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# Directed Dihydroxylation of Cyclic Allylic Alcohols and Trichloroacetamides Using $OsO_4$/TMEDA

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The oxidation of a range of cyclic allylic alcohols and amides with $OsO_4$/TMEDA is presented. Under these conditions, hydrogen bonding control leads to the (contrasteric) formation of the syn isomer in almost every example that was examined. Evidence for the bidentate binding of TMEDA to $OsO_4$ is presented and a plausible mechanism described.

## Introduction

Over the past few years, we have been engaged in a program of research that aims to develop the directed dihydroxylation of substituted alkenes. Perhaps the most useful class of compounds that could be subjected to such a protocol would be cyclic allylic alcohols because Kishi demonstrated some years ago that these substrates are dihydroxylated with a strong bias for the anti isomer;[1] directed dihydroxylation would necessarily form the all-syn isomer, which is difficult to access by other means, Figure 1.

While our early attempts to design a protecting group for allylic alcohols that would coordinate to osmium were unsuccessful, we did discover that hydrogen bonding between an allylic donor and $OsO_4$ (as an acceptor) was a useful method of forming the all-syn isomers.[2] In particular, we found that (in dichloromethane) the nature of the amine additive used to speed up the reaction was crucial to the degree of hydrogen bonding ability shown by the oxidant. In fact, TMEDA additive was found to produce a complex that was a very good hydrogen bond acceptor and that was also capable of dihydroxylating alkenes at −78 °C.[3] We now wish to discuss in full our results from oxidation of a wide variety of substituted cyclic alkenes using the $OsO_4$/TMEDA reagent.

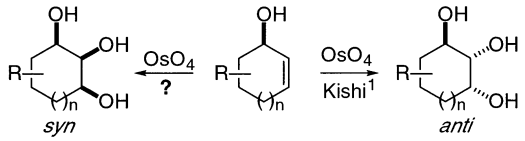


**FIGURE 1.** Syn versus anti selectivity for dihydroxylation.

## Results and Discussion

**Oxidation of Cyclic Allylic Alcohols.** We began our studies with five-membered allylic alcohols (all made via literature routes) and subjected four differently substituted compounds to oxidation with the $OsO_4$/TMEDA reagent, Scheme 1.[3a] Pleasingly, all of these compounds gave the syn isomer as the major product, although the level of stereoselectivity depended upon the substitution pattern. In each example, the selectivity observed under Upjohn conditions[4] is also given so that a comparison can be made between the result of a directed dihydroxylation and that of a more standard dihydroxylation protocol. One should be aware that with five-membered rings, both allylic and homoallylic substituents can sometimes give rise to syn products without recourse to hydrogen bonding (allylic strain may be responsible, vide infra).[5] Despite this caveat, it can be seen that good levels of syn selectivity are obtained with $OsO_4$/TMEDA. In fact, minimization of allylic strain between the hydroxyl and the alkene methyl group may be responsible for the increased preference for compound **3** to give syn products relative to compound **1**.

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‡ University of Manchester.
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|| AstraZeneca Pharmaceuticals.
⊥ GlaxoSmithKline.

(1) (a) Cha, J. K.; Christ W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3947. (c) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247. (d) Cha, J. K.; Kin, N.-S. *Chem. Rev.* **1995**, *95*, 1761.

(2) (a) Donohoe, T. J.; Garg, R.; Moore, P. R. *Tetrahedron Lett.* **1996**, *37*, 3407. (b) Donohoe, T. J.; Moore, P. R.; Beddoes, R. L. *J. Chem. Soc., Perkin Trans. 1* **1997**, 43.

(3) (a) Donohoe, T. J.; Moore, P. R.; Waring, M. J.; Newcombe, N. J. *Tetrahedron Lett.* **1997**, *38*, 5027. (b) Donohoe, T. J.; Blades, K.; Moore, P. R.; Winter, J. J. G.; Helliwell M.; Stemp, G. *J. Org. Chem.* **1999**, *64*, 2980. (c) Donohoe, T. J.; Waring M. J.; Newcombe, N. J. *Tetrahedron Lett.* **1999**, *40*, 6881. (d) Donohoe, T. J.; Mitchell, L.; Waring, M. J.; Bell, A.; Newcombe, N. J. *Tetrahedron Lett.* **2001**, *42*, 8951.

(4) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(5) Poli, G. *Tetrahedron Lett.* **1989**, *30*, 7385. See also: Ward, S. E.; Holmes, A. B.; McCague, R. *Chem. Commun.* **1997**, 2085.

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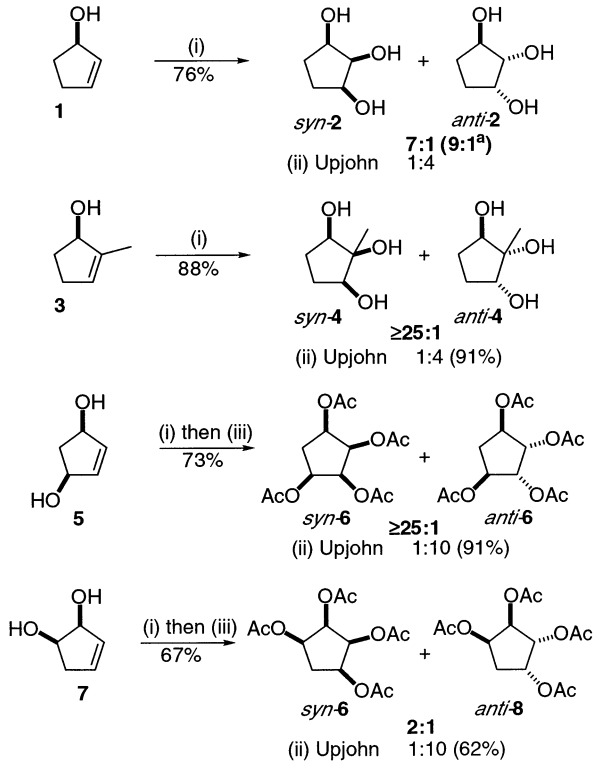
**SCHEME 1**[a]



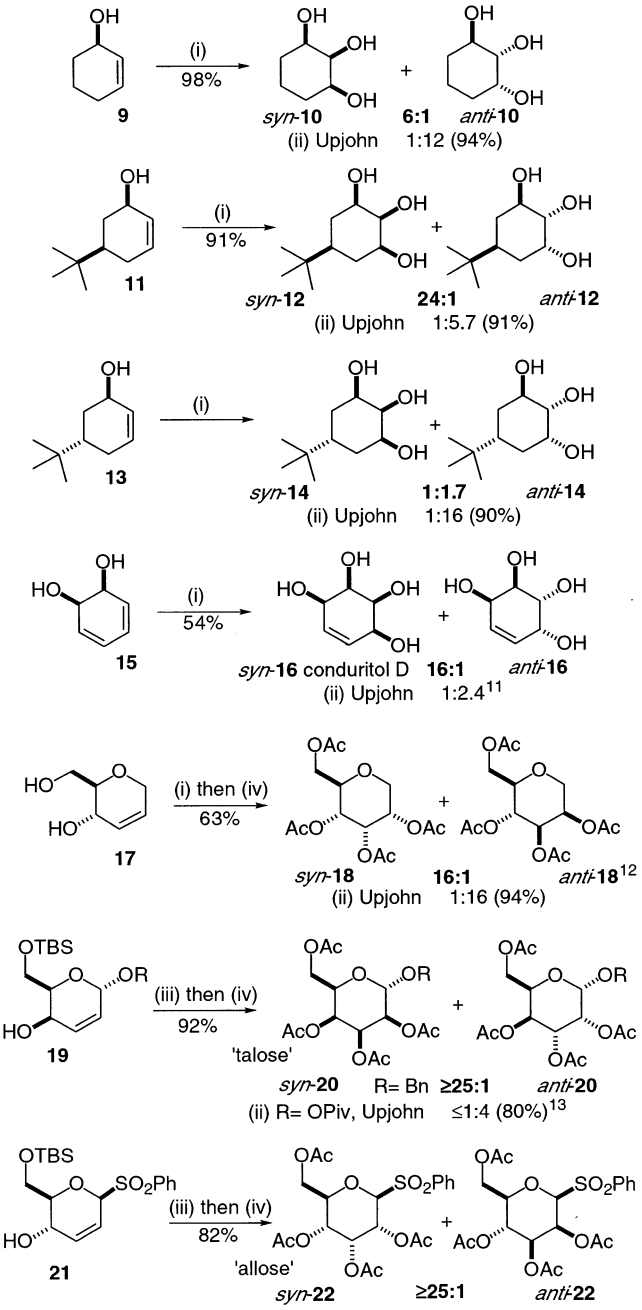

[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then $NH_2CH_2CH_2NH_2$; (ii) $OsO_4$ (cat.), acetone, $H_2O$, NMO, rt; (iii) $Ac_2O$, py.

Moreover, we presume that the lower level of selectivity displayed by **7** (relative to **1** and **5**) is a consequence of intramolecular hydrogen bonding within the substrate, which reduces its ability to hydrogen bond to an incoming reagent.

The ratios of stereosiomers were determined by $^1H$ NMR spectroscopy in conjunction with the crude reaction mixtures. In each example shown in Scheme 1, the relative stereochemistry was easy to assign because of the different symmetry properties of the alcohol (or peracetate) products; for example, the $^{13}C$ NMR spectrum of syn-**2** consisted of three peaks.

One of the first observations to be made about the $OsO_4$/TMEDA oxidation is that it is not catalytic in osmium; in fact, one forms an osmate ester by mixing $OsO_4$ (1 equiv), TMEDA (1 equiv), and alkene (1 equiv) in $CH_2Cl_2$ at low temperature, vide infra. This osmate ester must be cleaved during workup to liberate the diol. Three methods have been used by the group: (1) $Na_2SO_3$ (aqueous) THF, Δ;[6] (2) MeOH, HCl;[3b] and (3) $H_2NCH_2CH_2NH_2$ in $CH_2Cl_2$.[3c] Although all three methods work well, generally, acidic methanol is the method of choice even though silyl protecting groups do not often survive this regime.[7] Sodium sulfite is a reducing agent and is presumed to reduce osmium(VI) and thereby facilitate hydrolysis of the glycol ligand from the metal. The other two sets of conditions are neither oxidizing nor reducing and probably liberate the glycol ligand directly by displacement; our attempts to characterize the osmium-containing byproducts from these hydrolyses (especially with ethylenediamine) failed.

**SCHEME 2**[a]




[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then $Na_2SO_3$; (ii) $OsO_4$ (cat.), acetone, $H_2O$, NMO, rt; (iii) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then HCl/MeOH; (iv) $Ac_2O$, py.

We then moved on to oxidize six-membered allylic alcohols under directed dihydroxylation conditions, Scheme 2. The results showed that the directing effect was a general one, and a variety of cyclic compounds were oxidized with good levels of stereoselectivity. In fact, oxidation of compound **13** represents one of the few cases where our reagent is ineffective, forming syn- and anti-**14** with disappointing selectivity. This may be rationalized by considering the cleft into which the oxidant must

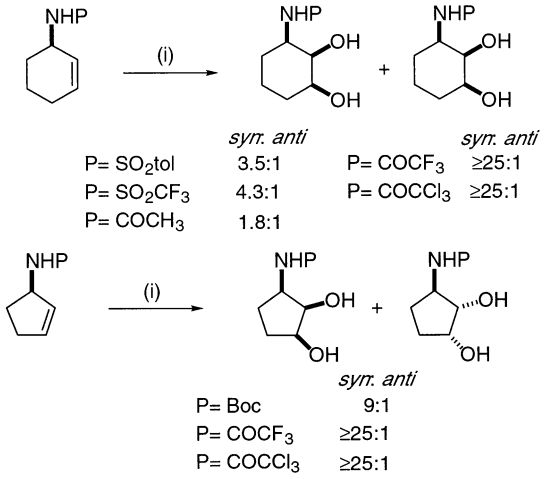
(6) See Schroeder, M. *Chem. Rev.* **1980**, *80*, 187 and ref 24.
(7) If retention of silyl groups is required, then an aqueous sodium sulfite workup is recommended; see ref 25(b).

fit as it approaches the alkene: clearly, a pseudoaxial hydroxyl group provides more hindrance to the osmium reagent than a pseudoequatorial hydroxyl group. Also, electronic deactivation of the alkene may be more prevalent with a pseudoaxial electronegative group. In support of this hypothesis, an analogous difference in selectivity has been observed for the directed epoxidation of these two allylic alcohols.[8]

Examination of the sugar derived alkenes **17**, **19**, and **21** appears to show the opposite trend, as compound **19** contains a pseudoaxial hydroxyl group and is dihydroxylated with higher diastereoselectivity than compound **17**. However, the configuration at the anomeric center should not be ignored here, as both alcohols **19**[9] and **21**[10] have anomeric configurations chosen to aid the directing effect. Using this methodology, concise syntheses of usefully protected forms of the sugars allose and tallose can now be accomplished. Moreover, the selective, contrasteric, oxidation of cyclohexadiene diol **15** represents a one-step (and stereoselective) synthesis of conduritol D.[11]

While most of the starting materials used in this section were known in the literature, many of the products (especially the syn isomers) are novel compounds. The structures of the syn isomers of compounds **10**, **12**, and **14** were deduced from their symmetry when compared to the corresponding anti isomers (syn-**10** has four resonances in its $^{13}C$ NMR spectrum). The spectroscopic data from compound syn-**16**, produced from the dihydroxylation of **15**, were an exact match with those of conduritol D. The anti isomer of **18** is a known compound[12] and could be identified as the minor component of the TMEDA-mediated oxidation of dihdyropyran **17**. Moreover, the structure of syn-**20** was assigned by $^1H$ NMR spectroscopy, which showed a W coupling between the hydrogen atoms on C-2 and C-4, in agreement with the literature precedent reported by Doherty.[13] Finally, the stereochemistry of syn-**22** was determined by examination of the coupling constants on the tetrahydropyran ring; for example, the coupling between H(C-1) and H(C-2) is 10 Hz, clearly indicative of a trans diaxial arrangement of these two hydrogen atoms.

**SCHEME 3**[a]




[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then aqueous $Na_2SO_3$ Δ.

From these results, one can conclude that as long as the allylic alcohol is not in a particularly hindered environment then the directed dihydroxylation reaction is an efficient way of producing a useful range of syn allylic alcohols in one step.

Moreover, the structure of the fully protected allose monosaccharide syn-**22** was assigned unambiguously by X-ray crystallography; see Supporting Information.

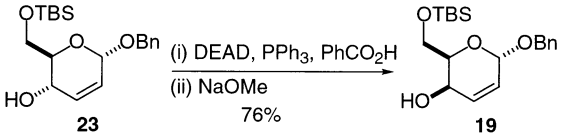
**Oxidation of Protected Allylic Amines.** Our next objective was to examine the directed dihydroxylation of (protected) cyclic allylic amines, hoping for a similar sense and level of stereoselectivity. Preliminary studies concentrated on finding the optimum protecting group that would encourage hydrogen bonding. Various derivatives of both cyclopentenyl- and cyclohexenylamine were prepared and then dihydroxylated under directing conditions Scheme 3. As far as carbonyl-based protecting groups are concerned, there was a clear correlation between p$K_a$ of the CON*H* and the directing ability of a particular protecting group; acetates and Boc groups were reasonably good hydrogen bond donors, while the acidic trifluoro- and trichloracetamides proved to be excellent at promoting high syn selectivity (≥25:1 selectivity means that we could not detect the other diastereoisomer by high-field NMR spectroscopy of the crude reaction mixture and with an authentic sample of the anti isomer for comparison).

In fact this correlation between p$K_a$ and syn selectivity can be taken as evidence in favor of hydrogen bonding control; the failure of the (more acidic) sulfonamides[14] to direct efficiently may be due to an increased steric interaction between the $SO_2$ unit and the oxidant, which disfavors effective hydrogen bonding.

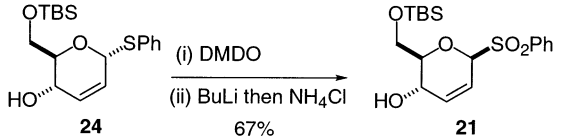
Of the two trihaloamide derivatives that showed promise as protecting and activating groups, we decided to investigate the trichloroacetamide group in detail because allylic trichloroacetamides are easy to prepare

(8) Chamberlain, P.; Roberts, M. L.; Whitham, G. H. *J. Chem. Soc. B* **1970**, 1374.

(9) Compound **19** was made via a Mitsunobu reaction on compound **23**.




(10) Compound **21** (unstable) was prepared from **24** in two steps; see: Valverde, S.; Garcia-Ochoa, S.; Martin-Lomas, M. *J. Chem. Soc., Chem. Commun.* **1987**, 383.



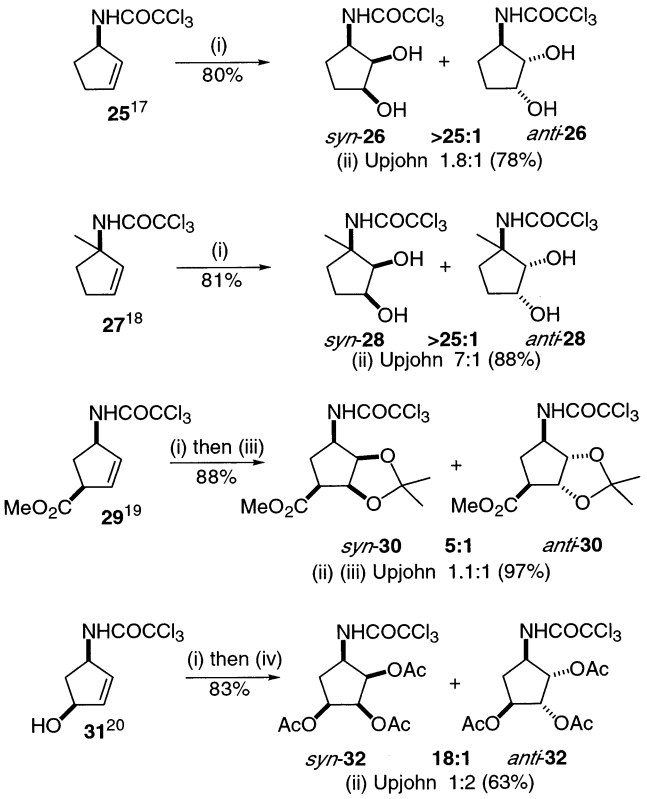

(11) Carless, H. A. J.; Busia, K.; Dove, Y.; Malik, S. S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2505. For a review of synthesis from cyclohexadiene diols, see: Hudlicky, T.; Gonzalez, D.; Gibson, D. T. *Aldrichimica Acta* **1999**, *32*, 35.

(12) Haque, M. B.; Roberts, B. P.; Tocher, D. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2881.

(13) (a) Harris, J. M.; Keranen, M. D.; O'Doherty, G. A. *J. Org. Chem.* **1999**, *64*, 2982. (b) Haukaas, M. H.; O'Doherty, G. A. *Org. Lett.* **2001**, *3*, 3899.

(14) (a) Xu, D.; Park, C. Y.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 2495. (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

**SCHEME 4**[a]




[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then HCl/MeOH; (ii) $OsO_4$ (cat.), acetone, $H_2O$, NMO, rt; (iii) dimethoxypropane, TFA; (iv) $Ac_2O$, py.

via the Overman rearrangement,[15] which would, therefore, provide a general and convenient route to the oxidation precursors.

Pleasingly, the directed dihydroxylation of a series of five-membered allylic trichloroacetamides was high-yielding and extremely stereoselective for the syn isomer Scheme 4. We presume that the enhanced acidity of the trichloroacetamide (and also the trifluoro analogue) relative to that of the corresponding allylic alcohol ($pK_a$ values are approximately 11.2 and 14.7, respectively)[16] means that hydrogen bonding to the $OsO_4$/TMEDA reagent is more effective: this manifests itself as a more syn-selective oxidation reaction. It is noteworthy that under Upjohn conditions, none of the substrates shown below give high levels of stereoselectivity; and this failure to produce the anti isomer may be a manifestation of allylic strain, as noted earlier by Poli. In fact, in this five-membered ring series, it may be that access to the anti stereoisomer is more problematic than access to the syn diastereoisomer!

The relative stereochemistry of the diols shown in Scheme 4 was more difficult to ascertain by NMR spectroscopy, so we made extensive use of X-ray crystallography. An X-ray structure of syn-**28**, anti-**30**, and anti-**32** proved the relative stereochemistry in these series unambiguously (see Supporting Information); the identity of syn-**26** was assigned by analogy to that of the corresponding trifluoro analogue (see Figure 5).

As expected, oxidation of the six-membered cyclic trichloroacetamides (also made via the Overman rearrangement)[21] gave excellent levels of syn diastereoselectivty, Scheme 5, while the Upjohn reaction lead to decent levels of anti selectivity. Again, the pseudoaxially locked amide **39** did not give high levels of stereoselectivity, in line with that observed for the corresponding alcohol **13**. The directed dihydroxylation of dihydropyran template **43** proved to be an efficient way of preparing protected talosamine syn-**44**[22] in high yield. Pleasingly, the seven-membered substrate **45** also responded well to directed dihydroxylation, giving syn-**46** as the sole product from oxidation, although the nonselective dihydroxylation under Upjohn conditions is surprising.

The stereochemistry of syn- and anti-**36** was assigned by $^1$H NMR spectroscopy on the respective TMEDA osmate esters. In $^1$H NMR spectroscopy derived from the syn isomer, the C-2 hydrogen appeared as a pseudo triplet with $J = 3.8$ Hz, while that from the anti isomer showed C2(H) as a dd with $J = 3.9$ and 9.5 Hz, clearly indicating the stereochemical outcome of the reaction. X-ray crystallographic analysis of the (syn) osmate ester derived from **38** proved to be informative (see Figure 5) and served to secure the stereochemistry of syn-**38** itself. The structures of syn-**40** (isopropylidine acetal), syn-**42**, and syn-**46** were also determined by X-ray crystallography so that the relative stereochemistry could be assigned with confidence; see Supporting Information. Stereochemistry in the talosamine series was assigned by removal of the trichloroacetamide group from syn-**44** (NaOH) and peracetylation ($Ac_2O$) to form a tetraacetate that had spectroscopic data identical to those reported in the literature.[22,23]

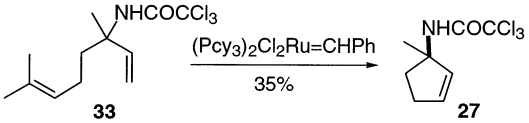
**Mechanism of the Directed Dihydroxylation.** With a comprehensive set of results detailing the behavior of the $OsO_4$/TMEDA mixture toward alkenes, we wish to comment on the mechanism of oxidation. Clearly, our first question relates to obtaining proof that hydrogen

(15) (a) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901. (b) Overman, L. E. *Acc. Chem. Res.* **1980**, *13*, 218. (c) Overman, L. E.; Clizbe, L. A.; Freerks, R. L.; Marlowe, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 2807. (d) Nishikawa, T.; Asai, M.; Ohyabu, N.; Isobe, M. *J. Org. Chem.* **1998**, *63*, 188.

(16) These are calculated $pK_a$s (Advanced Chemistry Development, $pK_a$ Predictor Programme version 5.12).

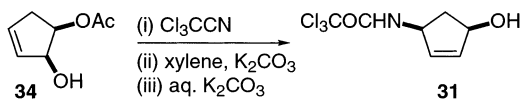
(17) Compound **25** was prepared via Overman rearrangement of the corresponding alcohol (80%).

(18) Compound **27** was prepared from **33** (see ref 15a) via metathesis.




(19) Daluge, S.; Vince, R. *Tetrahedron Lett.* **1976**, *17*, 3005.

(20) Compound **31** was prepared from a mixture of monoacetates **34** (one shown), themselves formed from oxidation of cyclopentadiene with $Pb(OAc)_4$; see: Banwell, M. G.; Ebenbeck, W.; Edwards, A. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 114.

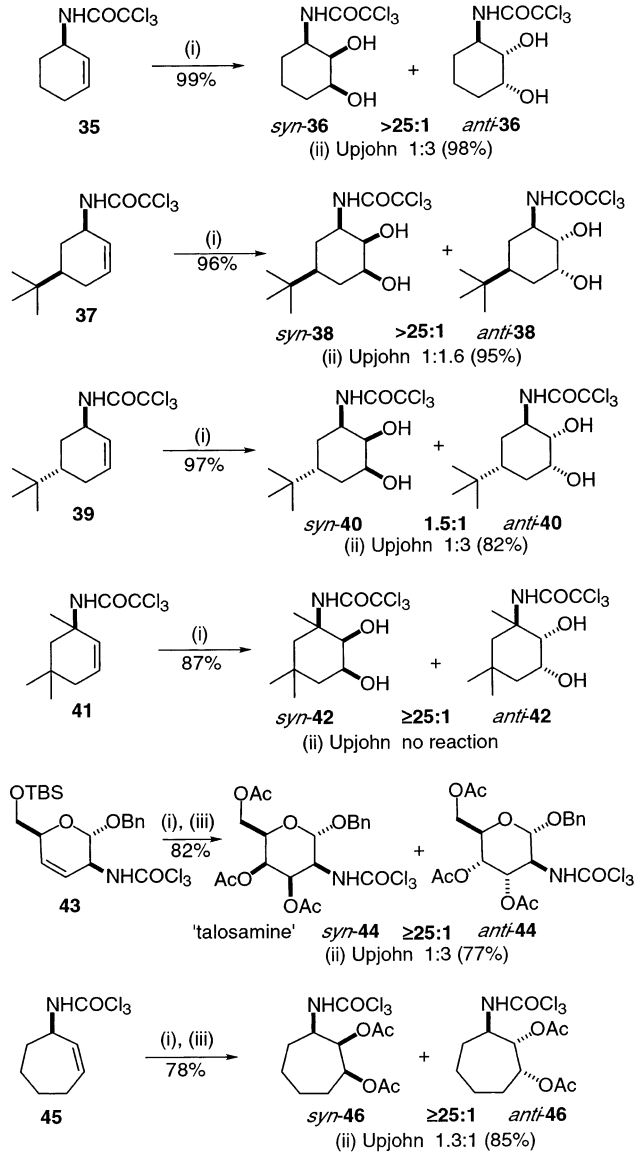



(21) Novel compounds **37** (76%), **39** (12%), **43** (94%), and **45** (59%) were prepared via Overman rearrangement.

(22) Donohoe, T. J.; Blades, K.; Helliwell, M. *Chem. Commun.* **1999**, 1733.

(23) Banaszek A.; Karpiesiuk, W. *Carbohydr. Res.* **1994**, *251*, 233.

**SCHEME 5**[a]

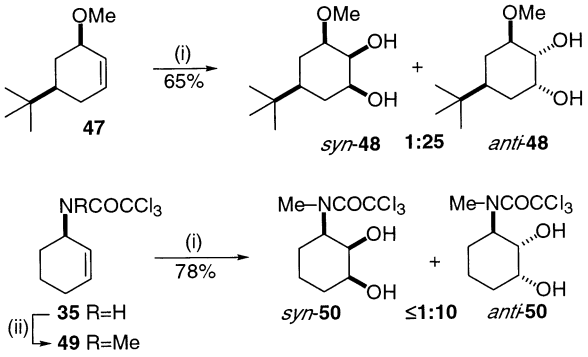



[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then HCl/MeOH; (ii) $OsO_4$ (cat.), acetone, $H_2O$, NMO, rt; (iii) $Ac_2O$, py.

bonding is responsible for the syn selectivity that we observe. This was proven convincingly when the *O*-methyl ether **47** and the *N*-methyl amide **49** were prepared and then subjected to dihydroxylation with $OsO_4$/TMEDA, Scheme 6. Not only were both of these oxidations slower than those of the parent alcohol or amide, but each gave a single diastereoisomer that was formed from oxidation from the *least* hindered face of the alkene. Anti-**48** is a known compound,[2b] and the stereochemistry of anti-**50** was correlated to a sample of anti-**36** that was *N*-methylated.

Being convinced that the allylic alcohols and amides were acting as hydrogen bond donors, we next examined the role of osmium tetroxide and its complexes as hydrogen bond acceptors. In previous work, we had shown that the complex of $OsO_4$ with $Me_3N$ was a better hydrogen bond acceptor than $OsO_4$ alone. A simple explanation for this is that coordination of a Lewis base

**SCHEME 6**[a]




[a] Reagents: (i) $OsO_4$ (1 equiv), TMEDA (1 equiv), $CH_2Cl_2$, −78 °C, then HCl/MeOH; (ii) NaH, MeI.

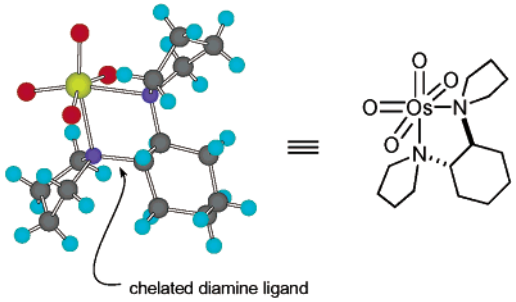



**FIGURE 2.** Corey's X-ray structure of an $OsO_4$·diamine complex.

to the metal increases the electron density on osmium and, in so doing, reduces back-bonding by the oxo ligands, thus making these atoms more electron rich. Of course, electron-rich oxo ligands are prone to efficient hydrogen bonding.

A logical extension of this argument supposes that TMEDA forms a bidentate complex with osmium tetroxide, making both the metal and oxo groups even more electron-rich again.

At the outset of this work, these (formally **20e**) complexes were unknown in the literature and were only recently identified by Corey, who obtained a crystal structure of a chiral 1,2-diamine bound to $OsO_4$, Figure 2.[24] In this complex, the bidentate nature of the chiral 1,2-diamine ligand can be seen clearly. In fact, there is significant precedent for the reaction of a bidentate amine with osmium tetroxide and an alkene.[25] However, despite their enhanced reactivity and potential for asymmetric induction, the ability of these complexes to act as hydrogen bond acceptors had not been uncovered.

Our own studies had concentrated on NMR spectra of the $OsO_4$/TMEDA reagent (which is only stable at temperatures ≤−50 °C). Both $^1H$ (300 MHz) and $^{13}C$ NMR (75 MHz) of a 1:1 mixture of $OsO_4$ and TMEDA at −78 °C showed the presence of a single compound, with two

(24) Corey, E. J.; Sarshar, S.; Azimiora, M. D.; Newbold R. C.; Noe, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 7851.

(25) (a) Tomioka, K.; Nakajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 573. (b) Corey, E. J.; DaSilva Jardine, P.; Virgil, S.; Yuen, W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243. (c) Hanessian, S.; Meffre, P.; Girard, M.; Beaudoin, S.; Sancéau, J.-Y.; Bennani, Y. *J. Org. Chem.* **1993**, *58*, 1991. (d) Oishi, T.; Iida, K. I.; Hirama, M. *Tetrahedron Lett.* **1993**, *34*, 3573. (e) Vedejs, E.; Galante, R. J.; Goekjian, P. G. *J. Am. Chem. Soc.* **1998**, *120*, 3613.

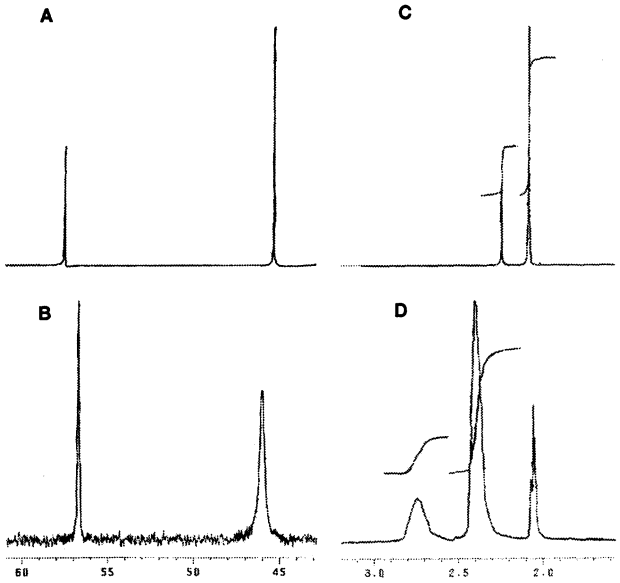



**FIGURE 3.** Overlay of low-temperature NMR spectra, $(CD_3)_2CO$, −78 °C: (A) $^{13}C$ NMR of TMEDA; (B) $^{13}C$ NMR of $OsO_4$/TMEDA; (C) $^1H$ NMR of TMEDA; (D) $^1H$ NMR of $OsO_4$/TMEDA.

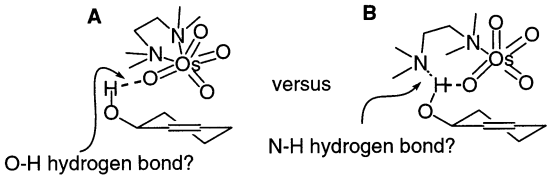



**FIGURE 4.** Plausible interactions of TMEDA with $OsO_4$.

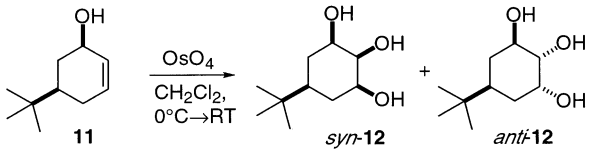
peaks for the TMEDA ligand, and no uncomplexed TMEDA was observed (Figure 3); these data are consistent with a bidentate complex.

In addition, we also measured the low temperature (−78 °C, $CH_2Cl_2$) IR spectra of $OsO_4$ and $OsO_4$/quinuclidine and $OsO_4$/TMEDA in order to qualitatively assess the Os=O bond order in this series. Under these conditions, $OsO_4$ absorbs at 953 $cm^{-1}$, $OsO_4$/quinuclidine at 910 $cm^{-1}$, and $OsO_4$/TMEDA at 880 $cm^{-1}$. This trend toward absorption at a lower wavenumber as the electron density on the metal increases correlates well with our observation that hydrogen bonding ability (and therefore syn selectivity) increases in the order $OsO_4$ < $OsO_4$·monodentate amine < $OsO_4$·chelating diamine. Naturally, caution is called for here because the three complexes have different shapes, and therefore we cannot be certain that we are observing the same type of absorption in each case. Therefore, we present these data as circumstantial evidence in favor of the electronic nature of the $OsO_4$/TMEDA complex.

If TMEDA forms (and then reacts via) a bidentate complex, then this must hydrogen bond to the substrate through an oxo ligand; see **A**, Figure 4. However, if the reactive species contains TMEDA bound in a monodentate fashion, then its extraordinary reactivity must be explained by hydrogen bonding through the nonligated amino group of TMEDA (**B**, Figure 4).

To investigate this second possibility, we performed the oxidation of alcohol **11** using a series of bifunctionalized

**SCHEME 7**




| amine | *syn:anti* | amine | *syn:anti* |
|---|---|---|---|
| none | 1:1.7 | $Me_2NCH_2NMe_2$ | 1.6:1 |
| $Me_3N$ | 1.2:1 | $Me_2NCH_2CH_2NMe_2$ | **4.6:1** |
| $Me_2NCH_2CH_2OMe$ | 1.1:1 | $Me_2NCH_2CH_2CH_2NMe_2$ | **2.8:1** |
| $Me_2NCH_2CH_2OH$ | 1.1:1 | | |

analogues of TMEDA. Oxidation using $OsO_4$ and $Me_3N$ is 1.2:1 syn selective, which is the selectivity expected from a standard monodentate ligand that has no extra possibilities for hydrogen bonding through the amine ligand. The amines shown in Scheme 7 clearly fall into two distinct categories: (i) those that can form a chelate with osmium and (ii) those that cannot. The former give high stereoselectivity, while the latter give lower levels of control. If model **B** were correct, then amines with a pendant methoxy or hydroxyl group should give levels of syn selectivity that approach that of TMEDA; however, they do not. The methylamine-derived compound ($Me_2NCH_2NMe_2$) should also be able to participate in a transition structure such as **B** but cannot form a four-membered chelate with osmium. The result shown in Scheme 7 shows that this ligand is not much better than trimethylamine in promoting hydrogen bonding, so credence is given to model **A**.

As mentioned earlier, the product of the reaction between an alkene, $OsO_4$, and TMEDA produces an osmate ester, which must be hydrolyzed to produce the diol product. Unusually, these osmate esters (18 electrons) are quite stable and can be purified by chromatography on silica. In fact, it is the stability of these complexes that precludes the use of chelating diamines with catalytic $OsO_4$, which cannot be regenerated from the osmate ester in situ by an oxidizing agent.[26] Examination of the crystal structures of *syn*-osmate esters **51** and **52** derived from (TMEDA) $OsO_4$-mediated dihydroxylation of the parent alkenes is informative and reveals two interesting features. First, the chelated nature of the TMEDA ligand is evident. Second, the proximity of the amide N and glycolate oxygen attached to osmium is noteworthy: these two atoms are closer than the sum of Van der Waal's radii, which is indicative of a hydrogen bond, between them (Figure 5). Intramolecular hydrogen bonding is also suggested by the NMR spectra of these osmate esters, which show a particularly low-field signal for the amide N*H* ($\delta$ 7−8 ppm) that is not present in the corresponding anti osmate esters (typically N*H* at $\delta$ 6−7 ppm). While these two features of compounds **51** and **52** are clearly those of the product of osmylation, they need not necessarily have been conserved from the preceding transition states for osmylation, so caution is appropriate when interpreting these results.

One aspect of the $OsO_4$/TMEDA reagent not discussed so far is the profound influence that TMEDA has on the

(26) However, see: Jonsson, S. Y.; Adolfsson, H.; Backväll, J.-E. *Org. Lett.* **2001**, *3*, 3463.

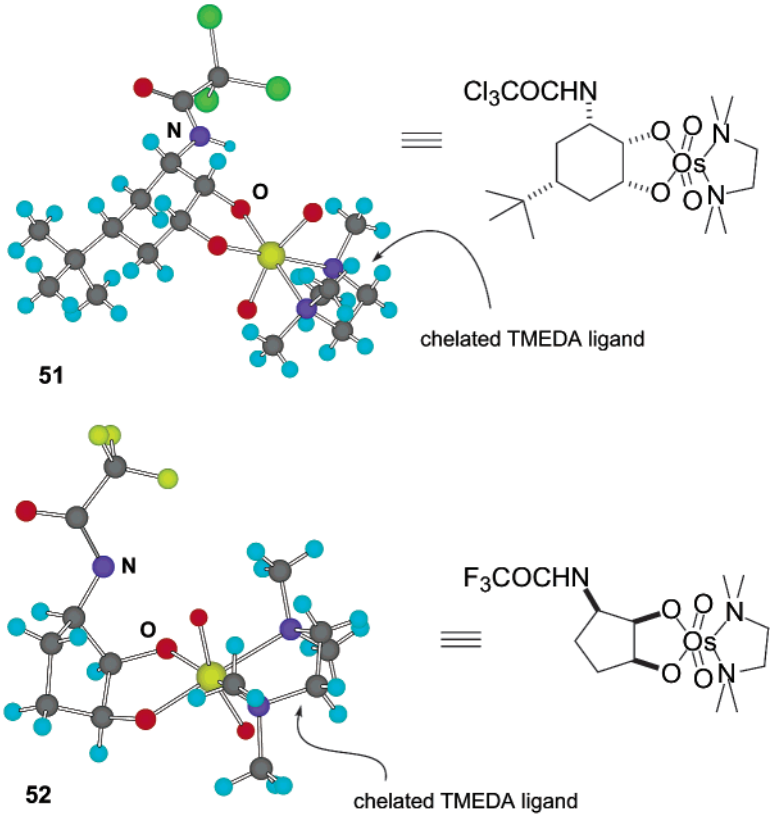



**FIGURE 5.** N···O distance in **51** is 2.67 Å and N···O distance in **52** is 2.61 Å.

reactivity of $OsO_4$ toward alkenes. Sharpless has measured the rate enhancement that quinuclidine imparts onto the dihydroxylation reaction to be an approximately 100-fold increase (depending on the alkene substitution pattern).[27] Moreover, Corey states that bidentate (chiral) diamine complexes are more reactive than complexes of $OsO_4$ with monodentate amines, again by a factor of $\geq 100$;[24] clearly, this means that $OsO_4$/TMEDA is expected to be 10 000 times more reactive than $OsO_4$. This estimate is borne by our observations that $OsO_4$/TMEDA accomplishes the osmylation of alkenes in minutes at −78 °C, under which conditions $OsO_4$·quinuclidine or $OsO_4$ are inert: this fact alone demands an explanation involving a unique role for TMEDA. From our own studies, we also know that the $OsO_4$/TMEDA reagent does not show the same levels of discrimination for electron-rich alkenes over electron-poor alkenes as $OsO_4$, which fits with it being a relatively electron-rich oxidizing agent. So, how can we explain the fact that TMEDA makes the oxidant more electron rich and yet much more reactive, even toward already electron-rich alkenes? Our observations on this difficult question center around the role of the metal during oxidation. Osmium tetroxide is a 16 electron complex, whereas an osmate ester formed after osmylation is a 14 electron species and (inasmuch as these compounds have a desire to attain an 18 electron configuration) more electron deficient. For example, osmate esters can readily bind two moles of a cinchona alkaloid ligand, whereas coordination of only one such alkaloid is observed for $OsO_4$.[28] If the metal becomes significantly more electron deficient during osmylation, then the presence of a chelating diamine, increasing electron density on $OsO_4$ beforehand, should help to assuage this loss of electron density and promote the reaction.

In summing up our data on the mechanism, we have shown that the $OsO_4$ TMEDA reagent is chelated, with respect to the metal, both before and after the osmylation event. The most logical extrapolation of these observations is to assume that the ligand remains bidentate throughout the course of the oxidation: such a role for the ligand also helps to explain the dramatically increased reactivity of the complex relative to $OsO_4$.quinuclidine. Of course, this particular mechanism requires that the oxidant behave as a hydrogen bond acceptor through its oxo ligands, a conclusion that is also supported by experiments with a range of different analogues of TMEDA. This reaction pathway leads directly to the osmate ester as shown above with contrasteric (syn) stereoselectivity.

Whatever the precise details of the osmylation reaction, we have uncovered an interesting and useful variant of the dihydroxylation reaction that shows excellent hydrogen bonding ability with a wide range of allylic alcohols and amides giving access to all syn triol and amino-diol motifs in five-, six-, and seven-membered rings. The information gained about the effect of an amine additive on the hydrogen bonding ability of the oxidant should

(27) Anderson, P. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 7047.

(28) Jacobsen, E. N.; Marko, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 737.

(29) For example, see: Blades, K.; Donohoe, T. J.; Winter, J. J. G.; Stemp, G. *Tetrahedron Lett.* **2000**, *41*, 4701.

prove to be useful in designing new dihydroxylating systems, especially ones that are catalytic in transition metal.[29]

## Experimental Section

**General Details.** All reactions were carried out under an atmosphere of dry nitrogen. Proton nuclear magnetic resonance spectra (NMR) were recorded at 300, 400, or 500 MHz. $^{13}$C NMR spectra were recorded at 75, 100, or 125 MHz. Coupling constants (*J*) are given in Hz. Infrared spectra (IR) were recorded as evaporated films. Chemical ionization (CI) was performed using $NH_3$. Microanalysis was obtained from the microanalytical section of the University of Manchester's Chemistry Department. All solvents and reagents requiring purification were purified using standard laboratory techniques according to methods published in *Purification of Laboratory Chemicals* by Perrin, Armarego, and Perrin (Pergamon Press, 1966).

**General Procedures for Dihydroxylation: $OsO_4$·-TMEDA.** To a solution of substrate (0.01 M) and TMEDA (1.1 equiv) in dichloromethane precooled to −78 °C was added a solution of $OsO_4$ (1.05 equiv) in dichloromethane (∼1 mL). The solution turned deep red and then brown−black. The solution was stirred until complete (TLC analysis, ca. 1 h) before being allowed to warm to room temperature.

**Workup A with Sodium Sulfite.** The solvent was removed in vacuo and replaced with THF (10 mL) and (aqueous) sodium sulfite (10 mL). This mixture was heated at reflux for 3 h and the product extracted as indicated.

**Workup B with Acidic Methanol.** The solution was concentrated under reduced pressure and the resulting residue redissolved in methanol (10 mL). Hydrochloric acid (concentrated, ∼5 drops) was then added and the solution stirred for 2 h after which time the solvent was removed under reduced pressure and the product isolated as indicated.

**Workup C with Ethylenediamine.** Ethylenediamine (5.0 equiv) was added to the crude reaction mixture at room temperature and the resulting solution stirred for 48 h during which time a brown precipitate formed. The solution was then concentrated under reduced pressure and the product isolated as indicated.

**Upjohn Conditions.** To a stirred solution of substrate (0.01 M) and *N*-methylmorpholine-*N*-oxide monohydrate (3.0 equiv) in 4:1 acetone−water was added $OsO_4$ (1 crystal, ∼1 mol %) and the solution stirred until complete (TLC analysis, ca. 4 h). Sodium sulfite solution (saturated, 10 mL) was then added and the solution stirred for an additional 30 min. The solvent was then evaporated under reduced pressure and the product isolated as outlined below.

***syn*-Cyclopentan-1,2,3-triol Syn-2.** 2-Cyclopentenol **1** (100 mg, 1.19 mmol) was oxidized with $OsO_4$/TMEDA using the ethylamine diamine workup. The residue was redissolved via sonication in a mixture of ethanol (7.5 mL) and ethyl acetate (40 mL) and the resulting solution filtered through celite and concentrated under reduced pressure to yield the crude mixture of syn and anti triols in a 7:1 ratio (by $^1$H NMR). The products were purified by flash chromatography (EtOAc) to yield the title compound, as a mixture of isomers, as a clear oil (107 mg, 76%). Pure *syn*-cyclopentane-1,2,3-triol **2** was then separated by further chromatography: $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 4.02−4.09 (m, 2 H), 3.82 (t, $J$ = 5 Hz, 1 H), 1.76−1.95 (m, 4 H); $^{13}$C NMR (75 MHz, $CD_3OD$) $\delta$ 71.9, 69.9, 27.1; IR (film) 3365 (br), 2962, 2926 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 154 (100%, M2$NH_4$), 90 (40); $C_5H_{14}NO_3$ requires *M* 136.0974, found $MNH_4^+$ 136.0979.

***syn*-2-Methylcyclopentan-1,2,3-triol Syn-4.** 2-Methylcyclopent-2-en-1-ol **3** (50 mg, 0.51 mmol) was oxidized with $OsO_4$/TMEDA using the ethylamine diamine workup. The residue was redissolved via sonication in a mixture of ethanol (7.5 mL) and ethyl acetate (40 mL) and the resulting solution filtered through celite and concentrated under reduced pressure to yield the crude product (as a single isomer by $^1$H NMR). The crude product was purified by flash chromatography (2:1 dichloromethane−methanol) to yield the title compound as a colorless oil (59 mg, 88%): $^1$H NMR (200 MHz; $CD_3OD$) $\delta$ 3.80−3.72 (m, 2 H), 2.00−1.68 (m, 4 H), 1.22 (s, 3 H); $^{13}$C NMR (75 MHz; $CD_3OD$) $\delta$ 77.93, 77.62, 29.49, 23.25; IR (film) 3314 (br), 2968, 2944, 1058 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 133 ($MH^+$, 30%,); $C_6H_{16}NO_3$ requires 150.1130, found $MH^+$ 150.1131.

***syn*-1,2,3,4-Tetraacetoxycyclopentane Syn-6.** *cis*-Cyclopent-2-en-1,4-diol **5** (100 mg, 1.0 mmol) was oxidized with $OsO_4$/TMEDA using the ethylamine diamine workup. The residue was redissolved in pyridine (10 mL) and acetic anhydride (10 mL), and *N*,*N*-(dimethylamino)pyridine (5 mg, catalytic) was added. The mixture was then heated at 80 °C for 12 h. It was then allowed to cool and diluted with diethyl ether (200 mL). The solution was then filtered through celite and washed with dilute hydrochloric acid (100 mL, 2 M), potassium carbonate solution (saturated, 100 mL), and brine (100 mL). The ethereal layer was then dried ($MgSO_4$) and concentrated under reduced pressure to yield the crude mixture of peracetylated products (>25:1 mixture by $^1$H NMR), which were then purified by flash chromatography (10:1 light petroleum−EtOAc) to yield the title compound as a colorless oil (220 mg, 73%): $^1$H NMR (300 MHz, $CDCl_3$, $Me_4Si$) $\delta$ 5.21 (dd, $J$ = 4 and 2 Hz, 2 H), 5.08−5.16 (m, 2 H), 2.60 (dt, $J$ = 15 and 8 Hz, 1 H), 2.02 (s, 6 H), 2.00 (s, 6 H), 1.92−2.04 (m, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.0, 169.6, 70.4, 69.1, 34.6, 20.6, 20.5; IR (film) 2994, 2941, 1744, 1435, 1372, 1231 cm$^{-1}$; CIMS *m*/*z* $C_{13}H_{22}NO_8$ requires *M* 320.1345, found $MNH_4^+$, 320.1358. Anal. Calcd for $C_{13}H_{18}O_8$: C, 51.66; H, 6.00. Found: C, 51.89; H, 6.29.

***anti*-1,2,3,4-Tetraacetoxycyclopentane Anti-8.** *cis*-1-Cyclopenten-3,4-diol **7** (100 mg, 1.0 mmol) was oxidized using Upjohn conditions. The peracetylation and workup procedure, which was identical to that for syn-**6**, gave the crude mixture of isomers (10:1 mixture by $^1$H NMR). Purification by flash chromatography (10:1 light petroleum−EtOAc) gave the title compound as a colorless oil (182 mg, 62%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.43 (qd, $J$ = 4 and 1 Hz, 2 H), 5.34 (dd, $J$ = 4 and 2 Hz, 2H), 2.28 (t, $J$ = 5 Hz, 2H), 2.09 (s, 6H), 2.08 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 169.9, 169.8, 73.5, 68.2, 34.8, 20.7, 20.5; IR (film) 2921, 2851, 1744, 1372, 1229 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 320 (100%, $MNH_4^+$); $C_{13}H_{22}NO_8$ requires 320.1345, found $MNH_4^+$ 320.1345.

***syn*-Cyclohexane-1,2,3-triol Syn-10.** 2-Cyclohexene-1-ol **9** (50 mg, 0.51 mmol) was oxidized with $OsO_4$/TMEDA using the sodium sulfite workup. The crude reaction mixture was then concentrated in vacuo to a gray powder. Ethanol (30 mL) was added and the suspension stirred at room temperature for 1 h. Filtration of this suspension through Celite and concentration under reduced pressure gave a colorless solid (80 mg). Flash chromatography (1:7 petrol−EtOAc) gave inseparable syn- and anti-**10** (66 mg, 98%) in a ratio of 9:1. Syn-**10**: $^1$H NMR (300 MHz, $D_2O$) $\delta$ 3.81 (t, $J$ = 2.6 Hz, 1 H), 3.52 (ddd, $J$ = 10, 4.6 and 2.6 Hz, 2 H), 1.8−1.0 (m, 6 H); $^{13}$C NMR (75 MHz, $D_2O$) $\delta$ 72.55, 70.27, 26.29 and 18.77; IR (film) 3192 and 2927 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 150 (100%, $MNH_4^+$); $C_6H_{16}NO_3$ requires *M* 150.1130, found $MNH_4^+$ 150.1128.

***syn*-5-*tert*-Butylcyclohexane-1,2,3-triol Syn-12.** *cis*-5-*tert*-Butylcyclohex-2-enol **11** (50 mg, 0.32 mmol) was oxidized with $OsO_4$/TMEDA using the sodium sulfite workup; the isolation procedure, which was identical to that shown for syn-**10**, gave a colorless solid. Chromatography through a small plug of silica (eluting with 6:1 EtOAc/EtOH) gave syn-**12** as a colorless crystalline solid (55 mg, 91%) in a ratio of 24:1 ($^1$H NMR). The spectroscopic data for this compound matched that in the literature.[2b]

**Conduritol D Syn-16.** *cis*-Cyclohexa-3,5-diene-1,2-diol **15** (50 mg, 0.45 mmol) was oxidized with $OsO_4$/TMEDA using the sodium sulfite workup; the isolation procedure, which was identical to that shown for syn-**10**, gave a light brown oil (70

mg). Flash chromatography (9:1 EtOAc/MeOH) gave an inseparable mixture of tetraols as a colorless oil (35 mg, 54%). $^1$H NMR spectroscopy (200 MHz/$D_2O$) showed a mixture of conduritol D and conduritol E in a ratio of 16:1.[11]

**2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-allitol Syn-18.** Diol **17** (100 mg, 0.77 mmol) was oxidized with $OsO_4$/TMEDA using the sodium sulfite workup. The aqueous mixture was concentrated under reduced pressure and then dried in vacuo to a gray solid. This solid was powdered, and pyridine (10 mL), acetic anhydride (5 mL), and 4-(dimethylamino)pyridine (catalytic) were added. The resulting black suspension was stirred at room temperature under an atmosphere of nitrogen for 48 h. Diethyl ether (100 mL) was added and the mixture filtered through Celite (washing with additional volumes of diethyl ether). The combined filtrate was washed with 2 M HCl (100 mL), aqueous sodium hydrogen carbonate (100 mL), and brine (100 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to a light brown oil (201 mg). $^1$H NMR spectroscopy (300 MHz, $CDCl_3$) showed a 1:6 mixture of tetraacetates anti and syn-**18**. Flash chromatography (6:1 petrol−EtOAc) gave 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-allitol syn-**18** (161 mg, 63%) as a colorless oil: $[\alpha]^{27}_D$ +7.5 (*c* 0.2, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.60 (t, $J$ = 2.6 Hz, 1 H), 4.95 (ddd, $J$ = 10, 5.5 and 2.6 Hz, 1 H), 4.84 (ddd, $J$ = 10 and 2.6 Hz, 1 H), 4.10−4.14 (m, 2 H), 3.78−3.88 (m, 2 H), 3.60 (t, $J$ = 10 Hz, 1 H), 2.10 (s, 3 H), 2.02 (s, 3 H), 1.94 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.69, 169.89, 169.30, 169.11, 71.71, 67.77, 66.40, 66.27, 63.45, 62.49, 20.70 (2) and 20.55 (2); IR (film) 2996 and 1747 cm$^{-1}$; CIMS *m/z* (rel intensity) 350 (10%, $MNH_4^+$) and 249 (100); $C_{14}H_{24}NO_9$ requires $M$ 350.1451, found $MNH_4^+$ 350.1454.

**2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-mannitol Anti-18.** Diol **17** (50 mg, 0.39 mmol was oxidized using Upjohn conditions. The peracetylation and workup procedure, which was identical to that for syn-**18**, gave a crude mixture of isomers. $^1$H NMR spectroscopy (300 MHz, $CDCl_3$) of this oil showed a mixture of the two tetraacetates anti-**18** and syn-**18** in a ratio of 16:1. Flash chromatography (4:1 petrol−EtOAc) gave anti-**18** as a colorless oil (89 mg, 70%). The spectroscopic data for this compound matched that in the literature.[12]

**2,3,4,6-Tetraacetoxy-1-benzyloxy-talose Syn-20.** Alcohol **19** (0.19 g, 0.54 mmol) was oxidized with $OsO_4$/TMEDA using the methanolic workup. The resulting crude tetraol was dissolved in pyridine (20 mL), and to this was added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The product was purified by column chromatography (40% ethyl acetate in petroleum ether 40−60) to afford syn-**20** as a clear oil (0.22 g, 92%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.40−7.27 (m, 5 H), 5.34−5.28 (m, 2 H), 5.13 (dt, $J$ = 3.8 and 1.2 Hz, 1 H), 4.95 (d, $J$ = 1.2 Hz, 1 H), 4.71 (d, $J$ = 11.8 Hz, 1 H), 4.54 (d, $J$ = 11.8 Hz, 1 H), 4.27 (dt, $J$ = 1.2 and 7.2 Hz, 1 H), 4.19−4.15 (m, 2 H), 2.12 (s, 3 H), 2.12 (s, 3 H), 2.10 (s, 3 H), 1.97 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.3, 170.1, 169.9, 169.6, 136.1, 128.5, 128.2, 128.1, 97.3, 69.6, 67.5, 66.8, 65.9, 65.6, 62.0, 20.8, 20.7, 20.6, 20.5; IR (thin film) 3032, 1769, 1372, 1225, 1069 cm$^{-1}$; CIMS *m/z* (rel intensity) 456 (100%, $MNH_4^+$), 331 (70); $C_{21}H_{30}NO_{10}$ requires $M$ 456.1870, found $MNH_4^+$ 456.1866.

**2,3,4,6-Tetraacetoxy-6-benzenesulfonyl allose Syn-22.** $\beta$-Sulfone **21** (0.10 g, 0.26 mmol) was oxidized with $OsO_4$/TMEDA using the methanolic workup. The resulting crude tetraol was dissolved in pyridine (20 mL), and to this was added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The product was purified by column chromatography (60% diethyl ether in petroleum ether 40−60) to afford the tetraacetate syn-**22** as a colorless crystalline solid (0.10 g, 82%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.90 (d, $J$ = 7.5 Hz, 2 H), 7.71 (t, $J$ = 7.4 Hz, 1 H), 7.57 (t, $J$ = 7.5 Hz, 2 H), 5.61 (t, $J$ = 2.8 Hz, 1 H), 5.21 (dd, $J$ = 2.8 and 10.1 Hz, 1 H), 4.78 (dd, $J$ = 2.8 and 10.1 Hz, 1 H), 4.71 (d, $J$ = 10.0 Hz, 1 H), 4.19 (dd, $J$ = 1.9 and 12.3 Hz, 1 H), 4.08 (dd, $J$ = 4.7 and 12.3 Hz, 1 H), 4.03 (ddd, $J$ = 1.9, 4.7 and 10.0 Hz, 1 H), 2.17 (s, 3 H), 2.11 (s, 3 H), 1.98 (s, 3 H), 1.96 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.2, 169.5, 168.8, 168.7, 134.9, 134.4, 130.3, 128.8, 86.7, 72.6, 68.0, 65.4, 64.8, 61.4, 20.6, 20.5, 20.4; IR (thin film) 1756, 1373 and 1227 cm$^{-1}$; CIMS *m/z* (rel intensity) 490 (100%, $MNH_4^+$), 490 (100%, $MNH_4^+$); $C_{20}H_{28}NO_{11}S$ requires $M$ 490.1383, found $MNH_4^+$ 490.1383; mp 165 °C. Anal. Calcd for $C_{20}H_{24}O_{11}S$: C, 50.82; H, 5.08. Found: C, 50.87; H, 4.98.

***syn*-*N*-(2,3-Dihydroxycyclopentyl)-2′,2′,2′-trichloroacetamide Syn-26.** Trichloroacetamide **25** (100 mg, 0.438 mmol) was subjected to standard TMEDA dihydroxylation conditions using the methanolic workup to produce a brown solid, which was purified by column chromatography (60% ethyl acetate/petrol) to produce syn-**26** (92 mg, 80%) as a colorless solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.55 (br s, 1 H), 4.20−4.27 (m, 2 H), 4.08 (dd, $J$ = 5.2 and 4.4 Hz, 1 H), 3.04 (br s, 1 H), 2.08−2.17 (m, 1 H) and 1.80−1.98 (m, 3 H); $^{13}$C NMR (75 MHz, $(CD_3)_2$-CO) $\delta$ 160.6, 92.8, 72.8, 72.6, 52.3, 29.7 and 27.6; IR (film) 3305, 2925, 1693 and 1515 cm$^{-1}$; CIMS *m/z* (rel intensity) 262 (100%, $MH^+$), 283 (28), 281 (100), 279 (93), 266 (21), 264 (73) and 262 (70); $C_7H_{11}NO_3Cl_3$ requires $M$ 261.9804, found $MH^+$ 261.9804; mp 112−114 °C. Anal. Calcd for $C_7H_{10}NO_3Cl_3$: C, 32.0; H, 3.8; N, 5.3. Found: C, 32.2; H, 4.0; N, 5.3.

***anti*-*N*-(2,3-Dihydroxycyclopentyl)-2′,2′,2′-trichloroacetamide Anti-26.** Trichloroacetamide **25** (100 mg, 0.438 mmol) was subjected to standard Upjohn conditions, and the products were purified by column chromatography (60% ethyl acetate/petrol) to give two white solids; syn-**26** (58 mg) and anti-**26** (32 mg) overall yield 78%. Anti-**26**: $^1$H NMR (300 MHz, $(CD_3)_2CO$) $\delta$ 8.00 (br s, 1 H), 3.80−4.10 (m, 3 H), 3.64 (br s, 1 H), 1.80−1.97 (m, 2 H) and 1.38−1.63 (m, 2 H); $^{13}$C NMR (75 MHz, $(CD_3)_2CO$) $\delta$ 161.5, 77.1, 71.3, 57.3, 29.0 and 25.8; IR (film) 3318, 2931, 1694 and 1517 cm$^{-1}$; CIMS *m/z* (rel intensity) 283 (28%), 281 (100), 279 (95), 266 (20), 264 (60) and 262 (57); $C_7H_{11}NO_3Cl_3$ requires $M$ 261.9804, found $MH^+$ 261.9809; mp 146−148 °C.

***syn*-*N*-(2,3-Dihydroxy-1-methyl-cyclopentyl)-2′,2′,2′-trichloroacetamide Syn-28.** Trichloroacetamide **27** (70 mg, 0.29 mmol) was subjected to standard TMEDA dihydroxylation conditions using the methanolic workup and the resulting brown oil purified by column chromatography (80% diethyl ether/petrol) to give syn-**28** (65 mg, 81%) as a colorless solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.61 (br s, 1 H), 4.28 (br q, $J$ = 6 Hz, 1 H), 3.70 (d, $J$ = 6 Hz, 1 H), 3.20 (br s, 2 H), 2.34−2.49 (m, 1 H), 1.88−2.02 (m, 1 H), 1.60−1.76 (m, 2 H), 1.43 (s, 3 H); $^{13}$C NMR (75 Mz, $CDCl_3$) $\delta$ 160.9, 93.5, 78.8, 71.6, 61.3, 33.0, 30.2 and 23.1; IR (film) 3368, 2972, 2940, 1702 and 1505 cm$^{-1}$; CIMS *m/z* (rel intensity) 297 (35%), 295 (95), 293 (100, $MH^+$), 280 (20), 278 (50) and 276 (60); $C_8H_{13}NO_3Cl_3$ requires $M$ 293.0226, found $MH^+$ 293.0230; mp 62−64 °C.

**2,2-Dimethyl-6-(2′,2′,2′-trichloroacetylamino)-tetrahydro-cyclopenta[1,3]dioxole-4-carboxylic Acid Methyl Ester Syn-30.** Trichloroacetamide **29** (100 mg, 0.349 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup, and the resulting brown oil was purified by column chromatography (60% ethyl acetate/petrol) to give a 5:1 mixture of inseparable *syn*- and *anti*-diols (98 mg, 88%) as colorless oils. A small sample of these diols was converted into its acetonide, see below, for separation: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.24 (br d, $J$ = 7.6 Hz, 1 H), 4.90 (t, $J$ = 6.0 Hz, 1 H), 4.63 (t, $J$ = 6.0 Hz, 1 H), 4.00−4.19 (m, 1 H), 3.76 (s, 3 H), 2.80 (dt, $J$ = 12.5 and 6.0 Hz, 1 H), 2.28 (dt, $J$ = 12.5 and 6.0 Hz, 1 H), 2.05 (q, $J$ = 12.5 Hz, 1 H), 1.49 (s, 3 H), 1.37 (s, 3 H); $^{13}$C NMR (75 Mz, $CDCl_3$) $\delta$ 170.0, 161.4, 111.5, 92.3, 79.5, 78.2, 52.0, 51.9, 45.7, 29.2, 25.5, 24.1; IR (film) 3383, 2921, 1737, 1692 and 1524 cm$^{-1}$; CIMS *m/z* (rel intensity) 381 (30%), 379 (90) and 377 (100, $MNH_4^+$); $C_{12}H_{17}NO_5Cl_3$ requires $M$

360.0172, found $MH^+$ 360.0167; mp 186−187 °C. Anal. Calcd for $C_{12}H_{16}NO_5Cl_3$: C, 40.0; H, 4.5; N, 3.9. Found: C, 39.9; H, 4.5; N, 3.8.

**2,2-Dimethyl-6-(2′,2′,2′-trichloroacetylamino)-tetrahydro-cyclopenta[1,3]dioxole-4-carboxylic Acid Methyl Ester Anti-30.** Trichloroacetamide **29** (100 mg, 0.35 mmol) was subjected to standard Upjohn conditions; the crude product was redissolved in acetone (20 mL), and then 2,2-dimethoxypropane (182 mg, 5 equiv) and trifluoroacetic acid (3 drops) were added. The mixture was stirred for 1 h, concentrated in vacuo, and purified by column chromatography (20% ethyl acetate/petrol) to separate syn-**30** (58 mg, 46%) and anti-**30** (64 mg, 51%) acetonides as two colorless solids; overall, a 1:1.1 syn:anti ratio was observed (122 mg, 97%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.16 (br d, $J$ = 7.1 Hz, 1 H), 4.77 (d, $J$ = 5.4 Hz, 1 H), 4.47 (d, $J$ = 5.4 Hz, 1 H), 4.33 (t, $J$ = 7.1 Hz, 1 H), 3.69 (s, 3 H), 3.08 (d, $J$ = 8.3 Hz, 1 H), 2.46 (ddd, $J$ = 7.1, 8.3 and 14.8 Hz, 1 H), 1.96 (d, $J$ = 14.8 Hz, 1 H), 1.40 (s, 3 H), 1.22 (s, 3 H); $^{13}$C NMR (75 Mz, $CDCl_3$) $\delta$ 176.5, 161.5, 111.1, 92.4, 85.8, 83.5, 57.6, 52.8, 51.0, 30.8, 26.4, 24.0; IR (film) 3383, 2992, 1737, 1692, 1524 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 381 (25%), 379 (82), 377 (100, $MNH_4^+$), 364 (22), 362 (71) and 360 (73); $C_{12}H_{20}N_2O_5Cl_3$ requires *M* 377.0438, found $MNH_4^+$ 377.0430; mp 92−94 °C. Anal. Calcd for $C_{12}H_{16}NO_5Cl_3$ C, 40.0; H, 4.5; N, 3.9. Found: C, 40.3; H, 4.5; N, 3.8.

***syn*-2,3,4-Triacetoxy-(2,2,2-trichloroacetylamino)-cyclopentane Syn-32.** Trichloroacetamide **31** (120 mg, 0.49 mmol) was subjected to standard TMEDA conditions, with the methanolic workup. The resulting brown oil was dissolved in pyridine (20 mL), and to this were added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The residue was purified by column chromatography (80% diethyl ether in petroleum ether 40−60) to yield syn-**32** as a colorless solid (165 mg, 83%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.24 (brd, $J$ = 8.4 Hz, 1 H), 5.48 (t, $J$ = 4.4 Hz, 1 H), 5.30−5.22 (m, 2 H), 4.68−4.56 (m, 1 H), 2.74 (ddd, $J$ = 8.4, 8.4 Hz, and 15.1 Hz, 1 H), 2.14 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.93 (ddd, $J$ = 4.1, 6.0 and 15.1 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 169.6, 169.1, 168.8, 161.1, 92.3, 71.8, 70.1, 69.5, 49.7, 34.8, 20.5, 20.5, 20.3; IR (film) 3422, 3348, 2941, 1723, 1519, 1224, 822 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 421 (90%, $MNH_4^+$), 404 (5, $MH^+$); $C_{13}H_{20}N_2O_7Cl_3$ requires *M* 421.0336, found $MNH_4^+$ 421.0332; mp 88 °C.

***anti*-2,3,4-Triacetoxy-(2,2,2-trichloroacetylamino)-cyclopentane Anti-32.** Trichloroacetamide **31** (150 mg, 0.50 mmol) was subjected to standard Upjohn conditions, and the resulting brown oil was dissolved in pyridine (20 mL); to this were added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The products were purified by column chromatography (80% diethyl ether in petroleum ether 40−60) to yield the title compounds as a colorless oil (126 mg, 63%). Separation of pure anti-**32** was possible by chromatography: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.30 (brd, $J$ = 7.7 Hz, 1 H), 5.36−5.28 (m, 2 H), 5.07 (ddd, $J$ = 2.1, 4.5 and 7.8 Hz, 1 H), 4.34 (qt, $J$ = 7.8 Hz, 1 H), 2.98 (ddd, $J$ = 7.8, 7.8 and 14.8 Hz, 1 H), 2.12 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.93 (ddd, $J$ = 4.5, 7.7 and 14.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.9, 169.5, 169.3, 162.0, 92.0, 74.4, 74.0, 73.8, 53.9, 34.0, 20.8, 20.6, 20.5; IR (film) 3420, 3020, 1746, 1714, 1371, 1224, 822 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 421 (90%, $MNH_4^+$), 404 (5, $MH^+$); $C_{13}H_{20}N_2O_7Cl_3$ requires *M* 421.0336, found $MNH_4^+$ 421.0338; mp 117 °C.

***syn*-*N*-(2,3-Dihydroxycyclohexyl)-2′,2′,2′-trichloroacetamide Syn-36.** Trichloroacetamide **35** (0.100 g, 0.412 mmol) was subjected to the standard TMEDA dihydroxylation conditions with methanolic workup, and the resulting orange mixture was purified by column chromatography (60% ethyl acetate/petrol) to yield syn-**36** (111 mg, 99%) as a colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.86 (br s, 1 H), 3.86−4.06 (m, 3 H), 3.00−3.70 (br m, 2 H), 1.58−1.84 (m, 5 H), 1.32−1.46 (m, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 161.8, 92.6, 70.8, 70.3, 52.1, 28.4, 26.1, 18.2, IR (film) 3407, 2942, 1698, 1515 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 295 (91%) and 293 (100, $MNH_4^+$); $C_8H_{13}NO_3Cl_3$ requires *M* 275.9961, found $MH^+$ 275.9966.

***anti*-*N*-(2,3-Dihydroxycyclohexyl)-2′,2′,2′-trichloroacetamide Anti-36.** Trichloroacetamide **35** (100 mg, 0.412 mmol) was subjected to the standard Upjohn reaction conditions, and the resulting brown oil was purified by column chromatography (60% ethyl acetate/petrol) to produce a colorless oil (35 mg, 31%) and a white solid (77 mg, 68%). $^1$H NMR showed the oil to be a mixture of syn:anti diols and the solid to be anti-**36**: $^1$H NMR (300 MHz, $(CD_3)_2CO$) $\delta$ 7.90 (br s, 1 H), 4.00−4.13 (m, 2 H), 3.79 (s, 2 H), 3.63−3.71 (br m, 1 H), 1.72−2.02 (m, 3 H), 1.40−1.60 (m, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ (*C*Cl3 not observed) 162.9, 75.2, 69.6, 52.8, 30.3, 30.1, 18.2; IR (film) 3407, 2943, 1699, 1514 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 295 (28%), 293 (30, $MNH_4^+$), 280 (32), 278 (88) and 276 (100); $C_8H_{13}NO_3Cl_3$ requires *M* 275.9961, found $MH^+$, 275.9956.; mp 115−117 °C.

***syn*-*N*-(5-*tert*-Butyl-2,3-dihydroxycyclohexyl)-2′,2′,2′-trichloroacetamide Syn-38.** Trichloroacetamide **37** (50 mg, 0.17 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup and then purified by column chromatography (40% ethyl acetate/petrol) to give syn-**38** (55 mg, 96%) as a colorless solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.19 (br d, $J$ = 7.7 Hz, 1 H), 3.90 (s, 1 H), 3.78 (ddd, $J$ = 3.9, 7.7 and 12 Hz, 1 H), 3.64 (br d, $J$ = 12 Hz, 1 H), 2.90 (br s, 1 H), 2.42 (br s, 1 H), 1.66 (br d, $J$ = 12 Hz, 2 H), 1.31 (qt, $J$ = 12 Hz, 2 H), 1.27 (br q, $J$ = 12 Hz, 1 H), 0.91 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 161.2, 92.6, 71.3, 70.1, 51.9, 42.9, 32.2, 28.6, 27.4, 26.0; IR (film) 3409, 2962, 1704, 1512 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 351 (93%), 349 (100, $MNH_4^+$), 336 (22), 334 (63) and 332 (69); $C_{12}H_{24}N_2O_3Cl_3$ requires *M* 349.0852, found $MNH_4$ 349.0853; mp 112−113 °C. Anal. Calcd for $C_{12}H_{20}NO_3Cl_3$: C, 43.3; H, 6.1; N, 4.2. Found: C, 43.2; H, 6.1; N, 4.1.

***anti*-*N*-(5-*tert*-Butyl-2,3-dihydroxycyclohexyl)-2′,2′,2′-trichloroacetamide Anti-38.** Trichloroacetamide **37** (50 mg, 0.17 mmol) was subjected to standard Upjohn conditions and the resulting black solid purified by column chromatography (40% ethyl acetate/petrol) to give syn-**38** and anti-**38** diols (53 mg, 95%) as white solids: $^1$H NMR (300 MHz, $(CDCl_3)$ $\delta$ 6.70 (br d, $J$ = 7.0 Hz, 1 H), 4.02−4.18 (m, 2 H), 3.43−3.52 (m, 1 H), 3.22 (br d, $J$ = 6.2 Hz, 1 H), 2.63 (br s, 1 H), 2.07 (ddd, $J$ = 3.0, 6.9 and 12.3 Hz, 1 H), 2.02 (ddd, $J$ = 2.8, 6.5 and 12.3 Hz, 1 H), 1.73 (tt, $J$ = 2.8 and 12.3 Hz, 1 H), 1.25 (dt, $J$ = 2.8 and 12.3 Hz, 1 H), 1.09 (q, $J$ = 12.3 Hz, 1 H), 0.89 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 163.0, 92.4, 75.6, 69.6, 53.0, 39.2, 31.8, 31.7, 31.6, 27.4; IR (film) 3304, 2962, 1686 and 1529 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 351 (82) and 349 (100, $MNH_4^+$); $C_{12}H_{24}N_2O_3Cl_3$ requires *M* 349.0852, found $MNH_4$ 349.0858; mp 181−182 °C. Anal. Calcd for $C_{12}H_{20}NO_3Cl_3$: C, 43.3; H, 6.1; N, 4.2. Found: C, 43.2; H, 6.0; N, 4.1.

***syn*-*N*-(5-*tert*-Butyl-2,3-dihydroxy-cyclohexyl)-2′,2′,2′-trichloroacetamide Syn-40 and *anti*-*N*-(5-*tert*-Butyl-2,3-dihydroxy-cyclohexyl)-2′,2′,2′-trichloroacetamide Anti-40.** Trichloroacetamide **39** (100 mg, 0.335 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup, and the resulting brown solid was purified by column chromatography (60% ethyl acetate/petrol) to yield a 1.5:1 mixture of syn-**40** and anti-**40** isomers (107 mg, 97%) as a colorless solid. The diol diastereoisomers were inseparable and characterized together: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.75 (br d, $J$ = 8.2 Hz, 1 H), 6.71 (br d, $J$ = 7.6 Hz, 1 H) 3.66−4.40 (m, 2 × 4 H), 3.60 (br s, 1 H), 3.05 (br s, 1 H), 1.05−2.05 (m, 2 × 5 H), 0.89 (s, 9H) and 0.92 (s, 9 H); $^{13}$C NMR (75 MHz; $CDCl_3$) $\delta$ 162.5, 161.5, 92.9, 92.1, 70.9, 69.6, 69.3, 68.5, 52.6, 52.3, 41.5, 34.6, 32.1, 31.9, 31.5, 29.9, 29.2, 27.3 (2), and 24.4; IR film 3454−3320 (br), 2961, 1702 and 1515 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 351 (45%), 332 (100, $MH^+$); $C_{12}H_{21}NO_3Cl_3$

requires *M* 332.0587, found $MH^+$ 332.0580. Anal. Calcd for $C_{12}H_{20}NO_3Cl_3$: C, 43.3; H, 6.1; N, 4.2. Found: C, 43.5; H, 6.3; N, 4.1.

***syn*-*N*-(2,3-Dihydroxy-1,5,5-trimethylcyclohexyl)-2′,2′,2′-trichloroacetamide Syn-42.** Trichloroacetamide **41** (100 mg, 0.351 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup to a produce a brown solid, which was purified by column chromatography (60% ethyl acetate/petrol) to yield syn-**42** (97 mg, 87%) as a colorless crystalline solid: $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 3.42 (d, $J$ = 3 Hz, 1 H) 3.38−3.32 (m, 1 H), 2.35 (dd, $J$ = 14 and 2 Hz, 1 H), 1.86−1.78 (m, 1 H), 1.58 (s, 3 H), 1.58−1.48 (m, 1 H), 1.39 (d, $J$ = 14 Hz, 1 H), 1.20 (s, 3H) and 0.82 (s, 3 H); $^{13}$C NMR (75 MHz; $CDCl_3$) $\delta$ 161.9, 94.6, 76.1, 71.3, 59.7, 45.2, 43.8, 34.1, 31.0, 29.7 and 24.3; IR (film) 3424 (br), 2925) and 1704 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 318 (100%, $MH^+$); $C_{11}H_{19}NO_3Cl_3$ requires *M* 318.0519, found $MH^+$ 318.0514; mp 167−169 °C. Anal. Calcd for $C_{11}H_{18}NO_3Cl_3$ C, 41.5; H, 5.7; N, 4.4. Found: C, 41.4; H, 5.8; N, 4.4.

**(1*R*,2*S*,4*R*,5S,6*S*)-3,4,6-Triacetoxy-1-(benzyloxy)-2-(2,2,2-trichloroacetylamino)-tetrahydropyran Syn-44.** Trichloroacetamide **43** (179 mg, 0.362 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup to a produce a brown solid. The resulting crude tetraol was dissolved in pyridine (20 mL), and to this were added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The product was purified by column chromatography (10% ethyl acetate in petroleum ether 40−60) to afford syn-**44** as a colorless oil (0.156 mg, 82%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.60 (d, $J$ = 6 Hz, 1 H), 7.40−7.25 (m, 5 H), 5.43 (s, 1 H), 5.41 (t, $J$ = 4 Hz, 1 H), 5.00 (s, 1 H), 4.66 (AB, $J$ = 12 Hz, 2 H), 4.44 (dd, $J$ = 5 and 10 Hz, 1 H), 4.32 (td, $J$ = 7 and 1 Hz, 1 H), 4.21−4.08 (m, 2 H), 2.20 (s, 3 H), 2.08 (s, 3 H), 2.00 (s, 3 H); $^{13}$C NMR (75 MHz; $CDCl_3$) $\delta$ 170.2, 169.2, 169.0, 161.7, 135.9, 128.6, 128.3, 128.1, 98.22, 92.41, 70.0, 67.26, 66.62, 64.72, 61.57. 50.47, 20.70, 20.59, 20.38; CIMS *m*/*z* (rel intensity) 559 (100%), 557 (100, $MNH_4^+$); $C_{21}H_{28}N_2O_9Cl_3$ requires *M* 557.0860, found $MNH_4^+$ 557.0868.

***syn*-*N*-(2,3-Diacetoxyoxycycloheptyl)-2′,2′,2′-trichloroacetamide Syn-46.** Trichloroacetamide **45** (100 mg, 0.39 mmol) was subjected to standard TMEDA conditions, with methanolic workup, and the resulting brown oil was dissolved in pyridine (20 mL); to this were added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The products were purified by column chromatography (40% diethyl ether in petroleum ether 40−60) to yield the title compound as a colorless solid (115 mg, 78%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.72 (brd, $J$ = 7.2 Hz, 1 H), 5.20−5.10 (m, 2 H), 4.38−4.23 (m, 1 H), 2.17 (s, 3 H), 2.08 (s, 3 H), 2.06−1.60 (m, 8 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.1, 169.5, 161.0, 92.6, 76.2, 74.4, 51.8, 28.5, 28.1, 24.5, 21.7, 21.1, 20.8; IR (film) 3341, 2942, 1710, 1513, 1243 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 391 (100%, $MNH_4^+$), 374 (5, $MH^+$); $C_{13}H_{22}N_2O_5Cl_3$ requires *M* 391.0594, found $MNH_4^+$ 391.0596; mp 90 °C.

***anti*-*N*-(2,3-Diacetoxyoxycyclohexyl)-2′,2′,2′-trichloroacetamide anti-46.** Trichloroacetamide **45** (100 mg, 0.39 mmol) was subjected to standard Upjohn conditions, and the resulting brown oil was dissolved in pyridine (20 mL); to this were added acetic anhydride (5 mL) and a catalytic amount of DMAP. The reaction was allowed to stir overnight at room temperature. The pyridine was removed in vacuo until a dry black solid was obtained. The products were purified by column chromatography (40% diethyl ether in petroleum ether 40−60) to yield the title compounds as a colorless solid (124 mg, 85%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.02 (br d, $J$ = 8.2 Hz, 1 H), 5.22 (br d, $J$ = 9.2 Hz, 1 H), 5.08 (dd, $J$ = 2.1 and 9.2 Hz, 1 H), 4.32−4.20 (m, 1 H), 2.12 (s, 3 H), 2.04 (s, 3 H), 2.08−1.60 (m, 8 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.1, 170.2, 161.3, 92.5, 76.0, 72.4, 53.3, 30.8, 27.7, 23.1, 22.7, 21.0, 20.8; IR (film) 3339, 2939, 1713, 1523, 1240 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 391 (100%, $MNH_4^+$), 374 (5, $MH^+$); $C_{13}H_{22}N_2O_5Cl_3$ requires *M* 391.0594, found $MNH_4^+$ 391.0594; mp 70 °C.

***anti*-*N*-(2,3-Dihydroxycyclohexyl)-*N*-methyl-2′,2′,2′-trichloroacetamide Anti-50.** Trichloroacetamide **49** (100 mg, 0.39 mmol) was subjected to standard TMEDA dihydroxylation conditions with methanolic workup, and the resulting orange solid was purified by column chromatography (60% ethyl acetate/petrol) to give the title compound (88 mg, 78%) as a colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.47 (br s, 1 H), 3.86 (dd, $J$ = 2.0 and 11.7 Hz, 1 H), 3.68 (dt, $J$ = 3.4 and 11.7 Hz, 1 H), 2.85 (s, 3 H), 1.96−2.18 (m, 3 H), 1.16−1.81 (m, 5 H); IR (film) 3433, 2941, 1742 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 311 (33%), 309 (96) and 307 (100, $MNH_4^+$); $C_9H_{14}NO_3Cl_3$ requires *M* 289.0039, found $M^+$ 289.0037.

***syn*-*N*-(5-*tert*-Butyl-2,3-osmadioxycyclohexyl)-2′,2′,2′-trichloroacetamide]-[*N*′,*N*′,*N*″,*N*″-tetramethylethylenediamine] Osmate Diester Syn-51.** *cis*-Trichloroacetamide **37** (50 mg, 0.17 mmol) was subjected to standard TMEDA osmylation conditions to produce a brown oil, which was purified by column chromatography (10% methanol/dichloromethane) to give the title compound (106 mg, 96%) as a brown crystalline solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.95 (br d, $J$ = 7.3 Hz, 1 H), 4.30−4.48 (m, 2 H), 3.75−3.86 (m, 1 H), 3.13 (s, 4 H), 2.91 (s, 3 H), 2.89 (s, 3 H), 2.85 (s, 3 H), 2.84 (s, 3 H), 1.88−1.98 (m, 1 H), 1.70−1.80 (m, 1 H), 1.49−1.63 (m, 1 H), 1.57−1.27 (m, 2 H), 0.90 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 160.8, 93.3, 87.7, 86.5, 64.6, 64.1, 52.1, 51.7 (2), 51.6, 51.5, 42.7, 32.4, 28.2, 27.9, 27.6; IR (film) 3393, 2958, 2866, 1710, 1498 cm$^{-1}$; CIMS *m*/*z* (rel intensity) 672 (38%), 670 (48, $MH^+$) and 668 ($MNH_4^+$ 30%); $C_{18}H_{38}N_4O_5Cl_3Os$ requires 670.1257, found $MH^+$ 670.1264.

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**Supporting Information Available:** Detailed procedures and spectroscopic data for compounds **19**, **21**, **27**, **31**, **37**, **39**, **43**, and **45** and X-ray pictures and CIF data for syn-**22**, syn-**28**, anti-**30**, anti-**32**, syn-**40**, syn-**42**, syn-**46**, **51**, and **52**. This material is available free of charge via the Internet at http://pubs.acs.org.

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