The generation of gem-difluoroallyllithium by the transmetalation reaction

3,3-Difluoroallytrimethyltin was prepared by reaction of chlorodifluoromethane with the ylide reagent \( \text{Ph}_3\text{P} = \text{CHCH}_2\text{SnMe}_2 \). gem-Difluoroallyllithium, which was generated by the reaction of \( \text{n-butyllithium} \) with 3,3-difluoroallyltrin in THF at \(-95^\circ\text{C}\), was of very limited stability at that temperature. However, in situ procedures and alternate incremental addition procedures allowed its application in the synthesis of \( \text{CH}_2\text{CHCF}_2\text{C(OH)Et}_2 \) from 3-pentanone.
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TRANSMETALATION REACTION

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THE GENERATION OF GEM-DIFLUROALLYLLITHIUM

BY THE TRANSMETALATION REACTION

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Summary

3,3-Difluoroallyltrimethyltin was prepared by reaction of chlorodifluoromethane with the ylide reagent Ph₃P=CHCH₂SnMe₃.

gem-Difluoroallyllithium, which was generated by the reaction of n-butyllithium with 3,3-difluoroallyltrimethyltin in THF at -95°, was of very limited stability at that temperature. However, in situ procedures and alternate incremental addition procedures allowed its application in the synthesis of 1,1-difluoroallylsilanes from chlorosilanes and of CH₂=CHCF₂C(OH)-Et₂ from 3-pentanone.

gem-Dichloroallyllithium, which can be prepared in good yield by the transmetalation reaction between Ph₃PbCH₂CH=CCl₂ and n-butyllithium in THF and which is stable in THF below -80°, is an ambident nucleophile which shows unusual regioselectivity in its reactions with carbonyl compounds (1). We have extended our studies of allyllithium chemistry to gem-difluoroallyllithium, a reagent, which, if accessible, would permit the synthesis of diverse unsaturated organofluorine compounds and whose regioselectivity in C=O addition would be of interest to examine.
An appropriate starting material of type CF2=CHCH2Z or ZCF2CH=CH2 is required for the preparation of gem-difluoroallyllithium either by direct lithiation (Z=H), ether cleavage with metallic lithium (Z = PhO) or transmetalation (Z = R3Sn, R3Pb, RHg). We have developed a procedure based on the latter reaction using Me3SnCH2CH=CF2 as the difluoroallyl anion source.

The 3,3-difluoroallyltrimethyltin required for this study was prepared in good yield using a trimethyltin-substituted Wittig reagent (eq. 1-3). In the first reaction of this sequence, ethereal triphenylphosphinemethylene is added to an ether solution of iodomethyltrimethyltin (2). The phosphonium halide which precipitates, 1, generally is contaminated with 10-15% of [Ph3PCH3]I. It can be purified by fractional crystallization to give analytically pure material, mp 122.5-123.5° (dec). However, for use in the eq. 2,3 sequence it need not be purified, as the CH2=CF2 formed from the [Ph3PCH3]I impurity (via Ph3P=CH2) is too volatile to interfere
in product isolation.

In the second step of this sequence the phosphonium salt is added to the cooled (ice bath) THF solution of lithium diisopropylamide* in THF to give a cranberry-red ylide solution.

* Organolithium reagents, e.g., PhLi, cannot be used since they attack at tin as well as at the protons α to phosphorus.

Removal of the diisopropylamine formed in reaction 2 is essential in order to obtain good product yields in the subsequent step and to effect this, the volatiles are removed at 0.02 torr and 50° by trap-to-trap distillation into a receiver at —196°. The ylide which remains is redissolved in diethyl ether and treated, at 0°, with one-half molar equivalent of chlorodifluoromethane, following the procedure of Burton (3). The precipitated phosphonium salt is filtered and the filtrate is distilled. The product, Me₃SnCH₂CH=CF₂, bp 129-131°, n²⁵D 1.4465, is obtained in 74% yield and triphenylphosphine is recovered from the distillation residue in 79% yield.

Further experiments examined the preparation of gem-difluoroallyllithium from 3,3-difluoroallyltrimethyltin (eq. 4).

\[
\text{Me}_3\text{SnCH}_2\text{CH}=\text{CF}_2 + \text{n-BuLi} \rightarrow \text{Me}_3\text{Sn}(\text{CF})\text{H}_2\text{C}\text{Li}^+ + \text{n-BuSnMe}_3
\]  

(4)

All experiments which were carried out to preform a solution of this reagent in this manner, prior to addition of the substrate, at temperatures between -95° and -130°, have failed thus far. The transmetalation does occur since n-
butyltrimethyltin is formed in good yield (73% in one such experiment which was carried out at -95°, together with a 12% recovery of unconverted \( \text{Me}_3\text{SnCH}_2\text{CH}=\text{CF}_2 \)). However, chlorosilanes can be converted to 1,1-difluoroallylsilanes in high yield by an in situ procedure in which \( n \)-butyllithium in hexane (\( \approx \) 2 molar equivalents) is added slowly at -95° to a mixture of \( \approx 1 \) molar equivalent of \( \text{Me}_3\text{SnCH}_2\text{CH}=\text{CF}_2 \) and \( \approx 4 \) molar equivalents of \( \text{R}_3\text{SiCl} \) in THF. Prepared in this manner were \( (\text{n—C}_3\text{H}_7)_3\text{SiCF}_2\text{CH}=\text{CH}_2 \) (86%), \( \text{PhMe}_2\text{SiCF}_2\text{CH}=\text{CH}_2 \) (75%) and \( \text{Me}_3\text{SiCF}_2\text{CH}=\text{CH}_2 \) (64%) (yields by GLC after trap-to-trap distillation of the reaction mixture and concentration of the distillate).

It is of interest to note that the products had the structures shown, and not the isomeric \( \text{R}_3\text{SiCH}_2\text{CH}=\text{CF}_2 \) structure. It would appear that as in the case of the \( \text{gem} \)-dichloroallyllithium-trimethylchlorosilane reaction, which gives \( \text{Me}_3\text{SiCCl}_2\text{CH}=\text{CH}_2 \) exclusively (4), these reactions of \( \text{gem} \)-difluoroallyllithium are subject to kinetic control of product formation. The structure of the \( \text{R}_3\text{SiCF}_2\text{CH}=\text{CH}_2 \) products was indicated clearly by their proton NMR spectra which showed only complex multiplets in the vinyl region (\( \approx 4.9-6.4 \) ppm), in addition to the resonances due to the \( \text{R} \) groups. In addition, the isomeric \( \text{Me}_3\text{SiCH}_2\text{CH}=\text{CF}_2 \) was prepared (in 90% yield) for comparison by the general route shown in eq. 1-3, with the differences that \( \text{Me}_3\text{SiCH}_2\text{I} \) was used in eq. 1 and that methyllithium was used to generate \( \text{Ph}_3\text{P}=\text{CHCH}_2\text{SiMe}_3 \) from \( \text{[Ph}_3\text{PCH}_2\text{CH}_2\text{SiMe}_3\text{]}\text{I} \) (eq. 2).

This silane, a known compound (5), had a very different proton NMR spectrum: \( \delta \) 0.04 (s, 9H, \( \text{Me}_3\text{Si} \)), 1.11-1.31 (d of t, \( 3J_{\text{HH}} \) 9 Hz, \( 4J_{\text{FH}} \) 1.5 Hz, 2H, CH\(_2\)Si) and 3.68-4.44 ppm (12 line pattern, \( 2J_{\text{HH}} \) 9 Hz, \( 3J_{\text{FH}} \)(cis) 3 Hz, \( 3J_{\text{FH}} \)(trans) 24 Hz, 1H, \( -\text{CH} \)) (in \text{CCl}_4, \text{CHCl}_3).

The in situ procedure could not be applied successfully to the difluoroallylation of carbonyl compounds since the rate of attack of \( n \)-butyllithium at C=O appears to be greater than its rate of attack at tin. A successful addition of \( \text{gem} \)-
difluoroallyllithium to 3-pentanone, however, could be effected by a procedure in which a solution of Me$_3$SnCH$_2$CH=CF$_2$ (6 mmol) in THF, cooled to -95°, was treated alternately with 1 mmol portions each of n-butyllithium in hexane (over a 15 sec. period, with 30 sec. of stirring) and 3-pentanone (followed by 3 min. of stirring). This procedure of 1 mmol alternate additions was repeated identically at 3 min. intervals until 25 mmol of each reactant had been added. The product alcohol was isolated and characterized as its trimethylsilyl ether, CH$_2$=CHCF$_2$CEt$_2$OSiMe$_3$, and was obtained in 75% yield.

These experiments have demonstrated that gem-difluoroallyllithium, although it is of very limited stability at -95°, can serve as a useful reagent, giving difluoroallyl group transfer in high yield, provided that appropriate procedures are used. Our further studies will examine its reactions with other substrates. Of special interest will be a study of its reactions with other carbonyl compounds. Its reaction with 3-pentanone parallels that of gem-dichloroallyllithium, which reacts with dialkyl ketones to give products of type R$_2$C(OH)CCl$_2$CH=CH$_2$ exclusively (1). It may be expected that gem-difluoroallyllithium will show similar regioselectivity, with the direction of addition to C=O being determined in the main by substrate electronic factors.

The availability of Ph$_3$P=CHCH$_2$SnMe$_3$ and Ph$_3$P=CHCH$_2$SiMe$_3$ provides a new and useful route for the synthesis of allylic tin and silicon compounds by Wittig reactions of our ylides with aldehydes and ketones. A separate report will detail our investigations in this area (6).

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References


