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# Novel 10-I-3 Hypervalent Iodine-Based Compounds for Electrophilic Trifluoromethylation

**Patrick Eisenberger, Sebastian Gischig, and Antonio Togni*[a]**

**Abstract:** The synthesis of a new family of 10-I-3 hypervalent iodine compounds is described in which the $CF_3$ functionality participates directly in the hypervalent bond. These materials are accessible by nucleophilic ligand substitution at iodine using $Me_3SiCF_3$ in the presence of a substoichiometric amount of fluoride. The expected T-shaped geometry at iodine was verified by X-ray crystallographic analyses of three of the products (1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one and two substituted 1-trifluoromethyl-1,3-dihydro-1,2-benziodoxoles). Preliminary results for the direct electrophilic transfer of the trifluoromethyl moiety onto organic nucleophiles show modest reactivity in polar aprotic solvents under relatively mild conditions. The overall process can be understood as a formal umpolung of the $CF_3$ group.

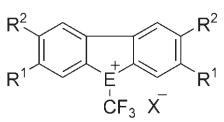
**Keywords:** hypervalent compounds · iodine · trifluoromethylation · umpolung

## Introduction

Fluorinated (and perfluorinated) organic compounds have been targeted increasingly in industry during recent decades.[1] Thus the trifluoromethyl unit is often present in synthetic drugs and agrochemicals, leading to altered physical and physiological behavior of these materials with respect to uptake, mode of action, and metabolism.[2]

Therefore, the introduction of fluorine or perfluoroalkylated groups is a desirable synthesis goal. Among the many existing strategies for the incorporation of the $CF_3$ functionality into organic molecules, the direct transfer of a $CF_3$ synthon is the most attractive approach since the use of $SF_4$, $SbF_3$, $BrF_3$, and HF (for example) for functional group conversion to $CF_3$ usually requires harsh conditions that are often incompatible with other desirable functionalities in the target molecule. For this reason, a lengthy building block strategy is usually necessary because of a lack of direct and relatively mild $CF_3$ transfer reagents. Methods for nucleophilic, electrophilic, and radical trifluoromethylation are now available; the nucleophilic approach is commonly the most successful, thanks to (trifluoromethyl)trimethylsilane ($Me_3SiCF_3$), known as Ruppert's reagent.[3] Although other methods are known,[4] such as the $CuCF_3$ system,[5] $Me_3SiCF_3$ is superior because of its convenience of handling and broad applicability. Recently, promising new approaches have been developed omitting the use of ozone-layer depleting persistent $BrCF_3$ (known as H-1301), which serves as a primary $CF_3$ source in the synthesis of $Me_3SiCF_3$.[6] Prakash and Olah could show that phenyl *S*-trifluoromethylsulfone or -sulfoxide reacts in a nucleophilic fashion in the presence of potassium *tert*-butanolate with aldehydes and ketones to give the trifluoromethylated alcohols.[7] More recently, the reaction of sodium trifluoroacetate ($CF_3COONa$) in the presence of a catalytic amount of $Cu^I$ was reported to give rise to the desired $CF_3$ anion via decarboxylation and subsequent reaction with aldehydes, ketones, or acid chlorides.[8]

In contrast to the nucleophilic $CF_3$ sources, the electrophilic reagents are less developed. The only known class of reagents are the *S*-, *Se*- and *Te*-(trifluoromethyl)dibenzothio-, -seleno- and -tellurophenium salts **1** (E = S, Se, Te; $R^1$ = H, $NO_2$; $R^2$ = H, *t*Bu; X = $SO_3CF_3$, $BF_4$),[9] respectively, invented by Umemoto and co-workers and based on work by Yagupolskii.[10] These reagents react with nucleophiles such as metal enolates of ketones and 1,3-dicarbonyl compounds, silylenolates, enamines, thiolates, and electron-rich aromatics affording trifluoromethylated products in quite useful yields depending on the substrate.

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[a] P. Eisenberger, S. Gischig,[+] Prof. A. Togni
Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology
ETH Hönggerberg, 8093 Zürich (Switzerland)
Fax: (+41) 44-632-1310
E-mail: togni@inorg.chem.ethz.ch

[+] X-ray crystallographic measurements.

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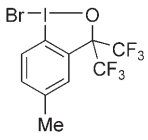
We speculated that an improved $CF_3$ transfer strategy might be based on hypervalent iodine, due to the unique reactivities of such molecules. Hypervalent iodine compounds have attracted much attention from the organic synthetic community; several books[11] and review articles[12] deal with the syntheses and applications of organic hypervalent iodine compounds. The first representative of this class of compounds, dichloroiodobenzene, was synthesized at the end of the 19th century by Willgerodt by passing chlorine gas through a solution of iodobenzene.[13] Furthermore, the chemistry of hypervalent molecules has experienced a renaissance in recent years. For example, hypervalent iodine derivatives are used as mild oxidizing agents for primary and secondary alcohols, giving aldehydes and ketones, respectively.[14] They are also used as group transfer reagents in asymmetric catalytic chlorination,[15] azidation,[16] and cyanation[17] reactions. The ability of the hypervalent iodine structural element to alter the reactivity of hypervalently bonded groups is well documented in the literature. A recent example in organic synthesis is the umpolung of α-hypervalent iodine-functionalized phosphonium ylides which are then able to react with nucleophiles to the corresponding α-substituted phosphonium ylides.[18]

A wide variety of structural motifs of hypervalent iodines with different ligand sets have emerged, ranging from cyclic to acyclic[19] molecules that are neutral or cationic and have the formal oxidation states +III and +V for the iodine atom. Typically, the covalently bonded functionality is usually an aryl or olefinic group, thus stabilizing the hypervalent bond by delocalization of the two electrons of the nonbonding orbital into the adjacent π system. The hypervalent bonding mode in 10-I-3[20] compounds leads to a distorted T-shaped geometry, as predicted by the VSEPR theory.

The heterocyclic derivatives based on the 1,2-benziodoxole fragment have proven to be especially useful in stabilizing atoms or functional groups hypervalently bonded to iodine, known to be otherwise unstable in acyclic derivatives. For instance, 1-bromo-1,3-dihydro-5-methyl-3,3-bis(trifluoromethyl)-1,2-benziodoxole **2**[39] is an isolable stable solid, whereas (dibromoiodo)benzene **3**[21] cannot be isolated.



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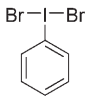
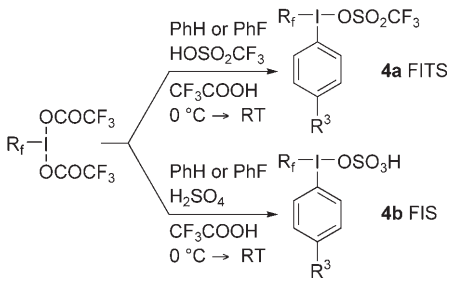


**3**

To our knowledge there are no reports so far of stable I-trifluoromethylated hypervalent iodine compounds suitable for electrophilic $CF_3$ transfer. Umemoto and co-workers attempted a synthesis of an acylic hypervalent I-trifluoromethylated structure following their general route (Scheme 1) to the FITS **4a** and FIS **4b** type of reagent[22] which is used efficiently in electrophilic perfluoroalkylation.[23] They were unable to isolate any product, however, due to the lack of stability of the starting material and presumably of the target molecule under the reaction conditions. They argued that the weak $CF_3$–I bond might be cleaved in this condensation step. For this reason we chose to follow a nucleophilic ligand displacement strategy instead of Yagupolskii's[24] and Umemoto's condensation approach. An alternative electrophilic source of the trifluoromethyl group based on hypervalent iodine is a desirable target because of relatively cheap starting materials and the potential opportunity to recycle the iodine-containing reduced species after the delivery of the $CF_3$ fragment.



Scheme 1. Synthesis of FITS (**4a**) and FIS (**4b**)-type reagents from perfluoroalkyliodides ($R^3$ = H, F; $R_f$ ($n$-$C_mF_{2m+1}$): $m$ = 10, 8, 7, 6, 3, 2; or $i$-$C_3F_7$).

Herein we describe our successful synthesis of the first stable hypervalent iodine compounds with a $CF_3$ group participating in the hypervalent bond. Starting from commercially available or easily accessible materials, we were able to synthesize several I-trifluoromethylated compounds in two steps, in reasonable isolated yields. Furthermore, some of the new compounds have been characterized crystallographically and preliminary reactivity studies show their potential in trifluoromethylation reactions.

## Results and Discussion

**Synthesis of hypervalent iodines**: In an attempt to prepare hypervalent *I*-trifluoromethyl compounds, we tried initially to trifluoromethylate acyclic starting materials such as iodosyltoluene, (dichloroiodo)toluene, (difluoroiodo)toluene, and bis(acetoxy)iodotoluene with $Me_3SiCF_3$ in the presence of tetrabutylammonium difluorotriphenylsilicate (TBAT) or CsF. Typically, the 10-I-3 iodine precursors were treated with $Me_3SiCF_3$ (1.0–2.2 equiv) in $CH_2Cl_2$, THF, or MeCN in the presence of CsF (5 mol%, up to 2.2 equiv) or TBAT. These reactions were carried out at −80 °C, −40 °C, 0 °C, or ambient temperature. In each case, the only products observed by $^{19}F$ NMR spectroscopy were $Me_3SiF$ (from the activation of $Me_3SiCF_3$), $Ph_3SiF$ when TBAT was used as an activator, or $CF_3H$. When difluoroiodotoluene reacted in MeCN in the absence of any fluoride source, $Me_3SiCF_3$ was consumed completely after six days and traces of $CF_3I$ were detected along with traces of by-products having a $^{19}F$ chemical shift $\delta \approx -60$ ppm, most likely arising from trifluoromethylated aromatics. The observation of $CF_3I$ indicates that the nucleophilic ligand substitution might take place, but the cleavage of the $I-C_{arom.}$ bond might be very facile under the reaction conditions. These initial discouraging results suggested that for additional stability of the product a more rigid and therefore more stable backbone is necessary.

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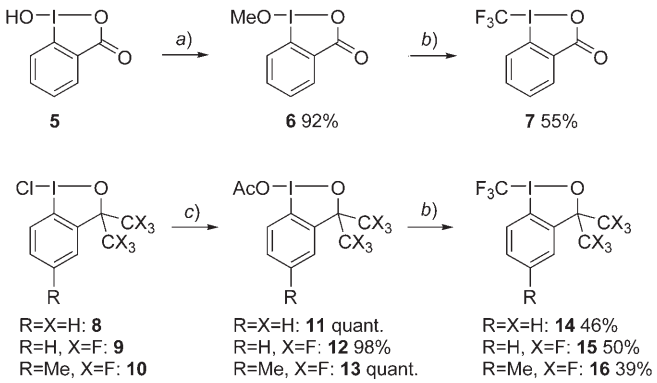
Starting from 2-iodosylbenzoic acid **5** in [$D_3$]MeCN with a catalytic amount of fluoride, the formation of a product displaying a signal at $\delta = -35.7$ ppm, together with a doublet with a $J_{C,F}$ coupling constant of 79.5 Hz at $\delta = -79.9$ ppm arising from $CF_3H$, was observed in the $^{19}F$ NMR spectra. $CF_3H$ is most likely formed by the abstraction of a proton from the medium by the strongly basic $CF_3^-$ ion. The reaction did not go to completion due to the polymeric nature of **5**, its insolubility, and the weak leaving group ability of the hydroxy function. We speculated that a more soluble starting material containing a better leaving group could provide **7** in higher yields if a substoichiometric amount of fluoride is used to initiate the reaction. Indeed, when we conducted the same type of reaction in MeCN with the methoxy compound **6**, almost complete conversion to product **7** was observed after 24 h at ambient temperature (Scheme 2).




Scheme 2. a) 1) AcOAc, reflux; 2) MeOH, reflux; b) $Me_3SiCF_3$, cat. $F^-$, MeCN, RT; c) AgOAc, MeCN, RT.

After filtration of the reaction mixture over neutral aluminum oxide (akt. I) to remove remaining starting material and traces of non-volatile side products, the desired product **7** was isolated in 50% yield. The methoxy anion liberated in the trifluoromethylation step acts as a nucleophile forming the pentacoordinate $[Me_3Si(CF_3)(OMe)]^-$, which is the active $CF_3$-transferring agent.[25] The resulting $Me_3SiOMe$ was identified in the $^{13}C$ NMR spectrum of the crude mixture ([$D_3$]MeCN, $\delta_C = -2.00$ ($(CH_3)_3Si$), 49.28 ppm ($OCH_3$)).

The analogous I-trifluoromethylated compounds **14**, **15**, and **16** become accessible following the same strategy. The acetoxy compounds **11**, **12**, and **13** are converted to the corresponding products with concomitant formation of $Me_3SiOAc$. CsF or TBAT can be used as a fluoride source to initiate the reaction, TBAT being superior due to its high solubility in the solvents used and its nonhygroscopicity. The isolated yields are in a useful range (**7** 50%, **14** 46%, **15** 49%, **16** 39%), but may be increased by applying optimized isolation and purification protocols. The typical conversion to product is greater than 80% based on the integration of the appropriate signals in the $^1H$ NMR spectrum. The products are stable crystalline solids: only **14** decomposes slowly at ambient temperature, and therefore must be stored at −18 °C. The synthesis of **14** easily allows a scale-up to multigram quantities, since only one distillation and two recrystallizations are necessary for the entire five-step route (starting from cheap, commercially available 2-iodobenzoic acid). Furthermore, the last two steps were also performed in a one-pot procedure, that is, without isolation of **11** after the filtration of the precipitated AgCl, with no loss of isolated product **14**. Thus, **14** is the ideal compound for reactivity studies because of its better synthetic accessibility.

The analytical data are in agreement with the proposed structures of the products **7**, **14**, **15**, and **16**. The NMR data of I-trifluoromethylated compounds relevant to the I–$CF_3$ functionality are summarized in Table 1. The carbon bearing

Table 1. NMR data for the I–$CF_3$ group of **7** and **14**–**16**.

| | $\delta_F$(I–$CF_3$)[c] | $\delta_C$(I–$CF_3$)[c] | $J_{C,F}$ [Hz] |
|---|---|---|---|
| **7**[a] | −33.8 | 107.1 | 380.2 |
| **14**[a] | −40.1 | 110.7 | 396.3 |
| **15**[b] | −36.5 | 107.3 | 390.0 |
| **16**[b] | −36.7 | 107.2 | 384.8 |

[a] In $CDCl_3$. [b] In $CD_2Cl_2$. [c] $\delta_F$ relative to $CFCl_3$ and $\delta_C$ to TMS, respectively.

the proton *ortho* to iodine shows a quartet in the $^{13}C$ NMR spectrum with a coupling constant $J_{C,F}$ of $\approx$3.0 Hz indicating a through-space interaction with the very close trifluoromethyl group. This is also visible in the $^1H$ NMR spectrum of **7** and **15**, where the signal of the proton *ortho* to iodine is shifted to higher frequency. The $^{19}F$ NMR shifts for the I–$CF_3$ groups are in the typical region for other previously reported molecules with an I–$CF_3$ fragment (Table 2). Note

Table 2. Selected bond lengths [Å], bond angles [°], and torsion angles [°] of **7**, **15**, and **16**.

| | **7** | **15** | **16** |
|---|---|---|---|
| I–C1 | 2.219(4) | 2.229(2) | 2.236(2) |
| I–O1 | 2.283(2) | 2.2014(15) | 2.1977(17) |
| I–C4 | 2.113(3) | 2.115(2) | 2.114(2) |
| C1-I-C4 | 93.74(14) | 92.37(8) | 93.61(9) |
| O1-I-C4 | 76.79(11) | 77.07(7) | 77.58(7) |
| C1-I-O1 | 170.49(12) | 169.40(7) | 171.07(8) |
| C1-I-C4-C5 | 0.7(3) | 11.75(19) | 4.3(2) |
| O1-I-C4-C5 | 179.9(3) | 169.13(19) | 177.2(2) |
| C1-I-C4-C3 | 179.5(3) | 167.01(16) | 175.36(17) |
| O1-I-C4-C3 | 0.3(2) | 12.11(15) | 3.21(16) |

that the $^{19}F$, $^{13}C$ NMR shifts, as well as the carbon–fluorine coupling constants for the I–$CF_3$ moiety, are closer to those of compounds formally belonging to the 10-I-2 family than of members of 10-I-3 compounds with equatorial $CF_3$ groups. This supports the structure of our new *I*-trifluoro-

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methyl compounds where the $CF_3$ group takes an apical position, thus being part of the hypervalent bond.

**Single-crystal X-ray analysis**: X-ray quality single crystals were obtained by diffusion of either $Et_2O$ into a saturated solution of **7** in MeCN, or pentane into a solution of **15** in $CH_2Cl_2$. Crystals of **16** were obtained directly from the reaction mixture. The X-ray analyses (Figure 1) clearly show the distorted T-shaped geometry around iodine, typical for members of the hypervalent iodine(III) class. The I–$CF_3$ bond lengths lie within the reported range for molecules containing the I–$CF_3$ fragment (Table 3). The bond lengths and $^{19}F$ NMR shifts of the series **7**–**15**–**16** exhibit a remarkable trend. The I–C1 bond length increases from **7** (2.219(4) Å), through **15** (2.229(2) Å), to **16** (2.236(2) Å) and simultaneously the I–O1 bond length decreases (**7**: 2.283(2) Å, **15**: 2.2014(15) Å, **16**: 2.1977(17) Å), whereas the I–C4 bond length remains constant within one standard deviation (2.114 Å). Within the same series the signal for the $CF_3$ group in the $^{19}F$ NMR spectrum shifts $\delta$ to lower frequencies (**7**: $\delta = -33.8$ ppm, **15**: $\delta = -36.5$ ppm, **16**: $\delta = -36.7$ ppm). So far we cannot judge whether or not these findings correlate with the relative reactivity in electrophilic trifluoromethylation reactions.

All three C1-I-O1 angles are significantly smaller than 180° due to the repulsion of the two lone pairs at iodine as predicted by VSEPR theory, and are within the range of those of closely related compounds (around 170°).[26,43] The O1-I-C4 angles around 77° indicate a rather strained situation in the five-membered ring. Values slightly larger than 90° (around 93°) were measured for the C1-I-C4 angles. This can be rationalized with a minimization of the van der Waals 1,4 interaction by pushing the $CF_3$ group away from the hydrogen attached to C5. However, the distance between the fluorine atoms of the I–$CF_3$ functionality and the hydrogen *ortho* to iodine is found in all three structures to be significantly shorter than the sum of their van der Waals radii. That there is an important through-space interaction in this part of the molecule is also indicated, as mentioned above, by the $^{13}C$ NMR spectrum, where the *C*H group *ortho* to *C*I shows a quartet with a carbon–fluorine coupling constant $J_{C,F}$ of ≈3.0 Hz. The five-membered heterocyclic ring in **15** displays an envelope-type conformation with the oxygen out of the π plane of the adjacent aryl ring, as indicated by the O1-I-C4-C3 torsion angle of 12.11(15)°. In **16** this torsion angle (O1-I-C4-C3 3.21(16)°) is found to be significantly smaller and the structure of **7** shows almost perfect coplanarity (torsion angle 0.3(2)°) with the adjacent π system.

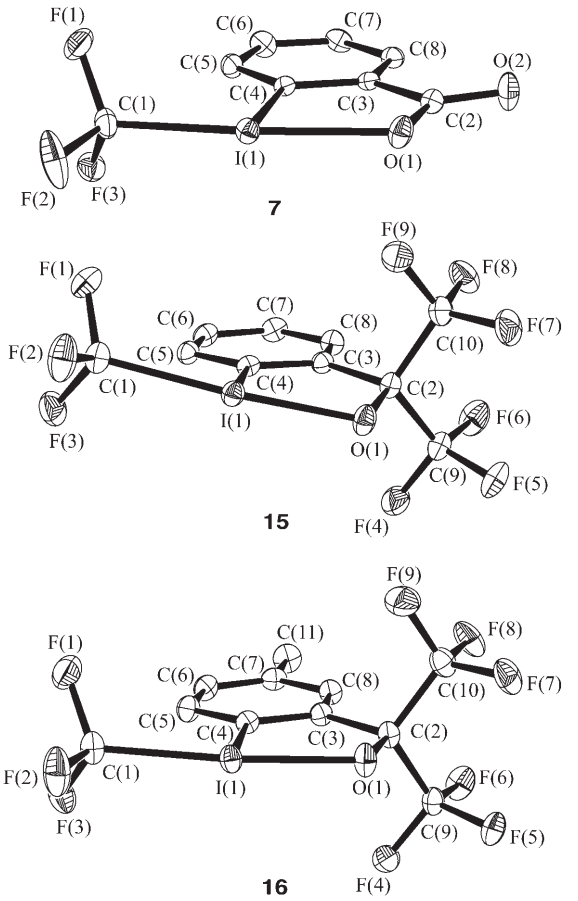


Figure 1. Molecular structures of **7**, **15**, and **16** (ORTEP drawings; 30% thermal ellipsoids, hydrogens omitted for clarity).

Table 3. Reported NMR shifts, coupling constants, and bond lengths of known I–$CF_3$ compounds.

| Entry | Compound[a] | $\delta_C$(I–$CF_3$)[b] | $\delta_F$(I–$CF_3$)[b] | Bond length [Å] |
|---|---|---|---|---|
| 1 | $CF_3I$ | 78.2 (q, $J_{C,F}$ = 344 Hz)[c] | −4.78[c] | – |
| 2 | $CF_3I(Cl)_2$ | 91.9 (q, $J_{C,F}$ = 365 Hz)[d] | −28.99[d] | 2.229(10)[d] |
| 3 | $CF_3I(Cl)F$ | – | −31.5[e] | 2.197(11)[f] |
| 4 | $CF_3I(F)_2$ | – | −33.7[g] | 2.174(6)[h] |
| 5 | $CF_3I(Cl)OMe$ | 83.09 (q, $J_{C,F}$ = 344 Hz)[i] | −29.68[i] | 2.212(8)[i] |
| 6 | $CF_3I(OMe)_2$ | 81.19 (q, $J_{C,F}$ = 344 Hz)[i] | −28.42[i] | 2.190(12)[i] |
| 7 | $CF_3I(ONO_2)_2$ | – | −26.1[j] | 2.212(4)[j] |
| 8 | $CF_3I(Cl)ONO_2$ | – | −28.8[j] | – |
| 9 | $CF_3I(Cl)OCOCF_3$ | – | −24.4[k] | 2.233(9)[k] |
| 10 | $CF_3I(OCOCF_3)_2$ | – | −25.4[g] | – |
| 11 | $[NMe_4]^+\cdot[I(CF_3)_2]^-$ | 117.9 (q q, $J_{C,F}$ = 442 Hz)[l] | −41.1[l] | – |
| 12 | $[NMe_4]^+\cdot[CF_3IOCF_3]^-$ | 106.08 ($J_{C,F}$ = 356 Hz)[m] | −36.2[m] | – |
| 13 | $[NMe_4]^+\cdot[CF_3IF]^-$ | 106.04 ($J_{C,F}$ = 353 Hz)[m] | −35.6[m] | – |

[a] For entries 2–10 the $CF_3$ group is in a pseudo equatorial position (10-I-3 compound), whereas for entries 11–13 it is in an apical position (10-I-2 compound). [b] $\delta_F$ is relative to $CFCl_3$ and $\delta_C$ to TMS, respectively. [c] Reference [27]. [d] Reference [28]. [e] Reference [29]. [f] Reference [30]. [g] Reference [31]. [h] Reference [32]. [i] Reference [33]. [j] Reference [34]. [k] Reference [35]. [l] Reference [36]. [m] Reference [37].

**Reactivity**: Preliminary reactivity tests showed that **14** reacts with β-ketoester **17** affording the α-trifluoromethylated β-ketoester **18** (Scheme 3). Concomitant formation of $CF_3H$

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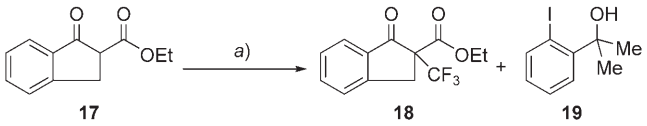


Scheme 3. a) **14**, $K_2CO_3$, cat. $NBu_4I$, solvent, RT.

and $CF_3I$ lowers the yield of **18** drastically. However, under phase-transfer catalysis (PTC) conditions **18** can be obtained in up to 67% yield (Table 4).[38] Polar, aprotic, and nucleophilic solvents are required for this transformation to occur

Table 4. Electrophilic α-trifluoromethylation of **17** under PTC conditions.

| Entry | Solvent | Conditions[a] | Yield of **18** [%] |
|---|---|---|---|
| 1 | $CH_2Cl_2$ | 48 h, RT | 25 |
| 2 | MeCN | 28 h, RT | 67 |
| 3 | THF | 28 h, RT | 19 |
| 4 | toluene | 28 h, RT | trace |
| 5 | DMF | 23 h, RT | 14 |

[a] 0.2 mmol **17**, 0.3 mmol **14**, 0.6 mmol $K_2CO_3$, and 0.02 mmol $NBu_4I$.

efficiently (Table 4, entry 2). The reaction proceeds in MeCN even in the absence of $K_2CO_3$ as base and $NBu_4I$ as a phase-transfer catalyst, but side reactions prevail and lower yields are obtained (maximum 30%). The iodo alcohol **19** can be easily recovered and reoxidized to **8** by *t*BuOCl. Thus, a formal recycling of the reagent is possible. Furthermore, **14** is about one order of magnitude less expensive than *S*-(trifluoromethyl)dibenzothiophenium tetrafluoroborate at present Aldrich prices.

## Conclusion

A new class of hypervalent iodine compounds based on the 1,2-benziodoxole fragment has been designed and prepared. The nucleophilic ligand displacement with "$CF_3^-$" proves to be a versatile method for the synthesis of I-trifluoromethylated hypervalent iodine compounds. In view of the promising reactivity features disclosed here, we are currently investigating our new 10-I-3 compounds with an emphasis on applications in electrophilic trifluoromethylation reactions, including asymmetric catalytic transformations.

## Experimental Section

**General**: All experiments were carried out under an argon or dinitrogen atmosphere using standard Schlenk techniques or in a dry box with oven-dried glassware and magnetic stirring.

All solvents were freshly distilled under argon from an appropriate drying agent before use (MeOH, MeCN, $CD_3CN$, $CH_2Cl_2$, and $CD_2Cl_2$ from $CaH_2$; $Et_2O$ from Na/benzophenone; pentane from Na/benzophenone/diglyme). Melting points were measured on a Griffin melting point apparatus by the sealed capillary method and are uncorrected. IR spectra were measured on a Perkin-Elmer Paragon 1000 (thin film) or on a Perkin-Elmer BX II spectrometer (neat). $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker DPX-250 (operating at 250.1 MHz and 62.9 MHz, respectively) or a Bruker DPX-300 (operating at 300.1 MHz and 75.5 MHz, respectively), and $^{19}F$ NMR spectra on a Bruker AC-200 (at 188.3 MHz). Shifts are relative to TMS as an external standard for $^1H$ and $^{13}C$ NMR spectra, and calibrated against the solvent residual peak. For $^{19}F$ NMR spectra, $CFCl_3$ was used as an external standard. Mass spectra were measured by the MS-Service des Labors für organische Chemie, ETH Zürich, Switzerland, and elemental analyses by the Mikroelementanalytisches Laboratorium der ETH Zürich. Neutral aluminum oxide activity I was purchased from ICN Biomedicals GmbH and silica gel 60 (230–400 mesh) from Fluka. TLC plates were obtained from Merck (silica gel 60 $F_{254}$, aluminum oxide 60 $F_{254}$).

**Compounds**: AcOAc, AgOAc, and CsF were obtained from Fluka, $Me_3SiCF_3$ from ABCR, and **5** from Lancaster; they were used as received. Noncommercial starting materials **8**,[39] **9**,[40] and **10**[39] were synthesized following published procedures. β-Ketoester **17** was synthesized as published,[41] except that toluene was used as solvent instead of benzene.

**1-Methoxy-1,2-benziodoxol-3-(1*H*)-one (6)**:[42] 1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (**5**) (7.0 g, 26.5 mmol) was heated to reflux for 15 min in acetic anhydride (19 mL) until a clear, slightly yellow solution was obtained. Upon cooling, white crystals began to separate. Crystallization was continued at −18 °C. The crystals were decanted, dried under vacuum for 15 h, and identified as 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one by NMR spectroscopy. M.p. 162–165 °C; $^1H$ NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 2.22 (s, 3H; $CH_3$), 7.67 (t, $J_{H,H}$ = 7.2 Hz, 1H; $CH_{arom.}$), 7.87–7.98 (m, 2H; $CH_{arom.}$), 8.19 ppm (d, $J_{H,H}$ = 7.5 Hz, 1H; $CH_{arom.}$); $^{13}C$ NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 20.3 ($CH_3$), 118.4 (CI), 129.0 ($CCO_2$), 129.3, 131.3, 133.1, 136.2 (CH), 168.1 ($CCO_2$), 176.3 ppm ($CH_3CO_2$); IR (neat): $\tilde{\nu}$ = 3094 (w), 3061 (w), 2927 (w), 1682 (s), 1637 (s), 1603 (m), 1587 (m), 1570 (m), 1455 (w), 1441 (m), 1367 (m), 1265 (s), 1239 (s), 1122 (s), 1110 (m), 1049 (w), 1021 (m), 1009 (m), 960 (w), 928 (m), 825 (m), 740 (s), 694 (m), 675 (s), 650 (m), 608 $cm^{-1}$ (w). After heating 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one in MeOH (35 mL) to reflux for 15 min until a clear, colorless solution was obtained and cooling to ambient temperature followed by crystallization at −18 °C, filtration, washing with a minimal amount of MeOH, and drying under vacuum, the desired product **6** (6.78 g, 24.4 mmol, 92%) was obtained as white crystals. M.p. 164–168 °C; $^1H$ NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 4.26 (s, 3H; $CH_3$), 7.64–7.76 (m, 2H; $CH_{arom.}$), 7.88 (t, $J_{H,H}$ = 7.7 Hz, 1H; $CH_{arom.}$), 8.24 ppm (d, $J_{H,H}$ = 7.7 Hz, 1H; $CH_{arom.}$); $^{13}C$ NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 62.2 ($CH_3$), 118.6 (CI), 126.0 (CH), 130.6 ($CCO_2$), 131.0, 132.8, 135.1 (CH), 168.0 ppm (CO); IR (neat): $\tilde{\nu}$ = 3081 (w), 3055 (w), 2965 (w), 2932 (w), 2826 (w), 1633 (s), 1602 (m), 1585 (m), 1562 (m), 1451 (m), 1439 (m), 1352 (w), 1306 (m), 1288 (s), 1270 (m), 1248 (m), 1160 (m), 1134 (s), 1009 (m), 960 (m), 888 (w), 828 (s), 804 (m), 747 (s), 690 (s), 674 (m), 648 $cm^{-1}$ (m).

**1-Trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (7)**: To a vigorously stirred suspension of 1-methoxy-1,2-benziodoxol-3-(1*H*)-one (**6**) (0.75 g, 2.70 mmol) in MeCN (12 mL) was added $Me_3SiCF_3$ (0.60 mL, 4.06 mmol, 1.5 equiv), followed by a suspension of CsF (0.020 g, 0.132 mmol, 3 mol% based on **6**) in MeCN (3 mL). After being stirred overnight (15 h) the light brown solution was evaporated to dryness under reduced pressure and the resulting solid was dried under vacuum. Chromatography with MeOH (p.a. grade) over aluminum oxide yielded the title compound **7** (0.47 g, 1.49 mmol, 55%) as white crystals after removal of the solvent. M.p. 122 °C (dec.); $^1H$ NMR (250 MHz, $CDCl_3$, 25 °C): $\delta$ = 7.26–7.85 (m, 3H; $CH_{arom.}$), 8.43–8.47 ppm (m, 1H; $CH_{arom.}$ *ortho* to I); $^{13}C$ NMR (63 MHz, $CDCl_3$, 25 °C): $\delta$ = 107.1 (q, $J_{C,F}$ = 380.2 Hz; $CF_3$), 114.8 (q, $J_{C,F}$ = 1.3 Hz; CI), 127.2 (q, $J_{C,F}$ = 3.1 Hz; CH *ortho* to CI), 131.9 (s; CH and $CCO_2$), 133.7, 135.7 (CH), 165.9 ppm (CO); $^{19}F$ NMR (188 MHz, $CDCl_3$, 25 °C): $\delta$ = −33.8 ppm (s, $J_{C,F}$ = 380.2 Hz, as calculated from the $^{13}C$ satellites; $CF_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 3621 (m), 3018 (m), 1660 (s), 1563 (w), 1444 (w), 1316 (w), 1220 (s), 1213 (s), 1158 (s), 1077 $cm^{-1}$ (s); elemental analysis: calcd (%) for $C_8H_4F_3IO_2$ (316.02): C 30.41, H 1.28, O 10.13, I 40.16; found: C 30.49, H 1.35, O 10.38, I 40.30.

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**1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (11)**:[43] 1-Chloro-1,3,-dihydro-3,3-dimethyl-1,2-benziodoxole (**8**) (2.02 g, 6.8 mmol) and AgOAc (1.18 g, 7.1 mmol) were placed under argon. MeCN (20 mL) was added and the resulting suspension was stirred overnight (15 h) at ambient temperature in the dark. Filtration under argon of the precipitated AgCl followed by removal of the solvent and drying under vacuum yielded the title compound **11** as a white solid in quantitative yield. $^1$H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 1.51 (s, 6H; $CH_3$), 1.98 (s, 3H; OCOC$H_3$), 7.16 (dd, $J_{H,H}$ = 1.8 Hz, $J_{H,H}$ = 6.9 Hz, 1H; $CH_{arom.}$), 7.45 (m, 2H; $CH_{arom.}$), 7.78 ppm (dd, $J_{H,H}$ = 1.5 Hz, $J_{H,H}$ = 7.5 Hz, 1H; $CH_{arom.}$); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 21.4 (OCO$CH_3$), 29.2 (C($CH_3$)$_2$), 84.5 (*C*($CH_3$)$_2$), 115.6 (CI), 126.2, 129.8, 129.9, 130.4 (CH), 149.4 (*CC*($CH_3$)$_2$), 177.3 ppm (CO).

**1-Acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (12)**: 1-Chloro-1,3,-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (**9**) (1.002 g, 2.48 mmol) and AgOAc (0.415 g, 2.49 mmol) were suspended in MeCN (15 mL). After being stirred overnight (14.5 h) in the dark, the precipitated AgCl was filtered off under argon and washed with MeCN. The mother liquor was evaporated to dryness to yield the title compound **12** (1.039 g, 2.43 mmol, 98%) as a white solid. $^1$H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 2.18 (s, 3H; $CH_3$), 7.61–7.79 (m, 3H; $CH_{arom.}$), 7.93 ppm (d, $J_{H,H}$ = 8.4 Hz, 1H; $CH_{arom.}$); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 20.4 ($CH_3$), 85.7 (m, *C*($CF_3$)$_2$), 115.8 (CI), 123.0 (q, $J_{C,F}$ = 214.3 Hz; $CF_3$), 129.7 (quintet (qu), $J_{C,F}$ = 2.4 Hz, CH), 130.2, 131.0 (CH), 131.5 (*CC*($CH_3$)$_2$), 133.4(CH), 176.5 ppm (CO); $^{19}$F NMR (188 MHz, $CDCl_3$, 25 °C): $\delta$ = −75.8 (d, $J_{H,F}$ = 0.8 Hz; $CF_3$).

**1-Acetoxy-1,3-dihydro-5-methyl-3,3-bis(trifluoromethyl)-1,2-benziodoxole (13)**: 1-Chloro-1,3-dihydro-5-methyl-3,3-bis(trifluoromethyl)-1,2-benziodoxole (**10**) (1.00 g, 2.40 mmol) and AgOAc (0.424 g, 2.54 mmol) were suspended in MeCN (20 mL) and stirred overnight (18 h) in the dark. The white precipitate was filtered off and washed with MeCN. The mother liquor was evaporated to dryness to yield product **13** quantitatively as white crystals (1.05 g, 2.40 mmol; 99%). $^1$H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta$ = 2.17 (s, 3H; OCOC$H_3$), 2.51 (s, 3H; $CH_3$), 7.50 (s, 1H; $CH_{arom.}$), 7.56 (d, $J_{H,H}$ = 8.7 Hz, 1H; $CH_{arom.}$), 7.75 ppm (d, $J_{H,H}$ = 8.4 Hz, 1H; $CH_{arom.}$); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C): $\delta$ = 20.4 (OCO$CH_3$), 21.0 ($CH_3$), 85.5 (qu, $J_{C,F}$ = 30.6 Hz, *C*($CF_3$)$_2$), 112.0 (CI), 123.1 (q, $J_{C,F}$ = 289.2 Hz, *C*$F_3$), 129.7 (CH), 130.2 (qu, $J_{C,F}$ = 2.3 Hz; CH *ortho* to CC($CF_3$)$_2$), 131.6 (*CC*($CF_3$)$_2$), 134.4 (CH), 141.9 (*CC*$H_3$), 176.5 ppm (CO); $^{19}$F NMR (188 MHz, $CDCl_3$, 25 °C): $\delta$ = −75.8 ppm (d, $J_{H,F}$ = 0.9 Hz; $CF_3$).

**1-Trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (14)**: To a solution of 1-acetoxy-1,3,-dihydro-3,3-dimethyl-1,2-benziodoxole (**11**) (2.06 g, 6.5 mmol) in MeCN (25 mL), $Me_3SiCF_3$ (1.5 mL, 10.15 mmol, 1.5 equiv) was added by using a syringe. A suspension of CsF (0.010 g, 0.066 mmol, 1 mol% based on **11**) in MeCN (5 mL) was added dropwise. The reaction mixture was stirred overnight (16 h) at ambient temperature. After removal of the solvent and all volatile compounds under vacuum, pentane (25 mL) was added to the resulting oily brown solid. The brown precipitate was filtered off under argon and the solvent was removed from the clear colorless solution under vacuum to yield the title compound **14** (1.00 g, 3.0 mmol, 46%) as a white solid. Sublimation gave an analytically pure sample. M.p. 54–56 °C; $^1$H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta$ = 1.46 (s, 6H; $CH_3$), 7.39 (m, 2H; $CH_{arom.}$), 7.51 ppm (t, $J_{H,H}$ = 6.9 Hz, 2H; $CH_{arom.}$); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta$ = 30.8 (C($CH_3$)$_2$), 76.5 (*C*($CH_3$)$_2$), 110.7 (q, $J_{C,F}$ = 396.3 Hz; $CF_3$), 110.6 (q, $J_{C,F}$ = 3.0 Hz; CI), 127.3 (CH), 127.8 (q, $J_{C,F}$ = 2.8 Hz, CH), 129.8, 130.6 (CH), 149.2 ppm (*CC*($CH_3$)$_2$); $^{19}$F NMR (188 MHz, $CDCl_3$, 25 °C): $\delta$ = −40.1 (s, $J_{C,F}$ = 396.0 Hz;[43] $CF_3$); IR (neat): $\tilde{\nu}$ = 2980 (w), 2926 (w), 1563 (w), 1461 (m), 1437 (m), 1376 (m), 1359 (m), 1270 (w), 1248 (m), 1164 (m), 1072 (br s), 1000 (s), 957 (s), 872 (m), 758 (s), 751 (s), 718 (m), 706 (w), 648 (w), 602 cm$^{-1}$ (s); elemental analysis: calcd (%) for $C_{10}H_{10}F_3IO$ (330.09): C 36.39, H 3.05, F 17.27, I 38.45; found: C 36.61, H 3.23, F 17.31, I 38.30.

**1-Trifluoromethyl-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (15)**: To a solution of 1-acetoxy-1,3,-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (**12**) (0.50 g, 1.17 mmol) in MeCN (5 mL) was added $Me_3SiCF_3$ (0.28 mL, 1.76 mmol, 1.5 equiv) by using a syringe. A suspension of CsF (0.003 g, 0.02 mmol, 2 mol% based on **12**) in MeCN (2 mL) was added dropwise via cannula. After the cloudy, orange solution had been stirred overnight (18 h), about four-fifths of the solvent was removed under vacuum. The resulting crystals were filtered off and washed with $Et_2O$ and pentane. The residue was taken up in $CH_2Cl_2$ and filtered. The mother liquor was concentrated to dryness under vacuum, yielding the title compound **15** (0.255 g, 0.58 mmol, 50%) as white crystals. M.p. 156 °C; $^1$H NMR (300 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = 7.69–7.80 (m, 3H; $CH_{arom.}$), 7.86–7.97 ppm (m, 1H; $CH_{arom.}$ *ortho* to I); $^{13}$C NMR (75 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = 81.4 (m, *C*($CF_3$)$_2$), 107.3 (q, $J_{C,F}$ = 390.0 Hz; I*C*$F_3$), 110.4 (CI), 123.5 (q, $J_{C,F}$ = 290.6 Hz; C(*C*$F_3$)$_2$), 128.9 (q, $J_{C,F}$ = 3.0 Hz; CH *ortho* to *C*I), 130.8 (qu, $J_{C,F}$ = 2.6 Hz; CH *ortho* to *C*C($CF_3$)$_2$), 130.9 (*CC*($CF_3$)$_2$), 131.4 (CH) , 133.7 ppm (CH); $^{19}$F NMR (188 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = −36.5 (s, $J_{C,F}$ = 384.7 Hz,[43] 3F, I$CF_3$), −76.1 ppm (s, 6F; C(*C*$F_3$)$_2$); IR (neat): $\tilde{\nu}$ = 1569 (w), 1471 (w), 1445 (w), 1300 (w), 1257 (m), 1228 (w), 1189 (m), 1143 (m), 1116 (s), 1071 (s), 1005 (w), 964 (m), 953 (m), 944 (s), 865 (w), 760 (m), 754 (m), 728 (m), 720 (m), 692 (m), 682 (m), 659 (m), 642 cm$^{-1}$ (m); ESI-HRMS: calcd (*m*/*z*) for $C_{10}H_{10}F_3IO$: 460.9061 ([*M*+Na$^+$]); found 460.9062 ([*M*+Na$^+$]); elemental analysis: calcd (%) for $C_{10}H_4F_9IO$ (438.03): C 27.42, H 0.92, F 39.04, I 28.97; found: C 27.26, H 1.03, F 39.06, I 29.20.

**1-Trifluoromethyl-1,3-dihydro-5-methyl-3,3-bis(trifluoromethyl)-1,2-benziodoxole (16)**: To a solution of 1-acetoxy-1,3-dihydro-5-methyl-3,3-bis-(trifluoromethyl)-1,2-benziodoxole (**13**) (0.93 g, 2.10 mmol) in MeCN (14 mL) was added $Me_3SiCF_3$ (0.5 mL, 3.38 mmol, 1.5 equiv) by using a syringe. To this mixture a solution of TBAT (0.011 g, 0.022 mmol, 1 mol% based on **13**) in MeCN (3 mL) was added dropwise by using a cannula. After the mixture had been stirred overnight (15 h), half of the solvent was removed under vacuum and the resulting white crystals were filtered off, washed with a minimal amount of $Et_2O$, and dried under vacuum. The white microcrystals were washed two times with a minimal amount of $CH_2Cl_2$ and dried under vacuum to yield the analytically pure **16** (0.371 g, 0.82 mmol, 39%). M.p. 165–166 °C; $^1$H NMR (300 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = 2.53 (s, 3H; $CH_3$), 7.57 (m, 2H; $CH_{arom.}$), 7.71 ppm (s, 1H; $CH_{arom.}$); $^{13}$C NMR (75 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = 20.7 ($CH_3$), 81.3 (qu, $J_{C,F}$ = 29.7 Hz; *C*($CF_3$)$_2$), 106.6 (CI), 107.2 (q, $J_{C,F}$ = 384.8 Hz; I*C*$F_3$), 123.5 (q, $J_{C,F}$ = 290.2 Hz; C(*C*$F_3$)$_2$), 128.3 (q, $J_{C,F}$ = 2.9 Hz; CH *ortho* to CI), 130.8 (*CC*($CF_3$)$_2$), 131.4 (qu, $J_{C,F}$ = 2.5 Hz; CH *ortho* to CC($CF_3$)$_2$), 134.6 (CH), 142.6 ppm (*CC*$H_3$); $^{19}$F NMR (188 MHz, $CD_2Cl_2$, 25 °C): $\delta$ = −36.7 (s, $J_{C,F}$ = 384.9 Hz,[43] 3F; I$CF_3$), −76.1 ppm (d, $J_{H,F}$ = 4.3 Hz, 6F; C($CF_3$)$_2$); IR (neat): $\tilde{\nu}$ = 1447 (w), 1261 (m), 1208 (m), 1193 (m), 1170 (m), 1130 (s), 1074 (s), 1015 (m), 978 (m), 962 (s), 950 (m), 892 (m), 838 (m), 804 (s), 748 (m), 731 (m), 718 (m), 688 (m), 679 (m), 658 cm$^{-1}$ (m); ESI-MS (*m*/*z*): 474.9 ([*M*+Na$^+$]), 452.8 ([*M*$^+$]), 383.9 ([*M*$^+$ −$CF_3$]); elemental analysis: calcd (%) for $C_{11}H_6F_9IO$ (452.05): C 29.23, H 1.34, F 37.82; found: C 29.19, H 1.36, F 37.78.

**Ethyl 1-oxo-2-trifluoromethylindane-2-carboxylate (18)**: To a vigorously stirred suspension of 1-oxoindane-2-carboxylic acid ethyl ester (**17**) (0.041 g, 0.2 mmol), $K_2CO_3$ (0.083 g, 0.6 mmol, 3.0 equiv), and *n*$Bu_4NI$ (0.0074 g, 0.02 mmol, 10 mol%) in MeCN (2 mL), solid **14** (0.099 g, 0.3 mmol, 1.5 equiv) was added at ambient temperature. After the mixture had been stirred for 28 h, saturated aqueous $NaHCO_3$ was added. Extraction of the aqueous phase three times with EtOAc, drying with $MgSO_4$, filtration, and evaporation of the solvent under reduced pressure yielded a brownish oil. After purification by chromatography (silica gel 60; eluent: hexanes/EtOAc (25:1)) **18** (0.036 g, 0.135 mmol, 67%) was obtained as a colorless oil. $^1$H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta$ = 1.24 (t, $J_{H,H}$ = 7.1 Hz, 3H; $CH_3$), 3.58 (d, $J_{H,H}$ = 17.8 Hz, 1H; $CH_2$), 3.74 (d, $J_{H,H}$ = 17.8 Hz, 1H; $CH_2$), 4.25 (m, 2H; $CH_2$), 7.43–7.55 (m, 2H; $CH_{arom.}$), 7.66–8.72 (m, 1H; $CH_{arom.}$), 7.84 ppm (d, $J_{H,H}$ = 7.8 Hz, 1H; $CH_{arom.}$); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C): $\delta$ = 13.8 ($CH_3$), 34.2 (q, $J_{C,F}$ = 1.9 Hz; $CH_2$), 62.8 ($CH_2$), 63.1 (q, $J_{C,F}$ = 26.0 Hz; C α to CO), 123.5 (q, $J_{C,F}$ = 281.5 Hz; $CF_3$), 125.6, 126.3, 128.5 (CH), 134.4 (q, $J_{C,F}$ = 1.6 Hz; C), 136.2 (CH), 151.7 (C), 165.1 (q, $J_{C,F}$ = 2.2 Hz; *C*OOEt), 193.0 ppm (q, $J_{C,F}$ = 1.0 Hz; CO); $^{19}$F NMR (188 MHz, $CDCl_3$, 25 °C): $\delta$ = −69.2 ppm (s, $J_{C,F}$ = 281.5 Hz;[43] $CF_3$); EI-MS: *m*/*z*: 272.04 ([*M*$^+$]), 227.01, 200.08, 199.04, 197.99, 180.06, 178.97 (100%), 168.99, 156.99, 152.5, 150.93, 147.00, 131.03, 109.00, 102.03, 101.01, 76.00, 75.00, 29.04,

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Table 5. Crystallographic data for **7**, **15**, and **16**.

| | **7** | **15** | **16** |
|---|---|---|---|
| empirical formula | $C_8H_4F_3IO_2$ | $C_{10}H_4F_9IO$ | $C_{11}H_6F_9IO$ |
| formula mass | 316.01 | 438.03 | 452.06 |
| temperature [K] | 200(2) | 200(2) | 200(2) |
| wavelength [Å] | 0.71073 | 0.71073 | 0.71073 |
| crystal system | monoclinic | orthorhombic | triclinic |
| space group | $P2_1/n$ | *Pbca* | $P\bar{1}$ |
| unit cell dimensions | | | |
| $a$ [Å] | 8.6543(7) | 9.6853(6) | 7.5749(10) |
| $b$[Å] | 8.2276(6) | 15.7911(9) | 9.7682(13) |
| $c$ [Å] | 12.4646(10) | 16.1417(9) | 10.3305(14) |
| $\alpha$ [°] | 90.00 | 90.00 | 93.484(2) |
| $\beta$ [°] | 90.829(2) | 90.00 | 109.920(2) |
| $\gamma$ [°] | 90.00 | 90.00 | 107.639(2) |
| volume [Å$^3$] | 887.44(12) | 2468.7(2) | 673.29(16) |
| $Z$ | 4 | 8 | 2 |
| $\rho_{calcd}$ [g cm$^{-3}$] | 2.365 | 2.357 | 2.230 |
| absorption coefficent [mm$^{-1}$] | 3.626 | 2.704 | 2.482 |
| crystal size [mm$^3$] | $0.70\times0.48\times0.47$ | $0.42\times0.38\times0.22$ | $1.13\times0.33\times0.22$ |
| collected reflns | 6427 | 23912 | 5963 |
| unique reflns | 2196 | 3058 | 2736 |
| $R_{int}$ | 0.0321 | 0.0215 | 0.0206 |
| refinement method | | full-matrix least-squares on $F^2$ | |
| data, restraints, parameters | 2196, 0, 128 | 3058, 0, 190 | 2736, 0, 200 |
| GOF | 1.075 | 1.079 | 1.084 |
| $R$ | 0.0356 | 0.0244 | 0.0213 |
| $R_w$ | 0.0767 | 0.0538 | 0.0520 |
| min./max. residual [e Å$^{-3}$] | 1.625/−1.851 | 0.557/−0.679 | 0.738/−1.076 |

27.07; elemental analysis calcd (%) for $C_{13}H_{11}F_3O_3$ (272.22): C 57.36, H 4.07; found: C 57.22, H 4.18.

CCDC-239458, CCDC-281919, and CCDC-281920 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Table 5 contains the key crystallographic data for compounds **7**, **15** and **16**.

## Acknowledgements

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[1] a) P. Kirsch, *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*, Wiley-VCH, Weinheim, **2004**; b) T. Hiyama, *Organofluorine Compounds: Chemistry and Applications*, Springer, Berlin, **2000**; c) Anon. , "Fluorine in the life science industry", *Chimia* **2004**, *58*(3), 92–162.

[2] a) M. Shimizu, T. Hiyama, *Angew. Chem.* **2005**, *117*, 218–234; *Angew. Chem. Int. Ed.* **2005**, *44*, 214–231; b) P. Jeschke, *ChemBioChem* **2004**, *5*, 570–589; c) H.-J. Böhm, D. Banner, S. Bendels, M. Kansy, B. Kuhn, U. Obst-Sander, M. Stahl, *ChemBioChem* **2004**, *5*, 637–643.

[3] I. Ruppert, K. Schlich, W. Volbach, *Tetrahedron Lett.* **1984**, *25*, 2195–2198.

[4] M. McClinton, D. A. McClinton, *Tetrahedron* **1992**, *48*, 6555–6666.

[5] a) Y. Kobayashi, I. Kumadaki, *Tetrahedron Lett.* **1969**, *10*, 4095–4096; b) Y. Kobayashi, K. Yamamoto, I. Kumadaki, *Tetrahedron Lett.* **1979**, *20*, 4071–4072.

[6] S. Solomon, D. L. Albritton, *Nature* **1992**, *357*, 33–37.

[7] G. K. S. Prakash, J. Hu, G. A. Olah, *Org. Lett.* **2003**, *5*, 3253–3256.

[8] Y. Chang, C. Cai, *Tetrahedron Lett.* **2005**, *46*, 3161–3164.

[9] a) T. Umemoto, S. Ishihara, *Tetrahedron Lett.* **1990**, *31*, 3579–3582; b) T. Umemoto, S. Ishihara, *J. Am. Chem. Soc.* **1993**, *115*, 2156–2164; c) T. Umemoto, K. Adachi, *J. Org. Chem.* **1994**, *59*, 5692–5699.

[10] L. M. Yagupolskii, N. V. Kondratenko, G. N. Timofeeva, *Zh. Org. Khim.* **1984**, *20*, 115–118.

[11] a) T. Wirth, *Topics in Current Chemistry, Vol. 224*: *Hypervalent Iodine Chemistry—Modern Developments in Organic Synthesis*, Springer, Heidelberg, **2002**; b) A. Varvoglis, *Hypervalent Iodine in Organic Synthesis*, Academic Press, San Diego, **1997**; c) A. Varvoglis, *The Organic Chemistry of Polycoordinated Iodine*, VCH, Weinheim, **1992**.

[12] a) P. J. Stang, *J. Org. Chem.* **2003**, *68*, 2997–3008; b) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2002**, *102*, 2523–2584; c) P. J. Stang, V. V. Zhdankin, *Chem. Rev.* **1996**, *96*, 1123–1178.

[13] C. Willgerodt, *J. Prakt. Chem.* **1886**, *33*, 154–160.

[14] a) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287; b) M. Frigerio, M. Santagostino, *Tetrahedron Lett.* **1994**, *35*, 8019–8022; c) S. H. Stickley, J. C. Martin, *Tetrahedron Lett.* **1995**, *36*, 9117–9120.

[15] H. Ibrahim, F. Kleinbeck, A. Togni, *Helv. Chim. Acta* **2004**, *87*, 605–610.

[16] a) P. Magnus, J. Lacour, P. A. Evans, M. B. Roe, C. Hulme, *J. Am. Chem. Soc.* **1996**, *118*, 3406–3418; b) V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mismash, J. T. Bolz, *J. Am. Chem. Soc.* **1996**, *118*, 5192–5197.

[17] V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, B. Mismash, J. K. Woodward, A. K. Simonsen, *Tetrahedron Lett.* **1995**, *36*, 7975–7978.

[18] a) Z. Huang, X. Yu, X. Huang, *J. Org. Chem.* **2002**, *67*, 8261–8264; b) R. M. Moriarty, I. Prakash, O. Prakash, W. A. Freeman, *J. Am. Chem. Soc.* **1984**, *106*, 6082–6084.

[19] We refer to "cyclic hypervalent compounds" whenever the iodine atom is part of a heterocyclic unit.

[20] *N*-X-*L* classification (N is the number of valence shell electrons formally associated with atom X with L directly bonded ligands) according to: C. W. Perkins, J. C. Martin, A. J. Arduengo, W. Lau, A. Alegria, J. K. Kochi, *J. Am. Chem. Soc.* **1980**, *102*, 7753–7759.

[21] J. Thiele, W. Peter, *Chem. Ber.* **1905**, *38*, 2842–2846.

[22] FIS = (perfluoroalkyl)phenyliodonium hydrogensulfate; FITS = (perfluoroalkyl)phenyliodonium trifluoromethanesulfonate; a) T. Umemoto, Y. Kuriu, H. Shuyama, O. Miyano, S.-I. Nakayama, *J. Fluorine Chem.* **1982**, *20*, 695–698; b) T. Umemoto, Y. Kuriu, H. Shuyama, O. Miyano, S.-I. Nakayama, *J. Fluorine Chem.* **1986**, *31*, 37–56.

[23] a) T. Umemoto, Y. Kuriu, *Tetrahedron Lett.* **1981**, *22*, 5197–5200; b) T. Umemoto, Y. Kuriu, S.-I. Nakayama, *Tetrahedron Lett.* **1982**, *23*, 1169–1172; c) T. Umemoto, Y. Kuriu, S.-I. Nakayama, O. Miyano, *Tetrahedron Lett.* **1982**, *23*, 1471–1474; d) T. Umemoto, Y. Kuriu, O. Miyano, *Tetrahedron Lett.* **1982**, *23*, 3579–3582; e) T. Umemoto, Y. Kuriu, S.-I. Nakayama, *Tetrahedron Lett.* **1982**, *23*, 4101–4102.

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[24] a) L. M. Yagupolskii, I. I. Maletina, N. V. Kondratenko, V. V. Orda, *Synthesis* **1978**, 835 –837; b) L. M. Yagupolskii, I. I. Maletina, N. V. Kondratenko, V. V. Orda, *Zh. Org. Khim.* **1980**, *16*, 232–233.
[25] G. K. S. Prakash, A. K. Yudin, *Chem. Rev.* **1997**, *97*, 757–786.
[26] a) V. V. Zhdankin, C. J. Kuehl, A. M. Arif, P. J. Stang, *Mendeleev Commun.* **1996**, *2*, 50–51; b) M. Ochiai, Y. Masaki, M. Shiro, *J. Org. Chem.* **1991**, *56*, 5511–5513.
[27] R. A. DeMarco, W. B. Fox, W. B. Moniz, S. A. Sojka, *J. Magn. Reson.* **1975**, *18*, 522–526.
[28] R. Minkwitz, M. Berkei, *Inorg. Chem.* **1999**, *38*, 5041–5044.
[29] R. Minkwitz, R. Bröchler, M. Schütze, *Z. Anorg. Allg. Chem.* **1995**, *621*, 1727–1730.
[30] R. Minkwitz, M. Berkei, *Inorg. Chem.* **2001**, *40*, 36–38.
[31] D. Naumann, J. Baumanns, *J. Fluorine Chem.* **1976**, *8*, 177–182.
[32] R. Minkwitz, M. Berkei, *Inorg. Chem.* **1998**, *37*, 5247–5250.
[33] R. Minkwitz, M. Berkei, R. Ludwig, *Eur. J. Inorg. Chem.* **2000**, 2387–2392.
[34] R. Minkwitz, T. Hertel, H. Preut, *Z. Anorg. Allg. Chem.* **1995**, *621*, 1552–1557.
[35] R. Minkwitz, M. Berkei, *Z. Anorg. Allg. Chem.* **2000**, *626*, 2325–2329.
[36] N. V. Kirij, Y. L. Yagupolskii, N. Maggiarosa, W. Tyarra, D. Naumann, *J. Fluorine Chem.* **2001**, *112*, 213–218.
[37] R. Minkwitz, R. Bröchler, M. Berkei, *Z. Anorg. Allg. Chem.* **1996**, *622*, 1749–1755.
[38] J.-A. Ma, D. Cahard, *J. Org. Chem.* **2003**, *68*, 8726–8729.
[39] R. L. Amey, J. C. Martin, *J. Org. Chem.* **1979**, *44*, 1779–1784.
[40] E. F. Perozzi, R. S. Michalak, G. D. Figuly, W. H. Stevenson III, D. B. Dess, M. R. Ross, J. C. Martin, *J. Org. Chem.* **1981**, *46*, 1049–1053.
[41] J. A. Nieman, B. A. Keay, *Tetrahedron: Asymmetry* **1995**, *6*, 1575–1583.
[42] Modified procedure: G. P. Baker, F. G. Mann, N. Sheppard, A. J. Tetlow, *J. Chem. Soc.* **1965**, 3721–3728.
[43] S. Akai, T. Okuno, M. Egi, T. Takada, H. Tohma, Y. Kita, *Heterocycles* **1996**, *42*, 47–51.

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