A Novel Method for Converting Aromatic Acids into Trifluoromethyl Derivatives using BrF_3

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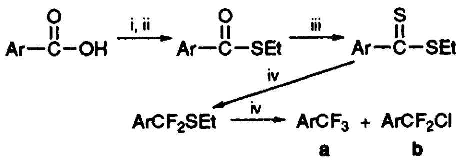
Aryltrifluoromethyl derivatives are obtained in good yields from the corresponding aryl carboxylic acids by reacting their dithionic esters with BrF_3 under very mild conditions.

Aryltrifluoromethyl derivatives are important starting materials for many pharmaceuticals and agrochemicals.[1] In general, they are prepared from the corresponding toluenes *via* radical chlorination followed by a catalysed high-pressure and -temperature halogen exchange reaction with HF.[2] Another possible route is the usually quite messy reaction of the corresponding acids with SF_4.[3]

We have shown recently that BrF_3, available commercially and also easily prepared from the corresponding elements,[4] is a very potent reagent for converting various carbonyls to the CF_2 group. Thus ketones, through their hydrazones, azines or oxime methyl ethers, were converted to the corresponding CF_2 compounds[5] while esters, after being transformed to *O*-substituted thioesters, were converted to difluoromethylene ethers.[4] This last reaction, which indicates that BrF_3 binds itself quite efficiently to sulfur atoms, prompted us to explore the possibility of constructing dithionic esters from carboxylic acids with the hope that at least two molecules of the fluorinating reagent would complex around the two sulfur atoms leading eventually to aryl trifluoromethyl compounds.

The dithionic esters are prepared by reacting the appropriate acyl halide with ethanethiol followed by reaction with Lawesson reagent.[6] The resulting ester (usually *ca.* 0.5 g) is then dissolved in *ca.* 30 ml of dry $CFCl_3$ and 3.5 equiv. of BrF_3 (dissolved in about 15 ml of the same solvent) are added during 5–10 min. at 0 °C.† Upon completion of the addition the reaction mixture is washed with thiosulfate until colourless and the product purified either by distillation or chromatography. The nature of the product is determined largely by the amount of the BrF_3 used. It is quite easy to see that when less than 3 equiv. of BrF_3 are employed, it is mostly the thiocarbonyl which is transformed into the CF_2 moiety resulting in $ArCF_2SR$. Increasing the BrF_3 : substrate ratio results in the replacement of the last sulfur atom by a third fluorine atom forming the desired CF_3 group. It should be noted that in several cases the product is accompanied by a small amount of the corresponding $ArCF_2Cl$ derivative arising apparently from a secondary reaction with chloride ions originating from side reactions between the $CFCl_3$ and the BrF_3 (Scheme 1).



Scheme 1 *Reagents*: i, SO_2Cl; ii, EtSH; iii, $[p\text{-}MeOC_6H_4P(S)S]_2$ (Lawesson reagent); iv, BrF_3

Table 1

Ar	$ArCF_3$ (%)	$ArCF_2Cl$ (%)
$4\text{-}NCC_6H_4$	75[7]	15[8]
$4\text{-}ClC_6H_4$	70[9]	15[10]
$2\text{-}ClC_6H_4$	70[11]	5
$3\text{-}BrC_6H_4$	75[11]	5
$4\text{-}CF_3C_6H_4$	65[11]	15[12]

Some examples of the above reaction are presented in Table 1. The yields of the trifluoromethyl derivatives are usually *ca.* 70–75%, but taking into account that in the literature derivatives of type **b** have been successfully converted to the desired products **a**[2] the potential yield of the reaction is even higher.

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Footnote

† **CAUTION**: BrF_3 should be treated with care since it reacts violently with oxygenated solvents such as H_2O and MeCOMe. Dry CCl_3F, $CHCl_3$ and CCl_4 are suitable as reaction solvents.

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