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From Alkyl Halides to Alkyltrifluoromethyls Using Bromine Trifluoride

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Under the right conditions, bromine trifluoride can be a useful tool for generating new types of reactions and compounds. Thus, tris(methylthio)alkyl derivatives, easily prepared from the corresponding alkyl bromides, were converted to the corresponding $RCHBrCF_2SMe$ or $RCHBrCF_3$ compounds. The bromine atom, however, could be easily reduced forming eventually $R'CF_2SMe$ or $R'CF_3$. If desired, the bromine atom can serve as an entry for constructing terminal difluoroolefins.

Introduction

The introduction of the trifluoromethyl group in organic substrates and its profound influence on biologically active molecules are often associated with its ability to increase the lipophilicity of the whole compound. Its high electronegativity, relative small size, and the extra stability it offers have contributed to its ever-rising popularity. Several new and exciting methods for the incorporation of this moiety have been described in the past decade, especially the use of trimethyl(trifluoromethyl)silane (Me_3SiCF_3). No wonder that several excellent reviews have appeared lately summarizing these methods.[1] We describe here a novel approach for the introduction of this group starting from readily accessible alkyl halides and bromine trifluoride.

Although BrF_3 has been used for the preparation of modern anesthetics such as desflurane[2] and sevoflurane,[3] it is still rarely mentioned in other fields of chemistry. In the past few years, however, we have started to unveil its synthetic potential for bromination of deactivated aromatic rings,[4] transforming carbonyls to the CF_2 group[5] and nitriles to the corresponding CF_3 group,[6] oxidizing alcohols to acyl fluorides,[7] constructing trifluoromethyl ethers,[8] and more.[9]

The above transformations have one thing in common. All substrates have a basic heteroatom serving as an anchor to the electrophilic bromine of the BrF_3. This provides an opportunity for the nucleophilic fluorine atoms in the reagent to react almost exclusively with the relatively electron depleted nearby carbon atom bonded to the heteroatom(s). In this paper, we concentrate on the sulfur atom as such an anchor. Tris(methylthio)-methyl derivatives are easily made by reacting tris-(methylthio)methane (**1**) with alkyl bromides under basic conditions. The conversion of this sulfur-containing moiety to the CF_3 group is the subject of this study.[10]

Results and Discussion

Reacting tris(methylthio)undecane (**2**), made from bromodecane (**3**), with 3-fold excess of BrF_3 resulted in the 1-methylthio-2-bromo-1,1-difluoroundecane (**4**) in 70% yield, while with 10-fold excess one obtains 2-bromo-1,1,1-trifluoroundecane (**5**) in 60% yield. The reaction conditions are mild and consist of reaction temperatures of 0 °C and reaction times of a few minutes. It should be noted that, if desired, the difluorinated products can be transformed to the trifluoro ones (e.g. **4** to **5**) by applying 3 equiv of bromine trifluoride. This provides an indication that the former are stable intermediates of the reaction leading to the latter (Scheme 1). In all cases, the bromine atom could be easily removed either by replacing it with hydrogen or by elimination reactions (see below). The reaction between BrF_3 and the tris(methylthio) derivatives can be applied to a number of aliphatic chains with similar results. Thus, heptyl, dodecyl, and cyclohexanemethyl bromides (**6**, **7**, and **8**) were all converted in good yields to the corresponding tris(methylthio) derivatives (**9**, **10**, and **11**) and then, depending on the reaction conditions, further transformed to the either difluoro

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(7) Rozen, S.; Ben-David, I. *J. Fluorine Chem.* **1996**, *76*, 145.

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(10) Preliminary results have been presented by us at the 13th European Symposium on Fluorine Chemistry, Bordeaux, France, p A8, 2001. Hiyama had described the fluorination of orthothioesters using $Bu_4NH_2F_3$ and 1,3-dibromo-5,5-dimethylhydantoin, resulting in $RCHBrCF_2SMe$ derivatives: Furuta, S.; Kuroboshi, M.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1939.

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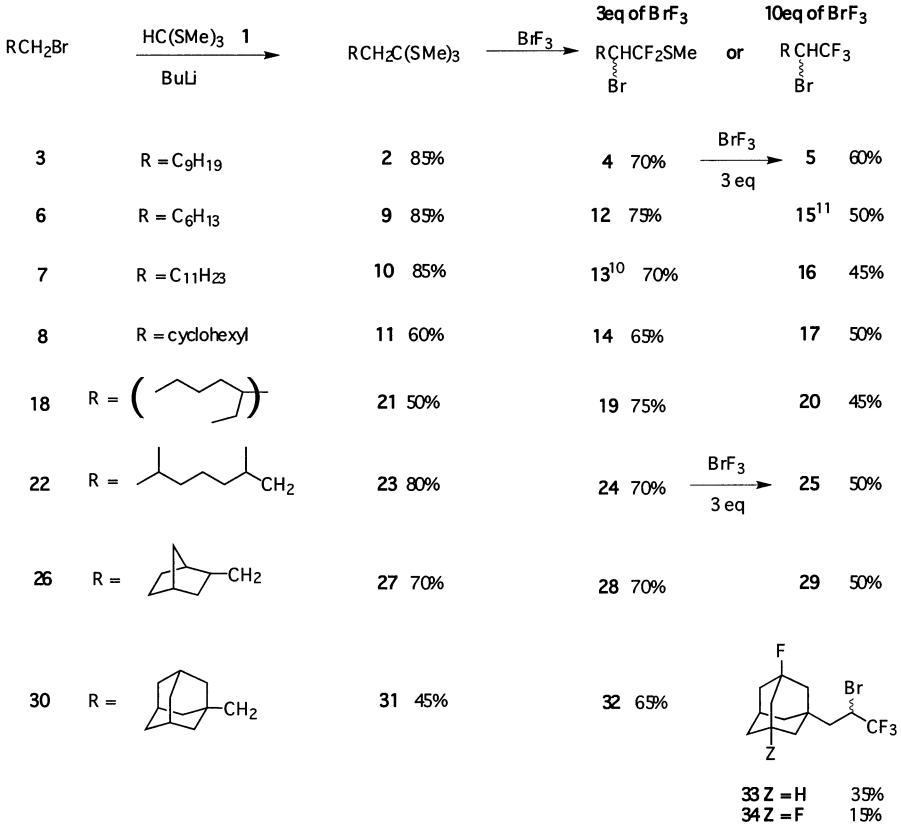
SCHEME 1



derivatives (**12**, **13**,[10] and **14**) or the trifluoromethyl ones (**15**,[11] **16**, and **17**).

It was documented that the fluorine atoms in bromine trifluoride can in certain cases act as electrophiles[12] and substitute tertiary hydrogens similarly to F_2.[13] It was of interest to see if the scope of this reaction includes substrates possessing such tertiary centers. We found out that the reaction around the sulfur atoms is by far the dominant one. Thus, no tertiary fluorination was observed with 2-ethylbromohexane (**18**). The reaction behaved as expected, producing the di- or trifluoro derivatives **19** or **20** via the corresponding 3-ethyl-1,1,1-tris(methylthio)heptane (**21**). Even when a second more remote, and therefore more reactive, tertiary center was present, as in 3,7-dimethyl bromooctane (**22**), the reaction proceeded smoothly and only around the methylthio moiety of **23**. As in the previous cases, one was able to obtain either the difluoro **24** or the trifluoro product **25** by varying the BrF_3 excess used. Working with bicyclo compounds such as 2-norbornaneethyl bromide (**26**) also resulted in no surprises. Its tris(methylthio) derivative **27** reacted fast with 3 mol equiv of BrF_3 to give 2-bromo-1,1-difluoro-1-methylthio-3-norbornylpropane (**28**), while the reaction with a larger excess of the reagent furnished the expected 2-bromo-1,1,1-trifluoro-3-norbornylpropane (**29**) in 50% yield. The only time we did notice a tertiary fluorination was in the case of 3-(adamant-1-yl)-1,1,1-tris(methylthio)propane (**31**) made from 2-(adamant-1-yl)ethyl bromide (**30**). When **31** was reacted with 3 mol equiv of bromine trifluoride, the expected difluoro sulfide **32** was obtained in 65% yield. Using 10-fold excess, however, two compounds were formed, both with extra fluorine atom(s) attached to the adamantane skeleton. The major one was identified as 3-(3-fluoroadamant-1-yl)-2-bromo-1,1,1-trifluoropropane (**33**) accompanied by 15% of 3-(3,5-difluoroadamant-1-yl)-2-bromo-1,1,1-trifluoropropane (**34**) (Scheme 1).

The mechanism of the reaction seems to be of ionic nature, since adding radical scavengers such as dinitrobenzene or oxygen did not change its outcome. We have noticed that the hydrogen atoms α to the tris(methylthio)-methyl moiety are labile and can be eliminated on heating along with one thiomethyl group, as exemplified by **2**, which was converted to 1,1-dimethylthioundec-1-ene (**35**). This compound was reacted with BrF_3 to produce again the difluoro derivative **4**, but unlike the reaction with **2**, it required less than 2 equiv of BrF_3 for completion. This indicates that at least 1 mol equiv of the reagent is needed for the first step of the reaction, which we believe forms the corresponding olefin. Since the hydrogen atoms α to the tris(methylthio)methyl group are somewhat acidic, they are capable of forming a strong hydrogen bond with the fluoride, followed by an eventual elimination of the elements of methanthiol. Consequently, bromine fluoride, always found in BrF_3 (a well known equilibrium reaction), can add itself across the resulting π center. A somewhat indirect evidence to the formation of this adduct was found in the reaction of **21** when not enough BrF_3 was employed. In this case, an elimination of HF took place, producing the bromo

(11) Fuchigami, T.; Hagiwara, T. Japanese Patent 10,287,596, 1998 (*Chem. Abstr.* **1998**, *129*, 343269z).
(12) Boguslavskaya, L. S.; Kartashov, A. V.; Chuvatkin, N. N. *Zh. Org Khim. (Eng. Transl.)* **1989**, *25*, 1835.
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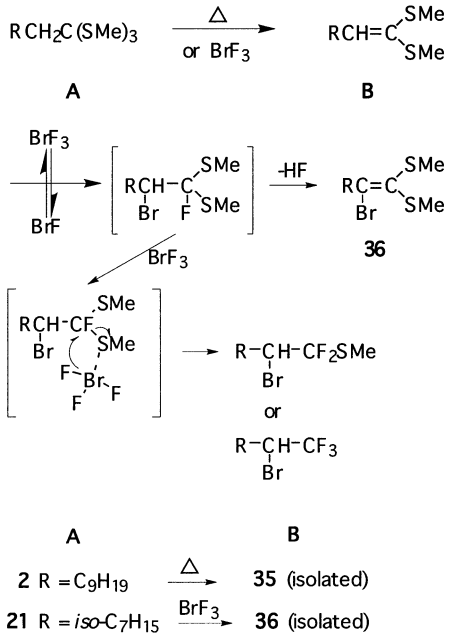
SCHEME 2



olefin **36**, which was isolated and characterized. Under the standard conditions (3-fold excess of BrF_3), however, the reagent is attracted by the sulfur atoms, resulting eventually in the displacement of the methylthio group by fluorides (Scheme 2).[14]

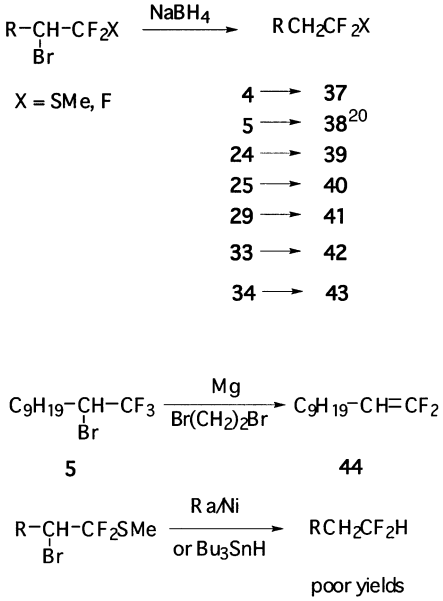
The bromine atom invariably found in the α position to either difluoromethyl sulfide or the CF_3 group can be replaced with a hydrogen atom by treating these compounds with $NaBH_4$. The reduction proceeds with 70−75% yield and does not affect the sulfide moiety when present. A few examples are outlined in Scheme 3, producing the bromine-free derivatives (**37**−**43**).

An elimination of [BrF] elements could also be achieved by treating the bromine-containing derivatives with Mg and 1,2-dibromoethane.[15] Thus, for example, 2-bromo-1,1,1-trifluoroundecane (**5**) was converted to 1,1-difluoroundeca-1-ene (**44**)[16] in 80% yield, providing a new method for the construction of the important terminal difluoroolefins[17] (Scheme 3).

We have also tried to reduce the sulfide group in order to obtain the desirable difluoromethyl moiety. However, using various conditions based on reactions with Bu_3SnH and Ra/Ni resulted in poor yields of about 10−15%, and we did not continue to pursue this line of research for the construction of this group.

In conclusion, we hope that this work will encourage chemists to think positively about BrF_3 and not dismiss it as an uncontrollable reagent unsuitable for organic

SCHEME 3



chemistry. About 20 years ago, F_2 was also considered as a reagent to avoid in organic chemistry, and today numerous laboratories use it routinely. We believe that BrF_3 will find its right place in the arsenal of reagents for synthetic purposes. Its present use for converting alkyl halides into trifluoromethyl derivatives is one more step toward this goal.

Experimental Section

^{1}H NMR spectra were recorded using a 200 MHz machine with $CDCl_3$ as a solvent and Me_4Si as an internal standard. Only the relevant and characteristic peaks are reported. The ^{19}F NMR spectra were measured at 188.1 MHz and are reported in parts per million upfield from $CFCl_3$ serving as an internal standard. The proton broad-band decoupled ^{13}C NMR spectra were recorded at 50.2 MHz. Here too, $CDCl_3$ served as a solvent with TMS as an internal standard. MS and GC−MS spectra were usually measured under CI conditions. In extreme cases where the CI method could not detect the molecular ion, we have successfully used the Amirav's supersonic GC−MS developed in our department. The main feature of this method is to provide electron ionization while the sample is vibrationally cooled in a supersonic molecular beam. This considerably enhances the relative abundance of the molecular ions.[18] The spectral properties of all products presented in this work are in excellent agreement with their structure, and where relevant, also with the ones described in the literature.

The term "worked up as usual" means termination by adding water to the reaction mixture, separation of layers, extraction of the the aqueous layer three times with ether, and drying of the combine organic layers over $MgSO_4$. Evaporation of the solvent followed by purification by column chromatography (Merck silica gel 60H), with petroleum ether and ethyl acetate serving as an eluent, completes the procedure.

Preparation and Handling BrF_3. Although commercially available, we prepare our own BrF_3 by simply passing 0.58 mol of pure fluorine through 0.2 mol of bromine placed in a copper reactor cooled to 0 ± 10 °C. At that temperature, the higher oxidation state—BrF_5—will not form in any appreciable

(14) One of the referees pointed that on one hand 3 mol equiv of BrF_3 were used for obtaining the CF_2SMe group and three more for converting it to the CF_3 one. On the other hand, 10 mol equiv were reacted with the starting alkyl bromide for that purpose. We do not have a definite answer for this apparent contradiction, and probably the reason is that in the two-steps reaction, work was conducted with relatively pure CF_2SMe derivatives, while in the one-step reaction, some BrF_3 was probably wasted on reactions with the resulting initial tars.

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(17) Kim, K, I.; McCarthy, J. R. *Tetrahedron Lett.* **1996**, *37*, 3223.

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amount,[19] although, we always use a small excess of bromine, thereby keeping the reagent from disproportionating to BrF_5. This is also responsible for the reddish coloration of the reagent. It can be stored in Teflon containers indefinitely. **CAUTION:** BrF_3 is a strong oxidizer and tends to react very exothermically with water and oxygenated organic solvents. The work with it should be conducted in a well-ventilated area and caution and common sense should be exercised.

General Procedure for Preparing the Tris(methylthio) Derivatives. To a cold (−78 °C) THF solution of 1.8 mL (13.6 mmol) of tris(methylthio)methane (**1**) was added 8.9 mL (14.24 mmol) of BuLi under nitrogen. After stirring for 2 h at this temperature, 12 mmol of neat alkyl bromide was added, the reaction was left for additional 2 h at −78 °C, and the mixture stirred for another hour at room temperature. The usual workup provides the corresponding tris(methylthio) derivatives pure enough for the next step. No attempts were made to obtain analytically pure samples of these materials.

General Procedure for the Reaction of Tris(methylthio) Derivatives with BrF_3. The tris(methylthio) derivates (1 mmol) were dissolved in 10−15 mL of dry $CFCl_3$ and cooled to 0 °C. About 3 mmol (for the difluoromethylmethyl sulfide products) or 10 mmols (for the trifluoromethyl compounds) of BrF_3 was dissolved in 10−15 mL of the same solvent, cooled to 0 °C, and added dropwise to the tris(methylthio) solution, at the same temperature, over a period of up to 3 min. The reaction mixture was then washed with aqueous Na_2SO_3 till colorless and worked up as usual. The same procedure applied when the difluoromethyl methyl sulfide compounds (1 mmol) were reacted with 3 mmol of BrF_3, converting them to the corresponding trifluoromethyl derivatives.

Reduction of the Bromine Atom. To 1 mmol of the bromo compound (di- or trifluorinated) was added 6 mmol of $NaBH_4$ dissolved in 15 mL of DMSO. The reaction mixture was stirred at 110 °C for 1−2 h. It was then acidified with aqueous HCl and worked up as usual.

1,1,1-Tris(methylthio)undecane (2) was prepared from 1-bromodecane (**3**) as described above in 85% yield: oil, ^{1}H NMR 2.10 (9 H, s), 1.91−1.83 ppm (2 H, m); ^{13}C NMR 70.8, 37.9, 29.4, 29.2, 24.6, 22.5, 13.9, 12.9 ppm.

2-Bromo-1,1-difluoro-1-methylthioundecane (4) was prepared from **2** as described above in 70% yield: oil; ^{1}H NMR 4.20−4.05 (1 H, m), 2.34 ppm (3 H, s); ^{13}C NMR 129.3 (t, J = 278 Hz), 54.3 (t, J = 26 Hz), 31.9, 31.6, 29.4, 29.2, 28.5, 22.5, 14.0, 10.1 ppm; ^{19}F NMR −83.4 (1 F, dd, J_1 = 204 Hz, J_2 = 9 Hz), −85.6 ppm (1 F, dd, J_1 = 204 Hz, J_2 = 11 Hz); MS *m*/*z* 316 and 318, both $(M + 1)^+$. Anal. Calcd for $C_{12}H_{23}BrF_2S$: C, 45.43; H, 7.31; Br, 25.18. Found: C, 45.61; H, 6.97; Br, 25.40.

2-Bromo-1,1,1-trifluoroundecane (5) was prepared from **2** in 60% yield: oil; ^{1}H NMR 4.12−4.00 ppm (1 H, m); ^{13}C NMR 124.1 (q, J = 275 Hz), 47.7 (q, J = 30 Hz), 31.6, 31.4, 29.5, 29.3, 28.6, 22.7, 14.1 ppm; ^{19}F NMR −72.6 ppm (d, J = 7 Hz); MS *m*/*z* 287 and 289, both $(M - 1)^+$. Anal. Calcd for $C_{11}H_{20}BrF_3$: C, 45.69; H, 6.97. Found: C, 45.39; H, 6.71.

1,1,1-Tris(methylthio)octane (9) was prepared from 1-bromoheptane (**6**) in 85% yield: oil; ^{1}H NMR 2.10 (9 H, s), 1.91−1.83 ppm (2 H, m); ^{13}C NMR 70.9, 38.1, 31.6, 29.4, 29.1, 24.7, 22.5, 13.9, 12.9 ppm.

2-Bromo-1,1-difluoro-1-methylthiooctane (12) was prepared from **9** in 75% yield: oil; ^{1}H NMR 4.20−4.05 (1 H, m), 2.34 ppm (3 H, s); ^{13}C NMR 129.0 (t, J = 278 Hz), 54.5 (t, J = 26 Hz), 32.9, 31.5, 28.3, 27.2, 22.5, 14.0, 10.5 ppm; ^{19}F NMR −78.17 (1 F, dd, J_1 = 204 Hz, J_2 = 8 Hz), −80.57 ppm (1 F, dd, J_1 = 204 Hz, J_2 = 11 Hz); MS *m*/*z* 275 and 277, both $(M + 1)^+$. Anal. Calcd for $C_9H_{17}BrF_2S$: C, 39.28; H, 6.23; Br, 29.04. Found: C, 39.98; H, 6.02; Br, 29.16.

2-Bromo-1,1,1-trifluorooctane (15)[11] was prepared from **9** in 50% yield: oil; ^{1}H NMR 4.10−4.00 ppm (1 H, m); ^{13}C NMR 124.1 (q, J = 277 Hz), 47.7 (q, J = 32 Hz), 35.8, 32.6, 28.2, 27.3, 22.5, 14.0 ppm; ^{19}F NMR −72.81 ppm (d, J = 7 Hz).

1,1,1-Tris(methylthio)tridecane (10) was prepared from 1-bromododecane (**7**) in 85% yield: oil; ^{1}H NMR 2.10 (9 H, s), 1.91−1.83 ppm (2 H, m); ^{13}C NMR 70.9, 43.9, 38.2, 31.9, 29.4, 29.3, 28.9, 25.6, 24.8, 22.6, 14.0, 13.0, 11.4 ppm.

2-Bromo-1,1-difluoro-1-methylthiotridecane (13)[10] was prepared from **10** in 70% yield: oil; ^{1}H NMR 4.20−4.05 (1 H, m), 2.34 ppm (3 H, s); ^{13}C NMR 129.0 (t, J = 279 Hz), 54.5 (t, J = 26 Hz), 32.8, 31.9, 29.6, 29.3, 29.1, 28.7, 27.2, 23.9, 22.7, 14.0, 10.4 ppm; ^{19}F NMR −78.48 (1 F, dd, J_1 = 204 Hz, J_2 = 8 Hz), −80.60 ppm (1 F, dd, J_1 = 204 Hz, J_2 = 11 Hz); MS *m*/*z* 345 and 347, both $(M + 1)^+$. Anal. Calcd for $C_{14}H_{27}BrF_2S$: C, 48.69; H, 7.88; Br, 23.14. Found: C, 48.59; H, 7.59; Br, 22.83.

2-Bromo-1,1,1-trifluorotridecane (16) was prepared from **10** in 45% yield: oil; ^{1}H NMR 4.14−4.00 ppm (1 H, m); ^{13}C NMR 124.0 (q, J = 276 Hz), 47.9 (q, J = 30 Hz), 32.5, 31.7, 31.5, 30.0, 29.5, 29.1, 28.9, 28.5, 22.6, 14.1 ppm; ^{19}F NMR −72.8 ppm (d, J = 7 Hz). Anal. Calcd for $C_{13}H_{24}BrF_3$: C, 49.22; H, 7.63. Found: C, 49.51; H, 7.33.

1,1,1-(Trismethylthio)methylcyclohexane (11) was prepared from bromomethylcyclohexane (**8**) in 60% yield: oil; ^{1}H NMR 2.11 ppm (9 H, s); ^{13}C NMR 71.1, 45.2, 35.2, 34.7, 32.8, 26.4, 13.3 ppm.

2-Bromo-2-cyclohexyl-1,1-difluoro-1-methylthioethane (14) was prepared from **11** in 65% yield: oil; ^{1}H NMR 4.20−4.00 (1 H, m), 2.35 ppm (3 H, s); ^{13}C NMR 128.8 (t, J = 276 Hz), 61.5 (t, J = 24 Hz), 32.1, 28.3, 26.2, 25.8, 10.6 ppm; ^{19}F NMR −73.3 (1 F, dd, J_1 = 204 Hz, J_2 = 9 Hz), −76.72 ppm (1 F, dd, J_1 = 204 Hz, J_2 = 14 Hz); MS *m*/*z* 273 and 275, both $(M + 1)^+$. Anal. Calcd for $C_9H_{15}BrF_2S$: C, 39.57; H, 5.53. Found: C, 39.31; H, 5.47.

2-Bromo-2-cyclohexyl-1,1,1-trifluoroethane (17) was prepared from **11** in 50% yield: oil; ^{1}H NMR 4.12−4.00 ppm (1 H, m); ^{13}C NMR 124.1 (q, J = 277 Hz), 54.5 (q, J = 30 Hz), 38.7, 31.2, 28.3, 26.6 ppm; ^{19}F NMR −68.13 ppm (d, J = 8 Hz). Anal. Calcd for $C_8H_{12}BrF_3$: C, 39.21; H, 4.94; Br, 32.60. Found: C, 39.23; H, 4.82; Br, 33.12.

3-Ethyl-1,1,1-tris(methylthio)heptane (21) was prepared from 2-ethylhexyl bromide (**18**) in 50% yield: oil; ^{1}H NMR 2.12 ppm (9 H, s); ^{13}C NMR 71.4, 42.5, 35.7, 33.7, 28.6, 26.9, 23.1, 14.1, 13.4, 10.5 ppm.

2-Bromo-3-ethyl-1,1-difluoro-1-methylthioheptane (19) was prepared from **21** (a mixture of two diastereoisomers) in 75% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.35−4.15 (1 H, m), 2.35 ppm (3 H, s); ^{13}C NMR (for the two diastereoisomers) 128.9 (t, J = 279 Hz), 58.8 (q, J = 24 Hz), 41.5 and 41.4, 30.9 and 30.5, 29.5 and 29.2, 25.0 and 23.7, 22.8 and 22.5, 14.0, 11.7 and 11.6, 10.5 ppm; ^{19}F NMR (for the two diastereoisomers) −73.05 and −73.15 (both 1 F, dd, J_1 = 204 Hz, J_2 = 14 Hz), −68.33 ppm (1 F, dd, J_1 = 204 Hz, J_2 = 8 Hz); MS *m*/*z* 289 and 291, both $(M + 1)^+$. Anal. Calcd for $C_{10}H_{19}BrF_2S$: C, 41.53; H, 6.62; Br, 27.63. Found: C, 41.34; H, 6.59; Br, 27.77.

2-Bromo-3-ethyl-1,1,1-trifluoroheptane (20) was prepared from **21** in 45% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.26−4.00 ppm (1 H, m); ^{13}C NMR (for the two diastereoisomers) 124.4 (q, J = 275 Hz), 51.7 (m), 40.5, 30.6 and 30.2, 29.4 and 29.2, 24.5 and 23.6, 22.8 and 22.6, 13.9, 11.6 ppm; ^{19}F NMR −68.2 ppm (m); MS *m*/*z* 259 and 261, both $(M - 1)^+$.

4,8-Dimethyl-1,1,1-tris(methylthio)nonane (23) was prepared from 1-bromo-3,7-dimethyloctane (**22**) in 80% yield: oil; ^{1}H NMR 2.09 ppm (9 H, s); ^{13}C NMR 70.9, 38.9, 36.8, 35.1, 32.4, 31.4, 27.6, 24.5, 22.4, 22.3, 19.5, 12.7 ppm.

2-Bromo-1,1-difluoro-4,8-dimethyl-1-methylthiononane (24) was prepared from **23** in 70% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.31−4.11 (1 H, m), 2.33 ppm (3 H, s); ^{13}C NMR (for the two diastereoisomers) 128.8 (t, J = 279 Hz), 52.5 (q, J = 24 Hz), 39.8 and 39.3, 38.8 and 37.3, 34.2, 30.1 and 30.0, 27.6, 24.3 and 23.6, 22.3, 22.2, 19.9, 17.7 ppm; ^{19}F NMR (for the two diastereoisomers) −81.09 and

(19) Stein, L. *J. Am. Chem. Soc.* **1959**, *81*, 1269.

−80.90 (both 1 F, dd, $J_1 = 214$ Hz, $J_2 = 12$ Hz), −78.35 ppm (1 F, wide d, $J_1 = 214$ Hz). Anal. Calcd for $C_{12}H_{23}BrF_2S$: C, 45.43; H, 7.31; Br, 25.18; S, 10.10. Found: C, 44.82; H, 7.21; Br, 25.23; S, 10.25.

2-Bromo-1,1,1-trifluoro-4,8-dimethylnonane (25) was prepared from **23** in 45% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.25−4.00 ppm (1 H, m); ^{13}C NMR (for the two diastereoisomers) 124.1 (q, $J = 275$ Hz), 45.9 (m), 38.9 and 38.6, 37.9 and 37.4, 34.5, 29.9 and 27.8, 24.4 and 23.9, 22.5, 22.3, 19.7, 17.8 ppm; ^{19}F NMR (for the two diastereoisomers) −72.07 and −72.91 ppm (both d, $J = 7$ Hz). Anal. Calcd for $C_{11}H_{20}BrF_3$: C, 45.69; H, 6.97; Br, 27.63. Found: C, 45.87; H, 6.85; Br, 27.51.

3-Norbornane-1,1,1-tris(methylthio)propane (27) was prepared from 2-norbornaneethyl bromide (**26**) in 70% yield: oil; ^{1}H NMR 2.11 ppm (9 H, s); ^{13}C NMR 70.1, 12.9 ppm.

2-Bromo-1,1-difluoro-1-methylthio-3-norbornylpropane (28) was prepared from **27** in 70% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.27−4.07 (1 H, m), 2.34 ppm (3 H, s); ^{13}C NMR (for the two diastereoisomers) 128.85 and 128.83 (both t, $J = 280$ Hz), 53.3 and 52.5 (both t, $J = 27$ Hz), 41.7 and 40.7, 39.3 and 39.2, 39.0 and 38.0, 36.6 and 36.4, 36.1 and 35.6, 35.0 and 34.5, 29.7 and 29.4, 28.4 and 28.2, 10.2 ppm; ^{19}F NMR (for the two diastereoisomers) −80.72 (1 F, dd, $J_1 = 204$ Hz, $J_2 = 11$ Hz), −78.53 and −78.42 ppm (both 1 F, dd, $J_1 = 204$ Hz, $J_2 = 8$ Hz). Anal. Calcd for $C_{11}H_{17}BrF_2S$: C, 44.16; H, 5.73; Br, 26.70. Found: C, 44.60; H, 5.65; Br, 25.92.

2-Bromo-1,1,1-trifluoro-3-norbornylpropane (29) was prepared from **27** in 50% yield: oil; ^{1}H NMR (for the two diastereoisomers) 4.18−3.98 ppm (1 H, m); ^{13}C NMR (for the two diastereoisomers) 123.89 and 123.87 (both q, $J = 270$ Hz), 46.8 and 46.5 (both q, $J = 32$ Hz), 41.5 and 39.1, 38.9 and 38.8, 37.8 and 37.7, 37.6 and 36.5, 36.3 and 36.1, 35.6 and 35.0, 29.7 and 29.4, 28.3 and 28.1 ppm; ^{19}F NMR (for the two diastereoisomers) −72.83 and −72.73 ppm (both d, $J = 7$ Hz). Anal. Calcd for $C_{10}H_{14}BrF_3$: C, 44.30; H, 5.20; Br, 29.47. Found: C, 44.20; H, 5.23; Br, 29.05.

3-(Adamant-1-yl)-1,1,1-tris(methylthio)propane (31) was prepared from 2-(adamant-1-yl)-ethylbromide (**30**) in 45% yield: mp 96 °C (from methanol); ^{1}H NMR 2.09 ppm (9 H, s); ^{13}C NMR 71.5, 42.4, 38.7, 37.1, 31.9, 30.5, 28.6, 12.9 ppm.

3-(Adamant-1-yl)-2-bromo-1,1-difluoro-1-methylthiopropane (32) was prepared from **31** in 65% yield: mp 48 °C (from methanol); ^{1}H NMR 4.25−4.05 (1 H, m), 2.36 (3 H, s), 2.08 (1 H, dd, $J_1 = 16$ Hz, $J_2 = 1$ Hz), 1.89 ppm (1 H, dd, $J_1 = 16$ Hz, $J_2 = 8$ Hz); ^{13}C NMR 129.3 (t, $J = 280$ Hz), 47.42, 47.1 (t, $J = 26$ Hz), 42.1, 36.5, 32.5, 28.2, 10.3 ppm; ^{19}F NMR −79.62 (1 F, dd, $J_1 = 202$ Hz, $J_2 = 8$ Hz), −81.33 ppm (1 F, dd, $J_1 = 202$ Hz, $J_2 = 12$ Hz). Anal. Calcd for $C_{14}H_{21}BrF_2S$: C, 49.56; H, 6.24. Found: C, 50.04; H, 6.32.

3-(3-Fluoroadamant-1-yl)-2-bromo-1,1,1-trifluoropropane (33) and 3-(3,5-difluoroadamant-1-yl)-2-bromo-1,1,1-trifluoropropane (34) were obtained from **31** as a mixture (35% by GC for **33** and 15% by GC for **34**). The MS (EI) for **33** showed *m*/*z* 311, 309, both $(M - 19)^+$, while **34** showed $(M - 19)^+$ peaks at *m*/*z* 329, 327. ^{1}H NMR (for **33** and **34**) 4.16−4.05 (1 H, m); ^{13}C NMR (for **33** and **34**, respectively) 124.0 and 123.8 (both q, $J = 277$ Hz), 93.0 (m) and 91.2 (m) ppm; ^{19}F NMR (for **33** and **34**, respectively) −73.50 and −73.60 (both d, $J = 7$ Hz), −132.2 and −137.3 ppm.

1,1-Dimethylthioundec-1-ene (35) was obtained in 90% yield by heating neat 1,1,1-Tris(methylthio)undecane (**2**) to 100 °C for 2 h: oil; ^{1}H NMR 5.90 (1 H, t, $J = 7$ Hz), 2.30 (2 H, m), 2.27 (3 H, s), 2.25 (3 H, s).

2-Bromo-1,1-dimethylthio-3-ethylhept-1-ene (36) was isolated in higher than 40% yield when **21** was reacted with less than 2 mol equiv of BrF_3: oil; ^{1}H NMR 3.47 (1 H, m), 2.39 (3 H, s), 2.26 ppm (3 H, s); ^{13}C NMR 139.5, 132.6, 48, 34.2, 29.3, 27.5, 22.6, 18.5, 16.9, 13.9, 11.7 ppm; MS (EI) *m*/*z* 296, 298, both $(M)^+$.

1,1-Difluoro-1-methylthioundecane (37) was obtained in 70% yield by reducing **4** as described above: oil; ^{1}H NMR 2.28 (3 H, s), 2.20−1.96 ppm (2 H, m); ^{13}C NMR 130.8 (t, $J = 274$ Hz), 38.9 (t, $J = 23$ Hz), 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 23.2, 22.6, 14.0, 10.1 ppm; ^{19}F NMR −76.74 (t, $J = 15$ Hz). Anal. Calcd for $C_{12}H_{24}F_2S$: C, 60.46; H, 10.15. Found: C, 60.31; H, 10.20.

1,1,1-Trifluoroundecane (38)[20] was obtained in 70% yield by reducing **5** as described above: oil; ^{1}H NMR 2.06−2.02 (2 H, m), 1.56−1.51 ppm (2 H, m); ^{13}C NMR 127.3 (q, $J = 275$ Hz), 33.8 (q, $J = 29$ Hz), 31.9, 29.6, 29.5, 29.4, 29.3, 28.8, 22.7, 21.9, 14.0 ppm; ^{19}F NMR −66.93 ppm (t, $J = 11$ Hz). Anal. Calcd for $C_{11}H_{21}F_3$: C, 62.83; H, 10.07. Found: C, 62.85; H, 9.77.

1,1-Difluoro-4,8-dimethyl-1-methylthiononane (39) was obtained in 75% yield by reducing **24** as described above: oil; ^{1}H NMR 2.28 (3 H, s); ^{13}C NMR 130.9 (t, $J = 273$ Hz), 39.1, 36.7, 36.5 (t, $J = 23$ Hz), 32.2, 29.8, 27.8, 24.5, 22.6, 22.5, 19.2, 9.8 ppm; ^{19}F NMR −76.90 (t, $J = 15$ Hz). Anal. Calcd for $C_{12}H_{24}F_2S$: C, 60.46; H, 10.15. Found: C, 60.46; H, 9.94.

1,1,1-Trifluoro-4,8-dimethylnonane (40) was obtained in 70% yield by reducing **25** as described above: oil; ^{1}H NMR 2.20−1.80 ppm (2 H, m); ^{13}C NMR 127.4 (q, $J = 274$ Hz), 39.1, 36.0, 31.9, 31.4 (q, $J = 28$ Hz), 28.5, 27.8, 24.5, 22.5, 22.4, 19.1 ppm; ^{19}F NMR −66.93 ppm (t, $J = 11$ Hz). Anal. Calcd for $C_{11}H_{21}F_3$: C, 62.83; H, 10.07. Found: C, 61.90; H, 9.77.

1,1,1-Trifluoro-3-norbornanepropane (41) was obtained in 75% yield by reducing **29** as described above: oil; ^{13}C NMR 129.2 (q, $J = 275$ Hz), 43.3, 42.8, 39.8, 38.4, 37.1, 34.2 (q, $J = 28$ Hz), 31.9, 30.5 ppm; ^{19}F NMR −66.83 ppm (t, $J = 12$ Hz); MS (super sonic molecular beam)[18] *m*/*z* 192 $(M)^+$.

3-(3-Fluoroadamant-1-yl)-1,1,1-trifluoropropane (42) and 3-(3,5-difluoroadamant-1-yl)-1,1,1-trifluoropropane (43) were obtained in combined yield of 75% by reducing the mixture of **33** and **34** as described above. Compound **42** was identified by HRMS calcd for $C_{13}H_{18}F_4$ 249.1272 $(M)^+$, found 249.1266. Compound **43** was identified by GC−MS (EI mode) *m*/*z* 249 $(M - 19)^+$ and 171 $(AdF_2)^+$. ^{13}C NMR (for **42** and **43**) 127.3 (q, $J = 274$ Hz), and 127.0 (q, $J = 274$ Hz), 27.9 (q, $J = 28$ Hz), 27.6 (q, $J = 28$ Hz), (for **42**) 92.5 (d, $J = 183$ Hz), 46.5 (d, $J = 17$ Hz), 41.8 (d, $J = 17$ Hz), 36.0 (d, $J = 10$ Hz), 30.8 ppm (d, $J = 10$ Hz), (for **43**) 92.7 (dd, $J_1 = 187$ Hz, $J_2 = 14$ Hz), 47.2 (t, $J = 19$ Hz), 37.3 (t, $J = 10$ Hz), 30.2 ppm (t, $J = 10$ Hz); ^{19}F NMR (for **42**) −66.96 (t, $J = 10$ Hz), −132.0 ppm (m), (for **43**) −63.93 (t, $J = 10$ Hz), −137.1 ppm (m).

Preparation of 1,1-difluoroundeca-1-ene (44)[16] was obtained by adding a dry THF solution of 1.3 g (4.5 mmol) of 2-bromo-1,1,1,-trifluoroundecane (**5**) to 1 g of Mg, activated with 1,2-dibromoethane in 10 mL of the same solvent, during a period of 10 min, after which the reaction was refluxed for an additional hour. The reaction was cooled to room temperature, dilute HCl was added, and the reaction mixture was worked up as usual: yield 80%; oil; ^{1}H NMR 4.13 (1 H, dtd, $J_1 = 25$ Hz, $J_2 = 8$ Hz, $J_3 = 3$ Hz), 2.34−1.90 ppm (4 H, m); ^{13}C NMR 156.1 (t, $J = 285$ Hz), 78.0 (t, $J = 21$ Hz), 31.8, 29.6, 29.5, 29.3, 29.2, 28.8, 22.6, 22.1, 14.0 ppm; ^{19}F NMR −90.2 (1 F, wide d, $J = 49$ Hz), −92.5 ppm (1 F, ddt, $J_1 = 49$ Hz, $J_2 = 25$ Hz, J3 = 2 Hz); For MS, the usual methods such as EI and CI found on commercial instruments fail to show any molecular ion peak. However, using Amirav's method provided the answer and indeed a strong molecular ion peak for **44** at *m*/*z* = 190 $(M)^+$ was observed.[18]

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