Simple Direct Synthesis of [Bis(trifluoroacetoxy)iodo]arenes

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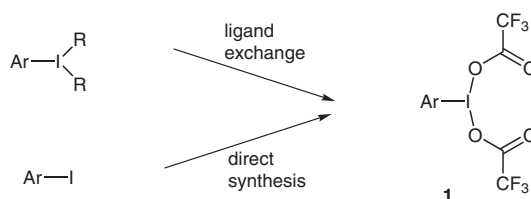Fax +44(29)20876968; E-mail: wirth@cf.ac.uk

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Abstract: A modified procedure for the direct synthesis of hypervalent [bis(trifluoroacetoxy)iodo]arenes is described. It avoids the use of hazardous reagents with the workup being only an aqueous extraction.

Key words: hydrogen peroxide, hypervalent compounds, iodine, oxidation

Scheme 1 Indirect and direct synthesis of [bis(trifluoroacetoxy)iodo]arenes **1**
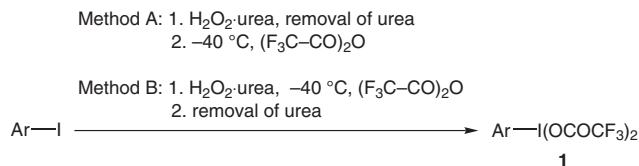
Hypervalent iodine compounds are now established reagents in organic synthesis. Their use as mild and efficient oxidants is important, but many more applications of these compounds have emerged recently. They range from the formation of carbon–carbon bonds in phenol-coupling reactions or as benzyne precursors in the generation of carbon–heteroatom bonds to the activation of carbon–hydrogen bonds. Depending on the substrate, rearrangements or fragmentations can also be induced by these reagents.[1] They are an alternative to metal-containing reagents due to their low toxicity, stability, ease of handling, and high efficiency. Although first reports on the catalytic use of hypervalent iodine reagents have recently appeared in the literature,[2] most of the applications still rely on stoichiometric quantities of these compounds. Of practical importance are hypervalent iodine compounds with halides (chloride, fluoride) and acetoxy or trifluoroacetoxy groups as ligands. Among the growing library of hypervalent iodine compounds are [bis(trifluoroacetoxy)iodo]arenes **1**, ArI(OCOCF$_3$)$_2$, originally prepared by Yagupolskii et al.[3] They have been applied as potent and often chemoselective oxidants, and have a broad appeal throughout organic synthesis.

Several methods have been published for the synthesis of [bis(trifluoroacetoxy)iodo]arenes. These reagents (**1**) can be prepared either by an indirect route, usually by a ligand-exchange reaction on an already-oxidized iodine(III) compound, or by direct oxidation from aryl iodide precursor molecules.

A commonly used procedure is the ligand-exchange reaction using (diacetoxyiodo)arenes and trifluoroacetic acid.[4] The success of this method is related to the electronic properties of the (diacetoxyiodo)arene – the reaction rate of electron-poor substrates can be very low. Other indirect methods include the reaction of (dichloroiodo)arenes with silver trifluoroacetate[5] or the reaction of iodosylarenes with trimethysilyl trifluoroacetate.[6]

The direct oxidation of iodoarenes, however, is still a more convenient method, although the choice of oxidants has to take into account the structure and the electronic properties of the iodoarene. Deactivated iodoarenes can be oxidized by either nitric acid[7] or sodium percarbonate[8] together with trifluoroacetic anhydride. The oxidation with trifluoroperacetic acid seems to be most convenient, but requires 80% hydrogen peroxide, which is dangerous and not commercially available.[9] Very recently, the use of potassium persulfate with trifluoroacetic acid anhydride was reported by Kitamura et al. in an efficient synthesis of [bis(trifluoroacetoxy)iodo]arenes.[10] Herein we report the direct synthesis of [bis(trifluoroacetoxy)iodo]arenes **1** using in situ generated trifluoroperacetic acid and describe a variation of the procedure reported by Zhdankin and Stang.[9]

The solubility of hydrogen peroxide is higher in organic solvents than in water.[11] Consequently, urea can be removed from solutions of the commercially available hydrogen peroxide–urea adduct in organic solvents by extraction with water. The remaining solution of hydrogen peroxide in an organic solvent can then, after drying, react with trifluoroacetic anhydride to generate trifluoroperacetic acid. If this reaction is performed in the presence of an aryl iodide, the corresponding hypervalent [bis(tri-
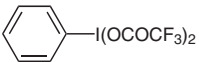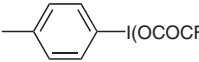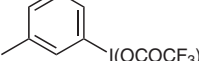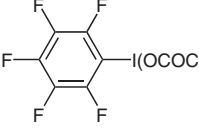
Method A: 1. $H_2O_2 \cdot$urea, removal of urea
            2. –40 °C, $(F_3C–CO)_2O$

Method B: 1. $H_2O_2 \cdot$urea, –40 °C, $(F_3C–CO)_2O$
            2. removal of urea

$$Ar—I \longrightarrow Ar—I(OCOCF_3)_2 \quad \mathbf{1}$$
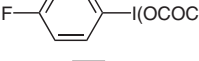
Scheme 2

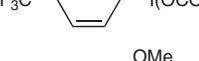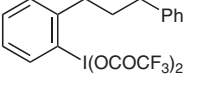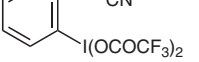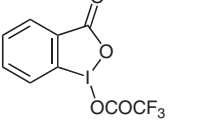fluoroacetoxy)iodo]arenes are obtained in good yields as shown in Table 1 and described in general procedure A.

As an alternative to this protocol, a mixture of the hydrogen peroxide–urea adduct and trifluoroacetic anhydride can be used directly for the generation of trifluoroperacetic acid. In the presence of an iodoarene, the hypervalent iodine species **1** are generated, but the urea has to be removed after the reaction. This protocol (general procedure B) is therefore only suitable for hypervalent iodine compounds that tolerate subsequent aqueous workup. The for-

Table 1   Direct Synthesis of [Bis(trifluoroacetoxy)iodo]arenes **1**

[Bis(trifluoroacetoxy)iodo]arenes **1**		Method	Yield (%)
Ph–I(OCOCF$_3$)$_2$	**1a**	B	96
4-Me-C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1b**	B	91
3-Me-C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1c**	A	65
C$_6$F$_5$–I(OCOCF$_3$)$_2$	**1d**	A	95
4-F-C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1e**	A	90
4-F$_3$C-C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1f**	A	81
2-[CH$_2$CH$_2$CH(OMe)Ph]C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1g**	B	59
2-[CH$_2$CN]C$_6$H$_4$–I(OCOCF$_3$)$_2$	**1h**	B	26
benziodoxolone–OCOCF$_3$	**1i**	A	50[a]

[a] Determined by NMR.

mation of trifluoroperacetic acid takes place around –30 °C, as shown by low-temperature NMR studies of hydrogen peroxide–trifluoroacetic anhydride mixtures.

In conclusion, we have improved an existing procedure and avoided the use of hazardous 80% hydrogen peroxide by replacement with hydrogen peroxide–urea adduct. This method allows the synthesis of hypervalent iodine reagents at low temperatures and should be applicable to a wide range of iodoarenes.

[Bis(trifluoroacetoxy)iodo]arenes 1; General Procedure, Method A

$H_2O_2 \cdot$urea (216 mg, 2.29 mmol) was dissolved in a minimum amount of deionized H_2O (0.5 mL) and extracted with CH_2Cl_2 (3 × 6 mL). The combined organic phases were dried (Na_2SO_4) and filtered to give a soln of H_2O_2 in CH_2Cl_2. This soln was cooled to –40 °C and trifluoroacetic anhydride (1.27 mL, 9.17 mmol) was added dropwise. After 30 min, the iodoarene (0.91 mmol) was added to the soln and the mixture stirred at –40 °C for a further 7 h. The soln was warmed up to r.t. and stirred for 1 h. The solvent was removed under reduced pressure to yield the corresponding [bis(trifluoroacetoxy)iodo]arene.

[Bis(trifluoroacetoxy)iodo]arenes 1; General Procedure, Method B

Trifluoroacetic anhydride (1.27 mL, 9.17 mmol) was added dropwise to a stirred soln of $H_2O_2 \cdot$urea (216 mg, 2.29 mmol) in CH_2Cl_2 (4 mL) at –40 °C. After 30 min, the appropriate iodoarene (0.91 mmol) was added, and the resulting soln stirred at –40 °C for 7 h. The soln was warmed up to r.t. and stirred for 1 h. The soln was quickly washed with a small quantity of H_2O, the organic phase separated, dried (MgSO$_4$) and the solvent removed under reduced pressure to yield the corresponding [bis(trifluoroacetoxy)iodo]arene.

Spectroscopic data for known compounds can be found in the literature: **1a**,[10] **1e**,[10] **1b**,[12] **1c**,[4b] **1d**,[7b] **1f**,[9] **1i**.[13]

1g

^{1}H NMR (500 MHz, CDCl$_3$): δ = 2.04 (m, 2 H, CH_2CHOMePh), 2.95 (m, 1 H, ArCH_2), 3.08 (m, 1 H, ArCH_2), 3.19 (s, 3 H, CH_3), 4.15 (dd, J = 8.0, 2.8 Hz, 1 H, CH$_2$CHOMe), 7.10–7.31 (m, 6 H, ArH), 7.5 (d, J = 8.2 Hz, 1 H, ArH), 7.58 (t, J = 7.6 Hz, 1 H, ArH), 8.21 (d, J = 8.14 Hz, 1 H, ArH).

^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 35.5 (CH$_2$CHOMe), 39.3 (ArCH$_2$), 56.6 (OCH$_3$), 83.4 (CH$_2$CHOMe), 112.9 (q, J_{CF} = 288 Hz, CF$_3$), 126.5, 126.8, 128.5, 128.7, 129.5, 131.1, 134.6 (CI), 138.3, 141.0, 144.5, 161.0 (q, J_{CF} = 40 Hz, COCF$_3$).

1h

^{1}H NMR (500 MHz, CDCl$_3$): δ = 4.30 (s, 2 H, CH_2), 7.57 (t, J = 7.7 Hz, 1 H, ArH), 7.87 (t, J = 7.6 Hz, 1 H, ArH), 7.98 (d, J = 7.7 Hz, 1 H, ArH), 8.40 (d, J = 7.9 Hz, 1 H, ArH).

^{13}C NMR (125.7 MHz, CDCl$_3$): δ = 27.5 (CH$_2$), 112.6 (q, J_{CF} = 289 Hz, CF$_3$), 115.2 (CN), 126.2 (CI), 130.7, 131.9, 134.0, 135.4, 138.2, 161.3 (q, J_{CF} = 41 Hz, COCF$_3$).

Acknowledgment

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