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# Perfluoroalkylated Sulfoximines as Analogues of Togni Reagents: The Crucial Role of Fluorine Atoms for the Stability of Hypervalent Iodine Scaffolds

Thibaut Duhail,<sup>[a]</sup> Jorna Kalim,<sup>[b]</sup> Jérôme Marrot,<sup>[a]</sup> Bruce Pégot,<sup>[a]</sup> Emmanuel Magnier,<sup>\*[a]</sup> and Elsa Anselmi<sup>\*[a, c]</sup>

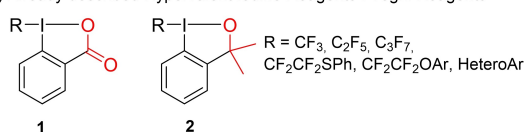
Hypervalent iodine compounds are described with perfluoroalkyl chains and *S*-perfluoromethyl sulfoximines as ligands of the halogen. The influence of these groups on the stability of the cyclic structure is studied. The crucial role of the trifluoromethyl

chain is clearly highlighted as an efficient ligand for the hypervalency. The structure and the reactivity of the new skeletons are discussed in detail.

## Introduction

Over the past two decades, hypervalent iodine compounds have emerged as an efficient group transfer platform, with Togni reagents being the most relevant examples for trifluoromethylation.<sup>[1]</sup> Two reagents are commonly used with R=CF<sub>3</sub>, the acid reagent **1** and the alcohol reagent **2** (Figure 1a), which are capable of transforming a variety of substrates and demonstrate the versatility of these scaffolds. Togni acid reagents **1** and **2** were extended to other perfluoroalkyl group transfer reagents comprising R=C<sub>2</sub>F<sub>5</sub>,<sup>[2]</sup> C<sub>3</sub>F<sub>7</sub>,<sup>[3]</sup> and CF<sub>2</sub>CF<sub>2</sub>SPh, CF<sub>2</sub>CF<sub>2</sub>OAr or CF<sub>2</sub>CF<sub>2</sub>HeteroAr.<sup>[4]</sup> In a similar vein, our group and the Togni group have recently described a novel trifluoromethylating agent **3a** (named Hypisul, Figure 1b) merging hypervalent iodine and sulfoximine groups.<sup>[5]</sup> We have shown that the reactivity of compound **3a** is comparable to the Togni reagent **1** and outperforms the latter

a) Already described Hypervalent Iodine Reagents : Togni Reagents



b) Previous work : R<sup>1</sup> = R<sup>2</sup> = CF<sub>3</sub> **3a** Hypisul

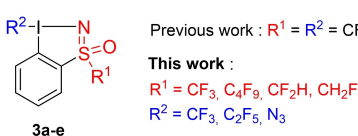


Figure 1. Example of hypervalent iodine used as transfer reagents.

for the trifluoromethylation of alcohols.<sup>[6]</sup> Moreover, the Hypisul scaffold offers the advantage of a potential double modification: on the sulfur atom and on the iodine atom, which we hoped would enable us to modulate reactivity and possibly also lead to the transfer of two fluoroalkyl groups.

The aim of this work is to take advantage of the versatility of perfluorinated sulfoximines to prepare other reagents **3b–e** (Figure 1b) enabling us to study the variation of the R<sup>2</sup> ligand and the influence of the R<sup>1</sup> group on the synthetic accessibility and stability of these new compounds. To begin this work, a preliminary study dedicated to the formation step of the hypervalent iodine-λ<sup>3</sup> species was developed, focusing on the key role played by the R<sup>1</sup> group for the stabilization of the scaffold.

## Results and Discussion

The methodology previously used to synthesize the Hypisul molecule **3a** was inspired by the synthesis of the Togni reagent **1**, with a few modifications (Scheme 1). During the optimization of our synthesis in 2019,<sup>[5]</sup> we took advantage of the presence of the CF<sub>3</sub> group on the sulfoximine moiety to monitor the first step (by <sup>19</sup>F NMR). We showed that the action of trichloroisocyanuric acid (TCICA) on the iodinated sulfoximine **4a**, at low temperature, led to the formation of an acyclic form **5a** as the

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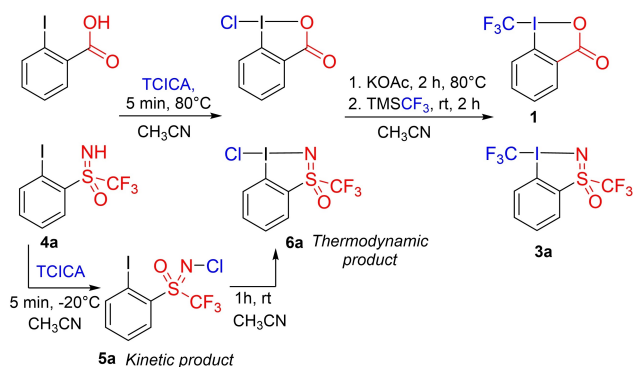
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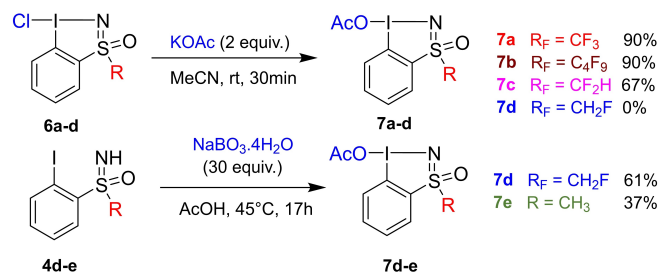
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Scheme 1. Synthesis of Togni reagent **1** and Hypisul reagent **3a**.

kinetic product of the reaction, which then evolved towards the hypervalent form **6a** corresponding to the thermodynamic product (Scheme 1), an observation not previously made whilst preparing reagents **1** and **2**. This crucial step of forming the hypervalent iodine molecule remains poorly mechanistically understood and we proposed in 2019 that an ionic mechanism involving an iodonium [8-I-2] species was a possible intermediate (see S11 scheme 2).

In order to gain more insight into the formation of **6a**, our conditions were applied to different fluorinated sulfoximines and a non-fluorinated one (Table 1). We were pleased to find that with a slight excess of chlorinating agent (0.34 equivalent, corresponding to 1.02 equivalents of cation Cl<sup>+</sup>), the C<sub>4</sub>F<sub>9</sub> sulfoximine **4b** led to the desired hypervalent **6b** form in a



Scheme 2. Syntheses of the acetylated hypervalent iodine products **7a-e** via two different procedures.

| Entry | R                              | Ratio <b>6b-d</b> / <b>5b-d</b> | Isolated Yield   |
|-------|--------------------------------|---------------------------------|------------------|
| 1     | C <sub>4</sub> F <sub>9</sub>  | 82/18                           | <b>6b</b> 63%    |
| 2     | CF <sub>2</sub> H              | 99/1                            | <b>6c</b> Quant. |
| 3     | CH <sub>2</sub> F              | 78/22                           | <b>6d</b> 71%    |
| 4     | CH <sub>3</sub> <sup>[a]</sup> | 0/100                           | <b>5e</b> 95%    |

[a] 80°C, 1 h.

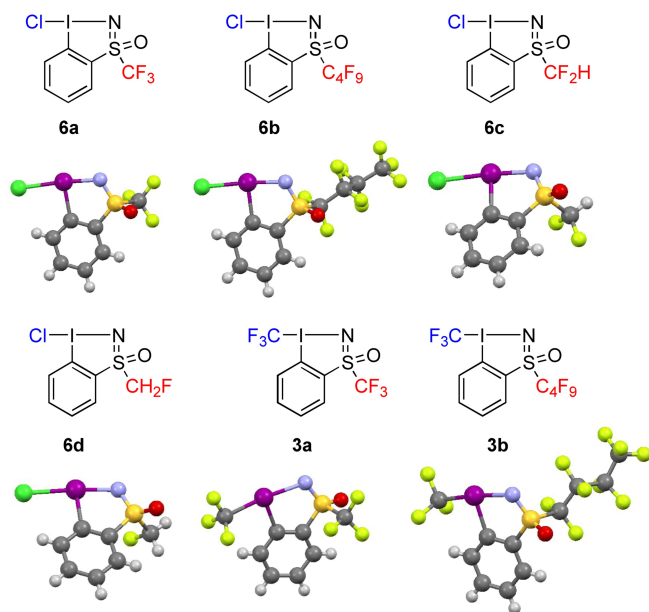
ratio of 82/18 with the “open” form **5b**, after 30 minutes, and was isolated in 63% yield (Table 1, entry 1). The hypervalent difluoromethylated sulfoximine **6c** was obtained in a ratio of 99:1 in a quantitative yield (Table 1, entry 2), while in the monofluorinated series the ratio of the hypervalent **6d** form to **5d** became 78/22 with 71% yield of isolated compound (Table 1, entry 3). Finally, from the S-methyl sulfoximine **4e**, only the chlorinated acyclic form **5e** could be obtained (Table 1, entry 4), whatever the conditions used.

Interestingly, the stability of each product in the reaction solvent (acetonitrile) was different (Table 2). While the cyclic products **6a** and **6b** were stable for a week at room temperature in acetonitrile (Table 2, entries 1 and 2), partial opening of the difluoromethylated and monofluorinated compounds **6c** and **6d** towards their respective isomers **5c** and **5d** was observed. In the case of the CF<sub>2</sub>H group, only 5% of the open form **5c** was detected after 7 days at room temperature in acetonitrile (Table 2, entry 3), whereas the isomer **5d** was the major product (60%, Table 2, entry 4) in the CH<sub>2</sub>F series. Not surprisingly, for the non-fluorinated open compound **5e** (Table 2, entry 5), no cyclization was observed under the same conditions. No further significant changes in the ratios were observed after a week, indicating that an equilibrium state had been reached. These results clearly highlight the necessary presence of fluorine atoms for the stability of the hypervalent iodine moiety.

All the new chlorinated hypervalent compounds **6b-d** were fully characterized and good quality crystals could be obtained in each case (see Figure 2).

Having compounds **6b-d** in hand, we then tried to synthesize the acetylated products **7b-d** (Scheme 2). An excellent yield was obtained for the formation of the non-fluorobutyl product **7b**, while the difluoromethylated substrate **6c** led to the desired product **7c** in a good yield. However, the monofluorinated substrate **6d** did not lead to the acetylated compound **7d** under the same conditions. Nevertheless, a procedure using NaBO<sub>3</sub> in acetic acid,<sup>[7]</sup> recently developed by Wirth *et al.* allowed the formation of the desired product **7e** from **4e**. To our delight, the derivative **4d** was

| Entry | R                             | Ratio after 7 days          |
|-------|-------------------------------|-----------------------------|
| 1     | CF <sub>3</sub>               | <b>6a</b> / <b>5a</b> 100/0 |
| 2     | C <sub>4</sub> F <sub>9</sub> | <b>6b</b> / <b>5b</b> 100/0 |
| 3     | CF <sub>2</sub> H             | <b>6c</b> / <b>5c</b> 95/5  |
| 4     | CH <sub>2</sub> F             | <b>6d</b> / <b>5d</b> 40/60 |
| 5     | CH <sub>3</sub>               | <b>6e</b> / <b>5e</b> 0/100 |



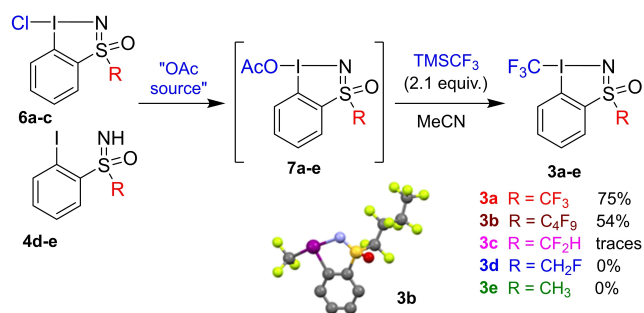
| bond length (Å)           | 6a    | 6b    | 6c    | 6d     | 3a    | 3b    |
|---------------------------|-------|-------|-------|--------|-------|-------|
| I-N                       | 2.102 | 2.101 | 2.080 | 2.077* | 2.284 | 2.289 |
| I-Cl or I-CF <sub>3</sub> | 2.576 | 2.571 | 2.595 | 2.595* | 2.250 | 2.251 |

\* Average over 3 forms obtained by X-ray.

**Figure 2.** Structures of the hypervalent iodine molecules and bond lengths between the iodine atom and the axial ligands in the hypervalent molecules **6a–c** and **3a–b**.<sup>[9]</sup>

transformed with the same methodology to the cyclic molecule **7d** in a satisfactory yield.

Finally, we attempted the last ligand exchange reaction to obtain the target trifluoromethylated compounds **3b–e**. Similarly to the previous protocol for compounds **1** and **3a**, the Ruppert-Prakash reagent was added to the acetylated compounds **7b–e** (formed *in situ*, scheme 3). Only the nonafluorobutyl substrate **7b** led to the desired product **3b** in an



**Scheme 3.** Attempted synthesis of products **3a–e** and structure of the new perfluorinated molecule **3b**.

acceptable yield (54%). From the difluorinated compound **7c**, only traces of what could be the desired product **3c** was detected by <sup>19</sup>F NMR. Various modifications of the conditions to obtain **3c** were unsuccessful (e.g., heating, excess TMSCF<sub>3</sub>, use of known activators such as KF, TBAF and *t*-BuOK). Furthermore, attempts to prepare **3c** from isolated **6c** or **7c** did not lead to the desired product **3c**. In the case of the monofluorinated series, no trace of the target product **3d** was observed by <sup>19</sup>F NMR, despite varying the conditions as described for the preparation of **3c**. Similarly, the non-fluorinated molecule **3e** could not be obtained.

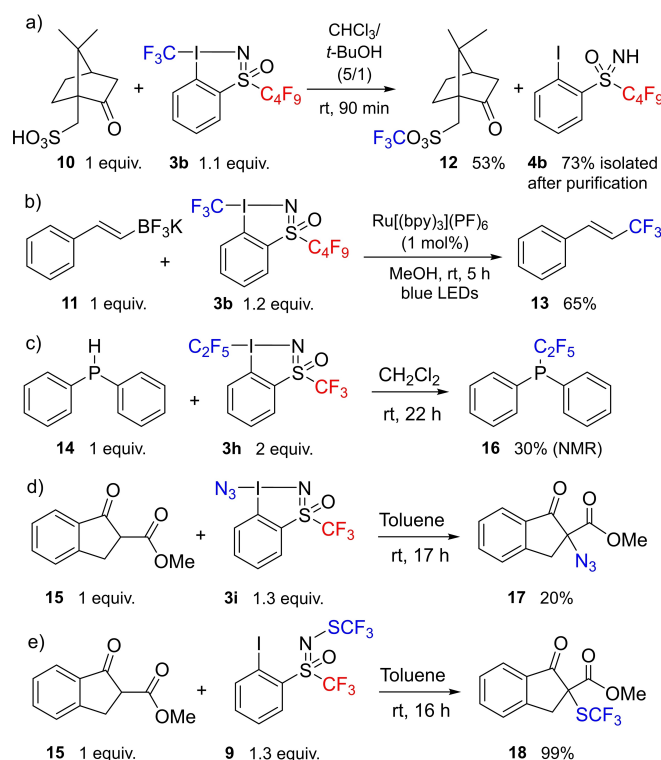
The stability of these new hypervalent iodine scaffolds is probably linked to the intensity of the ligand's trans effects. According to the literature,<sup>[8]</sup> iodane-λ<sup>3</sup> scaffolds are stable if the two axially positioned ligands exhibit either a moderate trans effect of close intensity, or if one of them has a strong trans effect and the other a weak trans effect. Two ligands L and L' having trans effects of close intensity imply furthermore similar I-L and I-L' bond lengths. On the contrary, opposite trans effects lead to a shortened I-L bond length for the ligand L with the strongest trans effect and an extended I-L' bond length for the ligand L' with the weaker trans effect. Based on the literature, we considered that the chlorine atom has a rather moderate trans effect, whereas a CF<sub>3</sub> ligand has a stronger trans effect relative to Cl. In our synthetic work dedicated to the chlorinated series (molecules **6a–d** and **5e**), we observed a decrease in stability of the molecular structure strongly correlated with a decrease in the number of fluorine atoms on the sulfoximine moiety. This trend suggests that the trans effect of sulfoximine ligands becomes either significantly stronger or significantly weaker than the effect of the chlorine atom. To discriminate between these two possibilities, the compounds with a I-CF<sub>3</sub> bond were considered (*vide supra*). The products **3a** and **3b** are isolable and stable, demonstrating a rather weak trans effect of perfluorinated sulfoximines as ligands. Inversely, for the difluoromethylated **3c**, monofluoromethylated **3d**, and methylated **3e** sulfoximine ligands the trans effect is too strong, precluding the formation of molecular scaffolds **3c–e**.

To corroborate this conclusion, we compared the I-N and I-Cl bond lengths of products **6a–d**, and also the I-N and I-CF<sub>3</sub> bond lengths of molecules **3a** and **3b**, obtained from X-ray data (Figure 2). Between chlorinated compound **6a** and trifluoromethylated compound **3a**, the I-N bond in **3a** (2.284 Å) is longer than in molecule **6a** (2.102 Å). This reflects the stronger trans effect of the CF<sub>3</sub> group compared to the Cl group as described in the literature. Regarding the chlorinated scaffolds **6a–d**, the fewer the fluorine atoms present on the sulfoximine CX<sub>3</sub> group, the longer the I-Cl bond (2.595 Å in **6d** to 2.576 Å in **6a**), and the shorter the I-N bond is (2.077 Å in **6d** to 2.102 Å in **6a**). This is in line with our hypothesis of a stronger trans effect for the sulfoximine ligands with fewer fluorine atoms. Molecules **6c** and **6d** have very similar I-N and I-Cl bond lengths, suggesting a similar trans effect for the mono and di-fluoromethylated sulfoximine ligands, and the same applies to the trifluoro and nonafluoromethylated sulfoximine ligands.

To complete this study, we further modulated the exocyclic ligand present on the hypervalent iodine atom in the presence of the trifluoromethylated sulfoximine to stabilize the hypervalent edifices. The method described above (Scheme 3) was extended to analogues of the Ruppert-Prakash reagent such as  $\text{TMSC}_2\text{F}_5$ ,  $\text{TMSCF}_2\text{H}$ ,  $\text{TMSCF}_2\text{Br}$  and  $\text{TMSN}_3$  (Scheme 4). In the case of  $\text{TMSCF}_2\text{H}$  and  $\text{TMSCF}_2\text{Br}$ , the desired products were not obtained despite using various conditions (e.g., heating, addition of  $\text{TMSR}_r$ , use of activators such as  $\text{KF}$ ,  $\text{TBAF}$  and  $\text{tBuOK}$ ). In the case of  $\text{TMSCF}_2\text{H}$ , the acetate compound **7a** did not react at all, while  $\text{TMSCF}_2\text{Br}$  led to a mixture of numerous products as indicated by  $^{19}\text{F}$  NMR. Variation with  $\text{TMSC}_2\text{F}_5$  gave the desired product **3h** in moderate yield despite a slow and incomplete conversion of the intermediate **7a** (around 40%). This mixture of product **3h** and intermediate **7a** was observed regardless of the amount of  $\text{TMSC}_2\text{F}_5$  used. Moreover, heating the reaction medium did not improve conversion and led to the decomposition of the hypervalent species. Exocyclic ligand exchange with the non-fluorinated agent  $\text{TMSN}_3$  was carried out under the conditions described by the Waser group<sup>[10]</sup> and led to the formation of the product **3i** in good yield (74%).

To conclude this part of the work on the variation of  $\text{R}^2$ , we wanted to introduce the  $\text{SCF}_3$  group as an exocyclic ligand in order to obtain a new trifluorothiomethylation reagent **8**. This modulation is described in the case of Togni's reagent as leading to the "open" form.<sup>[11]</sup> In 2020, Zhang and *al.* described the first hypervalent iodine (III) reagent having an  $\text{I}-\text{SCF}_3$  bond.<sup>[12]</sup> In our case, we also obtained the open form **9** in a poor yield of 30% from the chlorinated compound **6a** but with a better yield of 69% *via* the formation of a bromine intermediate with 1,3-dibromo-5,5-dimethylhydantoin (DBH) followed by the addition of  $\text{AgSCF}_3$  (see SI).<sup>[13]</sup>

To finalize this study, proof of concept group transfer reactions were conducted in both electrophilic and radical transformations, demonstrating the versatility of this type of reagent. We first transferred the trifluoromethyl group from the compound **3b** to camphorsulfonic acid **10** (electrophilic process, scheme 5a) giving compound **12** and to the styryl trifluoroborane potassium salt **11** (radical transformation, scheme 5b) giving compound **13**. These two results are slightly less favorable than those obtained with the Hypisul reagent **3a**.<sup>[5]</sup> We also showed that sulfoximine **4b** could be recovered in 73% yield (in the example of scheme 5) highlighting the

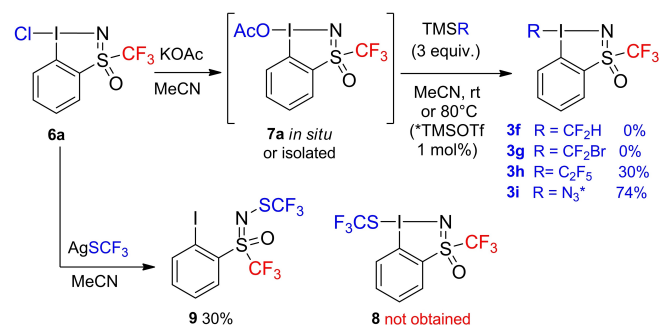


Scheme 5. Transfer of the exocyclic group by new hypervalent iodine sulfoximine reagents.

potential recyclability of reagent **3b** as in the  $\text{CF}_3$  series. We also verified that the new compounds **3h** and **3j** were electrophilic transfer agents of the  $\text{C}_2\text{F}_5$  group and the  $\text{N}_3$  group respectively, under the reaction conditions described previously with the Hypisul reagent (Scheme 5c and 5d). Although not optimized, the pentafluoroethylation of the diphenylphosphine **14** and the azidation of the  $\beta$ -keto ester **15** were successfully carried out, confirming the proof-of-concept of our new reagents. Pleasingly and to the best of our knowledge, this is the first example of a  $\text{C}_2\text{F}_5$  group transfer from a hypervalent iodine to a phosphorus atom. However, the reaction involving the introduction of an azido group to the  $\beta$ -keto ester **17** gave a lower yield than with the reagent developed by Waser.<sup>[10]</sup> These results add to our previous work on the trifluoromethylation of alcohols with reagent **3a**<sup>[6]</sup> or the alkynylation described by the Waser group.<sup>[14]</sup> Finally and to our delight, compound **9** enabled the transfer of the  $\text{SCF}_3$  group to the  $\beta$ -keto ester **15** in quantitative yield (Scheme 5e), comparable to that obtained by Buchwald.<sup>[11]</sup>

## Conclusions

In this work, the stability of molecular structures incorporating a hypervalent iodine linked to the nitrogen of a sulfoximine function was studied in detail. We discovered the necessity of the presence of a perfluoroalkyl chain ( $\text{CF}_3$  or  $\text{C}_4\text{F}_9$ ) on the sulfoximine group, which facilitated the formation of the hypervalent iodine moiety. Stability studies and bond lengths



Scheme 4. Preparation of various hypervalent iodine scaffolds.

(obtained from X-ray diffraction) were used to propose a classification of the trans effects of the different sulfoximines and clearly showed an increasing effect with the decrease in the number of fluorine atoms. Three new reagents based on hypervalent iodine structures were described and the transfer of several exocyclic groups ( $C_2F_5$ ,  $N_3$  and  $SCF_3$ ) was reported.

## Experimental Section

**1-Iodo-2-(S-(nonafluorobutyl)sulfonimidoyl)benzene 4b:** A solution of 2.5 M *n*-BuLi in hexane (25 mL, 60 mmol, 4 equiv.) was added dropwise to a solution of (S-(nonafluorobutyl)sulfonimidoyl)benzene (5.5 g, 15.3 mmol, 1 equiv.) in freshly distilled THF (100 mL) at  $-50^\circ\text{C}$ . The reaction temperature was slowly increased to  $-30^\circ\text{C}$  over 5 h. The reaction mixture was cooled to  $-50^\circ\text{C}$ , and solid  $I_2$  (60 mmol, 15.5 g) was added portionwise. The reaction mixture was allowed to warm to room temperature overnight and subsequently quenched with a saturated aqueous  $NH_4Cl$  solution (100 mL). The aqueous layer was extracted with  $Et_2O$  (3 x 100 mL), dried with anhydrous  $MgSO_4$ , filtered, and concentrated. The residue was purified by flash column chromatography using toluene (100%) as eluent to give **4b** as a pale yellow oil in 89% yield (6.6 g, 13.6 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.41 (d,  $J=8.1$  Hz, 1H), 8.26 (d,  $J=7.8$  Hz, 1H), 7.61 (t,  $J=7.8$  Hz, 1H), 7.33 (t,  $J=7.7$  Hz, 1H), 4.07 (s, 1H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ , 298 K):  $\delta$  144.8, 135.8, 135.1 (C–S), 134.6, 129.1, 94.8 (C–I);  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-81.20$  (t,  $J=9.8$  Hz, 3F),  $-105.79$ – $-110.31$  (m, 2F),  $-119.88$ – $-122.57$  (m, 2F),  $-126.30$  (t,  $J=14$  Hz, 2F); HRMS (ESI): Calcd for  $C_{10}H_6F_9INOS^+$  [ $M+H$ ] $^+$ : 485.9066, Found: 485.9074.

**3-Chloro-1-(nonafluorobutyl)benziodo[d]isothiazole 1-oxide 6b:** In a round-bottomed flask were charged TCICA (1.1 g, 4.6 mmol, 0.34 equiv.) and the nonafluorobutylated iodosulfoximine **4b** (6.6 g, 13.6 mmol, 1 equiv.) in MeCN (100 mL, 0.1 M). TFA (50  $\mu$ L, 0.68 mmol, 0.05 equiv.) was added to the suspension which was then stirred at room temperature for 24 h. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with MeCN and then concentrated. A solid was obtained in the filtrate and was washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **6b** as a white solid in 63% yield (4.4 g, 8.5 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.74 (d,  $J=8.3$  Hz, 1H), 8.17–7.97 (m, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K):  $\delta$  137.2, 132.4 (2 C), 130.8, 130.6, 118.8 (C–I). Carbons of  $C_4F_9$  group were not attributed;  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-81.11$  (t,  $J=9.8$  Hz, 3F),  $-106.16$ – $-109.62$  (m, 2F),  $-120.58$ – $-121.13$  (m, 2F),  $-126.39$  (t,  $J=14$  Hz, 2F); HRMS (ESI): Calcd for  $C_{10}H_5F_9ICINOS^+$  [ $M+H$ ] $^+$ : 519.8676, Found: 519.8699.

**3-1-Oxido-1-(nonafluorobutyl)benziodo[d]isothiazol-3-yl acetate 7b:** Solid KOAc (75 mg, 0.76 mmol, 2 equiv.) was dried under vacuum at room temperature for 5 min and **6b** (200 mg, 0.38 mmol, 1 equiv.) was added, the resulting powder was evacuated under vacuum and refilled with Ar. MeCN (10 mL, 0.04 M) was added and the resulting mixture degassed under vacuum, the suspension was stirred at room temperature for 1 hour. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with MeCN and then concentrated to give the desired product **7b** as a white solid in 90% yield (180 mg, 0.34 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.44 (d,  $J=8.2$  Hz, 1H), 8.07–7.96 (m, 2H), 7.94–7.84 (m, 1H), 2.14 (s, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K):  $\delta$  177.9 (C=O), 136.7, 132.8, 132.3, 132.2, 131.6, 130.7, 121.2 (C–I), 21.5 ( $CH_3$ ). Carbon of  $C_4F_9$  group were not attributed;  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-81.16$  (t,  $J=9.7$  Hz, 3F),  $-106.79$ – $-110.12$  (m, 2F),  $-120.77$ – $-121.17$  (m, 2F),  $-126.41$  (t,  $J=14$  Hz,

2F); HRMS (ESI): Calcd for  $C_{10}H_4F_9INOS^+$  [ $M$ ] $^+$ : 483.8915, Found: 483.8918.

**3-Trifluoromethyl-1-(nonafluorobutyl)benziodo[d]isothiazole 1-oxide 3b:** Solid KOAc (150 mg, 1.6 mmol, 2 equiv.) was dried under vacuum at room temperature for 5 min and **6b** (400 mg, 0.77 mmol, 1 equiv.) was added, the resulting powder was evacuated under vacuum and refilled with Ar. MeCN (10 mL, 0.1 M) was added and the resulting mixture degassed under vacuum, the suspension was stirred at room temperature for 30 minutes. Subsequently,  $TMSCF_3$  (240  $\mu$ L, 1.6 mmol, 2.1 equiv.) was added and the mixture was stirred at room temperature for 90 minutes. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with MeCN and then concentrated. The resulting brown residue was washed with a mixture of pentane and diethyl ether (3/1) to give the product **3b** as a brown-yellow solid in 54% yield (230 mg, 0.42 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.31–8.24 (m, 1H), 8.06–7.88 (m, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K):  $\delta$  136.2, 132.9 (d,  $J=3.2$  Hz), 132.5, 131.5 ( $C_1$ ), 129.6 (q,  $J=3.3$  Hz), 119.5 (q,  $J=4.0$  Hz,  $C_2$ ). Carbon of  $C_4F_9$  group were not attributed;  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-38.91$  (s, 3F,  $-CF_3$ ),  $-81.11$ – $-81.30$  (m, 3F),  $-107.17$ – $-111.13$  (m, 2F),  $-120.95$ – $-121.23$  (m, 2F),  $-126.30$ – $-126.53$  (m, 2F); HRMS (ESI): Calcd for  $C_{11}H_5F_{12}INOS^+$  [ $M+H$ ] $^+$ : 553.8939, Found: 553.8935.

**3-Chloro-1-(difluoromethyl)benziodo[d]isothiazole 1-oxide 6c:** In a round-bottomed flask were charged TCICA (68 mg, 0.29 mmol, 0.34 equiv.) and the difluoromethylated iodosulfoximine **4c** (270 mg, 0.85 mmol, 1 equiv.) in MeCN (4 mL, 0.2 M). The suspension was stirred at room temperature for 30 min. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with MeCN and then concentrated. A solid was obtained in the filtrate and was washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **6c** as a white solid in 99% yield (300 mg, 0.85 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.72 (d,  $J=8.4$  Hz, 1H,  $H_3$ ), 8.08–7.95 (m, 3H,  $H_{4,5,6}$ ), 6.28 (t,  $J=5.3$  Hz, 1H,  $CF_2H$ );  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K):  $\delta$  136.8, 132.3, 131.9 (d,  $J=3.0$  Hz,  $C_6$ ), 130.7, 130.7 ( $C_1$ ), 118.5 (dd,  $J=295$  Hz,  $J=286$  Hz,  $CF_2H$ ), 118.5 ( $C_2$ );  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-115.0$  &  $-119.3$  (part of an ABX system,  $J_{AB}=252$  Hz,  $J_{AX}=J_{BX}=53$  Hz, 2F); HRMS (ESI): Calcd for  $C_7H_6ClF_2INOS^+$  [ $M+H$ ] $^+$ : 351.8871, Found: 351.8869.

**3-1-Oxido-1-(difluoromethyl)benziodo[d]isothiazol-3-yl acetate 7c:** Solid KOAc (35 mg, 0.36 mmol, 2 equiv.) was dried under vacuum at room temperature for 5 min and **6c** (62 mg, 0.18 mmol, 1 equiv.) was added, the resulting powder was evacuated under vacuum and refilled with Ar. MeCN (2 mL, 0.1 M) was added and the resulting mixture degassed under vacuum, the suspension was stirred at room temperature for 30 min. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with MeCN and then concentrated. A solid was obtained in the filtrate and was washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **7c** as a white solid in 67% yield (45 mg, 0.12 mmol).  $^1H$  NMR (300 MHz,  $CDCl_3$ , 298 K):  $\delta$  8.45 (d,  $J=8.3$  Hz, 1H,  $H_3$ ), 7.96 (t,  $J=7.8$  Hz, 2H,  $H_{4,6}$ ), 7.86 (t,  $J=7.4$  Hz, 1H,  $H_5$ ), 6.54 (t,  $J=5.4$  Hz, 1H,  $CF_2H$ ), 2.13 (s, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K):  $\delta$  178.0 (C=O), 136.2, 132.8, 131.8 (d,  $J=3.3$  Hz,  $C_6$ ), 131.5 ( $C_1$ ), 131.4, 121.0 ( $C_2$ ), 118.7 (dd,  $J=295$  Hz,  $J=284$  Hz,  $CF_2H$ ), 21.9 ( $CH_3$ );  $^{19}F$  NMR (282 MHz,  $CDCl_3$ , 298 K):  $\delta$   $-115.8$  et  $-119.6$  (part of an ABX system,  $J_{AB}=251$  Hz,  $J_{AX}=J_{BX}=54$  Hz, 2F); HRMS (ESI): Calcd for  $C_7H_7F_2INOS^+$  [ $M-OAc+2H$ ] $^+$ : 317.9261, Found: 317.9258.

**3-Chloro-1-(monofluoromethyl)benziodo[d]isothiazole 1-oxide 6d:** In a round-bottomed flask were charged TCICA (100 mg, 0.43 mmol, 0.34 equiv.) and the monofluoromethylated iodosulfoximine **4d** (380 mg, 1.27 mmol, 1 equiv.) in MeCN (6 mL, 0.2 M). The suspension was stirred at room temperature for 30 min. The reaction medium was filtered through a Celite<sup>®</sup> pad, rinsed with

MeCN and then concentrated to give **6d** as a white solid in 71% yield (300 mg, 0.90 mmol). <sup>1</sup>H NMR (300 MHz, acetone-d<sub>6</sub>, 298 K): δ 8.69 (d, *J* = 7.8 Hz, 1H, H<sub>3</sub>), 8.19–8.10 (m, 3H, H<sub>4,5,6</sub>), 5.99 & 5.50 (part of an ABX system, *J*<sub>AB</sub> = 48 Hz, *J*<sub>AX</sub> = *J*<sub>BX</sub> = 10 Hz, 2H, CH<sub>2</sub>F); <sup>13</sup>C NMR (126 MHz, acetone-d<sub>6</sub>, 298 K): δ (ppm) 136.9, 136.6, 133.3, 131.4 (C<sub>6</sub>), 130.9, 117.4 (C<sub>2</sub>), 94.0 (d, *J*<sub>C-F</sub> = 220 Hz, CH<sub>2</sub>F); <sup>19</sup>F NMR (282 MHz, acetone-d<sub>6</sub>, 298 K): δ –201.2 (t, *J* = 46 Hz, CH<sub>2</sub>F).

### 3-1-Oxido-1-(monofluoromethyl)benziodo[d]isothiazol-3-yl

**acetate 7d**: In a round-bottomed flask were charged the monofluoromethylated iodoloximine **4d** (598 mg, 2 mmol, 1 equiv.) and glacial acetic acid (60 mL, 0.3 M). NaBO<sub>3</sub>·4H<sub>2</sub>O (10 g, 60 mmol, 30 equiv.) was added to this suspension which was then stirred at 45 °C for 17 h. The reaction medium was concentrated under vacuum and then the residue diluted in a mixture of CH<sub>2</sub>Cl<sub>2</sub> and water (1/1). Phases were then separated and the organic phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (three times), dried over MgSO<sub>4</sub> and concentrated under vacuum. A solid was obtained, washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **7d** as a white solid in 73% yield (520 mg, 1.46 mmol). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 298 K): δ 8.40 (d, *J* = 8.4 Hz, 1H, H<sub>3</sub>), 8.03–7.81 (m, 3H), 5.33 & 5.14 (part of an ABX system, *J*<sub>AB</sub> = 48 Hz, *J*<sub>AX</sub> = *J*<sub>BX</sub> = 10 Hz, 2H, CH<sub>2</sub>F), 2.12 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>, 298 K): δ 178.1 (C=O), 135.4, 134.3 (C<sub>1</sub>), 132.5, 131.6, 129.7, 119.6 (C<sub>2</sub>), 93.6 (d, *J* = 220 Hz, CH<sub>2</sub>F), 22.0 (CH<sub>3</sub>); <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>, 298 K): δ –200.3 (t, *J* = 48 Hz, CH<sub>2</sub>F); HRMS (ESI): Calcd for C<sub>7</sub>H<sub>8</sub>FINOS<sup>+</sup> [M-OAc + 2H]<sup>+</sup>: 299.9355, Found: 299.9359.

**1-Iodo-2-(N-(chloro)-S-(trimethyl)sulfonimidoyl)benzene 5e**: In a round-bottomed flask were charged TCICA (364 mg, 1.56 mmol, 0.34 equiv.) and the imino(2-iodophenyl)(methyl)-λ<sup>6</sup>-sulfanone **4e** (1.30 g, 4.6 mmol, 1 equiv.) in freshly distilled MeCN (35 mL, 0.1 M). The suspension was stirred at 80 °C for 1 hour. The reaction medium was filtered through a Celite® pad, rinsed with MeCN and then concentrated. A solid was obtained in the filtrate and was washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **5e** as a white solid in 95% yield (1.15 g, 3.6 mmol). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 298 K): δ 8.30 (dd, *J* = 8.1 Hz, *J* = 1.4 Hz, 1H, H<sub>3</sub>), 8.18 (d, *J* = 7.0 Hz, 1H, H<sub>6</sub>), 7.62 (t, *J* = 7.6 Hz, 1H, H<sub>4</sub>), 7.31 (td, *J* = 7.5, 1.4 Hz, 1H, H<sub>5</sub>), 3.46 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>, 298 K): δ 143.6 (C<sub>Ar</sub>), 138.5 (C<sub>1</sub>), 135.0 (C<sub>Ar</sub>), 133.6 (C<sub>Ar</sub>), 129.4 (C<sub>Ar</sub>), 93.5 (C<sub>2</sub>), 39.6 (CH<sub>3</sub>); HRMS (ESI): Calcd for C<sub>7</sub>H<sub>8</sub>I NOS<sup>+</sup> [M + H-Cl]<sup>+</sup>: 281.9444, Found: 281.9460.

**3-Pentafluoroethyl-1-(trifluoromethyl)benziodo[d]isothiazole 1-oxide 3h**: In a round-bottomed flask were charged **7a** (1.0 g, 2.5 mmol, 1 equiv.) in MeCN (50 mL, 0.05 M). TMSCF<sub>5</sub> (1.3 mL, 7.6 mmol, 3 equiv.) was added to this suspension which was stirred at room temperature for 17 h and then at 80 °C for 2 hours. The reaction medium was then concentrated under vacuum and the residue was covered with a mixture of pentane and diethyl ether (3/1) for 1 hour to precipitate. The solid obtained then washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **3h** as a brown solid in 30% yield (370 mg, 0.82 mmol). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 298 K): δ 8.24 (d, *J* = 6.2 Hz, 1H, H<sub>3</sub>), 8.04 (d, *J* = 7.1 Hz, 1H, H<sub>6</sub>), 7.97–7.94 (m, 2H, H<sub>4,5</sub>); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>, 298 K): δ 136.3, 132.8, 132.5, 131.3 (C<sub>1</sub>), 130.2 (q, *J* = 5.4 Hz, C<sub>6</sub>), 122.8 (q, *J* = 336 Hz, RSCF<sub>3</sub>), 118.5 (C<sub>2</sub>). Peaks from the C<sub>2</sub>F<sub>5</sub> were not attributed; <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>, 298 K): δ –77.7 (s, 3F, RSCF<sub>3</sub>), –81.2 (s, 3F, RCF<sub>2</sub>CF<sub>3</sub>), –96.3 (d, *J* = 11 Hz, 2F, RCF<sub>2</sub>CF<sub>3</sub>); HRMS (ESI): Calcd for C<sub>9</sub>H<sub>5</sub>F<sub>8</sub>I NOS<sup>+</sup> [M + H]<sup>+</sup>: 453.9003, Found: 453.9006.

**3-Azido-1-(trifluoromethyl)benziodo[d]isothiazole 1-oxide 3j**: In a round-bottomed flask were charged **7a** (200 mg, 0.54 mmol, 1 equiv.) in MeCN (15 mL, 0.04 M). TMSN<sub>3</sub> (215 μL, 1.6 mmol, 3 equiv.) and TMSOTf (1 μL, 0.005 mmol, 0.01 equiv.) were added to this suspension which was stirred at room temperature for 30 minutes. The reaction medium was then concentrated under

vacuum and the yellow residue was washed with a mixture of pentane and diethyl ether (3/1) to give the desired product **3j** as a yellow solid in 74% yield (150 mg, 0.40 mmol) with a purity close to 99% (some traces of **7a** are still present, around 1%). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN, 298 K): δ 8.41 (d, *J* = 8.4 Hz, 1H, H<sub>3</sub>), 8.20–8.08 (m, 2H), 8.03 (t, *J* = 7.3 Hz, 1H); <sup>13</sup>C NMR (126 MHz, CD<sub>3</sub>CN, 298 K): δ 138.3, 133.5, 132.7, 131.2, 130.6 (C<sub>1</sub>), 124.3 (q, *J* = 334 Hz), 120.9 (C<sub>2</sub>); <sup>19</sup>F NMR (282 MHz, CD<sub>3</sub>CN, 298 K): δ = –77.1 (s, CF<sub>3</sub>).

### 1-Iodo-2-(N-(trifluorothiomethyl)-S-(trifluoromethyl)sulfonimidoyl)benzene 9

**9**: In a round-bottomed flask was charged the iodoloximine **4a** (1.0 g, 3.0 mmol, 1 equiv.) in freshly distilled MeCN (25 mL, 0.1 M). DBH (1.1 g, 3.7 mmol, 1.2 equiv.) was then added and the reaction medium was stirred at room temperature for 17 h. AgSCF<sub>3</sub> (1.9 g, 9 mmol, 3 equiv.) was finally added in once and the reaction medium was stirred at room temperature for 1 h. The reaction medium was filtered through a Celite® pad, rinsed with MeCN and then concentrated. The crude was purified by chromatography on silica gel with pentane/diethyl ether (95/5) as eluent and the desired product **9** obtained as a pale-yellow solid in 69% yield (900 mg, 2.1 mmol). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 298 K): δ 8.31 (ddd, *J* = 12 Hz, *J* = 8.0 Hz, *J* = 1.4 Hz, 2H), 7.66 (td, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.40 (td, *J* = 7.7 Hz, *J* = 1.6 Hz, 1H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>, 298 K): δ 145.2, 136.6, 134.6, 133.2 (C<sub>1</sub>), 129.9 (q, *J* = 311 Hz), 129.4, 121.0 (q, *J* = 337 Hz, C<sub>7</sub>). 94.4 (C<sub>2</sub>); <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>, 298 K): δ –50.59 (s, 3F, F<sub>8</sub>), –69.03 (s, 3F, RSCF<sub>3</sub>, F<sub>7</sub>); HRMS (ESI): Calcd for C<sub>8</sub>H<sub>4</sub>F<sub>6</sub>I NOS<sub>2</sub> [M]: 434.8683, Found: 434.8688.

## Supporting Information

The data that support the findings of this study are available in the supplementary material of this article. The authors have cited additional references within the Supporting Information (Ref. [15–22]).

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## Conflict of Interests

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords:** hypervalent compounds · fluorine · iodine · sulfoximine · trifluoromethyl

- [1] a) P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579; b) J. Charpentier, N. Früh, A. Togni, *Chem. Rev.* **2015**, *115*, 650.  
 [2] Y. Li, A. Studer, *Angew. Chem. Int. Ed.* **2012**, *51*, 8221.  
 [3] L. Wang, A. Studer, *Org. Lett.* **2017**, *19*, 5701.  
 [4] V. Matoušek, J. Václavík, P. Hájek, J. Charpentier, Z. E. Blastik, E. Pietrasiak, A. Budinská, A. Togni, P. Beier, *Chem. Eur. J.* **2016**, *22*, 417.  
 [5] J. Kalim, T. Duhail, T.-N. Le, N. Vanthuyne, E. Anselmi, A. Togni, E. Magnier, *Chem. Sci.* **2019**, *10*, 10516.  
 [6] J. Kalim, T. Duhail, E. Pietrasiak, E. Anselmi, E. Magnier, A. Togni, *Chem. Eur. J.* **2021**, *27*, 2638.  
 [7] M. Elsherbini, A. Osi, H. Alharbi, F. Karam, T. Wirth, *Synthesis* **2023**, *55*, 307.  
 [8] M. Ochiai, T. Sueda, K. Miyamoto, P. Kiprof, V. V. Zhdankin, *Angew. Chem. Int. Ed.* **2006**, *45*, 8203.  
 [9] Deposition Numbers 2282933 (for **6b**), 2282934 (for **6c**), 2282935 (for **6d**), 2282936 (for **3b**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.  
 [10] M. V. Vita, J. Waser, *Org. Lett.* **2013**, *15*, 3246.  
 [11] E. V. Vinogradova, P. Müller, S. L. Buchwald *Angew. Chem. Int. Ed.* **2014**, *53*, 3125.  
 [12] X.-G. Yang, K. Zheng, C. Zhang *Org. Lett.* **2020**, *22*, 2026.  
 [13] C. Bohnen, C. Bolm, *Org. Lett.* **2015**, *17*, 3011.  
 [14] E. Le Du, T. Duhail, M. D. Wodrich, R. Scopelliti, F. Fadaei-Tirani, E. Anselmi, E. Magnier, J. Waser, *Chem. Eur. J.* **2021**, *27*, 10979.  
 [15] T.-N. Le, P. Diter, B. Pégot, C. Bournaud, M. Toffano, R. Guillot, G. Vo-Thanh, E. Magnier, *Org. Lett.* **2016**, *18*, 5102.  
 [16] T. Duhail, M. Zhu, C. Rombault, G. Dagousset, S. Messaoudi, E. Magnier, E. Anselmi, *Eur. J. Org. Chem.* **2022**, *29*, e202200173.  
 [17] S. Chaabouni, J.-F. Lohier, A.-L. Barthelemy, T. Glachet, E. Anselmi, G. Dagousset, P. Diter, B. Pégot, E. Magnier, V. Reboul, *Chem. Eur. J.* **2018**, *24*, 17006.  
 [18] R. Koller, Q. Huchet, P. Battaglia, J. M. Welch, A. Togni, *Chem. Commun.* **2009**, 5993.  
 [19] Y. Yasu, T. Koike, M. Akita, *Chem. Commun.* **2013**, *49*, 2037.  
 [20] A. K. Brisdon, C. J. Herbert, *Chem. Commun.* **2009**, *43*, 6658.  
 [21] J. Dhineshkumar, K. R. Prabhu, *Eur. J. Org. Chem.* **2016**, *2016*, 447.  
 [22] X. Shao, X. Wang, T. Yang, L. Lu, Q. Shen, *Angew. Chem. Int. Ed.* **2013**, *52*, 3457.

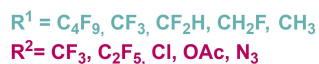
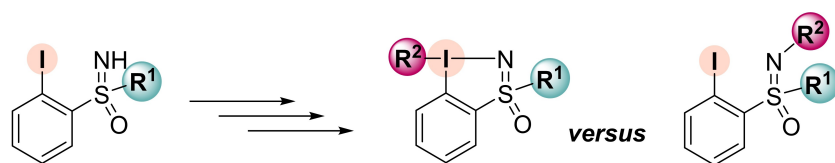
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stability. The cyclic derivatives are promising reagent to deliver the  $R^2$  group under electrophilic or radical mechanism.

The influence of both  $R^1$  and  $R^2$  groups for the stability of the hypervalent form were examined in detail. The presence of at least two fluorine atoms in  $R^1$  moiety is crucial for the

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**Perfluoroalkylated Sulfoximines as Analogues of Togni Reagents: The Crucial Role of Fluorine Atoms for the Stability of Hypervalent Iodine Scaffolds**

