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Preliminary communication

THE GENERATION OF GEM-DIFLUOROALLYLLITHIUM BY THE TRANSMETALATION REACTION

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Summary

3,3-Difluoroallyltrimethyltin was prepared by reaction of chlorodifluoromethane with the ylide reagent $Ph_3P{=}CHCH_2SnMe_3$. 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 $CH_2{=}CHCF_2C(OH)Et_2$ from 3-pentanone.

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gem-Dichloroallyllithium, which can be prepared in good yield by the transmetalation reaction between $Ph_3PbCH_2CH{=}CCl_2$ 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 $CF_2{=}CHCH_2Z$ or $ZCF_2CH{=}CH_2$ is required for the preparation of gem-difluoroallyllithium either by direct lithiation (Z=H), ether cleavage with metallic lithium (Z = PhO) or transmetalation (Z = R_3Sn, R_3Pb, RHg). We have developed a procedure based on the latter reaction using $Me_3SnCH_2CH{=}CF_2$ 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

$$Ph_3P{=}CH_2 + Me_3SnCH_2I \xrightarrow{Et_2O} \underset{\underline{1}}{[Ph_3PCH_2CH_2SnMe_3]I} \qquad (1)$$

$$[Ph_3PCH_2CH_2SnMe_3]I + (Me_2CH)_2NLi \xrightarrow{THF} Ph_3P{=}CHCH_2SnMe_3 + (Me_2CH)_2NH + LiI \qquad (2)$$

$$2\ Ph_3P{=}CHCH_2SnMe_3 + HCF_2Cl \longrightarrow Me_3SnCH_2CH{=}CF_2 + Ph_3P + [Ph_3PCH_2CH_2SnMe_3]Cl \qquad (3)$$

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 $[Ph_3PCH_3]I$. 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 $CH_2{=}CF_2$ formed from the $[Ph_3PCH_3]I$ impurity (via $Ph_3P{=}CH_2$) 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. 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

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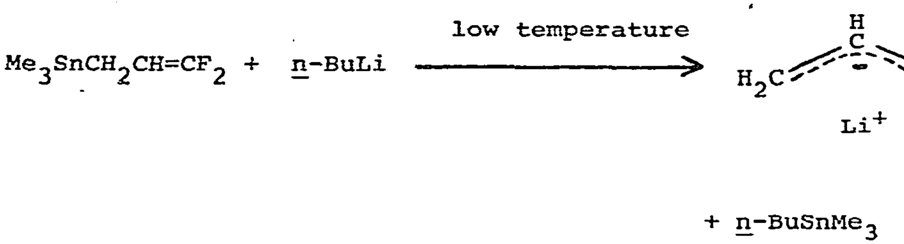
* Organolithium reagents, e.g., PhLi, cannot be used since they attack at tin as well as at the protons α to phosphorus.

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, $Me_3SnCH_2CH=CF_2$, bp 129-131°, $n^{25}D$ 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).



(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 $Me_3SnCH_2CH=CF_2$). However, chlorosilanes can be converted to 1,1-difluoroallylsilanes in high yield by an *in situ* procedure in which *n*-butyllithium in hexane (∿2 molar equivalents) is added slowly at -95° to a mixture of ∿1 molar equivalent of $Me_3SnCH_2CH=CF_2$ and ∿4 molar equivalents of R_3SiCl in THF. Prepared in this manner were $(n\text{-}C_3H_7)_3SiCF_2CH=CH_2$ (86%), $PhMe_2SiCF_2CH=CH_2$ (75%) and $Me_3SiCF_2CH=CH_2$ (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 $R_3SiCH_2CH=CF_2$ structure. It would appear that as in the case of the *gem*-dichloroallyllithium-trimethylchlorosilane reaction, which gives $Me_3SiCCl_2CH=CH_2$ exclusively (4), these reactions of *gem*-difluoroallyllithium are subject to kinetic control of product formation. The structure of the $R_3SiCF_2CH=CH_2$ products was indicated clearly by their proton NMR spectra which showed only complex multiplets in the vinyl region (~4.9-6.4 ppm), in addition to the resonances due to the R groups. In addition, the isomeric $Me_3SiCH_2CH=CF_2$ was prepared (in 90% yield) for comparison by the general route shown in eq. 1-3, with the differences that Me_3SiCH_2I was used in eq. 1 and that methyllithium was used to generate $Ph_3P=CHCH_2SiMe_3$ from $[Ph_3PCH_2CH_2SiMe_3]I$ (eq. 2). This silane, a known compound (5), had a very different proton NMR spectrum: δ 0.04 (s, 9H, Me_3Si), 1.11-1.31 (d of t, $^3J_{HH}$ 9 Hz, $^4J_{FH}$ 1.5 Hz, 2H, CH_2Si) and 3.68-4.44 ppm (12 line pattern, $^2J_{HH}$ 9 Hz, $^3J_{FH(cis)}$ 3 Hz, $^3J_{FH(trans)}$ 24 Hz, 1H, =CH) (in CCl_4, $CHCl_3$).

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 _gem_-difluoroallyllithium to 3-pentanone, however, could be effected by a procedure in which a solution of $Me_3SnCH_2CH=CF_2$ (~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, $CH_2=CHCF_2CEt_2OSiMe_3$, 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 $R_2C(OH)CCl_2CH=CH_2$ 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 $Ph_3P=CHCH_2SnMe_3$ and $Ph_3P=CHCH_2SiMe_3$ 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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