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Syntheses of selectively fluorinated cyclodecenones: the first deployment of the neutral oxy-Cope rearrangement in organofluorine chemistry

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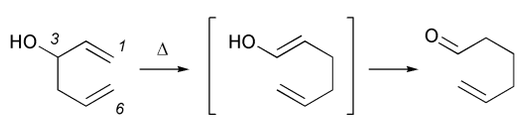
Metallated haloalkenes were used to open epoxides in moderate to good yield. The homoallylic alcohols obtained underwent Swern oxidation to afford three γ,γ-difluorinated β,γ-enones, which reacted with either vinyllithium, 2-lithio-2*H*-dihydropyran or another metallated haloalkene to afford substituted *trans*-1,2-divinylcyclohexanols of different degrees of stability. These intermediates underwent neutral thermal oxy-Cope rearrangements when heated in xylene in Ace® tubes. The first-formed enols ketonised without loss of HF to afford a range of cyclodecenones in moderate to good yield; X-ray crystallography was used extensively for product characterisation. All substrates rearranged more rapidly than a *cis*/*trans* mixture of 1,2-divinylcyclohexanols.

Introduction

In 1964, Berson and Jones recognized that the thermal (oxy-Cope) rearrangement of a 1,5-diene **1**, carrying an hydroxyl group at C-3, resulted in the formation of an enol **2** which underwent irreversible tautomerisation to a *δ*,ε-unsaturated carbonyl compound **3** (Scheme 1) driving the reaction from left to right.[1]



1 2 3

Scheme 1 Minimal framework for neutral oxy-Cope rearrangement.

The oxy-Cope rearrangement differs from the Cope rearrangement in several ways. Firstly, the oxy-Cope substrate can be prepared easily either by addition of a vinylmetal reagent to a β,γ-unsaturated carbonyl compound, or by the 1,2-addition of an allylmetal to an α,β-unsaturated carbonyl compound. Secondly, the rapid tautomerisation of the enol species to a carbonyl compound effectively removes the oxy-Cope product from the equilibrium and thus the rearrangement is irreversible.[2] This driving force can overcome the development of strain which impedes Cope rearrangements,[3] so, importantly for natural product synthesis, medium rings can be constructed easily. Furthermore, the product of the oxy-Cope rearrangement contains two remote and useful functional groups which may be manipulated or transformed further. The reaction can require high temperatures; although the overall driving force is significant, strong bonds must be broken in the rate determining step, and retro-ene reactions can compete, particularly with simple acyclic substrates. Hydroxyl group protection can block the fragmentation pathway,[4] but a simple change of reaction conditions affords the highest level of control.

Spectacular rate enhancements are available if the rearrangement is carried out *via* the conjugate base;[5] generation of the potassium alkoxide then allows rearrangement at temperatures as low as −78 °C, although temperatures at and above ambient are more common. The reaction leads directly to the formation of a reactive enolate which can be trapped, adding complexity or a convenient functionality for subsequent highly selective reactions. The *anionic* oxy-Cope has indeed become a tool of major strategic power[6] for the construction of complex cyclic systems.[7–12]

Although the conditions of the anionic oxy-Cope are milder, the methodology cannot be applied to certain classes of substrates. The alkoxide must be present as a loose ion pair (or may be more dissociated still) for the C3–C4 bond to be weakened significantly, so high nucleophilicity/basicity at oxygen is an inevitable consequence, and may lead to undesirable side reactions.

Our interest in the oxy-Cope rearrangement arose from the seminal observations of Dolbier and co-workers. Even a single fluorine atom affects the equilibrium position of the Cope rearrangement shown in Scheme 2,[13] though with a modest effect on $\Delta G^{\ddagger}$ compared to the isotopically labeled parent system described by Doering and co-workers.[14]

Progressive terminal difluorination of 1,5-hexadiene lowers $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ for the reaction, while $\Delta S^{\ddagger}$ increases. The $\Delta S^{\ddagger}$ values are consistent with passage through concerted chair transition states and the rearrangements of **4** and **5** are also effectively irreversible, the thermodynamic advantage of the products arising from the well known destabilising effect of CF_2 centres upon alkenes.[15] More complex situations arise with systems that are constrained to adopt boat conformations[16] to bring the diene termini together;[17] kinetic and computational insights are being developed to elucidate the role of biradical reaction pathways under these constraints.[18,19]

The oxy-Cope rearrangement involving fluorinated substrates has not, to our knowledge, been reported anywhere else.[20] We wished to know if we could use our alkenylmetal chemistry[21–23] to construct precursors to the oxy-Cope rearrangement easily and to determine qualitatively if the thermal neutral oxy-Cope rearrangement would be accelerated by the presence of one or two terminal CF_2 groups.[24–27] Because

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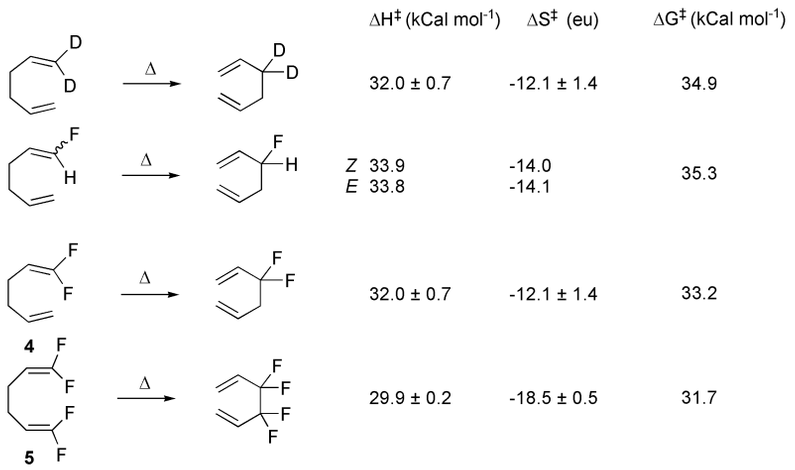
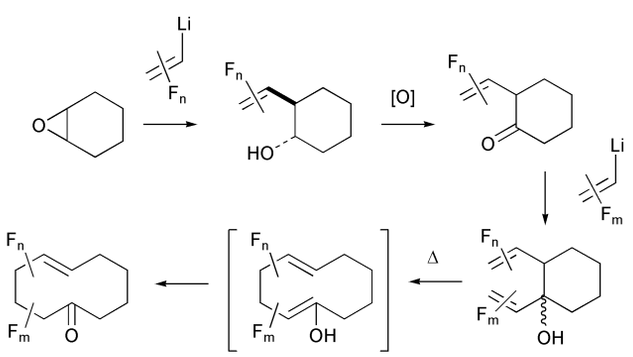


Scheme 2 Cope rearrangements reported by Doering,[14] and Dolbier[18] and co-workers.

difluoroalkenes are well known electrophiles and their exposure to potassium alkoxides would be expected to result in nucleophilic displacement of a fluoride ion,[28,29] we concentrated exclusively on the thermal neutral rearrangements.

As fluorinated cyclodecenones were unknown in the literature, we chose to investigate the ring expansion reaction of cyclohexyl templates; Scheme 3 shows the overall route. Nucleophilic ring opening of cyclohexene oxide, followed by Swern oxidation and the addition of a second vinylmetal would deliver divinylcyclohexanols suitable for rearrangement. Issues would arise with the relatively high basicity of the difluorovinyllithium reagents, the potential sensitivity of the β,γ-unsaturated ketone intermediate either during isolation or the addition of the second vinylmetal and the potential retro-ene side reaction. All of these issues are addressed in the manuscript.



Scheme 3 Proposed route to fluorinated cyclodecenones using metallated fluoroalkenes and the neutral oxy-Cope rearrangement.

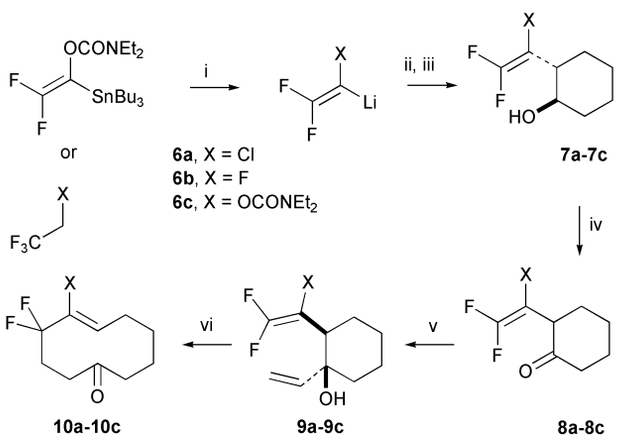
Results and discussion

Fluorinated alkenylmetals **6a** and **6b** were generated according to precedent directly from HCFC-133a[30] and HFC-134a[31,32] respectively; in the presence of freshly-distilled BF_3.etherate,[33] both ring opened cyclohexene oxide in good yield to afford the known homoallyl alcohols **7a** (69%) and **7b** (76%) (Scheme 4).

We generated known **6c** from the corresponding stannane[34] and used the same electrophile/Lewis acid combination to afford **7c** (64%). The use of the tin chemistry is undesirable but gave cleaner products than our original procedure. Coe *et al.* have described cyclisation reactions of homoallylic alcohols related to **7b**;[35] the stereochemistry of **7b** and the presence of the boron halide presumably prevent the cyclisation here.

Swern oxidation, selected because it is known to be mild, was carried out using a standard procedure[36] to deliver ketones **8a**–**8c** in moderate to good yield (Table 1).

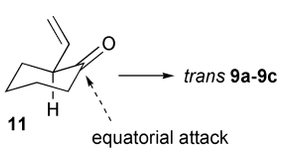
The former compounds were shown to be pure by capillary GC and characterised to HRMS while **8c** was obtained



Scheme 4 *Reagents and conditions:* i, *n*-BuLi, THF, −78 °C; ii, $BF_3.OEt_2$; iii, cyclohexene oxide; iv, DMSO, oxalyl chloride, DCM, then Et_3N, −78 °C; v, vinyllithium, THF, −78 °C then NH_4Cl; vi, Δ, xylene, Ace® tube (Table 1).

microanalytically pure. The ketones could be stored successfully without any trace of isomerisation. Formation of the dienolate or dienol followed by γ-protonation would move the alkenyl group into conjugation with the ketonic carbonyl while rehybridising the CF_2 centre from sp^2 to sp^3. We stirred **8c** with triethylamine in CD_2Cl_2 for one week but detected no change in the ^{19}F NMR spectrum, so these β,γ-unsaturated ketone intermediates are more robust than suspected.

Commercial vinylmagnesium bromide gave unacceptable results in subsequent attempts at vinylation and we were unable to obtain good yields of divinylcyclohexanols using the Gadwood method[37] for the preparation *in situ* of vinyllithium from vinyl bromide. However, transmetallation of vinyltributyltin with *n*-butyllithium followed by the addition of **8a**–**8c** at −78 °C delivered **9a**–**9c** in good to moderate yields. These intermediates were very difficult to purify fully; traces of tetraalkyltin compounds adhered through column chromatography but clean ^{19}F NMR spectra were obtained. These suggested strongly that only one of the two possible diastereoisomers had been formed (as a racemic modification). The sense of attack predicted (on **11** in Scheme 5) would lead to the *trans*-dienols **9a**–**c** based upon the known tendency of 2-methyl-



Scheme 5 Trajectory of nucleophilic attack upon vinylcyclohexanol predicted by Ashby.[38]

Table 1 Synthesis of first generation cyclodecenones

Alcohol	Yield(%)	Ketone	Yield(%)	Dienol	Yield(%)[a]	Enone	*T*/°C	*t*/hours	Yield(%)
7a	69	**8a**	83	**9a**	78	**10a**	125	8	67
7b	76	**8b**	72	**9b**	76	**10b**	125	46	72
7c	64	**8c**	52	**9c**	52	**10c**	125	32	68

[a] Estimated yield; see text.

Table 2 Syntheses of cyclodecenones incorporating dihydropyranyl units

	Ketone	Dienol	Yield(%)[a]	Enone	*T*/°C	*t*/hours	Yield(%)
	8a	**13a**	97	**14a**	150	3	65
	8b	**13b**	78	**14b**	140	17	84
	8c	**13c**	100	**14c**	155	9	62

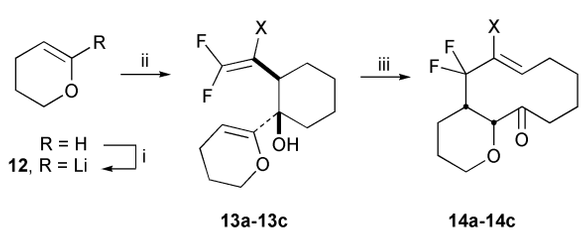
[a] Estimated yield; see text.

cyclohexanone to undergo equatorial attack with phenyllithium.[38]

The first rearrangements were carried out in xylene in Ace® tubes at 125 °C (also Table 1), with the periodic withdrawal of aliquots for monitoring by ^{19}F NMR. In all cases, the terminal vinylic ^{19}F signals (−88 to −122 ppm, $^{2}J_{F-F}$ 40–80 Hz) disappeared as the AB systems ($^{2}J_{F-F}$ ~250 Hz) arising from the rehybridised CF_2 centre developed; the fluorine atoms are diastereotopic because the cyclodecenone ring is chiral. All reactions were driven to completion before isolation of the crystalline products **10a**–**c** by evaporation of the xylene and column chromatography. The purity of the products was shown by GC but we were only able to obtain satisfactory microanalysis in one instance (**10c**) despite repeated attempts. It is likely that accurate combustion analysis was prevented by the presence of traces of tetrabutyltin which could not be fully removed. All three cyclodecenones invariably crystallised as fine needles preventing the collection of any X-ray data.

The alkene stereochemistry can be assigned in the case of **10b**; in the ^{1}H NMR spectrum, the alkenyl proton shows a large (33.7 Hz) coupling consistent only with the transoid H–C=C–F dihedral (the *Z*-alkene). The same geometry was inferred for **10a** and **10c**. There was modest broadening in the ^{19}F NMR spectrum and in the methylene region of the ^{1}H NMR spectrum of **10a**, presumably because of fluxional movements of the ring. We did not carry out VT NMR studies as there seemed little information to gain in these instances.

We were also able to add metallated dihydropyran **12** to **8a**–**8c** to afford three very unstable dienols **13a**–**13c** (Scheme 6).



Scheme 6 *Reagents and conditions*: i, *t*-BuLi, THP, 0 °C; ii, THF, cool to −78 °C then **8a**–**8c**; iii, Δ, xylene, Ace® tube (Table 2).

Dihydropyran was metallated in tetrahydropyran using the method of Meyers.[39] The adducts showed very clean ^{19}F NMR spectra, consistent with the formation of a single (racemic) diastereoisomer but resisted all attempts at purification, decomposing rapidly on silica gel. However, the crude products rearranged smoothly in xylene in Ace® tubes at 150 °C to afford crystalline products **14a**–**14c** in good yield (Table 2).

All afforded satisfactory microanalyses and in two cases, sufficiently good crystals could be grown for X-ray crystallographic analysis after vapour diffusion recrystallisation from dichloromethane (hexane precipitant).

Fig. 1 shows the X-ray crystal structure of **14b**; the alkene geometry can be seen clearly (the corresponding $^{3}J_{H-F}$ coupling is 34.8 Hz, supporting our assignment for **10b**), together with the *cis*-junction between the tetrahydropyranyl and cyclodecenone rings.

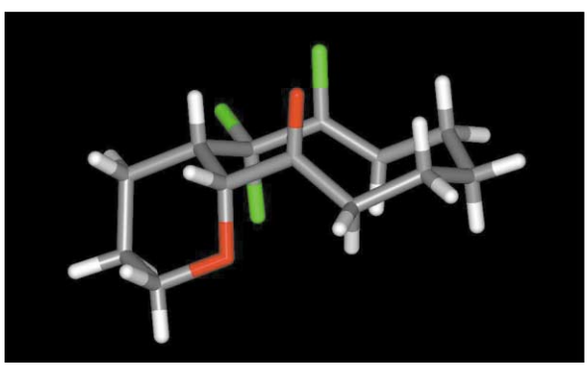


Fig. 1 X-Ray crystal structure of **14b**.

One of the fluorine atoms shows a large $^{3}J_{H-F}$ splitting to the H-10 proton (31.6 Hz in **14b**, 30.9 Hz in **14c**) consistent with the close to antiperiplanar dihedral relationship in both the crystal structure (175°) and the solution conformer. The alkene shows some twisting out of plane (4.9°) which is not unexpected for a transoid alkene in a 10-membered ring. The structure for **14a** showed essentially the same features.

Extensive 2D NMR analysis was undertaken to allow the assignment of the rather complex, though well-dispersed, ^{1}H NMR spectrum of **14b**. In the COSY spectrum (Fig. 2), almost all the possible correlations are visible. The alkene proton H-7 is clearly coupled to both H-6 protons and connectivity can be demonstrated around the ring into the H-3 methylene protons. The chemical shifts of the two H-3 protons differ by almost 1 ppm which is surprising. One possible explanation could be a transannular interaction with the alkenyl group which selectively and strongly deshields one proton in the methylene pair. The two H-13 protons next to the oxygen of the tetrahydropyranyl ring provide a convenient place to begin tracing the connectivity through the fused ring.

Confirmation of the assignment and support for the congruence between solid state and solution conformations came from an NOE experiment (GOESY[40]). Examination of the crystal structure suggests that the H-7 alkene proton lies close to one of each of the H-5 (at 2.55 Å) and H-3 (at 2.57 Å) methylene protons, which are mutually close (at 2.56 Å). The observed transannular transfer of magnetisation from H-7 to H-3 is

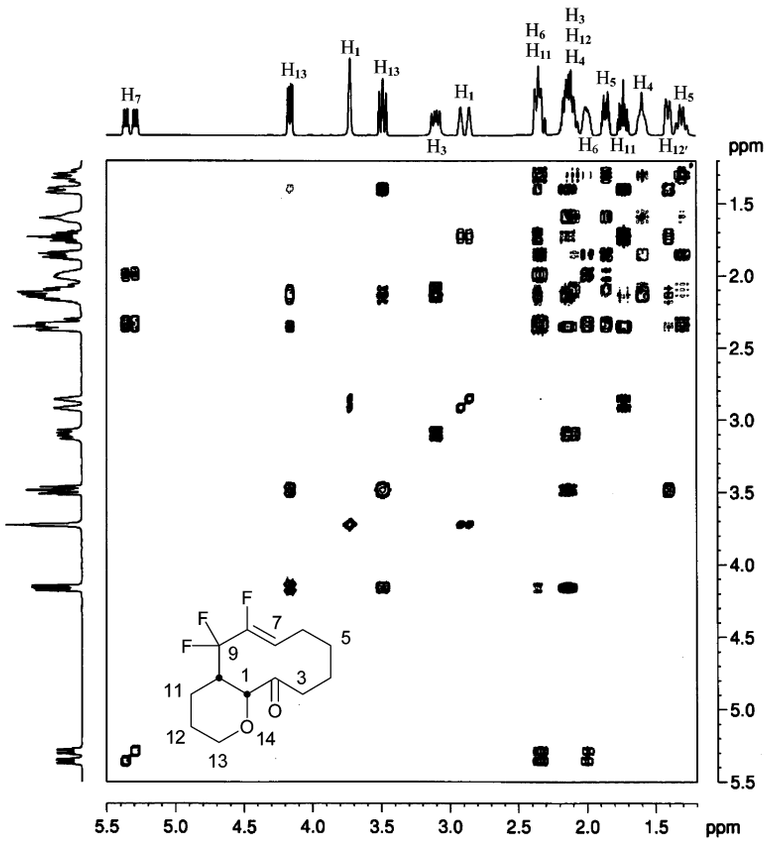
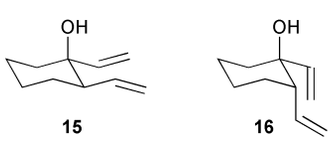


Fig. 2 500 MHz ^{1}H–^{1}H gradient COSY NMR spectrum for **14b**.

therefore to be expected and the H-7/H-5 and H-5/H-3 magnetisation transfers are consistent with these predictions. Sharp NMR spectra were obtained, consistent with lower degrees of ring mobility for **14a**–**c**.

These results were interesting because they showed that we could introduce further ring architecture and additional functionality *via* the second vinylmetal reagent. They also confirmed our ideas about the sense of stereoselection in the enone addition reaction; the most obvious explanation for the various stereochemical outcomes in **14a**–**14c** involves the rearrangement of a *trans*-dienol through a chair transition state **15**. However, **16**, which also leads to the correct alkene geometry cannot be excluded.

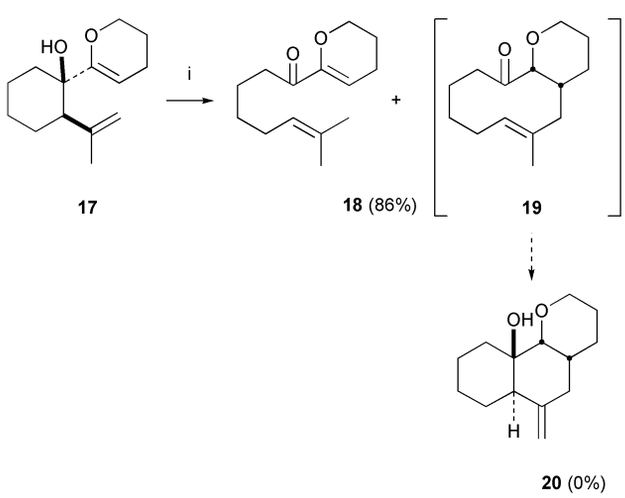


15 **16**

The results differ significantly from those described by Barriault and co-workers (Scheme 7).[41] Retro-ene reaction (a significant side reaction for simple acyclic species) dominates here. Vigorous heating of **17** in a sealed tube in toluene afforded **18** alone, and none of the expected **20** (a strain-relieving transannular-ene product from first-formed oxy-Cope educt **19**). Our outcome presumably arises from the considerably greater ease with which these systems (**9**,**13**) rearrange so that the fragmentation in Scheme 7 which leads to **18** does not compete with the neutral oxy-Cope.

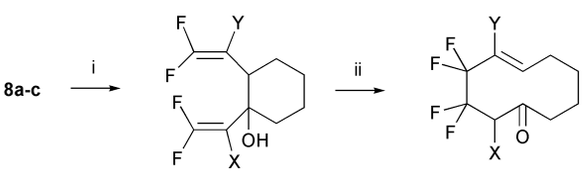
Further variation in the second alkenylmetal fragment was sought through the reactions of **6a** with **8b** and **8c**, to afford **21b** (46%) and **21c** (62%), and **6b** with **8a**–**8c** to afford **22a** (57% estimated yield), **22b** (62% estimated yield) and **22c** (56%) (Scheme 8).

These were very difficult compounds to purify fully, though we were satisfied as to their identity from multinuclear NMR. Although we could detect only a single diastereoisomer for



17 **18** (86%) **19** **20** (0%)

Scheme 7 *Reagents and conditions*: i, 180 °C, PhMe.[41]



21b, X = Cl, Y = F
21c, X = Cl, Y = $OCONEt_2$
22a, X = F, Y = Cl
22b, X = F, Y = F
22c, X = F, Y = $OCONEt_2$

23b, X = Cl, Y = F
23c, X = Cl, Y = $OCONEt_2$
24a, X = F, Y = Cl
24b, X = F, Y = F
24c, X = F, Y = $OCONEt_2$

Scheme 8 Reagents and conditions: i, **6a** (for **21b**,**c**) or **6b** (for **22a**–**c**), THF, −78 °C; ii, Δ, xylene, Ace® tube (see Table 3).

21b and **21c**, separable diastereoisomers were obtained for **22a** (2.3 : 1) and **22c** (1.8 : 1). We have not been able to propose the identity of the major stereoisomer by comparing ^{13}C and ^{19}F

Table 3 Preparation of more highly fluorinated cyclodecenones

Nucleophile	Ketone	Dienol	Yield(%)[a]	Enone	*T*/°C	*t*/hours	Yield(%)
6a	**8b**	**21b**	46	**23b**	110	40	69
6a	**8c**	**21c**	62	**23c**	150	2	71
6b	**8a**	**22a**	57	**24a**	150	1.75	73
6b	**8b**	**22b**	62	**24b**	100	47	54
6b	**8c**	**22c**	56	**24c**	100	30	66

[a] Estimated yield.

NMR chemical shifts, nor can we explain why a second stereoisomer should be formed in these cases alone. The NMR spectra of **21a** and **22b** require comment; for **22b**, most of the ^{13}C and ^{1}H NMR spectra were badly overlapped, making the identification of discrete multiplets impossible, but with integration of the ^{19}F NMR spectra, the two diastereoisomers could be identified clearly with discrete signals for 5 of the 6 different fluorine atoms in each diastereoisomer. The signals from the sixth fluorines in each diastereoisomer were overlapped so that the signal appeared as a doublet of triplets. We also note that a signal from the other internal fluorine in the minor diastereoisomer (−176.5 ppm, ddt, 111.6, 34.0, 5.0 Hz) contains a surprisingly large coupling to a proton. One 34.0 Hz splitting arises from a *cis*-coupling to another alkenyl fluorine but the third splitting must arise from a $^{3}J_{H-F}$ coupling to the allylic proton in **22b**. The origin of this splitting is far from clear, as similar interactions in **8b** result in much smaller coupling constants (7.6 Hz in **8b**). However, in **22a**, which has a simpler ^{1}H NMR spectrum, the putative $^{3}J_{H-F}$ coupling can be identified in the ^{19}F (31.8 Hz) and ^{1}H NMR (31.6 Hz) spectra, suggesting strongly that it represents a genuinely large allylic H–F coupling. The putative $^{3}J_{H-F}$ coupling also appears clearly in the ^{19}F NMR spectrum of **7b**, but is obscured by overlap in the ^{1}H NMR spectrum.

All five compounds underwent oxy-Cope rearrangement successfully (Table 3) to afford crystalline solids from which we obtained X-ray crystal structures as unambiguous proof of structure. Only *Z*-configured alkenes were obtained, although it is possible that we simply did not detect a second product in the rather complex ^{19}F NMR spectra of the crude material.

We were concerned that the first formed enols from the oxy-Cope would lose HF to form the conjugated enones. We saw no evidence of such products but we were careful to neutralise the tube contents before working with them. When mutually superimposed, the crystal structures for **23c** and **24c** show a high degree of congruence but differ significantly in the location of the C–Cl and C–F bonds (Fig. 3a).

The same issue arose with **23b** and **24a** (Fig. 3b). In both cases, the Cl–C–C–O dihedral angle is considerably closer to 90° (79.1°) than the H–C–C–O angle in the fluorocongener (64.3°). The expansion of this angle causes some distortion to the dihedral angles around the adjacent methylene groups. From studies of 2-halocyclohexanones,[42,43] different halogen stereoelectronic effects have been noted. The interaction between the C–X σ bond and the C=O π* orbital favours axial disposition of the C–Cl bond but is much weaker for the C–F bond because of the opposition between the high electronegativity of the fluorine atom and the X^{+} character required (Fig. 4).

The approach of the Cl–C–C–O dihedral angle towards 90° in these systems may reflect this preference, at least in the solid state. The antiparallel arrangement between the C–F and C=O bonds in **24a** and **24c** allows dipolar minimisation as in the calculated minimum energy conformation of *N*-methyl fluoroacetamide.[44] Unfortunately, the signals for the H-2 protons in the ^{1}H NMR spectra of **23b** and **23c** are too complex for the solution Cl–C–C=O dihedral to be estimated.

To make qualitative reactivity comparisons between the various systems, we prepared 1,2-divinylcyclohexanol **25** as a

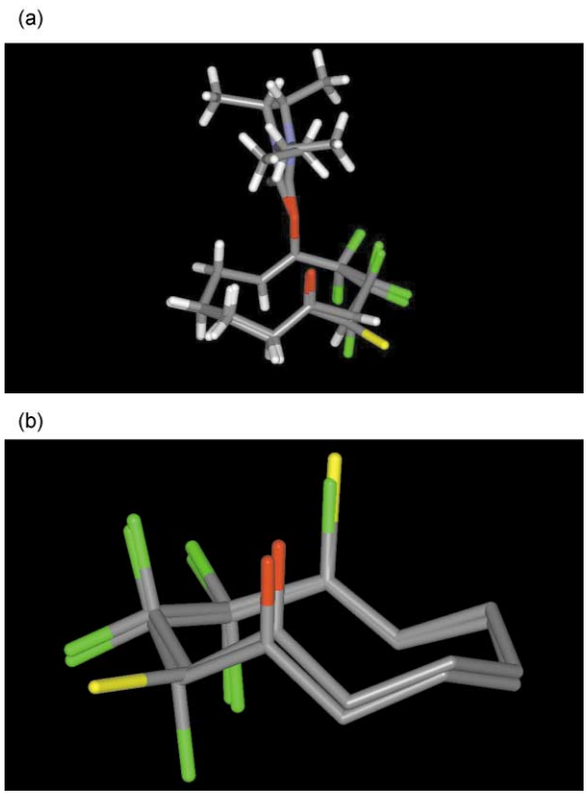


Fig. 3 (a) Superimposed X-ray crystal structures for **23c** and **24c** (fluorine atoms in green, chlorine atom in yellow). (b) Superimposed X-ray crystal structures for **23b** and **24a** (fluorine atoms in green, chlorine atoms in yellow, hydrogens hidden for clarity).

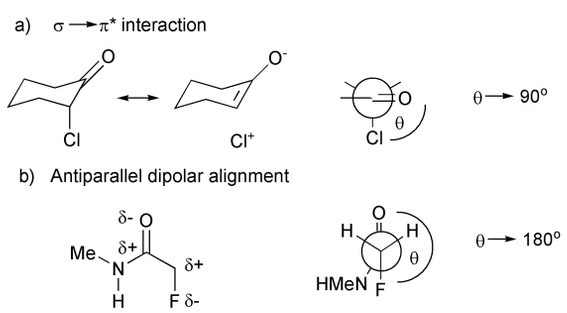
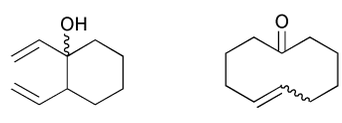


Fig. 4 Stereoelectronic effects of the conformations of α-halocarbonyl compounds.

cis/*trans* mixture following the procedure of Holt.[45] Choosing 150 °C as the rearrangement temperature, we found that **11a**, **14a** and **24a** all rearranged completely within 3 hours, whereas **25** was recovered unchanged.



25 **26**

We were able to form **26** but only after heating for 24 hours at 225 °C, in contrast to the literature observation.[46] Indeed all the fluorinated systems described in this manuscript rearrange more rapidly than **25**, consistent with the effects of CF_2 centres upon the Cope rearrangement and indicating that the thermal neutral oxy-Cope rearrangement could be an extremely valuable tool for the construction of cyclic molecules which are selectively fluorinated to different degrees. Furthermore, the addition of fluorinated and non-fluorinated vinylmetals to γ,γ-difluorinated vinylcyclohexenones appears to be a flexible, reliable and robust method of precursor synthesis. Further work will attempt to probe the importance of diradical character in these rearrangements.

Experimental

NMR spectra were recorded on a Bruker AC-300 spectrometer. ^{19}F-NMR (300 MHz) spectra were referenced to fluorotrichloromethane as the internal standard. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were referenced to residual chloroform at 7.26 ppm. ^{13}C-NMR spectra were recorded using the JMOD or PENDANT pulse sequences. 500 MHz ^{1}H-COSY and GOESY NMR spectra were recorded on a Bruker DRX-500 spectrometer. 400 MHz ^{19}F, ^{1}H-COSY and HSQC NMR spectra were recorded on a Bruker AMX-400 spectrometer. *J* values are reported in Hz. Low and high resolution mass analyses 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. A Micromass LCT mass spectrometer was also used for both low resolution (ES-TOF) mass spectra (using methanol mobile phase) and HRMS measurements (using a lockmass incorporated into the mobile phase). All mass data containing Cl refer to ^{35}Cl isotope.

Precoated aluminium-backed silica plates were supplied by E. Merck, A. G. Darmstadt, Germany. (silica gel 60 F_{254}, thickness 0.2 mm, Art.no. 5554). Anisaldehyde, potassium permanganate staining or ultraviolet light were employed for visualisation. Column chromatography was performed using silica gel (E. Merk, A. G. Kieselgel, Art. 9385). Infra red spectra were obtained from a Perkin Elmer 1600 series FTIR spectrometer, in the region 4000–500 cm^{-1}. Elemental analyses were performed at the University of North London. X-ray crystallographic analyses were performed, by the EPSRC X-ray crystallography service, at the University of Southampton.

Tetrahydrofuran was dried by refluxing with sodium metal and benzophenone under dry nitrogen, until a deep purple colour persisted. The solvent was then collected by syringe as required. Diethylether, hexane, toluene and DCM were dried by refluxing with calcium hydride under dry nitrogen then distilled and collected by syringe as required. HCFC-133a and HFC-134a were supplied by Fluorochem and used as received. Alcohol **7a** was prepared according to our published procedure.[30] 1-(*N*,*N*-diethylcarbamoyloxy)-2,2,2-trifluoroethane and 1-(*N*,*N*-diethyl-carbamoyloxy)-2,2-difluoroethenyl tributylstannane were prepared according to our published procedure.[34] Cyclohexene oxide, oxalyl chloride, dimethylsulfoxide, triethylamine and boron trifluoride etherate were purchased from the Aldrich Chemical Company and were freshly distilled before the reactions. *t*-Butyllithium and *n*-butyllithium were titrated using 1,3-diphenyl-2-propanone-*p*-toluene sulfonylhydrazone according to the procedure of Lipton and co-workers.[47] Sealed tube reactions were performed in Ace® pressure tubes (8648B). Light petroleum refers to the fraction boiling in the range 40–60 °C.

Crystallographic experimental †

Crystallographic data for **14a** were published in our communication of this work.[20] Other data appear after the preparative details for the compound.

trans-2-(1′-Chloro-2′,2′-difluoroethenyl)-cyclohexan-1-ol 7a

Alcohol **7a** was prepared according to our published procedure.[30]

trans-2-(1′,2′,2′-Trifluoroethenyl)-cyclohexan-1-ol 7b

A 2-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; THF (2.5 ml) was added to the evacuated flask which was sealed. 1,2,2,2-Tetrafluoroethane (50 ml, 2.1 mmol [V_m @ 20 °C = 24043 ml $mmol^{-1}$ *vs.* @ 0 °C (STP) = 22402 ml mol^{-1}.]) was used, then *n*-butyllithium (1.7 ml of a 1.8 M solution in hexane, 3.0 mmol) was added and the mixture was left to stir for 45 minutes at −78 °C. Work-up in the usual manner afforded an orange oil (0.29 g). Purification by column chromatography (10% diethyl ether in petroleum ether) gave **7b** (0.20 g, 76%) as a yellow oil; R_f (10% diethyl ether in petroleum ether) 0.10; ν_{max} (film)/cm^{-1} 3404 (OH), 1794, 1729 (C=C); δ_H (300 MHz, $CDCl_3$) 3.56–3.40 (1H, m, H-1), 3.30 (1H, s, O*H*), 2.28–1.87 (2H, m, H-2, H-6), 1.80–1.55 (3H, m, –CH_2), 1.52–1.33 (1H, m, –CH_2), 1.31–1.05 (3H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 153.9 (dd, $^1J_{C-F}$ 272.4, $^2J_{C-F}$ 47.5), 129.4 (ddd, $^1J_{C-F}$ 235.1, $^2J_{C-F}$ 52.0, $^2J_{C-F}$ 14.1), 69.0, 43.8 (d, $^2J_{C-F}$ 20.9), 34.2, 25.1, 25.0, 24.0; δ_F (282 MHz, $CDCl_3$) −105.2 (1F, dd, ^2J 89.0, $^3J_{cis}$ 31.8), −124.9 (1F, dd, $^3J_{trans}$ 113.2, ^2J 89.0), −185.0 (1F, d, $^3J_{trans}$ 113.2, $^3J_{cis}$ 31.8, $^3J_{H-F}$ 31.8); *m*/*z* (CI) 198 (80%, M + $[NH_4]^+$), 134 (100%). The data were in agreement with those reported by Dubuffet *et al.*[33]

2-[1′-(*N*,*N*-Diethylcarbamoyloxy)-2′,2′-difluoroethenyl]-cyclohexan-1-ol 7c

A solution of 1-(*N*,*N*-diethyl-carbamoyloxy)-2,2-difluoroethenyl tributylstannane[34] (0.61 g, 2 mmol) in dry THF (6 ml) was cooled to −78 °C. *n*-Butyllithium (1.21 ml of a 1.78 M solution in hexane) was added to the solution over 10 minutes and the mixture became yellow during this time. The suspension was stirred at −78 °C for 45 minutes, then boron trifluoride etherate (0.50 ml, 4 mmol) was added in one portion, followed by the addition of cyclohexene oxide (0.20 ml, 2.0 mmol). The solution was stirred for a further two hours at −78 °C before being allowed to warm slowly. At −30 °C, saturated aqueous ammonium chloride solution (25 ml) was added. The aqueous layer was extracted with ether (3 × 15 ml) and the combined organic extracts were washed with saturated sodium bicarbonate solution (2 × 15 ml), dried with magnesium sulfate and evaporated *in vacuo* to leave a yellow oil. Purification by flash chromatography (15% ethyl acetate in hexane) yielded the alcohol **7c** (0.354 g, 64%) as a pale yellow oil; R_f (15% ethyl acetate in hexane) 0.35; δ_H (300 MHz, $CDCl_3$) 4.25 (1H, d, $^3J_{H-H}$ 2.9, H-1), 3.40–3.20 (5H, m, NCH_2CH$_3$, O*H*), 2.30–2.15 (1H, m, H-2), 2.12–1.98 (1H, m, –CH_2), 1.82–1.61 (3H, m, –CH_2), 1.45–1.10 (10H, m, –CH_2, NCH$_2$CH_3); δ_C (75 MHz, $CDCl_3$) 155.2 (dd, $^1J_{C-F}$ 288.8, $^1J_{C-F}$ 282.6), 154.5, 112.1 (dd, $^2J_{C-F}$ 43.5, $^2J_{C-F}$ 14.1), 70.0, 68.0, 42.0, 39.0, 28.0, 26.0, 24.0 18.0; δ_F (282 MHz, $CDCl_3$) −96.8 (1F, d, $^2J_{F-F}$ 59.8), −110.2 (1F, d, $^2J_{F-F}$ 59.8); *m*/*z* (CI) 278 (100%, M + H)$^+$, 260 (7%, M − OH), 100 (30%, $CONEt_2$) in agreement with literature data.[34]

2-(1′-Chloro-2′,2′-difluoroethenyl)-cyclohexan-1-one 8a

A solution of dimethyl sulfoxide (5.8 ml, 28 mmol) in DCM (25 ml, 4.8M) was added dropwise to a stirred solution of oxalyl chloride (1.21 ml, 12.7 mmol) in DCM (14 ml) at −78 °C. The mixture was stirred for 30 minutes at −78 °C then **7a** (1.05 g, 5.86 mmol) was added over ten minutes at −78 °C as a solution in DMSO/DCM (6 ml, 1 : 1.9). The reaction mixture was stirred for a further 60 minutes at −78 °C. Triethylamine

† CCDC reference numbers 216343 and 219860–219864. See http://www.rsc.org/suppdata/ob/b3/b311261f/ for crystallographic data in .cif or other electronic format.

(4.06 ml, 29 mmol) was added slowly and the yellow solution was left stirring at −78 °C for one hour further and allowed to warm to −30 °C. The reaction was quenched at this temperature after 30 minutes with saturated aqueous bicarbonate solution (50 ml). The aqueous layer was extracted with dichloromethane (3 × 10 ml). The combined organic extracts were washed with brine (25 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to leave a yellow oil (1.15 g). Purification by flash chromatography (10% diethyl ether in petroleum ether) yielded **8a** (0.945 g, 83%, 99% by GC) as a yellow oil; R_f (10% diethyl ether in petroleum ether) 0.5; ν_{max} (film)/cm^{-1} 1748 (C=C), 1717 (C=O); δ_H (300 MHz, $CDCl_3$) 3.40 (1H, dd, $^3J_{H-H}$ 11.8, $^3J_{H-H}$ 5.5, H-2), 2.53 (1H, d, $^3J_{H-H}$ 14.3, H-6), 2.40–2.20 (1H, m, H-6), 2.18–1.92 (4H, m, –CH_2), 1.80–1.61 (2H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 206.1, 154.5 (t, $^1J_{C-F}$ 287.7), 90.7 (dd, $^2J_{C-F}$ 36.5, $^2J_{C-F}$ 38.0), 50.8, 41.7, 31.8, 27.1, 24.6; δ_F (282 MHz, $CDCl_3$) −87.3 (1F, d, $^2J_{F-F}$ 42.6), −92.3 (1F, d, $^2J_{F-F}$ 42.6); [HRMS (CI, [M + NH_4]$^+$) Found 194.03122. Calc. for $C_8H_9ClOF_2$ 194.03099]; *m/z* 194 (15 %, M$^+$), 159 (50 %, M − Cl), 39 (100%).

2-(1′,2′,2′-Trifluoroethenyl)-cyclohexan-1-one 8b

Ketone **8b** was prepared from **7b**, using the procedure for **8a** on the same scale. Flash chromatography (10% ethyl ether in petroleum ether) yielded **8b** (0.756 g, 72%, 98% by GC) as a yellow oil; R_f (10% ethyl ether in petroleum ether) 0.25; ν_{max} (film)/cm^{-1} 1797 (C=C), 1721 (C=O); δ_H (300 MHz; $CDCl_3$) 3.30–3.10 (1H, m, H-2), 2.45–2.35 (1H, m, H-6a), 2.30–2.20 (1H, m, H-6b), 2.15–1.95 (2H, m, H-3), 1.95–1.50 (4H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 205.0, 154.1 (ddd, $^1J_{C-F}$ 287.6, 273.5, $^2J_{C-F}$ 45.8), 126.5 (ddd, $^1J_{C-F}$ 236.2, $^2J_{C-F}$ 52.6, $^2J_{C-F}$ 16.9), 40.8 (d, $^2J_{C-F}$ 20.9), 40.5, 30.3, 29.8, 27.0; δ_F (282 MHz, $CDCl_3$) −104.1 (1F, dd, $^2J_{F-F}$ 85.2, $^3J^{cis}_{F-F}$ 33.7), −123.2 (1F, ddd, $^3J^{trans}_{F-F}$ 114.0, $^2J_{F-F}$ 85.2, $^4J_{F-H}$ 2.5), −180.4 (1F, ddd, $^3J^{trans}_{F-F}$ 114.0, $^3J^{cis}_{F-F}$ 33.7, $^3J_{F-H}$ 7.6); [HRMS (CI, M + [NH_4]$^+$) Found 196.0950. Calc. for $C_8H_{13}F_3NO$ 196.0949, found 196.0950]; *m/z* (CI) 196 (100%, M + [NH_4]$^+$), 178 (20, M$^+$), 158 (50, M − HF).

2-[1′-(*N*,*N*-Diethylcarbamoyloxy)-2′,2′-difluoroethenyl]-cyclohexan-1-one 8c

Ketone **8c** was prepared from **7c**, using the procedure for **8a** on the same scale. Flash chromatography (10% ethyl ether in petroleum ether) yielded **8c** (0.838 g, 52%) as a yellow oil; R_f (10% ethyl ether in petroleum ether) 0.2; (Found: C, 56.70; H, 7.00; N, 5.00. Calc. For $C_{13}H_{19}O_3F_2N$: C, 56.73; H, 6.91; N 5.09%); ν_{max} (film)/cm^{-1} 1777 (C=C), 1724 (C=O); δ_H (300 MHz; $CDCl_3$) 3.40–3.28 (5H, m, H-2, 2 × NCH_2), 2.58–2.45 (1H, m, H-6), 2.40–2.22 (2H, m, –CH_2), 2.15–1.82 (2H, m, –CH_2), 1.80–1.56 (3H, m, –CH_2), 1.20–1.05 (6H, m, CH_3); δ_C (75 MHz; $CDCl_3$) 205.9, 152.2 (dd, $^1J_{C-F}$ 289.4, $^1J_{C-F}$ 281.4), 152.9, 109.2 (dd, $^2J_{C-F}$ 44.6, $^2J_{C-F}$ 15.2), 50.2, 41.9, 41.8, 29.0, 26.0, 24.6, 13.8; δ_F (282 MHz; $CDCl_3$) −95.8 (1F, d, $^2J_{F-F}$ 61.0), −108.2 (1F, d, $^2J_{F-F}$ 61.0); *m/z* (CI) 275 (4%, M$^+$), 260 (M − Me), 100 (100%, $CONEt_2$).

trans-1-Ethenyl-2-(1′-chloro-2′,2′-difluoroethenyl)-cyclohexan-1-ol 9a

n-Butyllithium (0.53 ml of a 1.9 M solution in hexane, 1.0 mmol) was added dropwise to a stirred solution of 1-(tributylstannyl)ethene (0.316 g, 1.0 mmol) in THF (0.5 ml) at −78 °C. The mixture was left stirring for one hour at the same temperature then **8a** (0.194 g, 1.0 mmol) was added. The solution was allowed to warm to −40 °C after one hour and left for 30 minutes further at this temperature. The mixture was then quenched with saturated aqueous ammonium chloride solution (20 ml). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with saturated sodium bicarbonate solution (2 × 10 ml), brine (2 × 10 ml), dried (magnesium sulfate), filtered and concentrated *in vacuo.* Column chromatography (10% diethyl ether in light petroleum) afforded dienol **9a** (assumed *trans*) (0.151 g, 78%) as a clear oil; R_f (10% diethyl ether in light petroleum) 0.35; δ_H (300 MHz, $CDCl_3$) 5.81 (1H, dd, $^3J_{H-H}$ 16.9, $^3J_{H-H}$ 10.7, H-1′), 5.32 (1H, d, $^3J_{H-H}$ 16.9, H-2′), 5.12 (1H, d, $^3J_{H-H}$ 10.7, H-2′), 2.52 (1H, s, O*H*), 2.16–1.99 (1H, m, H-2), 1.90–1.20 (8H, m, –CH_2); δ_F (282 MHz, $CDCl_3$) −88.7 (1F, d, $^2J_{F-F}$ 43.2), −91.2 (1F, d, $^2J_{F-F}$ 43.2); *m/z* (CI) 240 (18%, M + [NH_4]$^+$), 222 (90%, M$^+$). The compound was not characterised more fully because it contained traces of tetrabutyltin which could not be removed.

trans-1-Ethenyl-2-(1′,2′,2′-trifluoroethenyl)-cyclohexan-1-ol 9b

Dienol **9b** was prepared using the same procedure as for **9a** from **8b** (0.178 g, 1.0 mmol) and 1-(tributylstannyl)ethene (0.316 g, 1.0 mmol). Work up in the usual manner afforded a yellow oil (0.29 g) which was purified by column chromatography (10% diethyl ether in light petroleum) to afford dienol **9b** (assumed *trans*) (0.14 g, 68%) as a colourless oil; R_f, (10% diethyl ether in petroleum ether) 0.1; ν_{max} (film)/cm^{-1} 3500 (OH), 1786, 1756, 1716 (C=C); δ_H (300 MHz, $CDCl_3$) 5.82 (1H, dd, $^3J_{H-H}$ 16.7, $^3J_{H-H}$ 10.7, H-1″), 5.31 (1H, d, $^3J_{H-H}$ 16.7, H-2″), 5.11 (1H, d, $^3J_{H-H}$ 10.7, H-2″), 2.42–2.30 (1H, m, H-2), 2.12–1.90 (1H, m, O*H*), 1.89–1.10 (8H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 153.9 (ddd, $^1J_{C-F}$ 287.6, $^1J_{C-F}$ 272.4, $^2J_{C-F}$ 48.0), 144.0, 130.2 (ddd, $^1J_{C-F}$ 236.8, $^2J_{C-F}$ 52.0, $^2J_{C-F}$ 14.7), 113.0, 58.0, 42.8 (dd, $^2J_{C-F}$ 18.6, $^3J_{C-F}$ 2.8), 38.5, 26.0, 24.5, 21.0; δ_F (282 MHz, $CDCl_3$) −105.5 (1F, dd, $^2J_{F-F}$ 85.2, $^3J^{cis}_{F-F}$ 31.8), −122.2 (1F, dd, $^2J_{F-F}$ 85.2, $^3J^{trans}_{F-F}$ 112.5, $^4J_{F-H}$ 3.8), −179.1 (1F, dt, $^3J^{trans}_{F-F}$ 112.5, $^3J^{cis}_{F-F}$31.8); *m/z* (CI) 224 (13%, M+[NH_4]$^+$), 206 (90%, M$^+$). The compound was not characterised more fully because it contained traces of tetrabutyltin which could not be removed.

trans-1-Ethenyl-2-(1′-[*N*, *N*-diethylcarbamoyloxy]-2′-difluoroethenyl)-cyclohexan-1-ol 9c

Dienol **9c** was prepared from **8c** (0.275 g, 1.0 mmol) and 1-(tributylstannyl)ethene (0.316 g, 1.0 mmol) as for **9c** except for the fact that the temperature was maintained at −78 °C for four hours after the addition of *n*-butyllithium to the stannane. The reaction was quenched at −78 °C with saturated ammonium chloride solution (20 ml). Work up in the usual manner followed by column chromatography (10% diethyl ether in light petroleum) afforded dienol **9c** (assumed *trans*) (0.206 g, 68%) as a colourless oil; R_f (10% diethyl ether in light petroleum) 0.3; ν_{max} (film)/cm^{-1} 3414 (OH), 1763 (C=O), 1703 (C=C); δ_H (300 MHz, $CDCl_3$) 5.89 (1H, dd, $^3J_{H-H}$ 17.3, $^3J_{H-H}$ 10.7, H-1″) 5.31 (1H, d, $^3J_{H-H}$ 17.3, H-2″), 5.09 (1H, d, $^3J_{H-H}$ 10.7, H-2″), 3.61 (1H, s, O*H*), 3.40–3.19 (4H, m, NCH_2), 2.48–2.37 (1H, m, H-2), 1.88–1.02 (8H, envelope, –CH_2); δ_C (75 MHz, $CDCl_3$) 155.5 (t, $^1J_{C-F}$ 282.0), 155.0, 144.8, 112.5, 112.4, 74.6, 44.9, 42.5, 37.6, 29.8, 26.2, 21.2, 13.8; δ_F (282 MHz, $CDCl_3$) −97.7 (1F, d, $^2J_{F-F}$ 56.6), −105.6 (1F, d, $^2J_{F-F}$ 56.6); [HRMS ES, Found 326.1539. Calc. for $C_{15}H_{23}O_3F_2NNa$ 326.1544]; *m/z* 304 (18%, [M + H]$^+$), 286 (20%, M − OH).

5-Chloro-4,4-difluoro-cyclodec-5*Z*-en-1-one 10a

A solution of dienol **9a** (0.222 g, 1.0 mmol) in xylene (5 ml) was sealed in an Ace® tube and heated to 125 °C in an oil bath. The reaction was followed by ^{19}F NMR of aliquots until the starting material was consumed completely (8 hours). Concentration and column chromatography (10% ether in light petroleum) afforded a white solid which was recrystallised from dichloromethane/hexane to afford **10a** (0.149 g, 67%) as colourless needles; mp 76–77 °C; R_f (10% ether in light petroleum) 0.3; ν_{max} (Nujol mull)/cm^{-1} 1715 (C=O); δ_H (300 MHz, $CDCl_3$) 6.11 (1H, t, $^3J_{H-H}$ 7.3, H-6), 3.20–1.10 (12H, envelope); δ_C (75 MHz, $CDCl_3$) 207.3, 131.9 (t, $^3J_{C-F}$ 5.1), 129.2 (t, $^2J_{C-F}$ 31.1), 119.7 (t, $^1J_{C-F}$ 247.3), 33.4 (t, $^2J_{C-F}$ 28.3), 56.4, 45.0, 37.1, 28.2, 22.3;

δ_F (282 MHz, $CDCl_3$) −97.8 (1F, br d, $^2J_{F-F}$ 233.9), −106.1 (1F, br d, $^2J_{F-F}$ 233.9); [HRMS (CI, [M + H]$^+$) Found: 240.096787. Calc. for $C_{10}H_{17}O^{35}ClF_2N$ 240.096674]; *m/z* 240 (100%, M + [NH_4]$^+$). Satisfactory microanalysis could not be obtained for this compound.

4,4,5-Trifluoro-cyclodec-5*Z*-ene-1-one 10b

From dienol **9b** (0.206 g, 1.0 mmol) at 125 °C (46 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **10b** (0.148 g, 72%) as fine colourless needles; mp 62–63 °C; R_f (15% ether in light petroleum) 0.2; ν_{max} (Nujol mull)/cm^{-1} 1719 (C=O); δ_H (300 MHz, $CDCl_3$) 5.21 (1H, dt, $^3J_{H-F}$ 33.7, $^3J_{H-H}$ 7.7, H-6), 3.10–2.75 (1H, m, –CH_2), 2.73–1.50 (10H, envelope, –CH_2), 1.50–1.12 (1H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 208.0, 150.2 (dt, $^1J_{C-F}$ 261.7, $^2J_{C-F}$ 32.2,), 117.1 (td, $^1J_{C-F}$ 244.7, $^2J_{C-F}$ 39.0), 112.0 (dt, $^2J_{C-F}$ 9.6, $^3J_{C-F}$ 3.4), 44.0, 36.9, 33.6 (td, $^2J_{C-F}$ 27.7, $^3J_{C-F}$ 2.3), 28.5, 23.5, 22.1; δ_F (282 MHz, $CDCl_3$) −104.8 (1F, dd, $^2J_{F-F}$ 253.0, ^3J 24.2), −112.2 (1F, dd, $^2J_{F-F}$ 253.0, $^3J_{F-F}$ 31.9), −123.8 (1F, dd, $^3J_{F-F}$ 31.9, $^3J_{F-F}$ 24.2); [HRMS (CI, [M + H]$^+$) Found: 224.127287. Calc. for $C_{10}H_{17}F_3NO$ 224.126224]; *m/z* 224 (100%, [M + NH_4]$^+$). Satisfactory microanalysis could not be obtained for this compound.

5-(*N,N*-Diethylcarbamoyloxy)-4,4-difluoro-cyclodec-5*Z*-en-1-one 10c

From dienol **9c** (0.303 g, 1.0 mmol) at 125 °C (32 hours). Concentration and column chromatography (10% ether in light petroleum) gave a colourless solid which recrystallised from dichloromethane/hexane to afford **10c** (0.206 g, 68%) as fine colourless needles; mp 83–85 °C; R_f (10% ether in light petroleum); 0.20; (Found: C, 59.68; H, 7.87; N, 4.30. Calc. for $C_{15}H_{23}F_2NO_3$: C, 59.39; H, 7.64; N, 4.62%); ν_{max} (Nujol mull)/cm^{-1} 1731 (C=O); δ_H (300 MHz, $CDCl_3$) 5.70 (1H, t, $^3J_{H-H}$ 7.7, H-6), 3.58–3.20 (4H, m, NCH_2), 3.00–2.30 (4H, envelope, H-2, H-10), 2.30–1.50 (8H, envelope, –CH_2), 1.40–1.05 (6H, m, –CH_3); δ_C (75 MHz, $CDCl_3$) 208.0, 153.2, 139.9 (t, $^2J_{C-F}$ 31.1), 123.2, 118.8 (t, $^1J_{F-F}$ 246.4), 42.1, 34.1 (t, $^2J_{C-F}$ 28.3), 45.8, 37.6, 29.1, 26.8, 22.9, 14.0; δ_F (282 MHz, $CDCl_3$) −104.8 (1F, br d, $^2J_{F-F}$ 242.2), −111.2 (1F, br dd, $^2J_{F-F}$ 242.2, $^3J_{F-H}$ 28.0); [HRMS (CI, [M + H]$^+$) Found: 304.172661. Calc. for ($C_{15}H_{24}O_3F_2N$) 304.172425]; *m/z* (EI) 303 (15%, M$^+$), 100 (CONEt$_2$, 100).

2-(1′-Chloro-2′,2′-difluoroethenyl)-1-(2″,3″-dihydropyranyl)-cyclohexan-1-ol 13a

t-BuLi (1.22 ml of a 1.64 M solution in *n*-pentane) was added dropwise to a solution of 2,3-dihydropyran (0.18 ml, 2.0 mmol) in dry tetrahydropyran (THP, 0.35 ml) at 0 °C. The mixture was stirred for 1 h then the solution was cooled to −78 °C. THF (0.25 ml) was added and the mixture was stirred for 5 minutes further. Ketone **8a** (0.275 g, 1.0 mmol) was added dropwise over 5 minutes; the mixture was stirred at −78 °C for one hour further and quenched with water (50 ml) The aqueous layer was extracted with ethyl ether (3 × 10 ml). The combined organic extracts were washed with saturated aqueous bicarbonate solution (3 × 10 ml), brine (3 × 10 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford dienol **13a** as an unstable yellow oil (0.267 g, 97% estimated yield). Only one diastereoisomer could be detected by ^{19}F NMR (assumed *trans*). δ_F (282 MHz, $CDCl_3$) −88.9 (1F, d, $^2J_{F-F}$ 39.4), −92.2 (1F, d, $^2J_{F-F}$ 39.4). The dienol was used for the subsequent step without further purification.

trans-2-(1′,2′,2′-Trifluoroethenyl)-1-(2″,3″-dihydropyranyl)-cyclohexan-1-ol 13b

Dienol **13b** was prepared from 2,3-dihydropyran (0.409 ml, 4.5 mmol) and **8b** (0.267 g, 1.5 mmol) as an unstable yellow oil (0.208g, 78% estimated yield). Only one diastereoisomer could be detected by ^{19}F NMR (assumed *trans*). δ_F (282 MHz, $CDCl_3$) −105.9 (1F, dd, $^2J_{F-F}$ 83.9, $^3J^{cis}_{F-F}$ 32.4), −122.6 (1F, ddd, $^2J_{F-F}$ 83.9, $^3J^{trans}_{F-F}$ 111.3, $^4J_{F-H}$ 3.8), −180.1 (1F, dtd, $^3J_{F-F}$ 111.3, $^3J_{F-F}$ 32.4, $^4J_{F-H}$ 5.1). The dienol was used for the subsequent step without further purification.

trans-2-[1′-(*N,N*-Diethylcarbamoyloxy)-2′,2′-difluoroethenyl]-1-(2″,3″-dihydropyranyl)-cyclohexan-1-ol 13c

Dienol **13c** was prepared from 2,3-dihydropyran (0.18 ml, 2.0 mmol) and **8c** (0.275 g, 1.0 mmol) as an unstable yellow oil (0.274g, 100% estimated yield). Only one diastereoisomer could be detected by ^{19}F NMR (assumed *trans*). δ_F (282 MHz, $CDCl_3$) −97.1 (1F, d, $^2J_{F-F}$ 55.9), −84.2 (1F, d, $^2J_{F-F}$ 55.9).

8-Chloro-9,9-difluoro-14-oxa-*cis*-bicyclo-[8.4.0]-tetradeca-7*Z*-en-2-one 14a

A solution of dienol **13a** (0.278 g, 1.0 mmol) in xylene (5 ml) was sealed in an Ace® tube and heated to 150 °C in an oil bath. The reaction was followed by ^{19}F NMR of aliquots until the starting material was consumed completely (3 hours). Concentration and column chromatography (10% ether in light petroleum) gave a colourless solid which recrystallised from dichloromethane/hexane to afford **14a** (0.181 g, 65%) as colourless rhombi; mp 137–138 °C; (Found: C, 56.20; H, 6.18. Calc. for $C_{13}H_{17}ClF_2O_2$: C, 56.02; H, 6.15%); R_f (10% ether in light petroleum) 0.1; ν_{max} (Nujol mull)/cm^{-1} 1710 (C=O); δ_H (500 MHz, $CDCl_3$); 6.25 (1H, d, ^3J 10.7, H-7), 4.16 (1H, dd, $^2J_{H-H}$ 11.5, $^3J_{H-H}$ 5.5, H-13a), 3.73–3.68 (1H, m, H-1), 3.48 (1H, dt, $^2J_{H-H}$ 11.5, $^3J_{H-H}$ 2.7, H-13b), 3.10 (1H, dd, $^2J_{H-H}$ 19.1, $^3J_{H-H}$ 10.3, H-3), 3.09–2.85 (1H, m, H-10), 2.48–2.28 (2H, m, H-6, H-12), 2.23–1.80 (4H, m, H-3, H-12, H-4, H-6), 1.79–1.51 (3H, m, H-11, H-4, H-5), 1.50–1.32 (2H, m, H-5, H-11); δ_C (126 MHz, $CDCl_3$) 207.5, 133.1, 129.3 (t, $^2J_{C-F}$ 30.5), 120.1 (dd, $^1J_{C-F}$ 257.7, $^1J_{C-F}$ 247.0), 83.2, 69.5, 40.3 (dd, $^2J_{C-F}$ 27.7, $^2J_{C-F}$ 20.9), 38.5, 29.1, 28.5, 23.1, 22.0, 20.5; δ_F (282 MHz, $CDCl_3$) −95.2(1F, dd, t, $^2J_{F-F}$ 239.7, $^3J_{F-H}$ 3.8), −102.8 (1F, dd, $^2J_{F-F}$ 239.7, $^3J_{F-H}$ 31.8); *m/z* (CI) 296 (10%, M + [NH_4]$^+$), 279 (8%, [M + H]$^+$), 258 (20, M − HF), 84 (100). The ^{1}H and ^{13}C NMR spectrum were assigned fully by COSY, GOESY and HSQC experiments.

8,9,9-Trifluoro-14-oxa-*cis*-bicyclo-[8.4.0]-tetradeca-7*Z*-en-2-one 14b[20]

Was prepared from dienol **14b** (0.262 g, 1.0 mmol) at 140 °C (17 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **14b** (0.220 g, 84%) as colourless rhombi; mp 93–94 °C; R_f (10% ether in light petroleum) 0.20; (Found: C, 59.68; H, 6.61. Calc. for $C_{13}H_{17}O_2F_3$: C, 59.54; H, 6.49%); ν_{max} (Nujol mull)/cm^{-1} 1712 (C=O); δ_H (500 MHz, $CDCl_3$); 5.32* (1H, ddq, $^3J_{H-F}$ 34.8, $^3J_{H-H}$ 12.2, ^3J $^4J_{H-F}$ 3.4, H-7), 4.16* (1H, br dd, $^2J_{H-H}$ 11.8, $^3J_{H-H}$ 5.5, H-13), 3.80–3.65 (1H, m, H-1), 3.48 (1H, ddt, $^3J_{H-H}$ 12.7, $^2J_{H-H}$ 11.8, $^3J_{H-H}$, $^4J_{H-H}$ 2.9, H-13), 3.10 (1H, dd, $^2J_{H-H}$ 19.1, $^3J_{H-H}$ 10.5, H-3), 2.88 (1H, dddd, $^3J_{H-F}$ 31.6, $^3J_{H-F}$ 10.8, $^3J_{H-H}$ 5.5, $^3J_{H-H}$ 2.9, H-10), 2.38–2.30 (2H, m, H-6, H-12), 2.19–2.05 (3H, m, H-3, H-12, H-4), 2.05–1.95 (1H, m, H-6), 1.85* (1H, d sept., $^2J_{H-H}$ 11.5, $^3J_{H-H}$, $^4J_{H-H}$ 2.9, H-5), 1.73* (1H, ttd, $^2J_{H-H}$ $^3J_{H-H}$ 13.7, $^3J_{H-H}$ 5.4, $^4J_{H-F}$ 1.0, H-11), 1.63–1.55 (1H, m, H-4), 1.40 (1H, d, $^2J_{H-H}$ 14.2, H-11), 1.35–1.23 (1H, m, H-5); δ_C (126 MHz, $CDCl_3$) 207.5, 150.5 (ddd, $^1J_{C-F}$ 260.5, $^2J_{C-F}$ 38.4, $^2J_{C-F}$ 27.7), 117.6 (ddd, $^1J_{C-F}$ 252.0, $^1J_{C-F}$ 244.7, $^2J_{C-F}$ 37.9), 113.4–113.0 (m), 83.2, 69.5, 40.9 (dd, $^2J_{C-F}$ 27.1, $^2J_{C-F}$ 21.5), 38.5, 29.1, 28.5, 23.1, 22.0, 20.5; δ_F (282 MHz, $CDCl_3$ −101.9 (1F, dd, $^2J_{F-F}$ 255.6, $^3J_{F-F}$ 26.7), −109.5 (1F, dd, $^2J_{F-F}$ 255.6, $^3J_{F-F}$ 31.6), −124.8 (1F, t, $^3J_{F-H}$ 34.8); *m/z* (CI) 280 (100%, [M + NH_4]$^+$). The ^{1}H and ^{13}C NMR spectra were assigned fully by COSY, GOESY and HSQC experiments. Gaussian and Lorentzian broadening was used to resolve the signals indicated* fully.

Crystallographic data for **14b**:† $C_{13}H_{17}F_3O_2$, crystal size 0.3 × 0.2 × 0.2 mm, M = 262.27, monoclinic, a = 10.1391(5), b = 8.2152(4), c = 14.6853(5) Å, β = 96.703(3) deg, U = 1214.85(9) Å^3, T = 150(2) K, space group $P2_1/c$, Z = 4, μ(Mo–Kα) = 0.125 mm^{-1}, 9829 reflections measured, 2130 unique (R_{int} = 0.0605) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0352, $wR2$ = 0.0858; R indices (all data) $R1$ = 0.0503, $wR2$ = 0.0933.

8-(*N*,*N*-Diethylcarbamoyloxy)-9,9-difluoro-14-oxa-bicyclo-[8.4.0]-tetradeca-7-en-2-one 14c

Was prepared from dienol **13c** (0.359 g, 1.0 mmol) at 155 °C (9 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **14c** (0.222 g, 62%) as colourless rhombi; mp 139–141 °C; R_f (10% ether in light petroleum) 0.3; (Found: C, 60.09; H, 7.75; N, 3.93. Calc. for $C_{18}H_{27}O_4F_2N$: C, 60.20; H, 7.50; N 3.90%); ν_{max} (Nujol mull)/cm^{-1} 1738, 1707 (C=O); δ_H (500 MHz, $CDCl_3$); 5.80 (1H, dd, $^3J_{H-H}$ 11.0, $^3J_{H-H}$ 2.6, H-7), 4.08 (1H, dd, $^2J_{H-H}$ 10.7, $^3J_{H-H}$ 5.5, H-13), 3.71–3.67 (1H, m, H-1), 3.50–3.28 (5H, m, H-13, 2 × NCH_2), 3.17–3.00 (1H, dd, $^2J_{H-H}$ 19.1, $^3J_{H-H}$ 9.9, H-3), 2.78 (1H, d, $^3J_{F-H}$ 30.9, H-10), 2.33 (1H, d, $^2J_{H-H}$ 14.0, H-6), 2.20–1.89 (4H, m, H-3, H-12, H-4), 1.86–1.48 (4H, m, H-11, H-4, H-5, H-6), 1.42–1.28 (2H, m, H-11, H-5), 1.25–1.02 (6H, m; 2 × –CH_3); δ_C (126 MHz, $CDCl_3$) 207.5, 152.5, 141.0 (dd, $^2J_{C-F}$ 33.9, $^2J_{C-F}$ 27.7), 123.5, 119.0 (dd, $^1J_{C-F}$ 255.4, $^1J_{C-F}$ 245.3), 83.2, 69.5, 42.0, 40.3 (dd, $^2J_{C-F}$ 28.3, $^2J_{C-F}$ 20.3), 38.5, 29.5, 26.5, 23.0, 22.0, 20.2, 13.8; δ_F (282 MHz, $CDCl_3$) −92.4 (1F, d, $^2J_{F-F}$ 246.0), −108.4 (1F, dd, $^2J_{F-F}$ 246.0, $^3J_{F-H}$ 31.8); [HRMS (CI, [M + H]$^+$) Found: 360.199311. Calc. for $C_{18}H_{28}O_4F_2N$: 360.198640]; *m/z* (CI) 360 (7%, [M + H]$^+$), 279 (12), 242 (13), 217 (10), 173 (14), 100 (CONEt$_2$, 100). The ^{1}H and ^{13}C NMR spectra were assigned fully by COSY, GOESY and HSQC experiments.

trans-1-(1′-Chloro-2′,2′-difluoroethenyl)-2-(1″,2″,2″-trifluoro-ethenyl)-cyclohexan-1-ol 21b

Was prepared from **6a** (1.5 mmol), generated as for **7a** and ketone **8b** (0.267 g, 1.5 mmol). After addition, the mixture was left stirring at −78 °C one hour, allowed to warm to −30 °C for 30 minutes then quenched by the addition of saturated aqueous ammonium chloride solution (20 ml). Work up in the usual manner followed by column chromatography (5% diethyl ether in petroleum ether) afforded **21b** (assumed *trans*) (0.191g, 46%) as a yellow oil; R_f (5% diethyl ether in petroleum ether) 0.1; δ_H (300 MHz, $CDCl_3$) 2.78 (1H, br dd, $^3J_{H-F}$ 31.6, $^3J_{H-H}$ 12.5, H-2), 2.28 (1H, s, OH), 2.20–1.50 (6H, m, –CH_2), 1.48–1.15 (2H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 153.9 (ddd, $^1J_{C-F}$ 326.6, $^1J_{C-F}$ 275.8, $^2J_{C-F}$ 47.5), 153.8 (dd, $^1J_{C-F}$ 293.3, $^1J_{C-F}$ 287.7), 130.2 (ddd, $^1J_{C-F}$ 235.7, $^2J_{C-F}$ 51.6, $^2J_{C-F}$ 15.8), 97.3 (dd, $^2J_{C-F}$ 27.7, $^2J_{C-F}$ 15.8), 75.5, 40.5 (d, $^2J_{C-F}$ 18.1), 35.8, 34.7, 34.2, 20.6; δ_F (282 MHz, $CDCl_3$) −79.9 (1F, d, $^2J_{F-F}$ 43.2), −85.4 (1F, d, $^2J_{F-F}$ 43.2), −102.8 (1F, dd, $^2J_{F-F}$ 80.1, $^3J^{cis}_{F-F}$ 31.8), −120.6 (1F, dd, $^3J^{trans}_{F-F}$ 111.9, ^2J 80.1), −181.2 (1F, dtd, $^3J^{trans}_{F-F}$ 111.9, $^3J^{cis}_{F-F}$ 31.8, $^3J_{F-H}$ 31.8, $^4J_{F-H}$ 5.1); [HRMS (EI, M$^+$) Found: 276.034783. Calc. for $C_{10}H_{10}{}^{35}ClF_5O$ 276.034034]; *m/z* (ES) 276 (75%, M$^+$), 256 (65, M − HF), 236 (60, M − H_2F_2), 221 (100, M − HF, Cl).

trans-1-(1′-Chloro-2′,2′-difluoroethenyl)-2-[1″-(*N*,*N*-di-ethylcarbamoyloxy)-2″,2″-difluoroethenyl)-cyclohexan-1-ol 21c

Was prepared from **6a** (1.5 mmol) and ketone **8c** (0.412 g, 1.5 mmol) which were stirred at −78 °C for three hours before being quenched with saturated aqueous ammonium chloride solution (20 ml). Work up in the usual manner followed by column chromatography (15% diethyl ether in petroleum ether) afforded **21c** (0.347 g, 62%) as a yellow oil; R_f (15% diethyl ether in petroleum ether) 0.2; ν_{max} (film)/cm^{-1} 3428 (OH), 1763 (C=O), 1719 (C=C); δ_H (300 MHz, $CDCl_3$) 3.40–3.23 (4H, m, NCH_2), 2.90 (1H, s, OH), 2.50 (1H, s, H-2), 2.21–1.29 (8H, m, –CH_2), 1.25–1.05 (6H, m, NCH$_2$CH_3); δ_C (75 MHz, $CDCl_3$) 155.0 (t, $^1J_{C-F}$ 284.3), 153.7 (d, $^1J_{C-F}$ 292.7), 152.2, 112.3 (dd, $^2J_{C-F}$ 40.1, $^2J_{C-F}$ 15.3), 99.0 (dd, $^2J_{C-F}$ 33.9, $^2J_{C-F}$ 16.4), 73.4, 41.8, 40.6, 33.1, 25.4, 21.8, 20.7, 13.2; δ_F (282 MHz, $CDCl_3$) −80.5 (1F, d, $^2J_{F-F}$ 40.7), −84.2 (1F, d, $^2J_{F-F}$ 40.7), −95.4 (1F, d, $^2J_{F-F}$ 54.7), −107.5 (1F, d, $^2J_{F-F}$ 54.7); *m/z* (ES) 396.1 (100%, [M + Na]$^+$).

cis- and *trans*-1-(1′,2′,2′-Trifluoroethenyl)-2-(1″-chloro-2″,2″-difluoroethenyl)-cyclohexan-1-ol 22a

1,2,2-Trifluoro-1-lithioethene **6b** (1.5 mmol) was generated according to the procedure used for **7b**, and ketone **8a** (0.292 g, 1.5 mmol) was added dropwise over 5 minutes. The reaction was stirred at −78 °C for three hours and quenched by the addition of saturated aqueous ammonium chloride solution (20 ml). The aqueous layer was extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with saturated sodium bicarbonate solution (2 × 15 ml) brine (2 × 15 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to leave a yellow oil. Purification by column chromatography (10% diethyl ether in petroleum ether) afforded **22a** (0.24 g, 57% total yield) as a mixture for diastereoisomers (2.3 : 1) as a yellow oil. Major diastereoisomer; R_f (10% diethyl ether in petroleum ether) 0.2 (0.165 g, 40%); ν_{max} (film)/cm^{-1} 3432 (OH), 1788 (C=C), 1725 (C=C); δ_H (300 MHz, $CDCl_3$) 2.82 (1H, d, $^3J_{H-H}$ 12.5, H-2), 2.45 (1H, s, OH), 2.10 (1H, d, $^3J_{H-H}$ 12.5, H-3ax), 1.90–1.52 (5H, m, –CH_2), 1.48–1.19 (2H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 154.2 (t, $^1J_{C-F}$ 289.3), 154.1 (ddd, $^1J_{C-F}$ 288.2, $^1J_{C-F}$ 282.0, $^2J_{C-F}$ 47.5), 131.8 (ddd, $^1J_{C-F}$ 240.7, $^2J_{C-F}$ 36.7, $^2J_{C-F}$ 14.7), 92.4 (dd, $^2J_{C-F}$ 41.2, $^2J_{C-F}$ 17.5), 73.7 (d, $^2J_{C-F}$ 22.0), 41.5, 37.1, 29.5, 25.5, 20.2; δ_F (282 MHz, $CDCl_3$) −86.1 (1F, d, $^2J_{F-F}$ 39.4), −90.7 (1F, d, $^2J_{F-F}$ 39.4), −100.2 (1F, dd, $^2J_{F-F}$ 84.6, $^3J^{cis}_{F-F}$ 35.0), −115.4 (1F, dd, $^3J^{trans}_{F-F}$ 113.9, $^2J_{F-F}$ 84.6), −178.7 (1F, ddd, $^3J^{trans}_{F-F}$ 113.9 $^3J^{cis}_{F-F}$ 35.0, $^4J_{F-H}$ 7.6); *m/z* (CI) 294 (100%, M + [NH$_4$]$^+$), 240 (15, M − HCl), 220 (12, M − HCl, HF); minor diastereoisomer R_f (10% diethyl ether in petroleum ether) 0.1 (0.069 g, 0.24 mmol, 17%); ν_{max} (film)/cm^{-1} 3464, 1724 (C=C); δ_H (300 MHz, $CDCl_3$) 2.95–2.80 (1H, m, H-2), 2.35–2.18 (1H, m, OH), 2.09–1.05 (8H, m, –CH_2); δ_F (282 MHz, $CDCl_3$) −85.3 (1F, d, ^2J 36.5), −90.1 (1F, d, ^2J 36.5), −100.2 (1F, dd, ^2J 83.9, $^3J_{cis}$ 35.0), −115.5 (1F, dd, ^2J 83.9, $^3J_{trans}$ 113.7), −178.7 (1F, ddd, $^3J_{trans}$ 113.7, $^3J_{cis}$ 35.0, $^4J_{F-H}$ 7.6); *m/z* (CI) 294 (35%, M + [NH$_4$]$^+$), 183 (30), 165 (52), 154 (73). The dienol was used for the subsequent step without further characterisation.

1,2-Di-(1′,2′,2′-trifluoroethenyl)-cyclohexan-1-ol 22b

Was prepared as for **22a** from **6b** (1.5 mmol) and ketone **8b** (0.267 g, 1.5 mmol). Work up in the usual manner followed by column chromatography (10% diethyl ether in petroleum ether) afforded **22b** (0.242 g 62% estimated yield) as an inseparable mixture of diastereoisomers (1.9 : 1, see text) R_f (10% diethyl ether in petroleum ether) 0.23; δ_H (300 MHz, $CDCl_3$) 3.75–3.65 (1H, m, OH), 2.91–2.55 (3H, m, –CH_2), 2.42–1.15 (5H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 158.1–149.8 (m), 133.9–127.8 (m), 73.2–71.8 (m), 44.0–41.0 (m), 35.8, 24.5, 23.0, 19.5; δ_F (282 MHz, $CDCl_3$) major diastereoisomer); −99.7 (dd, $^2J_{F-F}$ 83.6, $^3J^{cis}_{F-F}$ 34.9), −102.8 (dd, $^2J_{F-F}$ 79.3, $^3J^{cis}_{F-F}$ 32.5), −115.1 (dd, $^3J^{trans}_{F-F}$ 114.1, $^2J_{F-F}$ 83.6), −120.9 (ddt, $^3J^{trans}_{F-F}$ 111.9, $^2J_{F-F}$ 80.1, $^4J_{H-F}$ 4.0); minor diastereoisomer −99.4 (dd, $^2J_{F-F}$ 78.2, $^3J^{cis}_{F-F}$ 34.0), −121.4 (ddt, $^3J^{trans}_{F-F}$ 111.6, $^2J_{F-F}$ 78.2, $^4J_{H-F}$ 5.0), −103.2 (dd, $^2J_{F-F}$ 77.6, $^3J^{cis}_{F-F}$ 32.0), −113.1 (dd, $^3J^{trans}_{F-F}$ 111.3, $^2J_{F-F}$ 77.6); both diastereoisomers −180.8 (app. dt, $^2J_{F-F}$ 113,6, $^3J^{cis}_{F-F}$ 32.0); *m/z* (CI) 240 (60%, M + 1-HF), 149 (100%). The dienol was used for the subsequent step without further characterisation.

cis- and _trans_-1-(1′,2′,2′-Trifluoroethenyl)-2-[1′-(_N_,_N_-diethylcarbamoyloxy)-2′,2′ difluoroethenyl]-cyclohexan-1-ol 22c

Was prepared as for **22a** from **6b** (1.5 mmol) and ketone **8c** (0.412 g, 1.5 mmol). Work up in the usual manner followed by column chromatography (10% diethyl ether in petroleum ether) afforded **22c** (0.300 g, 56% total yield) as a mixture of diastereoisomers (1.8 : 1), as a yellow oil. The two diastereoisomers were separated and characterised: major diastereoisomer (assumed *trans*) (0.193 g, 36%); R_f (10% diethyl ether in petroleum ether) 0.25: δ_H (300 MHz, $CDCl_3$) 4.10 (1H, s, O*H*), 3.42–3.20 (4H, m, 2 × NCH_2), 2.62 (1H, d, $^3J_{H-H}$ 12.1, H-2), 2.14–2.08 (1H, m, H-3), 1.98–1.30 (6H, m, –CH_2), 1.20–1.08 (6H, m, 2 × –CH_3); δ_C (75 MHz, $CDCl_3$) 159.5–150.1 (m), 134.2 (ddd, $^1J_{C-F}$ 245.8, $^2J_{C-F}$ 35.6, $^2J_{C-F}$ 15.8), 111.1 (dd, $^2J_{C-F}$ 40.7, $^2J_{C-F}$ 15.3), 71.0 ($^2J_{C-F}$ 19.2), 42.0, 57.5, 39.5, 28.0, 26.5, 24.1, 13.5; δ_F (282 MHz, $CDCl_3$) −94.05 (1F, d, ^2J 53.4), −107.3 (1F, d, $^2J_{F-F}$ 53.4), −101.2 (1F, dd, $^2J_{F-F}$ 76.3, $^3J^{cis}_{F-F}$ 35.6), −111.5 (1F, dd, $^3J^{trans}_{F-F}$ 111.9 $^2J_{F-F}$ 76.3), −168.6 (1F, br d, $^3J^{trans}_{F-F}$ 111.9 (*cis* coupling invisible due to signal breadth); [HRMS (CI, [M + H]$^+$) Found: 358.14518. Calc. for [$C_{15}H_{20}F_5NO_3$] 358.14416; *m*/*z* (CI) 358 (37%, [M + H]$^+$), 340 (100%, M − OH): and minor diastereoisomer (0.107 g, 20%); R_f (10% diethyl ether in petroleum ether) 0.10: δ_H (300 MHz, $CDCl_3$) 4.55 (1H, s, O*H*), 3.42–3.20 (4H, m, 2 × NCH_2), 2.85–2.75 (1H, m, H-2), 1.90–1.25 (8H, m, –CH_2), 1.20–1.09 (6H, m, 2 × NCH$_2$CH_3); δ_C (75 MHz, $CDCl_3$) 159.5–150.1 (m), 134.2, 111.1, 55.5, 65.6, 42.3, 34.7, 25.5, 22.2, 19.9, 13.5; δ_F (282 MHz, $CDCl_3$) −95.05 (1F, d, $^2J_{F-F}$ 52.1), −100.6 (1F, dd, $^2J_{F-F}$ 84.5, $^3J^{cis}_{F-F}$ 33.7), −105.9 (1F, ddd, $^2J_{F-F}$ 52.1, $^4J_{H-H}$ 19.1, $^5J_{F-H}$, 3.1), −115.6 (1F, dd, $^3J^{trans}_{F-F}$ 113.2, $^2J_{F-F}$ 84.5), −176.8 (1F, ddd, $^3J^{trans}_{F-F}$ 113.2, $^3J^{cis}_{F-F}$ 33.7, $^4J_{F-H}$ 19.1); [HRMS (CI, [M + H]$^+$) Found: 358.143378. Calc. for $C_{15}H_{20}F_5NO_3$ 358.14416]; *m*/*z* (CI) 358 (10%, [M + H]$^+$), 340 (100%, M − OH).

2-Chloro-3,3,4,4,5-pentafluoro-cyclodec-5_Z_-en-1-one 23b

A solution of dienol **21b** (0.276 g, 1.0 mmol) in xylene (5 ml) was sealed in an Ace® tube and heated to 110 °C in an oil bath. The reaction was followed by ^{19}F NMR of aliquots until the starting material was consumed completely (40 hours). Concentration and column chromatography (10% ether in petroleum ether) then recrystallisation afforded **23b** (0.191 g, 69%) as colorless blocks: mp 82–83 °C; ν_{max} (Nujol mull)/cm^{-1} 1721 (C=O); δ_H (300 MHz, $CDCl_3$) 5.67–5.30 (1H, m, H-6), 4.60–4.29 (1H, m, H-2), 3.14–2.72 (1H, m, H-10), 2.70–2.23 (2H, m, H-10, –CH_2), 2.20–1.63 (4H, m, –CH_2), 1.61–1.18 (1H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 196.0, 117.2, 61.1 (t, $^2J_{C-F}$ 20.3), 56.8, 23.7, 23.5, 20.7; δ_F (376 MHz, PhMe-d$_8$, 213K) −106.4 (1F, dt, $^2J_{F-F}$ 256.5, $^3J_{F-F}$, $^3J_{F-H}$ 20.3), −118.2 (1F, br d, $^2J_{F-F}$ 266.5); −121.8 (1F, d, $^2J_{F-F}$ 256.5), −123.2 (br t, $^3J_{F-F}$ 27.3), −124.8 (1F, dd, $^2J_{F-F}$ 266.5, $^3J_{F-F}$ 19.0); [HRMS (CI, [M + H]$^+$) Found: 276.035289. Calc. for $C_{10}H_{10}ClF_5O$ 276.034034]; *m*/*z* 276 (28%, M$^+$). Satisfactory microanalysis could not be obtained for this compound.

Crystallographic data for **23b**:† $C_{10}H_{10}ClF_5O$, crystal size 0.3 × 0.3 × 0.2 mm, M = 276.63, monoclinic, a = 8.7576(4), b = 13.7337(10), c = 9.8743(4) Å, β = 106.530(2) deg, U = 1138.54(11) Å^3, T = 150(2) K, space group Pc, Z = 4, μ(Mo–Kα) = 0.383 mm^{-1}, 12683 reflections measured, 3664 unique (R_{int} = 0.0378) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0272, $wR2$ = 0.0594; R indices (all data) $R1$ = 0.0272, $wR2$ = 0.0604.

2-Chloro-3,3,4,4-tetrafluoro-5-(_N_,_N_-diethylcarbamoyloxy)-cyclodec-5_Z_-en-1-one 23c

Was prepared from dienol **21c** (0.373 g, 1.0 mmol) at 150 °C (2 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **23c** (0.265 g, 71%) colourless blocks; mp 99–102 °C; (Found: C, 48.44; H, 5.62; N, 3.58. Calc. For $C_{15}H_{20}ClF_4NO_3$: C, 48.20; H, 5.39; N, 3.75%); R_f (10% ether in light petroleum) 0.2; ν_{max} (Nujol mull)/cm^{-1} 1722 (C=O); δ_H (300 MHz, $CDCl_3$) 6.02–5.88 (1H, m, H-6), 4.52–4.38 (1H, m, H-2), 3.47–3.19 (4H, m, 2 × NCH_2), 3.00–2.75 (1H, m, H-10), 2.74–2.47 (1H, m, H-10), 2.29–2.01 (2H, m, H-7), 1.99–1.62 (3H, m, –CH_2), 1.52–1.30 (1H, m, –CH_2); 1.28–1.10 (6H, m, 2 × –CH_3); δ_C (126 MHz, $CDCl_3$) 194.5, 151.4, 136.3–135.6 (m), 127.9, 115.8–109.0 (m), 57.6–56.0 (m), 42.4, 42.0, 37.9, 26.6, 26.0, 20.9, 13.9, 13.2; δ_F (282 MHz, $CDCl_3$) −108.3 (1F, d, $^2J_{F-F}$ 271.2), −119.2 (1F, d, $^2J_{F-F}$ 290.0); −123.9 (1F, d, $^2J_{F-F}$ 271.2), −126.8 (d, $^2J_{F-F}$ 290.0); *m*/*z* 396.5 (100%, [M + Na]$^+$).

Crystallographic data for **23c**:† $C_{15}H_{20}ClF_4NO_3$, crystal size 0.4 × 0.3 × 0.2 mm, M = 373.77, monoclinic, a = 11.1981(5), b = 11.8463(7), c = 13.1682(6) Å, β = 94.524(3) deg, U = 1741.40(15) Å^3, T = 150(2) K, space group $P2_1/n$, Z = 4, μ(Mo–Kα) = 0.272 mm^{-1}, 14497 reflections measured, 3067 unique (R_{int} = 0.0583) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0416, $wR2$ = 0.1052; R indices (all data) $R1$ = 0.0643, $wR2$ = 0.1154.

5-Chloro-2,3,3,4,4-pentafluoro-cyclodec-5_Z_-en-1-one 24a

Was prepared from dienol **22a** (0.276 g, 1.0 mmol) at 150 °C (1.75 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **24a** (0.201 g, 73%) as colourless blocks; mp 92–98 °C; R_f (10% ether in light petroleum) 0.1; δ_H (300 MHz, $CDCl_3$) 6.55–6.40 (1H, m, H-6), 4.88 (1H, dtd, $^2J_{H-F}$ 46.7, $^3J_{H-F}$ 9.2, $^3J_{H-FC}$ 9.2, $^4J_{H-F}$ 4.4, H-2), 3.15–2.98 (1H, m, H-10), 2.60–2.45 (1H, m, H-10), 2.38–2.20 (2H, m, H-7), 2.10–1.18 (4H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 199.0, 129.9–128.0 (m), 90.2 (dt, $^1J_{C-F}$ 199.5, $^2J_{C-F}$ 24.4), 42.5, 38.0, 29.5, 20.5; distinct resonances for ring methylene carbons were not observed; δ_F (282 MHz, $CDCl_3$) −105.8 (1F, br d, $^2J_{F-F}$ 291.1), −107.4 (1F, d, $^2J_{F-F}$ 291.1); −107.8 (1F, d, $^2J_{F-F}$ 258.8), −111.0 (1F, d, $^2J_{F-F}$ 258.8), (−199.1)–(−199.7) (1F, m); *m*/*z* (CI) 294 (2.5%, [M + NH$_4$]$^+$), 167 (100%). Neither satisfactory microanalysis nor HRMS could be obtained for this compound.

Crystallographic data for **24a**:† $C_{10}H_{10}ClF_5O$, crystal size 0.2 × 0.2 × 0.3 mm, M = 276.63, orthorhombic, a = 7.979(1), b = 9.742(1), c = 14.053(2) Å, U = 1092.4(2) Å^3, T = 150(2) K, space group $P2(1)2(1)2(1)$, Z = 4, μ(Mo–Kα) = 0.399 mm^{-1}, 6657 reflections measured, 2190 unique (R_{int} = 0.0334) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0283, $wR2$ = 0.0598; R indices (all data) $R1$ = 0.0334, $wR2$ = 0.0621.

2,3,3,4,4,5-Hexafluoro-cyclodec-5_Z_-en-1-one 24b

Was prepared from dienol **22b** (0.260 g, 1.0 mmol) as mixture of two diastereoisomers (1.9 : 1 ratio) at 100 °C (47 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **24b** (0.140 g, 54%) as colorless blocks; mp 46–49 °C; R_f (10% ether in light petroleum) 0.1; ν_{max} (Nujol mull)/cm^{-1} 1724 (C=O); δ_H (500 MHz, $CDCl_3$) 5.57 (1H, ddd, $^3J_{H-F}$ 32.7, ^3J 7.4, 2.9, H-6), 4.90 (1H, app. ddt, $^3J_{H-F}$ 46.5, $^3J_{H-F}$ 9.0, $^3J_{H-F}$ 4.8, $^4J_{H-F}$ 4.8 H-2), 3.20–2.80 (1H, m, H-10a), 2.50–2.37 (1H, m, H-7a), 2.30 (1H, dd, ^3J 18.9, 9.2, H-9a), 2.16–1.98 (2H, m, H-7b, H-10b), 1.96–1.84 (1H, m, H-8a), 1.77–1.68 (1H, m, H-9b), 1.46–1.32 (1H, m, H-8b); δ_C (75 MHz, $CDCl_3$) 199.2 (d, $^2J_{C-F}$ 26.4), 146.1 (ddd, $^1J_{C-F}$ 262.2, $^2J_{C-F}$ 33.9, $^2J_{C-F}$ 26.6), 116.8–116.1 (m), 90.2 (dt, $^1J_{C-F}$ 201.8, $^2J_{C-F}$ 26.6); 57.5, 38.4, 23.8, 20.4; δ_F (282 MHz, $CDCl_3$) −113.4 (1F, br d, $^2J_{F-F}$ 287.4), −116.3 (1F, br d, $^2J_{F-F}$ 287.4); −120.1 (1F, br d, $^2J_{F-F}$ 277.2), −124.1 (1F, d, $^2J_{F-F}$ 277.2), (−127.1)–(−127.5) (1F, m), (−205.6)–(−206.1) (1F, m); [HRMS (CI [M + NH$_4$]$^+$) Found: 278.096651. Calc. for

$C_{10}H_{14}F_6NO$ 278.097959]; *m/z* (CI) 278 (50%, M + $[NH_4]^+$). The ^{1}H NMR spectrum was assigned partially by COSY analysis and by comparison with the fully-assigned ^{1}H NMR spectrum for **14b**. Satisfactory microanalysis could not be obtained for this compound.

Crystallographic data for **24b**:† $C_{10}H_{10}F_6O$, crystal size 0.3 × 0.3 × 0.2 mm, M = 260.18, triclinic, a = 5.996(1), b = 8.007(2), c = 11.386(2) Å, α = 80.90(3) deg, β = 87.03(3) deg, γ = 78.66(3), U = 529.10(18) Å^3, T = 150(2) K, space group P-1, Z = 2, μ(Mo–Kα) = 0.175 mm^{-1}, 6510 reflections measured, 2053 unique (R_{int} = 0.0578) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0425, $wR2$ = 0.1189; R indices (all data) $R1$ = 0.0493, $wR2$ = 0.1248.

5-(*N*,*N*-Diethylcarbamoyloxy)-2,3,3,4,4-pentafluoro-cyclodec-5*Z*-en-1-one 24c

Was prepared from dienol **22c** (0.357 g, 1.0 mmol) at 100 °C (30 hours). Concentration and column chromatography (10% ether in light petroleum) gave a white solid which recrystallised from dichloromethane/hexane to afford **24c** (0.234 g, 66%) as colourless rods; mp 105 °C; R_f (10% ether in light petroleum) 0.15; (Found: C, 50.40; H, 5.60; N, 3.80; Calc. For $C_{15}H_{19}NO_3F_2$: C, 50.40; H, 5.60; N, 3.90%); ν_{max} (Nujol mull)/cm^{-1} 1731 (C=O); δ_H (300 MHz, $CDCl_3$) 6.10–5.98 (1H, m, H-6), 4.88 (1H, ddd, $^2J_{H-F}$ 47.1, $^3J_{H-F}$ 9.2, $^3J_{H-F}$ 4.8, H-2), 3.48–3.20 (4H, m, NCH_2), 3.20–3.02 (1H, m, H-10), 2.40–1.52 (6H, m, –CH_2), 1.50–1.30 (1H, m, –CH_2), 1.27 (3H, t, ^3J 7.0, CH_3), 1.15 (3H, t, ^3J 7.0, CH_3); δ_C (75 MHz, $CDCl_3$) 199.0, 151.8, 128.3, 90.4 (dd, $^1J_{C-F}$ 202.3, $^2J_{C-F}$ 28.2), 41.9, 37.9, 27.1, 26.2, 20.3, 13.5; δ_F (282 MHz, $CDCl_3$) −112.1 (1F, d, $^2J_{F-F}$ 286.1), −115.3 (1F, d, $^2J_{F-F}$ 286.1); −118.1 (1F, d, $^2J_{F-F}$ 267.0), −123.3 (1F, dt, $^2J_{F-F}$ 267.0, $^3J_{F-F}$ 19.0), (−204.4)–(−204.8) (1F, m); [HRMS (CI, [M + H]$^+$) Found: 357.137280. Calc. for $C_{15}H_{20}F_5NO_3$ 357.136335]; *m/z* 358 (100%, M + $[NH_4]^+$), 375 (90%, [M + H]$^+$).

Crystallographic data for **24c**:† $C_{15}H_{20}F_5NO_3$, crystal size 0.3 × 0.3 × 0.1 mm, M = 357.32, monoclinic, a = 11.1132(2), b = 11.0996(2), c = 13.8507(3) Å, β = 102.8902(12) deg, U = 1665.46(6) Å^3, T = 150(2) K, space group $P2_1/n$, Z = 4, μ(Mo–Kα) = 0.134 mm^{-1}, 29759 reflections measured, 3396 unique (R_{int} = 0.0446) which were used in all calculations. Final R indices [$F^2 > 2\sigma(F^2)$] $R1$ = 0.0344, $wR2$ = 0.0800; R indices (all data) $R1$ = 0.0454, $wR2$ = 0.0854.

cis- and *trans*-1,2-Divinyl-cyclohexan-1-ols 25

Vinylmagnesium bromide (1.0 ml of a 1 M solution in THF, 1.0 mmol) was added dropwise over 10 minutes to a solution of 2-chlorocyclohexanone (0.132 g, 1.0 mmol) in dry THF (0.5 ml) at 0 °C. The mixture was stirred for two hours, then further vinylmagnesium bromide (1.0 ml of a 1 M solution in THF, 1.0 mmol) was added and the mixture was heated to reflux (63 °C),[45] stirred for three hours at this temperature and quenched carefully with saturated aqueous ammonium chloride solution (20 ml). The aqueous layer was extracted with diethyl ether (3 × 10 ml) and the combined organic extracts were washed with brine (2 × 15 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography (10% diethyl ether in petroleum ether) afforded **25** as a mixture of two diastereoisomers (0.1 g, 4.1 : 1, 73%). Major diastereoisomer: δ_H (300 MHz, $CDCl_3$) 5.99–5.80 (2H, m, H-1′, H-1″), 5.28–4.92 (4H, m, H-2′, H-2″), 2.50–2.35 (1H, m, OH), 2.18–2.02 (1H, m, H-2), 2.90–1.38 (7H, m, –CH_2), 1.37–1.15 (1H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 146.0, 138.9, 116.5, 112.2, 73.5, 42.0, 39.1, 25.3, 22.8; *m/z* (CI) 152 (12%, M$^+$), 151 (14%, M − 1); Minor diastereoisomer δ_H (300 MHz, $CDCl_3$) 6.30–6.16 (1H, m, H-1′), 5.69–5.32 (1H, m, H-1″), 5.33–4.90 (4H, m, H-2′-2″), 2.82–2.70 (1H, m, OH), 2.45–2.20 (1H, m, H-2), 2.15–1.15 (8H, m, –CH_2); δ_C (75 MHz, $CDCl_3$) 140.0, 138.8, 117.0, 114.0, 73.6, 53.1, 29.1, 27.0, 25.1, 23.3; *m/z* (CI) 152 (5%, M$^+$), 151 (7%, M − 1).

Cyclodec-5-en-1-one 26

A solution of dienols **25** (0.152 g, 1.0 mmol) in xylene (5 ml) was sealed in an Ace® tube and heated to 225 °C in an oil bath. The reaction was followed by ^{1}H NMR of aliquots until the starting material was consumed completely (24 hours). Concentration and column chromatography (10% ether in petroleum ether) afforded 124 (0.074 g, 49%) as colourless oil; ν_{max} (film)/cm^{-1} 1708 (C=O); δ_H (300 MHz, $CDCl_3$) 5.39–5.20 (1H, m, H-6), 5.18–4.98 (1H, m, H-5), 2.58–1.08 (14H, –CH_2), δ_C (75 MHz, $CDCl_3$) 212.9, 134.4, 131.2, 45.5, 43.1, 34.1, 33.3, 28.7, 27.9, 22.1; *m/z* 170 (18%, M + NH_4^+), 153 (25%, M + 1), identical with the data reported by Marvell and Whalley.[46]

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