Efficient, practical and reproducible reactions of a commercial hydrochlorofluorocarbon

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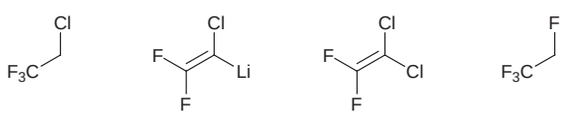
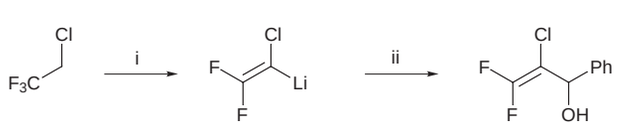
We report a reliable and reproducible procedure for the conversion of readily-available hydrochlorofluorocarbon 1-chloro-2,2,2-trifluoroethane (HCFC-133a) to a metallated difluoroalkene (1-chloro-1-lithio-2,2-difluoroethene) which can be trapped with a range of electrophiles to afford high isolated yields of products. 1-Chloro-1-lithio-2,2-difluoroethene generated by our method reacts efficiently with aldehydes and ketones, Group (IV) halides, an epoxide and a sulfur electrophile. Less reactive, softer electrophiles fail to trap the reactive intermediate.

As the range of methods available for the synthesis of selectively-fluorinated and highly-functionalised compounds from simple readily-available fluorine-containing starting materials widens,[1] the availability of new hydrochlorofluorocarbons (HCFC′s) in high tonnage quantities presents a range of novel opportunities to the organofluorine chemist. We became interested in exploring the synthetic potential of 1-chloro-2,2,2-trifluoroethane (HCFC-133a) **1**, which is readily available on an industrial scale. Dehydrofluorination–metallation would allow the generation of 1-chloro-1-lithio-2,2-difluoroethene **2** which could be trapped with electrophiles. Indeed Drakesmith,[2] Normant[3] and Okuhara[4] have all described the generation and trapping of **2**, usually from 1,1-dichloro-2,2-difluoroethene (CFC-1112a) **3**, a feedstock which is becoming less readily available. The dehydrofluorination–metallation approach has already been used profitably to convert trifluoroethanol into a diverse array of CF_2 compounds,[5] and shows great promise for the elaboration of 1,1,1,2-tetrafluoroethane (HFC-134a) **4** into useful materials.



1 **2** **3** **4**

The literature contained one example of the dehydrofluorination–metallation we wished to develop but no details were provided.[6] We therefore investigated the reaction shown in Scheme 1 under various conditions, using benzaldehyde as the electrophile in the first instance to determine the optimum conditions for the generation of **2**. Gaseous HCFC and solvent were loaded into a cold, evacuated flask *via* syringe. Nitrogen was admitted through a Rotaflo tap to release the remaining vacuum, then *n*-butyllithium was added, followed by the electrophile.



1 **2** **5**

Scheme 1 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C; ii, PhCHO, then NH_4Cl

Trapping after ten minutes with benzaldehyde in THF resulted in complete conversion of the aldehyde to difluoroallylic alcohol **5** by ^{1}H NMR of the crude product mixture. Following work-up and column chromatography, **5** could be isolated in excellent (96%) yield based on the amount of aldehyde used. In view of the availability of 1-chloro-2,2,2-trifluoroethane, and the ease of removal of both this, and the derived 1-chloro-2,2-difluoroethene (HCFC-1122) (both are gases at room temperature), an excess (1.5 equivalents) of 1-chloro-2,2,2-trifluoroethane was used throughout. Table 1 summarises further results obtained *via* this method.

The base of choice appeared to be *n*-butyllithium, rather than LDA (which gave acceptable yields but afforded very dark coloured crude products) and the reactions in hexane, diethyl ether or THF afforded similar (good to excellent) yields of alcohol **5**. Temperature control was important: the upper limit for the stability of **2** lies somewhere below −50 °C in hexane. Allowing a hexane solution of **2** to warm to −50 °C followed by the addition of benzaldehyde resulted in the formation of **5** in 25% yield compared to the 75% yield obtained when the metallated perhaloalkene was maintained at −78 °C in hexane. At −25 °C, <5% of the adduct was obtained. Hexane was chosen as the solvent for these studies as the solutions are colourless and a colour change would be expected as the metallated fluoroalkene decomposed.

The other allylic alcohols[7] **6**–**9** were obtained as the sole fluorine-containing products;[8,9] ^{1}H NMR spectra of the crude products showed that the non-fluorinated alcohols, products of the addition of *n*-butyllithium to the electrophile, were not formed. Most aldehyde and ketone electrophiles were well behaved though the products obtained from additions to furfural and cinnamaldehyde, **10** and **11** respectively, were extremely unstable, decomposing before characterisation could be completed (though satisfactory ^{19}F NMR spectra were obtained, Table 1). The low stability of these alcohols is not surprising given the propensity for rearrangement of difluoroallylic alcohols through loss of water and carbenium ion formation, facilitated by the high degree of conjugation available in **11**, and the extremely electron-rich aromatic system in **10**. Silane[10] and stannane[11] adducts **12** and **13** could be obtained in high yield and we were able to open cyclohexene oxide to **14** following the procedure described by Ganem.[12] With Trost's reagent (*S*-phenyl benzenethiosulfonate),[13] an unacceptable

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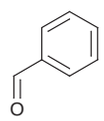
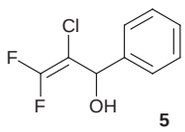
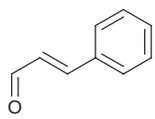
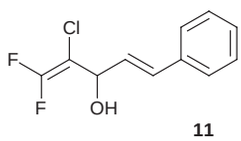
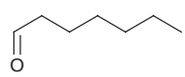
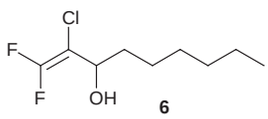
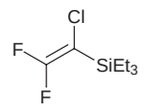
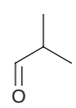
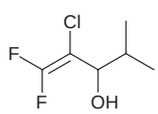
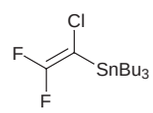
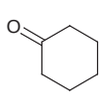
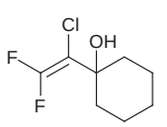
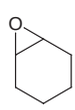
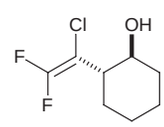
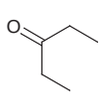
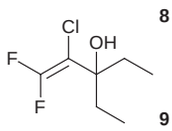
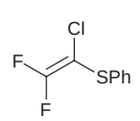
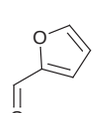
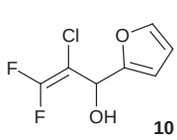
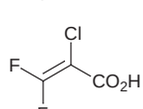
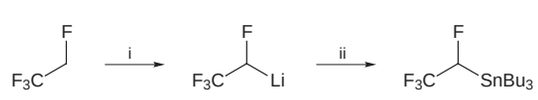
Table 1 Trapping reactions of **2** with electrophiles

Electrophile	Product	Yield (%)[a]	Electrophile	Product	Yield (%)[a]
	 **5**	96		 **11**	(—)[c]
	 **6**	98	Et_3SiCl	 **12**	89
	 **7**	92	Bu_3SnCl	 **13**	95
	 **8**	81		 **14**	71
	 **9**	78	PhO_2SSPh	 **15**	93[d]
	 **10**	(—)[b]	CO_2	 **16**	(—)[e]

[a] Isolated yeld after purification. [b] δ_F(282 MHz, $CDCl_3$) −85.9 (1F, d, $^2J_{F\text{-}F}$ 35.6), −89.6 (1F, d, $^2J_{F\text{-}F}$ 35.6). [c] δ_F(282 MHz, $CDCl_3$) −86.8 (1F, d, $^2J_{F\text{-}F}$ 38.8), −90.2 (1F, d, $^2J_{F\text{-}F}$ 38.8). [d] Diethyl ether was the reaction solvent. [e] δ_F(282 MHz, $CDCl_3$) −64.3 (1F, d, $^2J_{F\text{-}F}$ 18.4), −65.7 (1F, d, $^2J_{F\text{-}F}$ 18.4).

(33%) yield of the phenyl sulfide **15** was obtained in THF, but performing the reaction in diethyl ether was more successful (93% isolated yield after 2 hours' contact time).[14] Direct trapping with carbon dioxide afforded the perhaloacrylic acid **16** according to the ^{19}F NMR spectrum of the crude reaction mixture, but we were not able to purify this compound before decomposition occurred, nor could we esterify the crude material. Neither direct alkylation nor reaction with a typical imine succeeded. All attempts to deploy organocopper chemistry, effective in our metallated difluoroenol carbamate studies were unsuccessful.[15]

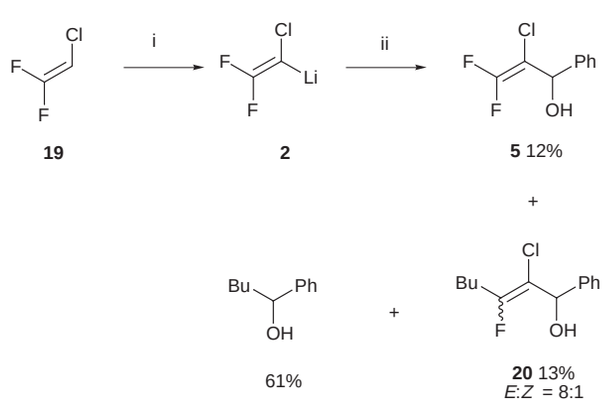
Without exception, the mechanism written for the dehydrofluorination–metallation sequence involves an $E1_cB$ pathway. Indeed, Burdon and co-workers presented *prima facie* evidence for the existence of an sp^3 hybridised carbanion **17** in the form of the detection of tributyltin chloride adduct **18**, during their study of 1,1,1,2-tetrafluoroethane (Scheme 2).[16]



4 **17** **18**

Scheme 2 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C; ii, Bu_3SnCl

By analogy, HF elimination from **1** affords 1-chloro-2,2-difluoroethene **19** *in situ* which would then undergo metallation more rapidly than the initial dehydrofluorination, given the higher acidity of protons attached to sp^2 centres. The dehydrofluorination step can be bypassed by the direct use of 1-chloro-2,2-difluoroethene. Generation of **2** will occur more rapidly as only metallation is required. To our surprise, all attempts to utilise 1-chloro-2,2-difluoroethene by direct metallation were *less* efficient, resulting in much lower yields of products than were obtained from 1-chloro-2,2,2-trifluoroethane.



19 **2** **5** 12%

20 13%
E:*Z* = 8:1

61%

Scheme 3 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C; ii, PhCHO then NH_4Cl

For example, Scheme 3 shows the outcome of a reaction using strict 1:1 HCFC:*n*-butyllithium stoichiometry. Monofluoro alcohol **20** was formed by stereoselective addition–elimination between *n*-butyllithium and the conjugate base of **5**.[17] Cleaner higher yielding reactions were obtained when 1-chloro-2,2-difluoroethene was used in excess, suggesting that the problem may lie in the high volatility of the chlorofluoroalkene which results in a relatively low concentration in solution. We were also aware that one equivalent of lithium fluoride was generated in the sequence from 1-chloro-2,2,2-trifluoroethane, and that lithium halide salts have been shown to modify the properties of lithium bases. However, the

presence of one equivalent of added lithium chloride had no effect on the yield or outcome of the reactions from 1-chloro-2,2-difluoroethene.

In conclusion, 1-chloro-2,2,2-trifluoroethane appears to be a useful new entry point to disubstituted difluoroalkenes, an important discovery in view of its availability on a large scale and anticipated longevity in the marketplace. We are investigating further methods for the manipulation of 1-chloro-2,2,2-trifluoroethane, 1-chloro-2,2-difluoroethene and products derived from them in our laboratory.

Experimental

All glassware was oven dried (80 °C) overnight. Tetrahydrofuran was dried by refluxing with sodium metal and benzophenone under dry nitrogen, until a deep purple colour persisted, then collected by syringe when required. Diethyl ether and hexane were dried by refluxing with calcium hydride under dry nitrogen. *n*-Butyllithium was titrated before use against 1,3-diphenylpropan-2-one *p*-tolylsulfonylhydrazone. HCFC-133a and HCFC-1122 were supplied by Fluorochem and used as received. The gases were collected in Optima® glass syringes. All electrophiles were distilled freshly before use, except for carbon dioxide and *S*-phenyl benzenethiosulfonate (Aldrich) which were used as supplied. Boron trifluoride–diethyl ether (Aldrich) was distilled *in vacuo* before use and stored under nitrogen. Light petroleum refers to that boiling in the range 40–60 °C

^{1}H NMR (300 MHz), ^{19}F NMR (282 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AC-300 spectrometer. ^{19}F NMR spectra were referenced to fluorotrichloromethane as the internal standard. ^{1}H and ^{13}C NMR spectra were referenced to residual chloroform. ^{13}C NMR spectra were recorded using the JMOD or PENDANT pulse sequences. *J* Values are reported in Hz. Mass spectra were recorded on a VG ProSpec mass spectrometer or a Kratos Profile mass spectrometer. Chemical ionisation (CI+) methods used ammonia as the reagent gas. For TLC, precoated aluminium-backed silica plates were supplied by E. Merck, A.G Darmstadt, Germany. (Silica gel 60 F254, thickness 0.2 mm.) Anisaldehyde and potassium permanganate staining; and ultraviolet light were employed for visualisation. Column chromatography was performed using silica gel (E. Merck, A.G kieselgel, Art. 9385). Column fractions were collected and monitored by thin layer chromatography. Gas chromatographic analyses were carried out on a Carlo Erba 8000 series (8130) chromatograph, fitted with a Megabore SGE BPX5 column (15 m × 0.53 mm). All new compounds were shown to be homogeneous by GC analysis.

General procedure for the dehydrofluorination–metallation and trapping of HCFC-133a: 2-chloro-1,1-difluoro-3-phenylprop-1-en-3-ol 5

A two-necked round bottomed flask was fitted with a Rotaflo tap and suba seal. The flask was evacuated through the Rotaflo tap and cooled to −78 °C. HCFC-133a {50 ml, 2.1 mmol [V_m @ 20 °C = 24 043 ml mol^{-1} *vs.* V_m @ 0 °C (STP) = 22 402 ml mol^{-1}]} and THF (2.5 ml) were added to the evacuated flask. The solution was stirred at −78 °C for 5 min.

The remaining vacuum was released to nitrogen through the Rotaflo tap and the reaction was stirred at −78 °C for a further 5 min. *n*-Butyllithium (1.7 ml of a 1.8 M solution in hexane, 3.0 mmol) was added dropwise to the stirred solution at −78 °C. The temperature was maintained at −78 °C for 10 min, during which time the reaction developed a brown colour. Benzaldehyde (0.15 ml, 1.5 mmol) was added dropwise. The reaction was stirred at −78 °C for 1 h further and then allowed to warm to −30 °C for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (20 ml) at −30 °C. The aqueous layer was extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with brine (25 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* affording an orange oil (0.41 g). Purification by column chromatography (R_f 0.23, 10% diethyl ether, 90% light petroleum) afforded **5** (0.29 g, 96%) as a colourless oil, δ_H(300 MHz; $CDCl_3$) 7.46–7.30 (5 H, m, Ph), 5.74 (1 H, dt, $^3J_{H\text{-}H}$ 6.6, $^4J_{H\text{-}F}$ 2.6, C*H*Ph) and 3.10 (1 H, d, $^3J_{H\text{-}H}$ 6.6, O*H*); δ_C(75 MHz; $CDCl_3$) 154.6 (dd, $^1J_{C\text{-}F}$ 291.6 and 288.8), 138.9, 128.5, 128.3, 125.7, 95.3 (dd, $^2J_{C\text{-}F}$ 46.1 and 15.3) and 68.7; δ_F(282 MHz; $CDCl_3$) −86.6 (1 F, d, $^2J_{F\text{-}F}$ 38.2) and −90.5 (1 F, dd, $^2J_{F\text{-}F}$ 38.2, $^4J_{H\text{-}F}$ 2.6) [HRMS (CI, M$^+$) Found: 204.0152. Calc. for $C_9H_7OF_2Cl$: 204.0153]; *m*/*z* (EI) 204 (66%, M$^+$), 184 (64), 169 (54), 107 (70) and 79 (100).

2-Chloro-1,1-difluorononon-1-en-3-ol 6. As for **5** but *n*-heptanal (0.21 ml, 1.5 mmol) was used as the electrophile. Work up in the usual way followed by column chromatography (R_f 0.20, 10% diethyl ether, 90% light petroleum) afforded **6** (0.31 g, 98%) as a colourless oil, δ_H(300 MHz; $CDCl_3$) 4.56–4.48 (1 H, m, C*H*OH), 1.88–1.54 [3 H, m, CH(OH)CH_2, O*H*], 1.43–1.16 (8 H, m, CH_2CH_2CH_2CH_2Me) and 0.88 (3 H, t, $^3J_{H\text{-}H}$ 6.6, Me); δ_C(75 MHz; $CDCl_3$) 153.9 (dd, $^1J_{C\text{-}F}$ 290.5 and 287.7), 95.1 (dd, $^2J_{C\text{-}F}$ 39.3 and 14.4), 67.2, 34.0, 31.6, 28.8, 25.0, 22.5 and 13.9; δ_F(282 MHz; $CDCl_3$) −87.7 (1 F, s) and −92.0 (1 F, s) {HRMS (CI, [M+H]$^+$) Found: 213.0865. Calc. for $C_9H_{16}OF_2Cl$: 213.0858}; *m*/*z* (CI) 230 (36%, [M+NH$_4$]$^+$), 212 (9, M$^+$), 192 (57), 159 (84) and 139 (100).

2-Chloro-1,1-difluoro-4-methylpent-1-en-3-ol 7. As for **5** but isobutyraldehyde (0.14 ml, 1.5 mmol) was used as the electrophile. Work up in the usual way followed by filtration though a silica column with diethyl ether afforded **7** (0.23 g, 92%) as an orange oil, δ_H(300 MHz; $CDCl_3$) 4.05 [1 H, dt, $^3J_{H\text{-}H}$ 9.6, $^4J_{F\text{-}H}$ 2.6, C*H*(OH)CHMe$_2$], 1.94–1.83 [1 H, m, CH(OH)C*H*Me$_2$], 1.70 (1 H, br s, O*H*), 1.09 (3 H, d, $^3J_{H\text{-}H}$ 6.6, CH_3CHMe) and 0.84 (3 H, d, $^3J_{H\text{-}H}$ 6.6, MeCHCH_3); δ_C(75 MHz; $CDCl_3$) 154.1 (dd, $^1J_{C\text{-}F}$ 290.5 and 287.1), 94.5 (dd, $^2J_{C\text{-}F}$ 39.9 and 14.4), 73.1, 31.6, 18.7 and 18.1; δ_F(282 MHz; $CDCl_3$) −88.8 (1 F, d, $^2J_{F\text{-}F}$ 42.0) and −92.3 (1 F, d, $^2J_{F\text{-}F}$ 42.0) [HRMS (CI, M$^+$) Found: 170.0308. Calc. for $C_6H_9OF_2Cl$: 170.0310]; *m*/*z* (EI) 170 (5%, M$^+$), 150 (16), 127 (100), 91 (34) and 43 (66).

1-(1-Chloro-2,2-difluoroethenyl)cyclohexanol 8. As for **5** but cyclohexanone (0.16 ml, 1.5 mmol) was used as the electrophile. Work up in the usual way followed by Kugelrohr distillation (75 °C, 8 mmHg) afforded **8** (0.24 g, 81%) as a colourless oil, δ_H(300 MHz; $CDCl_3$) 2.00–1.16 (11 H, envelope, CH_2CH_2CH_2-CH_2CH_2 and O*H*); δ_C(75 MHz; $CDCl_3$) 153.0 (dd, $^1J_{C\text{-}F}$ 292.8 and 286.9), 99.9 (dd, $^2J_{C\text{-}F}$ 32.9 and 14.9), 72.4 (d, $^3J_{C\text{-}F}$ 4.2), 35.9, 25.1 and 21.8; δ_F(282 MHz; $CDCl_3$) −81.3 (1 F, d, $^2J_{F\text{-}F}$ 42.6) and −85.3 (1 F, d, $^2J_{F\text{-}F}$ 42.6) [HRMS (CI, M$^+$) Found: 196.0466. Calc. for $C_8H_{11}OF_2Cl$: 196.0466]; *m*/*z* (CI) 196 (10%, M$^+$), 176 (100), 157 (37), 123 (18).

2-Chloro-1,1-difluoro-3-ethylpent-1-en-3-ol 9. As for **5** but pentan-3-one (0.15 ml, 1.5 mmol) was used as the electrophile. Work up in the usual way followed by filtration though a silica column with diethyl ether afforded **9** (0.22 g, 78%) as an orange oil, δ_H(300 MHz; $CDCl_3$) 1.87–1.59 (5 H, envelope, 2 × CH_2Me and O*H*) and 0.92 (6 H, t, $^3J_{H\text{-}H}$ 7.4, 2 × Me); δ_C(75 MHz; $CDCl_3$) 153.9 (dd, $^1J_{C\text{-}F}$ 291.3 and 286.3), 96.5 (dd, $^2J_{C\text{-}F}$ 31.9 and 15.0), 76.7 (d, $^3J_{C\text{-}F}$ 4.0), 31.2 (t, $^4J_{C\text{-}F}$ 2.6) and 7.4; δ_F(282 MHz; $CDCl_3$) −81.2 (1 F, d, $^2J_{F\text{-}F}$ 46.3) and −87.8 (1 F, d, $^2J_{F\text{-}F}$ 46.3) [HRMS (CI, M$^+$) Found: 184.0460. Calc. for $C_7H_{11}OF_2Cl$: 184.0466]; *m*/*z* (EI) 184 (7%, M$^+$), 164 (100), 145 (20), 111 (26).

1-Chloro-2,2-difluoro-1-(triethylsilyl)ethene 12. As for **5** but triethylsilyl chloride (0.28 ml, 1.7 mmol) was used as the electrophile. Work up in the usual way followed by filtration though an alumina column (Brockmann, Activity 1) with pentane afforded **12** (0.32 g, 89%) as a colourless oil (Found: C, 44.8; H, 6.9. Calc. for $C_8H_{15}F_2SiCl$: C, 45.2; H, 7.1%) δ_H(300 MHz; $CDCl_3$) 0.97 (9 H, t, $^3J_{H\text{-}H}$ 7.8, 3 × Me) and 0.80 (6 H, q, $^3J_{H\text{-}H}$ 7.8, 3 × CH_2Me); δ_C(75 MHz; $CDCl_3$) 158.9 (dd, $^1J_{C\text{-}F}$ 306.3

and 284.3), 84.9 (dd, $^2J_{C\text{-}F}$ 61.0 and 3.4), 6.8 and 2.5 (t, $^4J_{C\text{-}F}$ 1.7); δ_F(282 MHz; $CDCl_3$) −68.5 (1 F, d, $^2J_{F\text{-}F}$ 31.2) and −83.5 (1 F, d, $^2J_{F\text{-}F}$ 31.2) [HRMS (CI, M^+) Found: 212.0610. Calc. for $C_8H_{15}F_2SiCl$: 212.0600]; *m/z* (EI) 212 (22%, M^+), 183 (34), 105 (100), 77 (71) and 43 (38).

1-Chloro-2,2-difluoro-1-(tributylstannyl)ethene 13. As for **5** but tri-*n*-butyltin chloride (0.40 ml, 1.5 mmol) was used as the electrophile. Work up in the usual way followed by filtration though an alumina column (Brockmann, Activity 1) with toluene afforded **13** (0.55 g, 95%) as a colourless oil, δ_H(300 MHz; $CDCl_3$) 1.70–0.82 (27 H, envelope, 3 × $CH_2CH_2CH_2CH_3$); δ_C(75 MHz; $CDCl_3$) 157.8 (dd, $^1J_{C\text{-}F}$ 313.1 and 272.4), 84.1 (dd, $^2J_{C\text{-}F}$ 81.9 and 11.9), 28.6, 27.1, 13.6 and 10.6; δ_F (282 MHz, $CDCl_3$) −71.5 (1 F, d, $^2J_{F\text{-}F}$ 43.3) and −86.5 (1 F, d, $^2J_{F\text{-}F}$ 43.3) {HRMS (CI, $[M - CH_3CH_2CH_2CH_2]^+$) Found: 331.0074. Calc. for $C_{10}H_{18}F_2ClSn$: 331.0087; *m/z* (EI) 331 (100%, $[M - CH_3CH_2CH_2CH_2]^+$}, 275 (91), 217 (46), 139 (27), 57 (31) and 41 (45).

2-(1′-Chloro-2′,2′-difluoroethenyl)cyclohexan-1-ol 14. As for **5** but boron trifluoride–diethyl ether (0.38 ml, 3.0 mmol) and cyclohexene oxide (0.15 ml, 1.5 mmol) were added dropwise to a cold (−78 °C) solution of the organometallic reagent (2.1 mmol). The reaction was stirred at −78 °C for 1 h and then allowed to warm to −30 °C for 30 min. Work up in the usual way followed by column chromatography (R_f 0.11, 10% diethyl ether, 90% light petroleum) afforded **14** (0.21 g, 71%) as a colourless oil, δ_H(300 MHz; $CDCl_3$) 3.65–3.52 (1 H, m, C*H*OH), 2.46–2.34 (1 H, m, C*H*CCl), 2.10 (1 H, br s, O*H*) and 1.88–1.18 (8H, envelope, $CH_2CH_2CH_2CH_2$); δ_C(75 MHz; $CDCl_3$) 154.5 (dd, $^1J_{C\text{-}F}$ 287.1 and 284.8), 94.1 (dd, $^2J_{C\text{-}F}$ 41.8 and 16.4), 69.7 (t, $^4J_{C\text{-}F}$ 2.0), 45.4, 34.5, 28.8 (dd, $^3J_{C\text{-}F}$ 2.8 and 1.7), 24.9 and 24.5; δ_F(282 MHz; $CDCl_3$) −87.5 (1 F, d, $^2J_{F\text{-}F}$ 44.5) and −94.1 (1 F, dd, $^2J_{F\text{-}F}$ 44.5, $^4J_{H\text{-}F}$ 2.6) {HRMS (CI, $[M+NH_4]^+$) Found: 214.0814. Calc. for $C_8H_{15}ONF_2Cl$: 214.0810}; *m/z* (CI) 214 (100%, $[M+NH_4]^+$), 196 (3, M^+), 176 (18), 150 (39), 124 (52).

1-Chloro-2,2-difluoro-1-(phenylthio)ethene 15. A two-necked round bottomed flask was fitted with a Rotaflo tap and suba seal. The flask was evacuated through the Rotaflo tap and cooled to −78 °C. HCFC-133a (50 ml, 2.1 mmol) and diethyl ether (2.5 ml) were added to the evacuated flask. The solution was stirred at −78 °C for 5 min. The remaining vacuum was released to nitrogen through the Rotaflo tap and the reaction was stirred at −78 °C for a further 5 min. *n*-Butyllithium (1.7 ml of a 1.8 M solution in hexane, 3.0 mmol) was added dropwise to the stirred solution at −78 °C. The temperature was maintained at −78 °C for 2 h, during which time the reaction developed a yellow colour. A solution of *S*-phenyl benzenethiosulfonate (0.43 g, 1.5 mmol) in diethyl ether (2.5 ml) was added dropwise at −78 °C. The reaction was stirred at −78 °C for 1 h further and then allowed to warm to −30 °C for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (20 ml) at −30 °C. Work up in the usual way followed by column chromatography (R_f 0.69, 100% light petroleum) afforded **15** (0.29 g, 93%) as a yellow oil, δ_H(300 MHz; $CDCl_3$) 7.45–7.20 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 157.6 (dd, $^1J_{C\text{-}F}$ 301.8, 290.5), 131.9, 129.8, 129.5, 128.1 and 89.1 (dd, $^2J_{C\text{-}F}$ 40.1 and 26. 6); δ_F(282 MHz; $CDCl_3$) −73.3 (1 F, d, $^2J_{F\text{-}F}$ 10.2) and −79.4 (1F, d, $^2J_{F\text{-}F}$ 10.2) [HRMS (CI, M^+) Found: 205.9768. Calc. for $C_8H_5F_2SCl$: 205.9769]; *m/z* (EI) 206 (36%, M^+), 127 (100) and 77 (18).

2-Chloro-3-fluoro-1-phenylhept-2-en-1-ol 20. A two-necked round bottomed flask was fitted with a Rotaflo tap and suba seal. The flask was evacuated through the Rotaflo tap and cooled to −78 °C. HCFC-1122 (35 ml, 1.5 mmol) and THF (2.5 ml) were added to the evacuated flask. The solution was stirred at −78 °C for 5 min.

The remaining vacuum was released to nitrogen through the Rotaflo tap and the reaction was stirred at −78 °C for a further 5 min. *n*-Butyllithium (0.85 ml of a 1.8 M solution in hexane, 1.5 mmol) was added dropwise to the stirred solution at −78 °C. The temperature was maintained at −78 °C for 10 min, during which time the reaction developed a brown colour. Benzaldehyde (0.15 ml, 1.5 mmol) was added dropwise. The reaction was stirred at −78 °C for 1 h further and then allowed to warm to −30 °C for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (20 ml) at −30 °C and worked up in the usual way to afford **5** (0.037 g, 12%) and **20** (0.047 g, 13%) after column chromatography (R_f 0.29, 10% diethyl ether, 90% light petroleum), δ_H(300 MHz; $CDCl_3$) 7.44–7.26 (5 H, m, Ph), 6.05 (1 H, dd, $^3J_{H\text{-}H}$ 7.0, $^4J_{H\text{-}F}$ 2.0, C*H*COH), 2.50 (2 H, dt, $^3J_{H\text{-}F}$ 23.5, $^3J_{H\text{-}H}$ 7.4, CH_2CF), 2.32 (1 H, d, $^3J_{H\text{-}H}$ 7.4, OH), 1.66–1.52 (2 H, m, CH_2Et), 1.46–1.30 (2 H, m, CH_2Me) and 0.95 (3 H, t, $^3J_{H\text{-}H}$ 7.4); δ_C(75 MHz; $CDCl_3$) 158.8 (d, $^1J_{C\text{-}F}$ 257.7), 140.2 (d, $^4J_{C\text{-}F}$ 2.8), 128.4, 127.8, 125.7, 119.3 (d, $^2J_{C\text{-}F}$ 39.0), 68.2 (d, $^3J_{C\text{-}F}$ 5.7), 28.8 (d, $^2J_{C\text{-}F}$ 25.2), 27.7, 22.1 and 13.8; δ_F(282 MHz; $CDCl_3$) −109.1 (1 F, t, $^3J_{H\text{-}F}$ 22.9) [HRMS (CI, M^+) Found: 242.0881. Calc. for $C_{13}H_{16}FOCl$: 242.0874]; *m/z* (EI) 242 (14%, M^+), 224 (20), 180 (58), 165 (64), 145 (88), 102 (89) and 57 (100).

The following were also obtained using the general procedure from HCFC-133a but could not be characterised fully because of their instability. ^{19}F NMR data were obtained as follows.

2-Chloro-3,3-difluoro-1-(1′-furyl)prop-2-en-1-ol 10. δ_F(282 MHz; $CDCl_3$) −85.9 (1 F, d, $^2J_{F\text{-}F}$ 35.6) and −89.6 (1F, d, $^2J_{F\text{-}F}$ 35.6).

(4*E*)-2-Chloro-1,1-difluoro-5-phenylpenta-1,4-dien-3-ol 11. δ_F(282 MHz; $CDCl_3$) −86.8 (1 F, d, $^2J_{F\text{-}F}$ 38.8) and −90.2 (1F, d, $^2J_{F\text{-}F}$ 38.8).

2-Chloro-3,3-difluoropropenoic acid 16. δ_F(282 MHz; $CDCl_3$) −64.3 (1 F, d, $^2J_{F\text{-}F}$ 18.4) and −65.7 (1F, d, $^2J_{F\text{-}F}$ 18.4).

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References

1 J. M. Percy, *Contemp. Org. Synth.*, 1995, **4**, 251.
2 F. G. Drakesmith, R. D. Richardson, O. J. Stewart and P. Tarrant, *J. Org. Chem.*, 1968, **33**, 286.
3 D. Masure, R. Sauvêtre, J. F. Normant and J. Villieras, *Synthesis*, 1976, 761.
4 K. Okuhara, *J. Org. Chem.*, 1976, **41**, 1487.
5 J. M. Percy, *Top. Curr. Chem.*, 1997, **193**, 131.
6 J. Burdon, P. L. Coe, I. B. Haslock and R. L. Powell, *J. Fluorine Chem.*, 1997, **85**, 151.
7 For a recent application of related allylic alcohols, see T. Takagi, N. Okikawa, S. Johnoshita, M. Koyama, A. Ando and I. Kumadaki, *Synlett*, 1996, 82. The groups of Hiyama and Kumadaki have described (independently) routes to these allylic alcohols, though the published characterisations are often far from complete. The former group worked from the increasingly less readily-available 2,2,2-trichloro-1,1,1-trifluoroethane (CFC-113a) while the latter obtained poor to moderate yields of products from expensive inhalation anaesthetic Halothane (HCFC-123B1) *via* the so-called abnormal Grignard reaction. See: T. Takagi, J. Takahashi, H. Nakatsuka, M. Koyama, A. Ando and I. Kumadaki, *Chem. Pharm. Bull.*, 1996, **44**, 280; T. Takagi, A. Takesue, A. Isowaki, M. Koyama, A. Ando and I. Kumadaki, *Chem. Pharm. Bull.*, 1995, **43**, 1071; T. Takagi, A. Takesue, M. Koyama, A. Ando, T. Miki, I. Kumadaki and T. Sato, *J. Org. Chem.*, 1992, **57**, 3921. Also: M. Fujita and T. Hiyama, *Tetrahedron Lett.*, 1986, **27**, 3655. See also: M. Fujita, T. Morita and T. Hiyama, *Tetrahedron Lett.*, 1986, **27**, 2135; M. Fujita and T. Hiyama, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 4377; M. Fujita and T. Hiyama, *Tetrahedron Lett.*, 1986, **27**, 3659; M. Fujita, K. Kondo and T. Hiyama, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 4385.
8 Tamura formed **5** (62%) from benzaldehyde and 2,2-dichloro-1,1,1–trifluoroethane (HCFC-123): M. Tamura and A. Sekiya, *J. Fluorine Chem.*, 1995, **71**, 119.
9 For an electrochemical approach, see T. Shono, N. Kise and H. Oka, *Tetrahedron Lett.*, 1991, **32**, 6567.
10 In contrast, Drakesmith reported that these silane products were

unstable and could not be isolated in reactions from HCFC-1122. See F. G. Drakesmith, O. J. Stewart and P. Tarrant, *J. Org. Chem.*, 1968, **33**, 472. The triethylsilane was prepared because the chlorotrimethylsilane adduct was simply too volatile to isolate in a pure state. The reader should note that the chlorotrimethylsilane adduct of the conjugate base of HFC-134a was never actually purified: I. Haslock, Ph.D. Thesis, University of Birmingham, 1995.
11 The trimethylstannane was reported in 40–45% yield from CFC-1112a: A. Runge and W. W. Sander, *Tetrahedron Lett.*, 1990, **31**, 5453.
12 M. J. Eis, B. Ganem and J. E. Wrobel, *J. Am. Chem. Soc.*, 1984, **106**, 3693; similar chemistry was described by T. Dubuffet, R. Sauvêtre and J. F. Normant, *J. Organomet. Chem.*, 1988, **341**, 11.
13 B. M. Trost and M. K. T. Mao, *Tetrahedron Lett.*, 1980, **21**, 3523.
14 An alternative preparation of the vinyl sulfide from vinylidene difluoride (HFC-1132a) was reported; S. Piettre, C. Decock, R. Merenyi and H. G. Viehe, *Tetrahedron*, 1987, **43**, 4309.
15 P. J. Crowley, J. A. Howarth, W. M. Owton, J. M. Percy and K. Stansfield, *Tetrahedron Lett.*, 1996, **37**, 5975.
16 J. Burdon, P. L. Coe, I. B. Haslock and R. L. Powell, *Chem. Commun.*, 1996, 49.
17 D. Masure, C. Chuit, R. Sauvêtre and J. F. Normant, *Synthesis*, 1978, 458.

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