JOC The Journal of Organic Chemistry

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Use of Fluoroform as a Source of Difluorocarbene in the Synthesis of Difluoromethoxy- and Difluorothiomethoxyarenes

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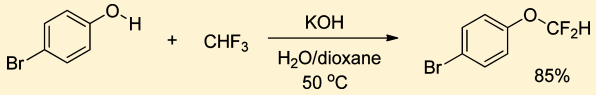
Supporting Information

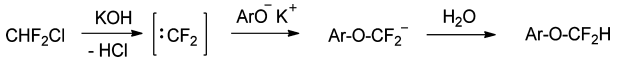
ABSTRACT: Fluoroform, CHF_3, a non-ozone-depleting, nontoxic, and inexpensive gas can be used as a difluorocarbene source in a process for the conversion of phenols and thiophenols to their difluoromethoxy and difluorothiomethoxy derivatives. The reactions are carried out at moderate temperatures and atmospheric pressure, using potassium hydroxide as base in a two-phase (water/dioxane or water/acetonitrile) process to provide moderate to good yields of the respective products.



The difluoromethyl ether functionality has become increasingly important as a structural component in pharmaceuticals, agrochemicals, and materials. However, the synthesis of molecules bearing the OCF_2H group, more specifically, aryl difluoromethyl ethers, has always proved problematic, with yields being generally modest and highly substrate-dependent.

Virtually all of the methodologies appear to have involved the use of a difluorocarbene-generating reaction, under basic conditions, in the presence of a proton donor, and one of the previously favored processes was one developed by Miller and Thanassi in 1960.[1] It involved the use of chlorodifluoromethane (CHF_2Cl, F22) as the difluorocarbene precursor (Scheme1). However, unfortunately, because CHF_2Cl is a

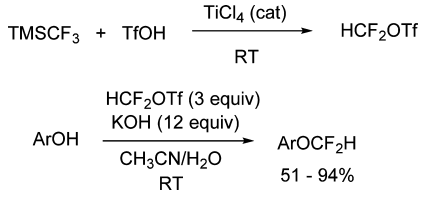
Scheme 1. Difluoromethyl Ethers from Difluorocarbene Reagents



significant ozone-depleter, this reaction has fallen out of favor for use in this or any other synthetic process. Two alternative and more recently developed methods use somewhat more exotic difluorocarbene-generating precursors, $(EtO)_2POCF_2Br$ or $PhCOCF_2Cl$, under very similar two-phase, basic conditions.[2,3]

Recently, an additional replacement for CHF_2Cl in this reaction has been found in the form of CHF_2OTf (Scheme 2).[4] When this new compound is used as the difluorocarbene precursor, again under conditions very similar to those of Miller and Thanassi, very good yields are obtained for a wide variety of phenol substrates.

Scheme 2. Hartwig–Fier HCF_2OTf Process



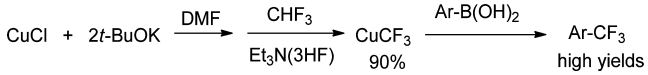
Although these three CHF_2Cl alternatives meet the needs of research chemists for laboratory synthesis of aryl difluoromethyl ethers (and thioethers), it nevertheless remains an important synthetic goal, particularly for the agrochemical industry, to find a less expensive difluorocarbene source that might accomplish similar results.

We believe that fluoroform (CHF_3) might well prove to be that precursor. Fluoroform is a byproduct of Teflon manufacture, but if desired, it could readily be manufactured as a commodity chemical by fluorine/chlorine exchange of chloroform; a gas with a boiling point of −83 °C, until recently it had attracted little interest as a synthetic fluorinated building block reagent, in spite of various reports by Shono, Normant, Troupel, and Langlois since 1991,[5−8] invoking its use to carry out nucleophilic trifluoromethylation of ketones. This earlier work set the stage for the recent series of important papers by Grushin, Prakash, and Shibata,[9−13] where they reported that one could conveniently utilize fluoroform in a great variety of nucleophilic trifluoromethylation reactions.

Grushin's work has thus far centered on the direct formation of CF_3Cu from fluoroform, followed by its utilization in nucleophilic trifluoromethylation reactions with aryl iodides, aryl boronic acids, and α-haloketones, as exemplified in Scheme 3.

Prakash's work involved direct trifluoromethylation of a variety of electrophilic substrates, with an example being given in Scheme 4, and Shibata was able to use a sterically demanding organic superbase to generate a stabilized trifluoromethyl anion

Scheme 3. Example of Grushin's Work



Received: July 2, 2013
Published: August 9, 2013

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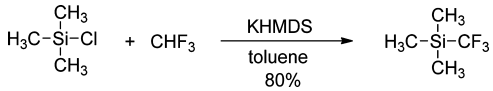
dx.doi.org/10.1021/jo401392f | J. Org. Chem. 2013, 78, 8904−8908

Scheme 4. Example of Prakash Chemistry



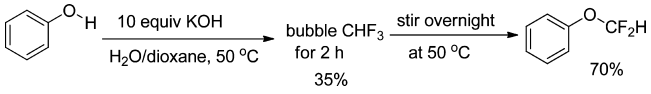
that will undergo nucleophilic addition to aromatic aldehydes and ketones.

However, to our knowledge, CHF_3 has never been reported as an effective reagent to elicit difluorocarbene chemistry. Mikami has recently reported the use of fluoroform to carry out "difluoromethylation of lithium enolates",[14] but difluorocarbene was not invoked as an intermediate in that reaction. Nevertheless, there are numerous reports of the trifluoromethyl anion, generated from organometallic precursors, undergoing α-elimination of fluoride ion to generate difluorocarbene in processes involving the synthesis of difluorocyclopropanes. The Seyferth reagent ($PhHgCF_3$) is perhaps the best known of these,[15] but Morrison also reported similar chemistry for $(CF_3)_2Cd$.[16] More recently, Hu's group reported the similar use of Me_3SiCF_3 as a source of difluorocarbene.[17,18] In all of these cases, the reaction of the so-generated difluorocarbene that was reported was addition to alkenes to form *gem*-difluorocyclopropanes.

In this paper, we report the use of fluoroform as difluorocarbene source in an efficient preparation of aryl difluoromethyl ethers and thioethers from the respective phenols and thiophenols. The reaction proceeds at atmospheric pressure, in a two-phase process, using KOH as base, conditions that are reminiscent of those reported earlier using CHF_2Cl as the difluorocarbene source.

Preliminary experiments, where CHF_3 was bubbled into a mixture of phenol and excess KOH in a dioxane/water mixture, gave very promising results (Scheme 5), and the conditions of

Scheme 5. Preliminary Results with Fluoroform



the reaction were optimized using 4-bromophenol, with the results of these experiments being given in Table 1. Varying the solvent, the cosolvent, the base, and the temperature, optimization reactions were carried out by bubbling CHF_3 through the solution for 2 h (which allowed addition of about 20 equiv of CHF_3), followed by immediate analysis using trifluoromethylbenzene as an internal standard.

Table 1. Optimization Experiments for Fluoroform Reaction

entry	base	cosolvent	*T*, °C	solvent	yield (%)
1	NaOH (10 equiv)	H_2O	50	diglyme	12
2	NaOH (10 equiv)	H_2O	50	THF	10
3	NaOH (10 equiv)	H_2O	50	DME	10
4	NaOH (10 equiv)	H_2O	50	dioxane	21
5	KOH (10 equiv)	H_2O	50	dioxane	27
6	*t*-BuOK (5 equiv)	none	50	dioxane	22
7	*t*-BuOK (6 equiv)	*t*-BuOH	50	dioxane	21
8	NaH (1.5 equiv)	none	rt	DMF	0
9	KOH (20 equiv)	H_2O	50	dioxane	31
10	KOH (25 equiv)	H_2O	50	dioxane	31
11	KOH (10 equiv)	H_2O	70	CH_3CN	13
12	KOH (10 equiv)	H_2O	70	dioxane	22
13	KOH (10 equiv)	H_2O	rt	CH_3CN	36
14	KOH (20 equiv)	H_2O	rt	dioxane	25
15	KOH (15 equiv)	H_2O	rt	CH_3CN	40
16	KOH (20 equiv)	H_2O	rt	CH_3CN	38

On the basis of these optimization experiments, it was found that KOH was clearly the best base to use, and that a two-phase system was superior to the use of homogeneous conditions (i.e., entries 1, 6, 7, and 8). Acetonitrile was determined to be the best solvent at room temperature (entry 15), whereas dioxane appeared to operate best at 50 °C (entry 5). In order to maximize conversion of the phenol substrates, the times of reaction and the amounts of fluoroform introduced were increased. Bubbling was continued for a total of 4 h for the dioxane reaction, with the reaction then being stirred at 50 °C for an additional hour (Method A), whereas 2 h was sufficient for the room temperature reaction in acetonitrile, plus the 1 h of additional stirring (Method B).

Because fluoroform has poor solubility in both acetonitrile and 1,4-dioxane under these reaction conditions, it seemed probable that most of the fluoroform that was introduced would pass through the reaction mixture unreacted. In order to estimate the amount of fluoroform actually consumed under the reaction conditions, an effort was made to trap the unreacted fluoroform. Thus, experiments were carried out using an apparatus with a slight N_2 flow that would carry the unused fluoroform into a tube trap cooled in liquid N_2 (depicted in the Supporting Information). When fluoroform was introduced from a weighed cylinder under conditions of Method A, analysis of the trap indicated that only 8 equiv of fluoroform was consumed, with 52 additional equiv being recovered in the trap. When the same procedure was repeated using Method B, 14.6 equiv of fluoroform was found to have been consumed, with 26.8 equiv of fluoroform being recovered in the trap (Scheme 6). Because of the uncertainty of the efficiency of the trapping of CHF_3, the number of equivalents reported as consumed in the reaction must be considered a *maximum* value. Nevertheless, there can be little doubt that at least some of the generated difluorocarbene that is generated must be destroyed by its known reaction with the hydroxide ion to form potassium formate.[2]

A broad selection of phenols and thiophenols was examined using Methods A and/or B, with the results being given in Table 2. It can be seen that the reaction has broad scope for the preparation of both difluoromethoxyarenes (**1a**–**1l**) and difluorothiomethoxyarenes (**2a**–**2d**).

The identities of the mostly known products were initially determined by ^{19}F NMR but were also confirmed by examination of their proton, and for some their carbon spectra. Moderate to good yields of difluoromethoxyarenes were obtained using both Method A and Method B. For the preparation of compounds **2g** and **2i**, the starting phenol substrates were not soluble in dioxane using the conditions of Method A. Therefore, Method B was used to obtain moderate yields of these compounds. Difluorothiomethoxyarenes could also be obtained in good yields using Method A, but additional base was required to obtain optimum yields. Yields of no more than 20% could be obtained when using *p*-nitrophenol as substrate, and the presence of amino or acetamido substituents with at least one N–H bond inhibited the reaction almost completely. 4-(*N*,*N*-Dimethylamino)phenol yielded 40% of product. No improvements in yield were observed when phase transfer agents such as benzyltrimethylammonium bromide or

dx.doi.org/10.1021/jo401392f | J. Org. Chem. 2013, 78, 8904–8908

Scheme 6. Two Methods for the Fluoroform Reaction

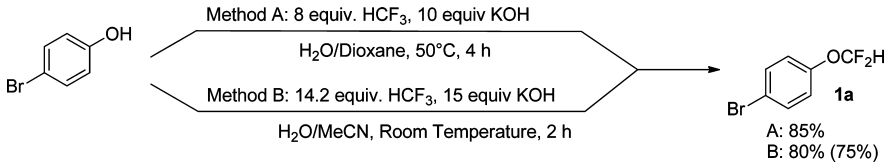
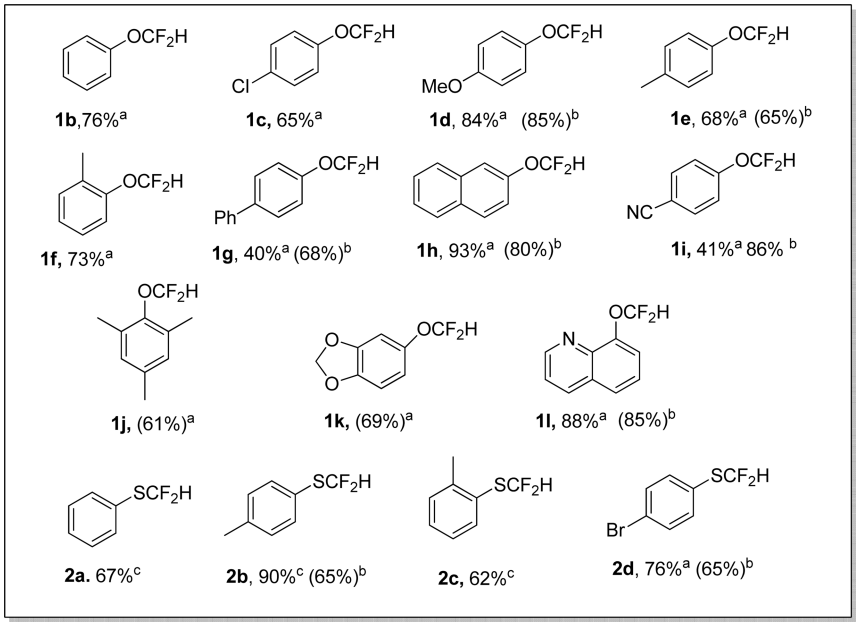


Table 2. Products and Yields from Phenols and Thiophenols



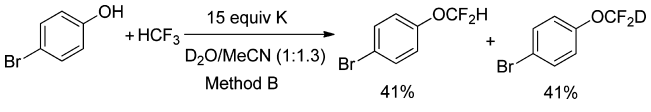
Parentheses indicate isolated yields. Other yields were calculated using ^{19}F NMR using trifluorotoluene as internal standard. [a]Yields obtained using Method A. [b]Yields obtained using Method B. [c]Using Method A but 20 equiv of KOH.

tris(2-(2-methoxyethoxy)ethyl)amine were added to the mixture, and when the reaction was carried out under pressure, in a closed system, the yields decreased dramatically.

The mechanism of the reaction almost certainly involves the intermediacy of difluorocarbene, which would be formed by deprotonation of CHF_3 by hydroxide followed by loss of fluoride ion. Reaction of the phenoxide with the intermediate CF_2, followed by protonation of the resultant carbanion, would produce the product. Direct nucleophilic substitution on CHF_3 by phenolate is not a mechanistic option because, under homogeneous conditions in acetonitrile, such substitution was not observed. Indeed, to our knowledge, there are no reported examples of a direct nucleophilic displacement of a fluoride ion from fluoroform. Although the proposed difluorocarbene intermediate was not able to be trapped under the reaction conditions by reactive alkene, α-methylstyrene, we still favor the carbene mechanism. It is likely that hydroxide and phenoxide simply compete better than the alkene in trapping the carbene.

Evidence for the proposed mechanism was provided by carrying out the reaction in D_2O instead of H_2O, as shown in Scheme 7. The unexpectedly significant proton contamination

Scheme 7. Reaction Using D_2O Instead of H_2O



that was observed in the product could be from product formation occurring in the relatively "dry" acetonitrile phase where CHF_3 could be the source of the proton. When the D_2O experiment was carried out using Method A, in dioxane, which would probably contain more D_2O, the ratio of $PhOCF_2D$ to $PhOCF_2H$ was 3:1. When difluoromethyl ether product **1a** is subjected to KOH/D_2O under the reaction conditions, it is not observed to undergo D/H exchange, so the carbene mechanism provides the best explanation for deuterium incorporation.

In conclusion, the results obtained in this work have demonstrated that fluoroform, a non-ozone-depleting, non-toxic, and inexpensive gas, can be used as the difluorocarbene source in a convenient process for conversion of phenols and thiophenols to their difluoromethoxy and difluorothiomethoxy derivatives. These two-phase, very clean reactions, carried out at moderate temperatures and atmospheric pressure, provide moderate to good yields, which should make this process very competitive with other methods for preparing these important compounds.

EXPERIMENTAL SECTION

General Information. The NMR spectra for ^1H, ^{13}C, and ^{19}F were recorded in $CDCl_3$ at 300, 75.46, and 282 MHz, respectively, with chemical shifts being reported in parts per million downfield from the respective internal standards (TMS for proton and carbon and $CFCl_3$ for fluorine spectra). HRMS data were obtained on a DSQ MS instrument.

Representative Procedures for the Conversion of Phenols to Difluoromethoxyaromatics. *Preparation of 4-Bromo(difluoromethoxy)benzene (**1a**). Method A.* A 25 mL, three-necked round-

dx.doi.org/10.1021/jo401392f | J. Org. Chem. 2013, 78, 8904−8908

bottomed flask was equipped with a stir bar. The vessel was then sealed with three septa, and the middle septum was fitted with a T tube in order to maintain a 1 atm N_2 environment, as well as to allow gases to escape from the flask. Escaping gases were passed through a liquid N_2-cooled trap and then through a paraffin oil bubbler to the atmosphere. A very small flow of N_2 was maintained throughout the reaction. Then, to the flask were added potassium hydroxide (1.68 g, 30 mmol, 10 equiv) and water (1.68 g), and the mixture was stirred until the KOH was almost completely dissolved. Then 4-bromophenol (0.52g, 3 mmol) was added, and the mixture stirred for 30 min, after which 1,4-dioxane (10 mL) was added via syringe and the mixture was heated to 50 °C. Fluoroform was then bubbled slowly into the mixture for 4 h from a small weighed cylinder, after which the resulting mixture was stirred for one additional hour with nitrogen flow being maintained throughout the entire process. Weighing of the trap indicated that 11 g (52 equiv) of CHF_3 had been condensed. Weighing of the source cylinder indicated that 12.4 g had been introduced into the flask, and that 1.4 g (8 equiv) had apparently been consumed in the reaction. The reaction was then quenched with water and the product extracted with ethyl acetate. The yield of the liquid product **1a** (85%) was measured by ^{19}F NMR, using trifluoromethylbenzene (15 mmol) as internal standard.

Method B. Using an identical apparatus as for Method A, potassium hydroxide (2.52 g, 45 mmol, 15 equiv) and water (2.52 g) were added to the reaction vessel and the mixture was allowed to stir until the potassium hydroxide was almost completely dissolved. Then, 4-bromophenol (0.52 g, 3 mmol) was added and the mixture stirred for 30 min, after which acetonitrile (10 mL) was added via syringe and the mixture stirred at room temperature. Fluoroform was then bubbled slowly into the mixture for 2 h, after which the resulting mixture was stirred for one additional hour. Analysis as described for Method A revealed that 5.6 g (26.8 equiv) had been condensed in the trap, with a total of 3 g (14.6 equiv) having been consumed in the reaction. After being quenched with water and extracted with ethyl acetate, the yield of the liquid product **1a** (80%) was measured by ^{19}F NMR.

Larger-Scale Reaction. A 250 mL, three-necked round-bottomed flask was equipped as described for Method A. Then, under an inert N_2 atmosphere, potassium hydroxide (25.2 g, 450 mmol, 15 equiv) and water (25.2g) were added to the vessel and the mixture was allowed to stir until the potassium hydroxide was almost completely dissolved. Then, 4-bromophenol (5.2 g, 30 mmol) was added and the mixture stirred for 30 min, after which acetonitrile (100 mL) was added via syringe and the mixture stirred at room temperature. Fluoroform was then bubbled slowly into the mixture for 10 h, with the resulting mixture being allowed to stir overnight. Analysis in the usual manner indicated that 56 g (26.8 equiv) of CHF_3 had been trapped, with 31 g (14.6 equiv) being consumed in the reaction. Then the reaction was quenched with water and extracted with ethyl acetate. The ethyl acetate layer was separated and concentrated, and additional impurities were removed via column chromatography on silica gel using an 80:20 mixture of hexanes/methylene chloride to provide 5.0 g (75%) of liquid product, 4-bromo(difluoromethoxyl)benzene, **1a**.

*4-Bromo(difluoromethoxy)benzene (**1a**):* ^1H NMR, δ 7.4 (d, J = 8.1 Hz, 2H), 6.9 (d, J = 8.1 Hz, 2H), 6.42 (t, $^2J_{HF}$ = 69.2 Hz, 1H); ^{19}F NMR, δ −81.5 (d, $^2J_{FH}$ = 71.5 Hz, 2F); ^{13}C NMR, δ = 150.0, 132.8, 121.5, 118.4, 115.6 (t, $^1J_{CF}$ = 260 Hz). The NMR data were consistent with those previously reported.[19,20]

*(Difluoromethoxy)benzene (**1b**):* Yields (Method A) 76% and (Method B) 68% (both by NMR); ^1H NMR, δ 7.25−7.0 (m, 5H), 6.42 (t, $^2J_{HF}$ = 69 Hz, 1H); ^{19}F NMR, δ −81 (d, $^2J_{FH}$ = 56.4 Hz, 2F). The NMR data were consistent with those previously reported.[19,20]

*4-Chloro(difluoromethoxy)benzene (**1c**):* Yield (Method A) 65% (by NMR); ^1H NMR, δ 7.4 (d, J = 8.1 Hz, 2H), 7.0 (d, J = 8.1 Hz, 2H), 6.42 (t, $^2J_{HF}$ = 69.2 Hz, 1H); ^{19}F NMR, δ −81.4 (d, $^2J_{FH}$ = 71.5 Hz, 2F). The NMR data were consistent with those previously reported.[19,20]

*4-Methoxy(difluoromethoxy)benzene (**1d**):* Yields (Method A) 84% (by NMR) and (Method B) liq, 0.44 g (85%) isolated; ^1H NMR, δ 7.1 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 6.41 (t, $^2J_{HF}$ = 74.4 Hz, 1H), 3.79 (s, 3H); ^{19}F NMR, δ −80.5 (d, $^2J_{FH}$ = 74.4 Hz, 2F); ^{13}C NMR, δ 157.2, 144.6 (t, J = 3 Hz), 121.2, 116.3 (t, J = 260 Hz), 114.7, 55.5). The NMR data were consistent with those previously reported.[19,20]

*4-Methyl(difluoromethoxy)benzene (**1e**):* Yields (Method A) 68% (by NMR) and (Method B) liq, 0.31 g (65%) isolated; ^1H NMR, δ 7.15 (d, J = 9.0 Hz, 2H), 7.0 (d, J = 8.4 Hz, 2H), 6.4 (t, $^2J_{HF}$ = 74.4 Hz, 1H), 2.25 (s, 3H); ^{19}F NMR, δ −80.4 (d, $^2J_{FH}$ = 74.4 Hz, 2F). The NMR data were consistent with those previously reported.[19]

*2-Methyl(difluoromethoxy)benzene (**1f**):* Yield (Method A) 73% (by NMR); ^1H NMR, δ 7.1 (d, J = 8.1 Hz, 2H), 6.92 (d, J = 8.1 Hz, 2H), 6.4 (t, $^2J_{HF}$ = 75 Hz, 1H), 2.22 (s,3H); ^{19}F NMR, δ −82.5 (d, $^2J_{FH}$ = 71.5 Hz, 2F). The NMR data were consistent with those previously reported.[19]

*4-Phenyl-(difluoromethoxy)benzene (**1g**):* Yields (Method A) 40% (by NMR) and (Method B) liq, 0.45 g (68%) isolated; ^1H NMR, δ 7.57 (m, 4H), 7.45 (m, 2H), 7.37 (m, 1H), 7.15 (d, J = 9 Hz, 2H), 6.55 (t, $^2J_{HF}$ = 74.1 Hz, 1H); ^{19}F NMR, δ −86.4 (d, $^2J_{FH}$ = 74.4 Hz, 2F); ^{13}C NMR, δ 150.8, 140.1, 138.6, 129.0, 128.6, 127.6, 127.1, 119.8, 115.9 (t, $^1J_{CF}$ = 260 Hz). The NMR data were consistent with those previously reported.[21]

*2-(Difluoromethoxy)naphthalene (**1h**):* Yields (Method A) 93% (by NMR) and (Method B) liq, 0.47 g (80%) isolated; ^1H NMR, δ 7.85 (m, 3H), 7.58 (m, 3H), 7.3 (m, 1H), 6.66 (t, $^2J_{HF}$ = 74.1 Hz, 1H); ^{19}F NMR, δ −80.4 (d, $^2J_{HF}$ = 73.0 Hz, 2F); ^{13}C NMR, δ 149.0 (t. J = 2.5 Hz), 133.8, 131.1, 130.1, 127.8, 127.5, 126.9, 125.7, 119.7, 116.2 (t, $^1J_{FC}$ = 260 Hz), 115.3. The NMR data were consistent with those previously reported.[20,22,23]

*4-Cyano(difluoromethoxy)benzene (**1i**):* Yields (Method A) 41% and (Method B) 86% (both by NMR); ^1H NMR, δ 7.6 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 6.59 (t, $^2J_{HF}$ = 75 Hz, 1H); ^{19}F NMR, δ −85.0 (d, $^2J_{FH}$ = 71.5 Hz, 2F). The NMR data were consistent with those previously reported.[19]

*2,4,6-Trimethyl(difluoromethoxy)benzene (**1j**):* Yield (Method A) liq, 0.34 g (61%) isolated; ^1H NMR, δ 6.89 (s, 2H), 6.3 (t, $^2J_{HF}$ = 75.3 Hz, 1H), 2.29 (s, 9H); ^{19}F NMR, δ −78.5 (d, $^2J_{FH}$ = 74.7 Hz, 2F); ^{13}C NMR, δ 146.6, 135.7, 131.2, 129.7, 117.8 (t, $^1J_{FC}$ = 260 Hz), 20.6, 16.5; HRMS (EI) m/z calcd for $C_{10}H_{12}OF_2$ 186.0856; found 186.0864.

*5-(Difluoromethoxy)benzo[d][1,3]dioxole (**1k**):* Yield (Method A) liq, 0.39 g (69%) isolated; ^1H NMR, δ 6.69 (d, J = 8.4 Hz, 1H), 6.67 (d, J = 0.6 Hz, 1H), 6.61 (dd, J = 0.6 Hz, J = 8.4 Hz,1H), 6.40 (t, $^2J_{FH}$ = 73.3 Hz, 1H), 5.98 (s, 2H); ^{19}F NMR, δ −80.7 (d, $^2J_{FH}$ = 73.3 Hz); ^{13}C NMR, δ 148.2, 145.5 (t, J = 3.1 Hz), 145.32, 116.2 (t, $^1J_{FC}$ = 261 Hz), 112.6, 108.0, 102.7, 101.8. The NMR data were consistent with those previously reported.[4]

*8-(Difluoromethoxy)quinoline (**1l**):* Yields (Method A) 88% (by NMR) and (Method B) solid, mp 68−72 °C; 0.50 g (85%) isolated; ^1H NMR, δ 7.11 (t, $^2J_{FH}$ = 75.6 Hz, 1H), 7.50 (m, 3H), 7.70 (m, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.98 (m, 1H); ^{19}F NMR, δ −81.94 (d, $^2J_{HF}$ = 75.6 Hz, 2F). The data were consistent with those previously reported.[20]

*(Difluorothiomethoxy)benzene (**2a**):* Yield (Method A) 67% (by NMR); ^1H NMR, δ 6.85 (t, 1H, $^2J_{FH}$ = 57.0 Hz), 7.36−7.48 (m, 3H), 7.56−7.64 (m, 2H); ^{19}F NMR, δ −93.58 (d, 2F, $^2J_{HF}$ = 58.7 Hz). The NMR data were consistent with those previously reported.[24]

*4-Methyl(difluorothiomethoxy)benzene (**2b**):* Yields (Method A) 90% (by NMR) and (Method B) liq, 0.34 g (65%) isolated; ^1H NMR, δ 7.49 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 6.68 (t, $^2J_{FH}$ = 56.4 Hz, 1H), 2.27 (s, 3H); ^{19}F NMR, δ −91.7 (d, $^2J_{HF}$ = 56.7 Hz, 2F). The NMR data were consistent with those previously reported.[22]

*2-Methyl(difluorothiomethoxy)benzene (**2c**):* Yield (Method A) 62% (by NMR); ^1H NMR, δ 7.41, 7.19 (m, 4H), 6.67 (t, $^2J_{FH}$ = 56.4 Hz, 1H), 2.34 (s, 3H); ^{19}F NMR, δ −92.3 (d, $^2J_{HF}$ = 56.7 Hz, 2F). The NMR data were consistent with those previously reported.[22]

*4-Bromo(difluorothiomethoxy)benzene (**2d**):* Yields (Method A) 76% (by NMR) and (Method B) liq, 0.47 g (65%) isolated; ^1H NMR, δ 7.53 (d, J = 11 Hz, 2H), 7.45 (d, J = 11 Hz, 2H), 6.80 (t, $^2J_{FH}$ = 57.0 Hz, 1H); ^{13}C NMR, δ 120.3 ($^1J_{FC}$ = 277 Hz), 124.7, 124.9, 132.6,

dx.doi.org/10.1021/jo401392f | J. Org. Chem. 2013, 78, 8904−8908

136.9; ^{19}F NMR, δ −91.6 (d, $^{2}J_{HF}$ = 57.0 Hz, 2F). The NMR data were consistent with those previously reported.[19]

■ ASSOCIATED CONTENT

Supporting Information

Diagram of apparatus; NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support of this research by a grant from Syngenta is acknowledged by the authors with thanks.

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