room temperature gave within 5 min satisfactory yields (45—65%) of the corresponding fluorodemercuration products† (Table 1). For

Table 1. Fluorinated aryl compounds from the displacement of a mercury group using MeCOOF.

Substrate	Yield[a] (%)	Ratio of fluoro products[b]			
		o	*m*	*p*	α
Anisole	85	3	—	1	—
p-$MeOC_6H_4HgOAc$	65	—	—	1	—
Acetanilide	67	2	—	1	—
p-$MeCONHC_6H_4HgOAc$	60	—	—	1	—
Phenol	75	3	—	2	—
o-HOC_6H_4HgCl	53	1	—	—	—
p-HOC_6H_4HgCl	47	—	—	1	—
Toluene	14	8	1	4	1
MeC_6H_4HgCl[c]	57	3	1	13	—
Benzene	18				
PhHgOAc	58				
PhHgCl	55				

[a] Based on MeCOOF (MeCOOF was prepared from F_2 in 80—90% chemical yield, so the radiochemical yields based on [^{18}F]F_2 are 20—30%); the standard deviation is *ca.* 5%. [b] Identified by g.c.–mass spectroscopy and by comparison of the retention times in reversed phase h.p.l.c. with those of authentic samples. [c] Mixture consisting of 18% *o*-, 6% *m*-, and 76% *p*-MeC_6H_4HgCl (ref. 5).

† The reaction is the same for compounds with different ligands (Cl^- or OAc^-) attached to the mercury atom. However, whenever possible, the –HgOAc group is preferred because in general RHgCl compounds have poor solubility in $MeCO_2H$. As it was found that a suspension of RHgCl in $MeCO_2H$ lowers the yield of the fluoro compounds, RHgCl compounds, when necessary, can be dissolved in $MeCO_2H$ by the addition of the salt $Hg(OAc)_2$; the presence of this salt during the reaction does not affect the yield of the fluoro products.

comparison, results are given of the reactions of the non-mercurated parent compounds with MeCOOF under the same conditions. It is of note that *o*:*p* ratios deviating from those measured by Lerman *et al.*[3] are found with the solvent that we used.

It is interesting to note that the reactions of MeCOOF with benzene and toluene result in low yields (see also Lerman *et al.*[3]), but good results are obtained with the mercurated derivatives, which indicates that unwanted side reactions are suppressed by using this method.

It is premature to discuss the mechanism of the fluorodemercuration, but it appears that the demercuration is very dependent on the solvent used. For example, when PhHgOAc was dissolved in MeCN, EtOAc, MeOAc, tetrahydrofuran, or EtOH, little or no yields of fluorobenzene were obtained by treatment with MeCOOF (which is always dissolved in acetic acid). For anisole the yields of the fluoroanisoles were almost the same in all of these solvents.

Given the relative ease with which mercury can be attached to aromatic systems,[6] the reaction with MeCOOF is a good synthetic method for obtaining specifically fluorinated aromatic compounds. In the context of ^{18}F chemistry for positron emission tomography the method is suitable for studies that require compounds with medium to low specific activities (<370 GBq/mmol *i.e.* <10 Ci/mmol).

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