

## Merging Hypervalent Iodine and Sulfoximine Chemistry: A New Electrophilic Trifluoromethylation Reagent

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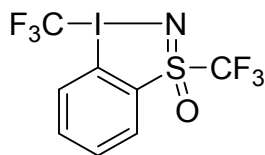
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## General Methods and Materials

All reactions were carried out under an argon atmosphere and prepared in freshly distilled acetonitrile over calcium hydride, or in anhydrous solvents purchased from commercial suppliers over molecular sieves in a sealed bottle which were used without further purification. Chemicals were purchased from commercial sources (Sigma–Aldrich, Alfa Aesar, Fluorochem or ABCR) and used without further purification. Organic solvents were purchased from Sigma–Aldrich and Carlo Erba companies. Reactions were monitored by thin-layer chromatography on silica gel 60F254, and/or by  $^{19}\text{F}$  NMR spectroscopy. Optical rotations were measured on a Jasco P-2000 polarimeter with a sodium lamp (589 nm), a halogen lamp (578, 546, 436, 405 and 365 nm), in a 10 cm cell, thermostated at 25°C with a Peltier controlled cell holder. NMR spectra were collected on a Bruker AC-300, Bruker AVANCE III 400 MHz or 500 MHz spectrometer fitted with a Bruker PABBO BB/19F-1H/D probe head, operating at the denoted spectrometer frequency given in MHz for the specified nucleus. Reported coupling constants and chemical shifts were based on a first order analysis. The internal reference for  $^1\text{H}$  NMR was the residual peak of  $\text{CH}_3\text{CN}$  (1.94 ppm), central peak of  $\text{CD}_3\text{CN}$  (1.32 ppm) for  $^{13}\text{C}$  NMR spectra, and  $\text{CFCl}_3$  (0.00 ppm) as internal reference for  $^{19}\text{F}$  NMR spectra. High resolution mass spectrometry (HRMS) was recorded on a Mass Spectrometer XEVO-QTOF in the Institute Lavoisier of Versailles – University of Versailles Saint Quentin. The chemical names use in this SI do not follow IUPAC's official rules. For convenience, we choose to use the nomenclature previously employed for the Togni reagents.

## Synthetic Procedures and Characterization

### 1,3-bis(trifluoromethyl)benziodo[*d*]isothiazole 1-oxide (**4**)



One pot-procedure from **5**: TCICA (235 mg, 1.01 mmol) was added to a solution of **5** (1.00 g, 2.98 mmol) in MeCN (30 mL, 0.1 M). TFA was added (12  $\mu$ L, 0.15 mmol) and the mixture was stirred at room temperature for 1 h. Solid KOAc (585 mg, 5.96 mmol) was then added and the suspension was stirred at room temperature for 30 min. Subsequently, TMSCF<sub>3</sub> (880  $\mu$ L, 5.96 mmol) was added and the mixture was stirred at room temperature for 6 h. The reaction medium was filtered through a celite pad, rinsed with MeCN and then concentrated. The resulting brown residue was washed with a mixture of pentane, Et<sub>2</sub>O and MeCN, to give the product as a white-yellow solid in 74% yield (895 mg, 2.22 mmol).

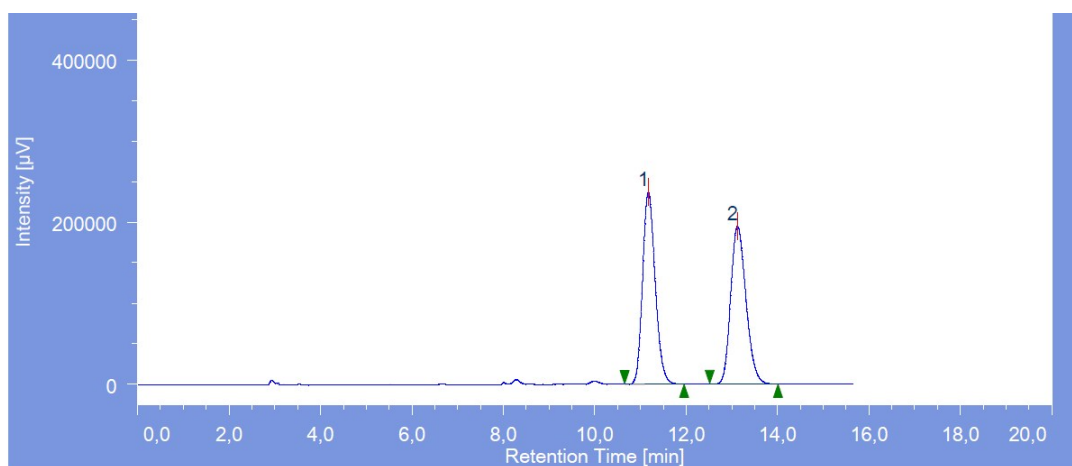
One pot-procedure from **5** on large scale: TCICA (2.35 g, 10.1 mmol) was added to a solution of **5** (10.0 g, 29.8 mmol) in MeCN (300 mL, 0.1 M). TFA was added (0.1 mL, 1.5 mmol) and the mixture was stirred at room temperature for 6 h. Solid KOAc (5.9 g, 59.6 mmol) was then added and the suspension was stirred at room temperature for 30 min. Subsequently, TMSCF<sub>3</sub> (9.3 mL, 62.6 mmol) was added and the mixture was stirred at room temperature overnight. The reaction medium was filtered through a celite pad, rinsed with MeCN and then concentrated. The resulting brown residue was washed with a mixture of pentane, Et<sub>2</sub>O and MeCN, to give the product as a white-yellow solid in 75% yield (9.0 g, 22.3 mmol).

From **10**: TMSCF<sub>3</sub> (520  $\mu$ L, 3.52 mmol) was added to a solution of **10** (690 mg, 1.76 mmol) in MeCN (35 mL, 0.05 M), the resulting mixture was stirred at room temperature for 2 h. The reaction medium was filtered through a celite pad, rinsed with MeCN and then concentrated. The resulting brown residue was washed with a mixture of pentane, Et<sub>2</sub>O and MeCN, to give the product as a white-yellow solid in 75% yield (895 mg, 2.22 mmol).

**IR**: 1679, 1661, 1450, 1292, 1265, 1167, 1145, 1049, 991. **<sup>1</sup>H NMR** (300 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  8.24-8.18 (m, 1H), 8.10-7.99 (m, 3H). **<sup>13</sup>C NMR** (126 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  (ppm) 137.9, 133.8, 132.9 (q,  $J$  = 1.2 Hz, 1C), 131.5, 131.1 (q,  $J$  = 3.3 Hz, 1C), 123.8 (q,  $J$  = 336 Hz, 1C), 119.8 (q,  $J$  = 3.5 Hz), 110.96 (q,  $J$  = 399 Hz). **<sup>19</sup>F NMR** (282 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  (ppm) -38.6, -77.6. **HRMS** (ESI): Calcd for C<sub>8</sub>H<sub>5</sub>F<sub>6</sub>INOS [M + H]<sup>+</sup>: 403.9035, Found : 403.9049.

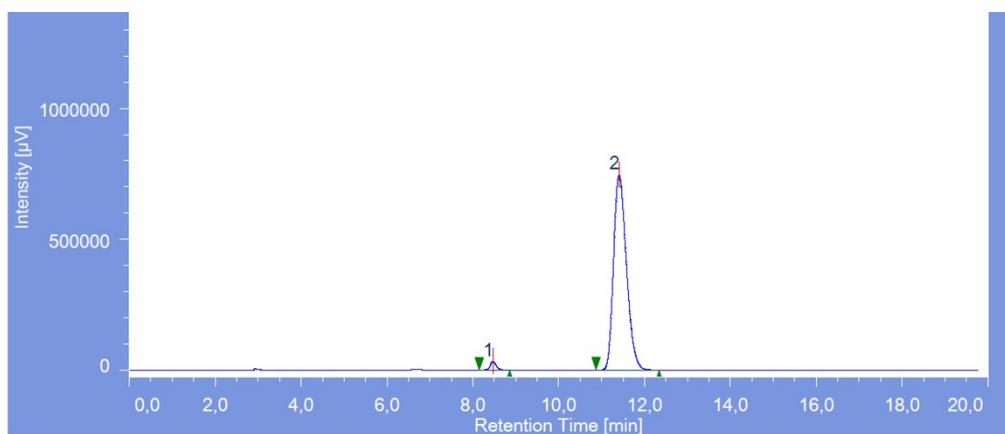
For the enantiomer **4** prepared from (+)-**5**:  $[\alpha]_{\lambda}^{20}$  (CH<sub>2</sub>Cl<sub>2</sub>,  $c$  = 0.01,  $\lambda$  = 589 nm): -34

For the enantiomer **4** prepared from (-)-**5**:  $[\alpha]_{\lambda}^{20}$  (CH<sub>2</sub>Cl<sub>2</sub>,  $c$  = 0.01,  $\lambda$  = 589 nm): +31



**Figure S1:** HPLC trace of racemic **4**. Chromatographic conditions: Chiralpak AS-H, *n*-heptane / isopropanol (90/10) as mobile phase, flow-rate = 1 mL/min, UV detection at 260 nm.

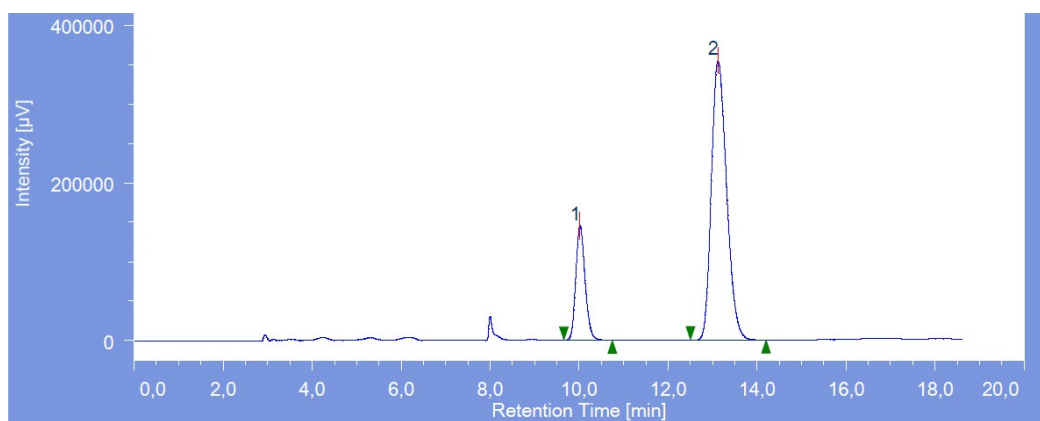
RT [min]	Area	Area%
11.170	6801306	50.010
13.122	6798575	49.990



**Figure S2:** HPLC trace of enantiopure **4** synthesized from (+)-**5**. Chromatographic conditions: Chiralpak AS-H, *n*-heptane / isopropanol (90/10) as mobile phase, flow-rate = 1 mL/min, UV detection at 260 nm.

The first peak corresponds to the enantiomer of the precursor (+)-**5**, and the second peak to the enantiopure product **4**. Minor degradation of **4** is observed during analysis, but no racemization.

RT [min]	Area	Area%
8.467	334669	2.109
11.402	15532667	97.891

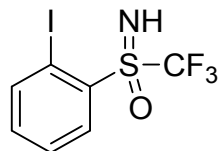


**Figure S3:** HPLC trace of enantiopure **4** synthesized from (–)-**5**. Chromatographic conditions: Chiralpak AS-H, *n*-heptane / isopropanol (90/10) as mobile phase, flow-rate = 1 mL/min, UV detection at 260 nm.

Peak 1 corresponds to the enantiomer of the precursor (–)-**5**, and peak 2 to the enantiopure product **4**. There is some degradation of the compound during analysis, but no racemization.

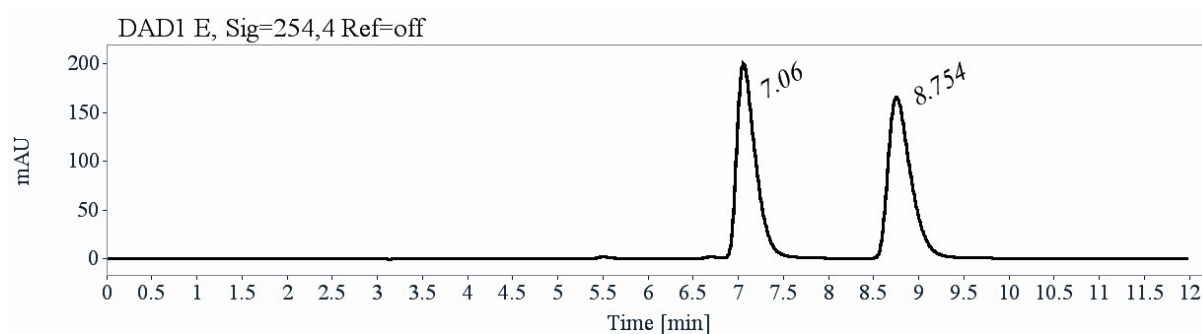
RT [min]	Area	Area%
11.170	144979	19.957
13.122	354219	80.043

### 1-iodo-2-(*S*-(trifluoromethyl)sulfonimidoyl)benzene (**5**)



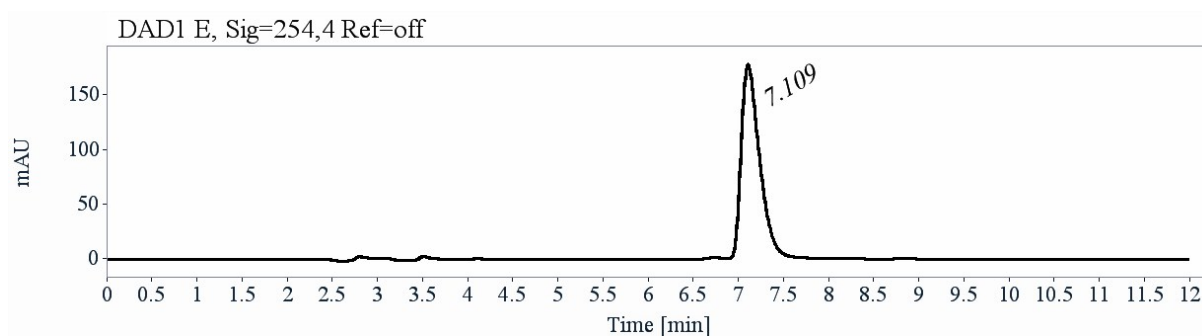
A solution of 2.5 M *n*-BuLi in hexane (96 mL, 240 mmol) was added dropwise to a solution of (*S*-(trifluoromethyl)sulfonimidoyl)benzene **8** (10.0 g, 48 mmol) in freshly distilled THF (300 mL) at -50 °C. The reaction temperature was slowly increased to -30 °C over 5 h. The reaction mixture was cooled to -50 °C, and solid I<sub>2</sub> (240 mmol, 60.9 g) was added portion-wise. The reaction mixture was allowed to warm to room temperature overnight and subsequently quenched with a saturated aqueous NH<sub>4</sub>Cl solution (200 mL). The aqueous layer was extracted with Et<sub>2</sub>O (3 x 200 mL), dried with anhydrous MgSO<sub>4</sub>, filtered, and concentrated. The residue was purified by flash column chromatography using toluene/MeOH (98/2) as eluent to give **5** as a pale yellow solid in 94% yield (15.1 g, 45 mmol). **R<sub>f</sub>** (toluene/MeOH 98/2): 0.7. **Mp** 47-48°C. **IR**: 3138, 1572, 1448, 1276, 1169, 1076, 1011, 949. **<sup>1</sup>H NMR** (300 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) 8.40 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.32 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.72 - 7.67 (m, 1H), 7.43 (td, *J* = 7.7, 1.5 Hz, 1H), 4.98 (br. s, 1H). **<sup>13</sup>C NMR** (75 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) 145.8, 137.2, 135.5, 135.2, 130.5, 121.8 (q, *J* = 333 Hz), 95.0. **<sup>19</sup>F NMR** (282 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) -75.4. **HRMS** (ESI): Calcd for C<sub>7</sub>H<sub>5</sub>F<sub>3</sub>ClNOS [M + H]<sup>+</sup>: 335.9161, Found : 335.9164.

### Semi-preparative separation of **5**:



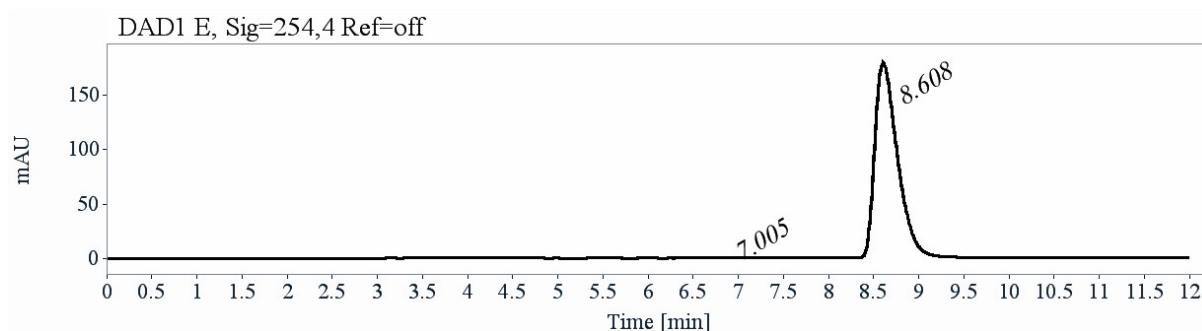
**Figure S4:** HPLC trace of racemic **5**. Chromatographic conditions: Chiralpak AS-H (250 x 10 mm), *n*-hexane/isopropanol (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 270 nm. Retention times: 7.06 min [(+)-**5**], 8.75 min [(-)-**5**].

RT [min]	Area	Area%
7.06	2830	49.46
8.75	2891	50.54



**Figure S5:** HPLC trace of enantiopure (+)-**5**. Chromatographic conditions: Chiralpak AS-H (250 x 10 mm), *n*-hexane/isopropanol (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 270 nm.

RT [min]	Area	Area%
7.11	2474	100.00



**Figure S6:** HPLC trace of enantiopure (-)-**5**. Chromatographic conditions: Chiralpak AS-H (250 x 10 mm), *n*-hexane/isopropanol (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 270 nm

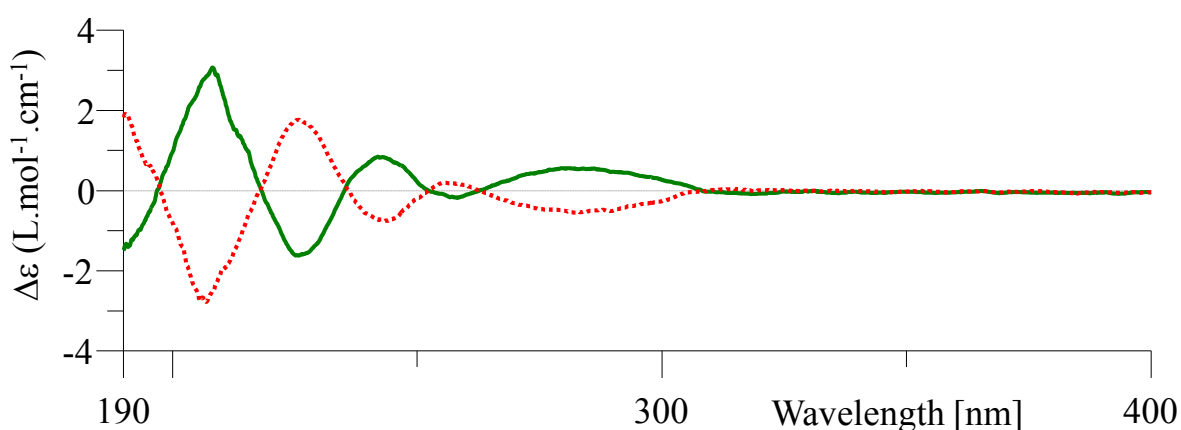
RT [min]	Area	Area%
7.00	7	0.23
8.61	3159	99.77

**Table S1:** Optical rotation of (+)-**5** (first eluted product) and (-)-**5** (second eluted peak). *c* = concentration.

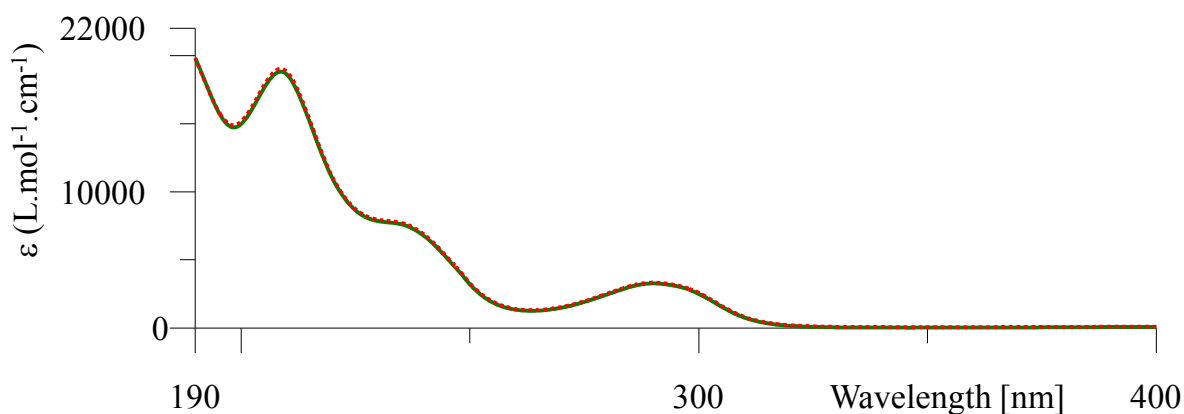
$\lambda$ (nm)	First eluted on Chiralpak AS-H $[\alpha]_{\lambda}^{25}$ (CH <sub>2</sub> Cl <sub>2</sub> , <i>c</i> = 0.23)	Second eluted on Chiralpak AS-H $[\alpha]_{\lambda}^{25}$ (CH <sub>2</sub> Cl <sub>2</sub> , <i>c</i> = 0.24)
589	+ 33	- 33
578	+ 34	- 34
546	+ 40	- 40
436	+ 73	- 73
405	+ 92	- 92
365	+ 137	-137

### Electronic Circular Dichroism

Electronic circular dichroism (ECD) and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at  $25.0 \pm 0.2^\circ\text{C}$ . A CD quartz cell of 1 mm of optical path-length was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted. The baseline was always measured for the same solvent and in the same cell as the samples. The spectra are presented without smoothing and further data processing. Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.



**Figure S7:** ECD spectrum of enantiopure **5**. Green solid line: (+)-**5** (first eluted enantiomer); *c* = 0.923 mmol·L<sup>-1</sup> in MeCN. Red dotted line: (-)-**5** (second eluted enantiomer); *c* = 0.903 mmol·L<sup>-1</sup> in MeCN.



**Figure S8:** UV spectrum of enantiopure **5**. Green solid line: (+)-**5** (first eluted enantiomer); MeCN. Red dotted line: (-)-**5** (second eluted enantiomer).

### 3-chloro-1-(trifluoromethyl)benziodo[*d*]isothiazole 1-oxide (**9**)



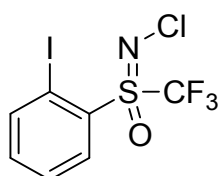
Solid TCICA (235 mg, 1.01 mmol) was added to a solution of **5** (1.00 g, 2.98 mmol) in MeCN (15 mL, 0.2 M). TFA was then added (12  $\mu$ L, 0.15 mmol) and the mixture was stirred at room temperature for 1 h. The reaction medium was filtered through a celite pad, rinsed with MeCN and then concentrated. The resulting white residue was washed with a mixture of pentane, Et<sub>2</sub>O and MeCN, to give the product as a white solid in 95% yield (1.05 g, 2.83 mmol).

**Mp:** 160-161 °C. **IR:** 3206, 3084, 2832, 1701, 1422, 1276, 1170, 1043, 989. **<sup>1</sup>H NMR** (300 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  (ppm) 8.68 (d, *J* = 8.4 Hz, 1H), 8.20 (ddd, *J* = 8.5, 6.1, 2.6 Hz, 1H), 8.09 (d, *J* = 6.2 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  (ppm) 138.8, 133.8, 132.8, 131.6, 131.0, 124.6 (q, *J* = 334 Hz), 119.3. **<sup>19</sup>F NMR** (282 MHz, CD<sub>3</sub>CN, 298 K):  $\delta$  (ppm) -76.8. **HRMS** (ESI): Calcd for C<sub>7</sub>H<sub>5</sub>F<sub>3</sub>ICINOS [M + H]<sup>+</sup>: 369.8772, Found: 369.8780.

For the enantiomer **9** prepared from (+)-**5**:  $[\alpha]_{\lambda}^{20}$  (acetone, *c* = 0.01,  $\lambda$  = 589 nm): +25

For X-ray crystallographic analysis for determining the absolute configuration of **9**, the enantiomer **9** prepared from (-)-**5** was used.

### 1-iodo-2-(*N*-(chloro)-*S*-(trifluoromethyl)sulfonimidoyl)benzene (**9'**)

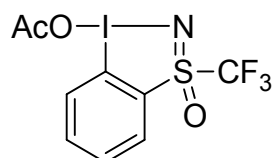


An oven dried crimp-cap vial was charged with **5** (20 mg, 0.06 mmol, 1 eq.), the vial was sealed,  $\alpha,\alpha,\alpha$ -trifluorotoluene (7  $\mu$ L, 0.06 mmol, 1.0 eq.) and anhydrous CD<sub>3</sub>CN (0.6 mL) was added and the suspension and cooled to -20 °C. An oven dried NMR tube fitted with a rubber septum was charged with TCICA (5.6 mg, 0.02 mmol, 0.4 eq.) and cooled to -20 °C, the solution of **5** was injected into the NMR tube. The suspension was vigorously shaken (ca. 30 s) until all solids were dissolved.



Spectroscopic data was obtained from the reaction mixture containing a 99:1 mixture of **9'** and **9** at -20 °C. **<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>CN, 253 K): δ (ppm) 8.36 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.27 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.76 (ddd, *J* = 8.1, 7.4, 1.3 Hz, 1H), 7.58 – 7.51 (m, 1H). **<sup>13</sup>C NMR** (101 MHz, CD<sub>3</sub>CN, 253 K; contains isocyanuric acid at 145.4 ppm): δ (ppm) 145.7, 138.2, 134.6, 130.94, 130.45, 121.5 (q, *J* = 339.4 Hz), 95.0. **<sup>19</sup>F NMR** (376 MHz, CD<sub>3</sub>CN, 253 K; contains remaining **5** at -76.04): δ (ppm) -64.8. **HRMS** (ESI): Calcd for C<sub>7</sub>H<sub>5</sub>F<sub>3</sub>IClNOS [M + H]<sup>+</sup>: 369.8772, Found : 369.8786.

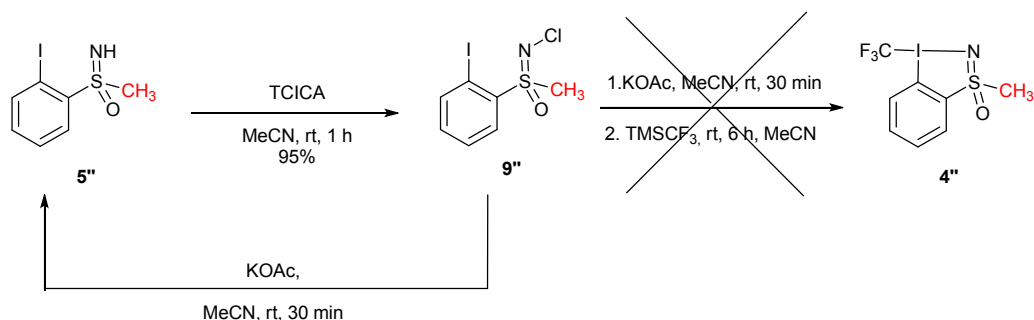
### 3-1-oxido-1-(trifluoromethyl)benziodo[*d*]isothiazol-3-yl acetate (**10**)



Solid KOAc (585 mg, 5.96 mmol) was dried under vacuum at room temperature for 5 min and **9** (1.00 g, 2.71 mmol) was added, the resulting powder was evacuated under vacuum and refilled with Ar. MeCN (75 mL, 0.036 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 pad, rinsed with MeCN and then concentrated to give **10** as a white solid in 90% yield (965 mg, 2.45 mmol). **Mp**: 117-118 °C. **IR**: 3101, 3069, 1640, 1366, 1270, 1188, 1165, 1055, 998. **<sup>1</sup>H NMR** (300 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) 8.38 (d, *J* = 8.3 Hz, 1H), 8.14-8.08 (m, 2H), 8.01-7.96 (m, 1H), 2.11 (s, 3H). **<sup>13</sup>C NMR** (75 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) 177.3, 138.4, 133.2, 133.1, 132.6, 130.5 (s, 1C), 124.7 (q, *J* = 335 Hz, 1C), 122.1, 21.3. **<sup>19</sup>F NMR** (282 MHz, CD<sub>3</sub>CN, 298 K): δ (ppm) -77.1. **HRMS** (ESI): Calcd for C<sub>9</sub>H<sub>7</sub>F<sub>3</sub>INO<sub>3</sub>S [M - OAc + H<sub>2</sub>O]<sup>+</sup>: 351.9111, Found : 351.9120.

### Attempt to synthesize **4''**, methylated analogue of **4**

Despite our efforts, synthesis of the analogous reagent **4''** starting from the corresponding SME sulfoximine **5''** was unsuccessful. The first step of the process leads to the formation of the open chlorinated compound **9''** without TFA, and the use of TFA did not result in cyclization. The synthesis of **4''** becomes then impossible and leads to the degradation of **9''** to **5''**.



**Scheme S1:** Attempt to synthesize hypervalent iodosulfoximine reagent **4''**. TCICA = Trichloroisocyanuric acid, TFA = Trifluoroacetic acid.

## Compilation of $^{19}\text{F}$ and $^{13}\text{C}$ Data for Iodine(I) and Iodine(III) Compounds

**Table S2:** Comparison of  $^{13}\text{C}$  and  $^{19}\text{F}$  chemical shifts of cyclic and acyclic iodoarene compounds in  $\text{CD}_3\text{CN}$ .  
[a]: NMR data obtained from the literature in  $\text{CDCl}_3$ .

Entry	Compound	$\text{C}_{\text{ipso}}$ Chemical Shift	$\text{CF}_3$ $^{19}\text{F}$ Chemical Shift
1 <sup>[a]</sup>		110.6 <sup>1a</sup>	–
2 <sup>[a]</sup>		114.8 <sup>1b</sup>	–
4		119.8	-77.6 -38.6
5		95.0	-75.4
9		119.3	-76.8
9'		94.9	-63.9
10		122.1	-77.1
11		–	-68.2 <sup>2</sup>

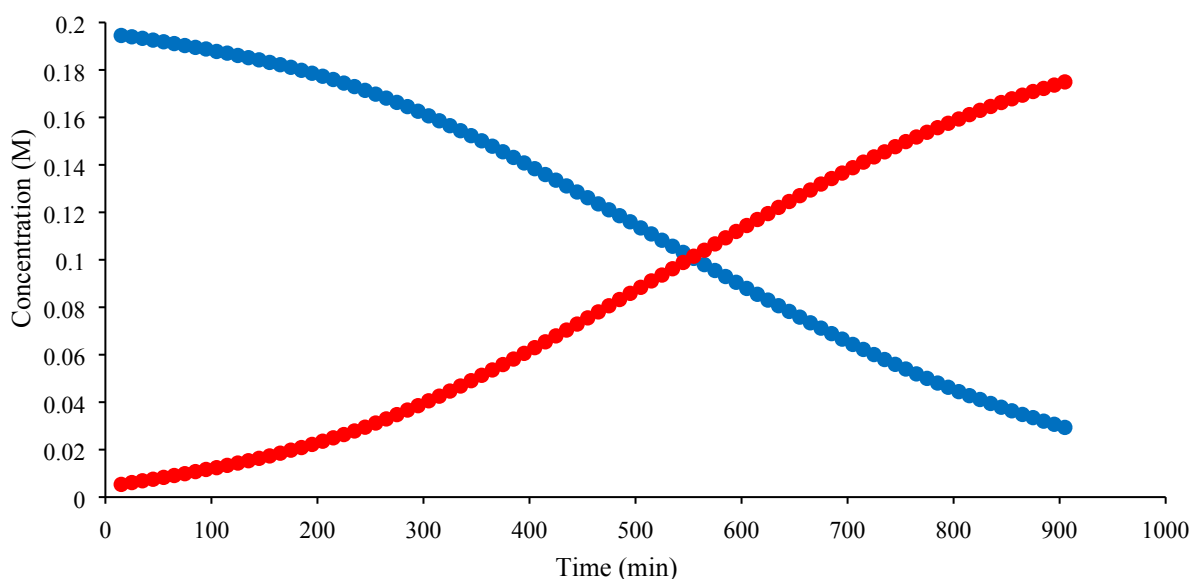
## NMR Investigations of the Tautomerization Mechanism

### General procedure for the $^{19}\text{F}$ NMR reaction monitoring of the tautomerization of **9'** to **9**

An oven dried crimp-cap vial was charged with **5** (0.06–0.12 mmol, 1.0 eq.) the vial was sealed and evacuated,  $\alpha,\alpha,\alpha$ -trifluorotoluene (1.0 eq.) and anhydrous MeCN (0.6 mL) was added, and the suspension cooled to  $-20\text{ }^\circ\text{C}$ . An oven dried NMR tube fitted with a rubber septum was charged with TCICA (0.4 eq.) and cooled to  $-20\text{ }^\circ\text{C}$ , the solution of **5** was injected into the NMR tube. The suspension was vigorously shaken (ca. 30–60 s) until all solids were dissolved. The NMR tube was inserted into the NMR instrument (Bruker AVANCE III 400 MHz or 500 MHz) at 298 K and the course of the reaction was followed by  $^{19}\text{F}\{\text{H}\}$  NMR. The probe had previously been tuned and matched with a sample of **5** in  $\text{CD}_3\text{CN}$ . After a pre-programmed 295 s delay (allowing the solution to warm to  $23\text{ }^\circ\text{C}$ ) the first spectrum was acquired (Relaxation time for acquisition,  $T_1 = 20\text{ s}$ ; measured starting material (**5**)  $T_1: 3.05\text{ s}$ ; 16 scans and 4 dummy scans per spectrum), with subsequent spectra acquired after 600 s (the duration of the pulse program was taken in to account to obtain accurate time values).

### Reaction Profile

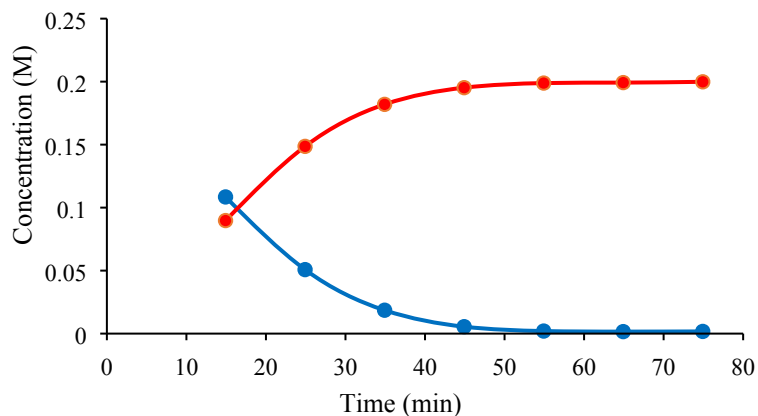
The general procedure was followed using **5** (41 mg, 0.12 mmol),  $\alpha,\alpha,\alpha$ -trifluorotoluene (15  $\mu\text{L}$ , 0.12 mmol, 1 eq.) and TCICA (11 mg, 0.048 mmol, 0.4 eq.) in MeCN (0.6 mL).



**Figure S9:**  $^{19}\text{F}$  NMR (376 MHz, 298 K) reaction profile of the conversion of **9'** (blue) into **9** (red) showing the induction period between the start of the acquisition and ca. 300 min.

### Effect of the addition of Brønsted acid

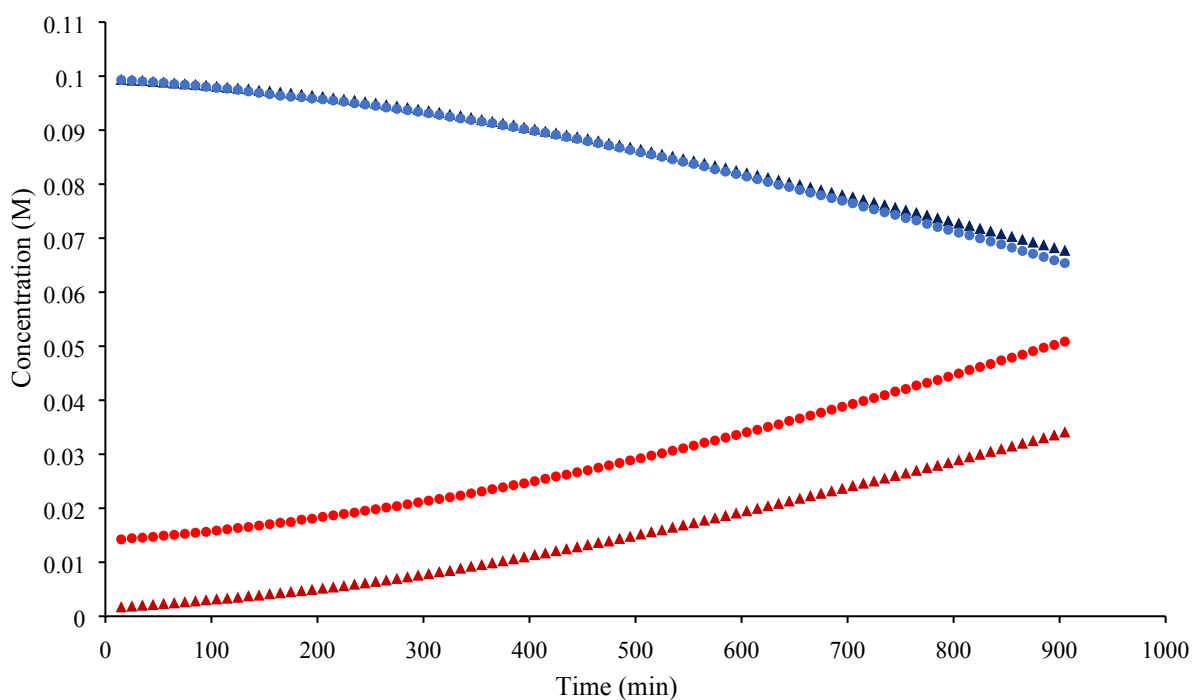
The general procedure was followed with the addition of TFA (1.5  $\mu\text{L}$ , 0.018 mmol) to the reaction mixture with **5** (41 mg, 0.12 mmol),  $\alpha,\alpha,\alpha$ -trifluorotoluene (15  $\mu\text{L}$ , 0.12 mmol) and TCICA (11 mg, 0.048 mmol, 0.4 eq.) in MeCN (0.6 mL).



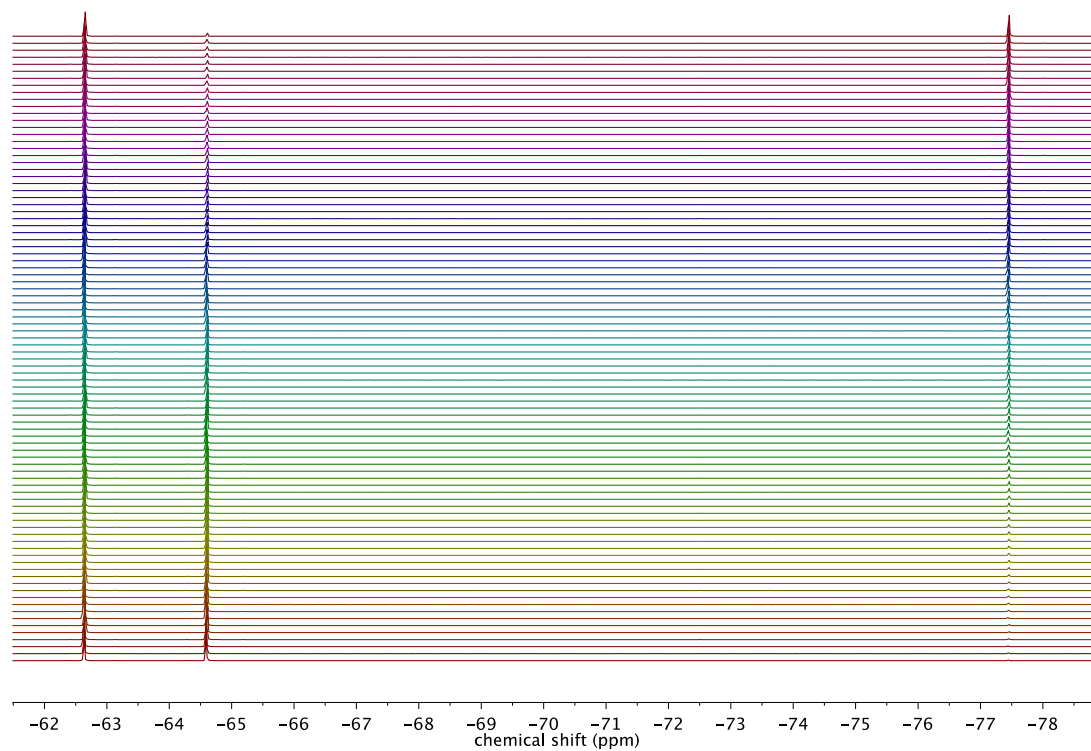
**Figure S10:**  $^{19}\text{F}\{\text{H}\}$  NMR (476 MHz, 298 K) profile of the tautomerization of **9'** (blue) to **9** (red) with the addition of 15 mol% TFA.

### Testing for an autocatalytic process

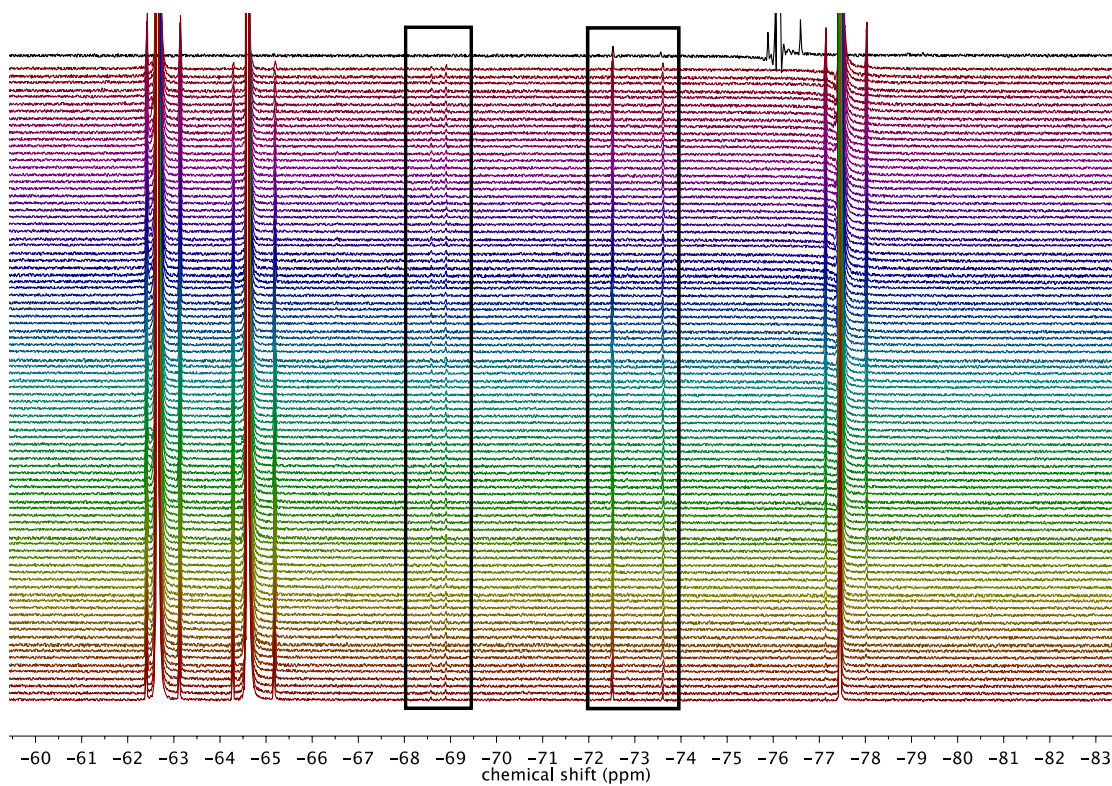
The general procedure was followed, two 0.1 M solutions were prepared, one with the addition of **9** (ca. 2.2 mg, 0.006 mmol, 0.1 eq.) to a solution of **5** (20 mg, 0.06 mmol),  $\alpha,\alpha,\alpha$ -trifluorotoluene (7  $\mu\text{L}$ , 0.06 mmol) and TCICA (5.6 mg, 0.024 mmol, 0.4 eq.) in MeCN (0.6 mL).



**Figure S11:**  $^{19}\text{F}\{\text{H}\}$  NMR (476 and 376 MHz, 298 K) reaction profile of the tautomerization process of **9'** to **9**. The solution was prepared with the addition of ca. 10 mol% of **9**; concentration of **9'** (blue circles); concentration of **9** (red circles). The solution was prepared without the addition of **9**; concentration of **9'** (blue triangle); concentration of **9** (red triangle). Conversion of **9'** over 905 min was found to be 32% for the reaction without the addition of **9**. When ca. 10% of **9** was added, 35% conversion of **9'** over 905 min was observed.



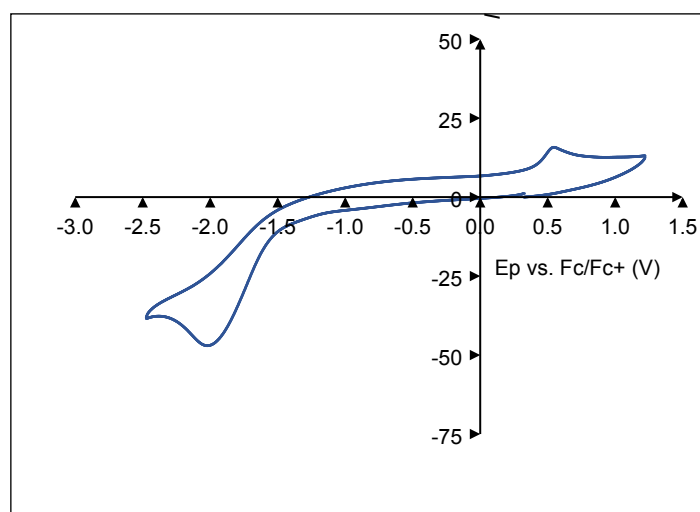
**Figure S12:** Sample  $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz, 298 K) reaction profile of the tautomerization of **9'** into **9**. Peaks at -62.6, -64.6 and -77.5 ppm correspond to  $\alpha,\alpha,\alpha$ -trifluorotoluene, **9'** and **9** respectively.



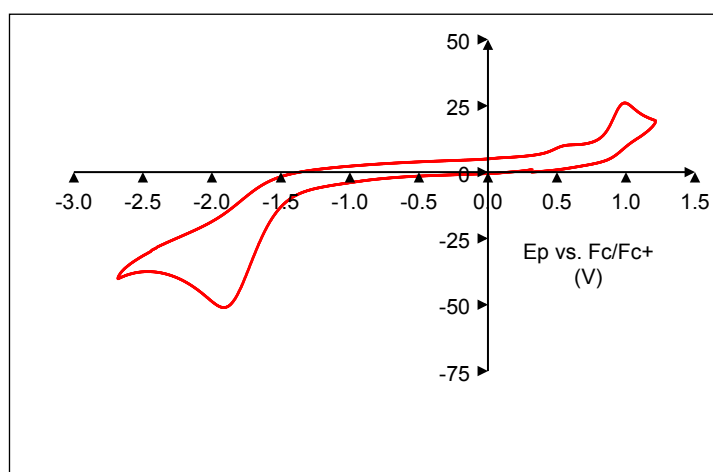
**Figure S13:** Sample  $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz, 298 K) reaction profile of the tautomerization of **9'** into **9** showing the baseline. Peaks at -73.6 and -72.5 ppm correspond to impurities present in starting material **5** (black line, top spectrum); peaks at -68.6 and -68.9 ppm correspond to presumed by-products in the reaction mixture.

## Cyclic Voltammetry

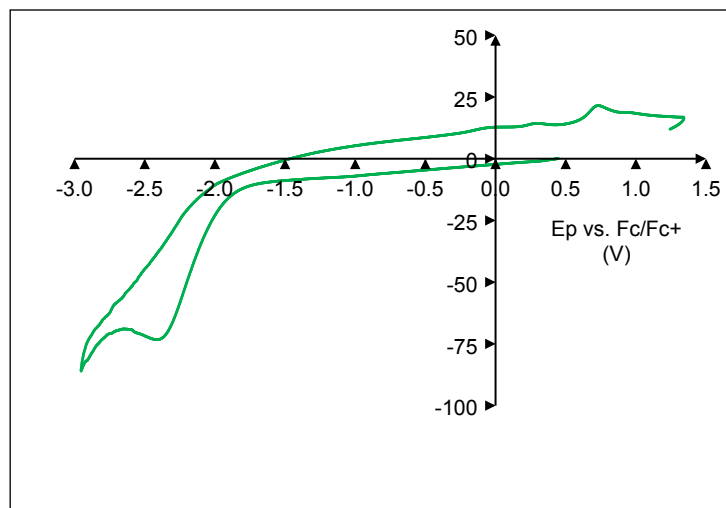
The potentiostat/function generator was a Metrohm Autolab PGSTAT128 (Metrohm Autolab, Utrecht, NL). The working electrode was glassy carbon (GC) (area 7.1 mm<sup>2</sup>) (Metrohm, Herisau, CH). The pseudo-reference electrode was Ag wire in 0.1 M *n*-Bu<sub>4</sub>NPF<sub>6</sub> in MeCN,  $E^\circ \approx -0.37$  vs. Fc<sup>+</sup>/Fc (built in-house). The counter electrode was a GC rod, the immersed surface area was 30 mm<sup>2</sup> (Metrohm, Herisau, CH). Supporting electrolyte was 0.1 M *n*-Bu<sub>4</sub>NPF<sub>6</sub> in MeCN for all measurements. Measurements and solutions were performed under the exclusion of oxygen and moisture. The potential of the reference electrode was determined by measuring its difference to the ferrocene/ferrocenium couple (+0.644 V in MeCN vs. aqueous SHE). The voltammetric sweep rate was 0.2 V/s.



**Figure S14:** Cyclic Voltammogram of **4** (blue) in anhydrous MeCN + 0.1 M *n*-Bu<sub>4</sub>NPF<sub>6</sub>, glassy carbon electrode, scan rate = 0.2 V/s.



**Figure S15:** Cyclic Voltammogram of Reagents **1** (red) in anhydrous MeCN + 0.1 M *n*-Bu<sub>4</sub>NPF<sub>6</sub>, glassy carbon electrode, scan rate = 0.2 V/s.



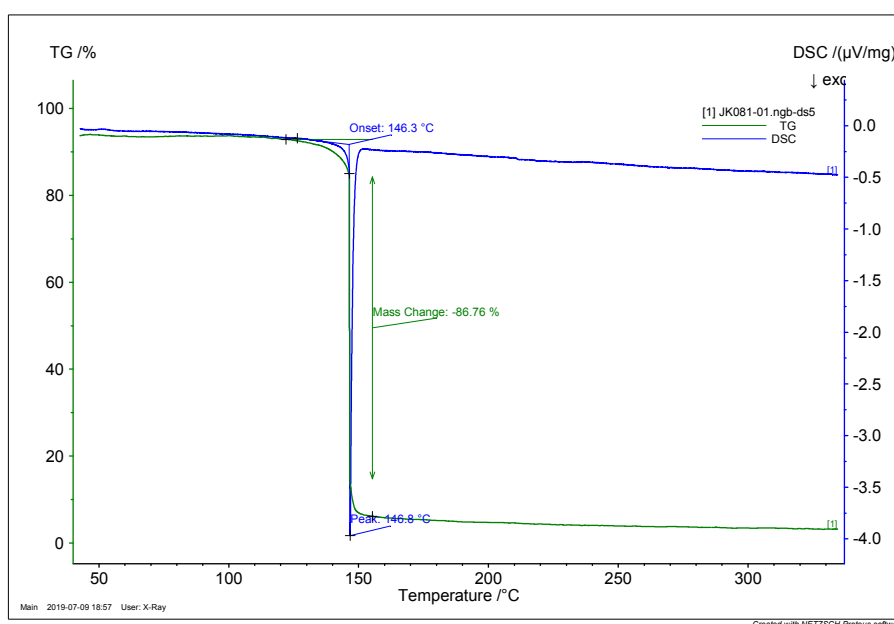
**Figure S16:** Cyclic Voltammogram of Reagents **2** (green) in anhydrous MeCN + 0.1 M  $n\text{-Bu}_4\text{NPF}_6$ , glassy carbon electrode, scan rate = 0.2 V/s.

**Table S3:** Conversion of first cathodic peak potentials ( $E_{pc}$ ) to SHE or SCE for reagents **1**, **2** and **4** in anhydrous MeCN + 0.1 M  $n\text{-Bu}_4\text{NPF}_6$ , glassy carbon electrode, scan rate = 0.2 V/s.

Reagent	$E_{pc}$ vs Fc/Fc <sup>+</sup> (V)	$E_{pc}$ vs H <sub>2</sub> /H <sup>+</sup> (V)	$E_{pc}$ vs SCE (V)
<b>1</b>	-1.91	-1.26	-1.51
<b>2</b>	-2.42	-1.78	-2.02
<b>4</b>	-2.02	-1.38	-1.62

## Thermogravimetric Analysis

Thermogravimetric analysis was performed on a Netzsch STA 449 F5 Jupiter TGA/DSC system coupled with a QMS, and analysed using Netzsch Proteus thermal analysis software.



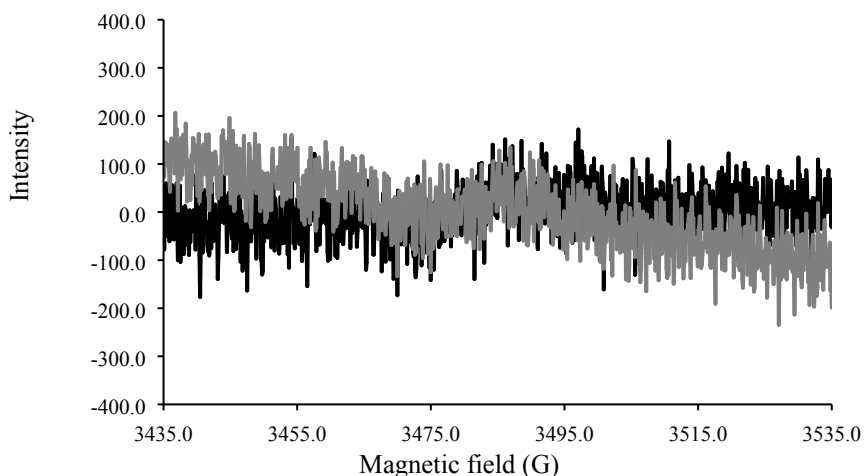
**Figure S17:** TGA/DSC plot of reagent **4** demonstrating decomposition before melting with an onset of thermal degradation at 146.3 °C and a maximum decomposition at 146.8 °C.

# Electron Paramagnetic Resonance

## EPR of the Tautomerization of 9' to 9

Electron Paramagnetic Resonance (EPR) was measured on a Bruker EMX continuous wave X-band spectrometer (Bruker Biospin EPR division, Ettlingen/Rheinstetten, Germany) equipped with an ER 4103TM Cylindrical Mode Resonator. The instrument was operated with a frequency,  $\nu = 9.76$  GHz at 293 K. An oven dried quartz flat cell from Wilmand LabGlass (Vineland, NJ, USA), 70 mm x 14 mm x 0.2 mm was used.

The measurement was run twice. The first was prepared with an isolated 9'/9 mixture in anhydrous MeCN; isolated from the reaction mixture by extraction with anhydrous *n*-hexane at -20 °C under Ar, the *n*-hexane layer was separated via cannula into a second Schlenck flask, then concentrated under high vacuum using an external cooling trap. The concentrated mixture was re-dissolved in anhydrous MeCN (end concentration ca. 0.01 M) and injected into a quartz flat cell. The second measurement was conducted directly from the reaction mixture prepared as a 0.1 M solution (Figure S18).



**Figure S18:** EPR measurement of the tautomerization of 9' into 9; conducted with the reaction mixture directly (grey), isolated 9'/9 mixture (black).



# $^1\text{H}$ , $^{13}\text{C}$ and $^{19}\text{F}$ NMR Spectroscopic Data

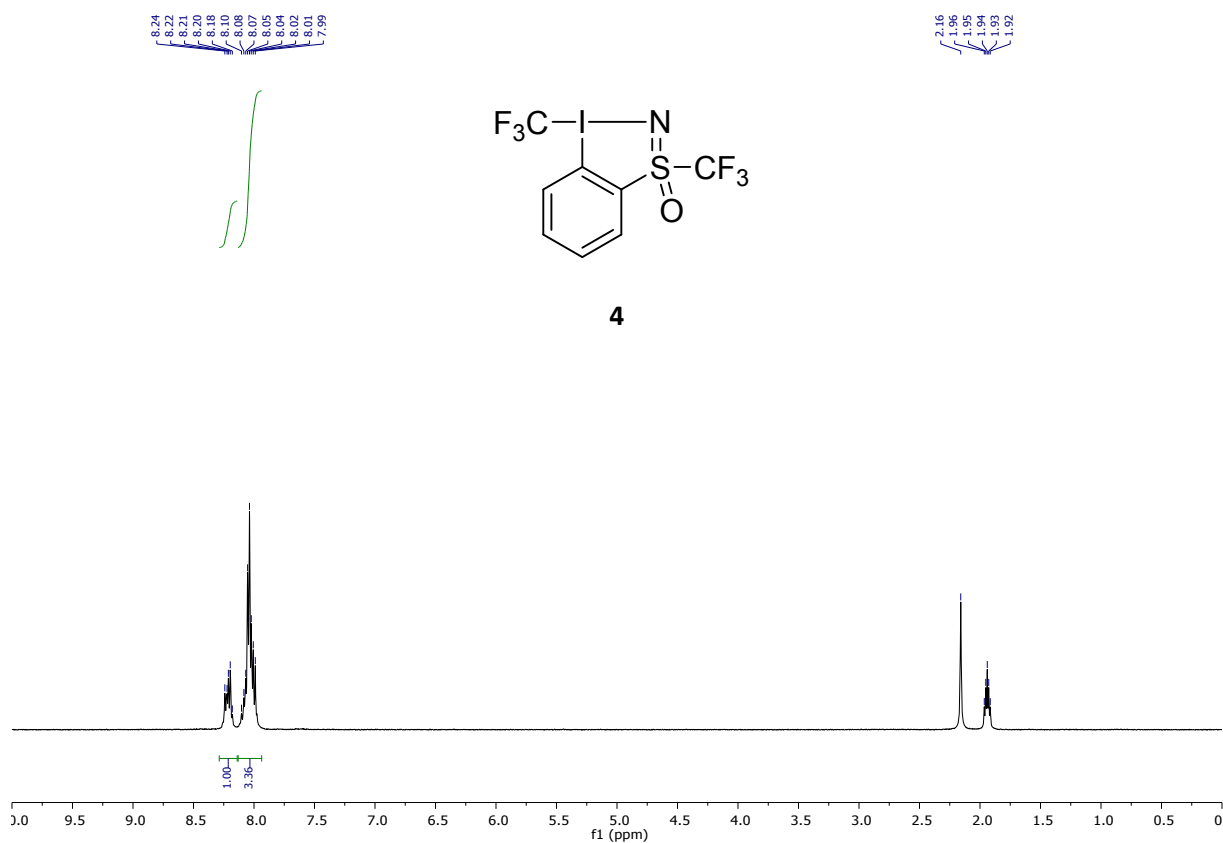


Figure S19:  $^1\text{H}$  NMR of **4**.

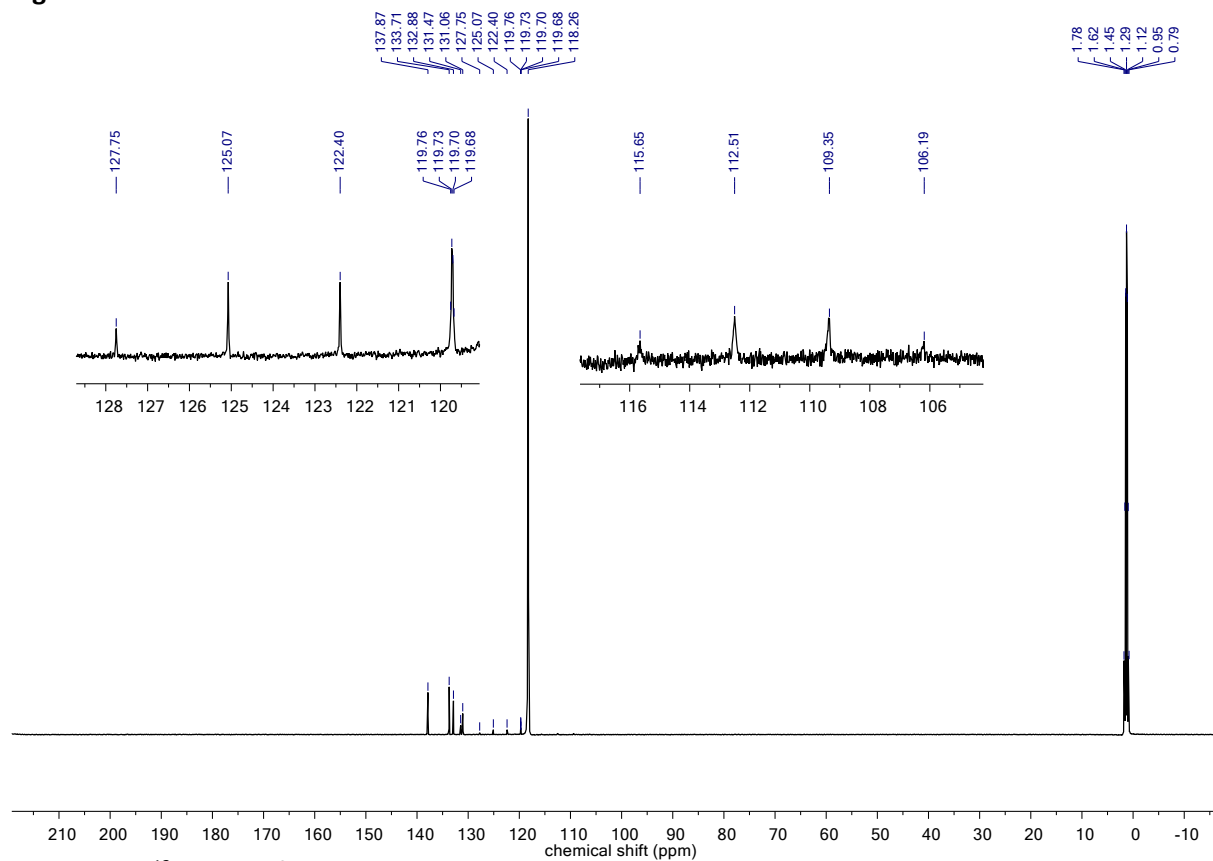


Figure S20:  $^{13}\text{C}$  NMR of **4**.

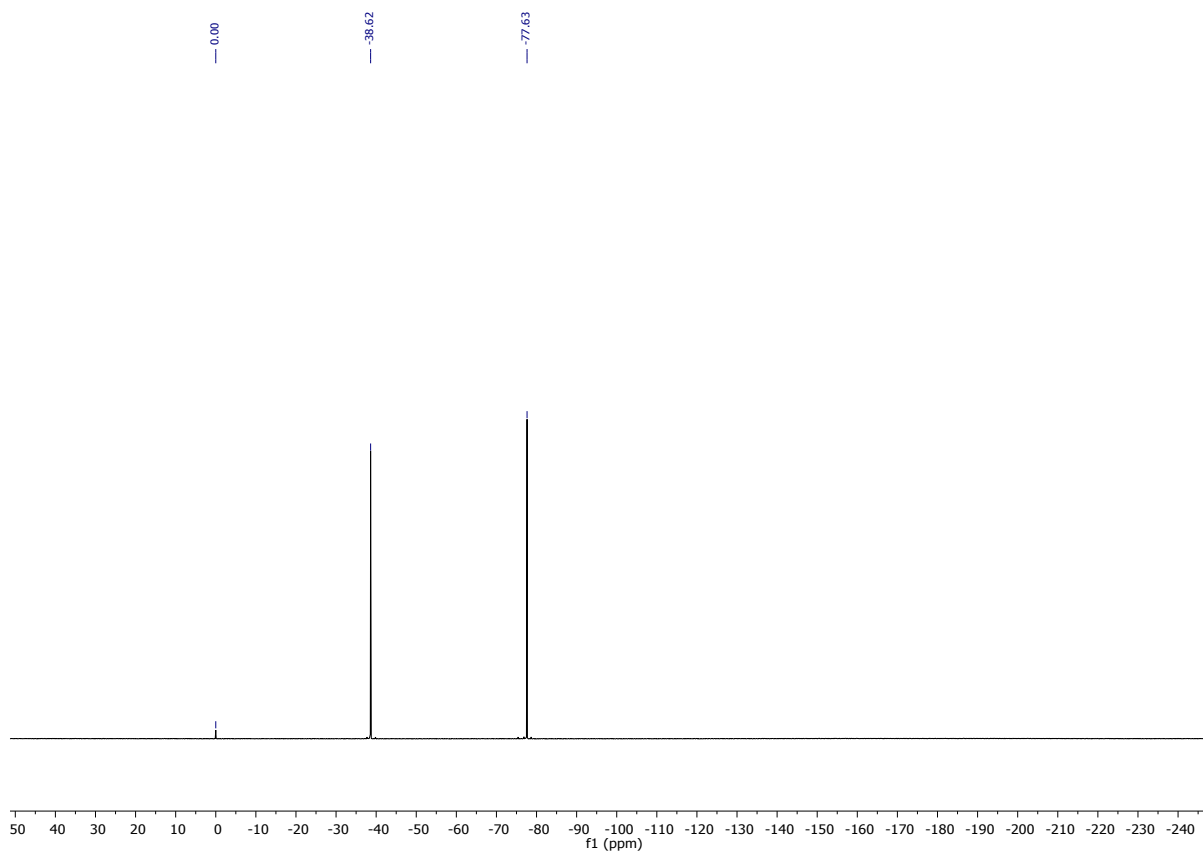


Figure S21:  $^{19}\text{F}$  NMR of **4**.

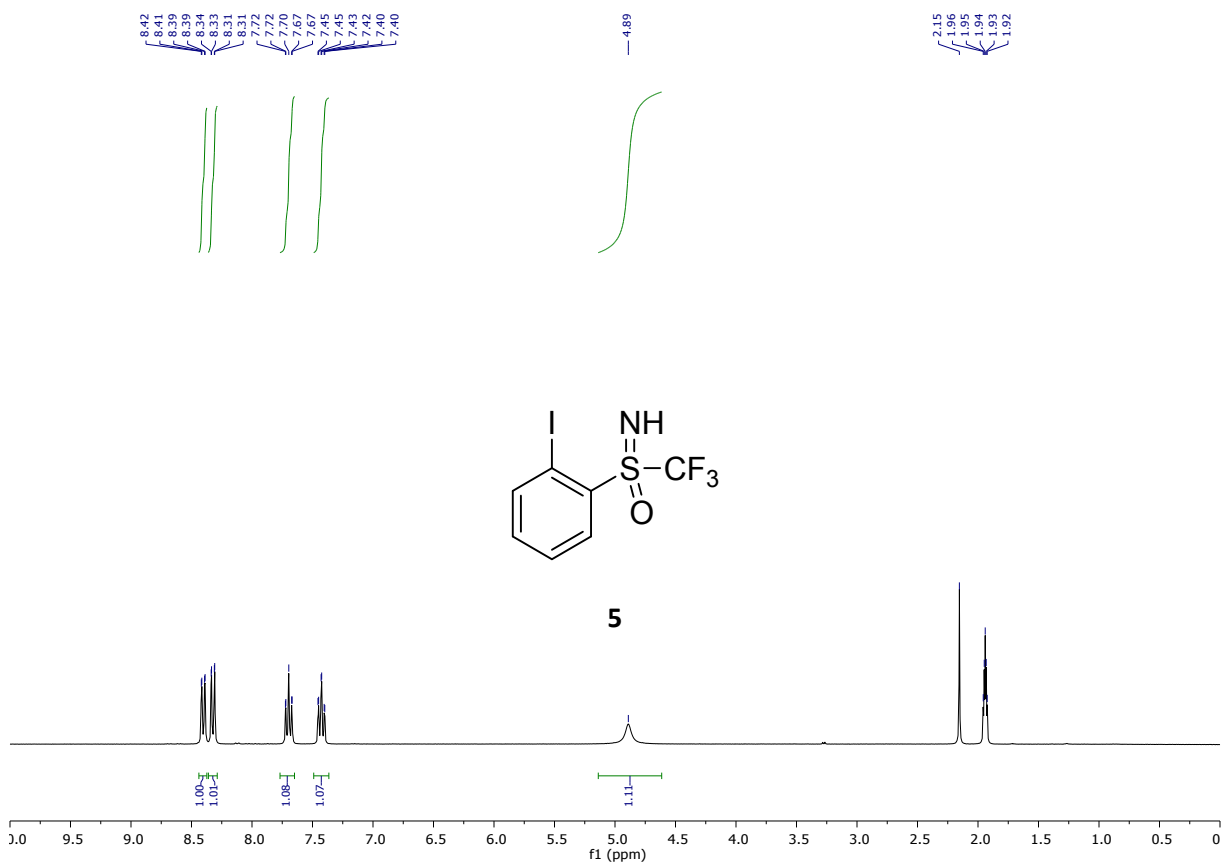


Figure S22:  $^1\text{H}$  NMR of **5**.

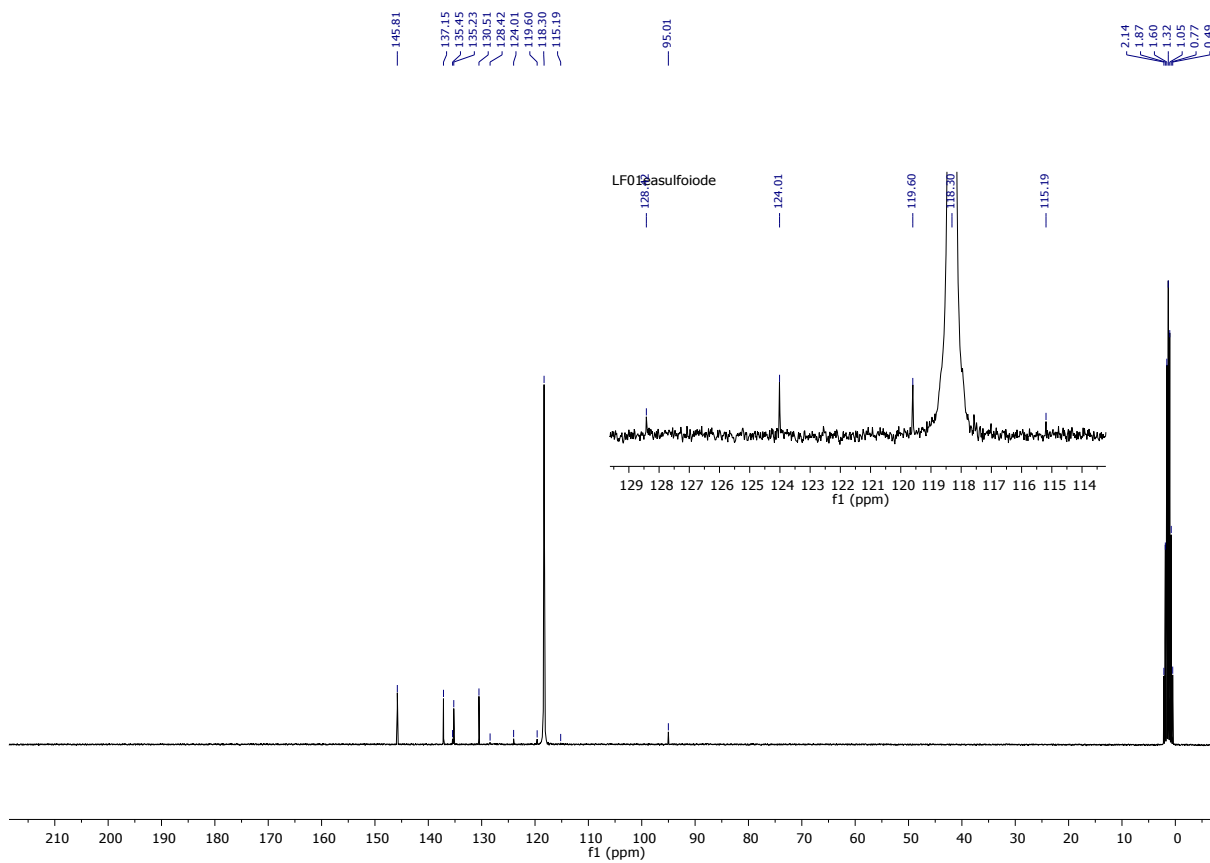


Figure S23:  $^{13}\text{C}$  NMR of 5.

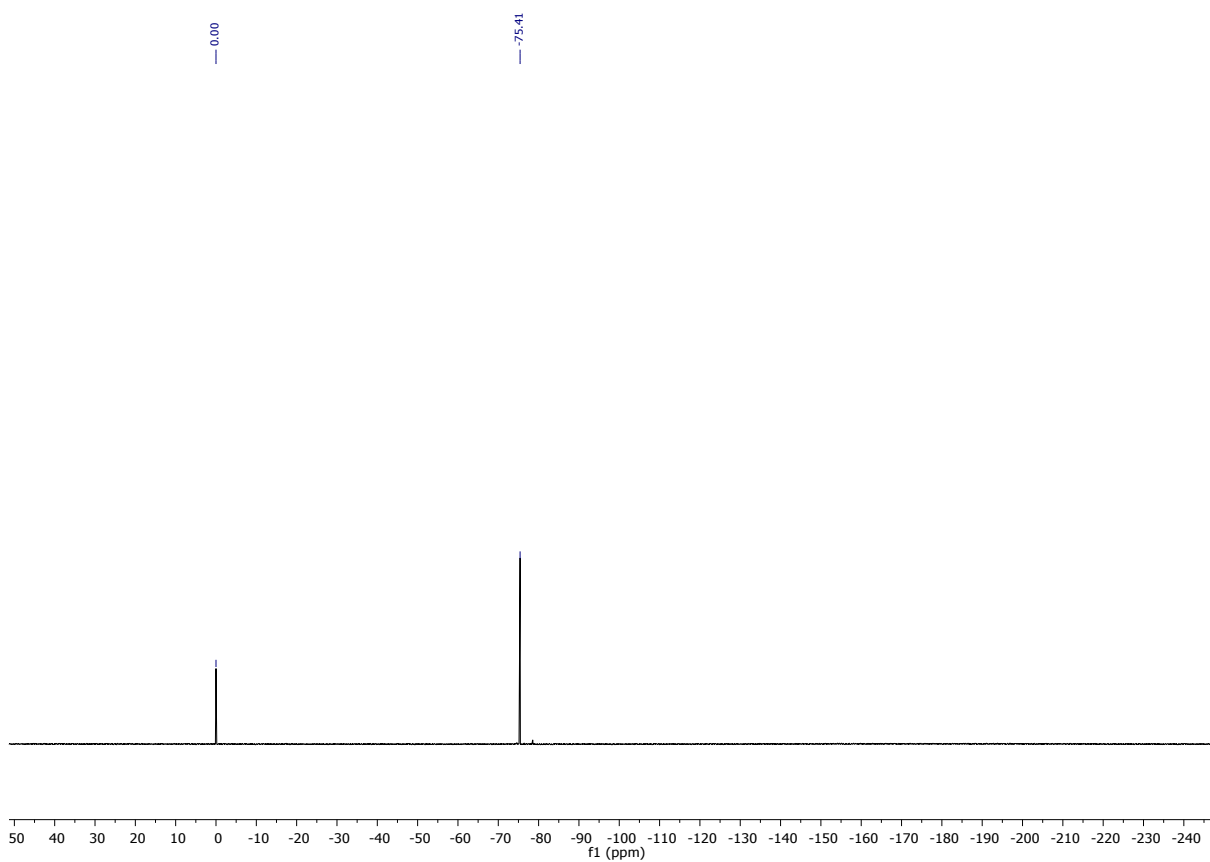


Figure S24:  $^{19}\text{F}$  NMR of 5.

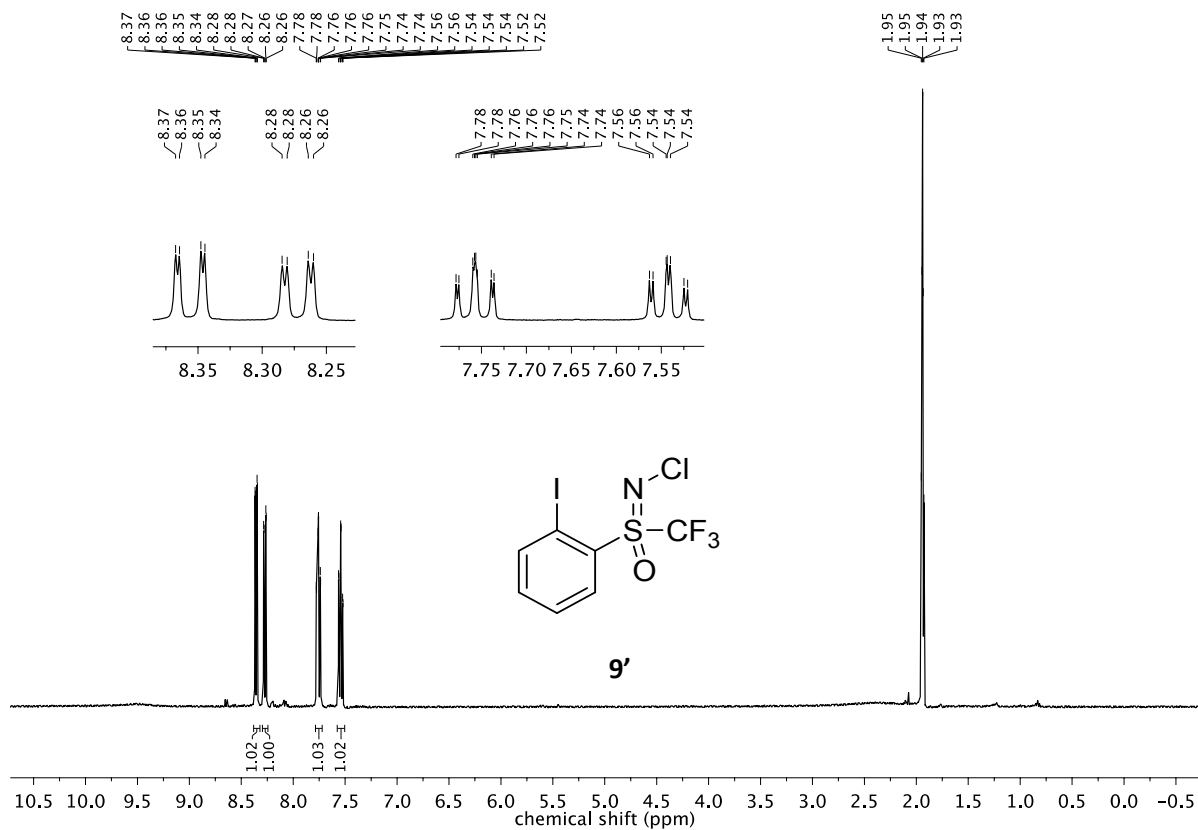


Figure S25: <sup>1</sup>H NMR of **9'**.

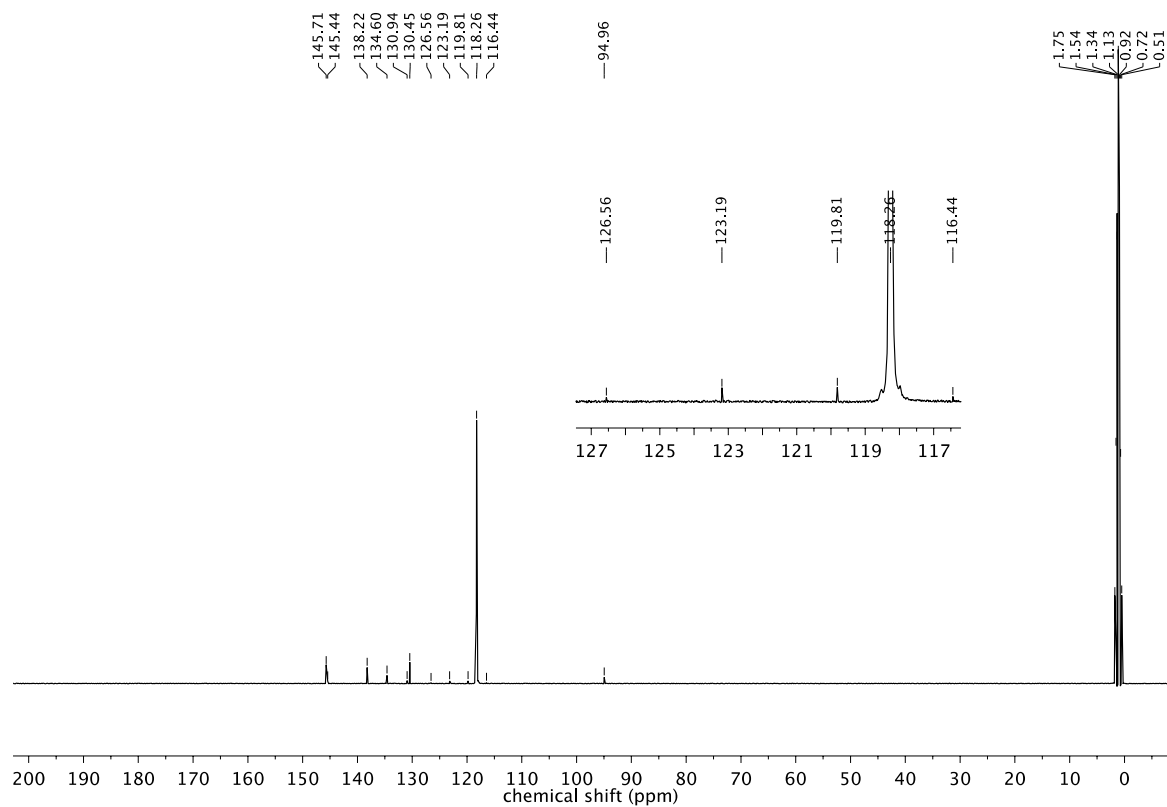


Figure S26: <sup>13</sup>C NMR of **9'**.

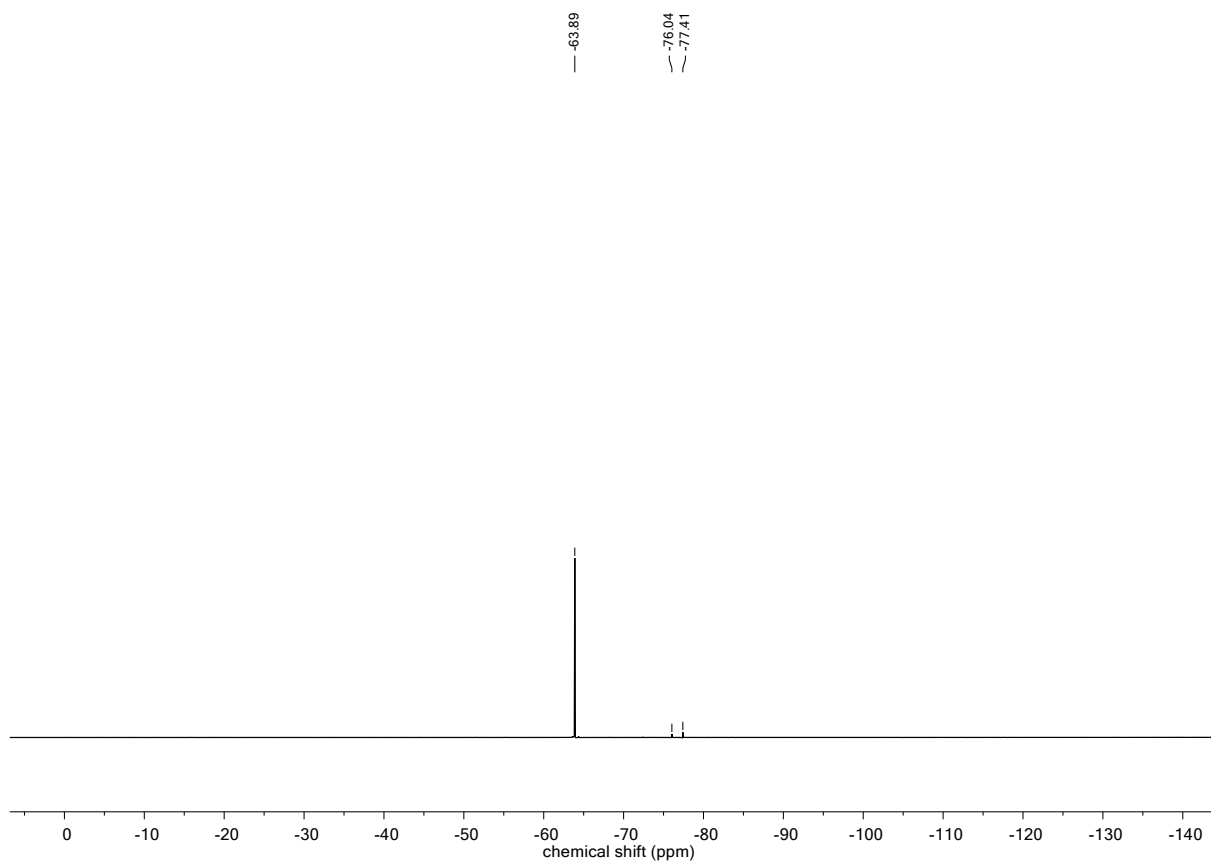


Figure S27:  $^{19}\text{F}$  NMR of **9'**.

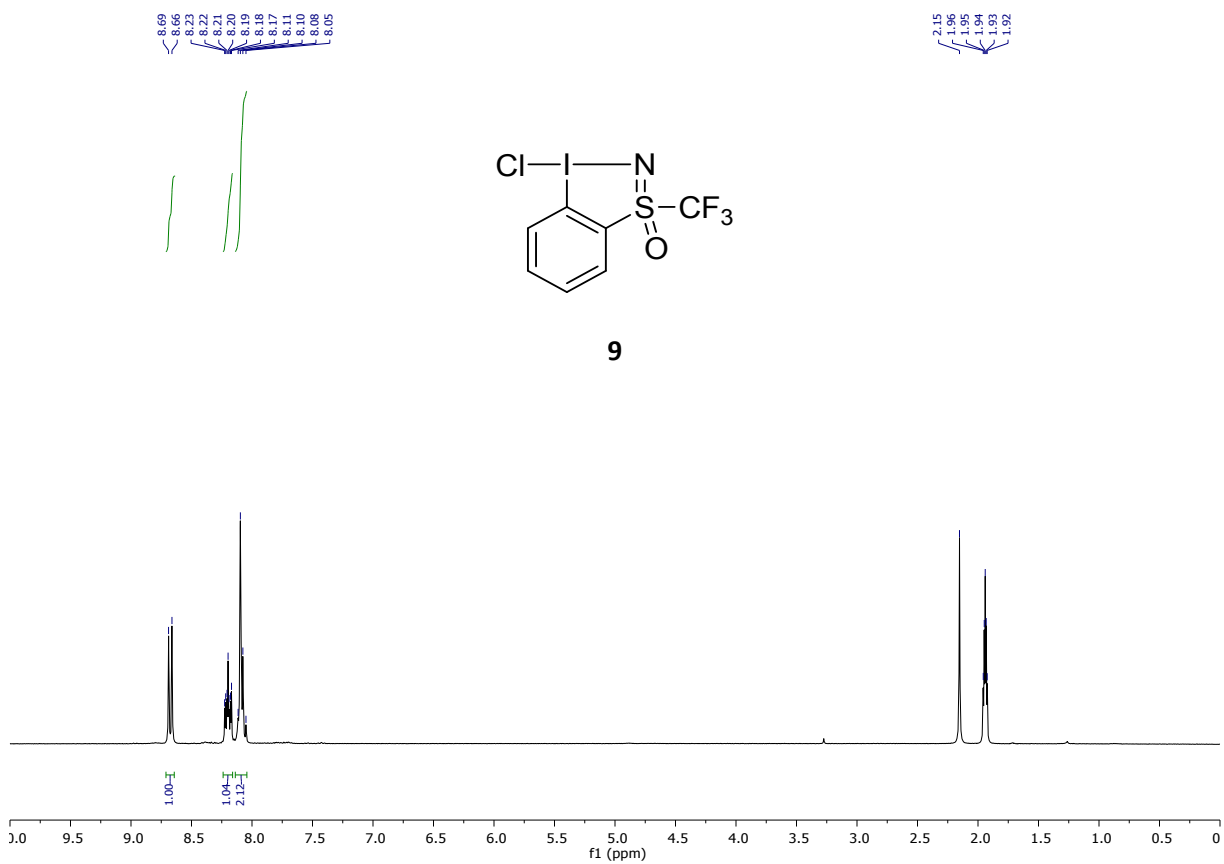


Figure S28:  $^1\text{H}$  NMR of **9**.

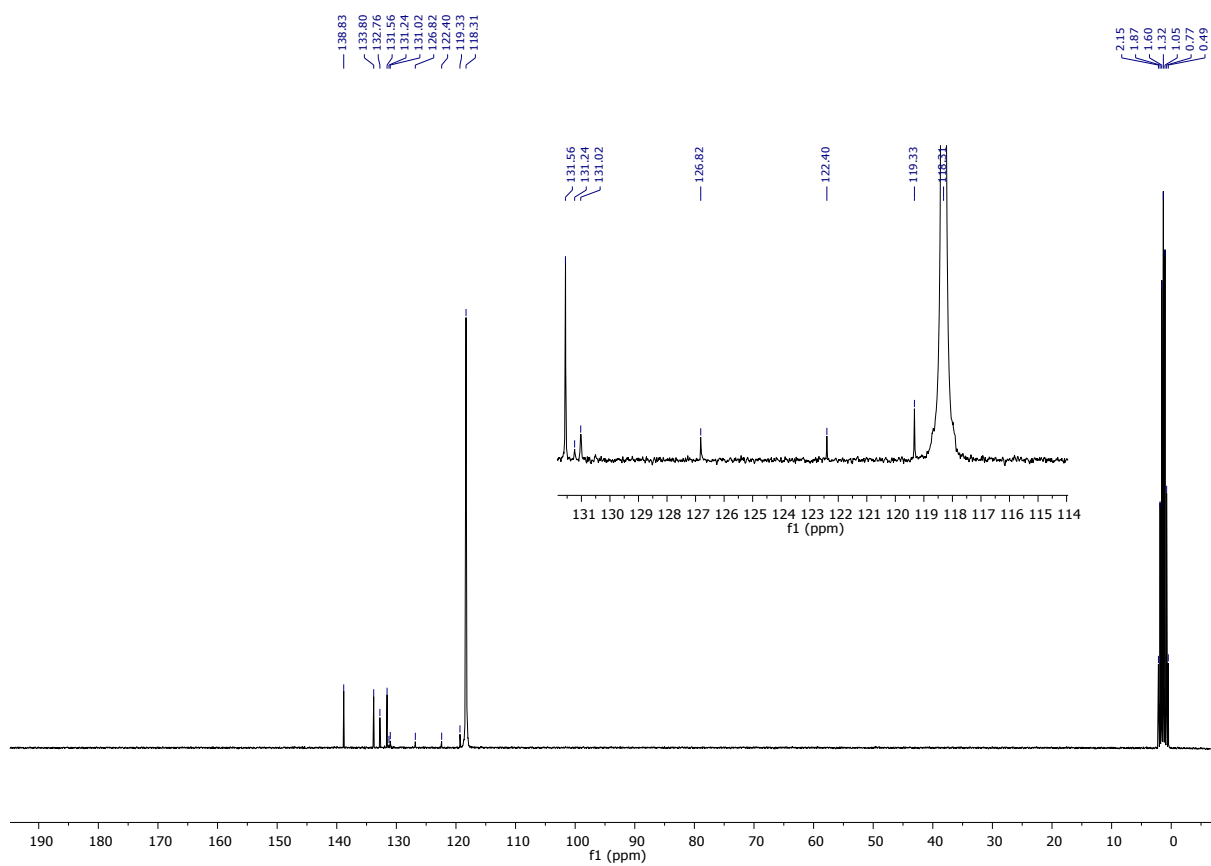


Figure S29:  $^{13}\text{C}$  NMR of **9**.

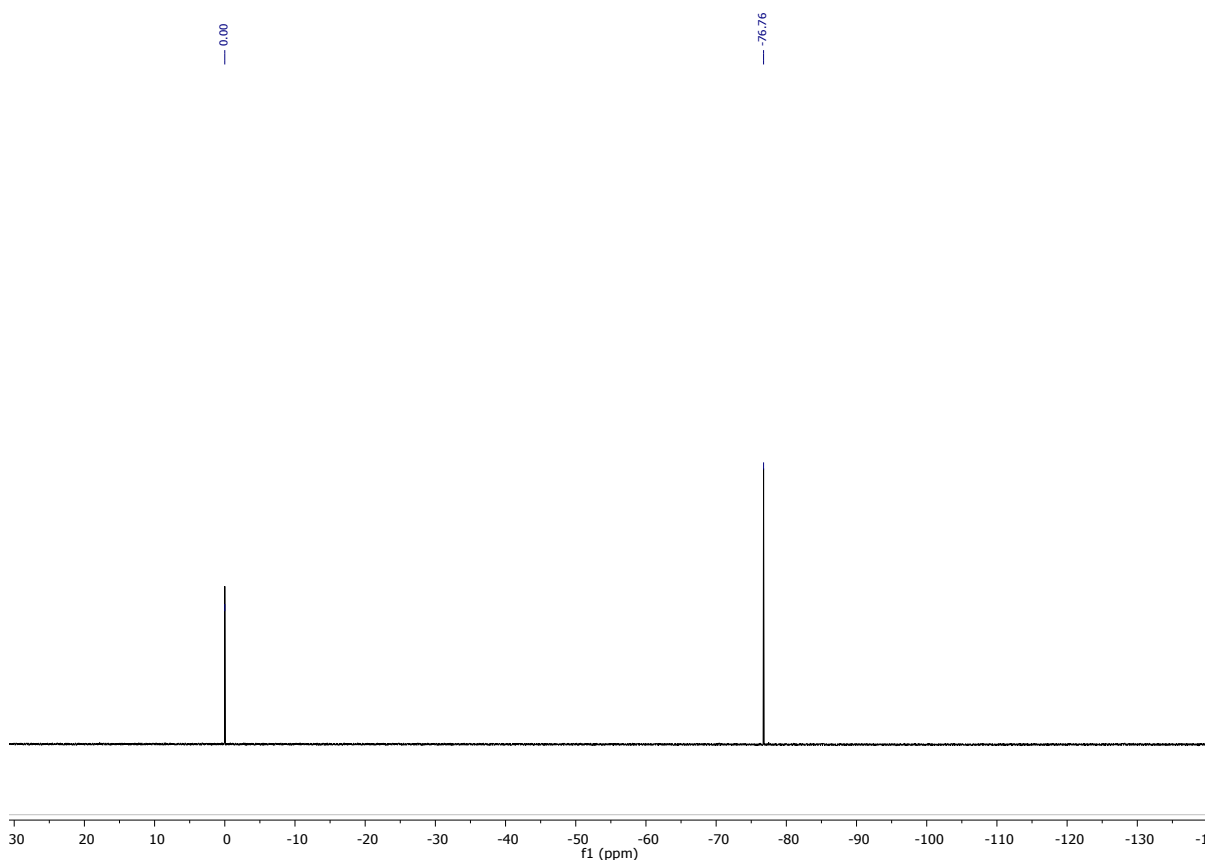
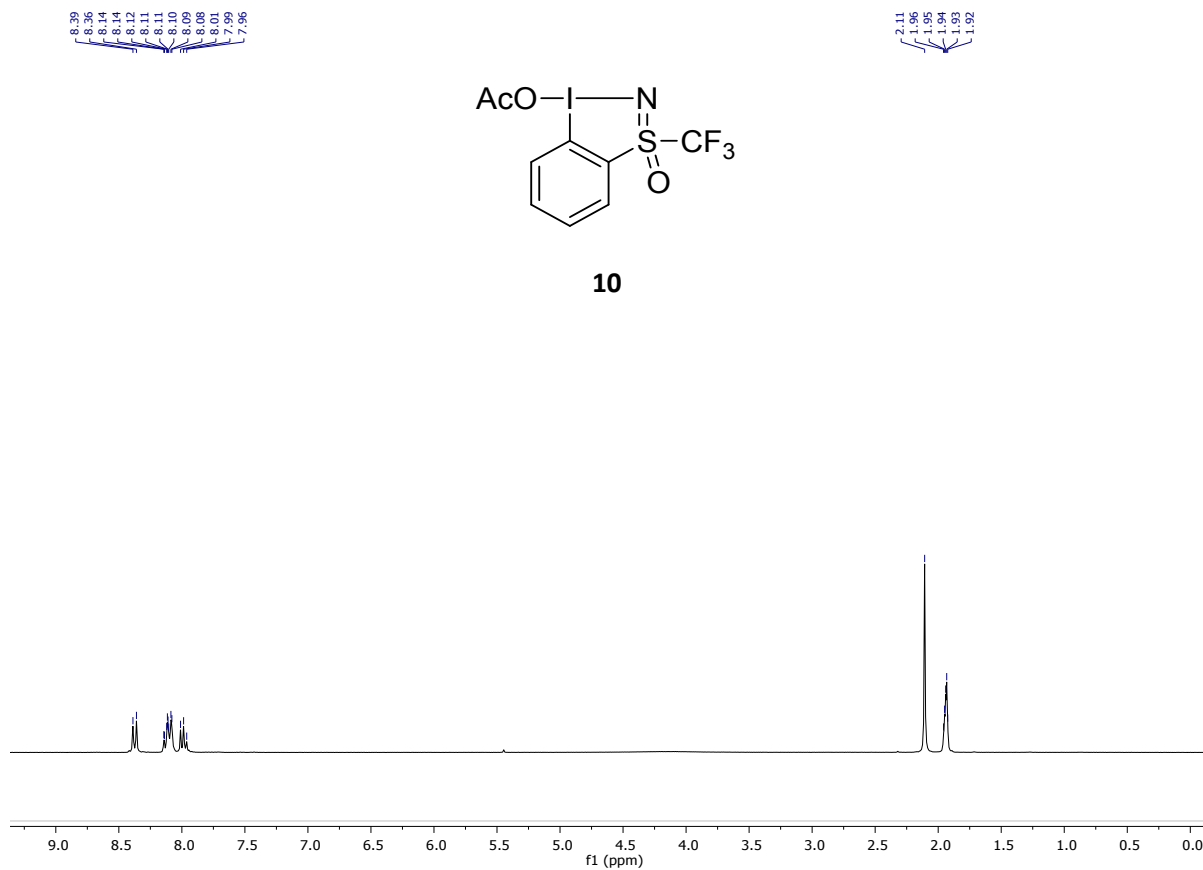
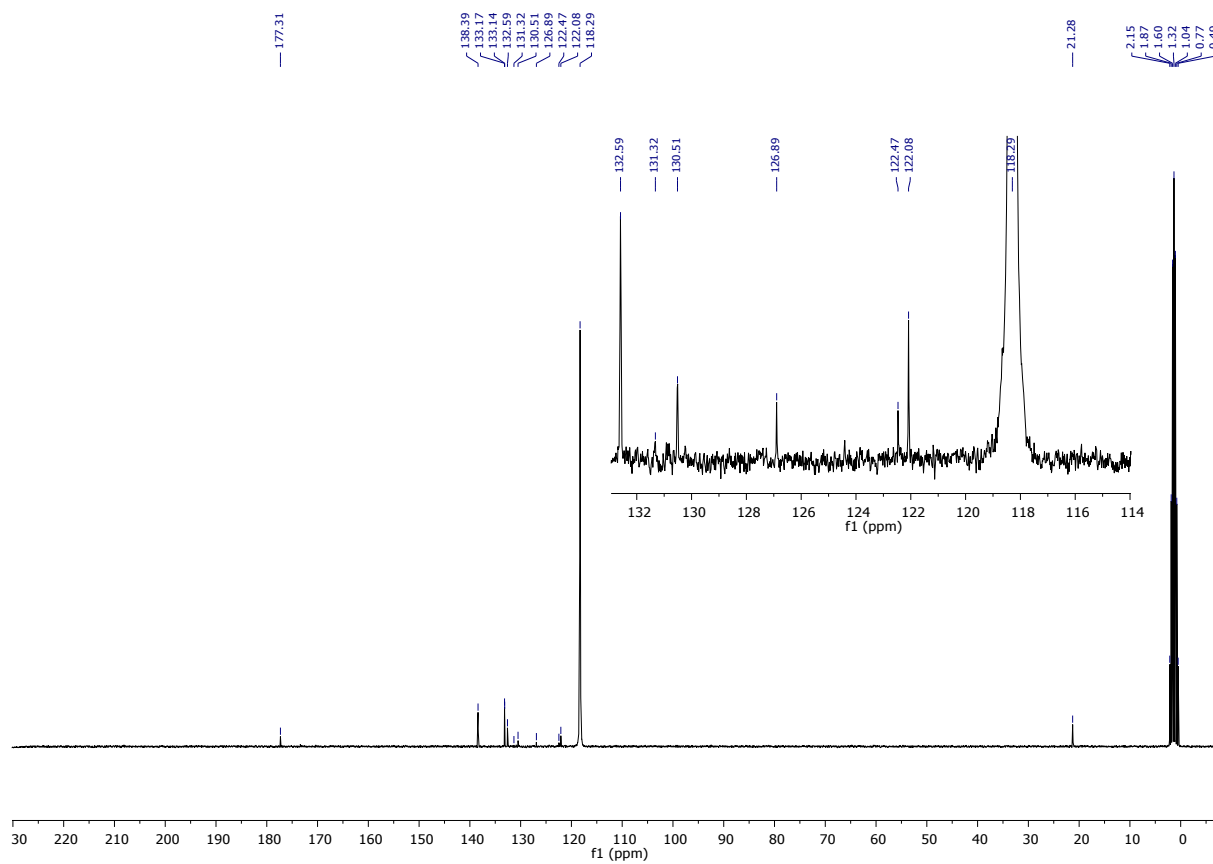


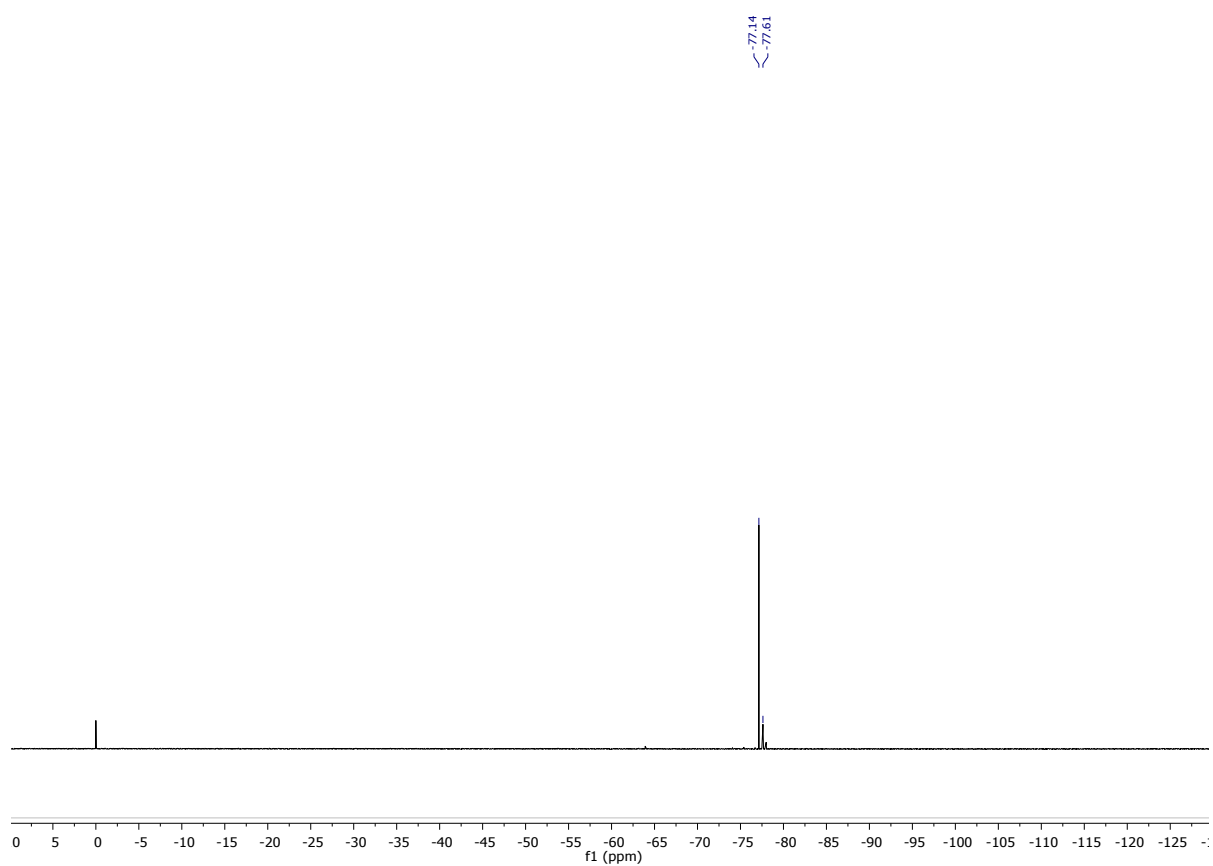
Figure S30:  $^{19}\text{F}$  NMR of **9**.



**Figure S31:**  $^1\text{H}$  NMR of **10**.



**Figure S32:**  $^{13}\text{C}$  NMR of **10**.



**Figure S33:**  $^{19}\text{F}$  NMR of **10**.



## DFT Calculations and Co-ordinates

All calculations are based on density functional theory (DFT) and carried out in Gaussian 09 (Rev. D.),<sup>3</sup> using the B3LYP functional.<sup>4</sup> The triple- $\zeta$  augmented correlation-consistent basis set, designated aug-cc-pVTZ, was employed for H, C, N, O, F;<sup>5</sup> d sets were added for second row element, S, using aug-cc-pV(T+d)Z.<sup>6</sup> For I, relativistic effective core potentials describing the inner core electrons were implemented using the aug-cc-pVTZ-PP (PP standing for pseudopotential) basis set.<sup>7</sup> Frequencies calculations were computed to obtain the thermodynamic parameters and to verify the stationary point to be a minimum. All computations were done in gas phase at 298.15 K and 1 atm. The generated MEPs were mapped onto the isodensity surface at a value of 0.001 au, which lies within the van der Waals contact distances and accounts for 96% of molecular electron density.<sup>8</sup>

### Cartesian coordinates

#### Reagent 1

C	0.53573100	1.98541100	-0.00013500
C	1.62390900	2.85417000	-0.00019600
C	2.92608100	2.36247600	-0.00020600
C	3.15748800	0.99540700	-0.00015400
C	2.08660700	0.10192800	-0.00009400
C	0.81066400	0.63062400	-0.00008800
I	-0.67873000	-0.91968300	0.00001000
C	2.31611600	-1.39250200	-0.00003200
O	1.20818500	-2.08985800	0.00008700
O	3.43728100	-1.85436200	0.00000100
C	-2.42490200	0.54067600	0.00012700
F	-2.47302400	1.33108500	1.08463900
F	-2.47329000	1.33092300	-1.08449200
F	-3.52844400	-0.22904900	0.00031900
H	-0.46732600	2.37815300	-0.00012700
H	1.44287700	3.92018300	-0.00023500
H	3.75972700	3.05080700	-0.00025300
H	4.15632400	0.58204500	-0.00016000

#### Reagent 2

C	-0.03681100	2.11137400	-0.00013200
C	-0.95696000	3.15269200	0.00001900

C	-2.31952100	2.87549500	0.00019300
C	-2.76566800	1.56251700	0.00020200
C	-1.86564300	0.49225300	0.00003900
C	-0.52302900	0.81441600	-0.00011800
I	0.72935800	-0.93832100	-0.00025100
C	-2.32635100	-0.97319000	0.00011500
O	-1.20611900	-1.82121300	-0.00048800
C	-3.15405700	-1.25950500	1.26591300
C	-3.15513200	-1.25938500	-1.26499600
C	2.66593700	0.30143300	0.00015800
F	2.84922700	1.08223200	1.08551200
F	2.84939900	1.08233100	-1.08512600
F	3.65549900	-0.62044800	0.00019500
H	1.01801900	2.32917500	-0.00026500
H	-0.60330600	4.17430000	0.00000100
H	-3.03602600	3.68550100	0.00032100
H	-3.82805000	1.36115100	0.00034500
H	-2.56040400	-1.06015600	2.15768700
H	-3.43689200	-2.31178200	1.27016400
H	-4.06137700	-0.65578900	1.30941000
H	-2.56225300	-1.05986000	-2.15724300
H	-4.06255700	-0.65576800	-1.30763300
H	-3.43786900	-2.31168800	-1.26915200

Reagent 4:

C	-1.01948100	2.19394100	0.10659300
C	-0.34428400	3.41146000	0.14694900
C	1.02655100	3.47836300	-0.07392900
C	1.74416000	2.32030700	-0.33479000
C	1.07821000	1.09758700	-0.35851500
C	-0.28461200	1.04867700	-0.14477800
I	-1.15071600	-0.93394900	-0.31061500

S	1.94466800	-0.42502500	-0.76661000
N	0.91828900	-1.49861400	-0.90625000
O	2.98081400	-0.14050800	-1.73466300
C	2.94944900	-0.69358500	0.82695000
F	2.11751100	-0.79579000	1.87490900
F	3.79993900	0.31366000	1.06654900
F	3.64107200	-1.82423200	0.71489000
C	-3.21701600	-0.13832600	0.34357600
F	-3.98470800	-1.24773700	0.37997700
F	-3.80251200	0.72681000	-0.50989400
F	-3.25435800	0.42004000	1.56852300
H	-2.08429400	2.17284600	0.26246900
H	-0.90705300	4.31343500	0.34394000
H	1.53387900	4.43241100	-0.05191800
H	2.80585200	2.35008700	-0.53200300

## Small Molecule X-Ray Crystal Structures

Single crystalline samples of compounds **4** and **9** were measured on a Bruker/Nonius Kappa APEX-II diffractometer with sealed tube Mo-K $\alpha$  radiation using mirror optics ( $\lambda = 0.71073 \text{ \AA}$ ). All measurements were carried out at 100 K using an Oxford Cryosystems Cryostream 700 sample cryostat. Data were integrated using SAINT from the Bruker Apex-II program suite and corrected for absorption effects using multi-scan method (SADABS).<sup>9</sup> The structures were solved by direct methods with SHELXS<sup>10</sup> and refined by full-matrix least-squares analysis (SHELXL)<sup>10,11</sup> using the program package OLEX2.<sup>12</sup> All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters (in terms of a riding model). CCDC 1947035 (**4**) and 1947034 (**9**) contain the supplementary crystallographic data for this paper, including structure factors and refinement instructions. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(1223)-336-033; e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk), or *via* <https://www.ccdc.cam.ac.uk/getstructures>).

Suitable crystals of compound **4** were grown by slow evaporation of a dichloromethane solution at room temperature to give colorless blocks.

**Table S4:** Crystal data and structure refinement for racemic **4**.

Identification code	CCDC 1947035
Empirical formula	C <sub>8</sub> H <sub>4</sub> NOF <sub>6</sub> SI
Formula weight	403.08
Temperature/K	101.2
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /n
a/Å	7.1787(13)
b/Å	10.1369(18)
c/Å	15.408(3)
$\alpha$ /°	90
$\beta$ /°	92.647(3)
$\gamma$ /°	90
Volume/Å <sup>3</sup>	1120.1(3)
Z	4
$\rho_{\text{calc}}$ /cm <sup>3</sup>	2.390
$\mu$ /mm <sup>-1</sup>	3.113

F(000)	760.0
Crystal size/mm <sup>3</sup>	0.25 × 0.22 × 0.18
Radiation	MoK $\alpha$ ( $\lambda$ = 0.71073)
2 $\theta$ range for data collection/°	4.812 to 56.554
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 13, -20 ≤ l ≤ 20
Reflections collected	20239
Independent reflections	2788 [R <sub>int</sub> = 0.0491, R <sub>sigma</sub> = 0.0297]
Data/restraints/parameters	2788/0/163
Goodness-of-fit on F <sup>2</sup>	1.052
Final R indexes [ $I \geq 2\sigma(I)$ ]	R <sub>1</sub> = 0.0220, wR <sub>2</sub> = 0.0415
Final R indexes [all data]	R <sub>1</sub> = 0.0276, wR <sub>2</sub> = 0.0433
Largest diff. peak/hole / e Å <sup>-3</sup>	0.58/-0.46

Suitable crystals of compound (S)-(-)-**9** were grown by slow evaporation of a dichloromethane solution at room temperature to give colorless needles.

**Table S5:** Crystal data and structure refinement for (S)-(-)-**9**

Identification code	CCDC 1947034
Empirical formula	C <sub>7</sub> H <sub>4</sub> ClF <sub>3</sub> INOS
Formula weight	369.52
Temperature/K	100.0
Crystal system	orthorhombic
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
a/Å	5.1427(6)
b/Å	7.2141(9)
c/Å	27.595(3)
$\alpha$ /°	90
$\beta$ /°	90
$\gamma$ /°	90
Volume/Å <sup>3</sup>	1023.8(2)

Z	4
$\rho_{\text{calc}}/\text{cm}^3$	2.397
$\mu/\text{mm}^{-1}$	3.606
F(000)	696.0
Crystal size/ $\text{mm}^3$	0.18 × 0.15 × 0.05
Radiation	MoK $\alpha$ ( $\lambda = 0.71073$ )
2 $\theta$ range for data collection/ $^\circ$	5.836 to 53.464
Index ranges	$-6 \leq h \leq 6, -9 \leq k \leq 9, -34 \leq l \leq 34$
Reflections collected	14295
Independent reflections	2177 [ $R_{\text{int}} = 0.0442, R_{\text{sigma}} = 0.0297$ ]
Data/restraints/parameters	2177/0/136
Goodness-of-fit on $F^2$	1.201
Final R indexes [ $I \geq 2\sigma(I)$ ]	$R_1 = 0.0321, wR_2 = 0.0690$
Final R indexes [all data]	$R_1 = 0.0328, wR_2 = 0.0692$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	1.61/-1.49
Flack parameter	0.008(12)

## References

1. a) P. Eisenberger, S. Gischig and A. Togni, *Chem. Eur. J.*, 2006, **12**, 2579; b) I. Kieltsch, P. Eisenberger and A. Togni, *Angew. Chem. Int. Ed.*, 2007, **46**, 754.
2. A. Prieto, P. Diter, M. Toffano, J. Hannedouche and E. Magnier, *Adv. Synth. Catal.*, 2019, **361**, 436.
3. Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, *Gaussian, Inc., Wallingford CT*, 2009.
4. a) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785; b) A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.
5. a) T. H. Dunning, *J. Phys. Chem. A*, 2000, **104**, 9062; b) R. A. Kendall, T. H. Dunning and R. J. Harrison, *J. Chem. Phys.*, 1992, **96**, 6796; c) K. A. Peterson, R. A. Kendall and T. H. Dunning, *J. Chem. Phys.*, 1993, **99**, 1930.
6. T. H. Dunning, K. A. Peterson and A. K. Wilson, *J. Chem. Phys.*, 2001, **114**, 9244.
7. a) K. A. Peterson, B. C. Shepler, D. Figgen and H. Stoll, *J. Phys. Chem. A*, 2006, **110**, 13877; b) K. A. Peterson, D. Figgen, E. Goll, H. Stoll, and M. Dolg, *J. Chem. Phys.*, 2003, **119**, 11113.
8. a) H. P. de Magalhães, A. Togni and H. P. Lüthi, *J. Org. Chem.*, 2017, **82**, 11799; b) M. H. Kolár and P. Hobza, *Chem. Rev.*, 2016, **116**, 5155; c) P. Politzer, J. S. Murray and T. Clark, *Phys. Chem. Chem. Phys.*, 2013, **15**, 11178; d) R. F. W. Bader, M. T. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.*, 1987, **109**, 7968; d) G. Cavallo, J. S. Murray, P. Politzer, T. Pilati, M. Ursini and G. Resnati, *IUCrJ* 2017, **4**, 411.
9. G. M. Sheldrick, *SADABS, Program for Empirical Absorption Correction of Area Detector Data*. Univ. of Göttingen, Göttingen, Germany, **1996**.
10. G. M. Sheldrick, *Acta Cryst.*, 2008, **A64**, 112.
11. G. M. Sheldrick, *Acta Cryst.*, 2015, **C71**, 3.
12. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339.