Organosilicon compounds have a multitude of applications in basic science, medicine, and industry due to their stability and non-toxicity, and natural abundance of silicon. For example, organosilicon compounds have received much attention in the cross-coupling reaction. However, the strategic functionalization of aliphatic carbon–silicon bonds is limited, for example, the trifluoromethoxy (OCF₃) group and trifluoromethylthiol (SCF₃) group are becoming increasingly important in medicinal, agro-chemical and materials science due to their strong electron-withdrawing effect and high lipophilicity. Thus, the development of efficient methods for the synthesis of OCF₃ and SCF₃ compounds is of great importance.

However, the trifluoromethoxylation and trifluoromethylthiolation of organosilanes are extremely underdeveloped. To the best of our knowledge, no trifluoromethoxylation of alkyllsilanes has been reported to date. Herein, we sought a strategy that would facilitate the direct conversion of aliphatic C–Si bonds into a variety of functional groups, including the trifluoromethoxylation and trifluoromethylthiolation of alkyllsilanes (Scheme 1).

Methods for aliphatic C–Si oxidation, halogenation, and azidation have been reported, but new reaction systems are typically required to promote each transformation. In addition, methods for trifluoromethoxylation of organosilanes are rare, and only two examples were reported. In 2008, using trifluoromethyltriflate as the trifluoromethoxylation reagent, the Kolomeitsev group reported the trifluoromethoxylation of aryynes from o-trimethylsilylphenyl triflate. In 2018, trifluoromethyl benzoate (TFBz) was reported as a new trifluoromethylation reagent by the Hu group and was used to prepare trifluoromethyl ether from trifluoromethoxylation–halogenation of arynes, which was in situ generated from o-trimethylsilylphenyl triflate.

Despite the advances in these methods, trifluoromethylation of alkyllsilanes has not been reported to date, so the development of a general approach for functionalization including trifluoromethylation of alkyllsilanes is highly desirable.

Inspired by our previous work of a hypervalent iodine-mediated fluorination of alkyllsilanes using fluoride ions as the fluorinating agent, we became interested in the possibility of functionalization of alkyllsilanes using other nucleophiles such as OCF₃. Recently, trifluoromethyl aroylsulfonfate (TFMS) as a new trifluoromethylation reagent was disclosed by our group, which was used to in situ generate AgOCF₃ in the presence of silver salts and fluoride ions. Thus, we envisioned whether the oxidative trifluoromethylation of alkyllsilanes could be achieved with OCF₃ which was in situ generated in the presence of fluoride ions and TFMS. Initial investigations focused on the reaction of alkyllsilane 1 with various fluoride sources in the presence of trifluoromethyl 4-methylbenzenesulfonfate (TFMS, 2) (Table 1, see more details in the ESI†). No desired product 3a was observed when Et₃N·3HF, CsF, TBAF or FeF₃ was used as the fluoride ion source (Table 1, entries 1–4). We were delighted to find that 61% yield of the desired product 3a was observed in the presence of AgF (Table 1, entry 5). Different ligands were evaluated, and 3,4,7,8-tetramethyl-1,10-phenanthroline gave the highest yield (Table 2).
Having established optimized reaction conditions, we extended the present system to a trifluoromethylthiolation of alkylsilanes by changing the ligand and silver salt. A primary alkylsilane, 3,4,7,8-tetramethyl-1,10-phenanthroline (dtbpy), was used, the corresponding products (Scheme 2a) were obtained in 80% yield. We note that in each system, both the silver salt and oxidant omitted. A nonsteroidal anti-inflammatory drug, celecoxib, was converted to the trifluoromethoxylated product (40a) in 31% yield or trifluoromethylthiolated product (40b) in 57% yield. In addition, we prepared compounds 5a and 5b at the gram scale under the standard reaction conditions in 44% and 69% isolated yields, respectively, which demonstrates the scalability of this method. However, trifluoromethylation and trifluoromethylthiolation of secondary alkylsilanes were observed with low yields (37 and 38), and alkynes were the major byproducts.

Encouraged by our success with trifluoromethylation and trifluoromethylthiolation of alkylsilanes, we investigated the use of other silver salts to develop the functionalization of alkylsilanes (Table 3). When AgObz, AgOCOCF3, or AgSCN was used, the corresponding products (42, 43, and 44) were obtained in moderate yields. Installation of an azide group has proven to be useful in chemical biology, medicinal chemistry, and materials science. The use of AgF and TsN3 enabled azidation of alkylsilane 1 to prepare the desired product 45 in 63% isolated yield. We note that in each system, both the silver salt and oxidant were necessary for productive reactivity. Although these reactions are not fully optimized, they provide a general strategy for the functionalization of alkylsilanes.

To gain some insight into the reaction mechanism, we performed some preliminary studies (Scheme 2a). A less than 10% trifluoromethoxylated or trifluoromethylthiolated product was formed when a radical inhibitor 2,6-di-tert-butyl-4-methylphenol (BHT) (8 equiv.) was added. In addition, when 4 equiv. of 2,2,6,6-tetramethyl-1-piperidinylxy (TEMPO) was added, the TEMPO adduct 46 or 47 was obtained in 25% and 38% isolated yield, respectively. Furthermore, the reaction of alkylsilanes under the standard reaction conditions (conditions B) gave the trifluoromethylthiolated product 48 (37%) along with the 5-exo-cyclization trifluoromethylthiolated product 48′ in 12% yield. Together, these observations strongly suggested that a radical-chain mechanism or single-electron transfer (SET) was involved in the reactions. In addition, a 28% trifluoromethoxylated product was obtained when AgF2 was used in the absence of AgF and Selectfluor, which indicated that AgF2 species could be involved in the reaction (see more details in the ESI†). Finally, a silver mirror was observed in the reaction, which suggested that Ag[0] was generated.

On the basis of these mechanistic investigations, we proposed the mechanism depicted in Scheme 2b. In the presence of ligand and Selectfluor, AgF, AgF (GC = OCF3, OBz, OCOCF3, SCF3, SCN, N3) is oxidized to produce Ag[1] intermediate 114th then R group transmetalation from silicon to Ag[1] intermediate 1 can afford alkylsilver species II. The

### Table 1. Optimized reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>OCF3 or SCF3</th>
<th>Ligand</th>
<th>Oxidant</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et3NF/3HF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>Selectfluor</td>
<td>3a, 0</td>
</tr>
<tr>
<td>2</td>
<td>CsF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>Selectfluor</td>
<td>3a, 0</td>
</tr>
<tr>
<td>3</td>
<td>TBAF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>Selectfluor</td>
<td>3a, 0</td>
</tr>
<tr>
<td>4</td>
<td>FeC2F9, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>Selectfluor</td>
<td>3a, 0</td>
</tr>
<tr>
<td>5</td>
<td>AgF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>Selectfluor</td>
<td>3a, 61</td>
</tr>
<tr>
<td>6</td>
<td>AgF, TFMS (2)</td>
<td>Phen</td>
<td>Selectfluor</td>
<td>3a, 45</td>
</tr>
<tr>
<td>7</td>
<td>AgF, TFMS (2)</td>
<td>Neocuproine</td>
<td>Selectfluor</td>
<td>3a, 8</td>
</tr>
<tr>
<td>8</td>
<td>AgF, TFMS (2)</td>
<td>4,7-Ph2Phen</td>
<td>Selectfluor</td>
<td>3a, 52</td>
</tr>
<tr>
<td>9</td>
<td>AgF, TFMS (2)</td>
<td>5,6-Dione-Phen</td>
<td>Selectfluor</td>
<td>3a, 2</td>
</tr>
<tr>
<td>10</td>
<td>AgF, TFMS (2)</td>
<td>dtbpy</td>
<td>Selectfluor</td>
<td>3a, 56</td>
</tr>
<tr>
<td>11</td>
<td>AgF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>NFSI</td>
<td>3a, 0</td>
</tr>
<tr>
<td>12</td>
<td>AgF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>PhIO</td>
<td>3a, 0</td>
</tr>
<tr>
<td>13</td>
<td>AgF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>PhI(OAc)2</td>
<td>3a, 0</td>
</tr>
<tr>
<td>14</td>
<td>AgF, TFMS (2)</td>
<td>3,4,7,8-Me2Phen</td>
<td>K2S2O8</td>
<td>3a, 0</td>
</tr>
<tr>
<td>15*</td>
<td>AgSCF3</td>
<td>dtbpy</td>
<td>Selectfluor</td>
<td>3b, 80</td>
</tr>
</tbody>
</table>

* General conditions: 1 (1.0 equiv.), silver salt (4.0 equiv.), TFMS (2) [5.0 equiv.], ligand (0.3 equiv.), oxidant (3.0 equiv.), MeCN/DCM (v/v 1 : 1), 50 °C, N2. ** AgSCF3 (0.4 equiv.), CsF (4.0 equiv.), dtbpy (0.4 equiv.), Selectfluor (3.0 equiv.), MeCN/dioxane (v/v 1 : 1), 50 °C, N2. 'Yields were determined by 19F NMR with benzotriazolylmethanesulfonimide (NFSI) and benzotriazolylmethanesulfonimide (NFSI).**
subsequent single-electron transfer between Ag(II) and the R group in intermediate II leads to the generation of the R radical and Ag(I) species III. Finally, the FG group transfer from the intermediate III to the R radical generates RFG and Ag(0). At present, we cannot rule out the possibility of an alternative mechanism in which the R radical intermediate is further oxidized to generate an R carbocation intermediate, which is trapped by the FG anion to form the desired product.

Table 2  Substrate scope for silver-mediated oxidative trifluoromethoxylation and trifluoromethylthiolation of alkylsilanes

<table>
<thead>
<tr>
<th>Condition A</th>
<th>Condition B</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-Si(OEt)₃</td>
<td>R-XCF₃</td>
</tr>
<tr>
<td>Me</td>
<td>X = O 57%</td>
</tr>
<tr>
<td>3a, X = O 57%</td>
<td></td>
</tr>
<tr>
<td>3b, X = S 80%</td>
<td></td>
</tr>
<tr>
<td>4a, X = O 56%</td>
<td></td>
</tr>
<tr>
<td>4b, X = S 67%</td>
<td></td>
</tr>
<tr>
<td>5a, X = O 63%</td>
<td></td>
</tr>
<tr>
<td>5b, X = S 70%</td>
<td></td>
</tr>
<tr>
<td>6a, X = O 63%</td>
<td></td>
</tr>
<tr>
<td>6b, X = S 43%</td>
<td></td>
</tr>
<tr>
<td>7a, X = O 59%</td>
<td></td>
</tr>
<tr>
<td>7b, X = S 64%</td>
<td></td>
</tr>
<tr>
<td>8a, X = O 59%</td>
<td></td>
</tr>
<tr>
<td>8b, X = S 62%</td>
<td></td>
</tr>
<tr>
<td>9, 66%</td>
<td></td>
</tr>
<tr>
<td>10, 66%</td>
<td></td>
</tr>
<tr>
<td>11, 59%</td>
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<td>12, 61%</td>
<td></td>
</tr>
<tr>
<td>13, 59%</td>
<td></td>
</tr>
<tr>
<td>14, 56%</td>
<td></td>
</tr>
<tr>
<td>15a, X = O 54%</td>
<td></td>
</tr>
<tr>
<td>15b, X = S 53%</td>
<td></td>
</tr>
<tr>
<td>16a, X = O 61%</td>
<td></td>
</tr>
<tr>
<td>16b, X = S 63%</td>
<td></td>
</tr>
<tr>
<td>17a, X = O 61%</td>
<td></td>
</tr>
<tr>
<td>17b, X = S 63%</td>
<td></td>
</tr>
<tr>
<td>18, 41%</td>
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</tr>
<tr>
<td>19a, X = O 62%</td>
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</tr>
<tr>
<td>19b, X = S 66%</td>
<td></td>
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<tr>
<td>20a, X = O 56%</td>
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</tr>
<tr>
<td>20b, X = S 65%</td>
<td></td>
</tr>
<tr>
<td>21a, X = O 51%</td>
<td></td>
</tr>
<tr>
<td>21b, X = S 62%</td>
<td></td>
</tr>
<tr>
<td>22a, X = O 65%</td>
<td></td>
</tr>
<tr>
<td>22b, X = S 61%</td>
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</tr>
<tr>
<td>23, 62%</td>
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<tr>
<td>24, 68%</td>
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<tr>
<td>25, 73%</td>
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<tr>
<td>26, 63%</td>
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</tr>
<tr>
<td>27, 64%</td>
<td></td>
</tr>
<tr>
<td>28, 58%</td>
<td></td>
</tr>
<tr>
<td>29, 61%</td>
<td></td>
</tr>
<tr>
<td>30, 68%</td>
<td></td>
</tr>
<tr>
<td>31a, X = O 41%</td>
<td></td>
</tr>
<tr>
<td>31b, X = S 64%</td>
<td></td>
</tr>
<tr>
<td>32a, X = O 64%</td>
<td></td>
</tr>
<tr>
<td>32b, X = S 71%</td>
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</tr>
<tr>
<td>33a, X = O 64%</td>
<td></td>
</tr>
<tr>
<td>33b, X = S 71%</td>
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<tr>
<td>34, 55%</td>
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</tr>
<tr>
<td>35a, X = O 61%</td>
<td></td>
</tr>
<tr>
<td>35b, X = S 58%</td>
<td></td>
</tr>
<tr>
<td>36, 38%</td>
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</tr>
<tr>
<td>37a, X = O 12%</td>
<td></td>
</tr>
<tr>
<td>37b, X = S 25%</td>
<td></td>
</tr>
<tr>
<td>38a, X = O 9%</td>
<td></td>
</tr>
<tr>
<td>38b, X = S 27%</td>
<td></td>
</tr>
<tr>
<td>39a, X = O 62%</td>
<td></td>
</tr>
<tr>
<td>39b, X = S 69%</td>
<td></td>
</tr>
<tr>
<td>40a, X = O 32%</td>
<td></td>
</tr>
<tr>
<td>40b, X = S 57%</td>
<td></td>
</tr>
<tr>
<td>41, 59%</td>
<td></td>
</tr>
</tbody>
</table>

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*a Conditions A: alkylsilanes (1.0 equiv.), AgF (4.0 equiv.), 3,4,7,8-tetramethyl-1,10-phenanthroline (0.3 equiv.), Selectfluor (3.0 equiv.), TFMS (2.0 equiv.), MeCN/DCM (v/v 7 : 2), N₂ atmosphere, 25 °C. Conditions B: alkylsilanes (1.0 equiv.), AgSCF₃ (4.0 equiv.), 4,4'-di-tert-butyl-2,2'-bipyridine (0.4 equiv.), Selectfluor (3.0 equiv.), CsF (4.0 equiv.), MeCN/dioxane (v/v 1 : 1), N₂ atmosphere, 50 °C. Yields of isolated products are given. b Yield was determined by 19F NMR with benzotrifluoride as a standard.
Table 3  Substrate scope for silver-mediated oxidative functionalization of alkylsilanes

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgFG</th>
<th>Ligand</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AgOBz (1.0 equiv.), CsF (4.0 equiv.), Selectfluor (3.0 equiv.), MeCN/DCE (v/v 1:1), 50 °C, N2</td>
<td></td>
<td>42, 61%</td>
</tr>
<tr>
<td>2</td>
<td>AgOCOCF3 (4.0 equiv.), CsF (4.0 equiv.), Selectfluor (3.0 equiv.), MeCN/DCE (v/v 1:1), 50 °C, N2</td>
<td></td>
<td>43, 61%</td>
</tr>
<tr>
<td>3</td>
<td>AgSCN (1.0 equiv.), AgF (4.0 equiv.), Selectfluor (3.0 equiv.), MeCN/DCE (v/v 1:1), 50 °C, N2</td>
<td></td>
<td>44, 43%</td>
</tr>
<tr>
<td>4</td>
<td>AgF + TsN3 (1.0 equiv.), AgOBz (4.0 equiv.), CsF (4.0 equiv.), Selectfluor (3.0 equiv.), MeCN/DCE (v/v 1:1), 50 °C, N2</td>
<td></td>
<td>45, 63%</td>
</tr>
</tbody>
</table>

Notes and references


Conclusions

In conclusion, we have developed a silver-mediated oxidative functionalization of alkylsilanes. This strategy enables accessing a range of functionalized products directly, thus obviating the need to develop a new methodology for each specific C-Si transformation. Furthermore, the first example of silver-mediated trifluoromethylation of alkylsilanes was developed using trifluoromethyl arylsulfonate (TFMS) as the trifluoromethylation reagent. Additionally, preliminary mechanistic studies suggested that this reaction may proceed through a radical mechanism.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We gratefully acknowledge the State Key Laboratory of Elemento-Organic Chemistry for generous start-up financial support. This work was supported by the National Key Research and Development Program of China (2016YFA0602900) and the National Natural Science Foundation of China (21522205 and 21672110) and the Fundamental Research Funds for the Central Universities.

Notes and references


