Organic & Biomolecular Chemistry

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Cite this: *Org. Biomol. Chem.*, 2011, **9**, 2801

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PAPER

Stereoselective synthesis of polyhydroxylated aminocyclohexanes†

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Received 23rd August 2010, Accepted 31st January 2011
DOI: 10.1039/c0ob00619j

The stereoselective synthesis of a series of di- and tri-hydroxylated aminocyclohexane derivatives has been developed. A one-pot, two step tandem process involving an Overman rearrangement and a ring closing metathesis reaction has been utilised for the asymmetric synthesis of (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene. Oxidation of this cyclohexene derivative was then studied leading to the preparation of two diol analogues in excellent stereoselectivity. (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene was then converted to a novel allylic alcohol *via* a 4,5-dihydro-1,3-oxazole. Functionalisation of this allylic alcohol by Upjohn dihydroxylation conditions or by a directed epoxidation/hydrolysis sequence of reactions allowed the synthesis of two dihydroconduramines in excellent stereoselectivity. The stereochemical assignment of all compounds prepared was confirmed by NOE experiments or X-ray structure determination.

Introduction

Conduramines such as conduramine C-1 (**2**) and E-1 (**3**) are purely synthetic aminocyclohexenetriols formally derived from conduritols (**1**) in which one of the hydroxyl groups is exchanged for an amino moiety (Fig. 1).[1,2] They constitute an increasingly important class of compound due to their ability to mimic oligosaccharides and act as inhibitors of glycosidases.[3] Conduramines are excellent synthetic precursors of amino- and diaminocyclitols many of which form the aglycon portions of the therapeutically useful aminoglycoside antibiotics.[2,4,5] They have also been used to prepare a variety of natural products such as alkaloids[6] and azasugars.[7] The importance of conduramines and their derivatives have led to a significant number of approaches for their preparation, usually *via* functional group manipulation of carbohydrates or other natural building blocks.[1,2,5,8] The most recent stereoselective syntheses of conduramines have involved nitroso-Diels–Alder reactions as the key step.[9] Studer and co-workers used a Cu(I)-catalysed enantioselective nitroso-Diels–Alder reaction between 2-nitrosopyridine and cyclohexa-1,3-dienes,[9a] while the research group of Liao used a homochiral nitroso dienophile derived from 10-camphorsulfonic acids with masked *o*-benzoquinones.[9b] In both cases, the cycloadducts were obtained in excellent yields and stereoselectivities and were easily converted to the corresponding conduramine core.

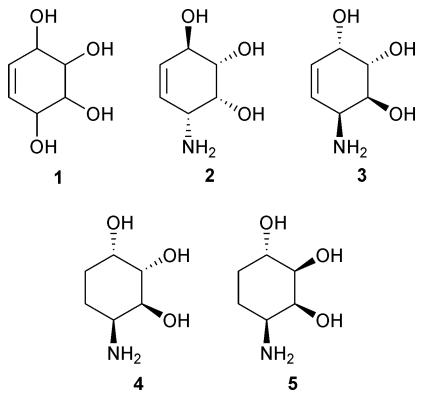

Fig. 1 Structures of **1**, **2**, **3**, **4** and **5**.

Very recently, we developed a new one-pot tandem process that utilises an Overman rearrangement[10] and a ring closing metathesis (RCM) reaction for the rapid and highly efficient synthesis of 5-, 6-, 7- and 8-membered carbocyclic amides.[11] A stereoselective variant has also been developed using chiral palladium(II)-catalysts for the Overman rearrangement step resulting in application of this tandem process for natural product synthesis.[11,12] Continuing our studies on new synthetic applications of the tandem process, we now report in full the asymmetric synthesis of an *N*-(cyclohexenyl)trichloroacetamide **7** and the subsequent investigation of the stereoselective oxidation of this synthetic intermediate leading to the preparation of polyhydroxylated aminocyclohexane derivatives (Scheme 1). In particular, we have used this approach for the highly stereoselective synthesis of dihydroconduramine E-1 **4** and the enantiomer of dihydroconduramine C-1 **5**.

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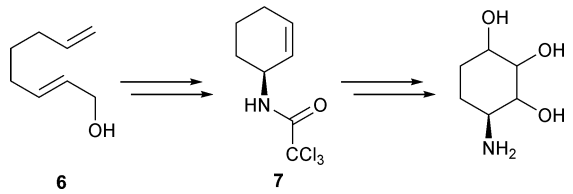
† Electronic supplementary information (ESI) available: Figure showing the key NOE enchancements for compounds **15**, **17**, **22** and **23**. CIF files for compounds **17** and **21**; CCDC reference numbers 809769 and 809770. ^{1}H and ^{13}C NMR spectra for all new compounds. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00619j



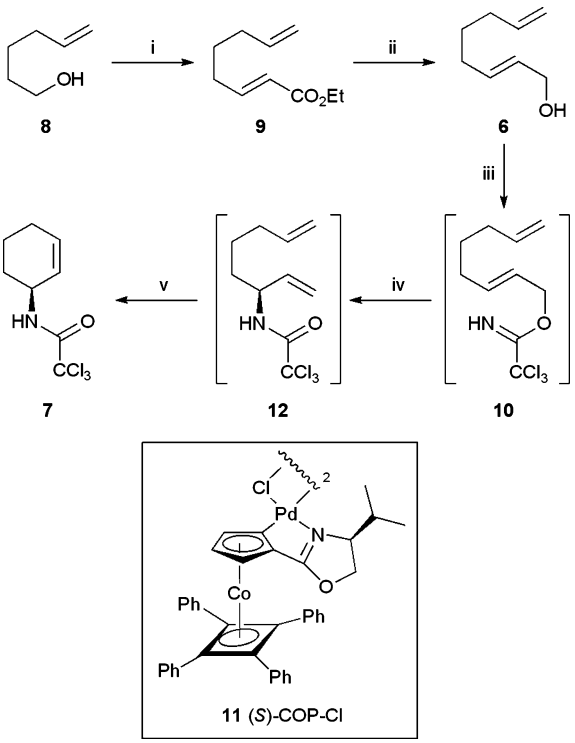
6 7

Scheme 1 Proposed route to polyhydroxylated aminocyclohexanes.

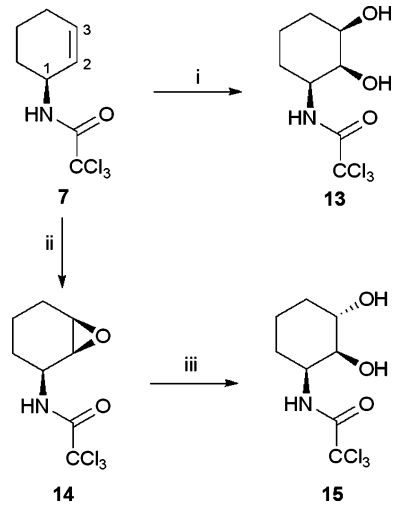
Results and discussion

The first stage of this project involved the development of a highly efficient asymmetric synthesis of *N*-(cyclohexenyl)-trichloroacetamide **7** (Scheme 2).[11a] The key substrate (2*E*)-octa-2,7-dien-1-ol (**6**) was prepared in two steps from 5-hexen-1-ol (**8**) using a one-pot Swern oxidation and Horner–Wadsworth–Emmons reaction to give *E*-α,β-unsaturated ester **9** followed by reduction of the ester functional group using DIBAL-H.[13] Allylic alcohol **6** was then converted to allylic trichloroacetimidate **10** using trichloroacetonitrile and a catalytic amount of DBU.[14] Without purification, allylic trichloroacetimidate **10** was then subjected to the one-pot tandem process using commercially available (*S*)-COP-Cl **11**[15,16] to catalyse the Overman rearrangement and Grubbs first generation catalyst[17] to effect the ring closing metathesis step. This allowed the isolation of (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene (**7**) in 90% yield from allylic alcohol **6** and in 88% enantiomeric excess.[18] The enantiomeric excess of **7** was improved to >99% on recrystallisation from a mixture of ethyl acetate and petroleum ether. It should be emphasised that this general approach permits the highly efficient and rapid synthesis of carbocyclic allylic amides such as **7** on a multi-gram scale (*e.g.* 75% overall yield of **7** from **8**).

Due to the considerable interest in the vicinal amino diol motif[19] and in particular 3-aminocyclohexane-1,2-diols,[20] we next investigated the dihydroxylation of (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene (**7**). An effective method for the *syn*-selective dihydroxylation of cyclic allylic trichloroacetamides has been reported by Donohoe and co-workers.[21] This method uses a reagent that is generated from osmium tetroxide and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA). This reagent then forms a complex with the substrate *via* hydrogen bonding and directed dihydroxylation occurs forming predominantly, the all *syn*-isomer. Dihydroxylation of **7** using this procedure gave 1,2-*syn*-2,3-*syn*-isomer **13** in 94% diastereomeric excess (by ^{1}H NMR spectroscopy) (Scheme 3).[21] Flash column chromatography allowed isolation of **13** as a single stereoisomer in 93% yield. Synthesis of the 1,2-*syn*-2,3-*anti*-isomer **15** was achieved using a two-step approach. Epoxidation of **7** was carried out using *meta*-chloroperbenzoic acid (*m*-CPBA) which gave *cis*-epoxide **14** *via* a substrate directed intermediate[22] in 90% diastereomeric excess (by ^{1}H NMR spectroscopy). As before, separation of the diastereomers by flash column chromatography was easily achieved allowing isolation of **14** as a single stereoisomer in 95% yield. Acid mediated hydrolysis of the epoxide then gave **15** in 75% yield as a single stereoisomer. The relative stereochemistry of **15** was confirmed by difference NOE experiments which clearly showed the 1,2-*syn*-2,3-*anti*-relationships of the trichloroacetamide and hydroxyl groups.[23]



Scheme 2 *Reagents and conditions*: i. $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C to RT, then DBU, LiCl, $(EtO)_2POCH_2CO_2Et$, MeCN, 88% over the two steps; ii. DIBAL-H (2.2 eq.), Et_2O, −78 °C to RT, 95%; iii. DBU, Cl_3CCN, CH_2Cl_2; iv. (*S*)-COP-Cl **11** (5 mol%), CH_2Cl_2, 45 °C; v. Grubbs' 1st generation catalyst (10 mol%), Δ, 90% from **6**.

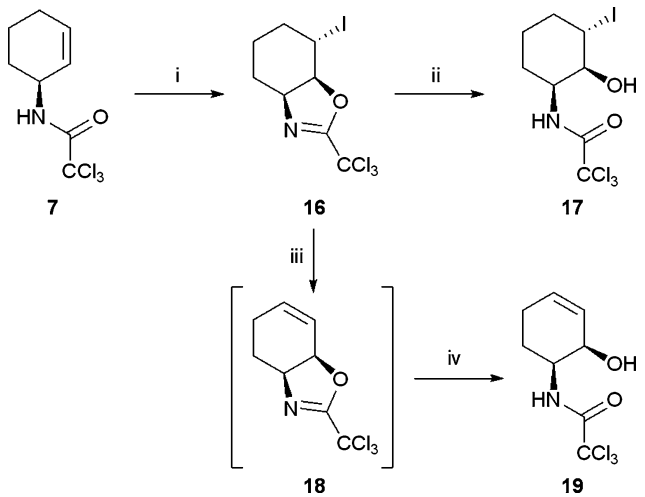


Scheme 3 *Reagents and conditions*: i. OsO_4, TMEDA, CH_2Cl_2, −78 °C, 93%; ii. *m*-CPBA, $NaHCO_3$, CH_2Cl_2, 95%; iii. 0.2 M H_2SO_4, 1,4-dioxane, 75%.

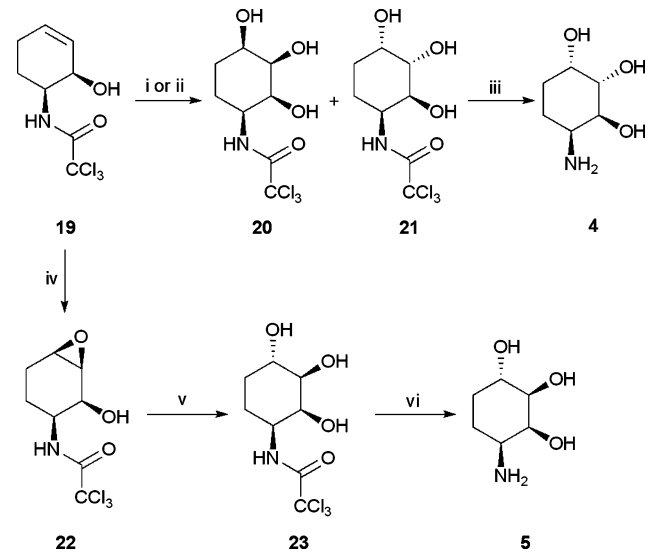
The next stage of our programme then focused on methods for the stereoselective introduction of three hydroxyl groups to (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene (**7**) that would allow access to dihydroconduramines **4** and **5**. Our proposed strategy involved stereoselective functionalisation of the alkene of **7** in such a way to introduce a hydroxyl group at C-2 and a leaving group at C-3 of the cyclohexane ring. Elimination of the leaving group and subsequent stereoselective oxidation of the

resulting alkene would then produce the conduramine derivatives. The first stage of this strategy was implemented by reaction of **7** with *N*-iodosuccinimide to give 4,5-dihydro-1,3-oxazole **16** in 85% yield (Scheme 4).[24] As **16** was found to be relatively unstable, it was subjected immediately to hydrolysis under acidic conditions which gave 1,2-*syn*-2,3-*anti*-iodoalcohol **17** in 76% yield and as a single stereoisomer. The relative stereochemistry of **17** was initially confirmed by difference NOE experiments.[23] However, recrystallisation of **17** provided crystals suitable for X-ray structural determination. Iodoalcohol **17** crystallises in the monoclinic space group $P2_1$ (Fig. 2, see also supporting information†) and the structure clearly shows the 1,2-*syn*-2,3-*anti*-relationship of the trichloroacetamide, hydroxyl and iodide substitutents.[25] Thus, reaction of **7** with *N*-iodosuccinimide must generate the iodonium intermediate *anti* to the trichloroacetamide group followed by *syn*-formation of the 4,5-dihydro-1,3-oxazole ring yielding **16**. Hydrolysis then takes place at C-2 of the 4,5-dihydro-1,3-oxazole ring to give **17**. On preparation of iodoalcohol **17**, elimination of the iodide to generate allylic alcohol **19** was then investigated. However, all attempts using a number of bases including DBU under reflux conditions returned only starting material. Instead, (1*S*)-*N*-(cyclohexenyl)trichloroacetamide **7** was again reacted with *N*-iodosuccinimide. Without purification, 4,5-dihydro-1,3-oxazole **16** was treated with DBU and the resulting intermediate **18** was subjected to hydrolysis under acidic conditions. This allowed the isolation of allylic alcohol **19** in 60% yield over the three steps.

With allylic alcohol **19** in hand, oxidation of the alkene moiety was then investigated (Scheme 5). Dihydroxylation of **19** using the Donohoe conditions gave a 3 : 1 mixture of two diastereomeric triols in 87% yield.[21] The major isomer was easily separated by flash column chromatography in 53% yield and recrystallisation allowed X-ray structural determination (Fig. 3, see also supporting information†).[26] Surprisingly, the X-ray structure revealed that the major diastereomer was 1,2-*syn*-2,3-*anti*-3,4-*syn* isomer **21**. Donohoe and co-workers have studied the use of 6-membered cyclic homoallylic trichloroacetamides as substrates for their directed dihydroxylation and found these to have poor stereoselectivity.[27] They proposed that the bulky trichloroacetamide group in these compounds likely adopts an equatorial position which prevents it from effectively directing the dihydroxylation. However, we reasoned that allylic alcohol **19** should be a good substrate for the Donohoe directed dihydroxylation. With the bulky trichloroacetamide group in an equatorial position, the adjacent hydroxyl group must be axial and thus, in a position to direct the dihydroxylation forming triol **20** as the major diastereomer. The isolation of triol **20** as the minor diastereomer suggests that while directed dihydroxylation *via* the alcohol may occur to some extent,



Scheme 4 *Reagents and conditions*: i. *N*-iodosuccinimide, $CHCl_3$, 85%; ii. 2.0 M HCl, MeOH, 76%; iii. DBU, toluene, Δ; iv. 2.0 M HCl, MeOH, 60% from **7**.



Scheme 5 *Reagents and conditions*: i. OsO_4, TMEDA, CH_2Cl_2, −78 °C, 87% (1 : 3 ratio of **20** and **21**, respectively); ii. OsO_4, NMO, acetone, H_2O, 56% (**21** only); iii. 2.0 M NaOH, MeOH, 68%; iv. *m*-CPBA, $NaHCO_3$, CH_2Cl_2, 69%; v. 0.2 M H_2SO_4, 1,4-dioxane, 87%, vi. 2.0 M NaOH, MeOH, 98%.

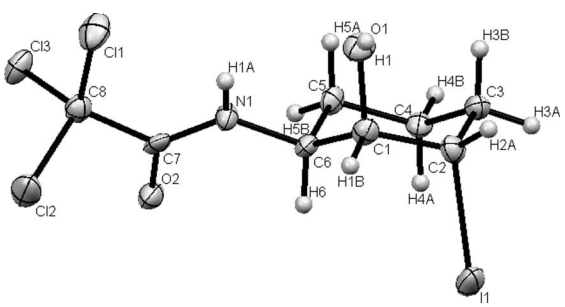


Fig. 2 Molecular structure of compound **17**. Displacement ellipsoids are drawn at the 50% probability level.

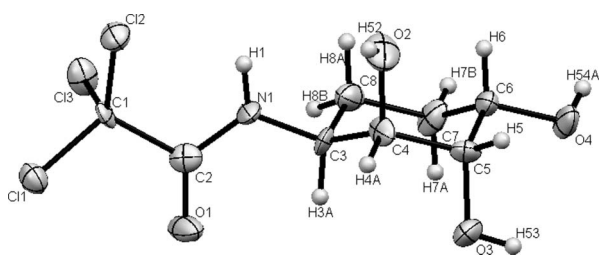


Fig. 3 Molecular structure of compound **21**. Displacement ellipsoids are drawn at the 50% probability level.

dihydroxylation preferably takes place from the least hindered face of the cyclohexene ring to give the trichloroacetamide derivative of dihydroconduramine E-1 **21** as the major product. To probe whether the minor product of this reaction, triol **20** was actually being formed by a directed dihydroxylation *via* the 2-hydroxyl group or just as the minor product of a face selective non-directed dihydroxylation, allylic alcohol **19** was also subjected to standard Upjohn conditions (OsO_4, NMO), a protocol where dihydroxylation takes place by a non-directed mechanism.[21,28] This gave triol **21** as a single stereoisomer (by ^{1}H NMR spectroscopy of the crude reaction material) and in 56% yield. The result from this Upjohn dihydroxylation of **19** shows that formation of triol **20** using the Donohoe conditions must occur by a directing effect *via* the 2-hydroxyl group. To access dihydroconduramine **4**, the trichloroacetyl protecting group of **21** was removed under base-mediated conditions. After purification by ion exchange chromatography, dihydroconduramine E-1 **4** was isolated in 68% yield.

It was proposed that the synthesis of the enantiomer of dihydroconduramine C-1, compound **5** could be achieved by a directed epoxidation of allylic alcohol **19** followed by hydrolysis, the same strategy used for the preparation of diol **15** (see Scheme 3). While dihydroxylation of **19** *via* a 2-hydroxyl directed reaction was not particularly effective, there was significant literature precedent for the directed epoxidation of cyclic allylic alcohols according to Henbest's rule using *m*-CPBA.[29,30] Treatment of **19** with *m*-CPBA gave epoxide **22** in 90% diastereomeric excess (Scheme 5). Purification by flash column chromatography gave the major product, the all *syn*-diastereomer **22** in 69% yield. Difference NOE experiments confirmed that the major diastereomer was the 1,2-*syn*-2,3-*syn*-3,4-*syn* isomer.[23] Hydrolysis of epoxide **22** under acidic conditions gave dihydroconduramine derivative **23** in 87% yield. Again, difference NOE experiments confirmed that the product formed was the 1,2-*syn*-2,3-*syn*-3,4-*anti* isomer.[23] Finally, hydrolysis of the trichloroacetamide group using sodium hydroxide gave dihydroconduramine **5** in 98% yield.

Conclusions

In summary, a one-pot tandem process involving an Overman rearrangement and RCM reaction has been used for the highly efficient multi-gram synthesis of (1*S*)-*N*-(cyclohexenyl)trichloroacetamide **7**. Oxidation of **7** has been studied leading to the preparation of two diol derivatives in excellent diastereoselectivity. Conversion of **7** to allylic alcohol **19** *via* 4,5-dihydro-1,3-oxazole **16** by a three-step process was followed by further oxidation leading to the preparation of two dihydroconduramines. These studies have generated further insight into the stereoselective functionalisation of substituted cyclohexenes and work is currently underway to extend these processes for the preparation of more complex biologically active compounds.

Experimental

All reagents and starting materials were obtained from commercial sources and used as received. All dry solvents were purified using a PureSolv 500 MD solvent purification system. Flash column chromatography was carried out using Fisher matrix silica 60. Macherey–Nagel aluminium-backed plates pre-coated with silica gel 60 (UV_{254}) were used for thin layer chromatography and were visualised by staining with potassium permanganate. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer with chemical shift values in ppm relative to tetramethylsilane as the standard. Assignment of ^{1}H and ^{13}C NMR signals are based on two-dimensional COSY and DEPT experiments, respectively. Infrared spectra were recorded using Golden Gate apparatus on a JASCO FTIR 410 spectrometer and mass spectra were obtained using a JEOL JMS-700 spectrometer. Melting points were determined on a Reichert platform melting point apparatus. Optical rotations were determined as solutions irradiating with the sodium D line ($\lambda = 589$ nm) using an Autopol V polarimeter. $[\alpha]_D$ values are given in units 10^{-1} deg cm^2 g^{-1}. The chiral HPLC methods were calibrated with their corresponding racemic mixtures. (*S*)-COP-Cl refers to di-μ-chlorobis[η^5-(*S*)-(ρ*R*)-2-(2′-(4′-methylethyl)oxazolinyl)cyclopentadienyl, 1-*C*, 3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium.

Ethyl (2*E*)-2,7-octadienoate (9)[31]

Dimethyl sulfoxide (7.10 mL, 0.10 mol) was added to a stirred solution of oxalyl chloride (5.08 mL, 0.06 mol) in dichloromethane (100 mL) at −78 °C under an argon atmosphere. The reaction mixture was stirred for 0.3 h before 5-hexen-1-ol (**8**) (4.00 g, 0.04 mol) in dichloromethane (50 mL) was slowly added. The mixture was stirred for a further 0.3 h before triethylamine (27.8 mL, 0.20 mol) was added. This reaction mixture was stirred for 0.5 h at −78 °C and then allowed to warm to room temperature and stirred for a further 2 h. Meanwhile, a solution of lithium chloride (2.97 g, 0.07 mol), triethyl phosphonoacetate (11.9 mL, 0.06 mol) and 1,8-diazabicyclo[5,4,0]undec-7-ene (8.97 mL, 0.06 mol) in acetonitrile (100 mL) was prepared and stirred for 1.0 h under an argon atmosphere. The Swern solution was concentrated *in vacuo*, then the Horner Wadsworth Emmons solution was added and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by the addition of a saturated solution of ammonium chloride (50 mL) and concentrated to give an orange residue, which was then extracted with diethyl ether (4 × 75 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated to give an orange oil. Flash column chromatography (petroleum ether/diethyl ether, 10 : 1) yielded ethyl (2*E*)-2,7-octadienoate (**9**) (5.91 g, 88% yield) as a colourless oil. Spectroscopic data consistent with literature.[31] ν_{max}/cm^{-1} (NaCl) 2933 (CH), 1721 (CO), 1655 (C=C), 1367, 1267, 1198, 1044; δ_H (400 MHz, $CDCl_3$) 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.52–1.58 (2H, m, 5-H_2), 2.06–2.12 (2H, m, 6-H_2), 2.18–2.25 (2H, m, 4-H_2), 4.17 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.96–5.06 (2H, m, 8-H_2), 5.73–5.96 (2H, m, 2-H and 7-H), 6.95 (1H, dt, *J* 15.5, 6.9 Hz, 3-H); δ_C (100 MHz, $CDCl_3$) 14.3 (CH_3), 27.1 (CH_2), 31.5 (CH_2), 33.1 (CH_2), 60.2 (CH_2), 115.1 (CH_2), 121.5 (CH), 138.0 (CH), 149.0 (CH), 166.7 (C); *m*/*z* (CI) 169.1232 (MH^+. $C_{10}H_{17}O_2$ requires 169.1229), 141 (90%), 123 (75), 95 (100), 81 (53), 55 (32).

(2*E*)-Octa-2,7-dien-1-ol (6)[31]

Ethyl (2*E*)-2,7-octadienoate (**9**) (5.00 g, 27.5 mmol) was dissolved in diethyl ether (100 mL) and cooled to −78 °C under argon. DIBAL-H (1.0 M in hexane) (60.5 mL, 60.5 mmol) was added dropwise and the reaction mixture was stirred at −78 °C for 3

h, before warming to room temperature overnight. The solution was cooled to 0 °C and quenched by the addition of a saturated solution of ammonium chloride (100 mL) and warmed to room temperature with vigorous stirring over 1 h producing a white precipitate. The reaction mixture was filtered through a pad of Celite® and washed with diethyl ether (500 mL). The filtrate was then dried ($MgSO_4$) and concentrated *in vacuo*. Flash column chromatography (petroleum ether/diethyl ether, 1 : 4) yielded (2*E*)-octa-2,7-dien-1-ol (**6**) (3.56 g, 95% yield) as a colourless oil. Spectroscopic data consistent with literature.[31] ν_{max}/cm^{-1} (NaCl) 3346 (OH), 2928 (CH), 1640 (C=C), 1439, 1090, 997, 970; δ_H (400 MHz, $CDCl_3$) 1.34 (1H, br s, OH), 1.46–1.51 (2H, m, 5-H_2), 2.02–2.10 (4H, m, 4-H_2 and 6-H_2), 4.07 (2H, d, *J* 4.6 Hz, 1-H_2), 4.94–4.97 (1H, m, 8-*H*H), 5.01 (1H, dq, *J* 17.0, 1.7 Hz, 8-H*H*), 5.60–5.73 (2H, m, 2-H and 3-H), 5.80 (1H, ddt, *J* 17.0, 10.2, 6.7 Hz, 7-H); δ_C (100 MHz, $CDCl_3$) 28.3 (CH_2), 31.6 (CH_2), 33.2 (CH_2), 63.7 (CH_2), 114.6 (CH_2), 129.2 (CH), 133.0 (CH), 138.6 (CH); *m*/*z* (CI) 109.1009 (MH^+-H_2O. C_8H_{13} requires 109.1017), 95 (16%), 81 (12), 67 (47).

(1*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)cyclohexa-2-ene (7)[32]

(2*E*)-Octa-2,7-dien-1-ol (**6**) (3.00 g, 23.8 mmol) was dissolved in dichloromethane (80 mL) and cooled to 0 °C under argon. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.90 mL, 5.94 mmol) was then added to the solution followed by trichloroacetonitrile (3.60 mL, 35.8 mmol). The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was then filtered through a short pad of silica gel and washed with diethyl ether (400 mL). The resulting filtrate was then concentrated to give allylic trichloroacetimidate **10**, which was used without further purification. Allylic trichloroacetimidate **10** (6.60 g) was dissolved in dichloromethane (200 mL) under an argon atmosphere. (*S*)-COP-Cl catalyst **11** (1.77 g, 1.21 mmol) was then added to the solution and the reaction mixture was stirred at 45 °C for 3 days. Grubb's 1st generation catalyst (1.98 g, 2.40 mmol) was then added and the reaction mixture was heated at 65 °C under reflux overnight. The mixture was cooled to room temperature, filtered through a short pad of Celite® and washed with diethyl ether (600 mL). The filtrate was then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (elution with petroleum ether/diethyl ether, 97 : 3) gave (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)cyclohexa-2-ene (**7**) (5.21 g, 90% yield over 3 steps) as a white solid. 88% ee determined by HPLC analysis using CHIRALPAK IB column (0.5% *iso*-propanol/hexane at 0.75 mL min^{-1}), retention time: t_S = 8.2 min, and t_R = 9.2 min. Mp 85–86 °C, lit.[32] 86–87 °C; ν_{max}/cm^{-1} (NaCl) 3421 (NH), 2941 (CH), 1676 (CO), 1519, 1073, 822; $[\alpha]_D^{23}$ –95.3 (*c* 2.1, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.62–1.79 (3H, m, 5-H_2 and 6-*H*H), 1.94–2.03 (1H, m, 6-H*H*), 2.03–2.16 (2H, m, 4-H_2), 4.42–4.54 (1H, m, 1-H), 5.65 (1H, ddt, *J* 10.0, 4.0, 2.2 Hz, 2-H), 5.98 (1H, dtd, *J* 10.0, 4.0, 1.9 Hz, 3-H), 6.60 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 19.4 (CH_2), 24.7 (CH_2), 28.6 (CH_2), 46.9 (CH), 92.7 (C), 125.7 (CH), 132.7 (CH), 161.1 (C); *m*/*z* (CI) 261.0144 (MNH_4^+. $C_8H_{14}{}^{35}Cl_2{}^{37}ClN_2O$ requires 261.0143), 259 (100%), 242 (23), 225 (9), 206 (21), 81 (10).

(1*S*,2*S*,3*R*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3-dihydroxycyclohexane (13)[21c]

(1*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)cyclohexa-2-ene (**7**) (0.10 g, 0.42 mmol) was dissolved in dichloromethane (10 mL) at −78 °C under argon. Tetramethylethylenediamine (0.07 g, 0.45 mmol) was added and the reaction mixture stirred for 0.1 h before the addition of osmium tetroxide (0.10 g, 0.43 mmol). The dark coloured solution was stirred for 1 h at −78 °C before warming to room temperature and stirred for a further 1 h. The solvent was removed *in vacuo* and the dark coloured solid was redissolved in methanol (10 mL). Concentrated hydrochloric acid (5 drops) was added and the reaction mixture stirred for 2 h. The solvent was removed *in vacuo* to afford a dark solid. Flash column chromatography (elution with petroleum ether/diethyl ether, 1 : 4) afforded (1*S*,2*S*,3*R*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2,3-dihydroxycyclohexane (**13**) (0.11 g, 93%) as a colourless oil. Spectroscopic data consistent with literature.[21c] ν_{max}/cm^{-1} (NaCl) 3407 (NH/OH), 2942 (CH), 1700 (CO), 1512, 1042, 821; $[\alpha]_D^{25}$ –3.8 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.30–1.43 (1H, m, 5-*H*H), 1.59–1.80 (5H, m, 4-H_2, 5-H*H* and 6-H_2), 2.56 (1H, br s, OH), 2.90 (1H, br s, OH), 3.83–3.93 (2H, m, 2-H and 3-H), 3.95–4.05 (1H, m, 1-H), 7.73 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 18.3 (CH_2), 26.1 (CH_2), 28.4 (CH_2), 52.1 (CH), 70.4 (CH), 70.9 (CH), 92.7 (C), 161.8 (C); *m*/*z* (CI) 275.9960 (MH^+. $C_8H_{13}{}^{35}Cl_3NO_3$ requires 275.9961), 242 (35%), 179 (12), 123 (89), 109 (88), 73 (100).

2′,2′,2′-Trichloro-*N*-[(1*S*,2*S*,3*R*)-oxabicyclo[4.1.0]hept-2-yl]acetamide (14)[22]

(1*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)cyclohexa-2-ene (**7**) (0.24 g, 0.97 mmol) was dissolved in dichloromethane (15 mL) along with sodium hydrogencarbonate (0.16 g 1.95 mmol). To the stirred suspension was added *meta*-chloroperoxybenzoic acid (0.34 g 1.95 mmol) at room temperature. The resulting suspension was stirred vigorously for 19 h. A 20% aqueous solution of sodium sulphite (10 mL) was added and the resulting two-phase mixture was stirred vigorously for 0.25 h. The two layers were separated and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with a 20% aqueous solution of sodium sulphite (10 mL) and a 5% aqueous solution of sodium hydrogencarbonate (2 × 20 mL), dried (Na_2SO_4) and evaporated under reduced pressure. Purification by flash column chromatography (petroleum ether/diethyl ether, 2 : 5) gave 2′,2′,2′-trichloro-*N*-[(1*S*,2*S*,3*R*)-oxabicyclo[4.1.0]hept-2-yl]acetamide (**14**) (0.24 g, 95%) as white solid. Spectroscopic data consistent with literature.[22] Mp 75–77 °C; ν_{max}/cm^{-1} (NaCl) 3421 (NH), 3020 (CH), 1712 (CO), 1363, 1217, 757; $[\alpha]_D^{25}$ –26.8 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.20–1.59 (4H, m, 5-H_2 and 6-H_2), 1.82–1.20 (2H, m, 4-H_2), 3.25 (1H, t, *J* 3.4 Hz, 2-H), 3.30 (1H, td, *J* 3.8, 3.4 Hz 3-H), 4.25–4.32 (1H, m, 1-H), 7.02 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 17.6 (CH_2), 23.1 (CH_2), 25.8 (CH_2), 47.5 (CH), 53.0 (CH), 54.6 (CH), 92.7 (C), 161.8 (C); *m*/*z* (CI) 257.9852 (MH^+. $C_8H_{11}{}^{35}Cl_3NO_2$ requires 257.9855), 224 (28%), 191 (6), 137 (21), 107 (45), 73 (100).

(1*S*,2*S*,3*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3-dihydroxycyclohexane (15)

2′,2′,2′-Trichloro-*N*-[(1*S*,2*S*,6*R*)-7-oxabicyclo[4.1.0]hept-2-yl]-acetamide (**14**) (0.10 g, 0.35 mmol) was added to a 1 : 1 mixture of 0.2 M sulfuric acid/1,4-dioxane (15 mL) and the reaction mixture was stirred at room temperature for 0.75 h. The reaction was then diluted with a saturated solution of sodium hydrogencarbonate (10 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/diethyl ether, 10 : 1) gave (1*S*,2*S*,3*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2,3-dihydroxycyclohexane (**15**) (0.08 g, 75%) as a colourless oil. ν_{max}/cm^{-1} (NaCl) 3408 (OH), 2942 (CH), 1700 (CO), 1512, 821; $[\alpha]_D^{25}$ +9.9 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.45–1.55 (2H, m, 4-*H*H and 5-*H*H), 1.58–1.77 (2H, m, 5-H*H* and 6-*H*H), 1.84–1.95 (2H, m, 4-H*H* and 6-H*H*), 3.01 (1H, br s, OH), 3.22 (1H, br s, OH), 3.77 (1H, dd, *J* 6.0, 3.6 Hz, 2-H), 3.82–3.89 (1H, m, 3-H), 4.15–4.21 (1H, m, 1-H), 7.16 (1H, d, *J* 7.6 Hz, NH); δ_C (100 MHz, $CDCl_3$) 18.6 (CH_2), 26.3 (CH_2), 28.5 (CH_2), 51.0 (CH), 70.5 (CH), 72.1 (CH), 92.7 (C), 162.1 (C); *m*/*z* (CI) 275.9959 (MH^+. $C_8H_{13}{}^{35}Cl_3NO_3$ requires 275.9961), 242 (59%), 208 (30), 158 (16), 113 (33), 69 (100).

(1*S*,2*S*,3*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2-hydroxy-3-iodocyclohexane (17)

To a solution of (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-cyclohexa-2-ene (**7**) (0.29 g, 1.20 mmol) in chloroform (15 mL), *N*-iodosuccinimide (0.40 g, 1.81 mmol) was added and the mixture stirred for 18 h under argon. The solvent was then removed *in vacuo*. The resulting residue was dissolved in ethyl acetate (20 mL) and the organic phase washed with water (4 × 30 mL). The organic layer was then dried ($MgSO_4$) and the solvent removed *in vacuo* to give (3a*S*,4*S*,7a*S*)-4-iodo-2-(trichloromethyl)benzoxazole (**16**) (0.37 g, 85% yield) as a colourless oil which was used without further purification. δ_H (400 MHz, $CDCl_3$) 1.50–1.69 (2H, m, 5-H_2), 1.90–2.23 (4H, m, 4-H_2 and 6-H_2), 4.17–4.30 (2H, m, 1-H and 3-H), 5.16 (1H, t, *J* 7.5 Hz, 2-H). To a solution of (3a*S*,4*S*,7a*S*)-4-iodo-2-(trichloromethyl)benzoxazole (**16**) (0.37 g, 1.01 mmol) in methanol (20 mL) was added 2.0 M hydrochloric acid (8 mL) and the reaction mixture was stirred at room temperature for 0.75 h. The reaction mixture was then diluted with a saturated solution of sodium hydrogencarbonate (10 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/diethyl ether, 10 : 1) gave (1*S*,2*S*,3*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2-hydroxy-3-iodocyclohexane (**17**) (0.30 g, 76%) as a white solid. Mp 103–105 °C; ν_{max}/cm^{-1} (NaCl) 3402 (OH), 2941 (CH), 1695 (CO), 1509, 1155, 821; $[\alpha]_D^{25}$ +60.8 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.58–1.66 (1H, m, 6-*H*H), 1.68–1.98 (4H, m, 4-H_2, 5-*H*H, 6-H*H*), 2.08–2.18 (1H, m, 5-H*H*), 2.32 (1H, br s, OH), 4.13 (1H, t, *J* 4.1 Hz, 2-H), 4.41 (1H, q, *J* 4.2 Hz, 3-H), 4.46–4.54 (1H, m, 1-H), 7.02 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 21.4 (CH_2), 26.2 (CH_2), 29.0 (CH_2), 32.9 (CH), 49.4 (CH), 72.8 (CH), 92.7 (C), 161.5 (C); *m*/*z* (CI) 387.8958 (MH^+. $C_8H_{12}{}^{35}Cl_2{}^{37}ClINO_2$ requires 387.8950), 352 (32%), 260 (100), 224 (64), 154 (42), 81 (21).

(1*S*,2*R*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2-hydroxycyclohexa-3-ene (19)

To a solution of (1*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-cyclohexa-2-ene (**7**) (4.00 g, 16.5 mmol) in chloroform (100 mL), *N*-iodosuccinimide (5.52 g, 25.0 mmol) was added and the mixture stirred for 18 h under argon. The solvent was then removed in *vacuo*. The resulting residue was dissolved in ethyl acetate (120 mL) and the organic phase washed with water (3 × 50 mL), dried ($MgSO_4$) and the solvent removed in *vacuo.* The residue obtained was dissolved in toluene (100 mL) and 1,8-diazabicyclo[5,4,0]undec-7-ene (3.70 mL, 24.8 mmol) was added. The reaction mixture was heated under reflux for 12 h under argon. The reaction mixture was then cooled and solvent was removed *in vacuo*. The resulting dark coloured solid was dissolved in methanol (80 mL). 2.0 M Hydrochloric acid (30 mL) was added and reaction mixture was stirred at room temperature for 1 h. The reaction mixture was then diluted with a saturated solution of sodium hydrogencarbonate (80 mL) and extracted with ethyl acetate (3 × 70 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/diethyl ether, 1 : 4) gave (1*S*,2*R*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2-hydroxycyclohexa-3-ene (**19**) (2.54 g, 60%) as white solid. Mp 105–109 °C; ν_{max}/cm^{-1} (NaCl) 3404 (OH), 2940 (CH), 1699 (CO), 1506, 1096, 909, 822; $[\alpha]_D^{25}$ −71.9 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.50 (1H, br s, OH), 1.64–1.75 (1H, m, 6-*H*H), 1.86–1.94 (1H, m, 6-H*H*), 2.20–2.26 (2H, m, 5-H_2), 3.97 (1H, ddd, *J* 11.9, 7.6, 3.6 Hz, 1-H), 4.14–4.21 (1H, m, 2-H), 5.85–5.91 (1H, m, 3-H), 6.00 (1H, dt, *J* 9.8, 3.6 Hz, 4-H), 7.36 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 22.4 (CH_2), 24.8 (CH_2), 51.4 (CH), 64.7 (CH), 92.5 (C), 127.2 (CH), 133.4 (CH), 162.5 (C); *m*/*z* (CI) 257.9857 (MH^+. $C_8H_{11}{}^{35}Cl_3NO_2$ requires 257.9855), 224 (98%), 190 (36), 153 (48), 113 (59), 81 (100).

(1*S*,2*S*,3*S*,4*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (21)

(1*S*,2*R*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2-hydroxycyclohexa-3-ene (**19**) (1.00 g, 3.89 mmol) was dissolved in dichloromethane (50 mL) at −78 °C under argon. Tetramethylethylenediamine (0.68 mL, 4.54 mmol) was added and the reaction mixture stirred for 0.1 h before the addition of osmium tetroxide (1.00 g 3.90 mmol). The dark coloured solution was stirred for 1 h at −78 °C before warming to room temperature and stirred for a further 1 h. The solvent was removed *in vacuo* and the dark coloured solid was dissolved in methanol (50 mL). Concentrated hydrochoric acid (1 mL) was added and the reaction mixture stirred for 2 h. The solvent was removed *in vacuo* to afford a dark solid. Column chromatography (elution with petroleum ether/diethyl ether, 1 : 4) afforded (1*S*,2*S*,3*S*,4*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (**21**) (0.60 g, 53%) as a white solid. Mp 151–153 °C; ν_{max}/cm^{-1} (NaCl) 3360 (OH), 2947 (CH), 1653 (CO), 1456, 1420, 1024; $[\alpha]_D^{25}$ −27.6 (*c* 0.9, MeOH); δ_H (400 MHz, CD_3OD) 1.63–1.83 (4H, m, 5-H_2 and 6-H_2), 3.83–3.92 (3H, m, 2-H, 3-H and 4-H), 4.10 (1H, ddd, *J* 10.6, 4.4, 2.9 Hz, 1-H); δ_C (100 MHz, $CDCl_3$) 24.7 (CH_2), 27.4 (CH_2), 50.6 (CH), 68.4 (CH), 72.3 (CH), 74.0 (CH), 93.8 (C), 163.0 (C); *m*/*z* (CI) 291.9908 (MH^+.

$C_8H_{13}{}^{35}Cl_3NO_4$ requires 291.9910), 258 (100%), 224 (50), 148 (22), 85 (12).

(1*S*,2*S*,3*S*,4*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (21)- Upjohn Reaction

A solution of (1*S*,2*R*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2-hydroxy-3-cyclohex-ene (**19**) (1.00 g, 3.89 mmol) in tetrahydrofuran (25 mL), *N*-methylmorpholine-*N*-oxide (0.60 g, 5.10 mmol) and osmium tetraoxide (0.06 g, 0.23 mmol) was added to a stirred solution of sodium hydrogencarbonate (0.40 g, 4.76 mmol) in *tert*-butyl alcohol (15 mL) and water (4 mL). The reaction mixture was stirred at room temperature for 24 h and then a 10% sodium sulfite solution (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3 × 30 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (elution with petroleum ether/diethyl ether, 1 : 4) gave (1*S*,2*S*,3*S*,4*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (**21**) (0.63 g, 56%) as a white solid. Spectroscopic data as described above.

(1*S*,2*S*,3*S*,4*S*)-1-Aminocyclohexane-2,3,4-triol (4)[8n]

(1*S*,2*S*,3*S*,4*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (**21**) (0.15 g, 0.52 mmol) was dissolved in methanol (15.0 mL) and 2.0 M sodium hydroxide (3.0 mL) was added. The reaction mixture was stirred for 12 h at room temperature and then concentrated *in vacuo*. Purification by ion exchange column chromatography (Dowex 50 W), eluting with 0.5 M ammonia solution gave (1*S*,2*S*,3*S*,4*S*)-1-aminocyclohexane-2,3,4-triol (**4**) as a white solid (0.052 g, 68%). Mp 96–97 °C, lit.[8n] 95–97 °C; ν_{max}/cm^{-1} (NaCl) 3326 (NH/OH), 2945 (CH), 1653, 1451, 1411, 1118, 1022; $[\alpha]_D^{23}$ +10.8 (*c* 1.0, MeOH); δ_H (400 MHz, CD_3OD) 1.51–1.67 (4H, m, 5-H_2 and 6-H_2), 3.09–3.14 (1H, m, 1-H), 3.73–3.76 (1H, m, 3-H), 3.77–3.83 (2H, m, 2-H and 4-H); δ_C (100 MHz, CD_3OD) 25.8 (CH_2), 27.1 (CH_2), 49.9 (CH), 68.7 (CH), 72.5 (CH), 73.7 (CH); *m*/*z* (CI) 148.0971 (MH^+. $C_6H_{14}NO_3$ requires 148.0974), 128 (6%), 112 (7), 85 (13), 79(42).

2′,2′,2′-Trichloro-*N*-[(1*S*,2*S*,3*R*,4*R*)-2-hydroxyoxabicyclo[4.1.0]hept-2-yl]acetamide (22)

(1*S*,2*R*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2-hydroxycyclohexa-3-ene (**19**) (1.20 g, 4.67 mmol) was dissolved in dichloromethane (40 mL) along with sodium hydrogencarbonate (0.86 g, 10.2 mmol). To the stirred suspension was added *meta*-chloroperoxybenzoic acid (1.76 g, 10.2 mmol) at room temperature. The resulting suspension was stirred vigorously for 24 h. A 20% solution of sodium sulfite (30 mL) was added and the resulting two-phase mixture was stirred vigorously for 0.25 h. The two layers were separated and the aqueous layer was extracted with dichloromethane (2 × 50 mL). The combined dichloromethane layers were washed with a 20% solution of sodium sulfite (40 mL) and a 5% solution of sodium hydrogencarbonate (2 × 40 mL), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by flash column chromatography (petroleum ether/diethyl ether, 2 : 5) gave 2′,2′,2′-trichloro-*N*-[(1*S*,2*S*,3*R*,4*R*)-2-hydroxyoxabicyclo[4.1.0]hept-2-yl]acetamide (**22**) (0.88 g, 69%) as a white solid. Mp 122–125 °C; ν_{max}/cm^{-1} (NaCl) 3389 (OH), 2951 (CH), 1705 (CO), 1510, 1223, 1078, 827, 756; $[\alpha]_D^{25}$ −125.3 (*c* 1.5, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.53–1.67 (2H, m, 6-H_2), 1.96–2.06 (1H, m, 5-*H*H), 2.20 (1H, dt, *J* 15.7, 5.4 Hz, 5-H*H*), 2.40 (1H, d, *J* 9.0 Hz, OH), 3.44–3.48 (2H, m, 3-H and 4-H), 3.83–3.91 (1H, m, 1-H), 4.14–4.21 (1H, m, 2-H), 7.51 (1H, br d, *J* 5.3 Hz, NH); δ_C (100 MHz, $CDCl_3$) 20.2 (CH_2), 22.1 (CH_2), 50.6 (CH), 54.5 (CH), 55.2 (CH), 64.9 (CH), 92.6 (C), 161.8 (C); *m*/*z* (CI) 273.9804 (MH^+. $C_8H_{11}{}^{35}Cl_3NO_3$ requires 273.9805), 240 (100%), 206 (31), 172 (8), 156 (9), 137 (14), 121 (17), 71 (25).

(1*S*,2*S*,3*R*,4*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (23)

2′,2′,2′-Trichloro-*N*-[(1*S*,2*S*,3*R*,4*R*)-2-hydroxyoxabicyclo[4.1.0]hept-2-yl]acetamide (**22**) (0.70 g, 2.56 mmol) was added to a 1 : 1 mixture of 0.2 M sulfuric acid/1,4-dioxane (20 mL) and the reaction mixture was stirred at room temperature for 8 h. The reaction mixture was diluted with a saturated solution of sodium hydrogencarbonate (30 mL) and extracted with ethyl acetate (3 × 40 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (petroleum ether/diethyl ether, 1 : 10) gave (1*S*,2*S*,3*R*,4*S*)-1-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (**23**) (0.65 g, 87%) as a white solid. Mp 112–114 °C; ν_{max}/cm^{-1} (NaCl) 3440 (OH), 2946 (CH), 1647 (CO), 1450, 1411, 1016; $[\alpha]_D^{24}$ +6.4 (*c* 2.2, MeOH); δ_H (400 MHz, CD_3OD) 1.34–1.43 (1H, m, 5-*H*H), 1.73–1.80 (2H, m, 6-H_2), 1.86–1.95 (1H, m, 5-H*H*), 3.50–3.54 (1H, m, 3-H), 3.79 (1H, td, *J* 7.8, 4.1 Hz, 4-H), 3.88–3.94 (1H, m, 1-H), 3.95 (1H, t, *J* 3.0 Hz, 2-H); δ_C (100 MHz, CD_3OD) 24.5 (CH_2), 30.9 (CH_2), 54.1 (CH), 70.6 (2 × CH), 76.2 (CH), 94.0 (C), 163.3 (C); *m*/*z* (CI) 291.9904 (MH^+. $C_8H_{13}{}^{35}Cl_3NO_4$ requires 291.9910), 258 (19%), 224 (5), 197 (5), 147 (14), 123 (12), 107 (100).

(1*S*,2*S*,3*R*,4*S*)-1-Aminocyclohexane-2,3,4-triol (5)

(1*S*,2*S*,3*R*,4*S*)-1-(2′,2′,2′-Trichloromethylcarbonylamino)-2,3,4-trihydroxycyclohexane (**23**) (0.15 g, 0.52 mmol) was dissolved in methanol (15 mL) and 2.0 M sodium hydroxide (3.0 mL) was added. The reaction mixture was stirred at room temperature for 12 h and then concentrated *in vacuo*. Purification by ion exchange column chromatography (Dowex 50 W), eluting with 0.5 M ammonia solution gave (1*S*,2*S*,3*R*,4*S*)-1-aminocyclohexane-2,3,4-triol (**5**) (0.075 g, 98%) as a white solid. Mp 64–66 °C; ν_{max}/cm^{-1} (NaCl) 3355 (OH), 3263 (NH), 2957 (CH), 1947, 1669, 1445, 1214, 1016; $[\alpha]_D^{22}$ +23.1 (*c* 0.9, MeOH); δ_H (400 MHz, CD_3OD) 1.11–1.25 (1H, m, 5-*H*H), 1.46–1.58 (2H, m, 6-H_2), 1.79 (1H, ddt, *J* 12.4, 8.4, 4.0 Hz, 5-H*H*), 2.71–2.79 (1H, m, 1-H), 3.18 (1H, dd, *J* 8.8, 2.5 Hz, 3-H), 3.53–3.61 (1H, m, 4-H), 3.7 (1H, t, *J* 2.5 Hz, 2-H); δ_C (100 MHz, CD_3OD) 27.2 (CH_2), 30.6 (CH_2), 53.0 (CH), 70.4 (CH), 73.9 (CH), 77.2 (CH); *m*/*z* (CI) 148.0975 (MH^+. $C_6H_{14}NO_3$ requires 148.0974), 137 (5%), 97 (41), 81 (68), 71 (100).

Acknowledgements

Financial support from the HEC, Pakistan and the University of Glasgow is gratefully acknowledged.

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