# A Simple, Novel Method for the Preparation of Trifluoromethyl Iodide and Diiododifluoromethane

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$CF_3I$ was synthesized in high yields by treatment of $XCF_2CO_2Me$ (X = Cl or Br) with iodine in the presence of potassium fluoride and copper iodide; if KI was used instead of KF under similar conditions, $CF_2I_2$ was obtained in moderate yields.

Trifluoromethyl iodide **1** and its analogues are useful reagents for the perfluoroalkylation of organic molecules.[1] Of special importance was the discovery that trifluoromethyl iodide reacted by free radical addition with alkenes or alkynes.[2] Numerous trifluoromethyl organometallic and organometalloid compounds of industrial as well as academic importance have also been prepared.[3] There has been considerable recent attention on novel methods, based on $CF_3I$, for introducing the trifluoromethyl group into aromatic or heterocyclic compounds because of the increasing use of such compounds in medicine and biochemistry.[4]

Unlike trifluoromethyl iodide, diiododifluoromethane **2** has been much less studied. It is a difluorocarbene precursor and source of the difluoroiodomethyl radical.[5] The differences in the range of applications of these two compounds may be ascribed to the differences in their availability.

Trifluoromethyl iodide **1** was originally synthesised by the reaction of $CI_4$ with $IF_5$[6] but this method has been replaced by a synthesis based on heating silver trifluoroacetate with excess of iodine at >100 °C (Hunsdiecker reaction); yields are >90%.[7] Sodium, potassium, barium, mercury and lead trifluoroacetates give lower yields of **1**, although the yield can be improved (80%) when sodium trifluoroacetate is treated with excess of iodine in the presence of CuI at 150 °C in dimethylformamide (DMF)[8] or in dimethyl sulfoxide (DMSO).[9] Trifluoroacetyl fluoride reacted with lithium iodide at high temperature to give **1** in 70% yield.[10] All these methods suffer from the need for exhaustively dried salts, excess of iodine and high temperatures.

Methods for the preparation of diiododifluoromethane **2** are much less developed. It has been obtained by the addition of difluorocarbene to iodine *via* a difficult low-yield procedure (<20%).[11] The fluorination of $CI_4$ with $HgF_2$ gives **2**, but the yield is unsatisfactory (27%).[5]

In our continuing studies on difluorocarbene chemistry, we found that methyl chlorodifluoroacetate **3**[†] can be used as a

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[†] Compound **3** is commercially available (Aldrich), and can also be prepared by the following method. Treatment of 2-chlorotetrafluoroethyl iodide, prepared by bubbling tetrafluoroethene into ICl, with fuming sulfuric acid gives $ClCF_2COF$, reaction of which with methanol affords **3** in near-quantitative yield. Compound **4** was prepared by the method in ref. 14.

For the preparation of **1** from **3**, a stirred mixture of $ClCF_2CO_2Me$ (10 mmol), dry KF (10 mmol), CuI (1 mmol), $I_2$ (10 mmol) and DMF (20 ml; dried with $CaH_2$) was heated at 120 °C for 3 h. The gas evolved was purified by trap-to-trap distillation to give pure $CF_3I$ (7.7 mmol, 77%), b.p. −21 to −23 °C (lit.[6] −22.5 °C); *m/z* 196 ($M^+$, 23.7%), 69 ($CF_3$, 100) and 127 (I, 2.7); $\delta_F$ (60 MHz, solvent $CCl_3D$, standard $CCl_3F$) $\delta$ −3.7. $CF_2I_2$ (10%) was a by-product: $\delta_F$ ($CCl_3D$) −18.0; *m/z* 304 ($M^+$, 24.1%), 177 (100, $CF_2I$), 50 (3.7, $CF_2$) and 127 (20.5, I).

For the synthesis of **2**, under $N_2$, a stirred mixture of DMF (30 ml), **5** (20 mmol), KI (20 mmol), $I_2$ (20 mmol) and CuI (20 mmol) was heated at 40 °C for 10 h; pure $CF_2I_2$ (10 mmol, 50%) was obtained by trap-to-trap distillation: b.p. 8–11 °C (10 Torr).[5]

trifluoromethylating agent *via* a difluorocarbene intermediate,[12] and so we attempted to prepare **1** and **2** from **3** or its analogues; this communication presents the results.

Treatment of **3** with KF and iodine (molar ratio 1:1:1) in the presence of a catalytic amount (10 mol%) of CuI in DMF at 100–120 °C for 2–3 h gave **1** in 70–80% yield, **2** as a by-product (10%) [reaction (1)]. The presence of both KF and CuI is essential. Without KF, **3** did not undergo decarboxylation and *N,N*-dimethylchlorodifluoroacetamide was the only product (14%). High yields of **1** require an equivalent amount of KF. In the absence of CuI, **1** was obtained in low yield (10%). The gases evolved in the reaction were identified as $CO_2$, $CF_3H$ and $CF_2{=}CF_2$.

$$\underset{\mathbf{3}}{\mathrm{ClCF_2CO_2Me}} + \mathrm{KF} + \mathrm{I_2} \xrightarrow{\mathrm{CuI}} \underset{\mathbf{1}}{\mathrm{CF_3I}} + \underset{\mathbf{2}}{\mathrm{CF_2I_2}} + \mathrm{MeI} + \mathrm{CO_2} + \mathrm{KCl} \tag{1}$$

Methyl bromodifluoroacetate **4** is also a convenient trifluoromethylating agent[13] and can be used to prepare **1**. Heating **4** with equimolar amounts of KF and $I_2$, and a catalytic amount of CuI in DMF at 80 °C for 5 h gave **1** in 70% yield [reaction (2)]. Interestingly, if KI was used instead of KF in reactions (1) and (2) under similar conditions, **2** was obtained in 50–60% yield (100% conversion of **3**) [reaction (3)]. A disadvantage of these two methods is the separation of traces of methyl iodide from the product **2**.

$$\underset{\mathbf{4}}{\mathrm{BrCF_2CO_2Me}} + \mathrm{KF} + \mathrm{I_2} \xrightarrow{\mathrm{CuI}} \underset{\mathbf{1}}{\mathrm{CF_3I}} + \mathrm{CO_2} + \mathrm{MeI} + \mathrm{KBr} \tag{2}$$

$$\underset{\substack{\mathbf{3},\ \mathrm{X} = \mathrm{Cl} \\ \mathbf{4},\ \mathrm{X} = \mathrm{Br}}}{\mathrm{XCF_2CO_2Me}} + \mathrm{KI} + \mathrm{I_2} \xrightarrow{\mathrm{CuI}} \underset{\mathbf{2}}{\mathrm{CF_2I_2}} + \mathrm{MeI} + \mathrm{CO_2} + \mathrm{KCl} \tag{3}$$

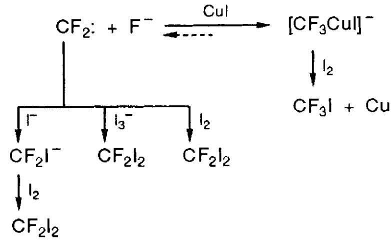
In order to obtain pure **2**, potassium bromodifluoroacetate **5** was found to be the best substrate. On heating **5** with equimolar amounts of KI and $I_2$ in DMF at 40 °C for 10 h, **2** was obtained in 50–60% isolated yield (80% by $^{19}$F NMR) with 90% conversion of **5** [reaction (4)]. Equimolar amounts of KI and CuI are necessary for high yields of **2**. Smaller proportions of CuI, or its absence, lead to low yield (10%).

$$\underset{\mathbf{5}}{\mathrm{BrCF_2CO_2K}} + \mathrm{KI} + \mathrm{I_2} \xrightarrow{\mathrm{CuI}} \underset{\mathbf{2}}{\mathrm{CF_2I_2}} + \mathrm{KX} + \mathrm{CO_2} \tag{4}$$

We suggest the following mechanism for the formation of **1** and **2**. The decomposition of **3** and **4** in the presence of CuI initially leads to $XCF_2CO_2Cu$,[12] which is readily decarboxylated to form difluorocarbene in a concerted process [reactions (5) and (6)]. Difluorocarbene and fluoride ion are in equilibrium with $CF_3^-$. In the presence of CuI the equilibrium readily shifts to the right forming $[CF_3CuI]^-$ species[12] which react with iodine to give **1**. In the presence of a high concentration of $I_3^-$ or $I^-$ rather than $F^-$ and $I_2$, difluorocarbene will react either with iodide ion, to form $ICF_2^-$, which then captures iodine to form **2**, or combine with $I_3^-$ to afford **2** and $I^-$. Compound **2** can also be formed from difluorocarbene insertion into iodine (Scheme 1).

$$\mathrm{ClCF_2CO_2Me} + \mathrm{CuI} \longrightarrow \mathrm{ClCF_2CO_2Cu} + \mathrm{MeI} \tag{5}$$

$$\mathrm{ClCF_2CO_2Cu} \longrightarrow \mathrm{CuCl} + \mathrm{CF_2\!:} + \mathrm{CO_2} \tag{6}$$



**Scheme 1**

Similarly the formation of $CF_2$: from **5** may take place as in reactions (7) and (8). In the absence of KF, in the synthesis of **1** [*cf.* reaction (1)], the formation of $ClCF_2CONMe_2$ may be ascribed to a simple displacement of **3** by $HNMe_2$, probably resulting from the decomposition of DMF [reaction (9)].

$$\mathrm{BrCF_2CO_2^-} + \mathrm{CuI} \rightarrow [\mathrm{BrCF_2CO_2CuI}]^- \tag{7}$$

$$[\mathrm{BrCF_2CO_2CuI}]^- \rightarrow \mathrm{CF_2\!:} + [\mathrm{CuBrI}]^- \tag{8}$$

$$\mathrm{ClCF_2CO_2Me} + \mathrm{HNMe_2} \rightarrow \mathrm{ClCF_2CONMe_2} \tag{9}$$

The formation of the by-products $CF_3H$ and $CF_2{=}CF_2$ may be explained by dimerisation of $CF_2$:, and its reaction with $F^-$ then $H_2O$.[12]

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