

Fluoride ion-initiated α -fluorovinylolation of carbonyl compounds with α -fluorovinyl-diphenylmethylsilane

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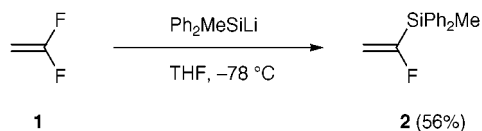
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α -Fluorovinyl-diphenylmethylsilane was synthesized in one step from 1,1-difluoroethylene; the TBAF-initiated reaction of the silane with carbonyl compounds smoothly proceeded to give the corresponding α -fluoroallylic alcohols in good yields.

Fluorinated allylic alcohols have recently received much attention due to their versatility as building blocks for complex structures.¹ These alcohols should be accessible from carbonyl compounds by fluorovinylolation in a straightforward way. Although the di- or tri-fluorovinylolation of carbonyl compounds to afford the corresponding fluorinated allylic alcohols has been reported,² to the best of our knowledge, no monofluorovinylolation as the simplest case has been reported so far. The reason seems to be the lack of the generation of the monofluorovinyl anion species.³ We have considered the title compound as a promising candidate for a monofluorovinylolation reagent which would generate the monofluorovinyl anion species by action of the fluoride source.⁴ This report describes the first preparation and reactions of the α -fluorovinyl-diphenylmethylsilane **2** as a useful reagent for introducing a monofluoroethylene moiety into carbonyl compounds.⁵

Our synthetic route for the preparation of α -fluorovinyl-diphenylmethylsilane is depicted in Scheme 1. Since we have recently reported the convenient preparation of α -fluorovinyl-diphenylphosphine from 1,1-difluoroethylene **1**,⁶ this method was applied to the preparation of the silane. As expected, the reaction of diphenylmethylsilyllithium⁷ and 1,1-difluoroethylene in THF at -78°C proceeded smoothly to give the desired product in 56% yield *in one step*.[†] We believe that the key to this reaction is use of chlorodiphenylmethylsilane instead of chlorophenyl-dimethylsilane. When the latter was employed under similar reaction conditions, the yield of the corresponding α -fluorovinylphenyl-dimethylsilane was low and the contaminant 1,2-diphenyl-1,1,2,2-tetramethyldisilane could not be separated from the desired α -fluorovinylphenyl-dimethylsilane.

We have examined the use of α -fluorovinyl-diphenylmethylsilane as a potential reagent for introducing an α -fluorovinyl group into various carbonyl compounds. The reaction of a slight excess of α -fluorovinyl-diphenylmethylsilane (1.2 equiv.) and benzaldehyde in the presence of a catalytic amount of TBAF (1 M THF solution, 10 mol%) in THF gave the desired product in 34% yield. Increasing the amount of catalyst (30 mol%) did not significantly improve the yield (39%). Based on TLC analysis of the reaction mixture, we observed that the α -fluorovinyl-diphenylmethylsilane was completely consumed although the benzaldehyde still remained. This finding may be explained as follows: the generated α -fluorovinyl anion species decomposed to the vinylcarbene or abstracted a proton from the



Scheme 1

Table 1 Reaction of α -fluorovinyl-diphenylmethylsilane with various carbonyl compounds

Entry	R	R'	Yield (%) ^a
1	Ph	H	61
2	4-MeOC ₆ H ₄	H	77
3	4-PhC ₆ H ₄	H	61
4	2-Naphthyl	H	65
5 ^b	(<i>E</i>)-PhCH=CH	H	60
6 ^c	CH ₃ (CH ₂) ₉	H	50
7	PhCH ₂ CH ₂	Me	18
8	Ph	Me	13

^a Isolated yield. ^b TBAF (20 mol%) was used. ^c TBAF was added to the reaction mixture at -70°C .

reaction medium due to its modest reactivity prior to its addition to benzaldehyde. On the basis of this idea, increasing the amount of the silane gave better results (1.5 equiv., 42%; 2.0 equiv., 61%). The reaction was applied to the silane and various carbonyl compounds under optimized conditions. These results are shown in Table 1. Although ketones afforded the adducts in low yields, probably due to their steric hindrance, aldehydes gave the adducts in fairly good yields. It is noteworthy that the reaction proceeded under mild conditions in contrast to the reaction of difluorovinyl-lithium.⁸ Attempts to improve the ketone adducts at an elevated reaction temperature (55°C) resulted in formation of a complex mixture of products.

A typical experimental procedure (Table 1, entry 2) is as follows: TBAF (1 M THF solution, 40.3 μl , 0.04 mmol, 10 mol%) was added to a mixture of α -fluorovinyl-diphenylmethylsilane (97.7 mg, 0.40 mmol) and 4-methoxybenzaldehyde (24.5 μl , 0.20 mmol) dissolved in THF (1 ml) at 0°C . The resulting mixture was stirred for 1 h at 0°C and for 16 h at room temperature. After the usual workup, column chromatography (silica gel, hexane-EtOAc = 9:1) of the residue afforded 28.5 mg of 2-fluoro-1-(4'-methoxyphenyl)-2-propen-1-ol (77% yield).[‡]

In conclusion, we have demonstrated the first preparation of α -fluorovinyl-diphenylmethylsilane from 1,1-difluoroethylene in one step. The generated α -fluorovinyl anion species derived from the silane by action of TBAF reacted with various carbonyl compounds to give the corresponding α -fluoroallylic alcohols in good yields. Further studies on its synthetic utility are now in progress in our laboratory.

Notes and references

[†] Preparation of **2**: To a solution of lithium wire (0.14 g, 20 mmol) in 10 ml of THF was added a catalytic amount of iodine and chlorodiphenylmethylsilane (1.03 ml, 5 mmol) at room temperature under argon. The solution was

irradiated with ultrasound for 30 min and a black–green color developed. After stirring for an additional 16 h, the solution was cooled to $-78\text{ }^{\circ}\text{C}$. At this temperature, argon was replaced with 1,1-difluoroethylene (balloon). The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min, gradually warmed to $0\text{ }^{\circ}\text{C}$, and carefully quenched with saturated aqueous NH_4Cl . After the usual workup, the residue was chromatographed on silica gel (hexane as an eluent) to give the desired product (683 mg, 56%): $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3071, 3050, 2963, 1620, 1429, 1256, 1160, 1115, 910, 881, 793, 729 and 698; $\delta_{\text{H}}(\text{CDCl}_3)$ 0.72 (3H, s), 4.86 (1H, dd, J 3.4, 61.5), 5.48 (1H, dd, J 3.4, 32.7), 7.34–7.66 (10H, m); m/z 242 (0.7%, M^+), 201 (100), 197 (59), 181 (58), 179 (26), 164 (31), 149 (31), 139 (82), 105 (21), 91 (28) (calcd. for $\text{C}_{15}\text{H}_{15}\text{FSi}$: C, 74.34; H, 6.24. Found: C, 74.43; H, 6.25%).

‡ Selected data for 2-fluoro-1-(4'-methoxyphenyl)prop-2-en-1-ol: $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3415, 2840, 1678, 1612, 1586, 1513, 1466, 1305, 1251, 1176, 1033, 942, 831 and 778; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.19 (1H, d, J 4.9), 3.81 (3H, s), 4.67 (1H, dd, J 2.9, 48.8), 4.76 (1H, dd, J 2.9, 17.3), 5.17 (1H, dd, J 4.9, 8.8), 6.91 (2H, d, J 8.8), 7.36 (2H, d, J 8.8); m/z 182 (24, M^+), 121 (100), 120 (30), 109 (98), 108 (38), 101 (35), 77 (81), 51 (35); (calcd. for $\text{C}_{10}\text{H}_{11}\text{FO}_2$: C, 65.92; H, 6.09. Found: C, 65.72; H, 6.21%).

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