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Scope of the directed dihydroxylation: application to cyclic homoallylic alcohols and trihaloacetamides

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The synthesis and directed dihydroxylation of a range of cyclic alkenes was investigated. Both homoallylic alcohols and homoallylic trihaloacetamides were found to be efficient directing groups, giving rise to good to excellent levels of remote asymmetric induction with OsO_4–TMEDA. Interestingly, in all cases examined, trifluoroacetamides were found to be superior to trichloroacetamides as directing groups and an argument is presented which rationalises this observation.

Introduction

The literature is replete with examples of stereoselective reactions of alkenes that are influenced by an allylic substituent; in particular, heteroatomic groups can participate in 'directed' reactions whereby they coordinate to an incoming reagent and affect a subsequent reaction with the substrate.[1] One of the largest and most useful subsets of 'directed' reactions relies on hydrogen bonding between the two reacting partners, usually to accomplish the formation of an otherwise unfavourable (contra-steric) product, *e.g.* the Henbest epoxidation of allylic alcohols with peracids.[2] In this regard, we have recently developed a reagent combination (OsO_4–TMEDA) that allows the directed dihydroxylation of allylic amides and alcohols using hydrogen bonding as a control element.[3] As part of a programme designed to develop and exploit this new oxidant, we decided to investigate the applicability of directed dihydroxylation towards homoallylic substituted alkenes. Homoallylic systems should prevent a more difficult challenge to the directed oxidation reaction, not least because of the difference in spatial orientation between the hydrogen bonding group, the reagent, and the alkene that such substrates could offer, Fig. 1.

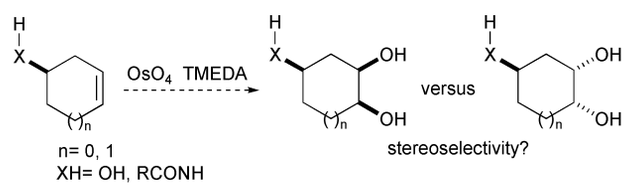


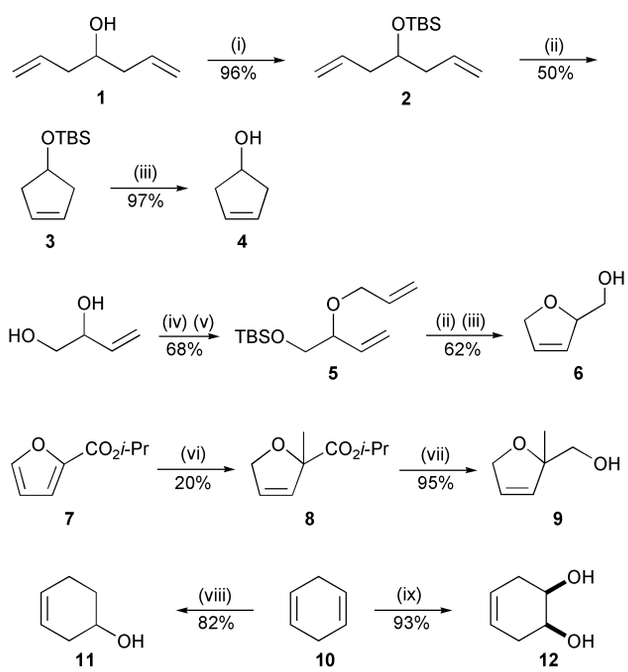
Fig. 1

This was also a challenging remit because the synthesis of a range of differently substituted cyclic homoallylic amides and alcohols was not as straightforward as that of the corresponding allylic analogues.[4] However, the opportunity to examine the synthesis of such substrates and the potential for using any subsequent remote stereoselectivity in synthetic applications made us decide to investigate this avenue of research further. Some of the results presented here have been the subject of a preliminary communication,[5] which we now wish to expand and discuss in full.

Results and discussion

Preparation and oxidation of homoallylic alcohols

A range of homoallylic alcohols was prepared in order that we could test their ability to direct dihydroxylation by hydrogen bonding to the OsO_4–TMEDA reagent: the synthetic sequences used to make these starting materials are shown in Scheme 1. The parent compound, cyclopent-3-en-1-ol **4**,[6] was prepared in three steps from the bis-homoallylic alcohol **1**, the key bond forming reaction in the sequence being the metathesis of **2**



Scheme 1 *Reagents*: i, TBSOTf, Et_3N; ii. (cat.) $Cl_2(Pcy_3)_2$ Ru=CHCH=CPh_2; iii. HCl, MeOH; iv. TBSCl, imidazole; v. KHMDS, allylbromide; vi. Li, naphthalene, THF, MeI; vii. $LiAlH_4$; viii. 9-BBN, H_2O_2; ix. (cat.) OsO_4, NMO.

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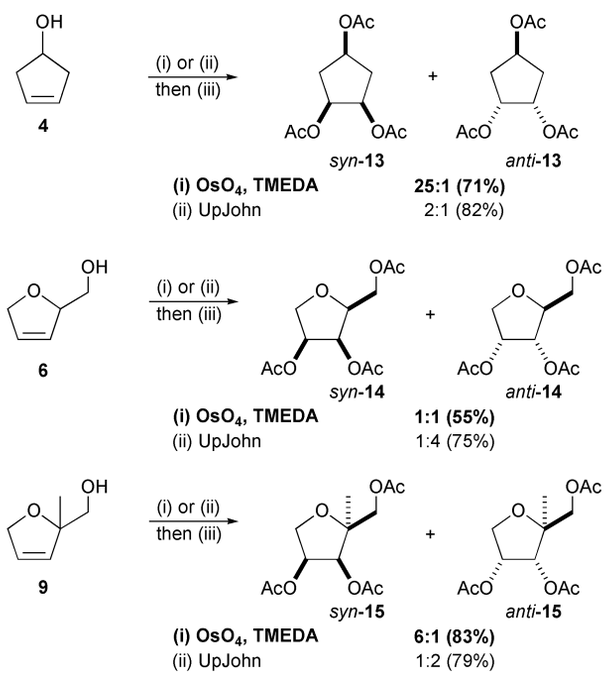
using Grubbs' catalyst (**2**⟶**3**). Metathesis was also instrumental in forming the heterocyclic ring within **6** by joining the alkenes of **5** together in good overall yield.

Moreover, the substituted dihydrofuran compound **9** was made from an ester of furoic acid **7**, which was reduced under 'ammonia free' Birch type conditions,[7] with *in situ* methylation; the volatile product **8** (hence the low yield) was immediately reduced with $LiAlH_4$ to furnish homoallylic alcohol **9** in good yield.

Finally, two six membered substrates were both prepared, *via* previously reported chemistry, from cyclohexadiene **10** which was either hydroborated or dihydroxylated to give compounds **11**[8] and **12**[9] respectively in good yields.

Our results after directed dihydroxylation of these test compounds are reported below, Scheme 2. In every case that we examined, dihydroxylation under UpJohn conditions[10] was also performed so that we could gauge the facial bias that each alcohol derivative gave under standard oxidising conditions. We found it more convenient to per-acetylate the crude reaction mixtures before examining the diastereoselectivity (by ^1H NMR on the mixtures prior to chromatography) for each oxidation.



Scheme 2 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. (cat.) OsO_4, NMO acetone, water; iii. Ac_2O, py.

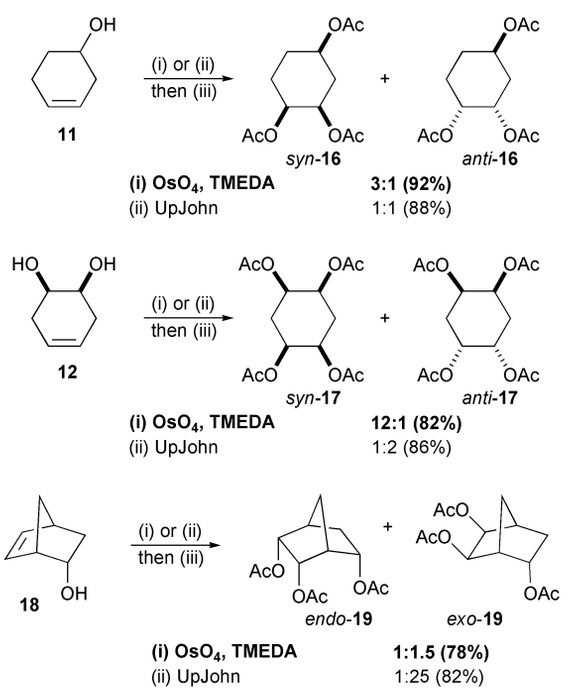
The five membered carbocycle **4** was dihydroxylated with OsO_4–TMEDA first, and gave excellent selectivity (≥25 : 1) for the all-*syn* isomer **13**, after peracetylation of the polar triol product. Oxidation under UpJohn conditions was only marginally selective (2 : 1) again in favour of the all-*syn* isomer.

Directed dihydroxylation of exocyclic alcohol **6** was disappointing, in that a non-selective reaction ensued, Scheme 2. That the parent alcohol **6** has a strong bias for formation of the *anti* isomer was shown by the production of mostly *anti*-**14** upon reaction under UpJohn conditions. Clearly, the exocyclic sidechain of **6** is sufficiently bulky to interfere with effective directed dihydroxylation and the OsO_4–TMEDA reagent is able only to make an otherwise *anti*-selective reaction non-selective.

As a consequence of the strong *anti* bias displayed by **6**, we decided to introduce an alkyl substituent to block the face of the alkene opposite to the hydroxymethyl group, see **9**. As expected, compound **9** had a much reduced bias for formation of the *anti* isomer (2 : 1) under UpJohn conditions and gave good selectivity for *syn*-**15** (6 : 1) under hydrogen bonding control.

In this sequence, proof of the stereochemistry of *syn*-**13** was obtained with an X-ray crystal structure of a derivative,‡ while the compound *anti*-**14** is known in the literature.[11] Although the relative stereochemistry of *syn*- and *anti*-**15** was not proven unambiguously, the fact that the two different oxidising conditions formed two different diastereoisomers gave us confidence in assigning them as shown.

Next, we turned our attention towards the oxidation of the six-membered homoallylic alcohols **11** and **12**, Scheme 3. Cyclohex-3-en-1-ol **11** was oxidised to **16** with reasonable *syn* selectivity using OsO_4–TMEDA and with no selectivity at all using UpJohn conditions. We presume that in these systems the directing group must adopt an axial position in order to be an effective director to the alkene, *vide infra*.[12] Therefore, *cis*-diol **12** which must have one hydroxy group in an axial position, was expected to be more effective in promoting *syn* selectivity. In fact, oxidation of **12** under directed dihydroxylation conditions gave the tetraacetate products **17** as a 12 : 1 mixture in favour of the all-*syn*-isomer. Interestingly, the ^1H NMR spectrum of *syn*-**17** shows two (2H each) separate double triplets (δ 2.35 and 1.84 ppm) clearly showing the non-equivalence of the methylene protons and proving the stereochemistry of directed dihydroxylation.



Scheme 3 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. (cat.) OsO_4, NMO acetone, water; iii. Ac_2O, py.

The oxidation of **18** (made by the Diels–Alder reaction of cyclopentadiene with 2-chloroacrylonitrile, followed by reaction with KOH and $NaBH_4$)[13] proved to be the most challenging substrate we had examined: this could be predicted from the result of the UpJohn reaction which was completely selective for *exo*-**19**. Therefore, we were not too surprised to find that the steric bias of alcohol **18** could not be overturned by OsO_4–TMEDA and instead a 1 : 1.5 ratio of *endo : exo* isomers was formed.

The stereochemistry of these compounds was assigned by correlation to the known compound *exo*-**19**;[14] the stereochemistry of *syn*-**16** (and therefore *anti*-**16**) was assigned by analogy.

Analysis of the results obtained so far shows that the *cis* directing effect is a reasonably powerful one, overturned only by

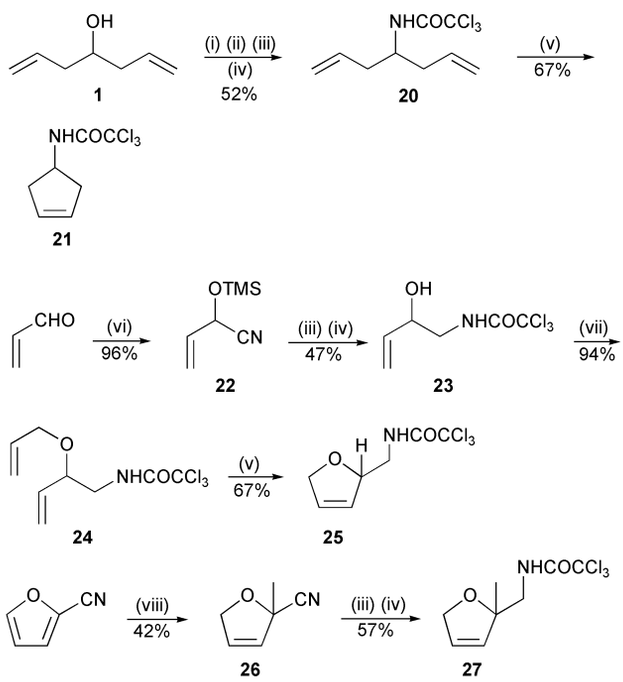
‡ CCDC reference numbers 207038 & 207039. See http://www.rsc.org/suppdata/ob/b3/b303081d/ for crystallographic data in .cif or other electronic format.

strong steric interactions. Examination of the literature reveals that with most of the substrates shown in Schemes 2 and 3, the OsO_4–TMEDA reagent gives levels of *syn* selectivity comparable or higher than the corresponding epoxidation with peracids.[15]

Preparation and oxidation of homoallylic amides

In an attempt to explore further the range of directing groups that could be effective as homoallylic hydrogen bond donors, we prepared a variety of cyclic trichloroacetamides. In a previous study, we had shown that allylic trichloroacetamides were better directing groups than the corresponding alcohols, probably because of their enhanced acidity (calculated pK_a ROH = 14.7, Cl_3CONHR = 11.2)[3d] which implies a better ability to act as a hydrogen bond donor. Therefore, we suspected that the homoallylic trichloroacetamides[16] would enhance the *syn* selectivity that was shown for homoallylic alcohols.

In each case examined, the synthesis of the requisite amide substrate proved more difficult than the analogous homoallylic alcohol.[4] The preparation of three five-membered homoallylic amides is described in Scheme 4. The preparation of amide **21** followed a route that was similar to that described for **4**, except that the protected nitrogen functionality was introduced *via* displacement (**20**) prior to ring closing metathesis.

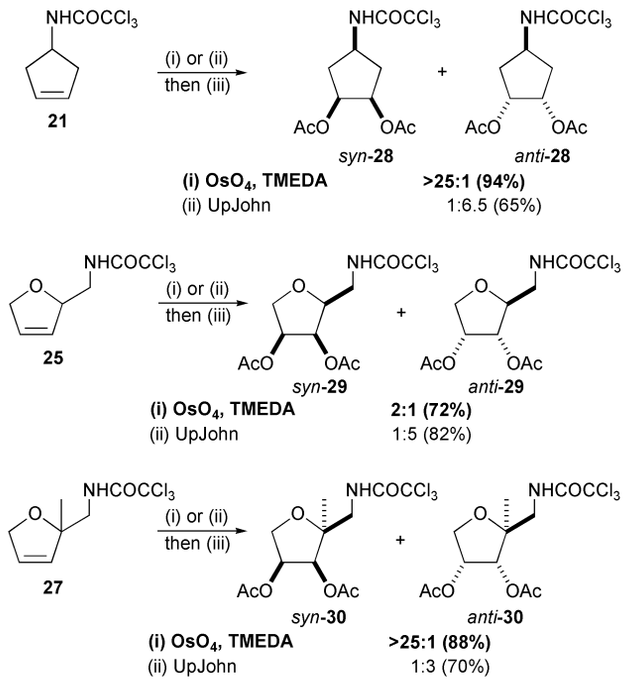


Scheme 4 *Reagents*: i. Ms_2O, Et_3N; ii. NaN_3, DMSO; iii. $LiAlH_4$, Et_2O; iv. Cl_3CCOCl, Et_3N; v. (cat.) $Cl_2(Pcy_3)_2$ Ru=CHPh; vi. TMSCN, ZnI; vii. allyltrichloroacetimidate, (cat.) TfOH; viii. Na, NH_3 then MeI.

The synthesis of **25** also used RCM methodology to form the heterocycle, starting from the TMS-cyanohydrin of acrolein **22**, Scheme 4. Reduction of the nitrile to a primary amine (with concomitant deprotection of the TMS group) was followed by protection of the nitrogen as a trichloroacetamide (**23**) before selective *O*-allylation under acidic conditions[17] (**24**) and metathesis as described below.

Finally, the synthesis of the more hindered five membered ring **27** was achieved by Birch reductive alkylation of 2-cyanofuran, quenching with methyl iodide: reduction of the nitrile **26** and acylation ensued to furnish **27** in reasonable yield.

The directed dihydroxylation of these five membered substrates illustrates that good to excellent ratios of *syn* selectivity can be achieved, Scheme 5. For example, directed oxidation of **21** gave the isomer *syn*-**28** with complete stereoselectivity. The exocyclic amide **25** was oxidised with some degree of *syn*



Scheme 5 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. (cat.) OsO_4, NMO acetone, water; iii. Ac_2O, py.

selectivity proving that, all things being equal, the amide is a better directing group than the corresponding alcohol in these systems (*cf*. the non-selective oxidation of **6**, Scheme 2). The hindered analogue **27** also proved the effectiveness of trichloroacetamides as homoallylic hydrogen bond donors and was oxidised with complete *syn*-selectivity under the action of OsO_4–TMEDA.

In each of the cases described above, the alternate, *anti*, diastereoisomer can be obtained with good selectivity using the UpJohn conditions. As well as being useful, this *anti*-selectivity enabled us to assess the stereoselectivity of the directed processes with ease from the crude ^{1}H NMR spectra. The stereochemistry of the stereoisomers of **29** and **30** was proven by NOE experiments on each isomer (or on osmate ester intermediates, see *syn*-**31**, Fig. 2); key enhancements are shown in Fig. 2 and they clearly indicate that the relative stereochemistry of the four products is as shown in Scheme 5. The structure of *syn*-**28** was assigned by X-ray crystallography on an osmate ester derivative (see Fig. 7).

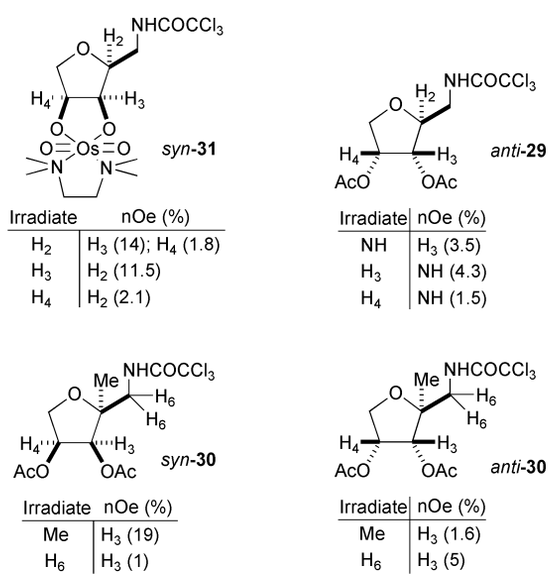
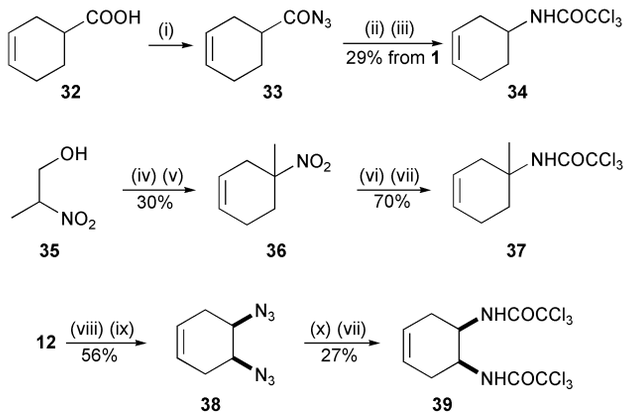


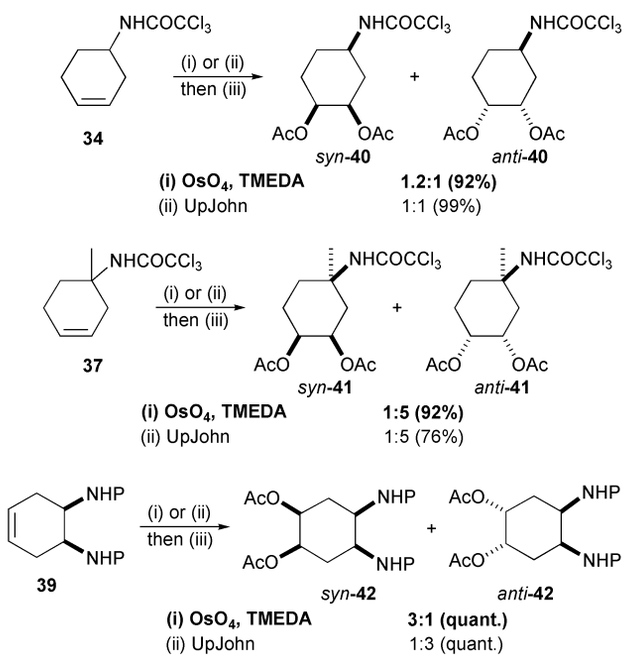
Fig. 2 Key NOE enhancements for *syn*-**31**, *anti*-**29** and *syn*- and *anti*-**30**.



Scheme 6 *Reagents*: i. $(PhO)_2PON_3$; ii. Δ; iii. Cl_3CCOOH, Δ; iv. Ac_2O; v. butadiene, NaOH, C_6H_6, Δ; vi. Li, NH_3, MeOH; vii. Cl_3CCOCl, Et_3N; viii. Ms_2O, Et_3N; ix. NaN_3, DMSO; x. $LiAlH_4$.

Next, we turned our attention towards the preparation of six-membered substrates, as shown in Scheme 6. As before, we utilised a wide range of synthetic reactions in order to make these compounds, ranging from the Curtius rearrangement (for **34**) through to Diels–Alder chemistry for the preparation of nitro-olefin **36** and simple displacement chemistry for **39**. Each of the three products had spectroscopic data that was completely consistent with the structures shown.

Directed dihydroxylation of these three compounds had some surprises in store, in that only one (**39**) gave any *syn* selectivity, while compound **34** was oxidised non-selectively under both sets of conditions tried, Scheme 7. Surprisingly, compound



Scheme 7 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. (cat.) OsO_4, NMO acetone, water; iii. Ac_2O, py.

37 gave *anti*-selective products with both OsO_4–TMEDA and under UpJohn conditions.

Given the lack of stereoselectivity observed during oxidation of **34**, the relative stereochemistry within the isomers of the adducts **40** was not proven. The *anti*-isomer of **41** was analysed by ^{1}H NMR spectroscopy and the stereochemistry within this isomer (which is the major one in both oxidations) assigned by NOE experiment. Both isomers of **42** were also assigned by difference NOE experiments and the key enhancements are shown in Fig. 3.

However one views the results shown in Scheme 7, the ability of a trichloroacetamide to direct dihydroxylation in six-membered rings is disappointing and not in keeping with the results shown in Scheme 5. Therefore, we decided to prepare the corresponding trifluoroacetamide analogues to examine the effect of using a smaller and more acidic (calculated pK_a's Cl_3CONHR = 11.2; F_3CONHR = 10.7)[18] directing group. Each substrate (**43**, **45**, **47**) was prepared according to the chemistry described for the trichloro-compounds, with the simple expedient of using F_3CCOCl as an acylating agent in the sequence. The results from the directed dihydroxylation of these compounds were very encouraging indeed, as each of the three compounds tried gave the all-*syn* diastereoisomer with OsO_4 and TMEDA, Scheme 8.

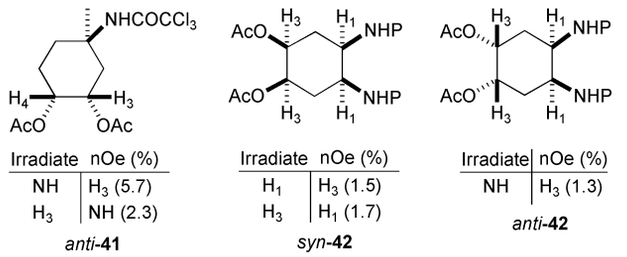
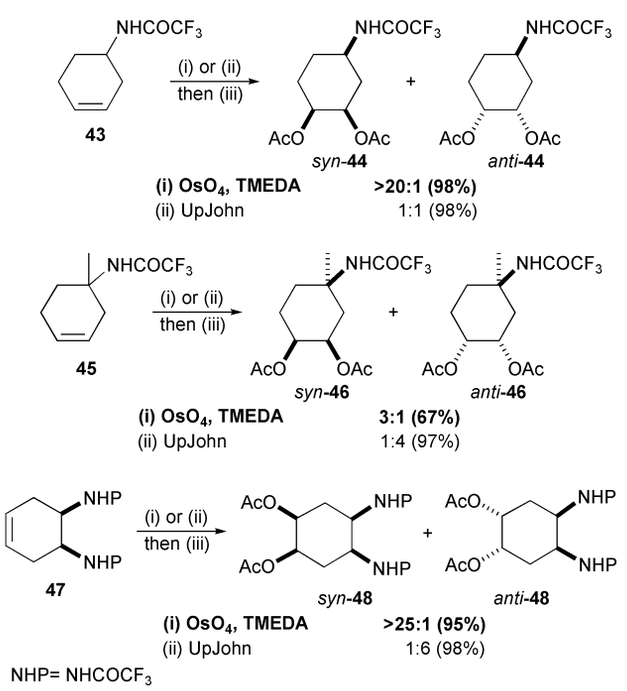


Fig. 3 Key NOE enhancements for *anti*-**41**, *syn*- and *anti*-**42**; NHP = $NHCOCCl_3$.



Scheme 8 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. (cat.) OsO_4, NMO acetone, water; iii. Ac_2O, py.

We used NOE experiments to confirm the stereochemistry of each of the diacetates shown in Scheme 8, see *syn*- and *anti*-**44**,**48**, Fig. 4. As far as compounds *syn*- and *anti*-**46** were concerned, the key NMR data were obtained on the TMEDA based osmate esters **49** obtained directly after directed dihydroxylation but before acidic methanol work-up (see later for a discussion of the mechanism). However, as the directed reaction is *syn* selective, an authentic sample of the *anti*-osmate ester (*anti*-**49**) was obtained by performing the directed dihydroxylation of **45** under protic (acetone–water) conditions (this was 3 : 1 selective for *anti*-**49**, *vide infra*).

Mechanism of the directed dihydroxylation of homoallylic substrates

The directed dihydroxylation is thought to proceed *via* the formation of a (reactive) bidentate complex **A** between OsO_4 and

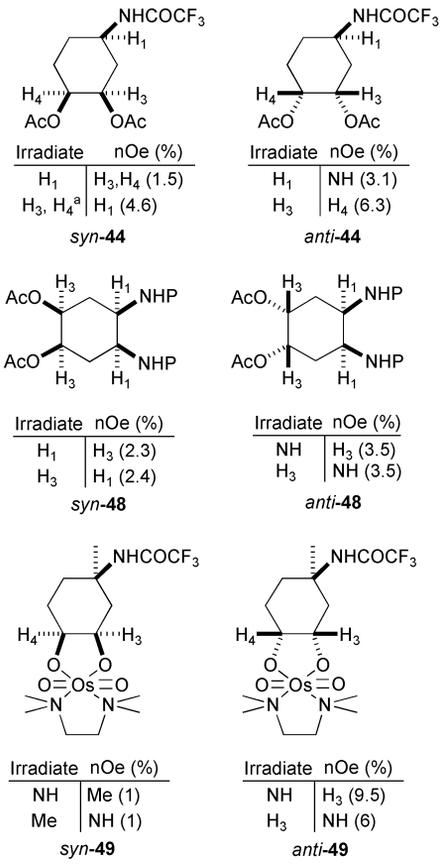


Fig. 4 Key NOE enhancements for *syn*- and *anti*-**44**, *syn*- and *anti*-**48**, and; *syn*- and *anti*-**49**; NHP = $NHCOCF_3$. [a]The signals for H_3 and H_4 overlap.

TMEDA, which is stable at low temperatures, Fig. 5.[3] The unique hydrogen bonding ability of this complex can be ascribed to the fact that addition of two electron donating nitrogen ligands to the transition metal increases electron density on the osmium, reduces back-bonding from the oxo groups and, in turn, makes them more electronegative. Consequently, increasing the electron density on the oxo ligands means that they are more capable of acting as hydrogen bond acceptors, which itself gives rise to contra-steric *syn* selectivity during oxidation of functionalised alkenes. We have previously reported the low temperature NMR spectra of this bidentate complex, which clearly shows the symmetrical nature of the ligand: moreover, low temperature IR experiments also show that, in this complex, the oxo ligands vibrate at a lower wavenumber than free OsO_4 itself, which can be taken as evidence in favour of a weakened Os=O bond order as predicted by the argument above.[3d] Significant evidence in favour of bidentate binding between OsO_4 and 1,2-diamines was obtained by Corey who published a crystal structure of the complex formed between OsO_4 and a chiral 1,2-diamine.[19] After addition of complex **A** to an alkene, the product is an osmate ester **B** (we have characterised several of these by X-ray) which still retains the chelated diamine ligand. Finally, the osmate ester is hydrolysed under acidic conditions to furnish the relevant 1,2-diol and osmium complexes of unknown composition.

During the course of our research programme, we have amassed a significant amount of evidence to implicate hydrogen

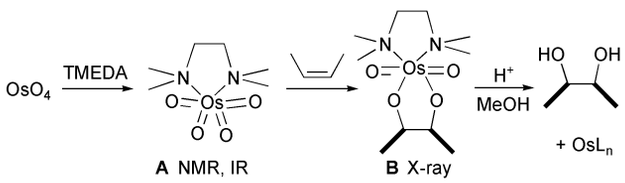
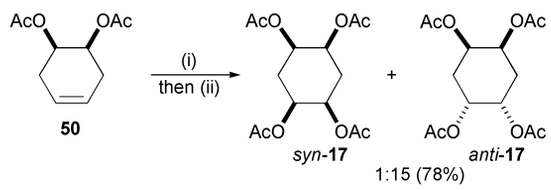


Fig. 5

bonding as the controlling element during directed dihydroxylation. As far as homoallylic systems are concerned, oxidation of the bis-acetate derivative **50** with OsO_4 and TMEDA was highly *anti*-selective, as would be expected for a substrate that is incapable of acting as a hydrogen bond donor, Scheme 9 (compare with the *syn* selective oxidation of **12**, Scheme 3). Moreover, repetition of several of the directed dihydroxylation reactions shown earlier, but in acetone–water solvent, showed little or no *syn* selectivity, which is consistent with the solvent disrupting the reagent–substrate hydrogen bonding interaction.



Scheme 9 *Reagents*: i. OsO_4 (1 eq.), TMEDA (1 eq.), CH_2Cl_2, −78 °C then HCl, MeOH; ii. Ac_2O, py.

The results from oxidation of the five membered rings using the OsO_4–TMEDA complex are clear-cut. Endocyclic homoallylic alcohols and amides both work very well indeed, giving high levels of *syn* selectivity, whereas exocyclic directing groups have more of a steric bias from the sidechain to overcome and the result is a less selective directed dihydroxylation.

However, the results from oxidation of the six membered substrates are more difficult to rationalise. Clearly the presence of a hydrogen bond donor in a homoallylic position presents a different environment to that in an allylic position. The first difference is that the hydrogen bond donor must adopt an axial orientation in order to be effective in the reaction, Fig. 6. This is not the case for allylic directing groups, and it has been shown convincingly here that pseudo-equatorial groups are more effective directing groups than their pseudo-axial counterparts.[3,20] This difference has ramifications for the effectiveness of the directing effect. For homoallylic systems, we not only have to consider the rate acceleration given by hydrogen bonding to favour contra-steric attack of the oxidant (*i.e.* is $k_{syn} > k^*_{syn/anti}$?) but also the energy penalty incurred in putting the directing group in a more hindered environment (*i.e.* *K*). As far as homoallylic alcohol **11** is concerned, this is governed by the Curtin–Hammett principle whereby the more stable conformer (OH equatorial) reacts more slowly than the less stable one with an axial OH. This balance is not always in our favour, as illustrated by the non-selective oxidation of the analogous trichloroacetamide **34**. Presumably, part of the reason that this compound is not oxidised selectively is the increased energy required to place a bulky amide directing group in an axial position. However, we do have suspicions that trichloroacetamide derivatives are not good as directing groups even when they are forced into an axial position, *vide infra*.

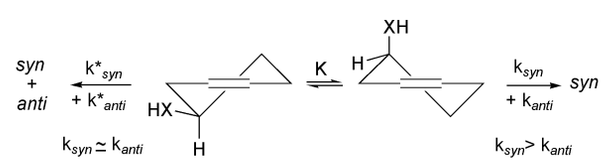


Fig. 6 The requirement for a homoallylic directing group (XH) to sit in an axial position.

Given the inability of **34** to be dihydroxylated with stereoselectivity, we were surprised to find that all of the trifluoroacetamides that we examined were then oxidised with enhanced selectivity for the *syn* isomer. Examination of the crystal structures of two osmate esters **51** and **52**, derived from allylic and homoallylic trichloroacetamides respectively, was

interesting because both show a hydrogen bond between an oxo-ligand on osmium and the directing group, Fig. 7. However, whereas in the case of **51** the hydrogen bond is clearly between N and O_1, the homoallylic amide derived osmate ester **52** has a stronger case for hydrogen bonding to the alternative oxo-ligand O_2 because the N–O_2 distance is shorter than that for N–O_1. In addition, within **52**, the Os=O bond is marginally longer for the proposed hydrogen bonding oxygen O_2 (*versus* the opposite, non hydrogen bonding, oxo group, O_3), whereas in **51**, both Os=O bonds are similar in length: this type of bond stretching might be expected if Os=O_2 were acting as a hydrogen bond acceptor.

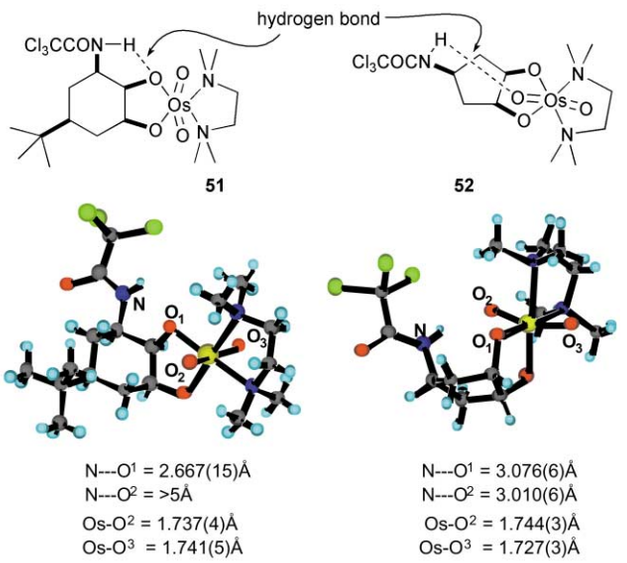


Fig. 7 X-Ray crystal structures of osmate esters **51** and **52**.

Clearly, these observations are pertinent to the osmate esters themselves, and the features of these compounds may not be conserved in the transition structures that preceded them. However, this observation does raise the intriguing possibility that the directed dihydroxylation involves hydrogen bonding to different oxo-ligands on osmium, depending upon the orientation of the directing group. Directing groups in an pseudo-equatorial orientation can hydrogen bond to the oxo-ligands that are attacking the alkene directly, whereas (homoallylic) axial directing groups may be able to hydrogen bond to the bystander Os=O ligands, Fig. 8. If this is true, then it helps to rationalise the enhanced directing effect of the trifluoroacetamides *versus* the trichloro-analogues. In the case of homoallylic directors, the angle of attack of the oxidant on the alkene brings it closer to the halo groups on the amide **D** and may provide a rationale for the poor performance of the trichloro compounds relative to the smaller trifluoro analogues. As far as allylic activating groups are concerned, the oxidant approaches the alkene from an angle that steers it well away from the halo-groups **C** and both trichloro- and trifluoroacetamides are oxidised with high selectivity.[3]

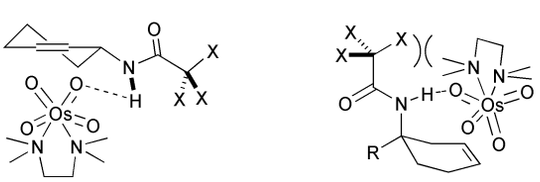


Fig. 8 **C**, directed dihydroxylation on an allylic trihaloacetamide; **D**, directed dihydroxylation on a homoallylic trihaloacetamide.

Of course, a simpler and more general explanation of the difference between the two halo derivatives is that the more acidic trifluoro derivative hydrogen bonds much more strongly to the oxidant and so increases the rate of directed dihydroxylation dramatically (*i.e.* k_{syn} is very large, Fig. 6), relative to the background, non-directed, rate of oxidation. At the same time, the $NHCOCF_3$ group is undoubtedly smaller than the $NHCOCCl_3$ group which makes it easier to adopt an axial position (*A* values: F 0.25–0.42; Cl 0.53–0.64[21]).

Given the poor performance of homoallylic trichloroacetamides within six membered rings, the *anti*-selective oxidation of **37** can be rationalised. In the absence of effective hydrogen bonding, disfavoured because of steric interactions between the oxidant and the CCl_3 group, complex **A** (Fig. 5) attacks from the face opposite to the bulky axially locked amide derivative. In addition, positioning the NH towards an incoming reagent means that the carbonyl group of the amide sits directly over the geminal methyl group (see **D**, Fig. 8, R = Me) which is expected to further decrease the amount of hydrogen bonding in the transition state.

The poor *syn* selectivity during oxidation of **39** (compare with the highly *syn* selective oxidation of **12**) may also be a consequence of the poor directing ability of (axial) homoallylic trichloroacetamides.

When we replace the trichloroacetamides with the trifluoro analogues, the *syn* selectivity is high in each case, presumably because of the enhanced directing group ability of the latter derivatives as discussed earlier.

To conclude, we have synthesised a variety of cyclic homoallylic alcohols and amides in order to define the substitution patterns that facilitate directed dihydroxylation. While both five and six-membered substrates are oxidised with good to excellent stereoselectivity, the presence of undue steric hindrance was shown to prevent efficient directed oxidation in a few examples. While, generally, amide derivatives are better directors than alcohols, there is a need to examine both trichloro- and trifluoroacetamides for any given substrate. Given the information now available about the optimum structure of the substrate, especially with respect to ring size and choice of directing group, we expect that this methodology will be useful in synthetic applications.

Experimental

General experimental

All reactions, except aqueous reactions, were carried out under an atmosphere of argon. Proton nuclear magnetic resonance spectra (NMR) were recorded on a Gemini 200 at 200 MHz, a Varian Unity Inova 300 at 300 MHz, a Varian Unity Inova 400 at 400 MHz and a Varian Unity Inova 500 at 500 MHz. ^{13}C nuclear magnetic resonance spectra were recorded on a Varian Unity Inova 300 at 75 MHz, a Varian Unity Inova 400 at 100 MHz and a Varian Unity Inova 500 at 125 MHz. Chemical shifts (δ) are quoted in parts per million (ppm), downfield from tetramethylsilane. Coupling constants (*J*) are quoted in Hz. Infrared spectra (IR) were recorded on an ATI Mattson Genesis FTIR as evaporated films (EF). Mass spectra were recorded on a Kratos Concept or a Fisson VG Trio 2000 using electron impact or chemical ionisation (CI). Melting points were obtained on a Kofler block and are uncorrected.

Tetrahydrofuran (THF) was dried and distilled from sodium metal using benzophenone as indicator, under an atmosphere of argon. Dichloromethane (DCM) was distilled over calcium hydride.

All chiral compounds are racemic.

4-(*tert*-Butyldimethylsilyloxy)hepta-1,6-diene 2[22]

To a solution of **1** (1.76 g, 15.7 mmol) and triethylamine (6.37 g, 63 mmol) in dichloromethane (100 ml) was added *tert*-butyldimethylsilyltrifluoromethanesulfonate (4.23 g, 16.0 mmol) dropwise at −78 °C. The resulting solution was warmed to room temperature and then concentrated *in vacuo*. Purification

by flash chromatography (petrol–EtOAc, 9 : 1) gave the title compound as a colourless oil (3.42 g, 96%). All spectroscopic data were consistent with that in the literature.

1-(*tert*-Butyldimethylsilyloxy)cyclopent-3-ene 3[23]

To a solution of **2** in degassed benzene (50 ml) was added Grubbs' catalyst ($(Cl_2(Pcy_3)_2Ru{=}CHCH{=}CPh_2$), 110 mg, 0.13 mmol) and the solution stirred at room temperature for 3 days. The mixture was then concentrated *in vacuo*. Purification by flash chromatography (petrol–EtOAc, 9 : 1) gave the title compound as a colourless oil (1.3 g, 50%) along with recovered starting material (0.98 g, 33%). All spectroscopic data were consistent with that in the literature.

Cyclopent-3-en-1-ol 4[6]

To a solution of 1-(*tert*-butyldimethylsilyloxy)cyclopent-3-ene **3** (500 mg, 2.5 mmol) in methanol (20 ml) was added hydrochloric acid (conc., 5 drops) and the solution stirred for 5 minutes. The solution was concentrated under reduced pressure and the residue redissolved in diethyl ether (100 ml) and washed with brine (50 ml). The ethereal layer was dried ($MgSO_4$) and concentrated to yield the crude product as a colourless oil. The resulting oil was purified by flash chromatography (petrol–Et_2O, 4 : 1) to afford the title compound as a colourless oil (202 mg, 97%); all data are consistent with those in the literature.

2-Allyloxy-1-(*tert*-butyldimethylsilyloxy)but-3-ene 5

To a solution of but-3-ene-1,2-diol (5.2 g, 0.059 mol) and imidazole (8.0 g, 0.12 mol) in dichloromethane (100 ml) was added *tert*-butyldimethylsilyl chloride (8.9 g, 0.059 mol) and the solution stirred for 4 hours. The mixture was poured into water (100 ml) and extracted with diethyl ether (3 × 100 ml). The combined ethereal extracts were dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude product as a colourless oil. The resulting oil was purified by flash chromatography (petrol–EtOAc, 10 : 1) to afford the mono-TBS compound as a colourless oil (10 g, 99%).

To a solution of 1-(*tert*-butyldimethylsilyloxy)but-3-en-2-ol (3.0 g, 0.017 mol) in tetrahydrofuran (50 ml) was added potassium bis(trimethylsilyl)amide (3.8 g, 0.019 mol) at 0 °C and the resulting solution stirred for 1 hour. Allyl bromide (2.5 g, 0.021 mol) was added and stirring continued for a further 4 hours. The solution was poured into brine (100 ml) and extracted with diethyl ether (3 × 100 ml). The combined ethereal extracts were dried ($MgSO_4$) and evaporated to yield the crude product as a colourless oil. The resulting oil was purified by flash chromatography (petrol–EtOAc, 10 : 1) to afford **5** as a colourless oil (2.5 g, 69%); ν_{max} (film)/cm^{-1} 2955, 2930, 2859, 1254, 1125, 1097, 838; δ_H (300 MHz; $CDCl_3$) 5.98–5.66 (2H, m), 5.34–5.10 (4H, m), 4.34–3.36 (5H, m), 0.89 (9H, s), 0.06, (6H, s); δ_C (75 MHz; $CDCl_3$) 136.1, 135.0, 117.7, 116.4, 81.1, 69.8, 66.2, 25.8, 18.3, −5.3.

2-(Hydroxymethyl)-2,5-dihydrofuran 6[24]

To a solution of 2-allyloxy-1-(*tert*-butyldimethylsilyloxy)but-3-ene **5** (2.5 g, 0.011 mol) in degassed benzene (50 ml) was added Grubbs' catalyst ($(Cl_2(Pcy_3)_2Ru{=}CHCH{=}CPh_2$), 0.45 g, 0.55 mmol) and the solution stirred for 3 days. The solution was exposed to air and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (petrol–EtOAc, 5 : 1) to afford 2-(*tert*-butyldimethylsilyloxy)methyl-2,5-dihydrofuran as a colourless oil (1.5 g, 64%); δ_H (300 MHz; $CDCl_3$) 5.95 (1H, m), 5.84 (1H, m), 4.85 (1H, m), 4.68–4.62 (2H, m), 3.69 (1H, dd, *J* 10 and 5), 3.60 (1H, dd, *J* 10 and 6), 0.92 (9H, s), 0.09 (6H, s). To a solution of 2-(*tert*-butyldimethylsilyloxy)methyl-2,5-dihydrofuran (1.5 g, 7.0 mmol) in methanol (10 ml) was added hydrochloric acid (conc., 3 drops) and the solution stirred for 5 minutes. The solution was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (light petroleum–Et_2O, 4 : 1) to afford the title compound **6** as a colourless oil (202 mg, 97%); all data were consistent with those in the literature.

Isopropyl 2-methyl-2,5-dihydrofuran-2-carboxylate 8[25]

A suspension of lithium (1.1 g, 0.16 mol) and naphthalene (21 g, 0.16 mol) in tetrahydrofuran (100 ml) was sonicated for 1 hour. The resulting green solution was cooled to −78 °C and a solution of isopropyl furan-2-carboxylate **7** (5.0 g, 32 mmol) and bis(2-methoxyethyl)amine (22 g, 0.16 mol) in tetrahydrofuran (50 ml) was added dropwise over 30 minutes (exotherm). The solution was stirred for 1 hour before the addition of iodomethane (27 g, 0.19 mol) (exotherm). The resulting solution was allowed to warm to room temperature over 5 hours. The solution was concentrated under reduced pressure and the residue redissolved in diethyl ether (500 ml) and washed with water (200 ml) followed by hydrochloric acid (2 M, 100 ml). The ethereal layer was dried ($MgSO_4$) and concentrated under reduced pressure (to ~100 ml volume). The solution was allowed to stand at 0 °C for 1 hour during which time a white solid crystallised. The solid was filtered off and the filtrate washed with methanol (chilled, 2 × 50 ml). The combined liquors were concentrated further to yield the crude product as a colourless oil. The resulting oil was purified by flash chromatography (petrol–Et_2O, 100 : 1⟶4 : 1) to afford the title compound as a colourless oil (1.1 g, 20%) (CARE: product volatile and unstable); ν_{max} (film)/cm^{-1} 2981, 2935, 2859, 1743, 1726; δ_H (300 MHz; $CDCl_3$) 5.98 (1H, dt, *J* = 1.7 and 4.5), 5.83 (1H, dt, *J* = 2.3 and 6.0), 5.02 (1H, septet, *J* = 6.3), 4.82–4.68 (2H, m), 1.52 (3H, s), 1.25 (6H, d, *J* = 6); δ_C (75 MHz, $CDCl_3$) 172.7, 130.1, 128.0, 90.0, 75.7, 68.4, 23.9, 21.6, 21.5; MS (CI, *m*/*z*) 188 (M + 18, 100%), 171 (M + 1, 73%); Found 170.0946 (EI) $C_9H_{14}O_3$ requires 170.0942.

2-Methyl-2-hydroxymethyl-2,5-dihydrofuran 9

To a stirred suspension of lithium aluminium hydride (0.45 g, 12 mmol) in tetrahydrofuran (50 ml) at −78 °C was added dropwise isopropyl 2-methyl-2,5-dihydrofuran-2-carboxylate **8** (1.0 g, 5.9 mmol) and the mixture stirred for 2 hours. The mixture was allowed to warm to room temperature and ammonium chloride (sat., 2 ml) was added. The resulting mixture was poured into brine (100 ml) and extracted with diethyl ether (3 × 100 ml). The combined ethereal extracts were dried ($MgSO_4$) and evaporated to yield the crude product as a colourless oil. This oil was purified by flash chromatography (petrol–Et_2O, 4 : 1) to afford the title compound **9** as a colourless oil (0.64 g, 95%). The product was found to be unstable, under going rapid air oxidation to the lactone and so characterisation was not possible.

Cyclohex-3-en-1-ol 11[8]

A solution of 9-BBN (0.5 M in tetrahydrofuran, 40 ml, 20 mmol) was added dropwise to cyclohexa-1,4-diene **10** (1.6 g, 20 mmol) and the solution stirred for 18 hours. Sodium hydroxide (3 M, 6 ml) was added followed by the dropwise addition of hydrogen peroxide (30%, 6 ml). The resulting solution was heated at reflux for 1 hour then allowed to cool. The mixture was poured into brine (100 ml) and extracted with diethyl ether (3 × 100 ml). The combined ethereal extracts were dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude product. The resulting oil was then purified by flash chromatography (petrol–Et_2O, 19 : 1) to afford the title compound as a colourless oil (1.6 g, 82%); all data are consistent with those in the literature.

***cis*-Cyclohex-4-ene-1,2-diol 12**[9]

To a solution of cyclohexa-1,4-diene **10** (1.6 g, 20 mmol) and *N*-methylmorpholine *N*-oxide (2.4 g, 20 mmol) in acetone–water (4 : 1, 50 ml) was added osmium tetraoxide (51 mg,

0.2 mmol) and the resulting solution stirred for 4 hours. Sodium sulfite (1 g) was added and stirring continued for 30 minutes. The solution was poured into brine (100 ml) and extracted with ethyl acetate (3 × 100 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to yield the crude product as a colourless oil. The resulting oil was purified by flash chromatography (petrol–EtOAc, 4 : 1) to afford the title compound **12** as a colourless oil (2.1 g, 93%); all data are consistent with those in the literature.

General procedure for OsO_4, TMEDA oxidation

To a solution of substrate (1.0 eq.) and TMEDA (1.1 eq.) in dichloromethane (50 ml) pre-cooled to −78 °C was added a solution of OsO_4 (1.1 eq.) in dichloromethane (~1 ml) in 1 portion. The solution turned deep red, then brown–black. The solution was stirred until reaction was complete (TLC analysis, *ca.* 30 minutes) and the solution was warmed to room temperature. The solvent was removed *in vacuo* to afford a dark brown oil. This concentrated osmate ester product was dissolved in methanol (~15 ml) and concentrated hydrochloric acid (4 drops) was added. The mixture was stirred at room temperature until complete reaction (TLC analysis for osmate ester disappearance, *ca.* 30 minutes). The products were concentrated *in vacuo*. The crude mixture was redissolved in 1 : 1 acetic anhydride and pyridine (~10 ml) and DMAP (10 mg) was added. The mixture was stirred at room temperature overnight and concentrated *in vacuo* on a hot bath (~80 °C). An NMR spectrum was obtained on the crude mixture.

General procedure for UpJohn oxidation

To a stirred solution of substrate (1.0 eq.) and *N*-methylmorpholine *N*-oxide monohydrate (3.0 eq.) in 4 : 1 acetone–water (50 ml) at room temperature was added OsO_4 (1 crystal, ~20 mg) and the solution was stirred until reaction was complete (TLC analysis, *ca.* 4 hours). The reaction mixture was concentrated *in vacuo* on a hot bath (~60 °C). The concentrated crude diol product was dissolved in 1 : 1 acetic anhydride–pyridine (~10 ml) and DMAP (10 mg) was added. The reaction mixture was stirred overnight and concentrated *in vacuo* on a hot bath (~80 °C). An NMR was obtained on the crude mixture.

***syn*-1,2,4-Triacetoxycyclopentane *syn*-13**

Cyclopent-3-en-1-ol **4** (50 mg, 0.60 mmol) was oxidised with OsO_4, TMEDA to yield the crude products [>25 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the title compound as a colourless oil (104 mg, 71%); ν_{max} (film)/cm^{-1} 2992, 2953, 1742, 1233, 1027; δ_H (300 MHz; $CDCl_3$) 5.16–5.02 (3H, m), 2.45 (2H, dt, *J* 14 and 7), 2.08 (6H, s), 2.06 (3H, s), 1.95 (2H, dt, *J* 14 and 4); δ_C (75 MHz; $CDCl_3$) 170.5, 170.1, 72.1, 70.4, 35.5, 35.4, 20.8; *m*/*z* (CI) 262 (100%, M + 18); Found (EI) 244.0942; $C_{11}H_{16}O_6$ requires 244.0947.

***syn*- and *anti*-1,2,4-Triacetoxycyclopentane *syn*- and *anti*-13**

Cyclopent-3-en-1-ol **4** (50 mg, 0.60 mmol) was oxidised using the UpJohn conditions to yield the crude products [2 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the title compounds as a colourless oil (120 mg, 82%) as an inseparable mixture of isomers. The *syn* isomer was identical (by ^{1}H and ^{13}C NMR) to *syn*-**13** prepared previously. For the minor isomer *anti*-**13**; δ_H (300 MHz; $CDCl_3$) 5.38–5.25 (3H, m), 2.30–2.05 (4H, m), 2.05 (6H, s), 2.04 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.4, 170.0, 72.2, 71.0, 36.0, 35.9, 20.9.

***anti*-2-(Acetoxymethyl)-3,4-diacetoxytetrahydrofuran *anti*-14** [11]

2-(Hydroxymethyl)-2,5-dihydrofuran **6** (50 mg, 0.50 mmol) was oxidised using UpJohn conditions to yield the crude products [4 : 1 (*anti* : *syn*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (petrol–EtOAc, 4 : 1) to afford the title compound as a colourless oil (98 mg, 75%); δ_H (300 MHz; $CDCl_3$) 5.37 (1H, t, *J* 5), 5.13 (1H, t, *J* 5), 4.33–4.05 (4H, m), 3.88 (1H, dd, *J* 10 and 5), 2.17 (3H, s), 2.10 (3H, s), 2.09 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.6, 170.0, 169.9, 77.9, 71.7, 71.1, 70.7, 63.4, 20.7, 20.6, 20.5. All data were consistent with that in the literature.

***syn*- *and anti*-2-(Acetoxymethyl)-3,4-diacetoxytetrahydrofuran *syn*- and *anti* 14**

2-(Hydroxymethyl)-2,5-dihydrofuran **6** (50 mg, 0.50 mmol) was oxidised using OsO_4, TMEDA to yield the crude products [1 : 1 (*anti* : *syn*) by ^{1}H NMR]. The resulting oil was then purified by flash chromatography (petrol–EtOAc, 4 : 1) to afford the pure products as a colourless oil (72 mg, 55%) as an inseparable mixture of diastereomers; the *anti* compound was identical (by ^{1}H and ^{13}C NMR) to *anti*-**14** prepared previously.

***syn*-2-Methyl-2-(acetoxymethyl)tetrahydrofuran *syn*-15**

2-Methyl-2-hydroxymethyl-2,5-dihydrofuran **9** (50 mg, 0.51 mmol) was oxidised using OsO_4, TMEDA to yield the crude products [6 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (petrol–EtOAc, 4 : 1) to afford the pure title compound as a colourless oil (116 mg, 83%); ν_{max} (film)/cm^{-1} 2977, 2929, 1746, 1374, 1230, 1046; δ_H (300 MHz; $CDCl_3$) 5.43 (1H, q, *J* 5), 5.17 (1H, d, *J* 5), 4.26–4.09 (3H, m), 3.89 (1H, dd, *J* 10 and 5), 2.10 (6H, s), 2.08 (3H, s), 1.36 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.6, 169.8, 169.5, 80.8, 76.2, 71.2, 68.9, 65.3, 22.3, 20.6, 20.4, 18.3; Found (CI) 292.1392, $C_{12}H_{22}NO_7 + NH_4$ requires 292.1396.

***anti*-2-Methyl-2-(acetoxymethyl)tetrahydrofuran *anti*-15**

2-Methyl-2-hydroxymethyl-2,5-dihydrofuran **9** (50 mg, 0.51 mmol) was oxidised using UpJohn conditions to yield the crude products [2 : 1 (*anti* : *syn*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (petrol–EtOAc, 4 : 1) to afford the product mixture as a colourless oil (110 mg, 79%) as an inseparable mixture of isomers (*anti* major compound); ν_{max} (film)/cm^{-1} 2989, 2944, 1746, 1379, 1232, 1046; δ_H (300 MHz; $CDCl_3$) 5.46–5.39 (1H, m), 5.26 (1H, d, *J* 6), 4.26–3.85 (4H, m), 2.11 (3H, s), 2.10 (6H, s), 1.26 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.4, 169.8, 169.6, 81.2, 72.7, 71.9, 69.3, 67.9, 20.7, 20.5, 20.4, 18.3; Found (CI) 292.1400, $C_{12}H_{22}NO_7$ requires 292.1396,

***syn*-1,2,4-Triacetoxycyclohexane *syn*-16**

Cyclohex-3-en-1-ol **11** (50 mg, 0.51 mmol) was oxidised using OsO_4, TMEDA to yield the crude mixture of products [3 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford a colourless oil (121 mg, 92%) as an inseparable mixture of isomers; mixture: ν_{max} (film)/cm^{-1} 2953, 1745, 1370, 1235, 1028; *syn*-**16** δ_H (300 MHz; $CDCl_3$) 5.17–5.11 (1H, m), 4.84–4.72 (2H, m), 2.04 (3H, s), 1.98 (3H, s), 1.86 (3H, s), 2.05–1.45 (6H, m); δ_C (75 MHz; $CDCl_3$) 170.1, 170.0, 169.9, 69.5, 69.3, 67.9, 31.4, 25.3, 24.7, 21.1, 20.9, 20.8: *anti*-**16**; δ_H (300 MHz; $CDCl_3$) 5.08–5.01 (1H, m), 4.81–4.67 (2H, m), 1.99 (9H, s), 2.05–1.45 (6H, m); δ_C (75 MHz; $CDCl_3$) 170.3, 170.2, 170.1, 69.7, 68.8, 68.6, 31.8, 25.9, 25.3, 23.6, 21.1, 20.9; mixture Found (CI) 276.1437, $C_{12}H_{22}NO_6$ requires 276.1447.

***anti*-1,2,4-Triacetoxycyclohexane *anti*-16**

Cyclohex-3-en-1-ol **11** (50 mg, 0.51 mmol) was oxidised using UpJohn conditions to yield the crude mixture of products [1 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the product mixture as a colourless oil (115 mg, 88%) as an inseparable mixture of

isomers; All data are consistent with *syn*- and *anti*-**16** prepared previously.

syn-1,2,4,5-Tetraacetoxycyclohexane *syn*-17

cis-Cyclohex-4-ene-1,2-diol **12** (50 mg, 0.44 mmol) was oxidised using OsO_4, TMEDA to yield the crude products as a colourless oil [12 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the title compound as a colourless solid (114 mg, 82%), mp 65–66 °C; ν_{max} (film)/cm^{-1} 2971, 2943, 1730, 1371, 1230, 1029; δ_H (300 MHz; $CDCl_3$) 5.11–5.03 (4H, m), 2.35 (2H, dt, *J* 14 and 7), 2.06 (12H, s), 1.84 (2H, dt, *J* 14 and 3); δ_C (75 MHz; $CDCl_3$) 170.0, 67.9, 28.0, 20.9; Found (CI) 334.1508, $C_{14}H_{24}NO_8$ requires 334.1502.

anti-1,2,4,5-Tetraacetoxycyclohexane *anti*-17 [14]

cis-Cyclohex-4-ene-1,2-diol **12** (50 mg, 0.44 mmol) was oxidised using UpJohn conditions to yield the crude products as a colourless oil [2 : 1 (*anti* : *syn*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the product mixture as a colourless solid (114 mg, 86%) as an inseparable mixture of isomers. The products were identical (by ^{1}H and ^{13}C NMR) to *syn*- and *anti*-**17** prepared by OsO_4–TMEDA oxidation of **12**.

2-*endo*-5-*endo*-6-*endo*-2,5,6-Triacetoxybicyclo[2.2.1]heptane *endo*-19

endo-Bicyclo[2.2.1]hept-5-en-2-ol **18** (100 mg, 0.90 mmol) was oxidised using OsO_4, TMEDA to yield the crude product [4 : 6 (*syn* : *anti*) by ^{1}H NMR] as a colourless oil. The resulting oil was then purified by flash chromatography (petrol–EtOAc, 2 : 1) to afford the mixture as a colourless oil (191 mg, 78%). A small sample of the title compound was separated from the mixture by further flash chromatography (light petroleum–EtOAc, 4 : 1); ν_{max} (film)/cm^{-1} 2970, 1731, 1241, 982; δ_H (300 MHz; $CDCl_3$) 5.59 (1H, d, *J* 6), 5.19 (1H, d, *J* 6), 5.02 (1H, dt, *J* 10 and 4), 2.97 (1H, d, *J* 5), 2.70 (1H, d, *J* 5), 2.28–2.12 (1H, m), 2.06 (9H, s), 1.26–0.97 (3H); δ_C (75 MHz; $CDCl_3$) 170.6 (3), 100.5, 96.0, 72.1 (3), 47.1, 43.6, 32.9, 30.7, 20.9.

2-*endo*-5-*exo*-6-*exo*-2,5,6-Triacetoxybicyclo[2.2.1]heptane *exo*-19 [15]

endo-Bicyclo[2.2.1]hept-5-en-2-ol **18** (50 mg, 0.45 mmol) was oxidised using UpJohn conditions to yield the crude product (single isomer by ^{1}H NMR) as a colourless oil. The resulting oil was purified by flash chromatography (petrol–EtOAc, 2 : 1) to afford the title compound as a colourless oil (100 mg, 82%); All data were consistent with that in the literature.

N-(1-Allylbut-3-enyl)-2,2,2-trichloroacetamide 20

To a stirred solution of hepta-1,6-dien-4-ol **1** (5.15 g, 46.0 mmol) and triethylamine (13.9 g, 138 mmol) in DCM (125 ml) at 0 °C under N_2 was added (CARE: exotherm) methanesulfonic anhydride (12.6 g, 72.4 mmol). The resulting solution was allowed to warm to room temperature over 1 hour and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (Et_2O–petrol, 1 : 1) to afford the mesylate compound as a colourless oil (8.63 g). To a stirred solution of mesylate (2.00 g, 10.5 mmol) in DMSO (50 ml) was added sodium azide (2.05 g, 31.6 mmol) and the reaction stirred at room temperature for 48 hours. The solution was poured into water (200 ml) and extracted with Et_2O (2 × 100 ml). The combined organic extracts were dried with magnesium sulfate and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (petrol) to afford the azide as a colourless oil (1.15 g). To a stirred suspension of lithium aluminium hydride (296 mg, 15.7 mmol) in Et_2O (25 ml) was added dropwise a solution of azide in Et_2O (25 ml) at −10 °C. The resulting solution was allowed to warm to room temperature over 15 minutes. Sodium sulfate decahydrate (~1 g) was slowly added until a white solid precipitated, then magnesium sulfate (~2 g) was added. The mixture was filtered and the residue washed with Et_2O (3 × 50 ml). The filtrate was concentrated *in vacuo* to afford the amine as a colourless oil. To a stirred solution of amine (702 mg, 6.27 mmol) in DCM (50 ml) was added triethylamine (1.90 g, 18.8 mmol) and the solution cooled to 0 °C. Trichloroacetyl chloride (1.25 g, 6.89 mmol) was added dropwise and the solution was warmed to room temperature over 2 hours. The mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 1 : 1) to yield a pale yellow solid which was recrystallised to afford the title compound as white needles (1.15 g, 52% from **1**), mp 61–63 °C (from hexane) (Found: C, 42.4; H, 4.4; N, 5.1; $C_9H_{12}Cl_3NO$ requires C, 42.1; H, 4.7; N, 5.5%); υ_{max} (film)/cm^{-1} 3318, 1690, 1532, 1274; δ_H (300 MHz; $CDCl_3$) 6.58 (1H, br s), 5.90–5.75 (2H, m), 5.23–5.14 (4H, m), 4.14–4.00 (1H, m), 2.50–2.28 (4H, m); δ_C (75 MHz; $CDCl_3$) 133.0, 118.9, 99.9, 50.1, 37.7 (no *C*Cl_3); MS (CI, *m*/*z*) 279 (5%), 277 (40), 273 (100); Found (CI) 273.0328, M + NH_4^+ $C_9H_{16}Cl_3N_2O$ requires 273.0328.

N-Cyclopent-3-enyl-2,2,2-trichloroacetamide 21

N-(1-Allylbut-3-enyl)-2,2,2-trichloroacetamide **20** (1.11 g, 4.34 mmol) was dissolved in DCM (15 ml) and the solution purged with nitrogen for 5 minutes. Grubbs' catalyst (($Cl_2(Pcy_3)_2Ru$=CHPh) 108 mg, 0.13 mmol) was added and the reaction stirred for 16 hours. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 1 : 1) to yield an off-white solid which was recrystallised to give white needles (662 mg, 67%), mp 84–86 °C (from hexane) (Found: C, 37.1; H, 3.4; N, 6.0; $C_7H_8Cl_3NO$ requires C, 36.8; H, 3.5; N, 6.1%); υ_{max} (film)/cm^{-1} 3424, 2974, 2253, 1703, 1513, 1256, 1048; δ_H (300 MHz; $CDCl_3$) 6.80 (1H, br s), 5.79 (2H, s), 4.65–4.52 (1H, m), 2.86 (2H, dd, *J* 15.9 and 7.6), 2.35 (2H, dd, *J* 15.9 and 3.4); δ_C (75 MHz; $CDCl_3$) 128.6, 50.9, 39.7 (no *C*=O, no *C*Cl_3); (CI, *m*/*z*) 251 (5%), 249 (30), 247 (90), 245 (100); Found (CI) 245.0019 (M + NH_4^+ $C_7H_{12}Cl_3N_2O$ requires 245.0015).

2-(Trimethylsilanoxy)but-3-enenitrile 22 [26]

To freshly distilled acrolein (2.82 g, 50.5 mmol) and trimethylsilyl cyanide (5.00 g, 50.5 mmol) was added freshly sublimed zinc(II) iodide (~10 mg) and the mixture heated at reflux for 90 minutes. The reaction mixture was cooled to room temperature and purified by short-path distillation to afford the title compound as a colourless oil (7.55 g, 96%). All data are consistent with that of the literature.

N-(2-Hydroxybut-3-enyl)-2,2,2-trichloroacetamide 23

To a stirred suspension of lithium aluminium hydride (2.55 g, 67.2 mmol) in Et_2O (50 ml) at 0 °C was added dropwise a solution of cyanohydrin **22** (5.00 g, 32.3 mmol) in Et_2O (50 ml). The solution was allowed to warm to room temperature over 2 hours. Sodium sulfate decahydrate (~2 g) was slowly added until a white solid precipitated, then magnesium sulfate (~2 g) was added. The mixture was filtered and the residue washed with Et_2O (3 × 75 ml). The solution was concentrated *in vacuo* to afford the aminol as a yellow oil (2.29 g). To a stirred solution of aminol (793 mg, 9.11 mmol) in DCM (50 ml) was added triethylamine (2.76 g, 27.3 mmol) at room temperature. The solution was cooled to 0 °C and trichloroacetyl chloride (1.82 g, 10.0 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature over 4 hours. The mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a white solid (1.21 g, 47% from **22**), mp 60–62 °C (Found: C, 31.4; H, 3.5; N, 6.0; $C_6H_8Cl_3NO_2$ requires C, 31.0; H, 3.5; N, 6.0%); υ_{max} (film)/cm^{-1} 3385 (br), 3056, 2986, 1713, 1694, 1530, 1517,

1505, 1428, 1265, 1141, 1074; δ_H (300 MHz; $CDCl_3$) 7.08 (1H, br s), 5.89–5.74 (1H, m), 5.32 (1H, dd, *J* 17.1 and 1.2), 5.21 (1H, dd, *J* 10.5 and 1.2), 4.37–4.21 (1H, m), 3.63–3.45 (1H, m), 3.34–3.12 (1H, m), 2.25 (1H, br d, *J* 3.2); δ_C (75 MHz; $CDCl_3$) 162.3, 136.9, 117.2, 71.0, 46.0 (no *C*Cl_3); Found (CI) 231.9697 ($M + H^+$ $C_6H_9Cl_3NO_2$ requires 231.9699).

N-(2-Allyloxybut-3-enyl)-2,2,2-trichloroacetamide 24

To a stirred solution of *N*-(2-hydroxybut-3-enyl)-2,2,2-trichloroacetamide **23** (1.50 g, 6.45 mmol) in DCM (10 ml) was added a solution of allyloxy trichloroacetimidate (2.61 g, 12.9 mmol) in hexane (30 ml). Trifluoromethanesulfonic acid was added until a white precipitate formed (6 drops). The reaction was heated at reflux for 16 hours. The mixture was cooled to room temperature and filtered. The filtrate was concentrated *in vacuo* onto silica and purified by flash chromatography (petrol–Et_2O, 20 : 1) to afford the title compound as a colourless oil (1.65 g, 94%); υ_{max} (film)/cm^{-1} 3425, 3349, 3081, 2986, 2938, 2865, 1713, 1696, 1646, 1517, 1426, 1266, 1137, 1086; δ_H (300 MHz; $CDCl_3$) 7.02 (1H, br s), 5.89–5.74 (1H, m), 5.64 (1H, ddd, *J* 17.4, 10.3 and 7.1), 5.36–5.06 (4H, m), 4.06 (1H, dd, *J* 12.8 and 5.2), 3.98–3.85 (1H, m), 3.82 (1H, dd, *J* 12.8 and 6.2), 3.56 (1H, ddd, *J* 13.8, 6.9 and 4.0), 3.24 (1H, ddd, *J* 13.8, 7.7 and 4.5); δ_C (75 MHz; $CDCl_3$) 134.7, 134.1, 119.5, 117.5, 77.7, 69.4, 44.8 (no *C*=O, no *C*Cl_3); (CI, *m*/*z*) 293 (40%), 291 (100), 276 (15), 274 (30), 257 (25), 255 (30), 238 (25), 219 (20); Found (CI) 289.0279 ($M + NH_4^+$ $C_9H_{16}Cl_3N_2O_2$ requires 289.0277).

2-[(2,2,2-Trichloroacetylamino)methyl]-2,5-dihydrofuran 25

N-(2-Allyloxybut-3-enyl)-2,2,2-trichloroacetamide **24** (522 mg, 1.92 mmol) was dissolved in DCM (25 ml) and the solution purged with nitrogen for 5 minutes. Grubbs' catalyst ((Cl_2-$(Pcy_3)_2$Ru=CHPh) 114 mg, 0.14 mmol) was added and the reaction stirred for 16 hours. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (petrol–Et_2O, 20 : 1 ⟶ 3 : 1) to afford the title compound as a beige solid (662 mg, 67%), mp 63–65 °C; υ_{max} (film)/cm^{-1} 2936, 2860, 1711, 1536, 1259, 1077; δ_H (300 MHz; $CDCl_3$) 6.98 (1H, br s), 6.10–6.03 (1H, m), 5.83–5.76 (1H, m), 5.09–5.00 (1H, m), 4.80–4.63 (2H, m), 3.66–3.51 (2H, m); δ_C (75 MHz; $CDCl_3$) 162.2, 129.2, 126.0, 84.5, 75.8, 44.6 (no *C*Cl_3); (CI, *m*/*z*) 265 (30%), 263 (100), 248 (10), 246 (25), 229 (20), 227 (25), 210 (15); Found (CI) 260.9967 ($M + NH_4^+$ $C_7H_{12}Cl_3N_2O_2$ requires 260.9964).

2-Methyl-2,5-dihydrofuran-2-carbonitrile 26

Sodium-dried ammonia (~30 ml) was distilled into an oven-dried 100 ml 3-necked flask equipped with a powerful magnetic stirrer at −78 °C. Distilled THF (30 ml) was then added followed by sodium metal (385 mg, 16.7 mmol) in small portions. The reaction mixture was stirred for 5 minutes to give a deep-blue solution. 2-Furonitrile (300 mg, 3.23 mmol) in THF (10 ml) was added dropwise over 5 minutes (dark blue ⟶ dark red colour change) and the reaction mixture was stirred at −78 °C for 15 minutes. Iodomethane (4.59 g, 32.3 mmol) was added in 1 portion and the mixture stirred for 15 minutes. Ammonium chloride (~2 g) was added and the mixture was allowed to warm to room temperature over 2 hours. Nitrogen was bubbled through the solution to evaporate excess ammonia. The mixture was diluted with Et_2O (50 ml), washed with water (30 ml) and brine (30 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* onto silica. The crude product was purified by flash chromatography to afford the title compound as a yellow oil (147 mg, 42%); δ_H (300 MHz; $CDCl_3$) 6.19 (1H, dt, *J* 6.0 and 1.6), 5.88–5.82 (1H, m), 4.83 (1H, ddd, *J* 16.6, 3.7 and 1.6), 4.80–4.73 (1H, m), 1.72 (3H, s); δ_C (75 MHz; $CDCl_3$) 130.5, 127.9, 119.4, 81.3, 75.9, 26.4; product volatile and unstable so full characterisation was not possible.

2-Methyl-2-[(2,2,2-trichloroacetylamino)methyl]-2,5-dihydrofuran 27

To a stirred suspension of lithium aluminium hydride (160 mg, 4.20 mmol) in Et_2O (20 ml) at 0 °C was added dropwise a solution of 2-methyl-2,5-dihydrofuran-2-carbonitrile **26** (147 mg, 1.40 mmol) in Et_2O (20 ml). The reaction was warmed to room temperature and stirred for 10 minutes. Sodium sulfate decahydrate (~1 g) was slowly added until a white solid precipitated, then magnesium sulfate (~1 g) was added. The mixture was filtered and the residue washed with Et_2O (3 × 75 ml). The solution was concentrated *in vacuo* to yield a yellow oil. The oil was dissolved in DCM (30 ml) and triethylamine (424 mg, 4.20 mmol) was added under stirring at room temperature. The mixture was cooled to 0 °C and trichloroacetyl chloride (260 mg, 1.4 mmol) was added dropwise. The mixture was allowed to warm to room temperature over 3 hours and concentrated *in vacuo* onto silica. The crude product was purified by flash chromatography to afford the title compound as a yellow solid (207 mg, 57% from **26**), mp 78–81 °C; υ_{max} (film)/cm^{-1} 3330, 2978, 2940, 2836, 1706, 1526, 1424, 1356, 1266, 1208, 1087, 1024; δ_H (300 MHz; $CDCl_3$) 6.87 (1H, br s), 5.88 (1H, dt, *J* 6.1 and 1.4), 5.62 (1H, dt *J* 6.1 and 2.5), 4.65 (1H, ddd, *J* 15.6, 2.5 and 1.4), 4.59 (1H, ddd, *J* 15.6, 2.5 and 1.4), 3.56 (1H, dd, *J* 13.8 and 7.5), 3.24 (1H, dd, *J* 13.8 and 4.7), 1.27 (3H, s); δ_C (75 MHz; $CDCl_3$) 130.6, 127.8, 89.8, 75.3, 48.6, 23.8 (no *C*=O, no *C*Cl_3); (CI, *m*/*z*) 279 (30%), 277 (100), 262 (20), 260 (60); Found (CI) 275.0128 ($M + NH_4^+$ $C_8H_{14}Cl_3N_2O_2$ requires 275.0121).

anti-*N*-(3,4-Diacetoxycyclopentyl)-2′,2′,2′-trichloroacetamide *anti*-28

N-Cyclopent-3-enyl-2,2,2-trichloroacetamide **21** (100 mg, 0.44 mmol) was oxidised using standard UpJohn conditions. The reaction mixture was concentrated *in vacuo* to yield the crude products [6.5 : 1.0 (*anti* : *syn*) by ^{1}H NMR]. The crude products were purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a colourless oil [6.5 : 1.0 (*anti* : *syn*) by ^{1}H NMR, 98 mg, 65%]; mp 113–114 °C; υ_{max} (film)/cm^{-1} 3345, 2989, 2951, 1742, 1712, 1524, 1435, 1374, 1243, 1165, 1063, 1029; δ_H (300 MHz; $CDCl_3$) 6.90 (1H, br d), 5.40–5.27 (2H, m), 4.58–4.44 (1H, m), 2.38–2.04 (3H, m), 1.99–1.84 (7H, m); δ_C (75 MHz; $CDCl_3$) 170.2, 161.5, 92.3, 72.7, 48.2, 35.5, 20.8; (CI, *m*/*z*) 367 (5%), 363 (20), 331 (20), 329 (25), 252 (40), 82 (100); Found (CI) 346.0018 ($M + H^+$ $C_{11}H_{15}Cl_3NO_5$ requires 346.0016).

syn-*N*-(3,4-Diacetoxycyclopentyl)-2′,2′,2′-trichloroacetamide *syn*-28

N-Cyclopent-3-enyl-2,2,2-trichloroacetamide **21** (100 mg, 0.44 mmol) was oxidised using standard OsO_4, TMEDA conditions with acidic methanol work-up. The mixture was concentrated *in vacuo* to yield the crude products [>25 : 1 (*syn* : *anti*) by ^{1}H NMR]. The crude products were purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a pale yellow solid [>25 : 1 (*syn* : *anti*) by ^{1}H-NMR, 143 mg, 94%], mp 85–86 °C; υ_{max} (film)/cm^{-1} 3424, 3056, 2986, 2955, 2255, 1744, 1714, 1515, 1373, 1264, 1249, 1081, 1059, 1024; δ_H (300 MHz; $CDCl_3$) 7.14 (1H, br d), 5.26–5.18 (2H, m), 4.44–4.30 (1H, m), 2.52–2.34 (2H, m), 2.01 (6H, s), 1.86–1.70 (2H, m); δ_C (75 MHz; $CDCl_3$) 169.6, 160.6, 73.0, 48.5, 36.1, 20.7 (no *C*Cl_3); (CI, *m*/*z*) 367 (5%), 363 (20), 350 (20), 346 (50), 314 (30), 312 (40), 290 (20), 286 (50), 252 (40), 186 (85), 81 (100); Found (CI) 346.0019 ($M + H^+$ $C_{11}H_{15}Cl_3NO_5$ requires 346.0016).

anti-3,4-Diacetoxy-2-[(2,2,2-trichloroacetylamino)methyl]-tetrahydrofuran *anti*-29

2-[(2,2,2-Trichloroacetylamino)methyl]-2,5-dihydrofuran **25** (100 mg, 0.41 mmol) was oxidised using standard UpJohn conditions. The reaction mixture was concentrated *in vacuo* to yield

the crude acetates as a mixture of diastereoisomers [5.3 : 1.0 (*anti : syn*) by ^{1}H NMR] which were purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a yellow oil [5.3 : 1.0 (*anti : syn*) by ^{1}H NMR, 122 mg, 82%]; mixture υ_{max} (film)/cm^{-1} 1746, 1710, 1524, 1372, 1246, 1095, 1080; *anti*-**29**; δ_H (300 MHz; $CDCl_3$) 7.04 (1H, br s), 5.32 (1H, dt, *J* 5.3 and 3.4), 4.88 (1H, dd, *J* 7.6 and 5.3), 4.18 (1H, dd, *J* 10.6 and 5.3), 4.02 (1H, ddd, *J* 7.6, 6.1 and 4.1), 3.82 (1H, dd, *J* 10.6 and 3.4), 3.68 (1H, ddd, *J* 14.1, 6.3 and 4.1), 3.42 (1H, dt, *J* 14.1 and 6.1), 2.04 (3H, s), 2.03 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.0, 169.8, 162.1, 77.7, 72.3, 71.1, 70.9, 42.3, 20.6, 20.5 (no CCl_3); mixture (CI, *m*/*z*) 383 (30%), 379 (100), 347 (30), 345 (40); Found (CI) 379.0239 (M + NH_4^+ $C_{11}H_{18}Cl_3N_2O_6$ requires 379.0230).

syn-3,4-Diacetoxy-2-[(2,2,2-trichloroacetylamino)methyl]-tetrahydrofuran *syn*-29

2-[(2,2,2-Trichloroacetylamino)methyl]-2,5-dihydrofuran **25** (100 mg, 0.41 mmol) was oxidised using standard OsO_4, TMEDA dihydroxylation conditions. The crude mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a colourless oil [2.0 : 1.0 (*syn : anti*) by ^{1}H NMR, 107 mg, 72%]; mixture: υ_{max} (film)/cm^{-1} 3054, 2986, 2305, 1747, 1718, 1518, 1422, 1372, 1265; *syn*-**29** δ_H (300 MHz; $CDCl_3$) 7.12 (1H, br s), 5.50–5.36 (2H, m), 4.19 (1H, dt, *J* 6.8 and 5.4), 4.02 (1H, dd, *J* 10.2 and 5.4), 3.93 (1H, dd, *J* 10.2 and 4.2), 3.62 (1H, ddd, *J* 14.3, 6.8 and 4.8), 3.54 (1H, ddd, *J* 14.3, 7.2 and 5.4), 2.11 (3H, s), 2.08 (3H, s); δ_C (75 MHz; $CDCl_3$) 169.9, 169.8, 161.8, 76.3, 71.7, 69.8, 40.7, 29.6, 20.6, 20.5 (no *C*Cl_3): mixture (CI, *m*/*z*) 383 (35%), 381 (100), 347 (45), 345 (60); Found (CI) 379.0226 (M + NH_4^+ $C_{11}H_{18}Cl_3N_2O_6$ requires 379.0230).

anti-2-Methyl-3,4-diacetoxy-2-[(2,2,2-trichloroacetylamino)-methyl]tetrahydrofuran *anti*-30

2-Methyl-2-[(2,2,2-trichloroacetylamino)methyl]-2,5-dihydrofuran **27** (70 mg, 0.27 mmol) was oxidised using standard UpJohn conditions. The reaction mixture was concentrated *in vacuo* to yield the crude acetates as a mixture of diastereoisomers [2.8 : 1.0 (*anti : syn*) by ^{1}H NMR] which were purified by flash chromatography (EtOAc–petrol, 1 : 1) to afford the title compounds as a yellow oil which were characterised as a mixture of diastereoisomers (71 mg, 70%); υ_{max} (film)/cm^{-1} 3020, 1744, 1720, 1522, 1372, 1247, 1216, 1065, 1026; *anti*-**30**; δ_H (300 MHz; $CDCl_3$) 6.98 (1H, br s), 5.36 (1H, dt, *J* 5.7 and 3.2), 4.93 (1H, d, *J* 5.7), 4.11 (1H, dd, *J* 10.8 and 5.7), 3.84 (1H, dd, *J* 10.8 and 3.2), 3.47 (1H, dd, *J* 13.9 and 6.1), 3.41 (1H, dd, *J* 13.9 and 6.1), 2.05 (3H, s), 2.03 (3H, s), 1.20 (3H, s); δ_C (75 MHz; $CDCl_3$) 169.8, 169.8, 162.2, 81.8, 73.4, 71.5, 69.4, 47.6, 29.6, 20.6, 20.4 (no *C*Cl_3); mixture (CI, *m*/*z*) 397 (30), 395 (90), 393 (100), 380 (15), 376 (35), 361 (30), 359 (50), 344 (20), 342 (40); Found (CI) 393.0384 (M + NH_4^+ $C_{12}H_{20}Cl_3N_2O_6$ requires 393.0386).

syn-2-Methyl-3,4-diacetoxy-2-[(2,2,2-trichloroacetylamino)-methyl]tetrahydrofuran *syn*-30

2-Methyl-2-[(2,2,2-trichloroacetylamino)methyl]-2,5-dihydrofuran **27** (70 mg, 0.27 mmol) was oxidised using standard TMEDA dihydroxylation conditions. The mixture was concentrated *in vacuo* and purified by flash chromatography (EtOAc–petrol, 1 : 3) to afford the title compound as a colourless oil [≥25 : 1 (*syn : anti*) by ^{1}H NMR, 90 mg, 88%]; υ_{max} (film)/cm^{-1} 3019, 2978, 2400, 1746, 1715, 1519, 1374, 1216, 1081, 1062, 1024; δ_H (300 MHz; $CDCl_3$) 7.02 (1H, br s), 5.39 (1H, dt, *J* 5.5 and 3.4), 5.08 (1H, d, *J* 5.5), 4.10 (1H, dd, *J* 10.8 and 5.5), 3.86 (1H, dd, *J* 10.8 and 3.4), 3.66 (1H, dd, *J* 14.0 and 5.0), 3.44 (1H, dd, *J* 14.0 and 6.6), 2.05 (3H, s), 2.04 (3H, s), 1.26 (3H, s); δ_C (75 MHz; $CDCl_3$) 169.7, 169.6, 161.8, 81.2, 76.5, 71.6, 69.3, 44.9, 22.9, 20.7, 20.4 (no *C*Cl_3); (CI, *m*/*z*) 397 (30%), 395 (90), 393 (100), 378 (50), 376 (60), 359 (20), 342 (25); Found (CI) 393.0381 (M + NH_4^+ $C_{12}H_{20}Cl_3N_2O_6$ requires 393.0386).

N-(Cyclohex-3-enyl)-2,2,2-trichloroacetamide 34

To a stirred solution of cyclohex-3-ene carboxylic acid **32** (5.00 g, 40.0 mmol) in toluene (100 ml) at 0 °C was added triethylamine (3.81 g, 38.0 mmol) and diphenylphosphonic azide (7.70 g, 38.0 mmol) and the reaction was stirred at 0 °C for 30 minutes. The reaction mixture was warmed to room temperature and then heated at reflux until nitrogen evolution was complete (~1 hour). Solvent was removed *in vacuo* and the crude mixture was redissolved in DCM (50 ml). To this solution was added trichloroacetic acid[27] (7.17 g, 44 mmol) and the reaction was stirred at reflux for 2 hours. The mixture was cooled to room temperature and washed with sodium bicarbonate (2 × 75 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The mixture was purified by flash chromatography (Et_2O–petrol, 1 : 20 ⟶ 1 : 5) to afford the title compound as a white solid which was recrystallised to afford white needles (2.67 g, 29%), mp 83–85 °C (Found: C, 39.9; H, 4.0; N, 5.5; $C_8H_{10}Cl_3NO$ requires C, 39.6; H, 4.2; N, 5.8%); υ_{max} (film)/cm^{-1} 3418, 3054, 2927, 2305, 1708, 1511, 1439, 1264, 1082; δ_H (300 MHz; $CDCl_3$) 6.60 (1H, br s), 5.74–5.46 (2H, m), 4.20–3.87 (1H, m), 2.48–2.28 (1H, m), 2.22–1.56 (5H, m); δ_C (75 MHz; $CDCl_3$) 161.1, 127.2, 123.5, 46.7, 30.7, 26.8, 22.8 (no *C*Cl_3); (CI, *m*/*z*) 265 (5%), 263 (40), 259 (100); Found (CI) 259.0168 (M + NH_4^+ $C_8H_{14}Cl_3N_2O$ requires 259.0172).

1-Methyl-1-nitrocyclohex-3-ene 36

To a stirred solution of 2-nitropropan-1-ol (15.6 g, 149 mmol) in DCM (80 ml) was added acetic anhydride (18.2 g, 178 mmol) and DMAP (~10 mg) and the reaction stirred at room temperature for 3 hours. Methanol (15 ml) was added and the reaction mixture stirred for 30 minutes. The crude mixture was concentrated *in vacuo* and purified by flash chromatography (100% Et_2O) to afford the nitroacetate as a pale green liquid (18.2 g). To a suspension of pyrogallol (330 mg, 2.62 mmol) in benzene (10 ml) was added 2-nitroacetoxypropane (9.00 g, 61.2 mmol) and sodium acetate (1.00 g, 12.2 mmol). The mixture was shaken vigorously for 5 minutes in a sealed tube. The cap of the sealed tube was replaced with a septum and the mixture cooled to −78 °C. Buta-1,3-diene (~ 10 ml) was distilled into the tube *via* a long syringe needle from a lecture bottle. After addition, the septum was carefully removed with the reaction mixture at −78 °C and the tube was sealed tightly. The reaction was allowed to warm to room temperature over 1 hour and the temperature slowly raised to 80 °C over a 4 hour period with vigorous stirring. The reaction was stirred at that temperature for 4 days. The mixture was cooled to room temperature and then cooled to −78 °C and the seal removed. The mixture was then allowed to warm to room temperature allowing the excess butadiene to evaporate off. The crude mixture was diluted with Et_2O (100 ml) and the organic layer washed with saturated sodium bicarbonate solution (1 × 40 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography (petrol ⟶ Et_2O–petrol, 1 : 5) to yield a colourless oil (2.68 g, 30% from **35**); υ_{max} (film)/cm^{-1} 3028, 2924, 1656, 1536, 1448, 1345, 1267, 1226, 1090, 1050; δ_H (300 MHz; $CDCl_3$) 5.76–5.60 (2H, m), 3.03–2.92 (1H, m), 2.42–2.04 (4H, m), 2.03–1.92 (1H, m), 1.62 (3H, s); δ_C (75 MHz; $CDCl_3$) 125.7, 123.0, 86.4, 34.9, 31.8, 25.6, 22.8; no mass ion obtainable from EI/CI, electrospray or FAB mass spectrometry techniques.

N-(1-Methylcyclohex-3-enyl)-2,2,2-trichloroacetamide 37

Ammonia (~30 ml) was distilled into a 100 ml three-necked flask at −78 °C under nitrogen. 1-Methyl-1-nitrocyclohex-3-ene

36 (2.06 g, 14.6 mmol) in methanol (4.53 g, 146 mmol) was added in 1 portion and the mixture stirred for 5 minutes. Lithium wire (819 mg, 117 mmol) was added in small portions over 10 minutes under vigorous stirring (a yellow to dark blue colour change was observed). The reaction mixture was stirred at −78 °C for 2 hours and then warmed to room temperature. Water (20 ml) was added dropwise (caution-exotherm) and the excess ammonia was allowed to evaporate. The aqueous layer was extracted with Et_2O (2 × 50 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford the amine as a colourless oil (1.34 g). To a stirred solution of amine (437 mg, 3.94 mmol) in DCM (50 ml) was added triethylamine (1.19 g, 11.6 mmol) and the solution was cooled to 0 °C. Trichloroacetyl chloride (879 mg, 4.72 mmol) was added dropwise and the solution was warmed to room temperature over 16 hours. The mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 1 : 3) to afford the title compound as a yellow solid (852 mg, 70% from **36**), mp 34–37 °C; υ_{max} (film)/cm^{-1} 3054, 2987, 2305, 1717, 1513, 1422, 1266; δ_H (300 MHz; $CDCl_3$) 6.41 (1H, br s), 5.74–5.63 (1H, m), 5.56–5.46 (1H, m), 2.34–1.91 (5H, m), 1.64–1.34 (4H, m); δ_C (75 MHz; $CDCl_3$) 160.7, 127.4, 122.8, 53.3, 37.6, 30.6, 24.5, 22.5 (no *C*Cl_3); (CI, *m*/*z*) 279 (5%), 277 (30), 273 (100); Found (CI) 273.0332 (M + NH_4^+ $C_9H_{16}Cl_3N_2O$ requires 273.0328).

cis-Cyclohex-4-ene-1,2-diazide 38

To a stirred solution of *cis*-cyclohex-4-en-1,2-diol **12** (2.80 g, 24.6 mmol) in DCM (50 ml) was added triethylamine (7.45 g, 73.8 mmol) at room temperature. The mixture was cooled to 0 °C and methanesulfonic anhydride (9.40 g, 54.0 mmol) was added in small portions (caution-exotherm) and the reaction was allowed to warm to room temperature over 1 hour. The mixture was concentrated *in vacuo* and purified by flash chromatography (100% DCM) to afford the mesylate as a white solid (4.94 g). To a stirred solution of mesylate (623 mg, 2.62 mmol) in DMSO (30 ml) at room temperature was added sodium azide (374 mg, 5.76 mmol) and the mixture stirred until full dissolution of sodium azide. The reaction mixture was then heated at 80 °C for 2 days and then cooled to room temperature. The mixture was poured into water (80 ml) and extracted with Et_2O (3 × 80 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (Et_2O–petrol, 1 : 4) afforded the title compound as a colourless oil (321 mg, 56% from **12**); υ_{max} (film)/cm^{-1} 2924, 2103, 1258; δ_H (300 MHz; $CDCl_3$) 5.68 (2H, t, *J* 1.5), 3.84 (2H, t, *J* 5.0), 2.47–2.40 (4H, m); δ_C (75 MHz; $CDCl_3$) 123.4, 58.6, 28.0; no mass ion detectable by EI/CI mass spectrometry techniques.

N-[6-(2,2,2-Trichloroacetylamino)cyclohex-3-enyl]-2,2,2-trichloroacetamide 39

To a stirred suspension of lithium aluminium hydride (1.43 g, 37.8 mmol) in Et_2O (25 ml) at 0 °C was added dropwise a solution of diazide **38** in Et_2O (25 ml). After complete addition, the reaction was stirred for 1 hour. Sodium sulfate decahydrate (~2 g) was slowly added until a white solid precipitated, then magnesium sulfate (~2 g) was added. The mixture was filtered and the residue washed with Et_2O (3 × 75 ml). The solution was concentrated *in vacuo* to yield the diamine as a yellow oil (825 mg). To a stirred solution of diamine (355 mg, 3.17 mmol) in DCM (50 ml) was added triethylamine (1.92 g, 19.0 mmol) at room temperature. The mixture was cooled to 0 °C and trichloroacetyl chloride (1.30 g, 6.97 mmol) was added dropwise followed by DMAP (~10 mg). The reaction was allowed to warm to room temperature overnight and the mixture was concentrated *in vacuo* onto silica. Flash chromatography (Et_2O–petrol, 1 : 4) yielded a yellow solid which was recrystallised to afford the title compound as a white solid (444 mg, 27% from **38**), mp 112–113 °C (from EtOAc–petrol) (Found: C, 29.7; H, 2.4; N, 6.9; $C_{10}H_{10}Cl_6N_2O_2$ requires C, 29.8; H, 2.5; N, 7.0%); υ_{max} (film)/cm^{-1} 3054, 2986, 2305, 1709, 1513, 1422, 1264; δ_H (300 MHz; $CDCl_3$) 7.47 (2H, br s), 5.81 (2H, t, *J* 1.5), 4.42–4.32 (2H, m), 2.89–2.76 (2H, m), 2.26–2.12 (2H, m); δ_C (75 MHz; $CDCl_3$) 163.1, 124.3, 92.1, 50.1, 28.8; (CI, *m*/*z*) 426 (3%), 424 (20), 422 (30), 420 (40), 407 (10), 403 (25), 401 (15), 78 (100); Found (CI) 417.9226 (M + NH_4^+ $C_{10}H_{14}Cl_6N_3O_2$ requires 417.9217).

syn- and *anti*-*N*-(3,4-Diacetoxycyclohexyl)-2′,2′,2′-trichloroacetamide *syn*- and *anti*-40

N-(Cyclohex-3-enyl)-2,2,2-trichloroacetamide**34** (100 mg, 0.41 mmol) was oxidised using standard UpJohn conditions. The reaction mixture was concentrated *in vacuo*, and purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compounds as a yellow oil which were characterised as a mixture of diastereoisomers [1.0 : 1.0 (*syn : anti*) by ^{1}H NMR, 147 mg, 99%]; υ_{max} (film)/cm^{-1} 3415, 3333, 3058, 2953, 2878, 1746, 1730, 1713, 1695, 1530, 1517, 1370, 1259, 1212, 1121, 1092, 1048; *syn*-**40** δ_H (300 MHz; $CDCl_3$) 7.34 (1H, br s), 5.30–5.15 (1H, m), 5.10–4.96 (1H, m), 4.13–3.97 (1H, m), 2.09 (3H, s), 2.05 (3H, s), 2.00–1.16 (6H, m); δ_C (75 MHz; $CDCl_3$) 170.0, 169.4, 160.9, 118.9, 92.6, 69.4, 69.3, 46.4, 31.8, 26.7, 21.0, 20.9: *anti*-**40**: δ_H (300 MHz; $CDCl_3$) 7.34 (1H, br d, *J* 7.3), 5.41–5.33 (1H, m), 4.87 (1H, ddd, *J* 10.3, 3.7 and 2.9), 4.24–4.05 (1H, m), 2.34–1.18 (12H, m); δ_C (75 MHz; $CDCl_3$) 170.3, 170.1, 161.3, 101.4, 92.4, 70.7, 68.3, 45.7, 34.0, 28.9, 24.4, 20.9; mixture (CI, *m*/*z*) 381 (35%), 379 (100), 377 (90), 347 (15), 345 (60), 343 (90); Found (CI) 377.0448 (M + NH_4^+ $C_{12}H_{20}Cl_3N_2O_5$ requires 377.0438).

N-(Cyclohex-3-enyl)-2,2,2-trichloroacetamide **34** (100 mg, 0.41 mmol) was oxidised using standard TMEDA dihydroxylation conditions. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compounds as a yellow oil which were characterised as a mixture of diastereoisomers [1.2 : 1.0 (*syn : anti*) by ^{1}H NMR, (137 mg, 92%].

anti-*N*-(1-Methyl-3,4-diacetoxycyclohexyl)-2′,2′,2′-trichloroacetamide *anti*-41

N-(1-Methylcyclohex-3-enyl)-2,2,2-trichloroacetamide **37** (100 mg, 0.41 mmol) was oxidised using standard UpJohn conditions and concentrated *in vacuo*. The reaction mixture was concentrated *in vacuo*, then purified by column chromatography (Et_2O–petrol, 4 : 1) to yield the title compounds as a mixture of diastereoisomers [5.0 : 1.0 (*anti : syn*) by ^{1}H NMR, 111 mg, 76%]; mixture: υ_{max} (film)/cm^{-1} 3412, 3055, 2986, 2306, 1741, 1721, 1515, 1449, 1422, 1368, 1265, 1220, 1052: *syn*-**41**: δ_H (300 MHz; $CDCl_3$) 7.42 (1H, br s), 5.52–5.44 (1H, m), 5.00–4.88 (1H, m), 2.40–1.16 (15H, m): *anti*-**41**: δ_H (300 MHz; $CDCl_3$) 6.46 (1H, br s), 5.30–5.24 (1H, m), 4.88 (1H, ddd, *J* 12.0, 4.4 and 2.8), 2.37–1.97 (8H, m), 1.92–1.81 (2H, m), 1.74–1.60 (2H, m), 1.47 (3H, s): mixture; δ_C (75 MHz; $CDCl_3$) 170.1, 170.0, 169.4, 160.8, 160.2, 70.5, 68.5, 67.7, 56.0, 53.7, 39.6, 35.4, 31.5, 29.6, 26.3, 25.4, 24.7, 22.4, 21.1, 21.0, 20.9 (no *C*Cl_3); (CI, *m*/*z*) 395 (20%), 393 (80), 391 (100), 389 (25), 359 (20), 357 (30), 349 (20), 186 (40), 169 (30); Found (EI) 373.0255 (M^+ $C_{13}H_{18}Cl_3NO_5$ requires 373.0251).

anti-*N*-(1-Methyl-3,4-diacetoxycyclohexyl)-2′,2′,2′-trichloroacetamide *anti*-41

N-(1-Methylcyclohex-3-enyl)-2,2,2-trichloroacetamide **37** (100 mg, 0.39 mmol) was oxidised using standard OsO_4, TMEDA conditions. The reaction mixture was concentrated *in vacuo* and the crude mixture was purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compounds as a colourless oil which were characterised as a mixture of diastereoisomers [5.0 : 1.0 (*anti : syn*) by ^{1}H NMR, 137 mg, 92%].

***anti*-*N*-(3,4-Diacetoxy-6-{2,2,2-trichloroacetylamino}-cyclohexyl)-2′,2′,2′-trichloroacetamide *anti*-42**

N-[6-(2,2,2-Trichloroacetylamino)cyclohex-3-enyl]-2,2,2-trichloroacetamide **39** (80 mg, 0.20 mmol) was oxidised using standard UpJohn conditions and concentrated *in vacuo*. The mixture was purified by flash chromatography (EtOAc–petrol, 1 : 1) to afford the title compounds as a pale yellow solid which was characterised as a mixture of diastereoisomers [3.0 : 1.0 (*anti : syn*) by ^{1}H NMR, 109 mg, 100%]; mixture υ_{max} (film)/cm^{-1} 3317, 1745, 1722, 1704, 1517, 1369, 1266, 1235, 1209, 1047; *syn*-**42**: δ_H (300 MHz; DMSO) 8.44 (2H, br s), 5.16–5.00 (2H, m), 4.30–4.10 (2H, m), 2.24–2.10 (2H, m), 2.04–1.87 (8H, m); δ_C (75 MHz, $CDCl_3$) 169.8, 161.4, 92.9, 68.9, 48.3, 28.2, 21.3; *anti*-**42**: δ_H (400 MHz; DMSO) 8.72 (2H, br d, *J* 7.2), 5.25–5.16 (2H, m), 4.38–4.10 (2H, m) 2.27–2.14 (2H, m), 2.04–1.91 (8H, m); δ_C (100 MHz, DMSO) 169.8, 161.7, 92.6, 67.4, 47.6, 28.4, 20.8; mixture (CI, *m*/*z*) 538 (5%), 334 (50), 237 (20), 94 (80), 60 (100); Found (CI) 535.9488 (M + NH_4^+ $C_{14}H_{20}C_{l6}N_3O_6$ requires 535.9483).

***syn*-*N*-(3,4-Diacetoxy-6-{2,2,2-trichloroacetylamino}-cyclohexyl)-2′,2′,2′-trichloroacetamide *syn*-42**

N-[6-(2,2,2-Trichloroacetylamino)cyclohex-3-enyl]-2,2,2-trichloroacetamide **39** (77 mg, 0.19 mmol) was oxidised using standard OsO_4, TMEDA conditions. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (EtOAc–petrol, 1 : 1) to afford the title compound as a pale yellow solid which was characterised as a mixture of diastereoisomers [3.0 : 1.0 (*syn : anti*) by ^{1}H NMR, 102 mg, 100%].

***N*-(Cyclohex-3-enyl)-2,2,2-trifluoroacetamide[27] 43**

To a stirred solution of cyclohex-3-enylamine (1.16 g, 11.9 mmol) in DCM (50 ml) was added triethylamine (3.61 g, 35.7 mmol) at room temperature. The solution was cooled to 0 °C and trifluoroacetic anhydride (3.01 g, 14.3 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature over 16 hours and then concentrated *in vacuo* onto silica. The crude product was purified by flash chromatography (Et_2O–petrol, 1 : 5) to yield a yellow solid which was recrystallised to afford the title compound as a beige solid (849 mg, 37%); all data were consistent with that in the literature.

***anti*-*N*-(3,4-Diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *anti*-44**

N-(Cyclohex-3-enyl)-2,2,2-trifluoroacetamide **43** (80 mg, 0.42 mmol) was oxidised using standard UpJohn conditions and concentrated *in vacuo*. The mixture was purified by flash chromatography (Et_2O–petrol, 1 : 1) to afford the title compounds as a colourless oil which were characterised as a mixture of diastereoisomers [1.0 : 1.0 (*syn : anti*) by ^{1}H NMR, 130 mg, 99%]; mixture: υ_{max} (film)/cm^{-1} 3319, 2952, 1746, 1730, 1714, 1555, 1443, 1371, 1257, 1234, 1210, 1184, 1160, 1045; *anti*-**44**: δ_H (400 MHz; $CDCl_3$) 6.37 (1H, br d, *J* 6.8), 5.39–5.32 (1H, m), 4.85 (1H, ddd, *J* 7.5, 4.6 and 2.9), 4.26–4.15 (1H, m), 2.23–1.80 (12H, m); δ_C (75 MHz; $CDCl_3$) 170.5, 170.2, 156.6 (q, *J* 37.2), 115.6 (q, *J* 288), 70.7, 68.2, 44.4, 34.2, 29.3, 24.3, 21.0, 20.9; mixture (CI, *m*/*z*) 330 (15%), 329 (100); Found (CI) 329.1331 (M + NH_4^+ $C_{12}H_{20}F_3N_2O_5$ requires 329.1324).

***syn*-*N*-(3,4-Diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *syn*-44**

N-(Cyclohex-3-enyl)-2,2,2-trifluoroacetamide **43** (80 mg, 0.42 mmol) was oxidised using standard OsO_4, TMEDA conditions. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 1 : 1) to afford the title compound as a colourless oil [>25 : 1.0 (*syn : anti*) by ^{1}H NMR, 127 mg, 98%]; υ_{max} (film)/cm^{-1} 3329, 2957, 1745, 1729, 1714, 1426, 1381, 1259, 1231, 1208, 1163, 1048; δ_H (300 MHz; $CDCl_3$) 7.13 (1H, br d, *J* 5.1), 5.23–5.05 (2H, m), 4.24–4.00 (1H, m), 2.20–1.60 (12H, m); δ_C (75 MHz; $CDCl_3$) 169.4, 168.9, 156.0 (q, *J* 36.6), 115.6 (q, *J* 288), 69.4, 68.5. 45.4, 31.5, 26.2, 23.9, 20.7, 20.6; (CI, *m*/*z*) 330 (15%), 329 (100); Found (CI) 329.1327 (M + NH_4^+ $C_{12}H_{20}F_3N_2O_5$ requires 329.1324).

***N*-(1-Methylcyclohex-3-enyl)-2,2,2-trifluoroacetamide 45**

To a stirred solution of 1-methylcyclohex-3-enylamine (121 mg, 1.09 mmol) in DCM (50 ml) at room temperature under nitrogen was added triethylamine (330 mg, 3.27 mmol) and the solution was cooled to −78 °C. Trifluoroacetyl chloride (~1 ml) was distilled directly into the reaction flask from a lecture bottle. The reaction mixture was allowed to warm to room temperature over 16 hours. Nitrogen was purged through the solution for 30 minutes to remove any excess trifluoroacetyl chloride and the solution was concentrated *in vacuo*. The crude mixture was purified by flash chromatography (Et_2O–petrol, 1 : 3) to afford the title compound as a white solid (189 mg, 84%), mp 49–51 °C; υ_{max} (film)/cm^{-1} 3420, 3055, 3033, 2986, 2929, 2845, 2306, 1724, 1535, 1447, 1423, 1378, 1336, 1266, 1205, 1162; δ_H (300 MHz; $CDCl_3$) 6.14 (1H, br s), 5.80–5.71 (1H, m), 5.63–5.54 (1H, m), 2.38–1.96 (5H, m), 1.62 (1H, ddd, *J* 14.9, 8.1 and 6.3), 1.49 (3H, s); δ_C (75 MHz, $CDCl_3$) 127.0, 122.8, 53.1, 37.4, 30.7, 24.4, 22.3 (no *C*=O, no *C*F_3); (CI, *m*/*z*) 256 (10%), 225 (100), 94 (45); Found (CI) 208.0949 (M + H^+ $C_9H_{13}F_3NO$ requires 208.0949).

***anti*-*N*-(1-Methyl-3,4-diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *anti*-46**

N-(1-Methylcyclohex-3-enyl)-2,2,2-trifluoroacetamide **45** (100 mg, 0.48 mmol) was oxidised using standard UpJohn conditions and concentrated *in vacuo*. The mixture was purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compounds as a colourless oil which was characterised as a mixture of diastereoisomers (3.5 : 1.0 (*anti : syn*) by ^{1}H NMR, 152 mg, 97%); mixture: υ_{max} (film)/cm^{-1} 3321, 2974, 2945, 1746, 1730, 1714, 1555, 1453, 1370, 1253, 1218, 1210, 1184, 1156, 1050, 1027; *anti*-**46**; δ_H (300 MHz; $CDCl_3$) 6.39 (1H, br s), 5.20–5.08 (1H, m), 4.97–4.86 (1H, m), 2.40–2.30 (1H, m), 2.24–2.14 (1H, m), 2.12 (3H, s), 2.02 (3H, s), 1.95–1.80 (2H, m), 1.74–1.64 (2H, m), 1.27 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.2, 170.1, 156.7 (q, *J* 36.6), 115.3 (q, *J* 289.3), 68.4, 67.7, 55.8, 35.4, 29.5, 26.6, 24.4, 21.0, 20.8; mixture (CI, *m*/*z*) 345 (3%), 344 (20), 343 (100); Found (CI) 343.1485 (M + NH_4^+ $C_{13}H_{22}F_3N_2O_5$ requires 343.1481).

***syn*-*N*-(1-Methyl-3,4-diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *syn*-46**

N-(1-Methylcyclohex-3-enyl)-2,2,2-trifluoroacetamide **45** (80 mg, 0.39 mmol) was oxidised using standard OsO_4, TMEDA conditions. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (Et_2O–petrol, 4 : 1) to afford the title compound as a colourless oil which was characterised as a mixture of diastereoisomers [3.0 : 1.0 (*syn : anti*) by ^{1}H NMR, 84 mg, 67%]; mixture: υ_{max} (film)/cm^{-1} 3331, 2953, 2926, 2853, 1729, 1553, 1451, 1434, 1370, 1249, 1210, 1181, 1155, 1050, 1026; *syn*-**46** δ_H (300 MHz; $CDCl_3$) 7.10 (1H, br s), 5.50–5.37 (1H, m), 4.92 (1H, ddd, *J* 10.8, 4.0 and 3.5), 2.65–2.50 (1H, m), 2.18 (1H, ddd, *J* 15.3, 4.6 and 2.9), 2.12 (3H, s), 2.02 (3H, s), 1.94–1.65 (4H, m), 1.54 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.1, 169.2, 155.7 (q, *J* 36.0), 115.6 (q, *J* 290), 70.3, 68.5, 53.6, 39.1, 31.8, 25.4, 22.2, 20.8, 20.6; mixture (CI, *m*/*z*) 344 (20%), 343 (100); Found (EI) 325.1137 (M^+ $C_{13}H_{18}F_3NO_5$ requires 325.1137).

***N*-[6-(2,2,2-Trifluoroacetylamino)cyclohex-3-enyl]-2,2,2-trifluoroacetamide 47**

To a stirred solution of diamine (500 mg, 4.46 mmol) in DCM (50 ml) was added triethylamine (2.71 g, 26.8 mmol) at room

temperature. The solution was cooled to −78 °C and trifluoroacetyl chloride (~2 ml) was distilled into the flask. The reaction mixture was allowed to warm to room temperature over 16 hours and then concentrated *in vacuo* onto silica. The crude product was purified by flash chromatography (Et_2O–petrol, 1 : 1) to afford the title compound as a colourless solid (876 mg, 65%), mp 135–136 °C (Found: C, 39.5; H, 3.0; N, 8.9; $C_{10}H_{10}F_6N_2O_2$ requires C, 39.5; H, 3.3; N, 9.2%); υ_{max} (film)/cm^{-1} 3414, 3306, 3055, 2987, 2306, 1730, 1713, 1549, 1538, 1441, 1423, 1260, 1205, 1185; δ_H (300 MHz; $CDCl_3$) 7.20 (2H, br s), 5.84–5.64 (2H, m), 4.37 (2H, app. q, *J* 5.9), 2.82–2.66 (2H, m), 2.26–2.10 (2H, m); δ_C (75 MHz, $CDCl_3$, Me_4Si) 124.2, 49.0, 28.7 (no *C*=O, *C*F_3); (CI, *m*/*z*) 323 (10%), 322 (100); Found (CI) 305.0719 (M + H^+ $C_{10}H_{11}F_6N_2O_2$ requires 305.0725).

anti-*N*-(2-Trifluoroacetamido-4,5-diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *anti*-48

N-[6-(2,2,2-Trifluoroacetylamino)cyclohex-3-enyl]-2,2,2-trifluoroacetamide **47** (50 mg, 0.17 mmol) was oxidised using standard UpJohn conditions and concentrated *in vacuo*. The mixture was purified by flash chromatography (EtOAc–petrol, 1 : 1) to afford the title compounds as an off-white solid which was characterised as a mixture of diastereoisomers [5.6 : 1.0 (*anti : syn*) by ^{1}H NMR, 68 mg, 98%]; mixture υ_{max} (film)/cm^{-1} 3308, 2955, 2926, 1725, 1550, 1370, 1234, 1212, 1179, 1160, 1042, 1025; *anti*-**48**; δ_H (400 MHz; DMSO) 9.32 (2H, br d, *J* 8.0), 5.42–5.32 (2H, m), 4.44–4.30 (2H, m), 2.06–1.88 (10H, m); δ_C (100 MHz; DMSO) 169.8, 156.9 (q, *J* 55.9), 115.8 (q, *J* 282), 67.2, 45.8, 28.3, 20.9; mixture (CI, *m*/*z*) 441 (15%), 440 (100), 334 (20), 322 (25); Found (CI) 440.1267 (M + NH_4^+ $C_{14}H_{20}F_6N_3O_6$ requires 440.1256).

syn-*N*-(2-Trifluoroacetamido-4,5-diacetoxycyclohexyl)-2′,2′,2′-trifluoroacetamide *syn*-48

N-[6-(2,2,2-Trifluoroacetylamino)cyclohex-3-enyl]-2,2,2-trifluoroacetamide **47** (50 mg, 0.17 mmol) was oxidised using standard OsO_4, TMEDA conditions. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (EtOAc–petrol, 1 : 1) to afford the title compound as an off-white solid [≥ 25 : 1.0 (*syn : anti*) by ^{1}H NMR, 66 mg, 95%]; mp 160–162 °C; υ_{max} (film)/cm^{-1} 3330, 2923, 1739, 1730, 1554, 1538, 1433, 1376, 1243, 1210, 1175, 1044; δ_H (400 MHz; DMSO) 8.52 (2H, br s), 5.12–5.04 (2H, m), 4.31–4.22 (2H, m), 2.19–2.08 (2H, m), 2.01–1.90 (8H, m); δ_C (75 MHz; DMSO) 169.5, 156.2 (q, *J* 36.6), 116.0 (q, *J* 289), 68.8, 46.8, 27.6, 20.9; (CI, *m*/*z*) 440 (100%); Found (CI) 440.1263 (M + NH_4^+ $C_{14}H_{20}F_6N_3O_6$ requires 440.1256).

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