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Indium-mediated allylation reaction of difluoroacetyltrialkylsilanes in aqueous media

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Abstract—Indium-mediated allylations of difluoroacetyltrialkylsilanes in aqueous media give homoallylic alcohols exclusively. The common Brook rearrangement *C*- to *O*-silyl group migration is totally suppressed with no detectable formation of enol silyl ethers. The influence of water on the allylation reaction is also described. © 2002 Elsevier Science Ltd. All rights reserved.

Acylsilanes, recognized as synthetic equivalents of aldehydes due to the facile excision of the silyl group by treatment with fluoride ion, have been used as versatile building blocks for the syntheses of complex organic molecules.[1] Fluorinated acylsilanes, in particular, are useful building blocks with diverse applications.[2] However, reactions of fluorinated acylsilanes with alkyl(aryl) Grignard compounds[3] and lithium reagents[2a] result in the formation of enol silyl ethers via Brook rearrangement[4] followed by defluorination (Scheme 1).

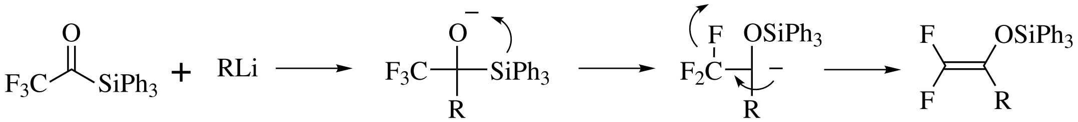
The hydroxy group and carbon–carbon double bond of the homoallylic alcohols that would be created by the allylation reaction[5] of fluoroacylsilanes suggests an entry to versatile building blocks for the formation of multi-functionalized fluorinated compounds.[6] Such compounds are well understood to possess diverse applications in pharmaceutical, agrochemical, and material science.[7] These attractive targets have been the aim of other researchers as well.[8]

As part of our research on the development of new fluorinated building blocks and our exploration of the synthetic utility of indium-mediated transformations,[9] we recently reported the syntheses of novel fluorinated acetyltrialkylsilanes[10] **1**. In this paper, we wish to present the results of our continuing studies on the synthetic utility of fluorinated acetyltrialkylsilanes **1**, in particular, the transformation of those substances to homoallylic alcohols by allylation reactions using indium in aqueous media.

Organic reactions carried out under aqueous conditions possess significant advantages relative to those employing organic solvents,[11] e.g. avoidance of flammable or anhydrous solvents, reduced environmental and economic impact and simplified processing in protection–deprotection schemes of reactive functional groups. As such, allylation reactions of carbonyl compounds using various metals such as Zn,[12] In,[13] Bi,[14] Sn,[15] Mg,[16] Mn,[17] Sb,[18] Pb,[19] and Hg[20] in aqueous media have been reported.

In this work the results of a series of allylation reactions of compound **1a** with allyl bromide and indium, where various concentrations of water in THF were employed, are summarized in Table 1.

Both water and THF are essential for the allylation reaction as can be seen from the formation of trace amounts of homoallylic alcohol when pure water or



Scheme 1. Formation of enol silyl ether via Brook rearrangement and defluorination.

Keywords: indium; allylation; difluoroacetyltrialkylsilane; homoallylic alcohol; enol silyl ether; Brook rearrangement.

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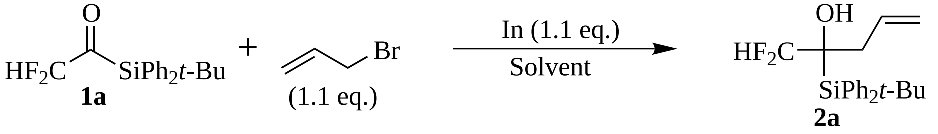
Table 1. The influence of water concentration on indium-mediated allylation reactions in aqueous THF



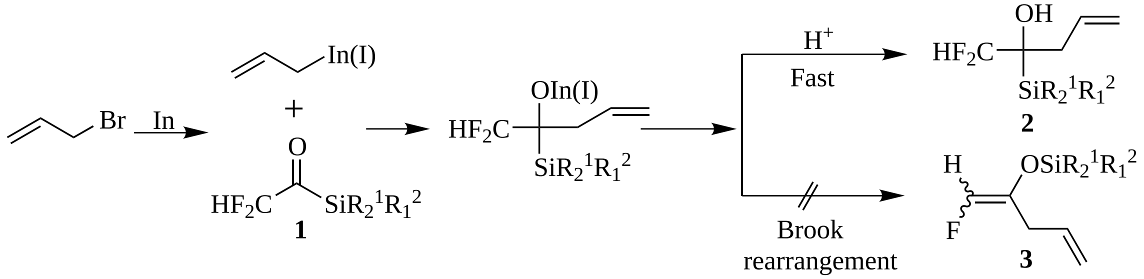
Entry	Solvent	Reaction time (h)	Ratio[a]	
			1a (%)	**2a** (%)
1a	100% THF	24	>99	<1
1b	90% THF:10% H_2O	24	0	100
1c	50% THF:50% H_2O	24	0	100
1d	20% THF:80% H_2O	24	9	91
1e	10% THF:90% H_2O	48	31	69
1f	100% H_2O	48	>99	<1

[a] Determined by GC and ^{19}F NMR.

anhydrous THF was employed (entries **1a**, **1f**). However, the importance of THF in this reaction relative that of water is evident in both longer reaction times and lower conversions as the concentration of water increased. This outcome may be rationalized by recognizing that the solubility of difluoroacetyltrialkylsilane is diminished in increasingly aqueous solvents. It is worth noting that the homoallylic alcohol was formed exclusively under these reaction conditions. Enol silyl ether **3**,[2a,3] found as a major product in the reactions of fluorinated acylsilanes with organometallic compounds via Brook[4] rearrangement and defluorination was not found. Furthermore, not only the strong absorption of hydroxyl group at 3514 cm^{-1} observed by IR spectroscopy but also the disappearance of the hydroxy proton peak at 2.3 ppm in ^1H NMR spectrum by deuterium exchange confirm that the product of allylation is the homoallylic alcohol.

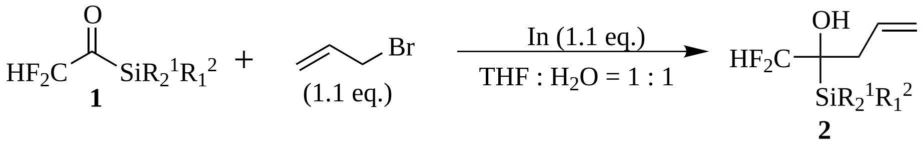
The reaction mechanism of indium-mediated allylations in aqueous media is still not clear. Recently, Chan et al.,[21] proposed allylindium(I) as an intermediate species, which on addition to the carbonyl group forms an indium alkoxide that undergoes a simultaneous proton–metal exchange, obviating the Brook rearrangement (Scheme 2).

As summarized in Table 2, the generality of the indium-mediated allylation reaction was explored with various difluoroacetyltrialkylsilanes **1** in a water:THF mixture (1:1). Desired homoallylic alcohols are synthesized in good yields without the formation of enol silyl ether **3**.



Scheme 2. The formation of homoallylic alcohol.

Table 2. Indium-mediated allylation of difluoroacetyltrialkylsilanes in aqueous media



Compound	R^1	R^2	Yield (%)[a]
2a	Phenyl	*t*-Butyl	91
2b	Ethyl	Ethyl	83
2c	*i*-Propyl	*i*-Propyl	85

[a] Isolated yield and compound is identified by ^1H, ^{13}C, ^{19}F NMR.

Substituents on silicon have no effect on the product formation.

A general reaction procedure for the preparation of compound **2** is as follows. To a mixture of allyl bromide (1.1 mmol) and difluoroacetyltrialkylsilanes **1** (1 mmol) in THF (5 mL) and H_2O (5 mL) was added indium (1.1 mmol, 126 mg of 100 mesh powder), and the resulting mixture was stirred for 1 day. The reaction was quenched with saturated NH_4Cl solution then extracted with dichloromethane. The organic layer was dried over $MgSO_4$, filtered and concentrated. Purification by silica gel column chromatography afforded compound **2** as a light yellow oil.

In conclusion, the indium-mediated allylation reactions of difluoroacetyltrialkylsilanes **1** gave homoallylic alcohols **2** exclusively in good yields without formation of enol silyl ether. Furthermore, both water and THF are necessary for homoallylic alcohol formation.

Acknowledgements

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