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Zinc Bromide Promoted Allylation of Aluminum Acetals Derived from Perfluoro Carboxylic Acid Esters and Diisobutylaluminum Hydride. New Convenient Access to α-Perfluoroalkylated Homoallyl Alcohols

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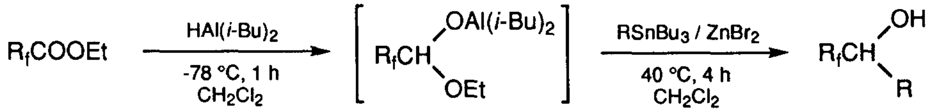
Abstract: The reaction of aluminum acetals, generated *in situ* by the reduction between perfluoro carboxylic acid esters and diisobutylaluminum hydride, with a variety of allylstannanes efficiently proceeds in the presence of zinc bromide at 40 °C to afford the corresponding α-perfluoroalkyl-substituted homoallyl alcohols in good yields.

Allylation of aldehydes and their acetals is a very useful and fundamental reaction for the synthesis of homoallylic alcohols and a large number of methods for this transformation[1-4] have hitherto been accumulated in the literature. Among them there exist several methods permitting the allylation of per- or polyfluoro aldehydes and acetals[3,4] to lead to α-per- or -polyfluoroalkylated homoallyl alcohols, one of the most important organofluorine building blocks in synthesis. However, these methods suffer serious disadvantages, such as variable yields of products and difficulties in accessibility or handling of such starting materials[5] due to their volatility, miscibility with water, and/or instability. It is of great value, therefore, to develop an effective and convenient method for preparing per- or polyfluoroalkyl-substituted homoallylic alcohols.

In this communication is described, for the first time, zinc bromide promoted allylation of *in situ* generated aluminum acetal intermediates[6] with various allylstannanes, which offers a new promising and efficient method for the synthesis of α-perfluoroalkylated homoallylic alcohols (**4**-**6**) in good yields starting from readily available perfluoro carboxylic acid ethyl esters (**1**-**3**).



1: $R_f = CF_3$
2: $R_f = CHF_2$
3: $R_f = CF_3CF_2$

4: $R_f = CF_3$
5: $R_f = CHF_2$
6: $R_f = CF_3CF_2$

The allylation reactions were conducted under various reaction conditions by using ethyl trifluoroacetate (**1**) and tributylmethallylstannane (Table 1). As shown in Table 1, the presence of Lewis acid is found to be essential for allowing the reaction to proceed successfully. Thus, even when an alumi-

Table 1. Allylation of the Aluminum Acetal Derived from **1** with Tributylmethallylstannane

Entry	Lewis acid	Solvent	Temp./°C	Time/h	Yield[a]/% of **4b**
1	$ZnBr_2$	CH_2Cl_2	r.t.	4	55
2	$ZnBr_2$	CH_2Cl_2	40	4	83
3	ZnI_2	CH_2Cl_2	40	4	80
4	$SnCl_4$	CH_2Cl_2	40	4	45
5	$BF_3{\cdot}OEt_2$	CH_2Cl_2	40	4	tr
6	$TiCl_4$	CH_2Cl_2	r.t.	2	tr
7	none	CH_2Cl_2	40	4	tr
8	$ZnBr_2$	Et_2O	r.t.	4	52
9	$ZnBr_2$	Et_2O	40	4	77
10	$ZnBr_2$	DME	r.t.	4	47
11	$ZnBr_2$	MeCN	r.t.	4	33
12	$ZnBr_2$	THF	r.t.	4	9

a) Measured by ^{19}F NMR using α,α,α-trifluorotoluene as standard.

num acetal species resulted from the reduction of **1** with diisobutylaluminum hydride (DIBAL)[7] was treated with methallylstannane in the absence of Lewis acid at 40 °C for 4 h, the expected allylic alcohol **4b** was scarcely obtained and instead trifluoroacetaldehyde ethyl hemiacetal was produced (Entry 7). Out of the Lewis acids examined, such as zinc bromide, zinc iodide, tin(IV) chloride, boron trifluoride etherate, and titanium(IV) chloride, the latter two Lewis acids were inefficacious for the reaction (Entries 5 and 6) and tin(IV) chloride provided only moderate yield of **4b** (Entry 4), whereas zinc bromide and zinc iodide efficiently promoted the reaction to give **4b** in 83% and 80% yields, respectively (Entries 2 and 3).

Use of dichloromethane (CH_2Cl_2) or diethyl ether as solvent led to the most satisfactory results. Although 1,2-dimethoxyethane (DME) and acetonitrile could also be used, they either made the reaction insufficient or made it remarkably troublesome to isolate the product to result in decreasing the yields of **4b** (Entries 10 and 11). The reaction performed at room temperature was extremely sluggish to give a low yield of the product **4b** (Entries 1 and 8). It should be mentioned that the aluminum acetal intermediate did not undergo the present reaction at all with allylsilanes regardless of forced reaction conditions being employed, probably due to lower nucleophilicity of the silane than that of the stannane.

A typical procedure for the reaction is as follows. To a CH_2Cl_2 solution of ethyl ester **1** was dropwise added a 1M hexane solution of DIBAL (1.1 equiv) at -78 °C and this mixture was stirred at the same temperature for 1 h. The resultant solution of the aluminum acetal and tributylmethallylstannane[8] (1.1 equiv) were successively added *via* syringe to a CH_2Cl_2 solution of zinc bromide, prepared from acid-washed zinc dust[9] (1.25 equiv) and 1,2-dibromoethane (1.25 equiv). After being stirred at 40 °C for 4 h under an argon atmosphere, the mixture was hydrolyzed with a 1:1 mixture of NH_4Cl and 10% HCl aqueous solution, followed by extraction with CH_2Cl_2, drying over Na_2SO_4, and concentration. The residue was chromatographed on silica-gel column using hexane and CH_2Cl_2 as eluents to give analytically pure 1,1,1-trifluoro-4-methyl-4-penten-2-ol (**4b**)[10] in 69% yield. Table 2 summarizes the results of the allylation reactions of the aluminum acetals derived from **1**-**3** with various allylic stannanes.

Table 2. Allylation of Aluminum Acetals Derived from **1**-**3** with Allylic Stannanes

Entry	Fluoro ester		Allylstannane	Product	Yield[a]/%
13	CF_3COOEt	(**1**)	$CH_2{=}CHCH_2SnBu_3$	(**4a**)	64[b] (82)
14	CF_3COOEt	(**1**)	$CH_2{=}C(Me)CH_2SnBu_3$	(**4b**)	69 (83)
15	CF_3COOEt	(**1**)	$MeCH{=}CHCH_2SnBu_3$[c]	(**4c**)	60 (71)[d,e]
16	CF_3COOEt	(**1**)	$PhCH{=}CHCH_2SnBu_3$	(**4d**)	54[d,e]
17	CF_3COOPh	(**1'**)	$CH_2{=}C(Me)CH_2SnBu_3$	(**4b**)	65 (75)
18	CHF_2COOEt	(**2**)	$CH_2{=}CHCH_2SnBu_3$	(**5a**)	56[b] (81)
19	CHF_2COOEt	(**2**)	$CH_2{=}C(Me)CH_2SnBu_3$	(**5b**)	70 (78)
20	CHF_2COOEt	(**2**)	$MeCH{=}CHCH_2SnBu_3$[c]	(**5c**)	59 (66)[d,e]
21	CF_3CF_2COOEt	(**3**)	$CH_2{=}CHCH_2SnBu_3$	(**6a**)	50[b] (71)
22	CF_3CF_2COOEt	(**3**)	$CH_2{=}C(Me)CH_2SnBu_3$	(**6b**)	71 (86)

a) Yields are of isolated products. The figures in parentheses refer to yields determined by ^{19}F NMR. b) Isolated by distillation. c) Contained ca. 50% of 1-methyl-2-propenyltributylstannane. See ref. 8. d) Obtained as a mixture of two regioisomers. e) The reaction time is 7 h.

As shown in Table 2, the aluminum acetal species generated not only from trifluoroacetate (**1**) but also from difluoroacetate (**2**) reacted smoothly with various allylic stannanes under the above-described conditions to afford good yields of the corresponding α-trifluoromethylated and α-difluoromethylated homoallyl alcohols **4** and **5**,[10] respectively. It is worthwhile to note that in the reaction with cinnamylstannane (Entry 16) two regioisomers, 1,1,1-trifluoro-3-phenyl-4-penten-2-ol (γ-product) and 1,1,1-trifluoro-5-phenyl-4-penten-2-ol (α-product), were formed in a ratio of 56 : 44. Phenyl trifluoroacetate (**1'**) also participated well in the reaction leading to a nearly comparable yield of **4** (Entry 17). The present allylation reaction could equally be applied to longer perfluoroalkanoic acid esters. Thus, on similar treatment of the aluminum acetal from pentafluoropropanoic acid ethyl ester (**3**) and DIBAL with allylstannanes, α-pentafluoroethylated homoallyl alcohols **6**[10] were obtained in good yields (Entries 21 and 22).

Of much significance is that these reactions do not give any allylic ethers that may arise from the replacement of the (diisobutylaluminum)oxyl group by an allylic part of the stannanes. Although exact elucidation of the reaction mechanism should await further investigations, the reaction seems to occur *via* a mechanism involving initial coordination of zinc bromide to the ethoxyl group in the aluminum acetals followed by nucleophilic attack of the stannanes to form the alcohols **4-6**.

Studies on synthetic applications of this reaction as well as its mechanism are actively being continued in our laboratory.

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8. The allylstannanes employed in this study were prepared according to the literature method. For example, Naruta, Y.; Nishigaichi, Y.; Maruyama, K. *Chem. Lett.* **1986**, 1857.
9. Commercially available zinc dust was washed successively with dilute HCl (3%), methanol, and diethyl ether, followed by drying under vacuum.
10. All isolated products exhibited spectral and analytical data which are fully consistent with the assigned structures.

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