Synthesis of propargylic fluorides from allenylsilanes†

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Allenylsilanes reacted at room temperature in acetonitrile with Selectfluor, an electrophilic fluorinating reagent, to give secondary propargylic fluorides in moderate to good yields; mechanistically, a side-product resulting from a 1,2-silyl shift testifies to the presence of a cationic intermediate.

The remarkable characteristics of the fluorine group make it an ideal substituent to produce compounds with unique properties.[1] Although numerous important fluorinated building blocks are accessible and used for further functional manipulation,[2] little has been done on the synthesis and reactivity of propargylic monofluorides, apart from the work of Grée.[3] The most common synthetic approach to propargylic fluorides relies on a dehydroxyfluorination of propargylic alcohols using nucleophilic sources of fluorine with reagents such as fluoroenamine,[4] Yarovenko's reagent,[5] tetrabutylammonium fluoride,[6] sulfur tetrafluoride[7] or *N*,*N*-(diethylamino)sulfur trifluoride (DAST).[3,8] It is noteworthy that piperidinosulfur trifluoride has been used in the nucleophilic substitution of a protected trimethylsilylated propargylic alcohol in the synthesis of structurally elaborated prostacyclin analogues.[9]

We report in this communication the first route to propargylic monofluorides based on the use of an electrophilic fluorinating reagent (Fig. 1). We reasoned that exposure of allenylsilanes to commercially available and easy to handle N–F reagents would result in the formation of the corresponding propargylic fluorides. This idea was substantiated by the recent advances in the area of electrophilic fluorodesilylation of structurally diverse organosilanes for the preparation of fluorinated targets[10] and the established reactivity of allenylsilanes with other electrophiles.[11]

For this study, various allenylsilanes were prepared in high yields from the corresponding silylated propargylic alcohols using one of two procedures (Scheme 1).† The first procedure began with the mesylation of the silylated propargylic alcohol followed by organocuprate substitution using the requisite organolithium combined with CuCN and LiCl (eqn (1), Scheme 1).[12] The yields

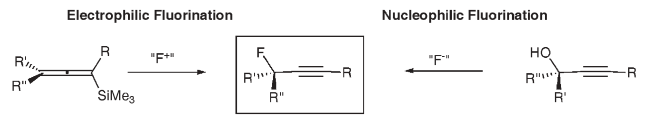

Fig. 1 Two approaches towards propargylic fluorides.

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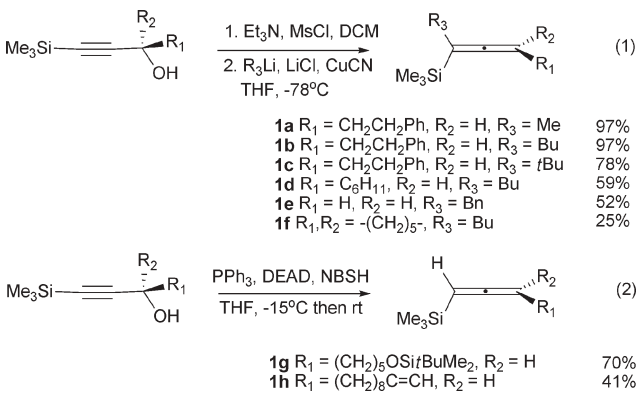
† Electronic supplementary information (ESI) available: Procedures for the preparation of the allenylsilanes and propargylic fluorides are provided as well as full characterisation of all new compounds. See DOI: 10.1039/b610013a

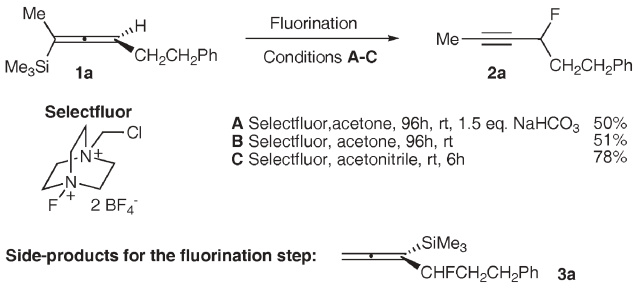
for the conversion of the mesylates into the allenylsilanes are good to excellent, ranging from 52% to 97%, except for allenylsilane **1f** due to the propensity of the quaternary mesylate to decompose rapidly at room temperature. The second procedure, developed by Myers, is an expedient one-step synthesis converting the silylated propargylic alcohol into the desired allenylsilanes upon treatment with diethyl azodicarboxylate (DEAD), triphenylphosphine and *o*-nitrobenzenesulfonylhydrazine (NBSH).[13] This second strategy was applied for the preparation of allenylsilanes **1g** and **1h** which were obtained in 70% and 41% yield respectively (eqn (2), Scheme 1).

An initial evaluation of the proposed route was performed with allenylsilane **1a** in the presence of Selectfluor [1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)] as the electrophilic fluorinating reagent. The desired propargylic fluoride **2a** was obtained within 96 hours in 50% yield when the reaction was carried out in acetone and in the presence of 1.5 eq. of $NaHCO_3$. The base was used primarily to avoid possible protodesilylation.[14] Under these conditions, a side-product was isolated in 13% yield and unambiguously identified as the fluorinated allenylsilane **3a**. The base was found unnecessary as a similar yield of 51% was obtained in its absence, with no trace of a non-fluorinated alkyne resulting from a protodesilylation process. Further studies revealed that acetonitrile was a better solvent than acetone for this transformation, allowing a shorter reaction time (6 h) and a higher isolated chemical yield for **2a** (78%). Under these conditions, the side-product **3a** could not be detected in the crude reaction mixture (Scheme 2).

Having established the optimal conditions for the electrophilic fluorodesilylation of **1a**, we examined the scope and limitations of this reaction with allenylsilanes **1b–h** featuring various substitution patterns. The fluorodesilylations were carried out in acetonitrile at room temperature (Table 1). As is evident from the examples of



Scheme 1 Synthesis of allenylsilanes **1a–h**.

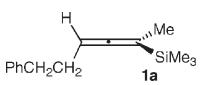
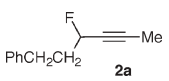
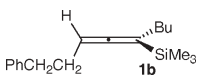
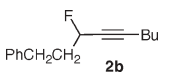
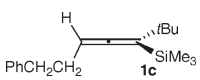
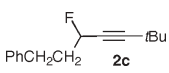
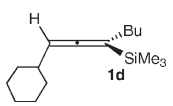
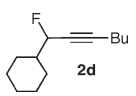
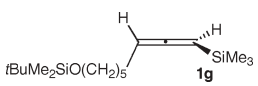
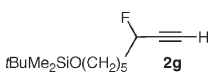
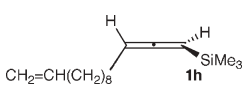
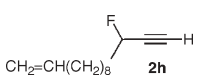
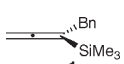
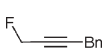
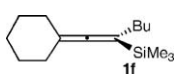
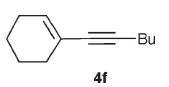


Scheme 2 Fluorination of allenylsilane **1a**.

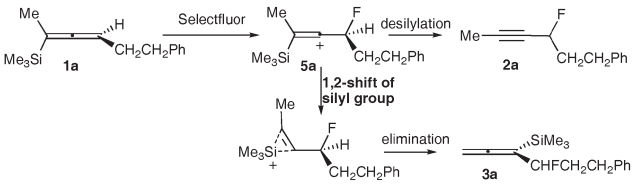
Table 1, the method is suitable for the preparation of various terminal and non-terminal secondary propargylic fluorides with isolated yields ranging from 40% to 78%. The reaction tolerates alkyl, alkenyl and silyloxy groups (entries 1–6). However, only traces of the primary propargylic fluoride **2e** (entry 7) were observed using this method due to the lack of reactivity of the disubstituted allenylsilane **1e**, which was recovered almost intact after work-up. In contrast, tetrasubstituted allenylsilane **1f** reacted rapidly but the corresponding propargylic fluoride **2f** featuring a quaternary fluorinated carbon could not be isolated due to the propensity of this compound to eliminate HF rapidly under the reaction conditions, a process resulting in the formation of the corresponding enyne (entry 8).†

Mechanistically, the C–Si bond in trimethylsilylallenes such as **1a** is oriented *cis* coplanar to the allylic π bond and thus can afford

Table 1 Fluorodesilylation of allenylsilanes **1a–h**

Entry	Allenylsilane	Product	Yield (%)[a]
1			78
2			69
3			40[b]
4			59
5			51
6			56
7			5
8			57[c]

[a] Isolated yields. [b] Reaction in acetone with 1.5 eq. of $NaHCO_3$. [c] No propargylic fluoride could be isolated.



Scheme 3 Suggested mechanism for the fluorodesilylation of **1a**.

direct stabilisation to the transition state resulting from electrophilic addition of Selectfluor at C3. This process provides a stabilised fluorinated vinyl cation, which upon desilylation affords the desired propargylic fluoride **2a**. If a 1,2-shift of the trimethylsilyl group occurs prior to the desilylation,[15] an isomeric vinyl cation is formed and eliminates to give a terminal allenylsilane which does not react further under the reaction conditions as seen for **1e**. This secondary reaction pathway accounts for the formation of the side-product **3a** observed during our optimisation studies. The presence of this compound further testifies to the formation of the carbocationic intermediate **5a** (Scheme 3).

In summary, we have established a new reaction that leads to propargylic monofluorides. This mild and operationally simple reaction based on the use of an electrophilic source of fluorine and carried out at room temperature is suitable for the formation of secondary propargylic fluorides. Further studies on this novel transformation are ongoing in our laboratory with a focus on the preparation of enantiopure functionalised propargylic fluorides from the corresponding non-racemic chiral allenylsilanes.‡

Notes and references

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