Preparation and Reactivity of Some Fluorovinyllithium Reagents

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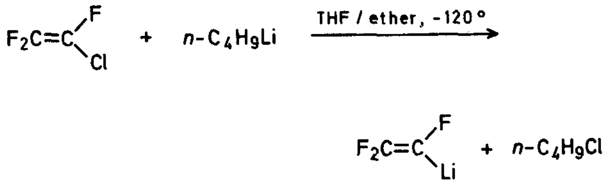
We have recently described[1] a simple preparation of trifluorovinyllithium[2] (**1**) via metal-halogen exchange. We have now extended the scope of this reaction to the preparation of the new reagents **2**, **3**, **4**, and **5**.



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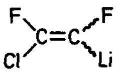

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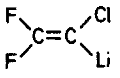

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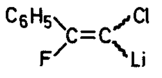

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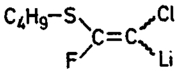

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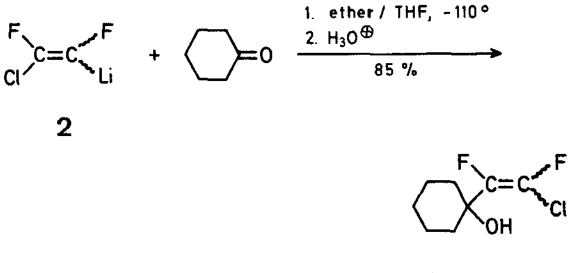
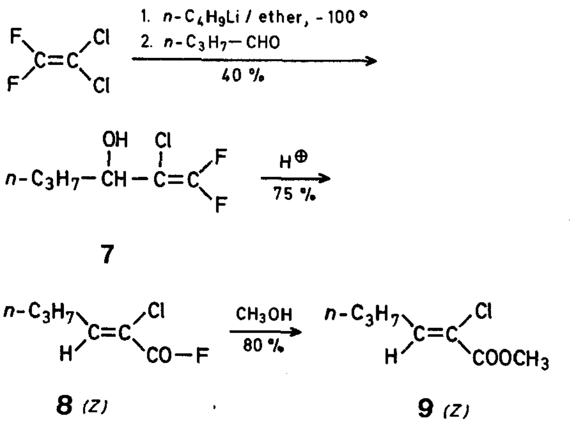
Our interest in these compounds involved determination of their decomposition thresholds and to use them for the selective introduction of fluorine atoms on to various substrates. The compounds were characterised by hydrolysis or hydroxyalkylation reactions.

Compound **2** is prepared from 1,2-dichloro-1,2-difluoroethene [(*E*)/(*Z*) = 30/70 as determined by N.M.R. spectrometry] by reaction with *n*-butyllithium at −115° in ether/tetrahydrofuran. Compound **2** is more stable than reagent **1**, and can be used at temperatures below −80°, e.g. for the conversion of cyclohexanone to the cyclohexanol derivative **6**.

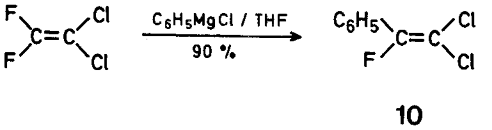


6 (*E*/*Z* = 30/70)

Compound **3** is more difficult to prepare as the lithium-chlorine exchange with 1,1-dichloro-2,2-difluoroethene is much more difficult. In ether, a maximum yield of 40% of **3** is obtained. Reagent **3** is advantageously trapped by reaction *in situ* with *n*-butanal to give 2-chloro-1,1-difluoro-3-hydroxy-1-hexene (**7**). Compound **7** is a useful precursor for α-chlorovinyl acid fluorides (**8**)—and esters (**9**)—by simple treatment with sulfuric acid.



Aromatic Grignard reagents react easily with 1,1-dichloro-2,2-difluoroethene to give 1,1-dichloro-2-fluoro-2-phenylethene (**10**)[3] which we used as the precursor for 1-chloro-2-fluoro-1-lithio-2-phenylethene (**4**).



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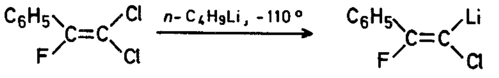
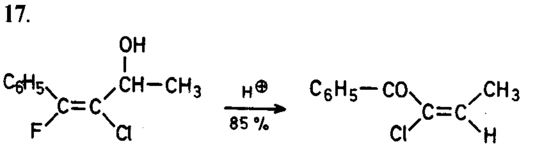
Treatment of 4 with acid represents an easy route to pure (Z)-1-chloro-2-fluoro-2-phenylethene (**11**). Carbonylation of vinyllithium compounds proceeds with retention of configuration[4]; thus treatment of **4** with carbon dioxide leads to pure (Z)-2-chloro-3-fluoro-3-phenyl-2-propenoic acid (**12**). Finally, reaction of **4** with aldehydes gives rise to various allylic alcohols with *(Z)* geometry.



10 4

The acid-induced allylic rearrangement of the alcohols **13** and **14** gives rise to pure *(E)*-α-chlorovinyl ketones **15** and **16**, respectively. Similarly reaction of **4** with acetone and subsequent treatment with acid leads to the vinyl ketone **17**.



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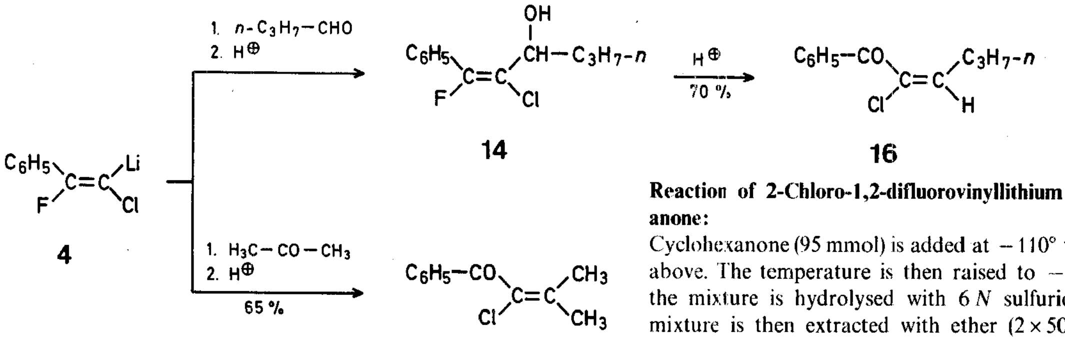
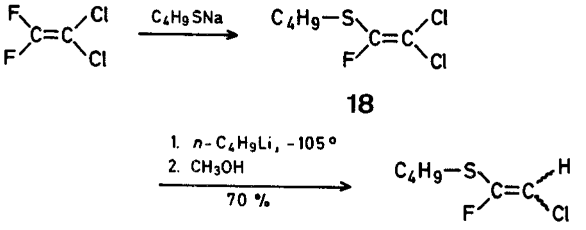


14 16 4 17

We have also shown that sodium alkylthiolates react cleanly with 1,1-dichloro-2,2-difluoroethene[5] to give the corresponding sulfide (e.g. **18**) which is easily metallated to give **5**, however without selectivity, and reacted *in situ* with methanol to give the vinyl sulfide **19** as an *(E)*:*(Z)*=55:45 mixture.



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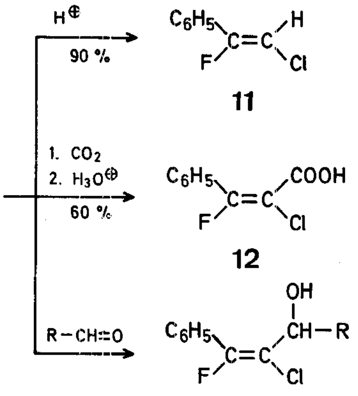
19 (E/Z = 55/45)

In conclusion, it can be stated that the metal-halogen exchange reaction of various chlorofluoroethenes represents a useful way to introduce a halovinyl moiety to acids, ketones, or alcohols. We have observed a total selectivity with the styrene **10** and no selectivity in the case of the thioethene **18**.

All reactions are performed under dry argon (or nitrogen). N.M.R. spectra are recorded on a JEOL MH 100 spectrometer using CCl_4/TMS for ^1H spectra and trifluoromethylbenzene/CCl_4 for ^{19}F spectra. I.R. spectra were recorded on a Perkin-Elmer 157G apparatus, liquids as films and solids as KBr discs.

Preparation of 2-Chloro-1,2-difluorovinyllithium (2):

A 1.5 *M* solution of butyllithium in ether (100 mmol) is added dropwise with stirring to a solution of 1,2-dichloro-1,2-difluoroethene (105 mmol; (*E*)/(*Z*)=30/70) in a mixture of tetrahydrofuran (60 ml) and ether (100 ml) at −115°. After the addition is completed (20 min), the temperature is raised to −100° for 2 min. The solution is used directly.



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12

13 R = CH_3 (75%)

14 R = n-C_3H_7 (85%)

Reaction of 2-Chloro-1,2-difluorovinyllithium (2) with Cyclohexanone:

Cyclohexanone (95 mmol) is added at −110° to the solution from above. The temperature is then raised to −80° for 10 min and the mixture is hydrolysed with 6 *N* sulfuric acid (30 ml). The mixture is then extracted with ether (2 × 50 ml) and the ether extracts dried with magnesium sulfate. Distillation from sodium hydrogen carbonate gives *1-(2-chloro-1,2-difluoroethenyl)-1-cyclohexanol* (**6**); yield: 85% as a 30:70 *(E)*:*(Z)* mixture; b.p. 45°/0.05 torr.

$C_8H_{11}ClF_2O$	calc.	C 48.85	H 5.59	Cl 18.06
(196.6)	found	48.72	5.43	18.37

I.R.: ν_{max} = 3380 (OH), 1730, 1705 cm^{-1} ($\gt C=C \lt$).

^{19}F-N.M.R.: (*Z*)-**6** (70%): $\delta = -55.2$ (=C<u>F</u>Cl), −87.5 ppm (—C<u>F</u>=CFCl), $^3J_{FF}$ = 130 Hz.

(*E*)-**6** (30%): $\delta = -38.5$ (=C<u>F</u>Cl), −74.7 ppm (—C<u>F</u>=CFCl), $^3J_{FF}$ = 16 Hz.

Preparation of 1-Chloro-2,2-difluorovinyllithium (3):

The preparation is analogous to that for **2** except that lower yields are obtained in the presence of tetrahydrofuran and thus ether alone is used as solvent.

Reaction of 1-Chloro-2,2-difluorovinyllithium (3) with Butanal:

Butanal (90 mmol) in ether (10 ml) is added dropwise to a solution of **3** (100 mmol) in ether (80 ml) at −110°. The mixture is stirred for 15 min at −100° for 15 min after the addition and is then hydrolysed by addition of 6 *N* sulfuric acid (30 ml). The resultant mixture is extracted twice with ether (2 × 50 ml), dried with magnesium sulfate, and distilled from sodium hydrogen carbonate to give *2-chloro-1,1-difluoro-3-hydroxy-1-pentene* (**7**); yield: 40%; b.p. 60–62°/13 torr; n_D^{20} = 1.4185.

$C_6H_9ClF_2O$	calc.	C 42.23	H 5.28	Cl 20.82
(170.6)	found	42.20	5.17	20.62

I.R.: ν_{max} = 3330 (OH), 1745 ($\gt C=C \lt$) cm^{-1}.

^{19}F-N.M.R.: $\delta = -29.1$ (F_a *trans* to Cl), -24.9 ppm (F_b *cis* to Cl); $^2J_{FF} = 43$ Hz, $^4J_{F_aH} = 2.5$ Hz, $^4J_{F_bH} = 1.5$ Hz.

Preparation of (*Z*)-2-Chloro-2-hexenoyl Fluoride (8):

The neat alcohol **7** (50 mmol) is added over 10 min at −10° to a stirred solution of 95% sulfuric acid (30 ml). Stirring is continued for 10 min at 0° and the mixture is poured on to crushed ice (50 g). The resultant mixture is extracted with ether (100 ml), the organic layer is quickly washed with saturated sodium hydrogen carbonate solution, dried with magnesium sulfate, solvent removed under reduced pressure, and the residue distilled from sodium carbonate (1 g); yield: 75%; b.p. 46–48°/13 torr; $n_D^{20} = 1.4335$.

I.R.: $\nu_{max} = 1820$ (>C=O), 1625 cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 1.0$ (t, 3H), 1.6 (m, 2H), 2.42 (d of t, 2H), 7.28 ppm (t, 1H) [evidence for (*Z*)-structure].

^{19}F-N.M.R.: $\delta = +77.2$ ppm (s).

Preparation of Methyl 2-Chloro-2-hexenoate (*Z*-9):

The fluoride **8** (50 mmol) is added dropwise to a mixture of methanol (100 mmol) and pyridine (100 mmol) at 25° and the mixture is stirred for 1 h. The mixture is worked up by addition of 6 *N* sulfuric acid (30 ml), extraction with ether (2 × 50 ml), drying ($MgSO_4$), and the product distilled to give (*Z*)-**9**; yield: 80%; b.p. 80–81°/13 torr; $n_D^{20} = 1.4570$.

$C_7H_{11}ClO_2$	calc.	C 51.69	H 6.77	Cl 21.84
(162.6)	found	51.55	6.70	21.68

I.R.: $\nu_{max} = 1735$ (>C=O), 1630 cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 1.0$ (t, 3H), 1.5 (m, 2H), 2.3 (d of t, 2H), 3.80 (s, 3H), 7.04 ppm (t, 1H) (calculated: 6.90 (*Z*): 6.47 (*E*)).[6]

Preparation of 1,1-Dichloro-2-fluoro-2-phenylethene (10):

Phenylmagnesium chloride (53 mmol) as a 2 *N* solution in tetrahydrofuran is added dropwise at 0° to a solution of 1,1-dichloro-2,2-difluoroethene (50 mmol). There is an exothermic reaction and at the end of the addition the temperature is 55° and no further reflux of the ethene is observed. The mixture is hydrolysed with 6 *N* sulfuric acid, extracted with ether (2 × 50 ml), dried with magnesium sulfate, and distilled to give **10**; yield: 90%; b.p. 91°/13 torr; $n_D^{20} = 1.5588$; Lit.[3] b.p. 89.0–89.9°/10.5 torr; $n_D^{26} = 1.5596$.

^{19}F-N.M.R.: $\delta = -33.5$ ppm (s).

Preparation of (*Z*)-1-Chloro-2-fluoro-2-phenylethene (11):

Reagent **4** (50 mmol) is prepared from **10** using the procedure described for **1**. The resultant solution is treated with methanol (10 ml) at −120° for 2 min, acidified with 6 *N* sulfuric acid, extracted with ether (2 × 50 ml), the ether extracts dried ($MgSO_4$), and the product distilled; yield: 90%; b.p. 84–85°/12 torr; $n_D^{20} = 1.5510$.

C_8H_6ClF	calc.	C 61.34	H 3.83	Cl 22.68
(156.6)	found	61.30	3.78	22.88

I.R.: $\nu_{max} = 1645$ cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 5.86$ ppm (d, 1H). Addition of methylnaphthalene shifts the signal by 0.3 ppm to higher field, proof of the (*Z*) configuration.

^{19}F-N.M.R.: $\delta = -50.8$ ppm (d, $^3J_{FH} = 25$ Hz).

Preparation of 2-Chloro-3-fluoro-3-phenyl-2-propenoic Acid (12; (*Z*)-α-Chloro-β-fluorocinnamic Acid):

A stream of dry carbon dioxide is passed over a stirred solution of **4** (50 mmol) in ether (80 ml) at −120°. The reaction is complete within a few minutes; the mixture is then hydrolysed with 6 *N* sulfuric acid (30 ml), extracted with ether (2 × 50 ml), and dried ($MgSO_4$). The solvent is removed on a rotary evaporator to give crude, crystalline **12**. N.M.R. spectral analysis indicates the presence of only one isomer (*Z*). Recrystallisation from ethanol gives the pure product; yield: 60%; m.p. 138°.

$C_9H_6ClFO_2$	calc.	C 53.86	H 2.99	Cl 17.70
(200.6)	found	54.00	3.15	17.60

I.R.: $\nu_{max} = 1690$ (>C=O), 1615 cm^{-1} (>C=C<).

^{19}F-N.M.R.: $\delta = -9.5$ ppm (s).

Preparation of (*Z*)-3-Chloro-4-fluoro-2-hydroxy-4-phenyl-3-butene (13):

Neat acetaldehyde (55 mmol) is added to a solution of **4** (50 mmol) in ether (80 ml) at −120°. The temperature is then raised to −100° for 5 min and the mixture hydrolysed with 6 *N* sulfuric acid (30 ml). The mixture is then worked up by extraction with ether (2 × 50 ml), drying ($MgSO_4$), and the product distilled from sodium hydrogen carbonate; yield: 75%; b.p. 90°/0.01 torr; $n_D^{20} = 1.5420$.

$C_{10}H_{10}ClFO$	calc.	C 59.85	H 4.99	Cl 17.70
(200.7)	found	60.03	5.01	17.71

I.R.: $\nu_{max} = 1670$ cm^{-1}.

^{1}H-N.M.R.: $\delta = 1.36$ (d, 2H, $J = 6$ Hz), 4.0 (s, 1H), 4.70 (d of q, 1H), 7.4 ppm (m, 5H_{arom}).

^{19}F-N.M.R.: $\delta = -30.0$ ppm (d, $^4J_{FH} = 2$ Hz).

Preparation of (*Z*)-2-Chloro-1-fluoro-3-hydroxy-1-phenyl-1-hexene (14):

The procedure described above was employed but the alcohol was not distilled; crude yield: 85%.

I.R.: $\nu_{max} = 1670$ cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 0.82$ (t, 3H), 1.28 (m, 2H), 1.78 (d of t, 2H), 4.40 (d of t, 1H), 7.4 ppm (m, 5H_{arom}).

^{19}F-N.M.R.: $\delta = -28.4$ ppm (d, $^4J_{FH} = 3$ Hz).

Preparation of (*E*)-2-Chloro-1-oxo-1-phenyl-2-butene (15) from 13:

The procedure used for the transformation of **7** to **8** is employed to give crude **15**; yield: 85%; N.M.R. analysis shows the presence of a single isomer (*E*). Recrystallisation from methanol gives the pure product; yield: 70%; m.p. 70°.

$C_{10}H_9ClO$	calc.	C 66.48	H 4.98	Cl 19.67
(180.6)	found	66.44	4.70	19.65

I.R.: $\nu_{max} = 1665$ (>C=O), 1625 cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 1.97$ (d, 3H), 6.64 (q, 1H), $^3J_{HH} = 7$ Hz), 7.4 ppm (m, 5H_{arom}).

Preparation of 2-Chloro-1-oxo-1-phenyl-2-hexene (16) from 14:

The procedure for the conversion of **7** to **8** is used; yield of distilled product: 70% (based on **10**); b.p. 90–92°/0.01 torr; $n_D^{20} = 1.5470$.

$C_{12}H_{13}ClO$	calc.	C 69.06	H 6.23	Cl 17.02
(208.7)	found	69.14	6.13	17.08

I.R.: $\nu_{max} = 1670$ (>C=O), 1620 cm^{-1} (>C=C<).

^{1}H-N.M.R.: $\delta = 1.0$ (t, 3H), 1.5 (t of q, 2H), 2.42 (d of t, 2H), 6.60 (t, 1H), 7.4 ppm (m, 5H_{arom}).

Preparation of 2-Chloro-3-methyl-1-oxo-1-phenyl-2-butene (17):

The reaction of **4** (50 mmol) in ether (80 ml) with acetone (50 mmol) is performed as described for the preparation of **13**. The crude alcohol is treated with 95% sulfuric acid (30 ml) as described for the conversion of **7** to **8**. The product is then obtained by distillation; yield: 65%; b.p. 75–76°/0.01 torr; $n_D^{20} = 1.5523$.

$C_{11}H_{11}ClO$	calc.	C 67.86	H 5.65	Cl 18.25
(194.5)	found	67.53	5.50	18.32

I.R.: $\nu_{max} = 1670$ cm^{-1} (>C=O).

^{1}H-N.M.R.: $\delta = 1.76$ (s, 3H), 1.98 (s, 3H), 7.2–8.0 ppm (m, 5H_{arom}).

Preparation of 2-Chloro-1-butylthio-1-fluoroethene (19):

The metal-halogen exchange reaction as described for the preparation of **2** is carried out with **18** (50 mmol). The resultant solution is stirred for 15 min at −105° and methanol (30 ml) is then added at this temperature. The mixture is then diluted with 3 *N* sulfuric acid (50 ml) and extracted with ether (2 × 50 ml). The product is obtained by distillation; yield: 70%; b.p. 63–66°/13 torr.

$C_6H_{10}ClFS$	calc.	C 42.73	H 5.93	Cl 21.07
(168.7)	found	42.63	5.92	21.01

^{1}H-N.M.R.: $\delta = 0.94$ (t, 3H), 1.6 (m, 4H), 2.75 (d of t, 2H), 5.80 (*E*: d, 1H), 6.18 ppm (*Z*: d, 1H), $^3J_{HF} = 19$ Hz (*E*), $^3J_{HF} = 7$ Hz (*Z*).

^{19}F-N.M.R.: $\delta = -25.0$ (*E*: d, $^3J_{FH} = 19$ Hz), -33.1 ppm (*Z*: d, $^3J_{FH} = 7$ Hz).

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