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2-(TRIFLUOROMETHYL)ALLYLTRIMETHYLSILANE. A USEFUL BUILDING BLOCK FOR TRIFLUOROMETHYLATED ORGANIC MOLECULES

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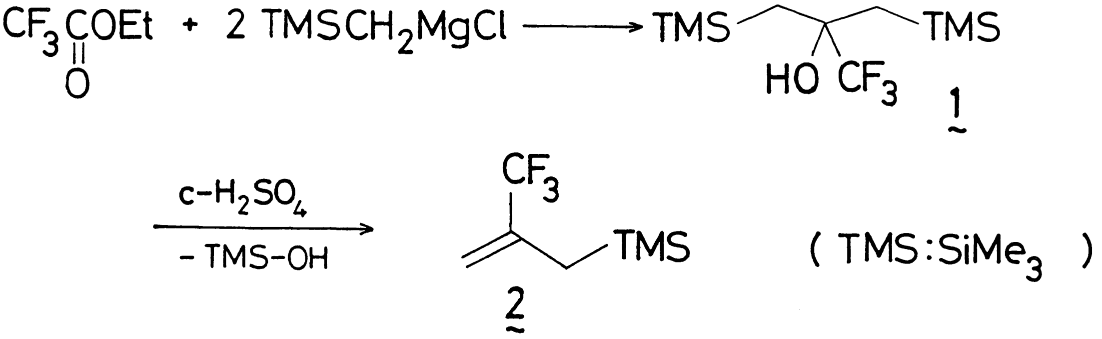
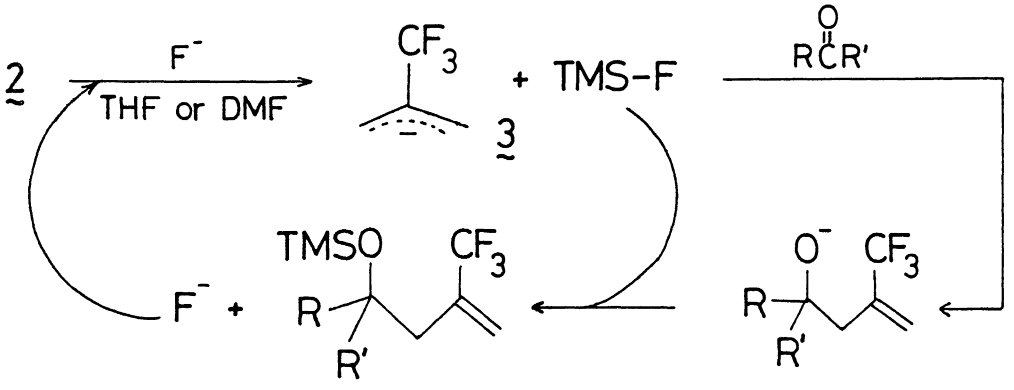
2-(trifluoromethyl)allyltrimethylsilane, a new building block for the introduction of trifluoromethyl group was prepared by the Grignard reaction of ethyl trifluoroacetate with (trimethylsilyl)methylmagnesium chloride. This allylsilane underwent the reaction with aldehydes and ketones to give the adducts in good yields.

In recent years, organic molecules bearing a trifluoromethyl group have been drawing attention because of their possible biological activities.[1,2a] A number of synthetic methods for trifluoromethylated compounds have been developed so far,[2b] which involve direct trifluoromethylation and use of building blocks containing a trifluoromethyl group. For examples of the latter case, (1) dimethyl (trifluoromethyl)malonate from octafluoroisobutene,[3] (2) 2- and 3-trifluoromethylpropionaldehydes and propionic acids from 3,3,3-trifluoropropene,[4] (3) trifluoroacetonitrile phenylimine from trifluoroacetaldehyde hydrate[5] are known as useful building blocks. In our continuing study for the introduction of a trifluoromethyl group into organic molecules, we wish here to report a new synthetic route to trifluoromethylated compounds which involves the synthesis and reactions of 2-(trifluoromethyl)allyltrimethylsilane (**2**) as a new building block.

The allylsilane **2** was prepared as follows.[6] Ethyl trifluoroacetate was employed for the source of the trifluoromethyl group because of its low cost, and two equivalents of the Grignard reagent made from chloromethyltrimethylsilane was added to the ester to produce 1,3-bis(trimethylsilyl)-2-trifluoromethylpropan-2-ol (**1**). Although the β-trimethylsilylalcohol **1** should give the allylsilane **2** by Peterson elimination,[7] all of conditions used by him gave an undesirable product, the structure of which was not identified. However, it was found that the compound **2** was yielded by dropping **1** slowly into concentrated sulfuric acid under reduced pressure, the product being collected in a trap cooled to -78 °C, and the overall yield after distillation (bp 106.5 - 107.0 °C) was 60%, calculated from the ester.



It is known that allylsilanes[8] or polyhalogenophenylsilanes[9] react with various electrophiles in the presence of a Lewis acid ($TiCl_4$, BF_3OEt_2, $AlCl_3$, *etc.*)[10] or fluoride ion (potassium fluoride,[9] tetra-*n*-butylammonium fluoride (TBAF),[11] *etc.*). Using Lewis acids, our trifluoromethyl-containing allylsilane **2** did not give any adducts with aldehydes because of the existence of a strongly electron withdrawing trifluoromethyl group. Meanwhile, the reaction of **2** in the presence of fluoride ion proceeded easily through the allylic anion (**3**) stabilized by the effect of trifluoromethyl group and gave adducts with various aldehydes and ketones. Then we tried the reaction of allylsilane **2** with these electrophiles promoted by TBAF or cesium fluoride, and the results were summarized in Table 1.



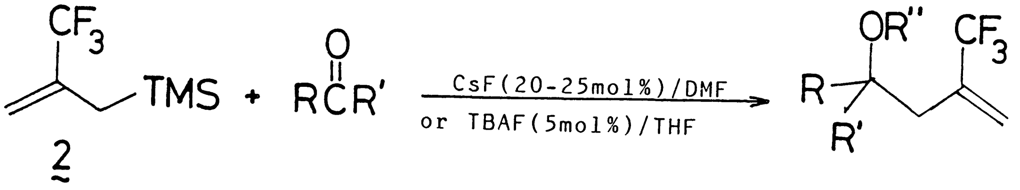
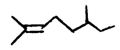


Table 1.

Entry	R	R'	R''	Reaction time / h	Isolated yield / % a)
1	Ph	H	H	2	99 (85)
2	n-C_6H_{13}	H	H	2	61 (82)
3	$PhCH(CH_3)$	H	H	5	77 (59)
4	Furfuryl	H	H	2	85 (89)
5		H	H	5	83 (80)
6	Cinnamyl	H	H	1	78 (48)
7	Ph	CH_3	$(CH_3)_3Si$	5	81 (56)
8	Ph	Ph	$(CH_3)_3Si$	5	94 (—)b)
9	$C_2H_5CH(CH_3)CH_2$	C_2H_5	$(CH_3)_3Si$	5	31 (—)b)
10	$-(CH_2)_5-$		H	5	41c) (—)b)

a) The yields were obtained by CsF/DMF system, although those in the parenthesis were done by TBAF/THF system.

b) Not tried. c) Determined by ^{19}F NMR using $PhCF_3$ as the internal standard.

The yields given by the reaction of **2** with aldehydes were fair to excellent. Cinnamaldehyde gave mainly 1,2-adduct although other products, one of which may be the 1,4-adduct, were detected by ^{19}F NMR. The reaction of **2** with ketones gave only moderate yields when R and R' are alkyl group due to the low electrophilicity of dialkyl ketones.

A typical procedure is described for the synthesis of 1-phenyl-3-trifluoromethyl-3-buten-1-ol. To a mixture of cesium fluoride (77.2 mg, 0.51 mmol, 24 mol%), 4A molecular sieves (50 mg), and 5 ml of dry dimethylformamide (DMF) was added benzaldehyde (0.24 ml, 2.4 mmol) and 2-(trifluoromethyl)allyltrimethylsilane (0.39 ml, 2.1 mmol) at room temperature with stirring under nitrogen. After 2 hours, the reaction mixture was quenched with MeOH-1N HCl (for entry 7-9, only water was used for quenching) and extracted with diethyl ether. This organic layer was washed with water, then with brine, and dried over $MgSO_4$. Evaporation of the solvent afforded an oil which was chromatographed to produce 446 mg of 1-phenyl-3-trifluoromethyl-3-buten-1-ol as a pale yellow colored oil (99% yield).

Related works are in progress.

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