JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

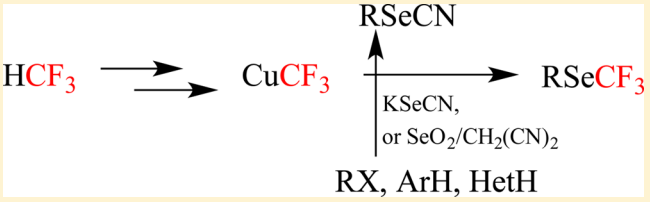
General Synthesis of Trifluoromethyl Selenides Utilizing Selenocyanates and Fluoroform

Shay Potash and Shlomo Rozen*

School of Chemistry, Tel-Aviv University, Tel-Aviv 69978, Israel

Supporting Information

ABSTRACT: Trifluoromethylated selenoethers are quite rare despite their potential and the interest that they generate. A series of trifluoromethylseleno derivatives, either primary and secondary aliphatic or aromatic and heterocyclic, is described herein by the reaction of easily prepared organic selenocyanates and $CuCF_3$. Another beneficial feature of this reaction is the use of fluoroform as a source for the CF_3 group, a compound whose chemistry is currently being intensively researched because it is a potent greenhouse gas that should not be released into the atmosphere.



INTRODUCTION

The trifluoromethyl group is of great interest because, among other features, it possesses remarkable biological properties, probably due to the increased lipophilicity that it grants to molecules attached to it.[1]

Thus, trifluoromethylation has been the subject of remarkable research efforts, especially over the last 2 decades. Among the various trifluoromethyl compounds, trifluoromethylated ethers and thioethers, $ROCF_3$ and $RSCF_3$, respectively, have attracted special interest because these families have some of the highest lipophilicity parameter values.[2] One general approach for their preparation is through the formation of carbon−fluorine bonds at specific sites,[3] whereas another concentrates on transferring the whole CF_3 group from an appropriate reagent.[4,5]

Although the procedures for the preparation of the aforementioned trifluoromethylated families are quite general and well-established, considerably less effort has been devoted to the development of synthetic methods toward trifluoromethylated selenoethers. Attaining this goal has become increasingly desirable because of their medicinal potential[6] and expected high lipophilicity[7] as well as the rapid expansion of organo selenium chemistry.[6,8]

Yagupolskii developed a trifluoromethylselenation applicable for some aryl iodides.[9] This synthetic method uses $CuSeCF_3$, made from copper and $CF_3SeSeCF_3$, which, in turn, is difficult to prepare.[10] Several groups reported the synthesis of $PhSeCF_3$ (**2e**) by the reaction of different trifluoromethylating agents with PhSeSePh (**3e**).[11] These reactions, aside from being limited to the formation of **2e**, suffer from the fact that half of the organic diselenide is generally lost in the form of a leaving group. Recently, a general procedure was reported for the synthesis of trifluoromethyl selenoethers by substituting the appropriate iodides or bromides[12] using the $[(bpy)Cu(SeCF_3)]_2$ complex, which is prepared in a two-pot reaction from $TMSCF_3$, CuI, KF, Se, and bipyridine in 41% yield.

Fluoroform, CHF_3, is, of course, one of the most attractive trifluoromethylation agents. It is a side product of the manufacturing of Teflon, PVDF, refrigerants, and fire extinguishing agents and is generated in large volumes of over 20 000 tons yearly.[5a,13] Unfortunately, although nontoxic and ozone-friendly, it is still a very potent greenhouse gas. As a result, the Kyoto protocol of 1997 obligated industrialized countries to reduce its emissions. Although it can be destroyed through a costly incineration process, it is preferable to use it as a feedstock for manufacturing, but this is a nontrivial challenge. Therefore, large quantities of it are stored without a great demand, turning CHF_3 into an inexpensive reagent indeed.[13]

In an effort to put this gas to good use, considerable research energy has been invested in turning it into a synthetic reagent.[14] Still, its current scope in organic chemistry is somewhat limited and confined mostly to formations of $C-CF_3$ bonds.[15] Recently, work in this field led to trifluoromethylation of B, Si, and S centers in addition to carbon ones.[13] An important reagent is fluoroform-derived $CuCF_3$, which has been used as a general reagent for the formation of different $C-CF_3$ bonds and enables convenient usage of fluoroform on a large scale.[5,16]

To develop a general synthesis of $RSeCF_3$ using the nucleophilic trifluoromethyl moiety of $CuCF_3$, a good electrophilic selenium source is needed. Organic selenocyanates, RSeCN, can fulfill this requirement.[17] Such compounds are easy to prepare by nucleophilic substitution of alkyl halides[18] with relatively inexpensive KSeCN or by electrophilic substitutions with a $SeO_2/CH_2(CN)_2$ mixture.[19]

RESULTS AND DISCUSSION

A $CuCF_3$ solution was prepared by following Grushin's procedure[5] by bubbling fluoroform gas through a DMF solution of CuCl and *t*-BuOK, with a slight variation in order to conduct

Received: October 6, 2014
Published: November 5, 2014

the reaction under atmospheric pressure and without any $Et_3N/3HF$. The resultant $CuCF_3$ solution (1.5 mol equiv) was reacted with 1-selenocyanatotetradecane (**1a**),[18] and the previously unknown *n*-tetradecyl(trifluoromethyl)selane (**2a**) was formed in quantitative yield after 1.5 h at room temperature. The progress of this reaction was monitored by ^{19}F NMR (vs a calibrated amount of $PhCF_3$).

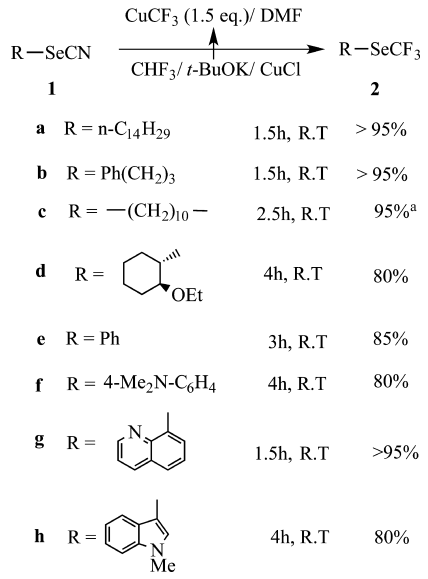
The $CuCF_3$ solution was reacted with (3-selenocyanatopropyl)-benzene (**1b**)[18] as well, quantitatively forming (3-phenylpropyl)-trifluoromethylselane (**2b**). In order to demonstrate the efficiency of this reaction, doubly selenated 1,10-diselenocyanatodecane (**1c**)[18] was reacted with 3 mol equiv of fluoroform-derived $CuCF_3$ (50% excess) for 2.5 h at room temperature, yielding the previously unknown 1,10-bis(trifluoromethylseleno)decane (**2c**) in 95% yield.

Cyclohexyltrifluoromethylselanes are of special interest because secondary trifluoromethylselanes in general and cyclohexyl ones in particular are not known. The reaction of cyclohexene with KSeCN and $CuCl_2$ in ethanol yielded mainly *trans*-1-ethoxy-2-selenocyanatocyclohexane (**1d**), with less than 10% being the *cis* isomer. The reaction of $CuCF_3$ with **1d** showed that the stereochemistry around the C−Se bond is retained, and the secondary trifluoromethylseleno ether, *trans*-(2-ethoxycyclohexyl)trifluoromethylselane (**2d**), was formed in 80% yeild in 4 h at RT.

Aromatic selenocyanates are also reactive toward the nucleophilic trifluoromethylating reagent $CuCF_3$. When commercial PhSeCN (**1e**) was added to this fluoroform-derived agent, the reaction was completed in 3 h, and phenyltrifluoromethylselane (**2e**) was formed in 85% yield. Trifluoromethylation is also suitable for electron-rich aromatic selenocyanates, which are readily prepared by electrophilic aromatic substitution. For example, treatment of *N*,*N*-dimethylaniline with selenium(IV) oxide and malononitrile gives para-substituted *N*,*N*-dimethyl-4-selenocyanatoaniline (**1f**).[19] When this compound was reacted with the $CuCF_3$ suspension for 4 h at RT, the *N*,*N*-dimethyl-4-(trifluoromethylselanyl)aniline (**2f**) was formed in 80% yield. The trifluoromethylation of selenocyanates with $CuCF_3$ is also effective with electron-poor aromatics, as is evident from the reaction of 8-selenocyanatoquinoline (**1g**)[20] with 1.5 equiv of fluoroform-derived $CuCF_3$, which led to quantitative formation of the previously unreported 8-(trifluoromethylselanyl)-quinoline (**2g**). In this case, the reaction rate was faster and completed within 1.5 h, probably due to copper−nitrogen interactions, which could hold the trifluoromethylating agent closer to the reaction center. Nitrogen heterocyclic substrates such as electron-rich 1-methyl-3-selenocyanato-1*H*-indole (**1h**), prepared by direct electrophilic aromatic substitution, also reacted with $CuCF_3$ to form the new 1-methyl-3-(trifluoromethylselanyl)-1*H*-indole (**2h**) in 80% yield after 4 h at RT (Scheme 1).

Although selenocyanates are probably the best starting point for the synthesis of trifluoromethylselenides, occasionally, diselenides (RSe−SeR) could be more readily available or prepared by air oxidation of the corresponding selenols (RSeH) and hence from the corresponding Cu or K salts. These diselenides[21] could also serve as substrates for trifluoromethyl selenides by using almost the same procedure as that with selenocyanates, and the reactions are even somewhat faster, as shown for **2e** and **2i**.[17] Although, mole per mole, the yields were about 90%, when based on the Se atoms, they are around 45%, with the balance being the corresponding selenide salts, RSeCu/K, ejected as the leaving group. These salts, of course,

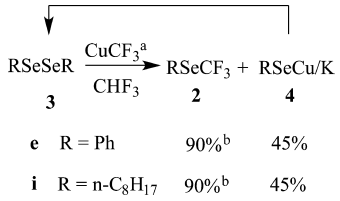
Scheme 1. From Selenocyanates to Trifluoromethyl Selenoethers



[a]Using 3 mol equiv of $CuCF_3$.

are easy to protonate by acidic workup to the corresponding selenols, RSeH, which, in turn, can be oxidized by air to the parent diselenides, **3**. Because the recovery is a simple, high-yield process, the recovered diselenides can be reused to form trifluoromethyl selenides, thus increasing the yield and minimizing waste (Scheme 2).

Scheme 2. From Diselenides to Trifluoromethyl Selenoethers



[a]1.5 mol equiv, 1 h, RT. [b]When calculated mole per mole; 45% when based on the Se atom.

■ CONCLUSIONS

A diverse series of trifluoromethylseleno derivatives was prepared from the corresponding alkyl, aryl, or heterocyclic selenocyanates. Because these trifluoromethylseleno compounds are expected to be highly lipophilic, their popularity is on the rise, and it was important to find a general and simple procedure that combines an easily accessible selenium source coupled with an attractive trifluoromethylating agent. These requirements are satisfied in the reaction of selenocyanates and fluoroform-derived $CuCF_3$. It was also shown that similar conditions are compatible for the reaction with diselenides serving as starting materials, resulting again in the corresponding trifluoromethylseleno compounds.

■ EXPERIMENTAL SECTION

General Procedures. The fluoroform cylinder was purchased from commercial sources. ^1H, ^{19}F, and ^{13}C NMR spectra were obtained with $CDCl_3$ as a solvent at 400, 376, and 100 MHz, respectively,

dx.doi.org/10.1021/jo5022844 | J. Org. Chem. 2014, 79, 11205−11208

with Me_4Si as an internal standard for the ^1H and ^{13}C NMR and $CFCl_3$ for the ^{19}F NMR spectra. HRMS samples of **2f** and **2g** were measured under ASAP conditions. In all other cases, this method could not detect any molecular ion, so we successfully used Amirav's supersonic GC−MS technique, which, without practically any exceptions, could reveal such ions. In these cases, the isotope abundance analysis provided very satisfactory results, as shown for the specific compounds. This type of analysis confirmed the proposed elemental formulas, as it ranked them first, hence making them the best choice, with very good matching factors of better than 940 (out of 999).[22]

Selenocyanates Formation. We have referenced the known selenocyanates. In particular, we have prepared primary selenocyanates **1a** and **1b** via the substitution of 1-bromotetradecane and 1-bromo-3-phenylpropane with 1.2 equiv of potassium selenocyanate in a refluxing ethanolic solution for 1 h (>95% yields). Bis-selenocyanate **1c** was similarly prepared using 2.5 equiv of potassium selenocyanate and 1,10-dibromodecane in 90% yield. Cyclic selenocyanate **1d** was prepared by the reaction of cyclohexene with 2 equiv of copper(II) chloride and potassium selenocyanate, each in refluxing ethanol, in 60% yield.[23] Selenocyanate **1g** was prepared by the diazotation of 8-aminoquinoline followed by substitution with potassium selenocyanate at 0 °C (60% yield). The preparation of electron-rich selenocyanates **1f** and **1h** was achieved by electrophilic aromatic substitutions using selenium(IV) oxide and malononitrile in DMSO, as described in ref 19, in 85 and 90% yields, respectively.

General Trifluoromethylation Procedure. To a two-necked flask equipped with a glass pipet inlet for argon was inserted 40 mL of dry DMF, and the solvent was degassed for 5 min followed by the addition of 4.7 g of finely ground potassium *tert*-butoxide. The suspension was stirred for about 5 min until most of the solid was dissolved. Two grams of copper(I) chloride was added, and the suspension turned black within a minute and was vigorously stirred while argon was passed through it for 1 h at room temperature. The argon inlet was replaced with a fluoroform inlet, and this gas was bubbled through the black solution for 5 min at a rate of about 600 mL/min (about 6 mol equiv, based on Cu). This procedure produced about 16 mmol of $CuCF_3$ (calibrated using ^{19}F NMR with $PhCF_3$ as a standard). A measured volume was added to the DMF solution of the selenocyanate, ensuring about a 50% excess of $CuCF_3$ over the starting selenocyanate, and the suspension was stirred under an argon atmosphere for 3−5 h until completion (monitored by TLC or UV for **2e**−**h**). The suspension was added to cold water and extracted with ether. The ethereal solution was passed through a short pad of Celite to remove inorganic salts and evaporated. The product was purified by flash column chromatography using pentane (compounds **2a**−**c**, **e**) or pentane/ether mixtures (compounds **2d**, **f**−**h**). Specific amounts of selenocyanates, $CuCF_3$ suspension, reaction times, and temperatures are specified herein. Because these reactions were conducted on a small scale, excess fluoroform was not destroyed; for large-scale applications, a continuous flow process for the preparation and reaction of $CuCF_3$ was reported.[16]

Tetradecyl(trifluoromethyl)selane (2a). Prepared from selenocyanate **1a** (0.80 g, 2.9 mmol) and about 4.0 mmol of $CuCF_3$ as described in the general procedure (quantitative yield, 0.91 g, clear oil). ^1H NMR 2.98 (2 H, t, J = 7.6 Hz), 1.78 (2 H, quin, J = 7.6 Hz), 1.40 (2 H, m), 1.26 (20 H, m), 0.88 (3 H, t, J = 6.4 Hz) ppm. ^{13}C NMR 122.8 (q, J = 328 Hz), 32.0, 30.3, 29.7−29.4 (8 C), 29.0, 25.9, 22.8, 14.2 ppm. ^{19}F NMR −39.5 ppm (3 F, s). The common MS methods failed to show any molecular peak. Amirav's supersonic GC-MS revealed a strong molecular ion peak of m/z 340.1 $(M)^+$ with an isotope abundance analysis matching factor of 998 out of 999. Anal. Calcd for $C_{15}H_{29}F_3Se$: C, 52.17; H, 8.46; F, 16.5. Found: C, 51.95; H, 8.45; F, 16.11.

(3-Phenylpropyl)(trifluoromethyl)selane (2b).[12] Prepared from selenocyanate **1b** (0.55 g, 2.4 mmol) and fluoroform-derived $CuCF_3$ (about 3.7 mmol) as described in the general procedure (quantitative yield, 0.65 g, clear oil). ^1H NMR 7.30−7.32 (2 H, m), 7.18−7.24 (3 H, m), 2.99 (2 H, t, J = 7.2 Hz), 2.75 (2 H, t, J = 7.6 Hz), 2.14 (2 H, quin, J = 7.2 Hz), ppm. ^{13}C NMR 141.6, 128.6, 128.5, 126.3, 122.7 (q, J = 328 Hz), 35.5, 31.8, 25.2 ppm. ^{19}F NMR −32.7 ppm (3 F, s).

1,10-Bis(trifluoromethylseleno)decane (2c). Prepared from selenocyanate **1c**[18] (0.80 g, 2.3 mmol) and fluoroform-derived $CuCF_3$ (about 5.7 mmol) as described in the general procedure (95% yield, 0.95 g, clear oil). ^1H NMR 2.98 (4 H, t, J = 7.2 Hz), 1.78 (2 H, quin, J = 7.6 Hz), 1.37−1.401 (4 H, m), 1.25−1.37 (8 H, m) ppm. ^{13}C NMR 122.8 (q, J = 330 Hz), 30.3, 29.6, 29.3, 28.9, 25.9 ppm. ^{19}F NMR −32.8 ppm (3 F, s). The common MS methods failed to show any molecular peak. Amirav's supersonic GC-MS revealed a strong molecular ion peak of m/z 426.0 $(M)^+$ with an isotope abundance analysis matching factor of 940 out of 999.

***trans*-(2-Ethoxycyclohexyl)(trifluoromethyl)selane (2d).** Prepared from selenocyanate **1d**[23] (1.0 g, 4.1 mmol) and fluoroform-derived $CuCF_3$ (about 6.5 mmol) as described in the general procedure (80% yield, 0.95 g, clear oil). ^1H NMR 3.28−3.68 (2 H, m), 2.04−2.35 (1 H, m), 1.60−1.79 (2 H, m), 1.18−1.43 (7 H, m), 0.83−0.91 (3 H, m) ppm. ^{13}C NMR 123.2 (q, J = 329 Hz), 96.2, 80.1, 64.5, 47.6, 31.2, 25.8, 23.2, 15.4 ppm. ^{19}F NMR −30.2 ppm (3 F, s). The common MS methods failed to show any molecular peak. Amirav's supersonic GC-MS revealed a strong molecular ion peak of m/z 270.0 $(M)^+$ with an isotope abundance analysis matching factor of 980 out of 999.

Phenyl(trifluoromethyl)selane (2e).[11] Prepared from commercial selenocyanate **1e** (3.00 g, 16.4 mmol) and fluoroform-derived $CuCF_3$ (about 24.7 mmol) as described in the general procedure (85% yield, 3.15 g, clear oil). ^1H NMR 7.74−7.77 (2 H, m), 7.46−7.50 (1 H, m), 7.38−7.42 (2 H, m) ppm. ^{13}C NMR 137.1, 130.4, 129.6, 122.6, 122.6 (q, J = 330 Hz) ppm. ^{19}F NMR −34.8 ppm (3 F, s).

***N,N*-Dimethyl-4-(trifluoromethylselanyl)aniline (2f).** Prepared from selenocyanate **1f**[18] (1.00 g, 4.4 mmol) and fluoroform-derived $CuCF_3$ (about 6.7 mmol) as described in the general procedure (80% yield, 0.95 g, pinkish solid). mp 58−59 °C. ^1H NMR 7.56 (2 H, d, J = 9.2 Hz), 6.66 (2 H, d, J = 8.8 Hz), 3.00 (6 H, s) ppm. ^{13}C NMR 152.3, 139.4, 123.3 (q, J = 332 Hz), 113.3, 107.7, 40.8 ppm. ^{19}F NMR −36.7 ppm (3 F, s). HRMS (ASAP): calcd. for $C_9H_{11}NF_3Se$ $(M + H)^+$, 266.0036; found, 266.0047. Anal. Calcd for $C_9H_{10}NF_3Se$: C, 40.31; H, 3.76; F, 21.26; N, 5.22. Found: C, 40.11; H, 3.63; F, 20.83; N, 4.71.

8-(Trifluoromethylselanyl)quinoline (2g). Prepared from selenocyanate **1g**[20] (0.61 g, 2.6 mmol) and fluoroform-derived $CuCF_3$ (about 3.9 mmol) as described in the general procedure (quantitative yield, 0.72 g, clear oil). ^1H NMR 8.88 (1 H, dd, J_1 = 4.3 Hz, J_2 = 1.7 Hz), 8.15 (1 H, dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz), 7.99 (1 H, t, J = 7.4 Hz), 7.76 (1 H, dd, J_1 = 8.2 Hz, J_2 = 1.1 Hz), 7.51 (1 H, t, J = 8.0 Hz), 7.45 (1 H, dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz) ppm. ^{13}C NMR 150.5, 146.5, 137.2, 131.3, 130.2, 129.1, 128.1, 124.2 (q, J = 330 Hz), 122.9 ppm ^{19}F NMR −35.2 ppm (3 F, s). HRMS (ASAP): calcd. for $C_{10}H_7F_3NSe$ $(M + H)^+$, 273.9723; found, 273.9727.

1-Methyl-3-(trifluoromethylselanyl)-1*H*-indole (2h). Prepared from selenocyanate **1h**[19] (0.52 g, 2.2 mmol) and fluoroform-derived $CuCF_3$ (about 3.3 mmol) as described in the general procedure (80% yield, 0.49 g, beige solid). mp = 59 °C. ^1H NMR 7.75 (1 H, d, J = 7.6 Hz), 7.26−7.39 (4 H, m), 3.85 (3 H, s) ppm. ^{13}C NMR 137.3, 137.1, 130.9, 122.9, 122.3 (q, J = 333 Hz), 121.2, 120.2, 109.8, 33.3 ppm. ^{19}F NMR −36.7 ppm (3 F, s). The common MS methods failed to show any molecular peak. Amirav's supersonic GC-MS revealed a strong molecular ion peak of m/z 273.0 $(M)^+$ with an isotope abundance analysis matching factor of 999 out of 999. Anal. Calcd for $C_{10}H_8NF_3Se$: C, 43.18; H, 2.90; F, 20.49; N, 5.04. Found: C, 43.17; H, 2.79; F, 20.94; N, 4.76.

Octyl(trifluoromethyl)selane (2i).[17] Prepared from diselenide **3i** (2.69 gr, 7.0 mmol) and about 10.5 mmol of $CuCF_3$, whose preparation was described in the general procedure. The suspension was stirred under an argon atmosphere for 1 h (monitored by TLC), added to cold 2% aqueous HCl, stirred for 5 min, and extracted with pentane. The organic solution was passed through a short pad of Celite to remove inorganic salts and evaporated. The product was purified by flash column chromatography using pentane. The product was isolated in 90% yield (45% based on Se atoms), 1.65 g, 6.3 mmol, clear oil. ^1H NMR 2.98 (2 H, t, J = 7.2 Hz), 1.78 (2 H, quin, J = 7.6 Hz),

dx.doi.org/10.1021/jo5022844 | J. Org. Chem. 2014, 79, 11205−11208

1.43−1.22 (10 H, m), 0.88 (3 H, t, J = 6.4 Hz) ppm. ^{13}C NMR 123.4 (q, J = 332 Hz), 32.5, 30.9, 30.3, 29.8, 29.6, 26.6, 23.3, 14.7 ppm. ^{19}F NMR −32.9 ppm (3 F, s).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: +972 3 640 9293. Tel.: +972 3 640 8378. E-mail: rozens@post.tau.ac.il.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Israel Science Foundation.

■ REFERENCES

(1) (a) Nishiumi, H.; Sato, K.; Kato, R. *Adv. Fluorine Sci.* **2006**, 131−164. (b) Filler, R.; Kirk, K. Biological properties of fluorinated compounds. In *Chemistry of Organic Fluorine Compounds II: A Critical Review*; Hudlicky, M., Pavlath, A. E., Eds.; ACS Monograph 187; American Chemical Society: Washington, DC, 1995.

(2) Hansch, C.; Leo, A.; Hoekman, D. H. *Exploring QSAR: Hydrophobic, Electronic and Steric Constants*; American Chemical Society: Washington, DC, 1995.

(3) (a) Ben-David, I.; Rechavi, D.; Mishani, E.; Rozen, S. *J. Fluorine Chem.* **1999**, *97*, 75−78. (b) Cohen, O.; Mishani, E.; Rozen, S. *Tetrahedron* **2010**, *65*, 3579−3582. (c) Rozen, S. *Acc. Chem. Res.* **2005**, *38*, 803−812.

(4) (a) Prakash, G. K. S.; Panja, C.; Vaghoo, H.; Surampudi, V.; Kultyshev, R.; Mandal, M.; Rasul, G.; Mathew, T.; Olah, G. A. *J. Org. Chem.* **2006**, *71*, 6806−6813. (b) Chen, M.; Buchwald, S. L. *Angew. Chem.* **2013**, *52*, 11628−11631.

(5) (a) Lishchynskyi, A.; Novikov, M. A.; Martin, E.; Escudero-Adan, E. C.; Novak, P.; Grushin, V. V. *J. Org. Chem.* **2013**, *78*, 11126−11146. (b) Konovalov, A. I.; Benet-Buchholz, J.; Martin, E.; Grushin, V. V. *Angew. Chem. Int. Ed.* **2013**, *52*, 11637−11641. (c) Novak, P.; Lishchynskyi, A.; Grushin, V. V. *J. Am. Chem. Soc.* **2012**, *134*, 16167−16170. (d) Novak, P.; Lishchynskyi, A.; Grushin, V. V. *Angew. Chem., Int. Ed.* **2012**, *51*, 7767−7770. (e) Zanardi, A.; Novikov, M. A.; Martin, E.; Benet-Buchholz, J.; Grushin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 20901−20913.

(6) *Organoselenium Chemistry: Synthesis and Reactions*; Wirth, T., Ed.; Wiley-VCH: Weinheim, Germany, 2012.

(7) Because SCF_3 compounds were determined to be more lipophilic than that of the corresponding OCF_3 and CF_3 derivatives, the less electronegative $SeCF_3$ compounds are expected to be even more lipophilic. See also ref 2.

(8) (a) *Organoselenium Chemistry: A Practical Approach*; Back, T. G., Ed.; Oxford University Press, Oxford, 1999. (b) Freudendahl, D. M.; Santoro, S.; Shahzad, S. A.; Santi, C.; Wirth, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 8409−8411. (c) Potash, S.; Rozen, S. *Eur. J. Org. Chem.* **2013**, 5574−5579.

(9) Kondratenko, N. V.; Kolomeytsev, A. A.; Popov, V. I.; Yagupolskii, L. M. *Synthesis* **1985**, 667−669.

(10) Haas, A. *J. Fluorine Chem.* **1986**, *32*, 415−439.

(11) (a) Cherkupally, P.; Beier, P. *Tetrahedron Lett.* **2010**, *51*, 252−255. (b) Pooput, C.; Dolbier, W. R., Jr.; Medebielle, M. *J. Org. Chem.* **2006**, *71*, 3564−3568. (c) Large, S.; Roques, N.; Langlois, B. R. *J. Org. Chem.* **2000**, *65*, 8848−8856.

(12) (a) Chen, C.; Ouyang, L.; Lin, Q.; Liu, Y.; Hou, C.; Yuan, Y.; Weng, Z. *Chem.—Eur. J.* **2014**, *20*, 657−661. (b) Zhu, P.; He, X.; Chen, X.; You, Y.; Yuan, Y.; Weng, Z. *Tetrahedron* **2014**, *70*, 672−677.

(13) Prakash, G. K. S.; Jog, P. V.; Batamack, P. T. D.; Olah, G. A. *Science* **2012**, *338*, 1324.

(14) Han, W.; Li, Y.; Tang, H.; Liu, H. *J. Fluorine Chem.* **2012**, *140*, 7−16.

(15) Large-Radix, S.; Billard, T.; Langlois, B. R. *J. Fluorine Chem.* **2003**, *124*, 147−149.

(16) Mazloomi, Z.; Bansode, A.; Benavente, P.; Lishchynskyi, A.; Urakawa, A.; Grushin, V. V. *Org. Process Res. Dev.* **2014**, *18*, 1020−1026.

(17) Billard, T.; Large, S.; Langlois, B. R. *Tetrahedron Lett.* **1997**, *38*, 65−68.

(18) (a) Huang, Y.; Chen, R. Y. *Synth. Commun.* **2000**, *30*, 377−381. (b) Rebane, E. *Acta Chem. Scand.* **1967**, *21*, 652−656.

(19) Kachanov, A. V.; Slabko, O. Y.; Baranova, O. V.; Shilova, E. V.; Kaminskii, V. A. *Tetrahedron Lett.* **2004**, *45*, 4461−4463.

(20) Sekido, E.; Fujiwara, I. *Talanta* **1972**, *19*, 647−655.

(21) Diselenides are easy to observe during column chromatography because they are generally more polar than the trifluoromethylated products and produce yellow bands.

(22) (a) Amirav, A.; Gordin, A.; Poliak, M.; Fialkov, A. B. *J. Mass Spectrom.* **2008**, *43*, 141−163. (b) Alon, T.; Amirav, A. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 2579−2588. (c) Fialkov, A. B.; Amirav, A. *J. Chromatogr.* **2004**, *1058*, 233−242.

(23) Toshimitsu, A.; Kozawa, Y.; Uemura, S.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1273−1278.