The generation of difluoroenolates from trifluoroethanol and reproducible syntheses of α,α-difluoro-β-hydroxy ketones

Andrew S. Balnaves,[a] Thomas Gelbrich,[c] Michael B. Hursthouse,[c] Mark E. Light,[c] Michael J. Palmer[b] and Jonathan M. Percy*[a]

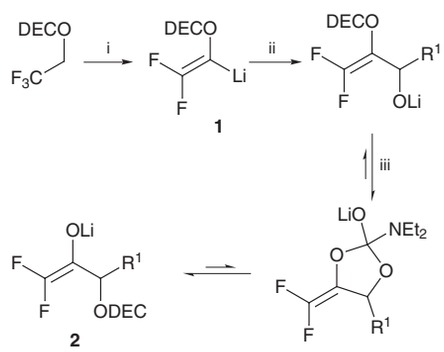
[a] *School of Chemistry, University of Birmingham, Edgbaston, Birmingham, UK B15 2TT*
[b] *Pfizer Central Research, Sandwich, UK CT13 9NJ*
[c] *EPSRC National X-Ray Crystallography Service, Department of Chemistry, University of Southampton, Highfield, Southampton, UK SO17 1BJ*

Received (in Cambridge) 14th April 1999, Accepted 21st June 1999

Metallated difluoroenol carbamate **1** reacted with aldehydes and ketones in the presence of highly oxophilic Lewis acid boron trifluoride–ethyl ether; the Lewis acid attenuated the transacylation reaction to the corresponding enolates so that allylic alcohols could be isolated. Treatment of the allylic alcohols with strong base afforded difluoroenolates which could be trapped cleanly in aldol reactions.

The synthesis of highly functionalised molecules containing a limited number of fluorine atoms remains a significant challenge to synthetic organic chemists.[1] One reason for continued interest lies in the enormous influence that fluorine atom substituents may exert upon adjacent or proximate functional groups. For example, certain molecules incorporating a difluoromethylene ketone motif have been shown to act as potent inhibitors of proteolytic enzymes,[2] including elastase,[3] HIV-1 protease,[4–6] (ICE),[7] HLE-1,[8] renin[9] and Human Heart Chymase.[10,11] In the typical mode of action, the CF_2 centre activates the ketonic carbonyl group towards hydration and the enzyme then binds the hydrated form reversibly.[12]

One method for installing the $–CF_2CO–$ group would be to exploit the ubiquitous aldol reaction[13,14] with a difluoroenolate, or synthetic equivalent. Precedents exist: difluoroenoxysilanes were prepared from chlorodifluoromethyl ketones by the action of zinc(0) in acetonitrile in the presence of chlorotrimethylsilane.[15–17] Later, zinc difluoroenolates were generated from α-chloro-α,α-difluoroketones upon exposure to zinc(0)–copper(I) and trapped with aldehydes to afford good yields of aldol products.[18] Acylsilanes have also been used as precursors; treatment of trifluoroacetyltriphenylsilane with Grignard reagents afforded alkoxide adducts in the first instance. These underwent Brook rearrangement, followed by fluoride ion loss, yielding difluoroenoxysilanes[19] which condensed with aldehydes in the presence of $TiCl_4$. In a significantly more straightforward and potentially very important modification, Portella has reacted acylsilanes with the trifluoromethyl anion equivalent Ruppert's reagent (CF_3SiMe_3) in the presence of a catalytic fluoride source, to produce difluoroenoxysilanes[20] which undergo aldol and Michael reactions *in situ*.[21,22] More recently Taguchi has reported the synthesis, by a dehydrochlorination approach, of stable α,α-difluorovinyl methyl ethers which condensed with aldehydes in the presence of Lewis acids, affording *O*-methylated aldol type products in a reaction which may have considerable generality.[23] Though many of these procedures are promising, some have not been reported in full, and all require the synthesis of either a chlorodifluoromethyl ketone or an acylsilane. Our trifluoroethanol chemistry seemed to offer a much more direct approach, in that the interception of our metallated enol carbamate **1**[24] with carbonyl electrophiles yielded alkoxides, which transacylated rapidly upon warming, releasing the more energetically favourable difluoroenolates **2**. In this way, a range of difluoroenolates could be generated *in situ* from a common fluorinated precursor and commercial aldehydes or ketones (Scheme 1).



Scheme 1 *Reagents and conditions*: i, 2.0 LDA, THF, −78 °C; ii, R^1CHO; iii, warm to 0 °C. DEC = Diethylcarbamoyl.

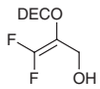
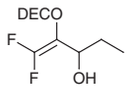
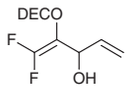
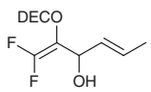
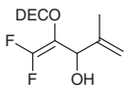
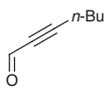
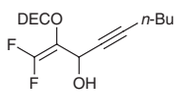
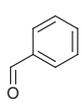
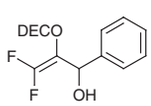
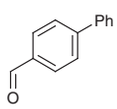
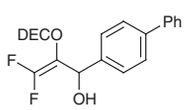
With the growing importance of rapid parallel synthesis in drug discovery, this seemed like an appealing feature. We had some initial success with a one-pot method from trifluoroethanol;[25] however, in subsequent studies, this method proved capricious and unpredictable. In many cases, the ^{19}F NMR spectra of crude reaction mixtures contained as many as eight AB quartet patterns; presumably, the mixture arose from incomplete trapping of the first carbonyl electrophile so that some metallated difluoroenol carbamate escaped to react with the second carbonyl electrophile. Two different enolates would then form following the transacylation step, and react with the remainder of the two electrophilic components. Products of Cannizaro reactions were also detected in some cases. Herein, we wish to describe in full, modified and reliable syntheses of novel difluoroallylic alcohols and of difluoroaldols derived from them.

In our improved synthesis, we found that it was possible to interrupt the transacylation process by intercepting the first-formed secondary alkoxide (in the case of an aldehyde electrophile) with the oxophilic Lewis acid boron trifluoride–ethyl ether (Scheme 2).

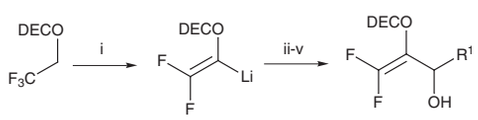
When coordinated to boron, the alkoxides appeared to be too weakly nucleophilic to trigger transacylation and difluoroallylic alcohols **3a–3h** were isolated upon work-up (Table 1).

Certain results require comment; for example, benzaldehyde, an ineffective electrophile in our original study was trapped

Table 1 Synthesis of difluoroallylic alcohols

Electrophile	Product[a]		Yield[b]
		**3a**	35
		**3b**	48
		**3c**	74
		**3d**	54
		**3e**	35
		**3f**	40
		**3g**	59
		**3h**	52

[a] DEC = diethylcarbamoyl. [b] Isolated yield after purification.



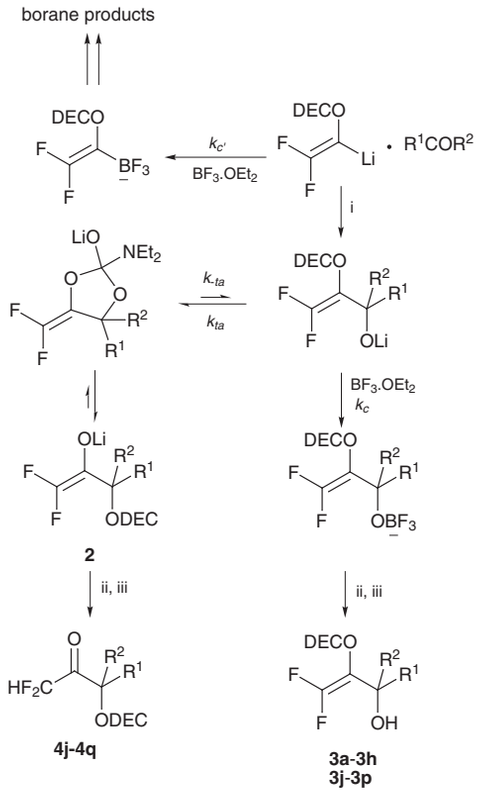
1 **3a-3h**

Scheme 2 *Reagents and conditions*: i, 2.0 LDA, THF, −78 °C; ii, R^1CHO 1 hr; iii, 1.0 $BF_3{\cdot}OEt_2$; iv, warm to 0 °C; v, NH_4Cl.

efficiently, and acrylaldehyde was also converted to difluoroallylic alcohol **3c** in good yield, without contamination from aldol and/or double bond migration products, encountered in the absence of Lewis acid as described previously.[24] We were also able to trap with monomeric formaldehyde generated according to the Schlosser procedure;[26] though the yield of **3a** was poor (due to difficulties in extracting the product completely and also due to the low reagent concentration necessitating an extended reaction time), the high potential utility of this three carbon difluorinated building block is a compensating factor. The yields quoted refer to isolated yields of purified products; the material balance in most cases cannot be accounted for with fluorinated side products. Indeed clean fluorine and proton NMR spectra were normally obtained at the crude stage after concentration *in vacuo*. We believe that yield losses occur during the isolation step.

When **1** was trapped with ketones (or aldehydes with bulkier substituents), mixtures of difluoroallylic alcohols **3j–3q** and difluoromethyl ketones **4j–4q** were obtained upon work-up (Table 2).

It is also interesting to note that the overall yields of isolated products are higher from the ketones. One difference between the reactions with aldehydes and ketones can be attributed to a small Thorpe–Ingold effect[27] upon the tentative mechanism proposed in Scheme 3.

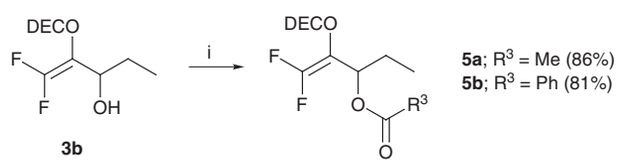


2 **4j-4q** **3a-3h** **3j-3p**

Scheme 3 *Reagents and conditions*: i, $BF_3{\cdot}OEt_2$, −78 °C; ii, warm to 0 °C; iii, NH_4Cl.

The initial assumption, (made before by Ganem *et al.*[28]) is that direct attack of the vinylmetal reagent upon the Lewis acid occurs very slowly at −78 °C ($k_{c'}$ is very small). Accelerated cyclisation (k_{ta} exceeds k_c) provides an escape route for the initial alkoxide adduct prior to capture by the Lewis acid. In all cases, alkoxide formation is relatively slow at −78 °C requiring one hour to reach completion. The importance of rapid (and irreversible) capture was also indicated by the failure of less oxophilic Lewis acids (such as $TiCl_4$, $SnCl_4$ or $ZnBr_2$) to inhibit transacylation (smaller k_c). These observations are in marked contrast to the behaviour of the desfluoro system described by Sengupta and Snieckus[29] and are consistent with the lower reactivity of both the difluorinated metallated enol carbamate and the enolate.

We also anticipated that the difluoroallylic alcohols would be relatively highly acidic and that treatment with even mild bases would trigger the transacylation reaction. However, **3b** was recovered unchanged after exposure to triethylamine in dichloromethane for 7 days and esters **5a** and **5b** could also be prepared in 86% and 81% yields respectively under conventional conditions (Ac_2O or PhCOCl, pyridine, DMAP, DCM) (Scheme 4) without formation of the difluoromethyl ketone.



3b

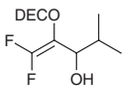
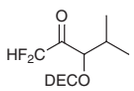
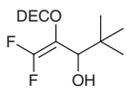
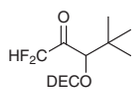
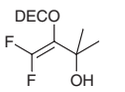
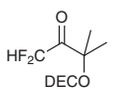
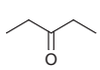
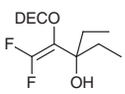
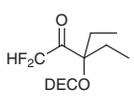
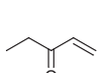
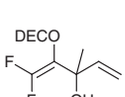
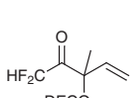
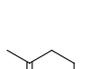
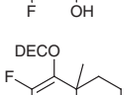
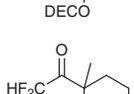
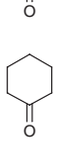
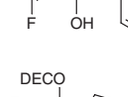
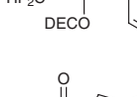
5a; R^3 = Me (86%)
5b; R^3 = Ph (81%)

Scheme 4 *Reagents and conditions*: i, 2.0 R^3COCl, DMAP, DCM, rt.

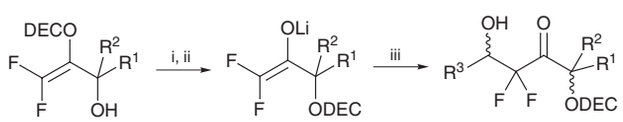
In contrast, treatment of **3l** with Grignard reagent (2.0 equivalents EtMgBr) at −10 °C for 18 hours afforded **4l** after conventional work-up following a slow transacylation (which was monitored by TLC).

With the purified allylic alcohols in hand, we were able to generate difluoroenolates cleanly by treatment with strong base

Table 2 Synthesis of difluoroallylic alcohols and difluoromethyl ketones

Electrophile	Alcohol[a]		Yield[b]	Ketone		Yield[b]
		**3j**	37		**4j**	13
		**3k**	57		**4k**	13
		**3l**	75		**4l**	20
		**3m**	44		**4m**	40
		**3n**	27		**4n**	21
		**3p**	38		**4p**	33
		**3q**	51		**4q**	30

[a] DEC = diethylcarbamoyl. [b] Isolated yield after purification.



3a-3h
3j-3p

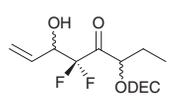
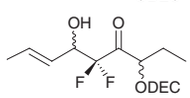
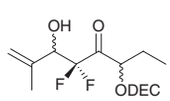
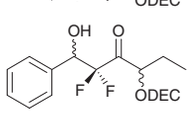
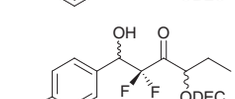
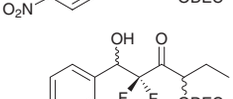
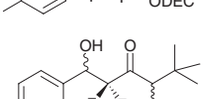
6a-6e
7a-7g

Scheme 5 *Reagents and conditions*: i, *n*-BuLi, THF, −78 °C; ii, warm to −10 °C; iii, R^3CHO; iv, NH_4Cl.

at low temperature (1.0 equivalent *n*-BuLi, THF, −78 °C), followed by warming to −10 °C (Scheme 5). Clearly amine bases would be unsuitable for performing the aldol reactions because proton return within the enolate–ammonium ion pair would compete with C–C bond formation. Grignard bases also proved unsuitable, presumably because the magnesium enolate is too weakly nucleophilic for transacylation to occur at a significant rate. The enolates were then reacted with non-enolisable aldehydes affording α,α-difluoro-β-hydroxy ketones **6a–6g** and **7a–7h** upon work-up, with minimal contamination from side products (Tables 3 and 4).

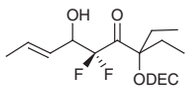
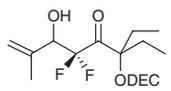
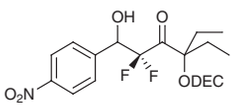
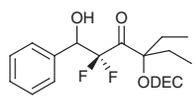
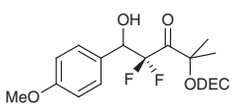
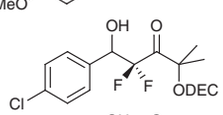
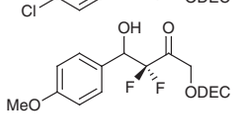
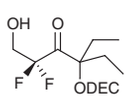
The suitability of solid paraformaldehyde (for **7h**) was a particularly pleasing result. In the case of **6c–6g**, purification by flash column chromatography allowed *syn*- and *anti*-stereoisomers to be separated and a correlation was made between the ^{19}F NMR chemical shift and the 1,4-relationship with the aid of a crystal structure determination for *syn*-**6e**.[30] The 1,4-stereoselectivity was poor[31] and was consistent with a reversible reaction, which was demonstrated upon deprotonation of purified racemic *syn*-stereoisomer of aldol **6e** (1.0 equivalent *n*-BuLi, THF, −78 °C). Upon warming to −10 °C and quenching after one hour, the ^{19}F NMR spectrum of the mixture showed the presence of the racemic *anti*-diastereoisomers formed upon *retro*-aldol and re-addition. Low temperature (−78 °C) quenching of the aldol reaction with ethanoic acid resulted merely in the recovery of difluoromethyl ketones indicating that the forward aldol reaction itself is quite slow with these difluorinated enolates. Enolate transmetallation is a possible tactic for performing a stereoselective reaction and we are pursuing this approach, but given the current interest in the generation of molecular diversity and the separability of *syn*- and *anti*-

Table 3 Synthesis of *syn*- and *anti*-difluoroaldols

Aldol[a]		Yield (%)	*syn*:*anti* Ratio[b]
	**6a**	50	1.5:1
	**6b**	47	1.4:1
	**6c**	58	1.2:1
	**6d**	61	1.1:1
	**6e**	45	1.5:1
	**6f**	49	1.2:1
	**6g**	62	1.1:1

[a] DEC = diethylcarbamoyl. [b] Ratios of diastereoisomers were determined by integration of the ^{19}F NMR spectra. All compounds are racemic modifications.

Table 4 Synthesis of difluoroaldols

Aldol[a]		Yield (%)
	**7a**	46
	**7b**	42
	**7c**	47
	**7d**	63
	**7e**	79
	**7f**	42
	**7g**	51
	**7h**	60

[a] DEC = diethylcarbamoyl.

diastereoisomers in most cases, we believe that even this non-stereoselective method could find significant use.

In conclusion, we have shown that not only are difluoroallylic alcohols available using this chemistry but that the "two pot" synthesis of difluoroaldols is general and reproducible. A wide range of aldehyde and ketone electrophiles may be incorporated at either side of the difluoromethylene position; this therefore suggests that a very powerful and concise method for the construction of highly oxygenated difluoro compounds will become available once the key problem of hydroxy group deprotection can be solved.

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 distilled and collected by syringe when required. *n*-Butyllithium was titrated before use against 1,3-diphenylpropan-2-one *p*-tolysulfonyl hydrazone (Lancaster). All electrophiles were distilled freshly before use. Boron trifluoride–diethyl ether (Aldrich) was distilled *in vacuo* before use and stored under nitrogen. Light petroleum refers to the fraction 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, Kratos Profile mass spectrometer or a VG ZabSpec mass spectrometer. Chemical ionisation (CI+) methods used ammonia as the reagent gas, whilst fast atom bombardment utilised LSIMS methods with caesium ions employed for ionisations. For TLC, precoated aluminium-backed silica plates were supplied by E. Merck A.G., Darmstadt, Germany (Art. no. 5554, Silica gel 60 F_{254}, thickness 0.2 mm). Anisaldehyde and potassium permanganate staining, and ultraviolet light were employed for visualisation. Flash column chromatography was performed using silica gel supplied by E. Merck A.G., Darmstadt, Germany, Kieselgel, Art. no. 9385. Microanalyses (CHN) were performed at the University of North London. When satisfactory microanalyses could not be obtained, new volatile compounds were shown to be homogeneous (>98%) by gas chromatographic analyses, carried out on a Carlo Erba 8000 series (8130) chromatograph, fitted with a Megabore SGE BPX5 column id (15 m × 0.53 mm). The homogeneity of new involatile compounds was established similarly by HPLC analysis, carried out on a Kontron HPLC system fitted with a Luna 5μ silica column (4.6 × 250 mm) with isochratic elution with 20% ethyl acetate in hexane using variable wavelength UV detection. X-Ray diffraction was carried out by the EPSRC service at the Universities of Cardiff and Southampton.

General procedure for the synthesis of difluoroallylic alcohols: 2-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoropent-1-en-3-ol (3b)

In a typical procedure, *n*-butyllithium (2.40 ml of a 2.0 M solution in hexanes, 4.8 mmol) was added dropwise to a solution of diisopropylamine (0.69 ml, 4.92 mmol) in THF (10 ml) at −78 °C. The resulting solution was allowed to warm to −30 °C to ensure complete LDA formation, before being cooled to −78 °C. 1,1,1-Trifluoro-2-(*N*,*N*-diethylcarbamoyloxy)ethane (0.39 ml, 2.4 mmol) was added dropwise over fifteen minutes; during this time, the clear, colourless solution became yellow. On stirring for a further twenty minutes, the colour changed through orange to red. Propanal (0.19 ml, 2.64 mol) was added in one portion, and the solution was stirred for one hour further before boron trifluoride–ethyl ether (0.33 ml, 2.64 mmol) was added in one portion. The solution faded in colour upon warming to 0 °C. After one hour at this temperature, the reaction was quenched with a saturated aqueous ammonium chloride solution (30 ml). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 30 ml). The combined organic extracts were washed with brine (30 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a pale yellow oil. Flash column chromatography (20% ethyl acetate in light petroleum) afforded **3b** as a colourless oil (0.30 g, 53%); R_f 0.39 (Found: C, 50.39; H, 7.26; N, 5.57. Calc. for $C_{10}H_{16}NO_3F_2$: C, 50.63; H, 7.22; N, 5.90%); ν_{max} (film)/cm^{-1} 3445 (OH), 1770 (C=CF_2), 1711 (C=O); δ_H (300 MHz; $CDCl_3$) 4.35–4.24 (1 H, m, C*H*OH), 3.76 (1 H, d, $^3J_{H-H}$ 5.0, CHO*H*), 3.33 (4 H, q, $^3J_{H-H}$ 7.0, N(CH_2Me)$_2$), 1.76–1.48 (2 H, m, CHCH_2), 1.23–1.13 (6 H, m, N(CH$_2$CH_3)$_2$), 0.92 (3 H, t, $^3J_{H-H}$ 7.0, CH$_2$CH_3); δ_C (75 MHz; $CDCl_3$) 154.8 (dd, $^1J_{C-F}$ 292.2 and 285.3), 154.0, 113.2 (dd, $^2J_{C-F}$ 26.8 and 14.2), 68.4, 42.8, 42.3, 26.7, 13.9, 13.2, 9.7. δ_F (282 MHz; $CDCl_3$) −97.0 (1 F, d, $^2J_{F-F}$ 56.0), −108.11 (1 F, d, $^2J_{F-F}$ 56.0); HRMS (Found: 238.1258. $C_{10}H_{17}NO_3F_2$: Calc. for 238.1255); *m*/*z* (CI) 238 (15%, $[M + H]^+$), 220 (100, $[M - OH]^+$), 100 (65, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoroprop-1-en-3-ol (3a). The alcohol **3a** was prepared as for **3b** from trifluoroethyl carbamate (0.78 ml, 4.80 mmol) and excess formaldehyde (100 ml of an approximate 0.6 M solution in THF). The mixture was stirred at −78 °C for three hours, then worked up in the usual manner, followed by flash column chromatography (20% ethyl acetate in light petroleum) to afford **3a** as a colourless oil (0.25 g, 25%); R_f 0.15; ν_{max} (film)/cm^{-1} 3445 (OH), 1774 (C=CF_2), 1716 (C=O); δ_H (300 MHz; $CDCl_3$) 4.16 (2 H, br s, CH_2OH), 3.71 (1 H, br s, CH(O*H*)), 3.27 (4 H, q, $^3J_{H-H}$ 7.1, N(CH_2Me)$_2$), 1.14–1.08 (6 H, m, $^3J_{H-H}$ 7.1, N(CH$_2$CH_3)$_2$); δ_C (75 MHz;

$CDCl_3$) 154.6 (dd, $^1J_{C-F}$ 293.0 and 285.0), 154.4, 112.4 (dd, $^2J_{C-F}$ 32.5 and 12.6), 57.6, 42.6, 42.2, 13.8, 13.1; δ_F (282 MHz; $CDCl_3$) −96.3 (1 F, d, $^2J_{F-F}$ 51.3), −106.8 (1 F, d, $^2J_{F-F}$ 51.3); HRMS (Found: 210.0926. Calc. for $C_8H_{14}NO_3F_2$: 210.0942); *m/z* (CI) 210 (100%, $[M + H]^+$), 100 (25, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoropenta-1,4-dien-3-ol (3c). The alcohol **3c** was prepared from trifluoroethyl carbamate (0.39 ml, 2.40 mmol) and acrylaldehyde (0.18 ml, 2.64 mmol). Work up in the usual manner followed by flash column chromatography (20% ethyl acetate in light petroleum) afforded **3c** as a colourless oil (0.42 g, 74%); R_f 0.28; ν_{max} (film)/cm^{-1} 3435 (OH), 2348 (C=C), 1770 ($C=CF_2$), 1713 (C=O); δ_H (300 MHz; $CDCl_3$) 5.81 (1 H, ddd, $^3J_{H-H}$ 17.0, 10.0 and 5.0, CHC*H*=CH_2), 5.39 (1 H, ddd, $^3J_{H-H}$ 17.0, $^2J_{H-H}$ 1.5, $^4J_{H-F}$ 1.0, =C*H*$_a$H$_b$), 5.20 (1 H, ddd, $^3J_{H-H}$ 10.0, $^2J_{H-H}$ 1.5, $^4J_{H-F}$ 1.0, =CH$_a$*H*$_b$), 4.93–4.87 (1 H, m, C*H*OH), 3.27 (4 H, q, $^3J_{H-H}$ 7.0, $N(CH_2Me)_2$), 1.11 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)_2$), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)_2$); δ_C (75 MHz; $CDCl_3$) 154.7, 154.5 (dd, $^1J_{C-F}$ 293.8 and 286.1), 135.1, 116.6, 112.9 (dd, $^2J_{C-F}$ 42.8, $^2J_{C-F}$ 12.5), 67.5, 42.8, 42.3, 13.8, 13.0; δ_F (282 MHz; $CDCl_3$) −96.3 (1 F, d, $^2J_{F-F}$ 51.9), −106.0 (1 F, d, $^2J_{F-F}$ 51.9); HRMS (Found: 236.1093. Calc. for $C_{11}H_{18}NO_3F_2$: 236.1098); *m/z* (CI), (15%, $[M + H]^+$), 218 (100, $[M - OH]^+$), 100 (50, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluorohexa-1,4-dien-3-ol (3d). The alcohol **3d** was prepared from trifluoroethyl carbamate (6.5 ml, 40 mmol) and crotonaldehyde (3.64 ml, 44 mmol). Work up in the usual manner followed by Kugelrohr distillation (65 °C, 0.1 mmHg) afforded **3d** as a colourless oil (5.92 g, 59%); ν_{max} (film)/cm^{-1} 3441 (OH), 2723 (C=C), 1734 ($C=CF_2$), 1677 (C=O); δ_H (300 MHz; $CDCl_3$) 5.79 (1 H, dqd, $^3J_{H-H}$ 15.1, 6.6, $^4J_{H-H}$ 1.47, C*H*CH_3), 5.51–5.43 (1 H, m, C*H*CHMe), 4.88–4.81 (1 H, m, C*H*(OH)), 4.04 (1 H, d, $^3J_{H-H}$ 5.9, CO*H*), 3.29 (2 H, q, $^3J_{H-H}$ 7.0, $N(CH_2Me)$), 3.30 (2 H, q, $^3J_{H-H}$ 7.0, $N(CH_2Me)$), 1.68 (3 H, d, $^3J_{H-H}$ 6.6, C*H*$_3$), 1.14 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.13 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$); δ_C (75 MHz; $CDCl_3$) 154.3 (dd, $^1J_{C-F}$ 293.2 and 285.8), 154.7, 128.4, 128.0, 113.0 (dd, $^2J_{C-F}$ 27.8 and 11.9), 67.4, 42.8, 42.3, 17.7, 13.8, 13.1; δ_F (282 MHz; $CDCl_3$) −96.4 (1 F, d, $^2J_{F-F}$ 51.4), −105.8 (1 F, d, $^2J_{F-F}$ 51.4); HRMS (Found: 250.1251. Calc. for $C_{11}H_{18}NO_3F_2$: 250.1255); *m/z* (CI), 250 (35%, $[M + H]^+$), 232 (100, $[M - OH]^+$), 100 (70, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoro-4-methylpenta-1,4-dien-3-ol (3e). The alcohol **3e** was prepared from trifluoroethyl carbamate (6.5 ml, 40 mmol) and methacrylaldehyde (2.97 ml, 60 mmol). Work up in the usual manner followed by flash column chromatography (30% diethyl ether in light petroleum) afforded **3e** as a colourless oil (3.53 g, 35%); R_f 0.25 (Found: C, 52.86; H, 6.89; N, 5.60. Calc. C, 53.01; H, 6.87; N, 5.62%); ν_{max} (film)/cm^{-1} 3432 (OH), 2360 (C=C), 1767 ($C=CF_2$), 1710 (C=O); δ_H (300 MHz; $CDCl_3$) 5.20 (1 H, d, $^2J_{H-H}$ 1.8, C*H*$_a$H$_b$), 5.00 (1 H, d, $^2J_{H-H}$ 1.8, CH$_a$*H*$_b$), 4.82–4.76 (1 H, m, C*H*(OH)), 4.48 (1 H, d, $^3J_{H-H}$ 6.6, CH(O*H*)), 3.38–3.17 (4 H, m, $N(CH_2Me)_2$), 1.69 (3 H, s, C*H*$_3$), 1.12 (6 H, t, $^3J_{H-H}$ 7.4, C*H*$_3$); δ_C (75 MHz; $CDCl_3$) 155.1, 155.2 (dd, $^1J_{C-F}$ 285.8 and 268.0), 142.1, 110.0 (dd, $^2J_{C-F}$ 28.0 and 11.6), 112.1, 69.8, 42.9, 42.4, 19.0, 13.8, 13.1; δ_F (282 MHz; $CDCl_3$) −95.0 (1 F, d, $^2J_{F-F}$ 49.6), −105.4 (1 F, dd, $^2J_{F-F}$ 49.6, $^4J_{H-F}$ 3.8); HRMS (Found: 250.1254. Calc. for $C_{11}H_{18}NO_3F_2$: 250.1255); *m/z* (CI), (3%, $[M + H]^+$), 232 (90, $[M - OH]^+$), 100 (90, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluorononan-1-en-4-yn-3-ol (3f). The alcohol **3f** was prepared from trifluoroethyl carbamate (0.78 ml, 4.80 mmol) and hept-2-yn-1-al (0.66 g, 5.28 mmol). Work up in the usual manner followed by flash column chromatography (15% ethyl acetate in light petroleum) afforded **3f** as a colourless oil (0.51 g, 63%); R_f 0.36; ν_{max} (film)/cm^{-1} 3429 (OH), 1769 ($C=CF_2$), 1712 (C=O); δ_H (300 MHz; $CDCl_3$) 5.20–5.13 (1 H, m, C*H*(OH)), 4.70 (1 H, d, $^3J_{H-H}$ 8.5, CH(O*H*)), 3.41–3.31 (4 H, m, $N(CH_2Me)_2$), 2.18 (2 H, td, $^3J_{H-H}$ 6.98, $^5J_{H-H}$ 2.2, CCC*H*$_2$), 1.45–1.38 (2 H, m, CCCH$_2$C*H*$_2$), 1.32–1.22 (2 H, m, C≡CCH$_2$CH$_2$C*H*$_2$), 1.21 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.18 (3 H, t, $^3J_{H-H}$ 7.4, $N(CH_2CH_3)$), 0.88 (3 H, t, $^3J_{H-H}$ 7.2, CH_2CH_3); δ_C (75 MHz; $CDCl_3$) 154.2 (dd, $^1J_{C-F}$ 293.7 and 286.8), 154.5, 112.6 (dd, $^2J_{C-F}$ 29.9 and 12.8), 87.0, 75.7, 58.3, 42.9, 42.4, 30.9, 28.1, 18.6, 11.0 (2 × NCH_2CH_3), 10.5; δ_F (282 MHz; $CDCl_3$) −95.8 (1 F, d, $^2J_{F-F}$ 47.0), −104.5 (1 F, d, $^2J_{F-F}$ 47.0); HRMS (Found: 304.1721. Calc. for $C_{16}H_{25}NO_3F_2$: 304.1724); *m/z* (CI) 304 (5%, $[M + H]^+$), 286 (34%, $[M - OH]^+$), 100 (100%, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-3,3-difluoro-1-phenylprop-2-en-1-ol (3g). The alcohol **3g** was prepared from trifluoroethyl carbamate (0.39 ml, 2.40 mmol) and benzaldehyde (0.27 ml, 2.64 mmol). Work up in the usual manner followed by flash column chromatography (15% ethyl acetate in light petroleum) afforded **3g** as a colourless oil (0.28 g, 59%); R_f 0.18 (Found: C, 58.83; H, 6.00; N, 4.97. Calc. for $C_{16}H_{24}NO_3F_2$: C, 58.94; H, 6.01; N, 4.91%); ν_{max} (film)/cm^{-1} 3429 (OH), 1766 ($C=CF_2$), 1709 (carbamate CO); δ_H (300 MHz; $CDCl_3$) 7.38–7.22 (5 H, m, Aromatic *H*), 5.64–5.60 (1 H, m, C*H*OH), 4.80 (1 H, br d, $^3J_{H-H}$ 6.3, CHO*H*), 3.24 (1 H, q, $^3J_{H-H}$ 7.0, N(C*H*$_a$H$_b$Me)), 3.23 (1 H, q, $^3J_{H-H}$ 7.0, N(CH$_a$*H*$_b$Me)), 3.17–2.94 (2 H, m, $N(CH_2CH_3)$), 1.08 (3 H, t, $^3J_{H-H}$ 7.2, $N(CH_2CH_3)$), 0.86 (3 H, t, $^3J_{H-H}$ 7.2, $N(CH_2CH_3)$); δ_C (75 MHz; $CDCl_3$) 154.7 (t, $^1J_{C-F}$ 290.0), 154.6, 139.4, 128.2, 127.6, 125.9, 113.6 (dd, $^2J_{C-F}$ 30.4 and 11.9), 68.6, 42.8, 42.2, 13.4, 13.0; δ_F −95.9 (1 F, br d, $^2J_{F-F}$ 49.6), −105.7 (1 F, br d, $^2J_{F-F}$ 49.6); HRMS (Found: 304.1721. Calc. for $C_{16}H_{25}NO_3F_2$: 304.1724); *m/z* (CI) 286 (7%, $[M + H]^+$), 268 (75%, $[M - OH]^+$), 100 (100%, $[CONEt_2]^+$).

1-(Biphenyl-4-yl)-2-(*N*,*N*-diethylcarbamoyloxy)-3,3-difluoroprop-2-en-1-ol (3h). The alcohol **3h** was prepared from trifluoroethyl carbamate (0.78 ml, 4.80 mmol) and biphenyl-4-carboxaldehyde (0.96 g, 5.28 mmol). Work up in the usual manner followed by flash column chromatography (10% ethyl acetate in light petroleum) afforded **3h** as a colourless crystalline solid (0.96 g, 55%); mp 64–66 °C; R_f 0.13 (Found: C, 66.63: H, 5.97; N, 3.94. Calc. for $C_{20}H_{21}NO_3F_2$: C, 66.47; H, 5.86; N, 3.94%); ν_{max} (Nujol mull)/cm^{-1} 3448 (OH), 1768 ($C=CF_2$), 1713 (C=O); δ_H (300 MHz; $CDCl_3$) 7.73–7.32 (9 H, m, Aromatic *H*), 5.78 (1 H, br s, CH(O*H*)), 5.03 (1 H, d, $^3J_{H-H}$ 5.3, C*H*(OH)), 3.38–3.01 (4 H, m, $N(CH_2Me)_2$), 1.13 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.94 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$); δ_C (75 MHz; $CDCl_3$) 154.9 (dd, $^1J_{C-F}$ 286.0 and 294.0), 154.7, 140.9, 140.6, 138.6, 128.9, 127.4, 127.1, 127.0, 126.6, 113.7 (dd, $^2J_{C-F}$ 42.1 and 11.7), 68.5, 42.9, 42.3, 13.6, 13.1; δ_F (282 MHz; $CDCl_3$) −95.7 (1 F, d, $^2J_{F-F}$ 50.9), −105.5 (1 F, d, $^2J_{F-F}$ 50.9); *m/z* (EI) 361 (3%, M^+), 100 (100%, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoro-4-methylpent-1-en-3-ol (3j) and 3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoro-4-methylpentan-2-one (4j). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.78 ml, 5.28 mmol) and 2-methylpropanal (0.48 ml, 5.28 mmol). Work up in the usual manner followed by flash column chromatography (10% ethyl acetate in light petroleum) afforded ketone **4j** as a colourless oil (0.61 g, 13%); R_f 0.40 (Found: C, 52.31; H, 7.53; N, 5.47. Calc. for $C_{11}H_{19}NO_3F_2$: C, 52.58; H, 7.62; N, 5.57%); ν_{max} (film)/cm^{-1} 1759 (ketonic C=O), 1694 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 6.00 (1 H, t, $^2J_{H-F}$ 50.0, CF_2H), 5.00 (1 H, dd, $^3J_{H-H}$ 5.1, $^4J_{H-F}$ 1.5, C*H*CH(Me)$_2$), 3.35–3.17 (4 H, m, $N(CH_2Me)_2$), 2.30–2.17 (1 H, m, C*H*(Me)$_2$), 1.15 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.07 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.01 (3 H, d, $^3J_{H-H}$ 7.0, CHCH(C*H*$_3$)), 0.96 (3 H, d, $^3J_{H-H}$ 7.0, CHCH(C*H*$_3$)); δ_C (75 MHz; $CDCl_3$) 197.2 (t, $^2J_{C-F}$ 22.1), 155.2, 109.3 (t, $^1J_{C-F}$ 252.0), 79.0, 42.2, 41.7, 29.4, 17.3, 13.9, 13.9, 13.3; δ_F (282 MHz; $CDCl_3$) −128.0 (1 F, dd, $^2J_{F-F}$ 310.3, $^2J_{H-F}$ 54.7), −130.4 (1 F,

dd, $^2J_{F-F}$ 310.3, $^2J_{H-F}$ 54.7); HRMS (Found: 252.1374. Calc. for $C_{11}H_{20}NO_3F_2$: 252.1374); *m*/*z* (CI) 252 (100%, $[M + H]^+$); and alcohol **3j** as a colourless oil (0.23 g, 37%); (R_f 0.14); ν_{max} (film)/cm^{-1} 3437 (OH), 1768 (C=CF_2), 1711 (C=O); δ_H (300 MHz; $CDCl_3$) 3.87–3.83 (2 H, m, C*H*OH and CHO*H*), 3.26 (4 H, q, $^3J_{H-H}$ 7.0, N(CH_2CH$_3$)), 1.78–1.66 (1 H, m, C*H*(Me)$_2$), 1.14–1.07 (6 H, m, N(CH$_2$CH_3)$_2$), 0.98 (3 H, d, $^3J_{H-H}$ 6.6, CHCH_{a3}-CH$_{b3}$), 0.80 (3 H, d, $^3J_{H-H}$ 7.0, CHCH$_{a3}$CH_{b3}); δ_C (75 MHz; $CDCl_3$) 155.0 (t, $^1J_{C-F}$ 288.7), 154.7, 112.6 (dd, $^2J_{C-F}$ 11.5 and 30.7), 72.3, 42.7, 42.2, 31.5, 18.8, 18.2, 13.8, 13.0; δ_F (282 MHz; $CDCl_3$) −96.2 (1 F, d, $^2J_{F-F}$ 54.0), −107.0 (1 F, d, $^2J_{F-F}$ 54.0); HRMS (Found: 252.1425. Calc. for $C_{11}H_{20}HNO_3F_2$: 252.1411). *m*/*z* (CI) 252 (20%, $[M + H]^+$), 234 (100, $[M - OH]^+$), 100 (30, $[CONEt_2]^+$). The ketone was reported previously at a lower level of characterisation.[24]

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoro-4,4-dimethylpent-1-en-3-ol (3k) and 3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoro-4,4-dimethylpentan-2-one (4k). The alcohol and ketone were prepared from trifluoroethyl carbamate (1.63 ml, 10 mmol) and trimethylacetaldehyde (1.20 ml, 11 mmol). Work up in the usual manner followed by flash column chromatography (10% diethyl ether in light petroleum) afforded ketone **4k** as a colourless oil (0.34 g, 13%); R_f 0.17 (Found: C, 54.37; H, 8.04; N, 5.21. Calc. for $C_{12}H_{21}NO_3F_2$: C, 54.33; H, 7.98; N, 5.28%); ν_{max} (film)/cm^{-1} 1759 (ketonic C=O), 1694 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.97 (1 H, t, $^2J_{H-F}$ 53.7, CF_2H), 4.82 (1 H, d, $^4J_{H-F}$ 1.1, C*H*(OCONEt$_2$)), 3.35–3.14 (4 H, m, N(CH_2Me)$_2$), 1.16 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.04 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.04 (9 H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 198.6 (t, $^2J_{C-F}$ 22.4), 155.5, 109.0 (t, $^1J_{C-F}$ 252.4), 79.8, 42.3, 41.7, 34.5, 26.0, 14.1, 13.4; δ_F (282 MHz; $CDCl_3$) −128.3 (1 F, dd, $^2J_{F-F}$ 348.4, $^2J_{H-F}$ 54.0), −129.3 (1 F, dd, $^2J_{F-F}$ 348.4, $^2J_{H-F}$ 54.0); *m*/*z* (CI) 266 (85%, $[M + H]^+$), 100 (100, $[CONEt_2]^+$); and alcohol **3k** as a colourless oil (1.51 g, 57%); R_f 0.09 (Found: C, 54.30; H, 7.92; N, 5.18. Calc. for $C_{12}H_{21}NO_3F_2$: C, 54.33; H, 7.98; N, 5.28%); δ_H (300 MHz; $CDCl_3$) 4.03 (1 H, br s, CH(O*H*)), 3.70 (1 H, d, $^4J_{H-F}$ 3.3, C*H*(OH)), 3.36–3.22 (4 H, m, N(CH_2Me)$_2$), 1.13 (3 H, t, $^3J_{H-H}$ 6.6, N(CH$_2$CH_3)), 1.11 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 0.92 (9 H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 154.8 (dd, $^1J_{C-F}$ 293.1 and 285.1), 154.2, 111.9 (dd, $^2J_{C-F}$ 40.0 and 12.1), 73.7, 42.7, 42.0, 35.7, 25.8, 13.9, 13.1 δ_F (282 MHz; $CDCl_3$) −96.2 (1 F, d, $^2J_{F-F}$ 53.1), −105.1 (1 F, dd, $^2J_{F-F}$ 53.1, $^4J_{H-F}$ 3.3); *m*/*z* 266 (7%, $[M + H]^+$), 248 (14, $[M - OH]^+$), 100 (30, $[CONEt_2]^+$).

3-(*N*,*N*-Diethylcarbamoyloxy)-4,4-difluoro-2-methylbut-3-en-2-ol (3l) and 3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoro-3-methylbutan-2-one (4l). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.39 ml, 2,40 mmol) and propan-2-one (0.19 ml, 2.64 mmol). Work up in the usual manner followed by flash column chromatography (20% ethyl acetate in light petroleum) afforded ketone **4l** as a colourless oil (0.11 g, 20%); R_f 0.35; ν_{max} (film)/cm^{-1} 1752 (ketonic C=O), 1682 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.89 (1 H, t, $^2J_{H-F}$ 53.7, CF_2H), 3.18–3.08 (4 H, m, N(CH_2Me)$_2$), 1.37 (6 H, s, C(CH_3)$_2$), 1.04–0.93 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 195.9 (t, $^2J_{C-F}$ 22.2), 155.1, 108.9 (t, $^1J_{C-F}$ 251.1), 80.8, 42.0, 41.6, 23.2, 7.4, 6.2; δ_F (282 MHz; $CDCl_3$) −125.7 (d, $^2J_{H-F}$ 53.7); HMRS (Found 238.1259. Calc. for $C_{10}H_{18}NO_3F_2$: 238.1255); *m*/*z* (CI) 238 (60%, $[M + H]^+$); and alcohol **3l** (0.43 g, 75%) as a colourless oil; R_f 0.14; ν_{max} (film)/cm^{-1} 3445 (OH), 1759 (C=CF_2), 1712 (C=O); δ_H (300 MHz; $CDCl_3$) 3.77 (1 H, s, O*H*), 3.29–3.13 (4 H, m, N(CH_2Me)$_2$), 1.28 (6 H, s, C(CH_3)$_2$), 1.12–0.94 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 154.1 (dd, $^1J_{C-F}$ 288.8 and 253.2), 154.1, 116.7 (dd, $^2J_{C-F}$ 37.1 and 12.8), 69.4, 42.6, 42.1, 27.5, 13.9, 13.1; δ_F (282 MHz; $CDCl_3$) −95.2 (1 F, d, $^2J_{F-F}$ 59.0), −101.8 (1 F, d, $^2J_{F-F}$ 59.0); HRMS (Found: 238.1261. Calc. for $C_{10}H_{18}NO_3F_2$: 238.1255); *m*/*z* (CI) 238 (100%, $[M + H]^+$).

3-Ethyl-2-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoropent-1-en-3-ol (3m) and 3-ethyl-3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoropentan-2-one (4m). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.39 ml, 2.40 mmol) and pentan-3-one (0.27 ml, 2.64 mmol). Work up in the usual manner followed by flash column chromatography (20% ethyl acetate in light petroleum) afforded ketone **4m** as a colourless oil (0.25 g, 40%); R_f 0.45 (Found: C, 54.30; H, 7.85; N, 5.20. Calc. for $C_{12}H_{21}NO_3F_2$: C, 54.33; H, 7.98; N, 5.28%); ν_{max} (film)/cm^{-1} 1759 (ketonic C=O), 1694 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.90 (1 H, t, $^2J_{H-F}$ 53.0, CF_2H), 3.24 (2 H, q, $^3J_{H-H}$ 6.5, N(CH_2Me)), 3.20 (2 H, q, $^3J_{H-H}$ 6.5, N(CH_2Me)), 1.99–1.83 (4 H, m, (CH_2CH$_3$)$_2$), 1.10 (3 H, t, $^3J_{H-H}$ 6.5, N(CH$_2$CH_3)), 1.04 (3 H, t, $^3J_{H-H}$ 6.5, N(CH$_2$CH_3)), 0.80 (6 H, t, $^3J_{H-H}$ 7.0, C(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 195.7 (t, $^2J_{C-F}$ 22.1), 155.0, 108.9 (t, $^1J_{C-F}$ 252.0), 85.6, 42.1, 41.7, 24.4, 13.9, 13.1, 6.8; δ_F (282 MHz; $CDCl_3$) −126.6 (d, $^2J_{H-F}$ 53.0); *m*/*z* (CI) 266 (99%, $[M + H]^+$) and alcohol **3m** as a colourless oil (0.28 g, 44%); R_f 0.28; ν_{max} (film)/cm^{-1} 3446 (OH), 1751 (C=CF_2), 1714 (C=O); δ_H (300 MHz; $CDCl_3$) 3.22 (4 H, q, $^3J_{H-H}$ 7.0, N(CH_2Me)$_2$), 3.10 (1 H, br s, CH(O*H*)), 1.60 (4 H, q, $^3J_{H-H}$ 7.5, C(CH_2Me)$_2$), 1.09 (6 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)$_2$), 0.83 (6 H, t, $^3J_{H-H}$ 7.5, C(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 154.8 (t, $^1J_{C-F}$ 287.9), 154.5, 114.6 (dd, $^2J_{C-F}$ 25.0 and 12.5), 75.0, 42.6, 42.0, 29.7, 13.8, 13.0, 7.5; δ_F (282 MHz; $CDCl_3$) −94.1 (1 F, d, $^2J_{F-F}$ 60.7), −103.0 (1 F, d, $^2J_{F-F}$ 60.7); HRMS (Found: 266.1576. Calc. for $C_{12}H_{22}$-NO_3F_2: 266.1568); *m*/*z* (CI) 266 (4%, $[M + H]^+$), 248 (100%, $[M - OH]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoro-3-methylpenta-1,4-dien-3-ol (3n) and 3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoro-3-methylpent-4-en-2-one (4n). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.78 ml, 4.8 mmol) and methyl vinyl ketone (0.44 ml, 5.28 mmol). Work up in the usual manner followed by flash column chromatography (5% ethyl acetate in light petroleum) afforded **4n** as a colourless oil (0.25 g, 22%); R_f 0.27; ν_{max} (film)/cm^{-1} 1745 (ketonic C=O), 1690 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 6.01 (1 H, dd, $^3J_{H-H}$ 17.5 and 12.5, C*H*=CH$_2$), 6.00 (1 H, t, $^2J_{H-F}$ 53.0, CF_2H), 5.38 (1 H, d, $^3J_{H-H}$ 12.5, CH=CH$_a$H$_b$), 5.33 (1 H, d, $^3J_{H-H}$ 17.5, CH=CH$_a$H$_b$), 3.36–3.22 (4 H, m, N(CH_2Me)$_2$), 1.52 (3 H, s, CH_3), 1.17 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)); δ_C (75 MHz; $CDCl_3$) 194.0 (t, $^2J_{C-F}$ 21.8), 155.1, 135.1, 117.2, 109.3 (t, $^2J_{C-F}$ 252.1), 83.5, 42.5, 42.0, 22.4, 14.2, 13.4; δ_F (282 MHz; $CDCl_3$) −125.2 (1 F, d, $^2J_{H-F}$ 53.0), −135.5 (1 F, d, $^2J_{H-F}$ 53.0); HRMS (Found: 250.1245. Calc. for $C_{11}H_{18}NO_3F_2$: 250.1255); *m*/*z* (CI) 250 (100%, $[M + H]^+$); and alcohol **3n** as a colourless oil (0.33 g, 27%); R_f 0.06; ν_{max} (film)/cm^{-1} 3446 (OH), 1757 (C=CF_2), 1713 (C=O); δ_H (300 MHz; $CDCl_3$) 5.83 (1 H, dd, $^3J_{H-H}$ 17.1 and 10.3, C*H*CH$_2$), 5.29 (1 H, br d, $^3J_{H-H}$ 17.1, CHCH_aH$_b$), 5.01 (1 H, br d, $^3J_{H-H}$ 10.3, CHCH$_a$$H_b$), 3.98 (1 H, br s, C(O*H*)), 3.21 (4 H, q, $^3J_{H-H}$ 7.0, N(CH_2CH$_3$)$_2$), 1.35 (3 H, s, C(OH)CH_3), 1.08–1.01 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 154.5 (dd, $^1J_{C-F}$ 297.7 and 281.2), 154.5, 140.6, 115.6 (dd, $^2J_{C-F}$ 25.9 and 13.0), 113.1, 71.8, 42.6, 42.0, 25.8, 13.7, 12.9; δ_F (282 MHz; $CDCl_3$) −93.6 (1 F, d, $^2J_{F-F}$ 53.9), −99.7 (1 F, d, $^2J_{F-F}$ 53.9).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoro-3-methylhepta-1,6-dien-3-ol (3p) and 3-(*N*,*N*-diethylcarbamoyloxy)-1,1-difluoro-3-methylhept-6-en-2-one (4p). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.78 ml, 4.8 mmol) and hex-5-en-2-one (0.61 ml, 5.28 mmol). Standard work-up followed by flash column chromatography (5% ethyl acetate in light petroleum) afforded the ketone **4p** as a colourless oil (0.55 g, 38%); R_f 0.20 (Found: C, 56.49; H, 7.68; N, 4.85. Calc. for $C_{13}H_{21}F_2NO_3$: C, 56.31; H, 7.63; N, 5.05%); δ_H (300 MHz; $CDCl_3$) 6.00 (1 H, t, $^2J_{H-F}$ 53.0, CF_2H), 5.84–5.70 (1 H, m, C*H*=CH$_2$), 5.01 (1 H, dd, $^3J_{H-H}$ 17.0, $^2J_{H-H}$ 2.1, CH=CH$_a$$H_b$), 4.94 (1 H, dd, $^3J_{H-H}$ 10.3, $^2J_{H-H}$ 2.1, CH=CH$_a$$H_b$), 3.32–3.14

(4 H, m, N(CH_2Me)$_2$), 2.14–1.97 (2 H, m, CH_2CH$_2$CH), 1.88–1.77 (2 H, m, CH$_2$CH_2CH), 1.52 (3 H, s, CH_3), 1.14 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.10 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)); δ_C(75 MHz; CDCl$_3$) 195.9 (t, $^2J_{C-F}$ 21.8), 155.0, 137.0, 115.1, 109.1 (t, $^1J_{C-F}$ 252.1), 83.1, 42.1, 41.1, 27.3, 24.9, 20.2, 13.8, 13.1; δ_F (282 MHz; CDCl$_3$) −126.3 (1 F, d, $^2J_{H-F}$ 53.4), −126.2 (1 F, d, $^2J_{H-F}$ 53.4); HRMS (Found: 278.1579. Calc. for $C_{13}H_{22}F_2NO_3$: 278.1568); *m/z* (CI) 279 (100%, [M + H+]); and alcohol **3p** as a colourless oil (0.45 g, 33%); R_f 0.10; ν_{max} (film)/cm^3 3447 (OH), 1757 (C=CF$_2$), 1712 (C=O); δ_H (300 MHz; CDCl$_3$) 5.69 (1 H, ddt, $^3J_{H-H}$ 17.3, 9.9 and 6.6, CHCH$_2$), 4.90 (1 H, dd, $^3J_{H-H}$ 17.3, $^2J_{H-H}$ 1.5, CHCH$_a$$H_b$), 4.82 (1 H, dd, $^3J_{H-H}$ 9.9, $^2J_{H-H}$ 1.5, CHCH$_a$$H_b$), 3.59 (1 H, s, C(O$H$)), 3.26–3.16 (4 H, m, N(CH_2Me)$_2$), 2.05–1.45 (2 H, m, CH$_2$CH_2CHCH$_2$), 1.71–1.58 (2 H, m, CH_2CH$_2$CHCH$_2$), 1.29 (3 H, s, C(OH)CH_3), 1.11–1.09 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; CDCl$_3$) 154.4 (t, $^1J_{C-F}$ 288.6), 154.2, 138.1, 115.9 (dd, $^2J_{C-F}$ 36.7 and 12.6), 114.3, 71.7, 42.6, 42.0, 39.2, 28.3, 25.1, 13.8, 13.0; δ_F (282 MHz; CDCl$_3$) −94.3 (1 F, d, $^2J_{F-F}$ 59.8), −101.9 (1 F, d, $^2J_{F-F}$ 59.8); HRMS (Found: 278.1575. Calc. for $C_{13}H_{22}NO_3F_2$: 278.1568); *m/z* (CI) 278 (11%, [M + H]$^+$), 260 (100, [M − OH]$^+$), 100 (41, [CONEt$_2$]$^+$).

1-[1-(*N*,*N*-Diethylcarbamoyloxy)-2,2-difluoroethenyl]cyclohexan-1-ol (3q) and 1-[1-(*N*,*N*-diethylcarbamoyloxy)cyclohexan-1-yl]-2,2-difluoroethan-1-one (4q). The alcohol and ketone were prepared from trifluoroethyl carbamate (0.78 ml, 4.8 mmol) and cyclohexanone (0.54 ml, 5.20 mmol). Standard work-up followed by flash column chromatography (10% ethyl acetate in light petroleum) afforded the ketone **4q** as a colourless oil (0.53 g, 30%); R_f 0.24 (Found: C. 56.54; H, 7.82; N, 5.02. Calc. for $C_{13}H_{21}F_2NO_3$: C, 56.31; H, 7.63; N, 5.05%); ν_{max} (film)/cm^{-1} 1734 (ketonic C=O), 1684 (carbamate C=O); δ_H (300 MHz; CDCl$_3$) 5.96 (1 H, t, $^2J_{H-F}$ 53.7, CF$_2$$H$), 3.33 (2 H, q, $^3J_{H-H}$ 7.0, N(CH_2Me)), 3.25 (2 H, q, $^3J_{H-H}$ 7.0, N(CH_2Me)), 2.16–2.01 (2 H, m), 1.74–1.64 (6 H, m), 1.57–1.49 (2 H, m), 1.17 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)); δ_C (75 MHz; CDCl$_3$) 196.4 (t, $^2J_{C-F}$ 21.8), 154.9, 109.1 (t, $^1J_{C-F}$ 251.7), 82.3, 42.1, 41.8, 30.8, 24.8, 21.2, 14.0, 13.3; δ_F (282 MHz; CDCl$_3$) −125.3 (d, $^1J_{H-F}$ 53.4); HRMS (Found: 278.1574. Calc. for $C_{13}H_{22}NO_3F_2$: 278.1568); *m/z* (CI) 278 (100%, [M + H]$^+$); and alcohol **3q** as a colourless oil (0.59 g, 51%); R_f 0.13; ν_{max} (film)/cm^{-1} 3446 (OH), 1752 (C=CF$_2$), 1707 (C=O); δ_H (300 MHz; CDCl$_3$) 3.70 (1 H, br s, CH(OH)), 3.28 (q, 4 H, $^3J_{H-H}$ 7.5, N(CH_2Me)$_2$), 1.80–1.53 (6 H, m), 1.47–1.23 (4 H, m), 1.19–1.05 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; CDCl$_3$) 154.9 (t, $^1J_{C-F}$ 290.1), 154.7, 116.4 (dd, $^2J_{C-F}$ 36.7 and 11.9), 71.2, 42.6, 42.1, 35.5, 25.3, 22.1, 13.9, 13.1; δ_F (282 MHz; CDCl$_3$) −93.0 (1 F, d, $^2J_{F-F}$ 54.7), −100.4 (1 F, d, $^2J_{F-F}$ 54.7); HRMS (Found: 278.1563. Calc. for $C_{13}H_{22}NO_3F_2$: 278.1568); *m/z* (CI) 278 (11%, [M + H]$^+$), 260 (100, [M − OH]$^+$), 100 (48, [CONEt$_2$]$^+$).

Typical procedure for the production of difluoroaldols *via* difluoroallylic alcohols: *syn*- and *anti*-3-(*N*,*N*-diethylcarbamoyloxy)-5,5-difluoro-6-hydroxyoct-7-en-4-one (6a)

n-Butyllithium (2.48 ml of a 1.7 M solution in hexanes, 4.21 mmol) was added dropwise over fifteen minutes, to a solution of alcohol **3b** (1.00 g, 4.21 mmol) in THF (20 ml). The solution was allowed to warm to −10 °C and stirred for a further fifteen minutes at this temperature to ensure complete enolate formation, before acrylaldehyde (0.31 ml, 4.63 mmol) was added in one portion. After stirring for one hour at −10 °C, a saturated ammonium chloride solution (50 ml) was added. The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 ml). The combined organic extracts were washed with brine (30 ml), dried (MgSO$_4$), and concentrated *in vacuo*. Column chromatography of the residue (20% diethyl ether in light petroleum) yielded aldols **6a** (an inseparable mixture of diastereoisomers, ratio 1.5:1) as a colourless oil (0.62 g, 50%); ν_{max} (mixture; film)/cm^{-1} 3382 (O–H), 1755 (ketonic C=O), 1684 (carbamate C=O); R_f 0.29; major diastereoisomer (*syn*) δ_H (300 MHz; CDCl$_3$) 5.99–5.82 (1 H, m, CH=CH$_2$), 5.56 (1 H, ddd, $^3J_{H-H}$ 17.3, $^4J_{H-H}$ 1.9, $^2J_{H-H}$ 1.5, CH=CH_aH$_b$), 5.41 (1 H, ddd, $^3J_{H-H}$ 10.7, $^4J_{H-H}$ 1.8, $^2J_{H-H}$ 1.5, CH=CH$_a$$H_b$), 5.20–5.08 (1 H, m, C$H$(OCONEt$_2$)), 4.60 (1 H, br s, CH(OH)), 4.55–4.38 (1 H, m, CH(OH)), 3.38–3.23 (4 H, m, N(CH_2CH$_3$)$_2$), 2.06–1.92 (1 H, m, CH_aH$_b$CH$_3$), 1.83–1.67 (1 H, m, CH$_a$$H_b$-CH$_3$), 2.94 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.04 (3 H, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75 MHz; CDCl$_3$) 200.0 (dd, $^2J_{C-F}$ 29.6, $^2J_{C-F}$ 21.5), 155.5, 130.2, 119.6, 116.0 (t, $^1J_{C-F}$ 259.9), 77.3, 73.1 (dd, $^2J_{C-F}$ 28.8, $^2J_{C-F}$ 23.7), 42.3, 41.9, 23.4, 13.8, 13.2, 9.9; δ_F (282 MHz; CDCl$_3$) −110.2 (1 F, d, $^2J_{F-F}$ 255.9), −133.3 (1 F, dd, $^2J_{F-F}$ 255.9, $^3J_{H-F}$ 22.6); minor diastereoisomer (*anti*) δ_H (300 MHz; CDCl$_3$) 5.99–5.82 (1 H, m, CH=CH$_2$), 5.27 (1 H, ddd, $^3J_{H-H}$ 17.3, $^2J_{H-H}$ 1.5, $^4J_{H-H}$ 1.5, CH=CH_aH$_b$), 5.35 (1 H, br d, $^3J_{H-H}$ 10.7, CH=CH$_a$$H_b$), 5.20–5.08 (1 H, m, C$H$(OCONEt$_2$)), 4.63 (1 H, br s, CH(OH)), 4.55–4.38 (1 H, m, CH(OH)), 3.32–3.14 (4 H, m, N(CH_2CH$_3$)$_2$), 2.06–1.92 (1 H, m, CH_aCH$_b$CH$_3$), 1.83–1.67 (1 H, m, CH$_a$CH_b-CH$_3$), 2.95 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.08 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.04 (3 H, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75 MHz; CDCl$_3$) 199.8 (dd, $^2J_{C-F}$ 26.4, $^2J_{C-F}$ 25.3), 155.5, 130.9, 120.2, 116.5 (t, $^1J_{C-F}$ 259.8), 78.2, 71.4 (t, $^2J_{C-F}$ 27.2), 42.3, 41.9, 23.2, 13.8, 13.2, 9.9; δ_F (282 MHz; CDCl$_3$) −117.0 (1 F, dd, $^2J_{F-F}$ 257.3, $^3J_{H-F}$ 9.3), −118.0 (1 F, dd, $^2J_{F-F}$ 257.3, $^3J_{H-F}$ 10.9); HRMS (Found: 294.1513. Calc. for $C_{13}H_{22}F_2NO_4$: 294.1517); *m/z* 294 (100%, [M + H]$^+$).

(*E*)-3-(*N*,*N*-Diethylcarbamoyloxy)-5,5-difluoro-6-hydroxynon-7-en-4-one (6b). The aldols **6b** were prepared from **3b** (0.90 g, 3.78 mmol) and crotonaldehyde (0.35 ml, 4.16 mmol). Usual work-up followed by column chromatography (15% diethyl ether in light petroleum) yielded **6b** (an inseparable mixture of diastereoisomers, ratio 1.4:1) as a colourless oil (0.60 g, 47%); ν_{max} (mixture; film)/cm^{-1} 3389 (O–H), 1754 (ketonic C=O), 1685 (carbamate C=O); R_f 0.25; δ_H (300 MHz; CDCl$_3$; signals for the major and minor diastereoisomers are coincident) 6.00–5.81 (1 H, m, CH$_3$CH), 5.60–5.42 (1 H, m, CH$_3$CHCH), 5.18–5.09 (1 H, m, CH(OCONEt$_2$)), 5.02 (1 H, br d, $^3J_{H-H}$ 3.7, CH(OH)), 4.40–4.25 (1 H, m, CH(OH)), 3.40–3.10 (4 H, m, N(CH_2CH$_3$)$_2$), 2.05–1.90 (1 H, m, CH_aH$_b$CH$_3$), 1.80–1.65 (1 H, m, CH$_a$CH_b-CH$_3$), 1.76–1.68 (3 H, m, CH_3CH), 1.17 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.07 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.02 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3); major diastereoisomer (*syn*) δ_C (75 MHz; CDCl$_3$) 199.8 (dd, $^2J_{C-F}$ 36.5, $^2J_{C-F}$ 22.0), 155.3, 132.3, 123.7, 116.4 (t, $^1J_{C-F}$ 261.7), 78.0, 71.4 (dd, $^2J_{C-F}$ 29.5, $^2J_{C-F}$ 23.2), 42.1, 41.7, 23.2, 17.9, 13.7, 13.1, 10.1; δ_F (282 MHz; CDCl$_3$), −109.9 (1 F, d, $^2J_{F-F}$ 256.1), −132.8 (1 F, dd, $^2J_{F-F}$ 256.1, $^3J_{H-F}$ 21.8); minor diastereoisomer (*anti*) (75 MHz; CDCl$_3$) 197.9 (dd, $^2J_{C-F}$ 31.7, $^2J_{C-F}$ 22.7), 155.3, 132.0, 123.0, 116.0 (t, $^1J_{C-F}$ 259.8), 77.2, 72.9 (t, $^2J_{C-F}$ 27.4), 42.1, 41.7, 23.1, 17.8, 13.7, 13.1, 10.0; δ_F (282 MHz; CDCl$_3$) −116.7 (1 F, d, $^2J_{F-F}$ 240.3), −118.4 (1 F, dd, $^2J_{F-F}$ 240.3, $^3J_{H-F}$ 10.7); HRMS (Found 336.1982. Calc. for $C_{16}H_{28}NO_4F_2$: 336.1986); *m/z* (CI) 336 (100%, [M + H]$^+$).

3-(*N*,*N*-Diethylcarbamoyloxy)-5,5-difluoro-6-hydroxy-7-methyloct-7-en-4-one (6c). The aldols **6c** were prepared from **3b** (0.91 g, 3.85 mmol) and methacrylaldehyde (0.35 ml, 4.24 mmol). Usual work-up followed by column chromatography (20% diethyl ether in petroleum ether) yielded **6c** (a separable mixture of diastereoisomers, 1.2:1 ratio) as colourless oils. Major diastereoisomers (*syn*) (0.33 g, 28%); R_f 0.37; ν_{max} (film)/cm^{-1} 3384 (O–H), 1755 (ketonic C=O), 1685 (carbamate C=O); δ_H (300 MHz; CDCl$_3$) 5.23–5.08 (4 H, m, CH(OH) + CH(OCONEt$_2$) + C=CH_2), 4.38 (1 H, dd, $^3J_{H-F}$ 25.0, $^3J_{H-H}$ 2.0, CH(OH)), 3.37–3.15 (4 H, m, N(CH_2CH$_3$)$_2$), 2.08–1.95 (1 H, m, CH_aH$_b$CH$_3$), 1.88 (3 H, s, CH_3C=CH$_2$), 1.84–1.67 (1 H, m, CH$_a$$H_bCH_3$), 1.20 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.10 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.06 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75

MHz; $CDCl_3$) 197.8 (dd, $^2J_{C-F}$ 35.1, $^2J_{C-F}$ 24.3), 155.4, 139.0, 116.9, 116.7 (dd, $^1J_{C-F}$ 302.3, $^1J_{C-F}$ 260.1), 78.1, 73.4 (dd, $^2J_{C-F}$ 29.2, $^2J_{C-F}$ 22.0), 42.1, 41.7, 23.1, 19.0, 13.7, 13.1, 9.8; δ_F (282 MHz; $CDCl_3$) −108.3 (1 F, d, $^2J_{F-F}$ 253.6), −133.6 (1 F, dd, $^2J_{F-F}$ 253.6, $^3J_{H-F}$ 25.0); minor diastereoisomers (*anti*) (0.36 g, 30%); R_f 0.24; ν_{max} (mixture; film)/cm^{-1} 3371 (O–H), 1748 (ketonic C=O), 1687 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.20–5.08 (3 H, m, =CH_2, CH(OCONEt$_2$)), 4.59 (1 H, ddd, $^3J_{H-F}$ 18.8, $^3J_{H-H}$ 7.0, $^3J_{H-F}$ 6.3, CH(OH)), 4.32 (1 H, d, $^3J_{H-H}$ 7.0, C(OH)), 3.41–3.18 (4 H, m, N(CH_2CH$_3$)$_2$), 2.08–1.91 (1 H, m, CH_aH$_b$Me), 1.84–1.68 (1 H, m, CH$_a$$H_b$Me), 1.86 (3 H, s, C(=CH$_2$)(C$H_3$)), 1.19 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.05 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75 MHz; $CDCl_3$) 197.5 (dd, $^2J_{C-F}$ 25.8, $^2J_{C-F}$ 10.2), 155.4, 139.3 , 116.7 (dd, $^1J_{C-F}$ 266.2, $^1J_{C-F}$ 253.9), 116.2, 77.1 (dd, $^2J_{C-F}$ 32.0, $^2J_{C-F}$ 31.4), 76.5, 42.2, 41.8, 23.5, 19.2, 13.8, 13.2, 9.8; δ_F (282 MHz; $CDCl_3$) −112.9 (1 F, dd, $^2J_{F-F}$ 258.1, $^3J_{H-F}$ 6.3), −121.5 (1 F, dd, $^2J_{F-F}$ 258.1, $^3J_{H-F}$ 18.8); HRMS (mixture of diastereoisomers); HRMS (Found 307.1588. Calc. for $C_{14}H_{23}NO_4F_2$: 307.1595); *m*/*z* (CI) 308 (100%, [M + H]$^+$), 100 (85, [CONEt$_2$]$^+$).

4-(*N*,*N*-Diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-1-phenylhexan-3-one (6d). Aldols **6d** were prepared from **3b** (0.40 g, 1.66 mmol) and benzaldehyde (0.21 ml, 1.83 mmol). Usual work-up followed by column chromatography (10% ethyl acetate in light petroleum) yielded **6d** (a separable mixture of diastereoisomers, 1.1 : 1 ratio) as colourless oils. *syn* Diastereoisomers (0.18 g, 32%); R_f 0.11 (Found: C, 59.63; H, 6.73; N, 3.97. Calc. for $C_{17}H_{23}NO_4F_2$: C, 59.47; H, 6.75; N, 4.08%); ν_{max} (Nujol mull) 3377 (OH), 1738 (ketonic C=O), 1682 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.53–7.50 (2 H, m, Aromatic *H*), 7.44–7.35 (3 H, m, Aromatic *H*), 5.47 (1 H, d, $^3J_{H-H}$ 2.9, CH(OH)), 5.29 (1 H, ddq, $^3J_{H-H}$ 8.5 and 1.8, $^4J_{H-H}$ 1.5, CH(OCONEt$_2$)), 4.49 (1 H, dd, $^3J_{H-F}$ 23.2, $^3J_{H-H}$ 2.9, CH(OH)), 3.41–3.18 (4 H, m, N(CH_2Me)$_2$), 2.09–1.95 (1 H, m, CH_aH$_b$Me), 1.85–1.70 (1 H, m, CH$_a$$H_bCH_3$), 1.22 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.13 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.07 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75 MHz; $CDCl_3$) 200.3 (t, $^2J_{C-F}$ 28.0), 155.7, 134.6, 128.8, 128.0, 128.0, 115.8 (dd, $^1J_{C-F}$ 262.1 and 259.0), 78.4, 72.5 (dd, $^2J_{C-F}$ 29.0, and 22.1), 42.4, 41.9, 23.3, 13.9, 13.3, 10.0; δ_F (282 MHz; $CDCl_3$) −107.1 (1 F, d, $^2J_{F-F}$ 254.7), −134.3 (1 F, dd, $^2J_{F-F}$ 254.7, $^3J_{H-F}$ 23.4); HRMS (Found: 344.1678. Calc. for $C_{17}H_{24}NO_4F_2$: 344.1673); *m*/*z* (CI) 344 (100%, [M + H]$^+$); *anti* diastereoisomer (0.17 g, 29%); R_f 0.06 (Found: C, 59.45; H, 6.79; N, 3.96. Calc. for $C_{17}H_{23}NO_4F_2$: C, 59.47; H, 6.75; N, 4.08%); δ_H (300 MHz; $CDCl_3$) 7.52–7.40 (2 H, m, Aromatic *H*), 7.38–7.30 (3 H, m, Aromatic *H*), 5.35–5.19 (2 H, m, CH(OH) and CH(OCONEt$_2$)), 4.54 (1 H, d, $^3J_{H-H}$ 6.3, CH(OH)), 3.44–3.21 (4 H, m, N(CH_2Me)$_2$), 2.09–1.93 (1 H, m, CH_aH$_b$Me), 1.86–1.70 (1 H, m, CH$_a$$H_b$Me), 1.20 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.12 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.07 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3); δ_C (75 MHz; $CDCl_3$) 197.7 (t, $^2J_{C-F}$ 26.0), 155.7, 134.6, 128.7, 128.7, 128.1, 115.8 (dd, $^1J_{C-F}$ 266.3, $^1J_{C-F}$ 252.5), 76.6, 73.3 (dd, $^2J_{C-F}$ 28.5 and 24.7), 42.4, 41.9, 23.6, 13.9, 13.3, 10.0; δ_F (282 MHz; $CDCl_3$) −112.6 (1 F, d, $^2J_{F-F}$ 260.7), −123.1 (1 F, dd, $^2J_{F-F}$ 260.7, $^3J_{H-F}$ 19.0); HRMS (Found: 344.1671. Calc. for $C_{17}H_{24}NO_4F_2$: 344.1673); *m*/*z* (FAB) 344.2 (65%, [M + H]$^+$), 100 (100, [CONEt$_2$]$^+$).

4-(*N*,*N*-Diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-1-(4-nitrophenyl)hexan-3-one (6e). The aldols **6e** were prepared from **3b** (0.48 g, 2.04 mmol) and *p*-nitrobenzaldehyde (0.36 g, 2.60 mmol), added as a solution in THF (2 ml). Usual work-up followed by column chromatography (10% ethyl acetate in light petroleum) yielded **6e** (a separable mixture of diastereoisomers, 1.25 : 1 ratio) as colourless solids. Major diastereoisomer (*syn*) (0.21 g, 25%); R_f 0.11 (Found: C, 52.43; H, 5.72; N, 7.27. Calc. for $C_{19}H_{22}N_2O_6F_2$: C, 52.58; H, 5.71; N, 7.21%); ν_{max} (Nujol mull)/cm^{-1} 3399 (OH), 1757 (ketonic C=O), 1684 (carbamate C=O); mp 101–103 °C; δ_H (300 MHz; $CDCl_3$) 8.20 (2 H, d, $^3J_{H-H}$ 8.5, (NO$_2$)CCH), 7.67 (2 H, d, $^3J_{H-H}$ 8.5, (NO$_2$)CCCH), 5.84 (1 H, br s, CH(OH)), 5.22–5.16 (1 H, m, CH(OCONEt$_2$)), 5.07 (1 H, d, $^3J_{H-F}$ 22.8, CH(OH)), 3.36–3.17 (4 H, m, N(CH_2Me)$_2$), 2.06–1.92 (1 H, m, CH_aH$_b$Me), 1.83–1.68 (1 H, m, CH$_a$$H_bCH_3$), 1.19 (3 H, t, $^3J_{H-H}$ 7.0, CH$_2$CH_3), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.04 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)); δ_C(75 MHz; $CDCl_3$) 197.7 (dd, $^2J_{C-F}$ 24.2 and 22.0), 155.6, 134.6, 128.8, 128.7, 128.0, 116.1 (dd, $^2J_{C-F}$ 266.4 and 252.9), 76.6, 73.3 (t, $^2J_{C-F}$ 26.4), 42.4, 41.9, 23.6, 13.9, 13.3, 10.0; δ_F (282 MHz; $CDCl_3$) −106.9 (1 F, d, $^2J_{F-F}$ 255.6), −134.4 (1 F, dd, $^2J_{F-F}$ 255.6, $^3J_{H-F}$ 22.9); *m*/*z* (CI) 413 (45%, [M + H]$^+$), 100 (100, [CONEt$_2$]$^+$); and the minor diastereoisomer (*anti*) (0.17 g, 20%); R_f 0.06; ν_{max} (film)/cm^{-1} 3307 (OH), 1756 (ketonic C=O), 1682 (carbamate C=O); mp 110–112 °C; δ_H (300 MHz; $CDCl_3$) 8.23 (2 H, d, $^3J_{H-H}$ 8.8, (NO$_2$)CCH), 7.67 (2 H, d, $^3J_{H-H}$ 8.8, (NO$_2$)CCCH), 5.35 (1 H, ddd, $^3J_{H-F}$ 18.4 and 5.2, $^3J_{H-H}$ 6.3, CH(OH)), 5.19 (1 H, br d, $^3J_{H-H}$ 8.4, CH(OCONEt$_2$)), 4.96 (1 H, d, $^3J_{H-H}$ 6.3, CH(OH)), 3.45–3.19 (4 H, m, N(CH_2Me)$_2$), 2.08–1.94 (1 H, m, CH_aH$_b$CH$_3$), 1.87–1.72 (1 H, m, CH$_a$$H_b$-Me), 1.21 (3 H, t, $^3J_{H-H}$ 7.4, CH$_2$CH_3), 1.13 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.09 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)); δ_C(75 MHz; $CDCl_3$) 196.6 (dd, $^2J_{C-F}$ 29.7, $^2J_{C-F}$ 24.8), 155.8, 148.2, 141.8, 128.8, 123.2, 115.8 (dd, $^2J_{C-F}$ 267.3 and 266.8), 76.7, 71.8 (t, $^2J_{C-F}$ 32.0), 42.5, 42.0, 23.6, 13.8, 13.3, 9.9; δ_F (282 MHz; $CDCl_3$) −113.5 (1 F, dd, $^2J_{F-F}$ 259.4, $^3J_{H-F}$ 5.2), −121.2 (1 F, dd, $^2J_{F-F}$ 259.4, $^3J_{H-F}$ 18.4).

1-(4-Chlorophenyl)-4-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluorohexan-3-one (6f). Aldols **6f** were prepared from alcohol **3b** (0.61 g, 2.55 mmol) and 4-chlorobenzaldehyde (0.43 g, 3.1 mmol) added as a solution in THF (1 ml). Usual work-up followed by column chromatography (10% ethyl acetate in light petroleum) yielded **6f** (a separable mixture of diastereoisomers, 1.2 : 1 ratio) as colourless solids. Major diastereoisomers (*syn*) (0.19 g, 22%); mp 93–95 °C; R_f 0.17 (Found: C, 54.15; H, 5.87; N, 3.69. Calc. for $C_{17}H_{22}ClF_2NO_4$: C, 54.04; H, 5.87; N, 3.69%); ν_{max} (Nujol mull)/cm^{-1} 3342 (OH), 1756 (ketonic C=O), 1678 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.43 (2 H, d, $^3J_{H-H}$ 8.5, ClCCH), 7.33 (2 H, d, $^3J_{H-H}$ 8.5, ClCCCH), 5.62 (1 H, br s, CH(OH)), 5.26–5.23 (1 H, m, CH(OCONEt$_2$)), 4.96 (1 H, d, $^3J_{H-F}$ 22.8, CH(OH)), 3.34–3.16 (4 H, m, N(CH_2Me)$_2$), 2.10–1.95 (1 H, m, CH(OCONEt$_2$)CH_aH$_b$), 1.82–1.67 (1 H, m, CH(ODEC)CH$_a$$H_b$), 1.18 (3 H, t, $^3J_{H-H}$ 7.0, C(CH$_2$CH_3)), 1.10–1.01 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 200.0 (dd, $^2J_{C-F}$ 34.6 and 21.5), 155.6, 134.6, 133.2, 129.6, 128.2, 115.6 (dd, $^2J_{C-F}$ 263.4 and 255.8), 78.3, 71.9 (dd, $^2J_{C-F}$ 28.9 and 22.3), 42.3, 41.9, 23.2, 13.8, 13.2, 9.8; δ_F (282 MHz; $CDCl_3$) −122.6 (1 F, d, $^2J_{F-F}$ 261.9, $^3J_{H-F}$ 22.8), −123.0 (1 F, dd, $^2J_{F-F}$ 261.9); HRMS (Found: 378.1291. Calc. for $C_{17}H_{23}NO_3F_2Cl$: 378.1284); *m*/*z* (CI) 378 (50%, [M + H]$^+$), 360 (25, [M − OH]$^+$), 100 (100, [CONEt$_2$]$^+$). Minor diastereoisomers (*anti*) (0.26 g, 27%); mp 98–100 °C; R_f 0.12 (Found: C, 54.18; H, 5.91; N, 3.79. Calc for $C_{17}H_{22}ClF_2NO_4$: C, 54.04; H, 5.87; N, 3.71%); ν_{max} (Nujol mull)/cm^{-1} 3353 (OH), 1757 (ketonic C=O), 1678 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.40 (2 H, d, $^3J_{H-H}$ 8.5, ClCCH), 7.33 (2 H, d, $^3J_{H-H}$ 8.5, ClCCCH), 5.30–5.15 (2 H, m, CH(OH), CH(OCONEt$_2$)), 4.73 (1 H, br s, CH(OH)), 3.39–3.21 (4 H, m, N(CH_2CH$_3$)$_2$), 2.05–1.93 (1 H, m, CH(OCONEt$_2$)CH_aH$_b$), 1.84–1.69 (1 H, m, CH-(OCONEt$_2$)CH$_a$$H_b$), 1.19 (3 H, t, $^3J_{H-H}$ 7.0, CH$_2$CH_3), 1.12–1.03 (6 H, m, N(CH$_2$CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 197.5 (dd, $^2J_{C-F}$ 30.5 and 25.9), 155.7, 134.6, 133.2, 129.3, 128.3, 115.9 (dd, $^2J_{C-F}$ 252.6 and 255.5), 76.6, 72.7 (dd, $^2J_{C-F}$ 28.8 and 24.3), 42.4, 41.9, 23.6, 13.9, 13.8, 9.9; δ_F (282 MHz; $CDCl_3$) −112.6 (1 F, dd, $^2J_{F-F}$ 261.9, $^3J_{H-H}$ 24.2), −123.0 (1 F, d, $^2J_{F-F}$ 261.9); HRMS (Found: 378.1288. Calc for $C_{17}H_{23}NO_3F_2Cl$: 378.1284); *m*/*z* (CI) 378 (48%, [M + H]$^+$), 100 (100, [CONEt$_2$]$^+$).

4-(*N*,*N*-Diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-5,5-dimethyl-1-phenylhexan-3-one (6g). Aldols **6g** were prepared from alcohol **3k** (0.37 g, 1.40 mmol) and benzaldehyde (0.16 g, 1.54 mmol). Usual work-up followed by column chromatography (30% diethyl ether in light petroleum) yielded **6g** (a separable mixture of diastereoisomers, 1.1 : 1 ratio) as colourless solids. *syn* Diastereoisomers (0.17 g, 33%); mp 66–68 °C; R_f 0.36 (Found: C, 61.54; H, 7.36; N, 3.81. Calc. for $C_{19}H_{27}F_2NO_4$: C, 61.44; H, 7.33; N, 3.77%); ν_{max} (Nujol mull)/cm^{-1} 3409 (OH), 1731 (ketonic C=O), 1689 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.55–7.48 (2 H, m, Aromatic *H*), 7.42–7.30 (3 H, m, Aromatic *H*), 5.46 (1 H, br s, CH(O*H*)), 5.11 (1 H, dd, $^3J_{H-F}$ 22.8, $^3J_{H-H}$ 1.8, C*H*(OH)), 5.10 (1 H, dd, $^4J_{H-F}$ 1.8 and 1.5, C*H*(OCONEt$_2$)), 3.37–3.16 (4 H, m, N(CH_2CH$_3$)$_2$), 1.22 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.11 (3 H, t, $^3J_{H-H}$ 7.4, N(CH_2CH$_3$)), 1.07 (9 H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 201.4 (t, $^2J_{C-F}$ 36.7), 155.7, 135.2, 128.7, 128.4, 128.0, 114.7 (dd, $^1J_{C-F}$ 267.5 and 255.8), 81.7, 72.6 (dd, $^2J_{C-F}$ 29.0 and 21.6), 42.5, 42.0, 35.5, 26.3, 14.0, 13.3; δ_F (282 MHz; $CDCl_3$) −102.4 (1 F, d, $^2J_{F-F}$ 261.9), −132.9 (1 F, dd, $^2J_{F-F}$ 261.9, $^3J_{H-F}$ 22.9); HRMS (Found: 372.1987. Calc. for $C_{19}H_{28}NO_4F_2$: 372.1986); *m*/*z* (FAB) 410 (15%, [M + Na]$^+$), 372 (100, [M + H]$^+$). *anti* Diastereoisomers (0.15 g, 29%); mp 98–100 °C; R_f 0.26 (Found: C, 61.37; H, 7.35; N, 3.68. Calc. for $C_{19}H_{27}F_2NO_4$: C, 61.44; H, 7.33; N, 3.77%); ν_{max} (film)/cm^{-1} 3409 (OH), 1736 (ketonic C=O), 1688 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.50–7.43 (2 H, m, Aromatic *H*), 7.40–7.35 (3 H, m, Aromatic *H*), 5.26 (1 H, ddd, $^3J_{H-F}$ 18.8 and 6.3, $^3J_{H-H}$ 4.8, C*H*(OH)), 5.02 (1 H, dd, $^4J_{H-F}$ 2.2 and 1.1, C*H*(OCONEt$_2$)), 4.50 (1 H, d, $^3J_{H-H}$ 6.3, CH(O*H*)), 3.43–3.22 (4 H, m, N(CH_2Me)$_2$), 1.21 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.14 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)) 1.07 (9 H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 199.4 (dd, $^2J_{C-F}$ 33.1 and 24.6), 155.8, 135.2, 128.6, 128.1, 128.0, 115.3 (dd, $^1J_{C-F}$ 263.2 and 257.3), 80.9, 74.1 (dd, $^2J_{C-F}$ 28.5 and 25.9), 42.5, 42.0, 35.6, 26.4, 14.1, 13.5; δ_F (282 MHz; $CDCl_3$) −111.3 (1 F, d, $^2J_{F-F}$ 259.4), −117.8 (1 F, dd, $^2J_{F-F}$ 259.4, $^3J_{H-F}$ 18.8); HRMS (Found: 372.1983. Calc. for $C_{19}H_{28}NO_4F_2$: 372.1986); *m*/*z* (CI) 372 (45%, [M + H]$^+$).

(*E*)-3-Ethyl-3-(*N*,*N*-diethylcarbamoyloxy)-5,5-difluoro-6-hydroxynon-7-en-4-one (7a). Aldol **7a** was prepared from alcohol **3m** (0.46 g, 1.74 mmol) and crotonaldehyde (0.10 ml, 1.90 mmol). Usual work up and column chromotography (15% ethyl acetate in light petroleum) afforded the aldol **7a** as a colourless oil (0.29 g, 46%); R_f 0.21; ν_{max} (film)/cm^{-1} 3433 (O–H), 1734 (ketonic C=O), 1677 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.89–5.77 (1 H, m, MeC*H*=CH), 5.48 (1 H, dd, $^3J_{H-H}$ 15.5 and 7.0, MeCH=C*H*), 4.64 (1 H, dd, $^3J_{H-F}$ 25.1, $^3J_{H-H}$ 7.0, C*H*(OH)), 3.94 (1 H, br s, CH(O*H*)), 3.27–3.14 (4 H, m, N(CH_2Me)$_2$), 2.02–1.92 (4 H, C(CH_2Me)$_2$), 1.68 (3 H, d, $^3J_{H-H}$ 6.0, CH_3CH=CH), 1.11 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.04 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 0.83–0.70 (6 H, m, C(CH$_2$-CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 197.8 (dd, $^2J_{C-F}$ 36.6 and 26.6), 155.4, 131.8, 124.5, 116.3 (dd, $^1J_{C-F}$ 256.0 and 267.1), 87.5, 73.3 (dd, $^2J_{C-F}$ 28.6 and 23.0), 42.3, 41.8, 24.3, 23.9, 17.9, 13.8, 13.2, 6.9, 6.7; δ_F (282 MHz; $CDCl_3$) −101.6 (1 F, br d, $^2J_{F-F}$ 275.9), −126.3 (1 F, br d, $^2J_{F-F}$ 275.9); HRMS (Found: 336.1993. Calc. for $C_{16}H_8NO_4F_2$: 336.1986); *m*/*z* 336 (100%, [M + H]$^+$), 100 (30, [CONEt$_2$]$^+$).

3-Ethyl-3-(*N*,*N*-diethylcarbamoyloxy)-5,5-difluoro-6-hydroxy-7-methyloct-7-en-4-one (7b). Aldol **7b** was prepared from alcohol **3m** (0.62 g, 2.35 mmol) and methacrylaldehyde (0.21 ml, 2.59 mmol). Usual work up and column chromatography (10% ethyl acetate in light petroleum) afforded the aldol **7b** as a colourless oil (0.33 g, 42%); R_f 0.26; ν_{max} (film)/cm^{-1} 3432 (O–H), 1734 (ketonic C=O), 1676 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 5.12 (1 H, br d, $^2J_{H-H}$ 2.9, =CH$_a$*H*$_b$), 5.08 (1 H, br d, $^2J_{H-H}$ 2.9, =C*H*$_a$H$_b$), 4.78 (1 H, d, $^3J_{H-F}$ 23.6, C*H*(OH)), 4.10 (1 H, d, $^3J_{H-H}$ 1.5, CH(O*H*)), 3.38–3.10 (4 H, m, N(CH_2Me)$_2$), 2.08–1.92 (4 H, m, C(CH_2Me)$_2$), 1.80 (3 H, br s, CH_3C=CH$_2$), 1.14 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 1.11 (3 H, t, $^3J_{H-H}$ 7.4, N(CH$_2$CH_3)), 0.85 (3 H, t, $^3J_{H-H}$ 7.5, C(CH$_2$CH_3)), 0.78 (3 H, t, $^3J_{H-H}$ 7.5, C(CH$_2$CH_3)); δ_C (75 MHz; $CDCl_3$) 197.8 (dd, $^2J_{C-F}$ 30.8 and 25.8), 155.8, 140.4, 117.0, 116.8 (dd, $^1J_{C-F}$ 270.7 and 116.8), 87.8, 73.7 (dd, $^2J_{C-F}$ 28.8, $^2J_{C-F}$ 20.9), 42.5, 42.0, 24.5, 24.0, 19.0, 13.9, 13.3, 7.1, 5.7; δ_F (282 MHz; $CDCl_3$) † −100.6 (1 F, br d, $^2J_{F-F}$ 271.7), −126.5 (1 F, br d, $^2J_{F-F}$ 271.7); HRMS (Found: 336.1981. Calc. for $C_{16}H_{28}NO_4F_2$: 336.1986); *m*/*z* (CI) 336 (100%, [M + H]$^+$), 100 (82, [CONEt$_2$]$^+$).

4-Ethyl-4-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-1-(4-nitrophenyl)hexan-3-one (7c). Aldol **7c** was prepared from alcohol **3m** (0.57 g, 2.15 mmol) and 4-nitrobenzaldehyde (0.36 g, 2.47 mmol) added as a solution in THF (1 ml). Usual work up and column column chromatography (10% ethyl acetate in light petroleum) afforded aldol **7c** as a colourless crystalline solid (0.42 g, 47%); mp 94–95 °C; R_f 0.13; ν_{max} (Nujol mull)/cm^{-1} 3325 (O–H), 1730 (ketonic C=O), 1666 (carbamate C=O) (Found: C, 54.78; H, 6.93; N, 6.76. Calc. for $C_{19}H_{26}N_2O_6F_2$: C, 54.80; H, 6.29; N, 6.73%); δ_H (300 MHz; $CDCl_3$) 8.23 (2 H, d, $^3J_{H-H}$ 8.8, (NO$_2$)CC*H*), 7.64 (2 H, d, $^3J_{H-H}$ 8.8, (NO$_2$)CCC*H*), 5.54 (1 H, d, $^3J_{H-F}$ 22.4, C*H*(OH)), 4.85 (1 H, br s, CH(O*H*)), 3.44–3.17 (4 H, m, N(CH_2CH$_3$)$_2$), 2.10–1.87 (4 H, m, C(CH_2CH$_3$)$_2$), 1.18 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 0.86 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.18 (3 H, t, $^3J_{H-H}$ 7.0, C(CH$_2$CH_3)), 1.17 (3 H, t, $^3J_{H-H}$ 7.0, C(CH$_2$CH_3)); δ_C (75 MHz; $CDCl_3$) 196.7 (dd, $^2J_{C-F}$ 29.5 and 24.9), 156.0, 148.1, 143.2, 129.4, 123.8, 115.7 (dd, $^1J_{C-F}$ 272.3 and 256.6), 87.8, 71.7 (dd, $^2J_{C-F}$ 27.3, $^2J_{C-F}$ 22.5), 42.6, 42.1, 24.4, 23.8, 13.9, 13.4, 7.01, 6.8; δ_F (282 MHz; $CDCl_3$) ‡ −97.3 (1 F, br d, $^3J_{H-F}$ 22.4), −128.8 (1 F, br d, $^3J_{H-F}$ 22.4); *m*/*z* (CI) 417 (48%, [M + H]$^+$), 100 (100, [CONEt$_2$]$^+$).

4-Ethyl-4-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-1-phenylhexan-3-one (7d). Aldol **7d** was prepared from alcohol **3m** (0.63 g, 2.40 mmol) and benzaldehyde (0.27 ml, 2.64 mmol). Usual work up followed by column chromatography (15% ethyl acetate in light petroleum) afforded the aldol **7d** as a colourless oil (0.56 g, 63%); R_f 0.29; ν_{max} (Nujol mull)/cm^{-1} 3329 (O–H), 1732 (ketonic C=O), 1668 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.49–7.47 (2 H, m, Aromatic H), 7.39–7.32 (3 H, Aromatic H), 5.44 (1 H, d, $^3J_{H-F}$ 23.2, C*H*(OH)), 4.57 (1 H, br s, CH(O*H*)), 3.37–3.18 (4 H, m, N(CH_2Me)$_2$), 2.13–1.94 (4 H, m, C(CH_2CH$_3$)$_2$), 1.19 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 1.18 (3 H, t, $^3J_{H-H}$ 7.0, N(CH$_2$CH_3)), 0.87 (3 H, t, $^3J_{H-H}$ 7.3, C(CH$_2$CH_3)), 0.71 (3 H, t, $^3J_{H-H}$ 7.7, C(CH$_2$CH_3); δ_C (75 MHz; $CDCl_3$) 197.7 (dd, $^2J_{C-F}$ 31.4 and 25.8), 155.8, 135.7, 128.7, 128.6, 128.5, 116.0 (dd, $^1J_{C-F}$ 270.8 and 255.0), 87.7, 72.3 (dd, $^2J_{C-F}$ 28.3 and 21.9), 42.5, 42.0, 24.4, 23.9, 13.9, 13.4, 7.0, 6.8; δ_F (282 MHz; $CDCl_3$) † −97.7 (1 F, br s), −129.6 (1 F, br s); HRMS (Found: 373.1977. Calc. for $C_{19}H_{28}NO_4F_2$: 372.1986); *m*/*z* (CI) 372 (100%, [M + H]$^+$).

4-(*N*,*N*-Diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-4-methyl-1-(4-methoxyphenyl)pentan-3-one (7e). Aldol **7e** was prepared from alcohol **3l** (0.58 g, 2.46 mmol) and 4-methoxybenzaldehyde (0.33 ml, 2.71 mmol). Usual work up and column chromotography (5% ethyl acetate in light petroleum) afforded the aldol **7e** as a colourless solid (0.73 g, 79%); mp 69–71 °C; R_f 0.18; ν_{max} (Nujol mull)/cm^{-1} 3437 (O–H), 1737 (ketonic C=O), 1677 (carbamate C=O) (Found: C, 58.64; H, 6.94; N, 3.52. Calc. for $C_{18}H_{25}NO_5F_2$: C, 58.90; H, 7.02; N, 3.62%); δ_H (300 MHz; $CDCl_3$) 7.38 (2 H, d, $^3J_{H-H}$ 8.5, C*H*(OMe)), 6.88 (2 H, d, $^3J_{H-H}$

† There was significant signal broadening in the ^{19}F NMR spectrum arising from exchange between rotamers and the expected $^3J_{H-F}$ coupling was not resolved.

‡ There was significant signal broadening in the ^{19}F NMR spectrum arising from exchange between rotamers and the expected $^3J_{F-F}$ coupling was not observed.

8.5, C*H*CH(OMe)), 5.33 (1 H, d, $^3J_{H-F}$ 22.5, C*H*(OH)), 4.36 (1 H, s, CH(O*H*)), 3.78 (3 H, s, OCH_3), 3.39–3.17 (4 H, m, $N(CH_2Me)_2$), 1.59 (3 H, s, $C(CH_{a3})(CH_{b3})$), 1.54 (3 H, s, $C(CH_{a3})(CH_{b3})$), 1.16 (6 H, t, $^3J_{H-H}$ 7.2, $N(CH_2CH_3)_2$); δ_C (75 MHz; $CDCl_3$) 198.5 (dd, $^2J_{C-F}$ 31.2 and 25.4), 159.9, 155.8, 129.6, 127.5, 116.2 (dd, $^1J_{C-F}$ 269.1 and 254.6), 113.4, 82.1, 72.1 (dd, $^2J_{C-F}$ 28.5 and 21.8), 55.2, 42.4, 41.9, 23.9, 23.8, 13.9, 13.4; δ_F −99.6 (1 F, dd, $^2J_{F-F}$ 275.9, $^3J_{H-F}$ 22.5), −126.1 (1 F, d, $^2J_{F-F}$ 275.9); HRMS (Found: 374.1762. Calc. for $C_{18}H_{25}NO_5F_2$: 374.1779); *m*/*z* (CI) 374 (100%, $[M + H]^+$).

1-(4-Chlorophenyl)-4-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-hydroxy-4-methylpentan-3-one (7f). Aldol **7f** was prepared from alcohol **3l** (0.65 g, 2.78 mmol) and 4-chlorobenzaldehyde (0.43 g, 3.06 mmol), added as a solution in THF (1 ml). Usual work up and column chromatography (15% ethyl acetate in light petroleum) afforded the aldol **7f** as a colourless crystalline solid (0.44 g, 42%); mp 88–89 °C; R_f 0.14 (Found: C, 54.16; H, 5.98; N, 3.82. Calc for $C_{17}H_{22}ClF_2NO_4$: C, 54.04; H, 5.87; N, 3.71%); ν_{max} (Nujol mull)/cm^{-1} 3513 (OH), 1722 (ketonic C=O), 1686 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.38 (2 H, d, $^3J_{H-H}$ 8.5, ClCC*H*), 7.29 (2 H, d, $^3J_{H-H}$ 8.5, ClCCC*H*), 5.33 (1 H, d, $^3J_{H-F}$ 22.1, C*H*(OH)), 4.59 (1 H, br s, CH(O*H*)), 3.31–3.13 (4 H, m, $N(CH_2Me)_2$), 1.56 (3 H, s, $C(CH_{a3})(CH_{b3})$), 1.52 (3 H, s, $C(CH_{a3})(CH_{b3})$), 1.12 (6 H, t, $^3J_{H-H}$ 7.2, $N(CH_2CH_3)_2$); δ_C (75 MHz: $CDCl_3$) 198.0 (dd, $^2J_{C-F}$ 31.7 and 24.9), 155.8, 134.4, 134.2, 129.8, 128.1, 115.9 (dd, $^2J_{C-F}$ 269.9 and 255.5), 82.1, 71.8 (dd, $^2J_{C-F}$ 28.5 and 22.0), 42.9, 41.9, 23.8, 23.7, 13.8, 13.3; δ_F (282 MHz; $CDCl_3$) −97.9 (1 F, d, $^2J_{F-F}$ 277.2), −127.6 (1 F, dd, $^2J_{F-F}$ 277.2, $^3J_{H-F}$ 22.1); HRMS (Found: 378.1266. Calc. for $C_{17}H_{23}NO_4F_2Cl$: 378.1284); *m*/*z* (ES) 400 (10%, $[M + Na]^+$), 378 (100, $[M + H]^+$).

1-(*N*,*N*-Diethylcarbamoyloxy)-3,3-difluoro-4-hydroxy-4-(4-methoxyphenyl)butan-3-one (7g). Aldol **7g** was prepared from alcohol **3a** (0.45 g, 2.15 mmol) and 4-methoxybenzaldehyde (0.29 ml, 2.37 mmol). Usual work up and column chromatography (20% ethyl acetate in light petroleum) afforded the aldol **7g** as a colourless solid (0.38 g, 51%); mp 105–107 °C; R_f 0.11 (Found: C, 55.72; H, 6.42; N, 3.88. Calc. for $C_{16}H_{21}NO_5F_2$: C, 55.82; H, 6.45; N, 3.90%); ν_{max} (Nujol mull)/cm^{-1} 3405 (OH), 1762 (ketonic C=O), 1691 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 7.37 (2 H, d, $^3J_{H-H}$ 8.8, (MeO)CC*H*), 6.89 (2 H, d, $^3J_{H-H}$ 8.8, (MeO)CCHC*H*), 5.11 (1 H, d, $^2J_{H-H}$ 18.0, CH_aH_b-(OCONEt$_2$)), 4.99 (1 H, ddd, $^3J_{H-F}$ 19.9 and 4.1, $^3J_{H-H}$ 4.4, C*H*(OH)), 4.89 (1 H, $^2J_{H-H}$ 18.0, CH_aH_b(OCONEt$_2$)), 4.14 (1 H, d, $^3J_{H-H}$ 4.4, CH(O*H*)), 3.79–3.34 (4 H, m, $N(CH_2CH_3)_2$), 1.16 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.09 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$); δ_C (75 MHz; $CDCl_3$) 196.9 (dd, $^2J_{C-F}$ 32.9 and 25.5), 160.0, 154.9, 129.1, 126.5, 115.6 (dd, $^1J_{C-F}$ 260.8 and 255.2), 113.6, 72.5 (dd, $^2J_{C-F}$ 29.5 and 23.3), 67.0, 55.2, 42.2, 41.6, 13.7, 13.2; δ_F (282 MHz; $CDCl_3$) −110.9 (1 F, d, $^2J_{F-F}$ 261.8, $^3J_{H-F}$ 4.1), −129.9 (1 F, dd, $^2J_{F-F}$ 261.8, $^3J_{H-F}$ 19.9); *m*/*z* (CI) 346 (100%, $[M + H]^+$).

4-Ethyl-4-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-hydroxyhexan-3-one (7h). Aldol **7h** was prepared from alcohol **3m** (0.80 g, 3.41 mmol) and solid paraformaldehyde (0.11 g, 3.82 mmol). Usual work up and column chromatography (20% ethyl acetate in light petroleum) afforded the aldol **7h** as a colourless oil (0.60 g, 60%); R_f 0.23 (Found: C, 52.66; H, 7.86; N, 4.69. Calc. for $C_{13}H_{23}NO_4F_2$: C, 52.87; H, 7.85; N, 4.74%); ν_{max} (film)/cm^{-1} 3436 (OH), 1731 (ketonic C=O), 1682 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 4.02 (2 H, td, $^3J_{H-F}$ 13.2, $^3J_{H-H}$ 6.6, CH_2(OH)), 3.28 (2 H, q, $^3J_{H-H}$ 7.0, $N(CH_2Me)$), 3.23 (2 H, q, $^3J_{H-H}$ 7.0, $N(CH_2Me)$), 3.08 (1 H, br t, $^3J_{H-H}$ 6.6, $CH_2(OH)$), 2.01 (4 H, q, $^3J_{H-H}$ 7.7, $C(CH_2Me)$), 1.16 (3 H, q, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 1.09 (3 H, q, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.82 (6 H, t, $^3J_{H-H}$ 7.7, $C(CH_2CH_3)$); δ_C (75 MHz; $CDCl_3$) 198.4 (t, $^2J_{C-F}$ 27.13), 155.5, 117.0 (t, $^1J_{C-F}$ 258.0), 87.2, 62.7 (t, $^2J_{C-F}$ 27.7), 42.3, 41.8, 24.0, 13.8, 13.3; δ_F (282 MHz; $CDCl_3$) −112.9 (2 F, t, $^3J_{H-F}$ 13.2); HRMS (Found: 296.1678. Calc. for $C_{13}H_{24}NO_4F_2$: 296.1673); *m*/*z* (CI) 296 (100%, $[M + H]^+$), 100 (57, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoropent-1-en-3-yl acetate 5a. Pyridine (0.10 ml, 1.28 mmol), 4-dimethylaminopyridine (0.02 g, 0.10 mmol) and acetic anhydride (0.24 ml, 2.54 mmol) were added to a solution of **3b** (0.30 g, 1.28 mmol) in dry dichloromethane (7 ml). The mixture was stirred for 48 hours at room temperature then concentrated *in vacuo*; the residue was taken up in diethyl ether (20 ml) then washed with water (3 × 10 ml) and dried ($MgSO_4$). Column chromatography (20% ethyl acetate in light petroleum) afforded the acetate **5a** as a colourless oil (0.31 g, 86%); R_f 0.45; ν_{max} (Nujol mull)/cm^{-1} 1775 (C=CF_2), 1733 (carbamate and ester C=O); δ_H (300 MHz; $CDCl_3$) 5.19 (1 H, td, $^3J_{H-H}$ 5.2, $^4J_{H-F}$ 1.8, C*H*(OAc)), 3.18 (4 H, q, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)_2$), 1.85 (3 H, s, CH_3CO), 1.65–1.50 (2 H, m, CH_2CH_3), 1.02 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.99 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.77 (3 H, t, $^3J_{H-H}$ 7.4, CH_2CH_3); δ_C (75 MHz; $CDCl_3$) 174.3, 155.2 (dd, $^1J_{C-F}$ 291.5, 287.2), 152.4, 109.1 (dd, $^2J_{C-F}$ 41.9, 15.4), 69.7, 42.5, 41.9, 23.0, 20.5, 13.7, 13.0, 9.3; δ_F (282 MHz; $CDCl_3$) −95.2 (1 F, d, $^2J_{F-F}$ 50.9), −105.2 (1 F, dd, $^2J_{F-F}$ 50.9, $^4J_{H-F}$ 2.5); HRMS (Found: 278.119631. Calc. for $C_{12}H_{18}NO_4F_2$: 278.120390); *m*/*z* (CI) 278 (2%, $[M + H]^+$), 218 (100%, $[M - (OCOCH_3)]^+$), 100 (90%, $[CONEt_2]^+$).

2-(*N*,*N*-Diethylcarbamoyloxy)-1,1-difluoropent-1-en-3-yl benzoate 5b. Pyridine (0.08 ml, 1.0 mmol), 4-dimethylaminopyridine (0.01 g, 0.1 mmol) and benzoyl chloride (0.15 ml, 1.1 mmol) were added to a solution of **3b** (0.13 g, 0.55 mmol) in dry dichloromethane (7 ml). The mixture was stirred for forty eight hours at room temperature then concentrated *in vacuo*; the residue was taken up in diethyl ether (20 ml) then washed with water (3 × 10 ml) and dried ($MgSO_4$). Column chromatography (20% ethyl acetate in light petroleum) afforded the benzoate **5b** (0.26 g, 81%) as a colourless oil; R_f 0.6; ν_{max} (film)/cm^{-1} 1775 (C=CF_2), 1734 (carbamate and ester C=O); δ_H (300 MHz; $CDCl_3$) 7.93 (2 H, br d, $^3J_{H-H}$ 7.0, *o*-Aromatic, *H*), 7.45–7.36 (1 H, m, *p*-Aromatic *H*), 7.34–7.24 (2 H, m, *m*-Aromatic *H*), 5.57 (1 H, td, $^3J_{H-H}$ 6.5, $^4J_{H-F}$ 3.0, C*H*(OBz)), 3.22–3.06 (4 H, m, $N(CH_2CH_3)_2$), 1.88–1.72 (2 H, m, CH_2CH_3), 1.10 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.97 (3 H, t, $^3J_{H-H}$ 7.0, $N(CH_2CH_3)$), 0.91 (3 H, t, $^3J_{H-H}$ 7.4, CH_2CH_3); δ_C (75 MHz; $CDCl_3$) 165.5, 155.4 (dd, $^1J_{C-F}$ 292.0, 287.2), 152.4, 133.0, 130.1, 129.6, 128.3, 109.4 (dd, $^2J_{C-F}$ 41.8, $^2J_{C-F}$ 15.6), 70.6, 42.7, 42.1, 14.0, 13.2, 9.6; δ_F (282 MHz; $CDCl_3$) −93.86 (1 F, d, $^2J_{F-F}$ 49.7), −104.35 (1 F, d, $^2J_{F-F}$ = 49.7); HRMS (Found: 342.153040. Calc. for $C_{17}H_{22}NO_4F_2$: 342.151690); *m*/*z* (EI) 341 (13%, $[M^+]$), 100 (100%, $[M + H]^+$).

Procedure for the transacylation of allylic alchols with ethyl magnesium bromide. Ethylmagnesium bromide (0.92 ml of a 1.0 M solution in tetrahydrofuran, 0.92 mmol) was added in one portion to a solution of **3b** (0.11 g, 0.46 mmol) in tetrahydrofuran (4 ml) under a nitrogen atmosphere at −10 °C. The solution was allowed to stir for eighteen hours at that temperature then a saturated ammonium chloride solution (5 ml) was added. The mixture was extracted with diethyl ether (3 × 10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The ^{19}F NMR spectrum of the crude material showed that complete conversion of **3b** to the corresponding difluoromethyl ketone[24] had been achieved.

Procedure for the epimerisation of aldol 6e

n-Butyllithium (0.064 ml of a 1.88 M solution in hexanes, 0.12 mmol) was added dropwise over five minutes to a solution of racemic *syn*-aldol **6e** (0.048 g, 0.12 mmol) in tetrahydrofuran

(0.5 ml) at −78 °C. The resulting solution was stirred at −78 °C for fifteen minutes then warmed to −10 °C over 1 hour. The solution was left to stir for one hour at that temperature, then quenched with saturated ammonium chloride (10 ml) and extracted with diethyl ether (3 × 5 ml). The combined organic extracts were dried ($MgSO_4$) then concentrated *in vacuo*. Analysis by ^{19}F NMR spectroscopy showed the presence of equal proportions of *syn*-**6e** and *anti*-**6e**.

Acknowledgements

The authors wish to thank the EPSRC and Pfizer Central Research for a CASE Award (to A. S. B.).

Notes and references

1 J. M. Percy, *Top. Curr. Chem.*, 1997, **193**, 131.
2 H. L. Sham, *ACS Symp. Ser.*, 1996, **639**, 184.
3 N. P. Peet, J. P. Burkhart, M. R. Angelastro, E. L. Giroux, S. Mehdi, P. Bey, M. Kolb, B. Neises and D. Schirlin, *J. Med. Chem.*, 1990, **33**, 394.
4 H. L. Sham, D. A. Betebenner, N. Wideburg, A. C. Saldivar, W. E. Kohlbrenner, A. Craigkennard, S. Vasavanonda, D. J. Kempf, J. J. Clement, J. E. Erickson, J. J. Plattner and D. W. Norbeck, *FEBS Lett.*, 1993, **329**, 144.
5 H. L. Sham, C. Zhao, K. C. Marsh, D. A. Betebenner, S. Q. Lin, E. McDonald, S. Vasavanonda, N. Wideburg, A. Saldivar, T. Robins, D. J. Kempf, J. J. Plattner and D. W. Norbeck, *Biochem. Biophys. Res. Comm.*, 1995, **211**, 159.
6 A. M. Silva, R. E. Cachau, H. L. Sham and J. W. Erickson, *J. Mol. Biol.*, 1996, **255**, 321.
7 R. P. Robinson and K. M. Donahue, *J. Org. Chem.*, 1992, **57**, 7309.
8 P. R. Bernstein, B. J. Kosmider, E. P. Vacek, C. A. Veale and B. C. Gomes, *Bioorg. Med. Chem. Lett.*, 1994, **4**, 2175.
9 A. M. Doherty, I. Sircar, B. E. Kornberg, J. Quin, R. T. Winters, J. S. Kaltenbronn, M. D. Taylor, B. L. Batley, S. R. Rapundalo, M. J. Ryan and C. A. Painchaud, *J. Med. Chem.*, 1992, **35**, 2.
10 M. Eda, A. Ashimori, F. Akahoshi, T. Yoshimura, Y. Inoue, C. Fukaya, M. Nakajima, H. Fukuyama, T. Imada and M. Nakamura, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 919.
11 M. Eda, A. Ashimori, F. Akahoshi, T. Yoshimura, Y. Inoue, C. Fukaya, M. Nakajima, H. Fukuyama, T. Imada and M. Nakamura, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 913.
12 K. M. Neder, S. A. French and S. P. F. Miller, *Tetrahedron*, 1994, **50**, 9847.
13 D. Schirlin, S. Baltzer, J. M. Altenburger, C. Tarnus and J. M. Remy, *Tetrahedron*, 1996, **52**, 305.
14 D. Schirlin, J. M. Rondeau, B. Podlogar, C. Tardif, C. Tarnus, V. Vandorsselaer and R. Farr, *ACS Symp. Ser.*, 1996, **639**, 169.
15 M. Yamana, T. Ishihara and T. Ando, *Tetrahedron Lett.*, 1983, **24**, 507.
16 For an application in the synthesis of a Kynureninase inhibitor, see J. P. Whitten, C. L. Barney, E. W. Huber, P. Bey and J. R. McCarthy, *Tetrahedron Lett.*, 1989, **30**, 3649.
17 For a recent electrogenerative approach, see K. Uneyama, K. Maeda, T. Kato and T. Katagiri, *Tetrahedron Lett.*, 1998, **39**, 3741.
18 M. Kuroboshi and T. Ishihara, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 428.
19 F. Q. Jin and Y. Y. Xu, *J. Fluorine Chem.*, 1993, **62**, 207.
20 T. Brigaud, P. Doussot and C. Portella, *J. Chem. Soc.*, *Chem. Commun.*, 1994, 2117.
21 T. Brigaud, O. Lefebvre, R. Plantierroyon and C. Portella, *Tetrahedron Lett.*, 1996, **37**, 6115.
22 O. Lefebvre, T. Brigaud and C. Portella, *Tetrahedron*, 1998, **54**, 5939.
23 Y. Kodama, H. Yamane, M. Okumura, M. Shiro and T. Taguchi, *Tetrahedron*, 1995, **51**, 12217.
24 J. A. Howarth, W. M. Owton, J. M. Percy and M. H. Rock, *Tetrahedron*, 1995, **51**, 10289.
25 J. A. Howarth, W. M. Owton and J. M. Percy, *J. Chem. Soc.*, *Chem. Commun.*, 1995, 757.
26 M. Schlosser, T. Jenny and Y. Guggisberg, *Synlett*, 1990, 704. For a similar application see S. T. Patel, J. M. Percy and R. D. Wilkes, *Tetrahedron*, 1995, **51**, 9201.
27 Described originally by Ingold (C. K. Ingold, *J. Chem. Soc.*, 1921, 119, 305), the effect is discussed more widely in the context of intramolecular reactions by Kirby (A. J. Kirby, *Adv. Phys. Org. Chem.*, 1980, **17**, 183). A number of examples exist in which the addition of a second alkyl group (creating a *gem*-pair) results in cyclisation rate increases of 10^2.
28 M. J. Eis, J. E. Wrobel and B. Ganem, *J. Am. Chem. Soc.*, 1984, **106**, 3693.
29 S. Sengupta and V. Snieckus, *J. Org. Chem.*, 1990, **55**, 5680. Transacylation could not be stopped in the desfluorosystem. Rapid (<5 s after the addition of carbonyl electrophile) quenching allowed methyl ketones to be isolated; more protracted reactions yielded aldol products. For a review of α-heteroatom substituted alk-1-enyllithium reagents, see M. Braun, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 430.
30 Crystal data for **3h**: $C_{20}H_{21}F_2NO_3$, $M = 361.38$, triclinic, $a = 7.7023(13)$, $b = 9.925(2)$, $c = 13.356(2)$ Å, $\alpha = 80.96(3)$, $\beta = 76.495(11)$, $\gamma = 70.767(13)°$, $U = 933.8(3)$ Å^3, $T = 150(2)$ K, space group $P\bar{1}$ (no. 2), $Z = 2$, μ(Mo-Kα) = 0.099 mm^{-1}, 3767 reflections measured, 2431 unique (R(int) = 0.0791) which were used in all calculations. The final $wR(F2)$ was 0.1054 (all data). Crystal data for **6e**: $C_{17}H_{22}F_2N_2O_8$, $M = 388.37$, monoclinic, $a = 7.7241(3)$, $b = 25.4363(8)$, $c = 10.1058(4)$ Å, $\beta = 103.0745(16)°$, $U = 1934.04(12)$ Å^3, $T = 150(2)$ K, space group $P2(1)/n$, $Z = 4$, μ(Mo-Kα) = 0.113 mm^{-1}, 24046 reflections measured, 3911 unique (R(int) = 0.0556) which were used in all calculations. The final $wR(F2)$ was 0.1512 (all data).
CCDC reference number 207/350. See http://www.rsc.org/suppdata/p1/1999/2525 for crystallographic files in .cif format.
31 There are few examples of 1,4-asymmetric induction in reactions of this type. Sengupta and Snieckus (ref. 29) reported a 4 : 1 excess of one diastereoisomeric series, though the 1,4-relationship (*syn* or *anti*) was not known. See also B. M. Trost and H. Urabe, *J. Org. Chem.*, 1990, **55**, 3982 for an example of 1,4-asymmetric induction in a Mukaiyama aldol reaction.

Paper 9/02966D