# Copper-catalyzed silylation of cyclopropenes using (trifluoromethyl)trimethylsilane†

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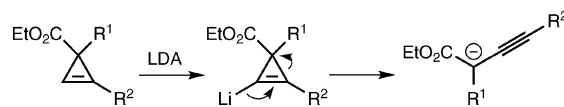A variety of cyclopropenes undergo direct silylation using (trifluoromethyl)trimethylsilane in the presence of a copper–bisphosphine catalyst; under these conditions, cyclopropenes that might otherwise undergo ring-opening are silylated efficiently.

Cyclopropenes have attracted much interest from synthetic chemists for many years.[1] Due to their significant ring strain, cyclopropenes undergo a range of unique transformations that represent enabling methodologies for organic synthesis.[1] For example, the alkene protons of cyclopropenes are relatively acidic ($pK_a \sim 30$),[2] allowing deprotonation and subsequent functionalization using strong bases. By undergoing addition reactions across the double bond,[1d] they serve as precursors to functionalized cyclopropanes, which are constituents of many biologically important compounds.[3] In addition, conformational constraints imposed by the rigidity of the three-membered ring make cyclopropenes excellent candidates for the development of new diastereo- and enantioselective reactions. As a result of these features, new methods to construct and functionalize cyclopropenes continue to be of value.

Cyclopropenes that contain a silyl substituent on the alkene are important synthetic intermediates. For example, they can serve as precursors to allenylsilanes through photochemical rearrangement.[4] Trimethylsilyl groups can efficiently control the regioselectivity of transformations such as cyclopropene carbometalation[5] and Pauson–Khand reactions.[6] Gevorgyan and co-workers have recently described the use of 1-silylcyclopropenes in sila-Morita–Baylis–Hillman reactions.[7] Since silyl groups are readily removed from the double bond of cyclopropenes with fluoride or hydroxide/alkoxide ions, they can also serve as protecting groups for the olefin protons. Common methods used to construct 1- or 2-silyl-substituted cyclopropenes include cyclopropenation of an alkynylsilane eqn (1), and silylation of a cyclopropenyl lithium species eqn (2).



$$(1)$$

$$(2)$$
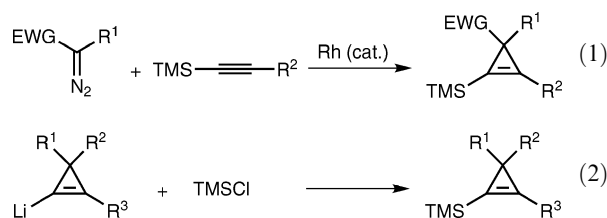
The first method often suffers from low efficiencies, requiring an excess of alkynylsilane relative to the diazo compound for acceptable results.[8] Although the second method works efficiently in many cases, it is often incompatible with base-sensitive functionality that is present on the cyclopropene. For example, anion-stabilizing substituents such as esters may promote undesired ring-opening (Scheme 1).[9a]



**Scheme 1** Ring-opening of cyclopropenyl lithium species.

While this problem may be overcome in certain cases by using an inverse addition procedure,[9b] or by employing free carboxylic acids in place of esters,[10] the development of a *direct* silylation process that proceeds under mild reaction conditions using an operationally simple protocol would be of utility. In this communication, we demonstrate that trimethylsilylation of cyclopropenes may be accomplished using (trifluoromethyl)trimethylsilane in the presence of a copper–bisphosphine catalyst.

We surmised that a milder cyclopropene silylation procedure might be realized by identification of conditions to generate softer, less basic cyclopropenyl metal species, which we hoped would react with a suitable silylating agent. On the basis that cyclopropenes often possess "alkyne-like" reactivity, and that metalation of terminal alkynes may be achieved using combinations of weak bases and soft Lewis acids,[11–13] we elected to examine reaction conditions based on the use of copper,[11] zinc,[12] and silver[13] salts. With the hope of simplifying the experimental procedure, we decided to eschew more conventional silylating reagents such as silyl chlorides or triflates (where an additional stoichiometric base is required) in favor of those that contain a functional group that could also function as the base to effect deprotonation of the cyclopropene. Our initial experiments began with cyclopropene **1a** (Table 1), which upon attempted silylation using LDA and TMSCl provided a complex mixture of products. Using commercially available *N*,*N*-dimethyltrimethylsilylamine as

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the silylating agent[14] and 5 mol% of CuI in toluene at room temperature, none of the desired product **2a** was observed (entry 1). Instead, complete conversion into furan **3** took place, which has precedence in the work of Ma and Zhang.[15] The use of Cu(acac)$_2$, AgOAc, or Zn(OTf)$_2$ led only to varying quantities of furan **3** and aldehyde **4**[16] in low to moderate conversions (entries 2–4). Changing the silylating agent to (trifluoromethyl)trimethylsilane[17] also afforded no product using Cu(acac)$_2$ (entry 5). However, we were gratified to observe that the combination of 5 mol% of Cu(acac)$_2$ and dppe[18] provided the desired product **2a** in an encouraging 40% yield (entry 6), the remainder of material being unreacted **1a**. Switching the solvent to THF increased the yield of **2a** to 88% (entry 7). A control experiment performed in the absence of Cu(acac)$_2$ demonstrated that both copper and dppe are required for reaction to occur (entry 8).

**Table 1** Identification of optimum reaction conditions for silylation of cyclopropene **1a**[a]



Side-products observed:

| Entry | Metal/ligand (5 mol% of each) | TMSX (2 equiv.) | Solvent | Yield of **2a** (%)[b] |
|---|---|---|---|---|
| 1 | CuI | TMSNMe$_2$ | Toluene | 0[c] |
| 2 | Cu(acac)$_2$ | TMSNMe$_2$ | Toluene | 0[d] |
| 3 | AgOAc | TMSNMe$_2$ | Toluene | 0[e] |
| 4 | Zn(OTf)$_2$ | TMSNMe$_2$ | Toluene | 0[e] |
| 5 | Cu(acac)$_2$ | TMSCF$_3$ | Toluene | 0 (SM) |
| 6 | Cu(acac)$_2$/dppe | TMSCF$_3$ | Toluene | 40 |
| 7 | Cu(acac)$_2$/dppe | TMSCF$_3$ | THF | 88 |
| 8 | dppe | TMSCF$_3$ | THF | 0 (SM) |

[a] Reactions were conducted using 0.20 mmol of **1a** in 0.7 mL of solvent. [b] Isolated yield. [c] Complete conversion into furan **3** was observed. [d] Ca. 72% of **3** and 8% of **4** was observed. [e] Ca. 20% of **4** was observed. dppe = 1,2-bis(diphenylphosphino)ethane. SM = starting material.

Having established satisfactory reaction conditions with cyclopropene **1a**, we proceeded to explore the scope of the direct silylation process with a range of other 1,3,3-trisubstituted cyclopropenes (Fig. 1). Analogues of **1a** containing other aromatic or alkyl substituents on the alkene successfully underwent silylation to provide silylcyclopropenes **2b–2e** in 69–99% yield. Replacement of one of the methyl esters at the 3-position with an aryl substituent, or both of the methyl esters with ethyl esters was also tolerated, leading to silylcyclopropenes **2f–2j** in 66–84% yield.[19] The efficiencies of these reactions are not markedly affected upon increasing the scale. For example, cyclopropene **2d** was formed in 99% and 93% yields on 0.20 and 2.00 mmol scales, respectively.
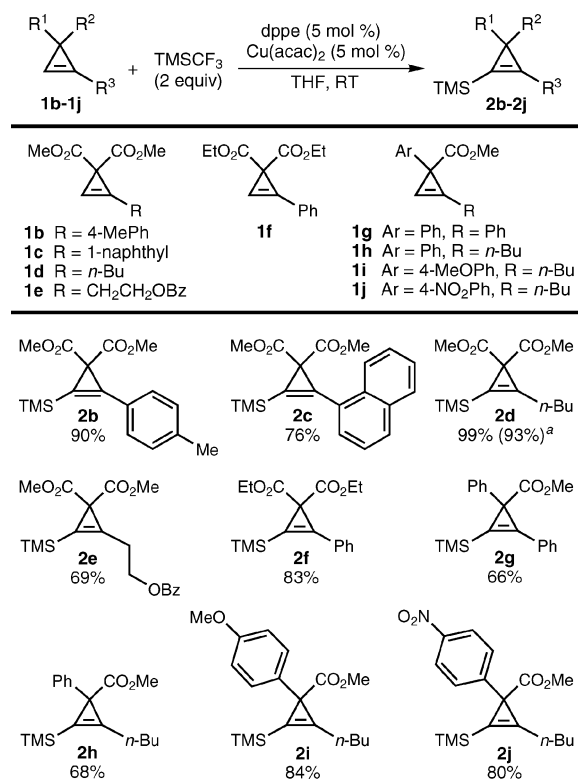


**Fig. 1** Direct silylation of assorted cyclopropenes. Unless otherwise stated, reactions were conducted using 0.20 mmol of cyclopropene, 0.01 mmol of Cu(acac)$_2$ and 0.01 mmol of dppe in THF (0.7 mL). Cited yields are of isolated material. [a] Yield in parentheses refers to a reaction conducted using 2.0 mmol of **1d**, 0.10 mmol of Cu(acac)$_2$ and 0.10 mmol of dppe in THF (7 mL).

To gain some insight into these reactions, the silylation of deuterated cyclopropene **5** (eqn (3)) was followed by $^{19}$F NMR spectroscopy (Fig. 2).† As the reaction proceeded, a new signal appeared at −80 ppm (t, $J_{FD}$ = 12.1 Hz), showing that DCF$_3$ was formed. Since substrate **5** was the only source of deuterium in the system, this observation suggests that at some stage a trifluoromethide species abstracted a deuteron from the substrate.
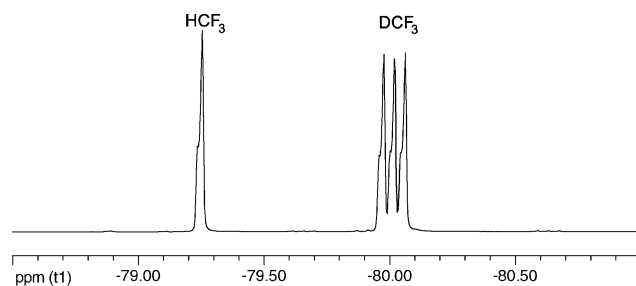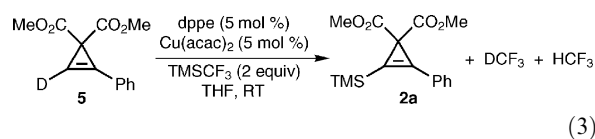


(3)



**Fig. 2** $^{19}$F NMR spectrum of the silylation of deuterated cyclopropene **5** (eqn (3)).

The production of DCF$_3$ was also accompanied by the formation of HCF$_3$ (eqn (3)), which most likely resulted from reaction of a trifluoromethide species with trace moisture present in the mixture. EPR and cyclic voltammetry experiments suggest that copper largely retains the +2 oxidation state in these reactions,† though we cannot exclude the possibility that the active catalytic species is a Cu(I) complex that exists as a minor component. With the information currently available, speculation about the exact nature of the mechanism of these reactions would be premature. Although on the basis of our original hypothesis (*vide supra*) it is tempting to suggest the involvement of bisphosphine-ligated copper–trifluoromethyl complexes (that give rise to cyclopropenyl copper species that then undergo silylation with TMSCF$_3$), alternative mechanisms involving electrophilic silylation[14] or hypervalent silicon intermediates[17a] cannot be excluded. A clearer picture of the mechanism of these reactions therefore awaits further investigations.

In summary, we have developed a new method for the direct silylation of cyclopropenes that employs TMSCF$_3$ as the silylating agent in conjunction with substoichiometric quantities of Cu(acac)$_2$ and dppe. These reactions take place under operationally more convenient conditions than traditional silylation procedures, and do not require the use of strong alkyl lithium or alkali metal amide bases which may affect base-sensitive functionality. Studies to broaden the scope of the process,[19] and further applications of this methodology will be the subjects of future reports from this laboratory.

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