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## Preliminary Note

# (3-Trifluoromethyl-but-3-en-1-ynyl)trimethylsilane as a potentially useful $CF_3$-containing building block: preparation and CsF/18-crown-6 ether-catalysed reactions with aldehydes

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## Abstract

A novel $CF_3$-containing building block, (3-trifluoromethyl-but-3-en-1-ynyl)trimethylsilane, has been prepared. It reacted readily with aldehydes in the presence of cesium fluoride and 18-crown-6 ether to afford 2-trifluoromethyl-1-alken-3-ynyl-5-ols.

Organic molecules bearing $CF_3$ groups have been attracting considerable attention in recent years because of their potential biological activities [1]. An interesting pathway for the synthesis of such compounds is to prepare some versatile intermediates which carry the $CF_3$ group and then utilise them as building blocks. Hence, the search for new versatile $CF_3$-containing building blocks, which contain functionalities that would allow further synthetic elaborations, is highly desirable. In this context, a number of $CF_3$-containing reagents useful as building blocks have already been reported [2, 3].

Silyl acetylenes are effective reagents for the introduction of alkynyl groups [4]. Thus, we have studied the preparation of an appropriate $CF_3$-substituted silyl acetylene and its utility as a precursor in the synthesis of a variety of trifluoromethylated molecules, in the hope that its normal reactivity would be retained. For this purpose, the title compound (**3**) was chosen since we expected that it would be amenable to fluoride anion-catalysed transformations [5]. Here we report the preparation of this novel compound and its fluoride anion-catalysed reactions with aldehydes.

For the preparation of **3**, the palladium-catalysed condensation of 2-bromo-3,3,3-trifluoropropene (**1**) with trimethylsilyl acetylene (**2**) was investigated (Scheme 1).

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TABLE 1

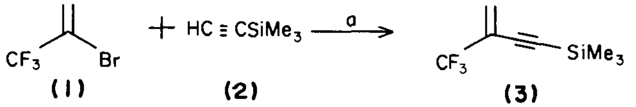
Preparation of $CF_3$-containing enynyl-substituted alcohols (**5**)[a]

| Entry No. | Aldehydes **4**, R= | Reaction time (h) | Product (**5**) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | Ph(**4a**) | 2 | **5a** | 84 |
| 2 | 4-$MeOC_6H_4$ (**4b**) | 3 | **5b** | 85 |
| 3 | 4-$MeC_6H_4$ (**4c**) | 2 | **5c** | 80 |
| 4 | 4-$ClC_6H_4$ (**4d**) | 3 | **5d** | 75 |
| 5 | 3-$ClC_6H_4$ (**4e**) | 3 | **5e** | 70 |
| 6 | 2-$ClC_6H_4$ (**4f**) | 3 | **5f** | 75 |
| 7 | 2-$BrC_6H_4$ (**4g**) | 2 | **5g** | 70 |
| 8 | 2-$C_4H_3O$ (**4h**)[c] | 3 | **5h** | 64 |
| 9 | i-$C_3H_7$ (**4i**) | 3 | **5i** | 50 |
| 10 | $C_2H_5$ (**4j**) | 3 | **5j** | 55 |

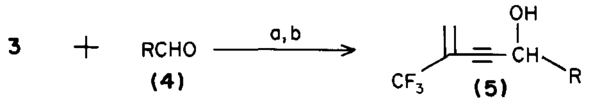
[a] Reactions were carried out in THF with compound **3** (1.2 equiv.), aldehyde (1 equiv.), CsF (0.05 equiv.) and 18-crown-6 (0.01 equiv.).

[b] Isolated yield based on the consumed aldehyde. Satisfactory spectral and microanalytical data were obtained for all new compounds (**5a**–**5j**).

[c] 2-Furyl.



Scheme 1. a, $PdCl_2(PPh_3)_2$ (1 mol%), CuI (1 mol%), $Bu_3N$, 60 °C.



Scheme 2. a, 5 mol% CsF, 1 mol% 18-crown-6, THF, −20 °C to r.t.; b, 2 N aq. HCl.

Thus, **1** (0.1 mol) [6], **2** (0.12 mol), $PdCl_2(PPh_3)_2$ (1 mmol), CuI (1 mmol) and $Bu_3{}^nN$ (30 ml) were mixed and stirred for 4 h at 60 °C under argon. The volatile components were then removed by careful fractional distillation and **3** was obtained as a colourless liquid in 95% yield, b.p. 120 °C*.

To demonstrate the synthetic utilities of **3**, it was subjected to fluoride anion-catalysed reaction with aldehydes in the presence of a catalytic amount of 18-crown-6 ether. Usual work-up and purification gave the $CF_3$-containing conjugated enynyl-substituted alcohols (Scheme 2 and Table 1).

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*Spectroscopic data for **3**: $^1H$ NMR (60 MHz, $CDCl_3$) $\delta$: 0.2 (s, 9 H); 6.0 (m, 2 H) ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: −9.0 (s) ppm. IR (neat) ($cm^{-1}$): 2200 (s); 1120 (s). MS (*m/z*): 192 ($M^+$); 177; 147. Analysis: Calc. for $C_8H_{11}F_3Si$: C, 50.00; H, 5.73%. Found: C, 50.18; H, 5.54%.

A typical procedure was as follows. Compound **3** (6 mmol) was added by means of a syringe to a well-stirred suspension of cesium fluoride (0.25 mmol), 18-crown-6 (0.05 mmol) and aldehyde ( 5 mmol) in THF (15 ml) at −20 °C under argon. The resultant mixture was stirred for 30 min at that temperature and then at room temperature for an additional 1.5–2.5 h. Hydrochloric acid (2 N, 20 ml) was added and stirring continued for 30 min. The product was then extracted with ether, the ethereal extract being washed successively with 5% aqueous sodium bicarbonate and brine and then dried ($Na_2SO_4$). Removal of the solvent under reduced pressure and purification by column chromatography on silica gel gave the pure product.

The results show that enynyl silane (**3**) possesses normal reactivity which is not adversely affected by the presence of the $CF_3$ substituent. As an alternative to CsF, KF may also be used as a catalyst.

The reaction is applicable to a wide range of aldehydes and on the basis of the consumed aldehyde the yields are good. Hence, this reaction provides a convenient route to $CF_3$-containing enynyl-substituted alcohol derivatives.

In summary, we have prepared a novel $CF_3$-containing enynyl silane and established its feasibility as a reagent possessing normal reactivity under fluoride anion-catalysed reaction conditions with aldehydes. Based on this and other known properties of silylacetylenes [7], a variety of other viable processes involving **3** should also be feasible. Exploration of further applications of **3** for the synthesis of trifluoromethylated molecules is in progress.

## Acknowledgment

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