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Synthesis of selectively fluorinated substrates via organometallic reagents derived from CF_2=CFCl, CF_2=CCl_2, CF_2=CH_2

Jean-F. Normant

Laboratoire de Chimie des Organoéléments, Université P. et M. Curie, Tour 44-45, 4 Place Jussieu, 75252, Paris Cedex 05 (France)

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Abstract

Selectively fluorinated reagents can be prepared via mono- or polyfluorinated vinyl-lithium reagents, obtained from cheap monomers by metal/halogen exchange or metallation. These organolithium reagents can be condensed with various electrophiles, and further rearrangements lead to the regio- and stereo-selective introduction of fluorine into organic molecules. Alternatively, they can be converted into zinc compounds of higher stability.

We have been interested for several years in developing new routes to selectively fluorinated ethylenic molecules. Biological organic chemistry increasingly requires such species, in which a fluorine atom, properly located, can promote biological activity or impede enzymatic transformations and/or be used to increase understanding of the relevant metabolism pathway [1]. Furthermore, in terms of basic organic chemistry it seems surprising that a whole array of methods is available [2] to prepare chloro, bromo, iodo alkenes of defined geometry (namely through P, Si, Sn, B, Cu, Zr chemistry) whereas the preparation of pure *E* or *Z* isomers of R–CH=CHF or R–CF=CHF is still a challenging problem. That there is this considerable leeway to make up is due to the fact that introduction of F often requires expensive, or toxic, or explosive reagents, with the exception of metal fluorides. However, some monomers, precursors of industrially produced fluorinated polymers, are readily available and cheap, but are generally polyfluorinated, and so we decided to study the selective metallation or metal/halogen exchange with CF_2=CFCl, CF_2=CCl_2, CF_2=CH_2 etc., with the aim of introducing a mono(bis) fluorovinyl group into a substrate, and to look for regio (stereo) selective rearrangements which might eventually lead to a regioselectively mono (bis) fluorinated compound.

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Metal/halogen exchange

During a study of the nucleophilic substitution of CF_2=CFCl [3] we observed that, in contrast to Grignard reagents, alkyllithiums undergo metal/halogen exchange, in an appropriate solvent mixture, to give a quantitative yield of trifluorovinyllithium (**1**) [4] (Eq. 1):

$$CF_2{=}CFCl + n\text{-}C_4H_9Li \xrightarrow[\substack{THF/ether/pentane\\(5/3/3)}]{-100\,^\circ C} CF_2{=}CFLi + n\text{-}C_4H_9Cl\ (quant.) \quad (1)$$

(**1**)

This avoids the use of the very expensive CF_2=CFBr, CF_2=CHF [5,6] and bypasses the preparation of $Ph_3SnCF{=}CF_2$, involved in the pioneering work by Seyferth [7].

The vinyllithium thus formed is of limited thermal stability (up to $-80\,^\circ C$) due to the presence of THF. Removal of the latter solvent, according to Eq. 2, leads to a better stability (up to $-30\,^\circ C$), and allows reactions which could not be carried out when the earlier pathway was used [8].

$$CF_2{=}CFCl + \text{s- or t-BuLi} \xrightarrow[-60\,^\circ C]{ether} CF_2{=}CFLi(quant.) \quad (2)$$

(**1**)

Such Li/Cl exchange is also possible when starting from various fluoro-chloro ethylenes [9]:

$$ClCF{=}CFCl + n\text{-BuLi} \xrightarrow[-115\,^\circ C]{ether/THF} CFCl{=}CFLi$$

($E/Z = 70/30$) (**2**, $E/Z = 30/70$)(85%)

The dichloro-species CF_2=CCl_2 is more difficult to metallate when pure diethyl ether is used [9a] but addition of 5% THF leads to a smooth reaction [9b], and $PhCF{=}CCl_2$ gives one greatly predominant isomer:

$$Ph{-}CF{=}CCl_2 \xrightarrow[ether]{n\text{-BuLi}\ -110\,^\circ C} \underset{F}{\overset{Ph}{\diagdown\!\!\diagup}}\!\!=\!\!\underset{Cl}{\overset{Li}{\diagdown\!\!\diagup}} \xrightarrow{H_3O^+} \underset{F}{\overset{Ph}{\diagdown\!\!\diagup}}\!\!=\!\!\underset{Cl}{\overset{H}{\diagdown\!\!\diagup}}$$

(**3**) ($Z/E = 94/6$) (90%)

In contrast, with alkyl thio analogs there is no selectivity:

$$BuSCF{=}CCl_2 \xrightarrow[n\text{-}BuLi]{-105\,^\circ C} BuSCF{=}CClLi \xrightarrow{MeOH} BuSCF{=}CHCl$$

($E/Z = 55/45$)(70%)

The above organolithium reagents are excellent reagents for the introduction of a fluorovinyl moiety into an organic substrate; for example [4]:

$$RCOR' \xrightarrow[2)\ H_2O]{1)\ \mathbf{1}\ (-100\,^\circ C)} CF_2{=}CF{-}\underset{OH}{\overset{R}{\overset{|}{C}}}{<}_{R'}$$

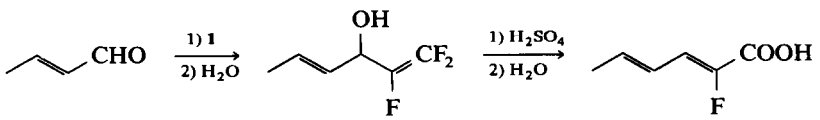
(**5**, 70–90%)

A few examples of this reaction had been previously reported by Tarrant et al. [5], who observed an acidic rearrangement of the allylic alcohols thus obtained (in

boiling 6 *N* hydrochloric acid) to give the parent acids: yields were highly dependent on the nature of the starting carbonyl derivative, but better than those obtained from CF_2=CFMgI [10]. When **1** was prepared as stated above, good yields (70–90%), of the desired carbinols were obtained from a large variety of carbonyl compounds, and we found that use of cold (−10 °C) concentrated sulfuric acid led smoothly to the isolable acid fluorides:

$$\text{AmCHO} \xrightarrow[2)\ H_2O]{1)\ \mathbf{1}} \underset{(83\%)}{\text{AmCHOHCF}=CF_2} \xrightarrow{\text{conc. } H_2SO_4} \underset{(80\%,\ Z \text{ pure})}{\text{AmCH}=\text{CFCOF}}$$

and hence to the corresponding esters, acids, or amides by quenching with alcohols, water, or amines. When a delocalized carbocation is formed, trapping by water occurs exclusively on the CF_2 terminus, to give α-fluorosorbic acid [4]:



(68%)

Analogous reactions can be performed starting from **2**, **3**, or **4**; for instance:

$$PhCF=CCl_2 \rightarrow \mathbf{4} \xrightarrow[2)\ H_2O]{1)\ \text{n-PrCHO}} \underset{(85\%)}{Ph-\overset{F}{\overset{|}{C}}=\overset{Cl}{\overset{|}{C}}-CHOHPr} \xrightarrow[2)\ H_2O]{1)\ H_2SO_4} PhCO-\overset{Cl}{\overset{|}{C}}=CHPr \quad (70\%)$$

Trifluorovinyl lithium can be carboxylated or sulfinated to give the interesting trifluoroacrylic acid or trifluorosulfinic acid [11] from which difluoroacrylic acid, or

$$\mathbf{1} \begin{cases} \xrightarrow[H_3O^+]{CO_2} CF_2=CFCOOH \quad (80\%) \\ \xrightarrow[H_3O^+]{SO_2} CF_2=CFSO_2H \quad (53\%) \end{cases}$$

2,3-difluoro-2-alkenoic acids can be prepared by addition–elimination of a metal hydride or an alkyl lithium (or Grignard) reagent:

$$CF_2=CF-COOLi \xrightarrow[2)\ H_3O^+]{1)\ LiAlH_4} \underset{(E/Z = 1/1)(50\%)}{CHF=CF-COOH}$$

$$CF_2=CF-COOLi \xrightarrow[2)\ H_3O^+]{1)\ 1 \text{ eq. BuLi or BuMgBr}} \underset{(E/Z = 40/60)(68\%)}{Bu-CF=CF-COOH}$$

By use of two equivalents of an alkyllithium, the 1-2 difluoroethylenic ketone can be prepared:

$$CF_2{=}CF{-}COOLi \xrightarrow[2)\ H_3O^+]{1)\ 2\ eq.\ n\text{-}BuLi} Bu{-}CF{=}CF{-}CO{-}Bu \quad (Z/E = 60/40)(55\%)$$

In contrast, the lithium sulfinate undergoes an elimination reaction when treated with butyl lithium, to generate $BuSO_2Li$ (90%). The trifluorovinyl carbinols **5** are also extremely electrophilic, and undergo nucleophilic attack by alkyllithiums or lithium aluminum hydride [12] to give difluoro alkenyl carbinols, which can be isomerised to α-fluoroethylenic ketones [13] (or aldehydes) [14]:

$$R{-}\underset{\displaystyle OH}{\overset{\displaystyle R'}{\overset{|}{\underset{|}{C}}}}{-}CF{=}CF_2 \xrightarrow[2)\ H_2O]{1)\ R'Li} R{-}\underset{\displaystyle OH}{\overset{\displaystyle R'}{\overset{|}{\underset{|}{C}}}}{-}CF{=}CF{-}R' \xrightarrow[2)\ H_2O]{1)\ H_2SO_4}$$

(5)

$$R'{-}\underset{\displaystyle R}{\overset{|}{C}}{=}CF{-}CO{-}R' \quad (60\text{–}65\%)$$

$$R{-}\underset{\displaystyle OLi}{\overset{|}{CH}}CF{=}CF_2 \xrightarrow[2)\ H_3O^+]{1)\ LiAlH_4} R{-}CHOH{-}CF{=}CHF \ (82\%) \xrightarrow[2)\ H_2O]{1)\ H_2SO_4}$$

$$R{-}CH{=}CF{-}CHO \quad (60\text{–}65\%)$$

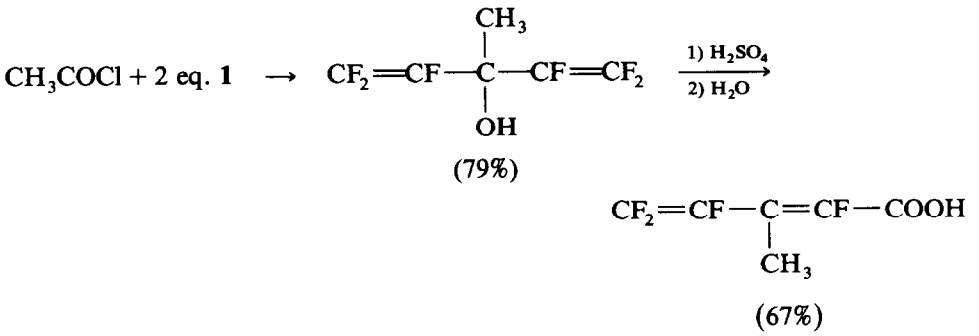
In contrast with the latter reaction scheme, when sodium borohydride is used, elimination of oxygen prevails over elimination of fluoride, and trifluoro alkenes are obtained in good yields [14,15]:

$$Am{-}\underset{\displaystyle OH}{\overset{|}{CH}}CF{=}CF_2 + NaBH_4 \xrightarrow{\text{diglyme}} Am{-}CH{=}CFCHF_2 \quad (Z)(65\%)$$

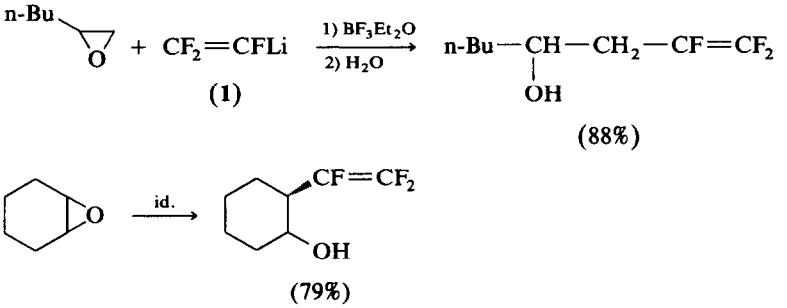
1,1-difluoro-2-alkenes can be prepared similarly:

$$Am{-}CHOH{-}CH{=}CF_2 \xrightarrow[\text{diglyme}]{NaBH_4} Am{-}CH{=}CH{-}CHF_2 \quad (E)(63\%)$$

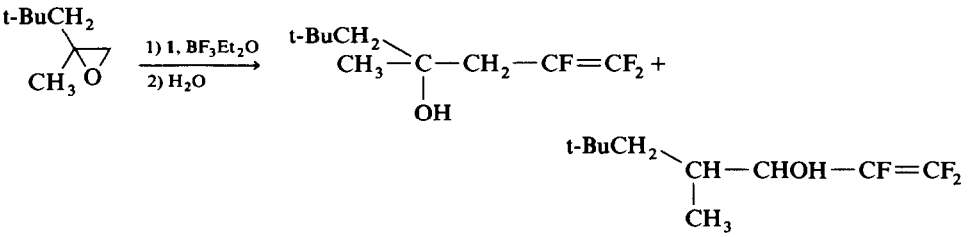
Acid halides also react with **1** at low temperature to give the symmetrical divinyl carbinol [8], which can be also isomerised in an acidic medium to 2,4,5,5-tetrafluoro-3-alkyl-pentadienoic acids:



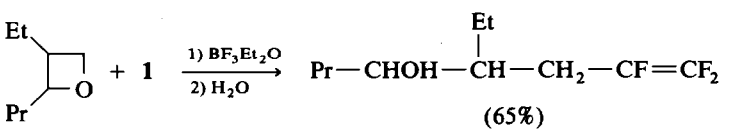
Reagent **1** is not stable enough to enter reaction with oxiranes, but activation of the latter by boron trifluoride etherate [16] allows a smooth reaction, even with 1,2-disubstituted oxiranes [8]:



With 1,1-disubstituted oxiranes, a carbocationic pathway gives rise to the formation of an allylic alcohol:



Oxetanes undergo a similar ring cleavage [17] regioselectively at the less hindered carbon:

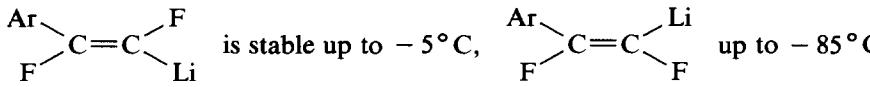


Although the preparation of RCF=CFCl (R aliphatic) is still a challenge, compounds ArCF=CFCl are readily obtained by addition–elimination of an aryl Grignard to chlorotrifluoroethylene:

$$CF_2{=}CFCl + ArMgX \rightarrow ArCF{=}CFCl$$

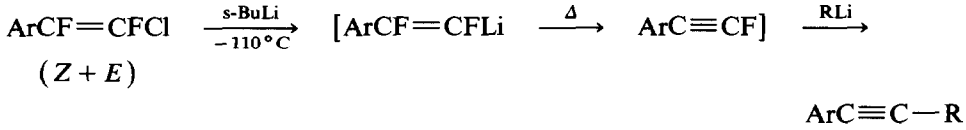
This reaction, disclosed by Tarrant [18] gave a 16% yield in ether, and we improved this to 82% in THF [3].

Lithium/chlorine exchange leads to the corresponding lithiostyrenes, which were characterized by protonolysis to give ArCF=CHF [19]. Ar = Ph: 70%; Ar = *p*-MeOPh: 90%.

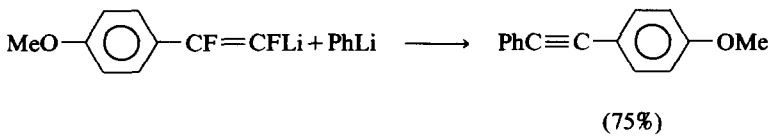


Addition of $MgCl_2$ gives the corresponding Grignard reagents, which are stable up to + 20 °C and − 40 °C respectively.

This study was carried out in order to seek a new way to fluoroalkynes and hence to disubstituted alkynes. Thus the metallation step, below the temperature threshold stated above, can be followed by addition of a second lithium derivative, and warming up leads to the desired product:



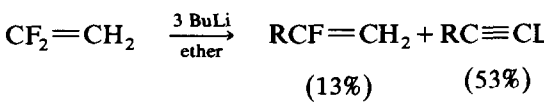
In this strategy the R group is introduced as a nucleophile, a process which widens the scope of such coupling reactions since tertiary alkyllithiums, aryl and vinyllithium, etc., can be used [19]:



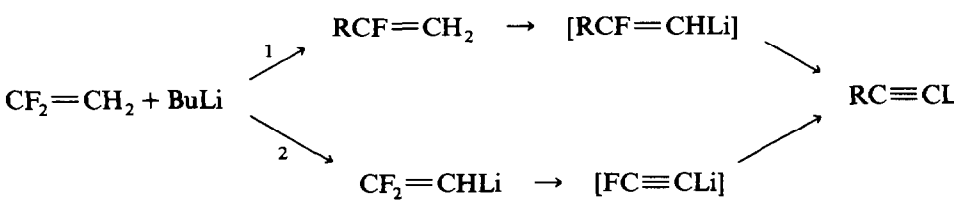
This contrasts with the usual procedure involving nucleophilic attack of an acetylide on an alkyl halide.

Metallation reactions

Another approach to fluorinated vinyl metals is the metal/halogen exchange. 1,1-difluoroethylene reacts with n-butyllithium in ether to give a mixture of products:



We found [20] that in THF the acetylide is the only product (84%), and is formed via two pathways: addition–metallation–elimination and metallation–elimination–coupling.



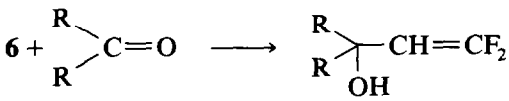
In respect of pathway 1, $RCF{=}CH_2$ has been characterized when the reaction is performed in ether. It is not formed in THF, and when independently prepared it is

not converted into the acetylide by n-BuLi in THF at a temperature below $-60\,^{\circ}C$. The second path is more interesting and can be exclusively followed when a strong base (s-BuLi) in a mixture (80/20) of THF and ether and a low temperature ($-110\,^{\circ}C$) are used:

$$CF_2{=}CH_2 \xrightarrow[-110\,^{\circ}C]{\text{s-BuLi}} CF_2{=}CHLi$$

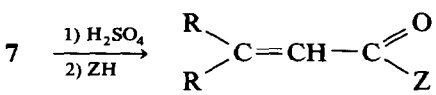
(6)(95%)

Reagent **6** is a good synthon for the preparation of 1,1-difluoro allylic alcohols [20]:



(7)(60–90%)

which can be isomerized (cold H_2SO_4) to α,β-unsaturated acid fluorides, acids, esters, etc. in excellent yields [21]:



Reagent **6** can also be quantitatively carboxylated to the lithium salt of β,β-difluoro acrylic acid [22], although liberation of the free acid leads to partial hydrolysis to malonic acid.

$$\mathbf{6} \xrightarrow[-105\,^{\circ}C]{CO_2} CF_2{=}CH{-}COOLi \text{ (quant.)}$$

(8)

Addition of Grignard reagents to **8** leads to β-fluoroethylenic acids:

$$\mathbf{8} + Bu{-}MgX \longrightarrow Bu{-}CF{=}CH{-}COOH$$

(9)(70%)

In contrast, alkyllithiums promote a β-elimination to give the parent α-acetylenic acid $RC{\equiv}CCOOH$.

Use of **9**, via its acid chloride (from oxalyl chloride) provides a route to β-fluoro-α-ethylenic esters, ketones, alcohols [22]; for example, lithium cuprates give β-fluoro-α-ethylenic ketones:

$$Bu{-}CF{=}CH{-}COCl + Et_2CuLi \longrightarrow BuCF{=}CH{-}CO{-}Et$$

(70%)

Reagent **6** is also an excellent precursor of the strongly electrophilic fluoroacetylene, according to the procedure described above for $PhC{\equiv}CF$:

$$\underset{\textbf{(6)}}{CF_2{=}CH_2} \xrightarrow[-110\,^{\circ}C]{\text{s-BuLi}} CF_2{=}CHLi \xrightarrow{-80\,^{\circ}C} \underset{\textbf{(10)}(\simeq 90\%)}{FC{\equiv}CH}$$

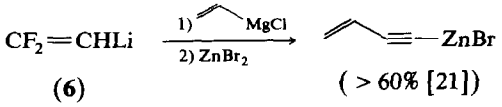
We were pleased to find that warming of **6** to $-80\,^{\circ}C$ leads to a smooth β-elimination of lithium fluoride and fluoroacetylene, which is resistant to its

precursor. Addition of another nucleophile produces metallated terminal acetylenes, which can be further elaborated by addition of electrophiles [23]:

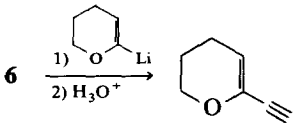
$$CF{=}CH_2 \longrightarrow [CF_2{=}CHLi \longrightarrow FC{\equiv}CH \xrightarrow{2Nu^-} NuC{\equiv}C^-] \xrightarrow{E^+Z^-} NuC{\equiv}C{-}E$$

Thus $CF_2{=}CH_2$ behaves as an equivalent of $^+C{\equiv}C^-$. The nucleophiles used were Grignards, lithium derivatives, amides; the electrophiles can be water, carbonyl compounds, alkyl halides, trimethylsilyl chloride, etc.

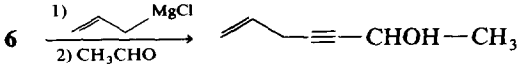
Examples:



(6) (> 60% [21])



(75%)



(58%)

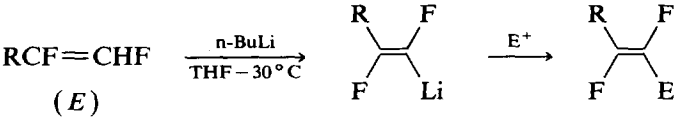
$CF_2{=}CHLi$ cannot be alkylated by alkyl halides. An efficient method, developed by Kobayashi et al to 1,1-difluoro-1-alkenes, achieves this via boron ate complexes [24]:

$$CF_3CH_2OTS \xrightarrow[2)\ BR_3]{1)\ 2LDA} CF_2{=}\underset{\displaystyle R}{\underset{|}{C}}{-}BR_2 \xrightarrow{AcOH} CF_2{=}CHR$$

Nakai et al. [25] used a Wittig approach:

$$RCH{=}O + PPh_3{=}CF_2 \longrightarrow RCH{=}CF_2$$

Later we obtained access (v.i.) to derivatives RCF=CHF (*E*) and RCF=CHCl (*E*), which were also subjected to metallation [8,26,27]:



((*E*)-**11**) (**12**)

For example: **12**, E = COOH from CO_2 (yields 70–90%), E = I, from I_2 (yields 80–90%), E = RCHOH from RCHO (yields 70–95%), E = $(CH_2)_3OH$ from oxetane [17]. Reagent (*E*)-**11** is stable up to −5 °C, whereas its isomer (*Z*)-**11** decomposes

already by −80 °C. The chloro-derivatives give the corresponding lithio compounds:

(*E*)

These are, surprisingly, much more unstable than (*E*)-**11**, and decompose above −50 °C; they must be prepared from s-butyl lithium at −100 °C [26].

Zinc derivatives

The limited thermal stability of the various fluorovinyl-lithium reagents considered so far led us to examine the use of the corresponding zinc reagents, which are much more stable, and easily prepared. Vinyl zinc derivatives are known [28,29] to enter several palladium-catalyzed reactions, and if the analogous fluorinated reagents would follow the same reaction path, a new route to fluorinated dienes, enones, etc., would be at hand. Such is indeed the case because these reagents are very stable, even at room temperature:

$$CF_2{=}CFLi \xrightarrow[-100\,^\circ C]{ZnCl_2} CF_2{=}CFZnCl$$

(13)

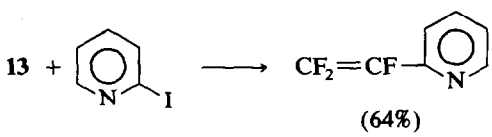
$$RCF{=}CFLi \xrightarrow[-30\,^\circ C]{ZnCl_2} RCF{=}CFZnCl\ (-100\,^\circ C \text{ for the } E \text{ isomer})$$

(*E*) (*Z*)

$$CF_2{=}CHLi \xrightarrow[-100\,^\circ C]{ZnCl_2} CF_2{=}CHZnCl$$

These reagents could be coupled, in the presence of Pd^0, at room temperature, with acid halides (15–60 min), iodo-alkenes and -arenes (12 to 24 h), β-iodo-α-enones and chloroformates (40 h) [30,31].

For example: in the presence of 3% $Pd(PPh_3)_4$ in THF the following reactions were carried out:



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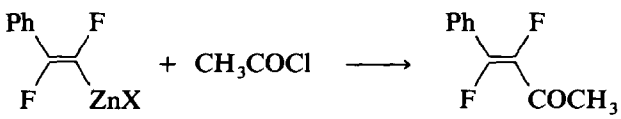

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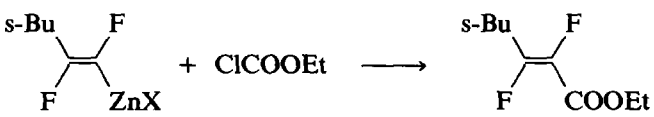
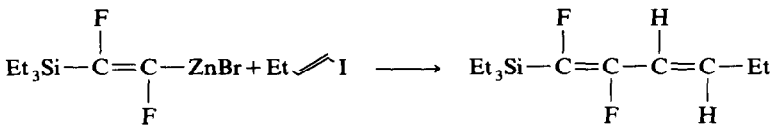


(73%)

iodoalkenes and iodoalkynes also couple, and a large variety of conjugated dienes, and enynes, with regioselectively positioned fluorine atoms can be prepared [32–34,42]:



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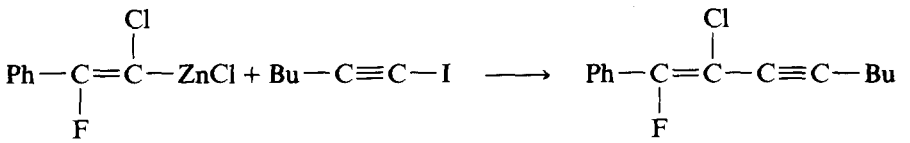

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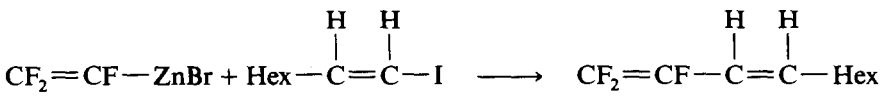
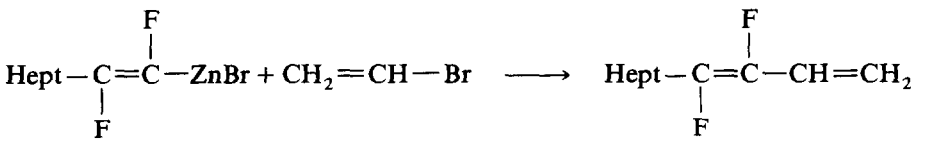
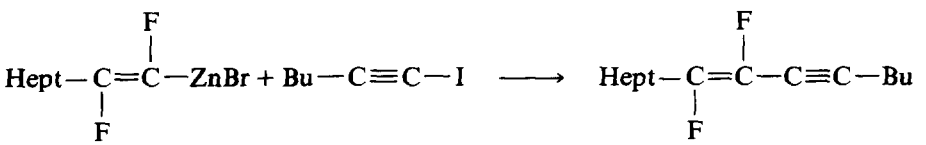


(53%)

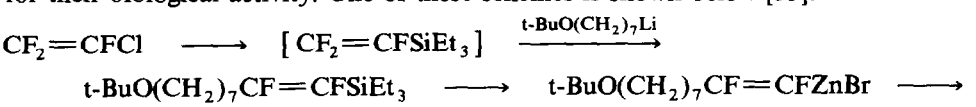


(61%)

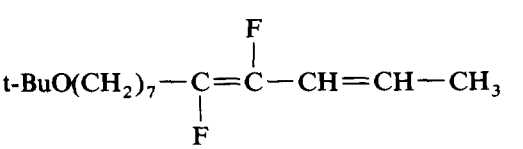


(90%)

This approach has led to the preparation of selectively fluorinated codlemones (a pheromone of *Laspereysia pomonella* (L), a pest of apple trees), which were tested for their biological activity. One of these schemes is shown below [35]:



(90% from CF_2 = CFCl)



(54%)

More recently, reagents CF_2=CFZnBr and CF_2=CFZnI have been prepared by

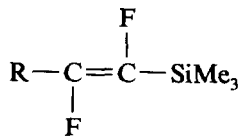
direct attack of CF_2=CFBr (or I) by zinc in DMF (85–95% yield) [36] and acylated in the presence of CuBr [37]. They behave like reagent **13** in Pd^0 catalyzed reactions: this preparation is straightforward, though the starting fluoro compound is rather costly.

Silyl derivatives

Trimethylsilyl trifluoroethylene was previously prepared by Seyferth [38]. Using our general procedure from **1** we were able to obtain a better overall yield from cheap materials [39]:

$$CF_2{=}CFCl \longrightarrow [\mathbf{1} \xrightarrow{Me_3SiCl} CF_2{=}CFSiMe_3] \xrightarrow{RLi}$$

(14)



(15)

Furthermore, **14** undergoes addition-elimination when treated in situ with an alkyllithium reagent, and gives directly the higher homologs **15** (R = primary-, secondary-, tertiary alkyl, vinyl) with yields in the 70–85% range. Derivatives **15** are of pure *Z* configuration, and can be protodesilylated (KF DMSO) to the corresponding (*E*)-1,2-difluoroalkenes:

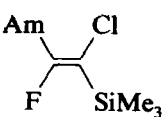
15 $\xrightarrow[DMSO]{KF,\ H_2O}$ 

(16)(76–90%)

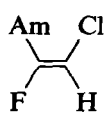
This is the only known route to such pure fluoro olefins.

CF_2=CCl_2 behaves similarly, leading to (*E*)-1-chloro 2-fluoro-1-alkene [26]:

$$CF_2{=}CCl_2 \longrightarrow \longrightarrow CF_2{=}CClSiMe_3 \xrightarrow{\text{n-AmLi}}$$



(17) (*E*/*Z* = 97/3)(85%)

17 $\xrightarrow[DMF]{KF,\ H_2O}$ 

(18) (*E*/*Z* = 98/2)(75%)

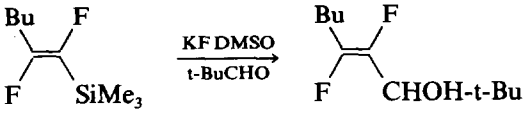
The metallation of **16** or **18** has been described above, but it is also possible to avo this multistep pathway, i.e.:

$$R-CF=CF-Si\lessdot \longrightarrow R-CF=CFH \longrightarrow$$

15

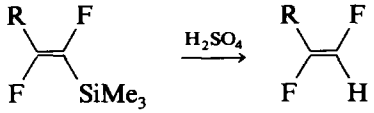
$$R-CF=CFLi \xrightarrow{E^+} RCF=CF$$

if **15** is treated by KF in the presence of an electrophile in anhydrous media [27



This process has been shown to work very efficiently by Hiyama et al [40] wh tris(diethyl amino)sulfonium difluoromethyl silicate is used as a catalyst: yields 50–85% are then obtained.

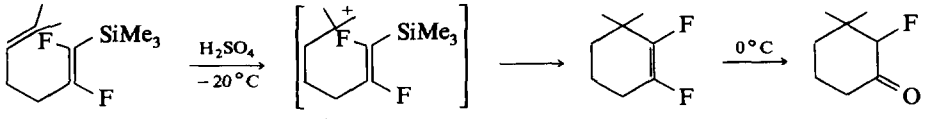
In contrast to basic protodesilylation, use of sulfuric acid leads to α-fluo methyl ketones by hydration of the intermediate difluoro alkenes:



$$\longrightarrow \quad RCOCH_2F$$

(R = alkyl)(66%)

Trisubstituted ethylenes are protonated more readily than difluoro alkenes, so th cyclisations can be carried out:



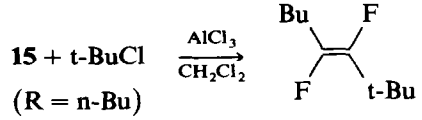
The corresponding difluorocycloalkene can be isolated, but within 1 h, at 0 °C it converted into the α-fluorocyclohexanone (63%) [41].

Even external carbocations derived from tertiary alcohols will promote th carbodesilylation [41]:

$$n\text{-}AmCF=CFSiMe_3 \xrightarrow[H_2SO_4]{5\ t\text{-}BuOH} n\text{-}AmCOCHF-t\text{-}Bu$$

(76%)

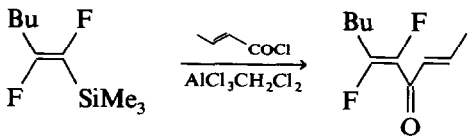
Another feature of the reactivity of difluoro vinyl silanes **15** is their nucleophil behaviour towards electrophilic reagents [27]:



(80%)

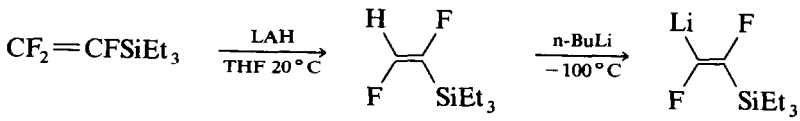
Such an alkylation is unknown with non-fluorinated vinyl silanes, and must l related to an intermediate carbocation located both β to silicon and α to fluorir

Acid halides lead to the corresponding α,β-difluoro-α-enones:



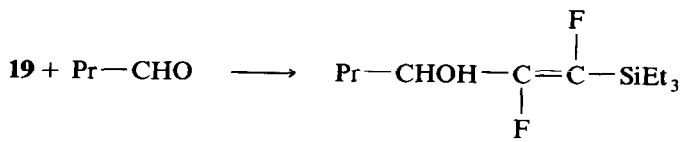
(82%)[42] (96% *E*,*E*)

Trifluorovinyl silanes can be regioselectively reduced to the corresponding difluorovinylsilane by lithium aluminium hydride [43]:

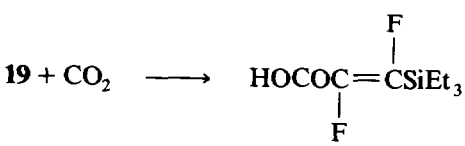


(19)

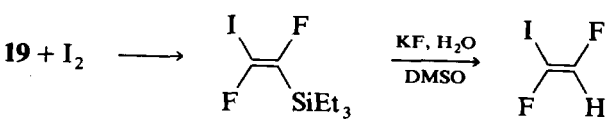
The latter is easily metallated, at low temperatures, to give a new functionalized C_2 synthon **19**, which is a precursor of new species: for example, of β-silyl-α,β-difluoro dienones [43]:



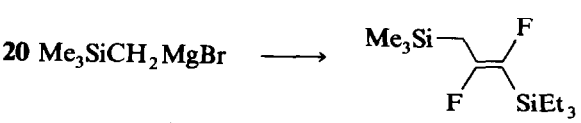
(78%)



(78%)

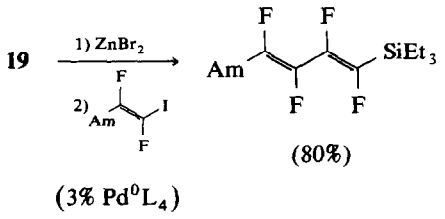


(66%)



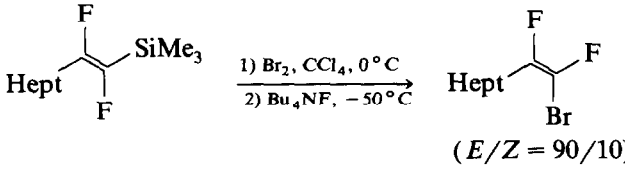
(85%)

The corresponding zinc reagent behaves normally:



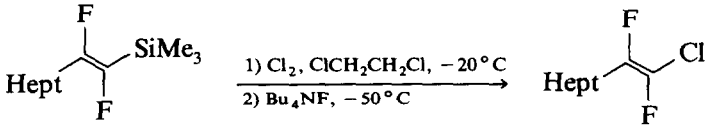
The halodesilylation of derivatives **15** shows different features from those observed in the well studied halodesilylations of non-fluorinated vinyl silanes.

Bromo desilylation gives an analogous stereochemical outcome, namely inversion of configuration [44]:



(*E*/*Z* = 90/10) (82%)

but chlorodesilylation with this aliphatic substrate, leads mostly to retention (in contrast to $RCH{=}CHSiMe_3$ analogs) [45]:



(*E*/*Z* = 7/93) (80%)

This difference is due partly to the greater ability of Br^- to attack the intermediate carbocation produced by "Br^+" attack, whereas the lower nucleophilicity of Cl^- promotes the direct evolution of the intermediate carbocation to the chloro-olefin with retention of configuration.

Conclusion

The use of commercially available C_2 fluorinated monomers, particularly $CF_2{=}CFCl$ and $CF_2{=}CH_2$, provides a valuable route, via organometallic chemistry, to a large array of mono-, bis-, and poly-fluorinated molecules, possessing one or more ethylenic units, and bearing a variety of other functions. The carbenoid nature of the lithium compounds accounts for their low thermal stability, but their high reactivity towards many electrophiles can be used at low temperatures. The corresponding zinc compounds, on the other hand, are stable, even when a halogen atom is located trans to the metal, and can be used in other types of reaction.

Acknowledgements

This survey covers part of the work of O. Reboul, J.P. Gillet, S. Martin, F. Tellier, Th. Dubuffet, P. Martinet, Th. Gouyon. I wish to acknowledge their enthusiastic collaboration, and courage, when they realized how far the organome-

tallic chemistry of fluorinated substrates is removed from the corresponding organometallic chemistry of hydrogenated substrates.

I wish to emphasize the participation of **R. Sauvêtre**: not only he started this chemistry in this laboratory years ago, but then took care of all the above-mentioned PhD researchers, and directed their progress, paying continuous attention to their work, and making many of the discoveries recorded above.

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