Stereoselective Ammonium-Directed Epoxidation in the

Asymmetric Syntheses of Dihydroconduramines (−)-A-2, (−)-B-2, (−)-C-3 and (+)-F-3

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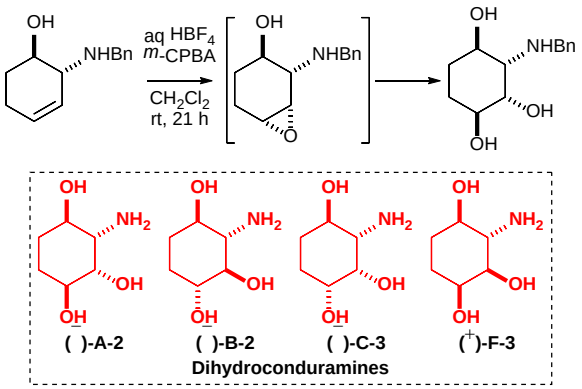


Epoxidation of racemic *trans*-2-(*N*,*N*-dibenzylamino)cyclohex-3-en-1-ol upon treatment with Cl_3CCO_2H then *m*-CPBA proceeded with poor levels of diastereoselectivity (~60:40 dr), whilst epoxidation of racemic *trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol under the same conditions proceeded with high diastereoselectivity (>95:5 dr) and was followed by completely regioselective and stereospecific ring-opening *in situ* to give, after methanolysis of the intermediate trichloroacetate ester, (1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*-benzylamino)cyclohexane-1,3,4-triol. Use of aq HBF_4 as the acid protecting agent gave the amino triol directly. The differing diastereoselectivities of these epoxidation reactions may be due to a predilection towards formation of an intramolecular hydrogen-bond in the former substrate disrupting the ability of the *in situ* formed ammonium moiety to act as a directing group for the incoming oxidant; the presence of two potential hydrogen-bond donors (i.e., two N−H bonds) in the latter substrate circumvents this limitation. With the criterion for a highly diastereoselective (ammonium-directed) epoxidation in this system established, a synthesis of enantiopure *trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol (>99% ee) was developed and the ammonium-directed epoxidation was then employed as a key synthetic step to facilitate the asymmetric syntheses of enantiopure dihydroconduramines (−)-A-2, (−)-B-2, (−)-C-3 and (+)-F-3 (>98% ee in each case) from 1,3-cyclohexadiene.

Introduction

Conduritol **1** (or cyclohex-5-en-1,2,3,4-tetraol) is a cyclitol with ten possible stereoisomeric forms, comprising six diastereoisomers of which four are chiral and two are meso compounds; two conduritols have so far been isolated from natural sources.[1,2] The relative configuration within a conduritol is distinguished in its specific name by appending a letter, A–F (Figure 1). Dihydroconduramines (DHC) **2** are a class of aminocyclitol that can be thought of as comprising saturated derivatives of conduritols in which any one of the hydroxyl groups has been formally replaced with an amino functionality. Therefore, two regioisomeric forms of dihydroconduramine exist: formal 'O for N' substitution at either C(1) or C(4) gives one possible regioisomer, whilst the same process at either C(2) or C(3) gives the other. Taking the latter process for example, the presence of internal symmetry within the parent conduritols A, B, D and E (σ or C_2) renders the formal 'O for N' substitution at C(2) or C(3) equivalent, so giving rise to only one possible corresponding dihydroconduramine. The lack of any such symmetry within the parent conduritols C and F means that the formal 'O for N' substitution at C(2) or C(3) is not equivalent, thus two possible dihydroconduramines are produced. This gives a total sixteen possible stereoisomeric forms in total, comprising eight diastereoisomers, each of which is chiral. Exactly the same argument applies to formal 'O for N' substitution at either C(1) or C(4) of the parent conduritols A–F. In order to distinguish each dihydroconduramine from all others, they are named for the parent conduritol but with the addition of a number, 1−4, to indicate the position of the amino functionality (Figure 1). Although none of the dihydroconduramine family has thus far been isolated from Nature, they have incited some interest in their synthesis due to their potential as glycosidase inhibitors.[3]

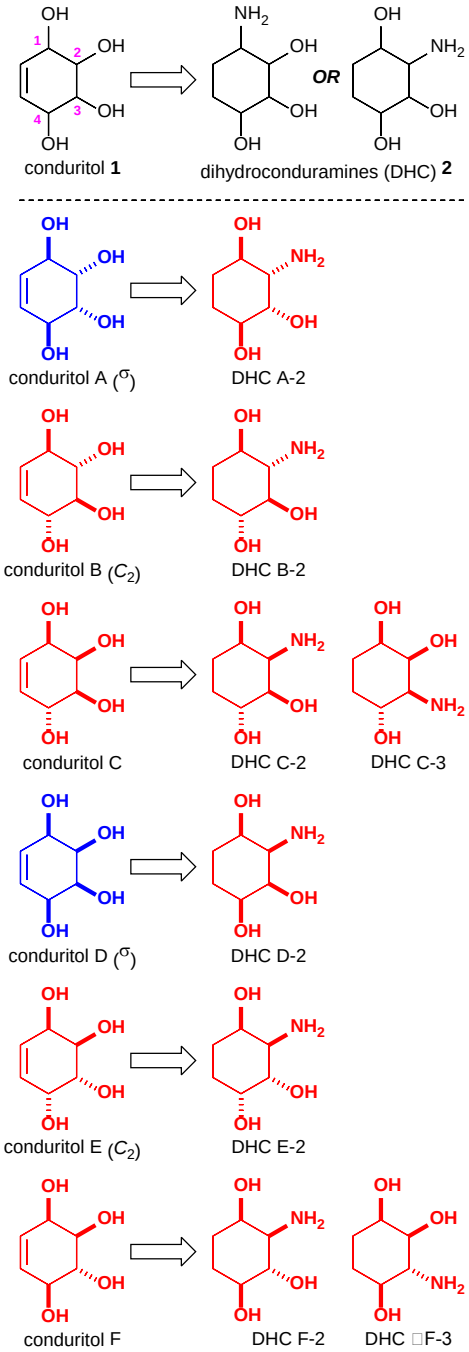


FIGURE 1. Generic structures of conduritol **1** and dihydroconduramines (DHC) **2**, structures of conduritols A–F and representative dihydroconduramines (DHC) A-2, B-2, C-2, C-3, D-2, E-2, F-2 and F-3. Achiral compounds are depicted in blue and chiral compounds in red. Relevant symmetry properties (σ or C_2) are indicated.

We have been actively engaged in a research program centred around the diastereoselective epoxidation of a range of chiral allylic amines.[4] We employed **3** as a model system for the development of this methodology and found that *in situ* conversion to the corresponding ammonium moiety upon treatment with a suitable Brønsted acid ($pK_a \leq 1$) not only offers protection against *N*-oxidation but also permits stereoselective epoxidation upon introduction of a peracid to the reaction flask, under the influence of hydrogen-bond direction to the proximal face of the olefin, giving epoxide **4**.[5] Although the epoxide **4** proved labile with respect to ring-opening under the reaction conditions, we were able to utilise this methodology for preparation of all four possible diastereoisomeric amino triols **6**–**9**;[6] this included the use of a three-step 'epoxide inversion' protocol to turn *syn*-epoxide **4** into *anti*-epoxide **5** (Figure 2).

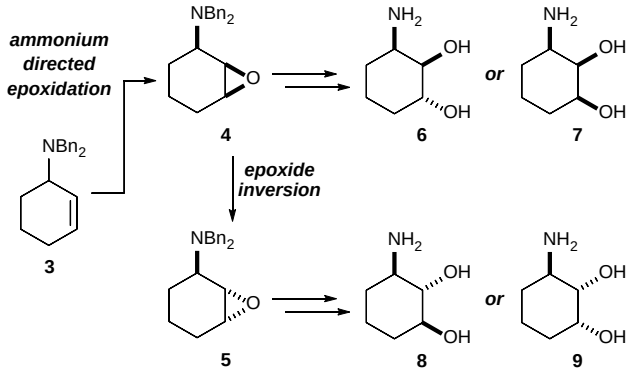


FIGURE 2. Synthesis of the for possible diastereoisomers of 3-aminocyclohexane-1,2-diol **6**–**9** using ammonium-directed epoxidation of **3** as one of the key steps.

We anticipated that epoxidation of *N*-protected 2-aminocyclohex-3-en-1-ols might similarly provide access to all possible stereoisomeric forms of the corresponding dihydroconduramines and we delineate herein the results of our preliminary investigations in this area concerning epoxidations of *N*-protected *trans*-2-aminocyclohex-3-en-1-ols **10** (Figure 3). Preparation of the substrates in racemic form is followed by evaluation of the efficacy of the ammonium-directed epoxidation for *trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol and *trans*-2-(*N*,*N*-dibenzylamino)cyclohex-3-en-1-ol. With the results of these studies in hand, a synthesis of enantiopure *trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol is developed, from which enantiopure dihydroconduramines (−)-A-2, (−)-B-2, (−)-C-3 and (+)-F-3 are prepared.

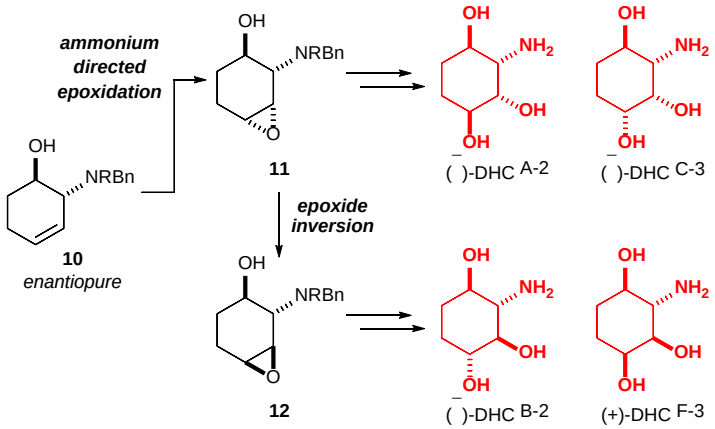


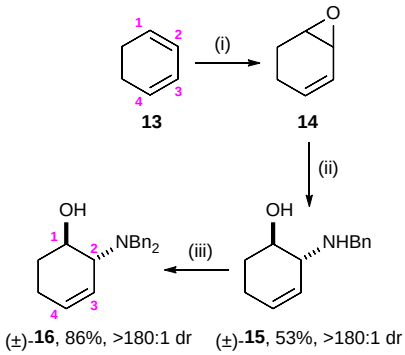
FIGURE 3. Proposed synthesis of enantiopure dihydroconduramines using ammonium-directed epoxidation of *N*-protected 2-aminocyclohex-3-en-1-ols **10** as one of the key steps.

Results and Discussion

The requisite substrates for these studies were prepared from 1,3-cyclohexadiene **13** via modification of a previously reported, related protocol.[7] Monoepoxidation of **13** upon treatment with AcOOH gave epoxide **14**, and then treatment of **14** with benzylamine in ^{i}PrOH at 80 °C gave complete conversion to (±)-**15** as a single regio- and diastereoisomer within 4 h; (±)-**15** was isolated in 53% yield (from **13**) and >180:1 dr, as determined by quantitative ^{1}H NMR spectroscopic analysis of the ^{13}C-^{1}H satellite peaks (Scheme 1).[8] The identity of and relative configuration within **15** was unambiguously established by single crystal X-ray

diffraction analysis of **15**·HCl, the corresponding HCl salt (Figure 4).[9] Use of an analogous procedure to prepare the corresponding *N*,*N*-dibenzyl-protected analogue (±)-**16** (using dibenzylamine to effect the epoxide ring-opening) gave incomplete consumption of starting material (tlc analysis) in the same time period, and even after 24 h the conversion was only 50% (^{1}H NMR spectroscopic analysis).[10] Subsequent attempts to optimise this approach did not prove fruitful, and therefore chemoselective *N*-benzylation of (±)-**15** (treatment with BnBr/^{i}Pr$_2$NEt/DMAP) was used to prepare (±)-**16**, in 86% isolated yield and >180:1 dr (Scheme 1).[11] The identity of and relative configuration within **16** was unambiguously established by single crystal X-ray diffraction analysis of both the free base and **16**·HCl, the corresponding HCl salt[9] (Figure 5 and Figure 6).

SCHEME 1[a]



[a]Reagents and Conditions: (i) AcOOH (39% w/w in AcOH), Na_2CO_3, CH_2Cl_2, 0 °C, 3.5 h; (ii) $BnNH_2$, ^{i}PrOH, 80 °C, 4 h; (iii) BnBr, ^{i}Pr$_2$NEt, DMAP, CH_2Cl_2, rt, 24 h.

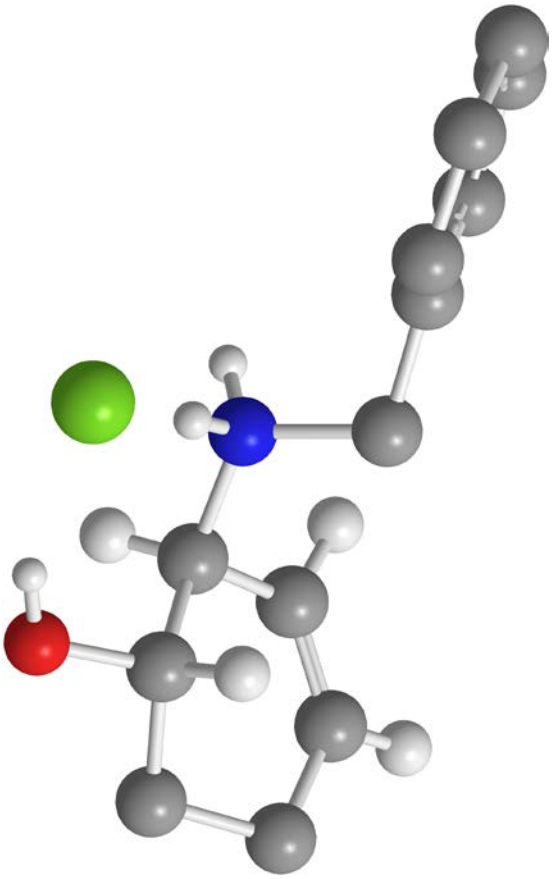


FIGURE 4. Chem3D representation of the X-ray crystal structure of (±)-**15**·HCl (selected H atoms are omitted for clarity).

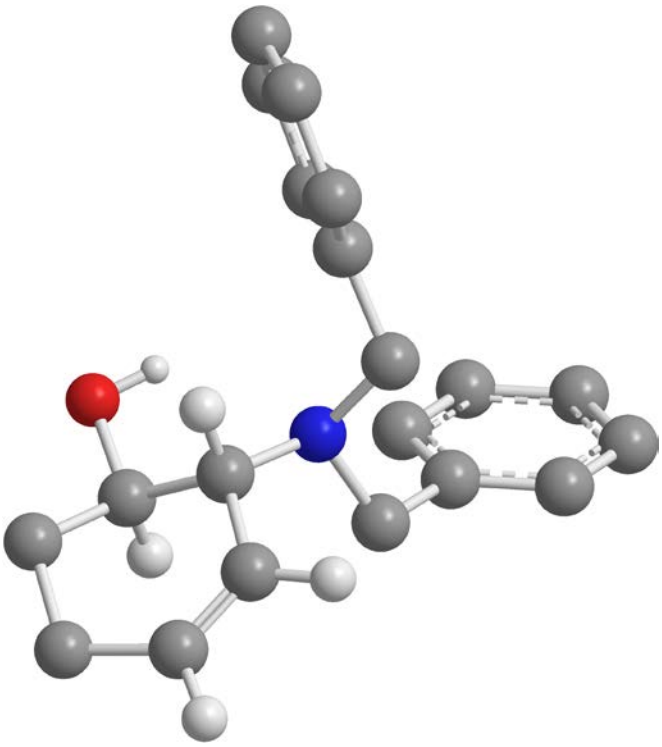


FIGURE 5. Chem3D representation of the X-ray crystal structure of (±)-**16** (selected H atoms are omitted for clarity).

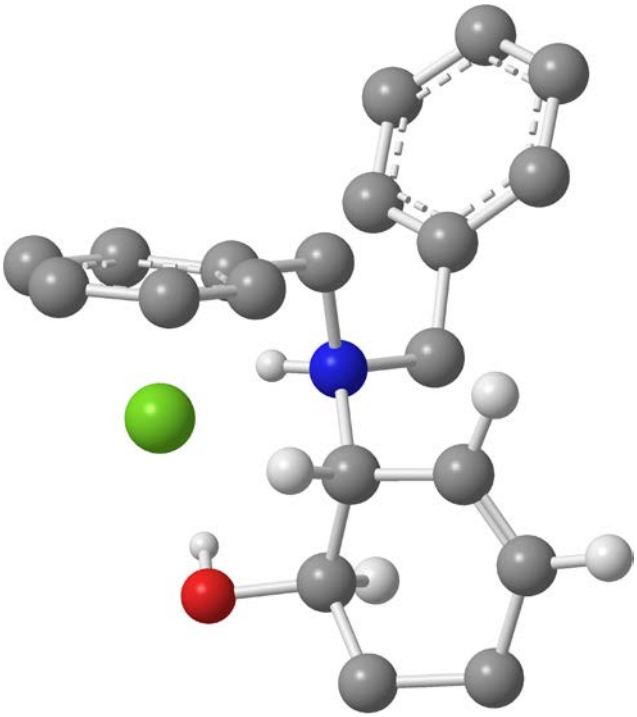
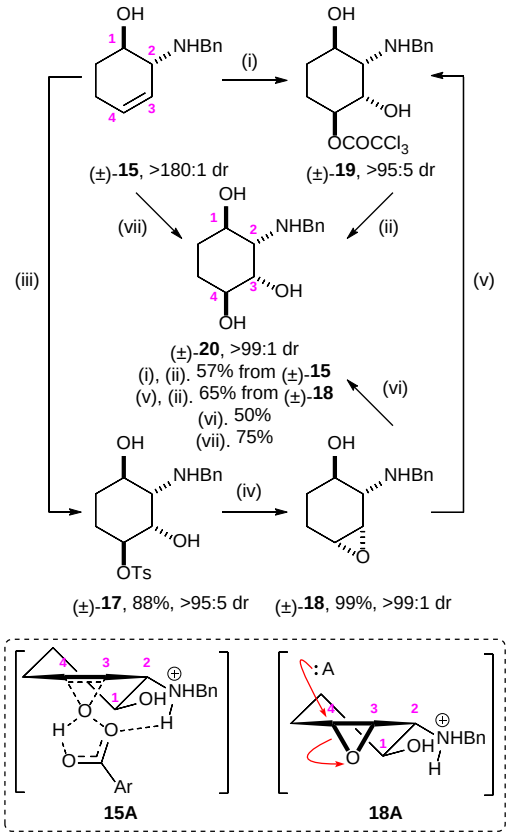


FIGURE 6. Chem3D representation of the X-ray crystal structure of (±)-**16**·HCl (selected H atoms are omitted for clarity).

Following our previously reported ^{1}H NMR "titration experiment" for monitoring the formation of the corresponding ammonium species,[5] Cl_3CCO_2H was added in 1 equiv portions to a 0.36 M solution of (±)-**15** in CD_2Cl_2 and the resultant solution was analysed by ^{1}H NMR spectroscopy. The changes in chemical shifts (Δδ) of C(1)*H*, C(2)*H* and C(3)*H* versus those of the free base (±)-**15** were determined, with the values of Δδ beginning to show a plateau around 5 equiv of Cl_3CCO_2H, so indicating that this would be a sufficient amount to confer resistance against oxidation of the nitrogen atom. Thus, the treatment of (±)-**15** with 5.0 equiv of Cl_3CCO_2H was followed by addition of 1.6 equiv of *m*-CPBA for 21 h,[5] which gave >95%

conversion to trichloroacetate ester (±)-**19** as a single regio- and diastereoisomer (>95:5 dr). It was possible to establish both the regiochemistry of and relative configuration within (±)-**19** from direct analysis of the ^{1}H NMR spectrum of the crude reaction mixture: the C*H*OCOCCl$_3$ proton displayed a characteristic chemical shift of δ_H ~5 ppm, whilst the relative configuration followed from ^{3}J coupling constant analysis, assuming a chair conformation was favoured in solution. Purification of (±)-**19** was not attempted due to the anticipated lability of the trichloroacetate ester moiety and instead it was subjected to transesterification upon treatment with K_2CO_3 in MeOH to give amino triol (±)-**20** as a single diastereoisomer (>95:5 dr), which was isolated in 57% yield from (±)-**15** after chromatography. When 40% aq HBF_4 was employed in place of Cl_3CCO_2H, amino triol (±)-**20** was obtained directly from (±)-**15**, in an improved 75% isolated yield. Meanwhile, epoxidation of (±)-**15** in the presence of TsOH under the same conditions resulted in >95% conversion to hydroxy tosylate (±)-**17** as a single regio- and diastereoisomer (>95:5 dr), in 88% yield (Scheme 2). Both the regiochemistry of and relative configuration within **17** were unambiguously established by single crystal X-ray diffraction analysis (Figure 7).[9,12] Treatment of (±)-**17** with DBU resulted in the formation of epoxide (±)-**18** in 99% yield and >99:1 dr after chromatography. The relative configuration within (±)-**18** was confidently assigned from the known configuration within the precursor (±)-**17**; this assignment was later confirmed by chemical correlation. Treatment of epoxide (±)-**18** with Cl_3CCO_2H gave (±)-**19**, again as a single regio- and diastereoisomer (>95:5 dr), with treatment of (±)-**19** with K_2CO_3 in MeOH giving amino triol (±)-**20** in 65% isolated yield from (±)-**18**, whilst treatment of (±)-**18** with 40% aq HBF_4 gave (±)-**20** directly, in 50% isolated yield, and in >99:1 dr in both cases. Taken together, all these data are entirely consistent with a mechanism which proceeds via transition state **15A**, involving ammonium-directed epoxidation to give the intermediate epoxide **18** (as the corresponding ammonium ion under the reaction conditions). Regioselective and stereospecific ring-opening of **18** upon attack of the conjugate base A (i.e., $Cl_3CCO_2^-$, TsO^- or H_2O) at C(4), the position distal to the ammonium moiety (transition state **18A**), gives the corresponding ring-opened derivative **17**, **19** or **20**, respectively (Scheme 2). This regioselectivity is favoured electronically (the destabilising effect of the inductively electron-withdrawing ammonium moiety on the transition state is minimised at the carbon atom distal to the ammonium moiety)[13,14] and stereoelectronically (ring-opening proceeds via the most stable chair-like transition state which places the ammonium moiety in a pseudo-equatorial position).[15] This regioselectivity is consistent with observations made by us[5,6,16–20] and others[21,22] in related systems (both cyclic and acyclic).

SCHEME 2[a]



[a]Reagents and Conditions: (i) Cl_3CCO_2H, *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) K_2CO_3, MeOH, rt, 16 h; (iii) TsOH, *m*-CPBA, CH_2Cl_2, rt, 21 h; (iv) DBU, CH_2Cl_2, rt, 24 h; (v) Cl_3CCO_2H, CH_2Cl_2, rt, 21 h; (vi) HBF_4 (40% aq), CH_2Cl_2, rt, 21 h; (vii) HBF_4 (40% aq), *m*-CPBA, CH_2Cl_2, rt, 21 h. A = $Cl_3CCO_2^-$, TsO^-, or H_2O.

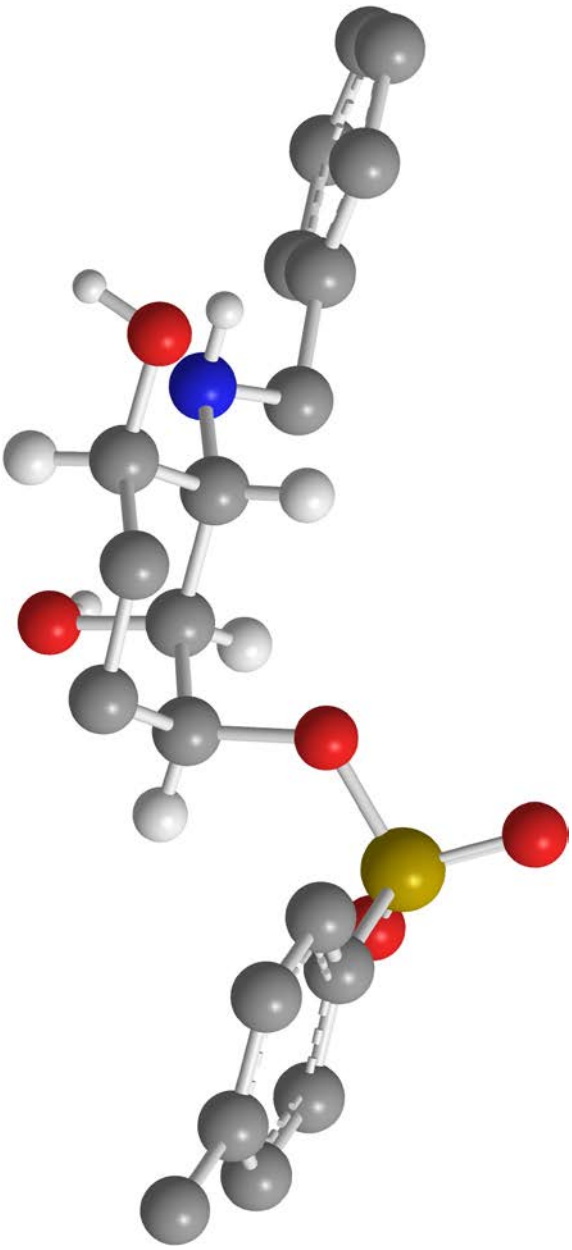
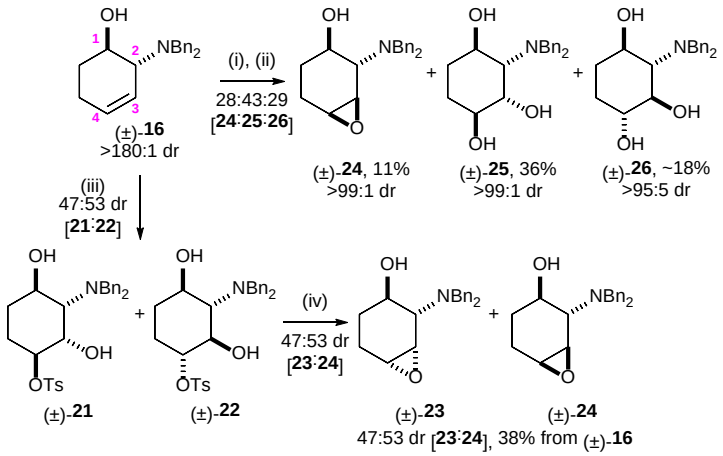


FIGURE 7. Chem3D representation of the X-ray crystal structure of (1*R*,2*S*,3*S*,4*S*)-**17** (selected H atoms are omitted for clarity).

A similar ^{1}H NMR "titration experiment" established that 5 equiv of Cl_3CCO_2H would be sufficient to confer resistance against oxidation to the nitrogen atom within *N*,*N*-dibenzyl-protected (±)-**16**. Treatment of (±)-**16** with 5.0 equiv of Cl_3CCO_2H then 1.6 equiv of *m*-CPBA for 21 h[5] resulted in incomplete consumption of starting material with formation of a mixture of products. When 5.0 equiv of *m*-CPBA was used, direct treatment of the crude reaction mixture with K_2CO_3 in MeOH revealed incomplete consumption of starting material to give a somewhat complex mixture, although a 28:43:29 ratio of epoxide (±)-**24** and the diastereoisomeric triols (±)-**25** and (±)-**26**, respectively, could be discerned. Purification via exhaustive flash column chromatography gave recovered starting material (±)-**16** in 4% yield, epoxide (±)-**24** in 11% yield, triol (±)-**25** in 36% yield, and triol (±)-**26** (impure sample) in ~18% yield (Scheme 3). The identities and relative configurations of **24**–**26** were established unambiguously by single crystal X-ray diffraction analyses (Figures 8–10).[9,23] Triols (±)-**25** and (±)-**26** both displayed the anticipated, favoured chair

conformation (with the *N*,*N*-dibenzylamino group occupying an equatorial position) in the solid-state, and ^{1}H NMR ^{3}J coupling constant analyses were entirely consistent with the same conformations being favoured in $CDCl_3$ solution. Use of 40% aq HBF_4 to promote the epoxidation reaction also resulted in formation of a complex mixture of products that contained (±)-**24**–**26** amongst other unknown species. Meanwhile, use of TsOH in the place of Cl_3CCO_2H resulted in the formation of a 47:53 mixture of hydroxy tosylates (±)-**21** and (±)-**22**. The connectivities within (±)-**21** and (±)-**22** were assigned by a combination of ^{1}H and ^{13}C NMR chemical shift analyses (the *CH*OTs moiety produced diagnostic proton and carbon chemical shifts: δ_H ~5 ppm; δ_C ~80 ppm) and ^{1}H–^{1}H COSY analyses. The relative configurations of (±)-**21** and (±)-**22** were thence assigned by ^{1}H NMR ^{3}J coupling constant analyses, assuming a chair conformation is adopted in solution. Treatment of the mixture of (±)-**21** and (±)-**22** with DBU gave a 47:53 mixture of the corresponding epoxides (±)-**23** and (±)-**24**, which proved inseparable by chromatography and which were isolated in 38% combined yield from (±)-**16**. These results suggest poorly diastereoselective epoxidation of (±)-**16** occurs to give a 47:53 mixture of epoxides (±)-**23** and (±)-**24**, both of which undergo completely regioselective and stereospecific ring-opening by TsOH under the reaction conditions to give a 47:53 mixture of the corresponding hydroxy tosylates (±)-**21** and (±)-**22** (Scheme 3).

SCHEME 3[a]



[a]Reagents and Conditions: (i) Cl_3CCO_2H (5 equiv), *m*-CPBA (5 equiv), CH_2Cl_2, rt, 21 h; (ii) K_2CO_3, MeOH, rt, 48 h; (iii) TsOH, *m*-CPBA, CH_2Cl_2, rt, 21 h; (iv) DBU, CH_2Cl_2, rt, 24 h.

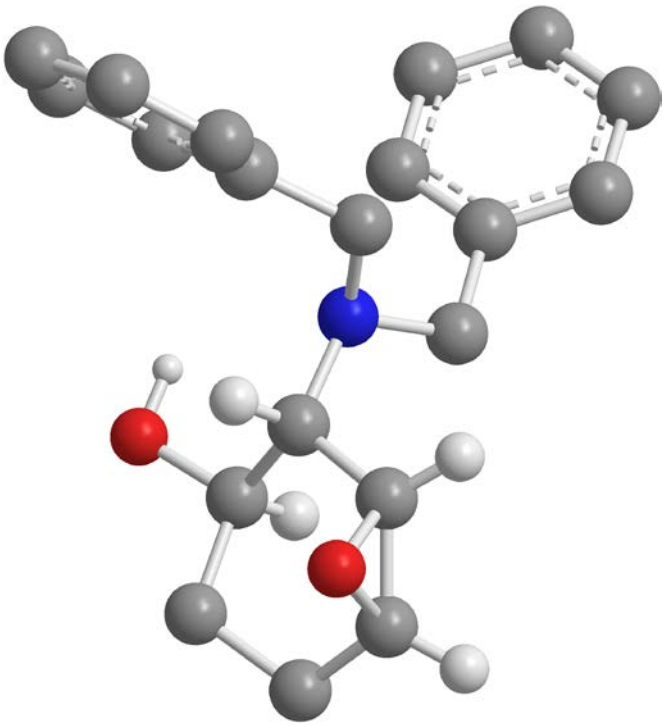


FIGURE 8. Chem3D representation of the X-ray crystal structure of (±)-**24** (selected H atoms are omitted for clarity).

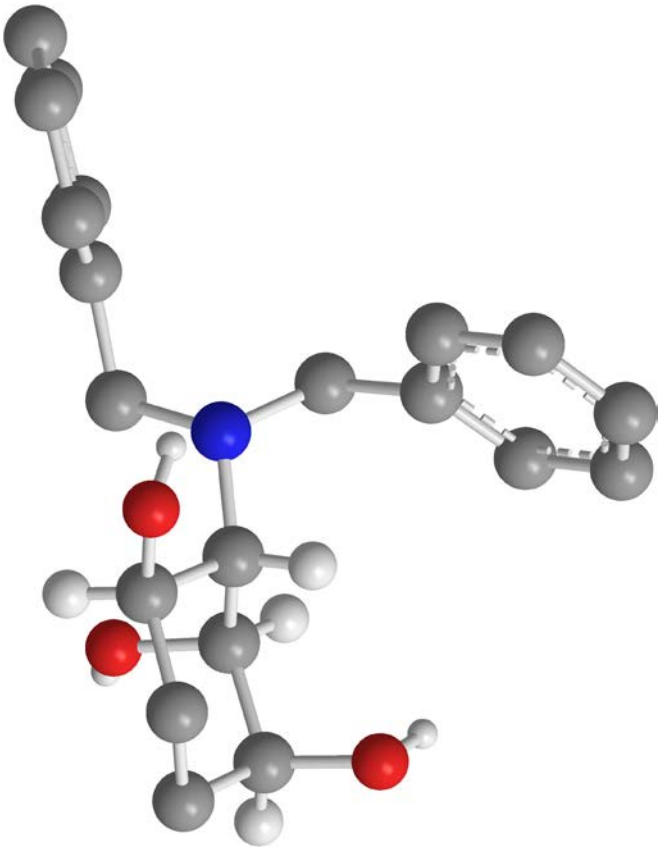


FIGURE 9. Chem3D representation of the X-ray crystal structure of (±)-**25** (selected H atoms are omitted for clarity).

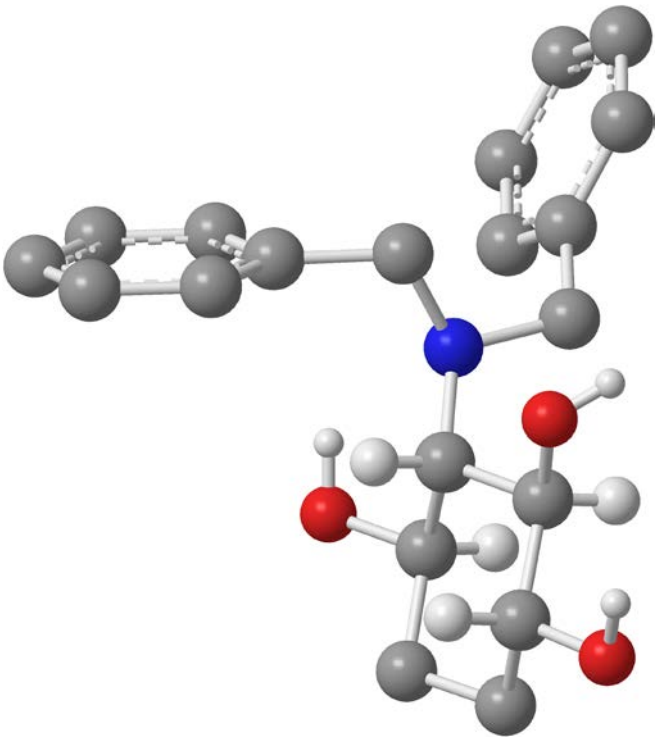
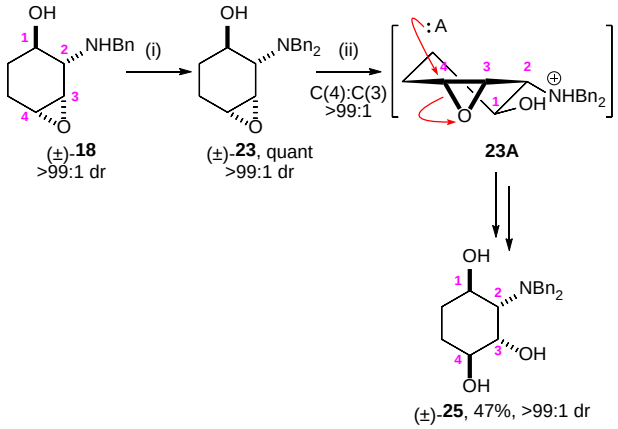


FIGURE 10. Chem3D representation of the X-ray crystal structure of (±)-**26** (selected H atoms are omitted for clarity).

The regioselectivity of ring-opening of epoxides (±)-**23** and (±)-**24** by Cl_3CCO_2H was next interrogated to provide further insight into this epoxidation reaction. Chemoselective *N*-benzylation of epoxide (±)-**18** gave a sample of (±)-**23** in quantitative yield, thus providing confirmation of the relative configuration assigned to both (±)-**18** and (±)-**23**. Treatment of (±)-**23** with Cl_3CCO_2H produced triol (±)-**25** as the only product, in 47% isolated yield after chromatography (Scheme 4). Meanwhile, under the same conditions epoxide (±)-**24** gave a 4:96 mixture of triols (±)-**25** and (±)-**26** that was isolated in 71% yield after chromatography (Scheme 5). These results demonstrate a very strong preference for ring-opening by Cl_3CCO_2H at the C(4)-position of both epoxides **23** and **24**, distal to the in situ formed ammonium moiety. In the former case, ring-opening of **23** at C(4) would presumably proceed from **23A** via a low-energy chairlike transition state which places the bulky *N*,*N*-dibenzylammonium moiety in a pseudoequatorial position. In contrast, ring-opening of epoxide **24** at C(4) must either proceed from **24A** via a twist-boatlike transition state or from **24B** via a chairlike transition state which places all of the substituents in pseudoaxial positions. Both of these alternatives would be anticipated to be somewhat disfavoured, which would be manifest in a slower rate of ring-opening in the latter case, consistent with the persistence of epoxide (±)-**24** in the crude reaction mixture upon epoxidation of (±)-**16**. With the regioselectivities of ring-opening of both epoxides (±)-**23** and (±)-**24** by Cl_3CCO_2H established, it can be extrapolated that epoxidation of (±)-**16** promoted by *m*-CPBA in the presence of Cl_3CCO_2H resulted in an approximate 43:57 mixture of the intermediate epoxides (±)-**23** and (±)-**24**, i.e., the ratio of (±)-**25** to the sum of (±)-**24** and (±)-**26**. The ratio of epoxides (±)-**23** and (±)-**24** obtained when using Cl_3CCO_2H (43:57 dr [**23**:**24**]) or TsOH (47:53 dr [**23**:**24**]) is

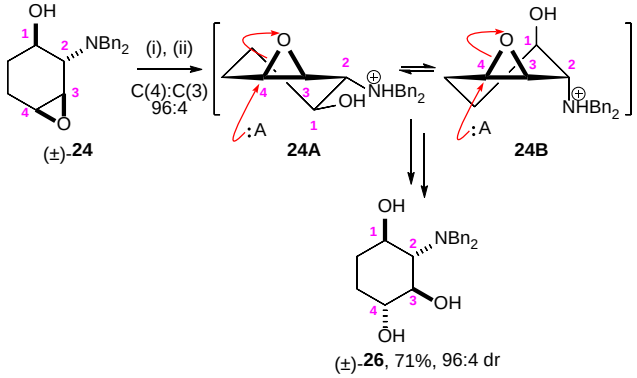
very similar, indicating little dependency of the epoxidation diastereoselectivity on the identity of the Brønsted acid protecting agent.

SCHEME 4[a]



[a]Reagents and Conditions: (i) BnBr, $^{i}Pr_2NEt$, DMAP, CH_2Cl_2, rt, 24 h; (ii) Cl_3CCO_2H, CH_2Cl_2, rt, 21 h; (iii) K_2CO_3, MeOH, rt, 16 h. A = $Cl_3CCO_2^-$.

SCHEME 5[a]



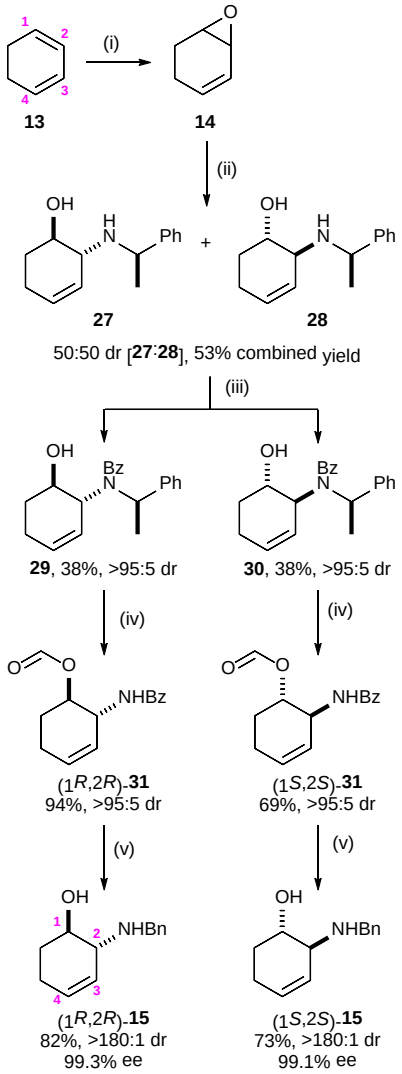
[a]Reagents and Conditions: (i) Cl_3CCO_2H, CH_2Cl_2, rt, 21 h; (ii) K_2CO_3, MeOH, rt, 16 h. A = $Cl_3CCO_2^-$.

The lack of diastereoselectivity upon epoxidation of *N*,*N*-dibenzyl protected **16** is in direct contrast to the high diastereoselectivities observed upon epoxidation of *N*,*N*-dibenzyl protected **3** and *N*-benzyl-protected **15** under these conditions. This could be the result of a competition between ammonium-directed and hydroxyl-directed pathways in the case of **16** (the *N*,*N*-dibenzylammonium moiety likely being a poorer directing group in comparison to the *N*-benzylammonium moiety, as we have previously established in related systems[24,25] allowing direction by the homoallylic hydroxyl group to compete). However, the homoallylic hydroxyl substituent would need to occupy a pseudo-axial position on a half-chair conformation of **16** to exert any directing effect, which would necessarily result in the ammonium moiety also being placed pseudo-axial; such a conformation is anticipated to be highly energetically disfavoured. It may be, therefore, that preferential formation of an intramolecular hydrogen-bond between the *N*,*N*-dibenzylammonium moiety (donor) and hydroxyl group (acceptor) means that there is then no capacity for the *N*,*N*-dibenzylammonium moiety to act as a hydrogen-bond donor to direct the incoming peracid. The stereochemical outcome of the epoxidation reaction would then be governed by steric/electronic factors

alone, which in this case results in essentially no diastereoselectivity. In the case of an *N*-benzylammonium moiety, however, there are two N−H bonds present and hence two potential hydrogen-bond donors, providing circumvention of this limitation.

Having established that an *N*-benzylamino substituent is prerequisite to enable diastereoselective ammonium-directed epoxidation in this system, the synthesis of the corresponding enantiopure substrate was pursued, again via modification of a previously reported, related protocol.[26] Starting from 1,3-cyclohexadiene **13**, mono-epoxidation was followed by ring-opening of **14** using (*R*)-α-methylbenzylamine (>99% ee), which gave an ~50:50 mixture of diastereoisomers **27** and **28** that were inseparable by chromatography and isolated in 53% combined yield. Treatment of this mixture with BzCl gave an ~50:50 mixture of the corresponding benzamides **29** and **30** which were separated chromatographically, giving **29** and **30** in 38% isolated yield and >95:5 dr in both cases (Scheme 6). The relative configuration within **29** was unambiguously established by single crystal X-ray diffraction analysis (Figure 11),[9] and thus its absolute configuration was assigned from the known (*R*)-configuration of the α-methylbenzyl stereocenter. This analysis also unambiguously established the absolute configuration of **30**. Treatment of **29** with formic acid at 60 °C effected removal of the *N*-α-methylbenzyl group and concomitant esterification of the hydroxyl group to give (1*R*,2*R*)-**31** in 94% yield, which upon reduction with $LiAlH_4$ gave enantiopure (1*R*,2*R*)-**15** (99.3% ee)[27] in 82% yield and >180:1 dr.[6] A similar two-step sequence applied to **30** gave enantiopure (1*S*,2*S*)-**15** (99.1% ee)[27] in 50% yield and >180:1 dr[6] over the two steps (Scheme 6).

SCHEME 6[a]



[a]Reagents and Conditions: (i) AcOOH (39% w/w in AcOH), Na_2CO_3, CH_2Cl_2, 0 °C, 3.5 h; (ii) (*R*)-α-methylbenzylamine, ^{i}PrOH, 80 °C, 4 h; (iii) BzCl, Na_2CO_3, THF, rt, 24 h; (iv) HCO_2H (90% aq), 60 °C, 18 h; (v) $LiAlH_4$, THF, 60 °C, 16 h.

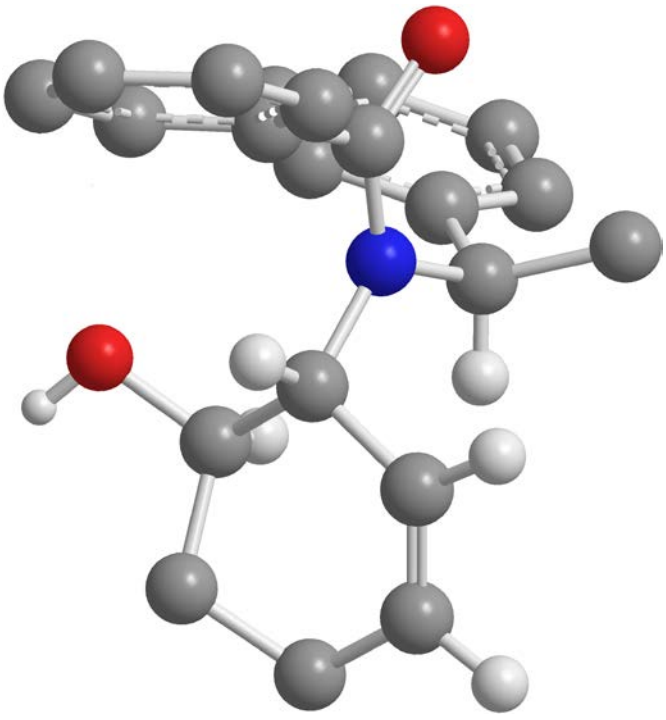
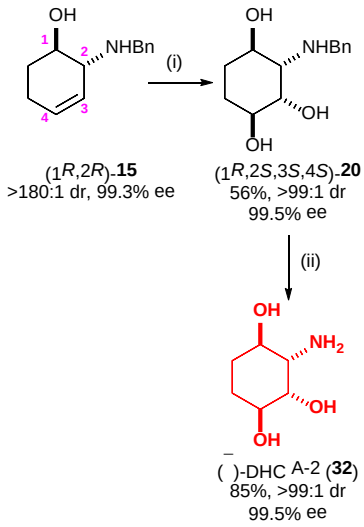


FIGURE 11. Chem3D representation of the X-ray crystal structure of **29** (selected H atoms are omitted for clarity).

Following the optimised conditions employed previously for racemic **15**, epoxidation of enantiopure (1*R*,2*R*)-**15** upon treatment with aq HBF_4 then *m*-CPBA gave enantiopure (1*R*,2*S*,3*S*,4*S*)-**20** in 56% yield and 99.5% ee,[28] which displayed ^{1}H and ^{13}C NMR spectroscopic data identical to those of the racemate. Hydrogenolysis of (1*R*,2*S*,3*S*,4*S*)-**20** gave (−)-dihydroconduramine A-2 (**32**) {$[\alpha]_D^{25}$ −25.8 (*c* 1.0 in MeOH)} in 85% yield and 99.5% ee[29] (Scheme 7).

SCHEME 7[a]

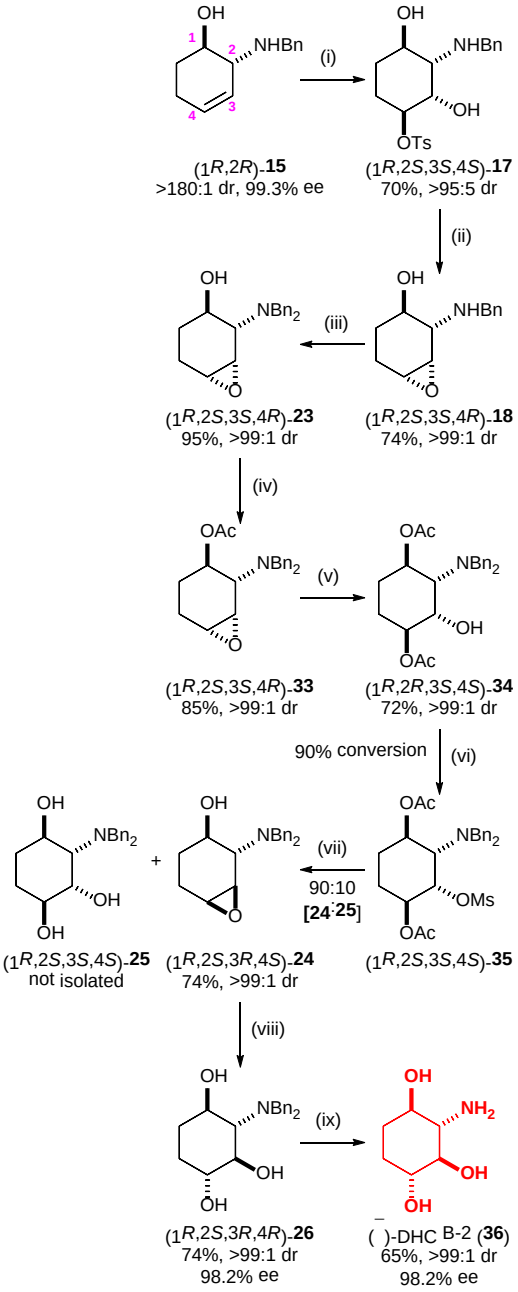


[a]Reagents and Conditions: (i) HBF_4 (40% aq), *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) H_2, $Pd(OH)_2$/C, MeOH, rt, 24 h.

Alternatively, oxidation of (1*R*,2*R*)-**15** using TsOH then *m*-CPBA gave enantiopure hydroxy tosylate (1*R*,2*S*,3*S*,4*S*)-**17** in 70% yield, which displayed ^{1}H and ^{13}C NMR spectroscopic data identical to those of the racemate. Treatment of (1*R*,2*S*,3*S*,4*S*)-**17** with DBU resulted in base-induced ring-closure to give the corresponding epoxide (1*R*,2*S*,3*S*,4*R*)-**18** in 74% yield, with chemoselective *N*-benzylation upon treatment with BnBr in the presence of ^{i}Pr$_2$NEt and DMAP then giving epoxide (1*R*,2*S*,3*S*,4*R*)-**23** in 95% yield; again, the ^{1}H and ^{13}C NMR spectroscopic data of these enantiopure samples of **18** and **23** were identical to those of the corresponding racemates. Our epoxide-inversion strategy was next deployed.[6] Initial treatment of (1*R*,2*S*,3*S*,4*R*)-**23** with Ac_2O was required in this case to give the corresponding acetate (1*R*,2*S*,3*S*,4*R*)-**33** in 85% yield, which was followed by regioselective and stereospecific (S_N2-type) epoxide ring-opening upon treatment with AcOH at 50 °C to give diacetate (1*R*,2*R*,3*S*,4*S*)-**34** in 72% yield. Treatment of (1*R*,2*R*,3*S*,4*S*)-**34** with MsCl in pyridine resulted in 90% conversion to the corresponding mesylate (1*R*,2*S*,3*S*,4*S*)-**35** which was treated with K_2CO_3 in methanol to give a 90:10 mixture of epoxide (1*R*,2*S*,3*R*,4*S*)-**24** and amino triol (1*R*,2*S*,3*S*,4*S*)-**25**, from which (1*R*,2*S*,3*R*,4*S*)-**24** was isolated in 74% yield. This is consistent with a mechanism involving transesterification of both acetate esters within (1*R*,2*R*,3*S*,4*S*)-**34** being followed by base-induced epoxide ring-closure to give (1*R*,2*S*,3*R*,4*S*)-**24**; the minor amino triol product (1*R*,2*S*,3*S*,4*S*)-**25** results from transesterification of the unreacted starting material (1*R*,2*R*,3*S*,4*S*)-**34** from the previous step. Treatment of epoxide (1*R*,2*S*,3*R*,4*S*)-**24** with aq HBF_4 at 40 °C gave amino triol (1*R*,2*S*,3*R*,4*R*)-**26** as the sole

product which was isolated in 74% yield and 98.2% ee[27] after chromatography; again, this sample displayed ^{1}H and ^{13}C NMR spectroscopic data identical to those of the racemate. This is consistent with the ring-opening of (1*R*,2*S*,3*R*,4*S*)-**24** occurring with complete regioselectivity and stereospecificity in this case.[30] Hydrogenolysis of (1*R*,2*S*,3*R*,4*R*)-**26** gave (−)-dihydroconduramine B-2 (**36**) {$[\alpha]_D^{25}$ −19.9 (*c* 1.0 in MeOH)} in 65% yield and 98.2% ee[29] (Scheme 8).

SCHEME 8[a]

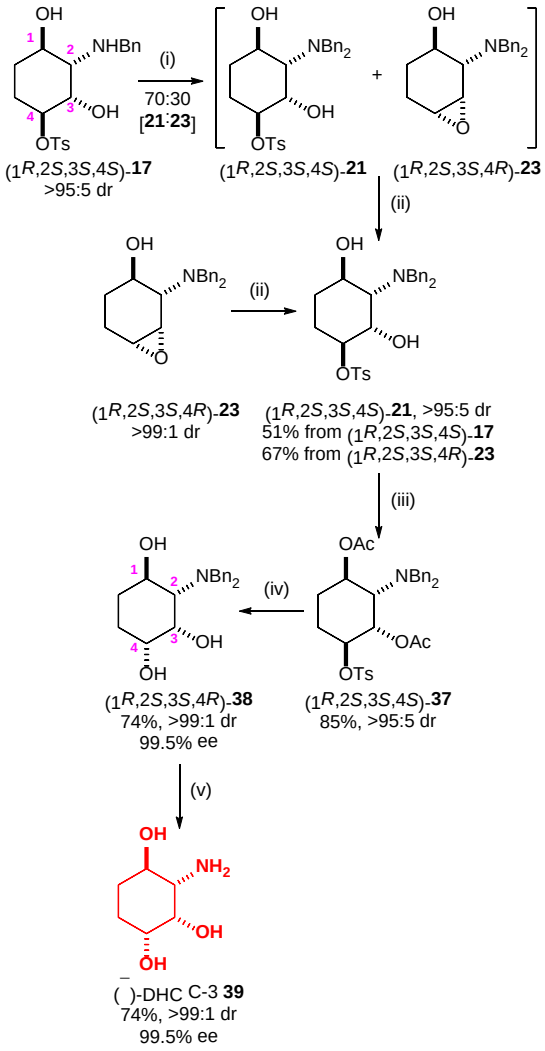


[a]Reagents and Conditions: (i) TsOH, *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) DBU, CH_2Cl_2, rt, 24 h; (iii) BnBr, $^{i}Pr_2NEt$, DMAP, CH_2Cl_2, rt, 24 h; (iv) Ac_2O, DMAP, pyridine, rt, 24 h; (v) AcOH, 50 °C, 36 h; (vi) MsCl, pyridine, rt, 16 h; (vii) K_2CO_3, MeOH, rt, 16 h; (viii) HBF_4 (40% aq), CH_2Cl_2, 40 °C, 24 h; (ix) H_2, $Pd(OH)_2/C$, MeOH, rt, 24 h.

A neighbouring group participation strategy (Winstein reaction) was implemented[6,31,32] to access the corresponding dihydroconduramine stereoisomers with a *cis*-configured 1,2-diol moiety. Treatment of epoxide (1*R*,2*S*,3*S*,4*R*)-**23** with TsOH gave hydroxy tosylate (1*R*,2*S*,3*S*,4*S*)-**21** in 67% yield, again consistent with completely regioselective and stereospecific (S_N2-type) epoxide ring-opening. Alternatively,

(1*R*,2*S*,3*S*,4*S*)-**21** could be accessed via chemoselective *N*-benzylation of (1*R*,2*S*,3*S*,4*S*)-**17** upon treatment with BnBr, $^{i}Pr_2NEt$ and DMAP, although this was accompanied by partial ring-closure to form epoxide (1*R*,2*S*,3*S*,4*R*)-**23**, and therefore the crude reaction mixture from this step was treated with TsOH, giving (1*R*,2*S*,3*S*,4*S*)-**21** in 51% isolated yield. Treatment of (1*R*,2*S*,3*S*,4*S*)-**21** with Ac_2O gave the corresponding diacetate derivative (1*R*,2*S*,3*S*,4*S*)-**37** in 85% yield, and then treatment of (1*R*,2*S*,3*S*,4*S*)-**37** with KOAc in EtOH/H_2O promoted a Winstein reaction,[31,32] resulting in displacement of the tosylate functionality via a mechanism involving neighbouring group participation from the adjacent acetate functionality; after treatment of the crude reaction mixture with K_2CO_3 in MeOH (to effect transesterification of all the acetate ester functionalities) the corresponding amino triol (1*R*,2*S*,3*S*,4*R*)-**38** was isolated in 74% yield and 99.5% ee (Scheme 9).[27] The relative configuration within **38** was unambiguously established by single crystal X-ray diffraction analysis (Figure 12),[9,33] and thus the absolute configuration of (1*R*,2*S*,3*S*,4*R*)-**38** was assigned from the known configurations of the C(1)- and C(2)-stereocenters derived from **29**. Hydrogenolysis of (1*R*,2*S*,3*S*,4*R*)-**38** gave (−)-dihydroconduramine C-3 (**39**) {$[\alpha]_D^{25}$ −31.3 (*c* 1.0 in MeOH)} in 74% yield and 99.5% ee[29] (Scheme 9).

SCHEME 9[a]



[q]Reagents and Conditions: (i) BnBr, $^{i}Pr_2NEt$, DMAP, CH_2Cl_2, rt, 24 h; (ii) TsOH, CH_2Cl_2, rt, 21 h; (iii) Ac_2O, DMAP, pyridine, CH_2Cl_2, rt, 24 h; (iv) KOAc, EtOH, H_2O, reflux, 72 h, then K_2CO_3, MeOH, rt, 24 h; (v) H_2, $Pd(OH)_2$/C, MeOH, rt, 24 h.

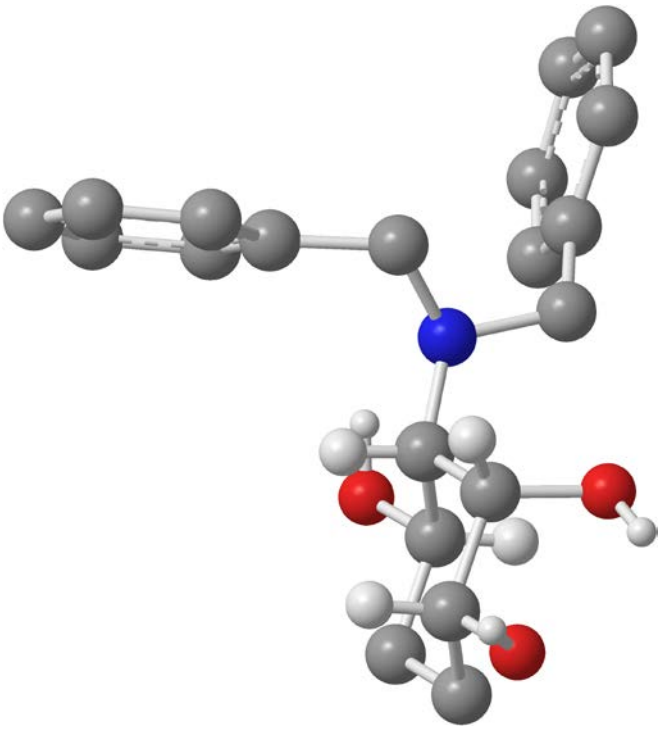
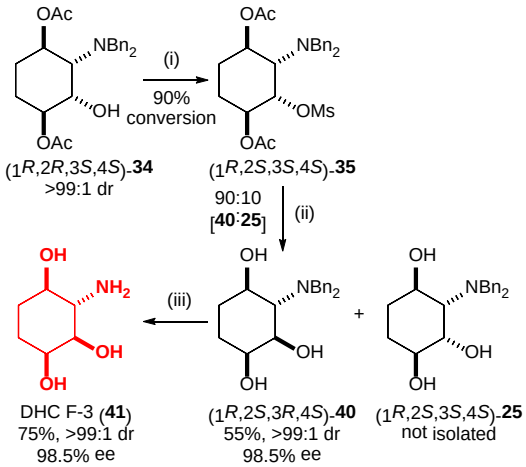


FIGURE 12. Chem3D representation of the X-ray crystal structure of (±)-**38** (selected H atoms are omitted for clarity).

Using a directly analogous approach, treatment of mesylate (1*R*,2*S*,3*S*,4*S*)-**35** [obtained, as before, in 90% conversion from (1*R*,2*R*,3*S*,4*S*)-**34**] with KOAc in EtOH/H_2O and then K_2CO_3 in MeOH gave a 90:10 mixture of amino triols (1*R*,2*S*,3*R*,4*S*)-**40** and (1*R*,2*S*,3*S*,4*S*)-**25** from which the major product (1*R*,2*S*,3*R*,4*S*)-**40** was isolated in 55% yield and 98.5% ee.[27] The formation of (1*R*,2*S*,3*R*,4*S*)-**40** is consistent with a Winstein reaction[31,32] occurring under these conditions, in which the mesylate functionality undergoes solvolysis via a mechanism involving neighbouring group participation of the adjacent acetate functionality, followed by transesterification of all of the acetate functionalities; the minor product (1*R*,2*S*,3*S*,4*S*)-**25** again simply arises from transesterification of the unreacted starting material (1*R*,2*R*,3*S*,4*S*)-**34** from the previous step (Scheme 10). The relative configuration within **40** was unambiguously established by single crystal X-ray diffraction analysis (Figure 13),[9,33] and thus the absolute configuration of (1*R*,2*S*,3*R*,4*S*)-**40** was assigned from the known configurations of the C(1)- and C(2)-stereocenters derived from **29**. Hydrogenolysis of (1*R*,2*S*,3*R*,4*S*)-**40** gave (+)-dihydroconduramine F-3 (**41**) {$[\alpha]_D^{25}$ +26.7 (*c* 1.0 in MeOH)} in 75% yield and 98.5% ee[29] (Scheme 10).

SCHEME 10[a]



[a]Reagents and Conditions: (i). MsCl, pyridine, rt, 16 h; (ii) KOAc, EtOH, H_2O, reflux, 72 h, then K_2CO_3, MeOH, rt, 24 h; (iii) H_2, $Pd(OH)_2$/C, MeOH, rt, 24 h

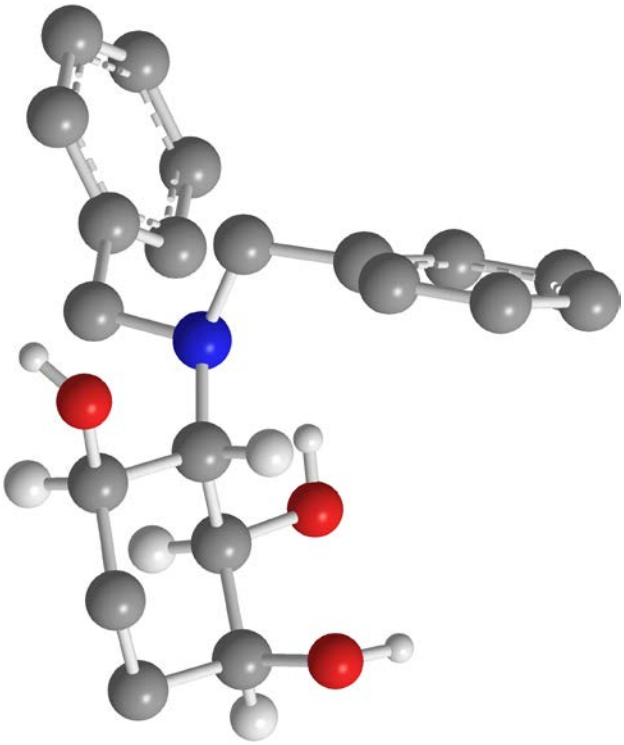


FIGURE 13. Chem3D representation of the X-ray crystal structure of (±)-**40** (selected H atoms are omitted for clarity).

Conclusion

In conclusion, epoxidation of enantiopure *trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol (>99% ee) upon treatment with a range of Brønsted acids (Cl_3CCO_2H, TsOH or aq HBF_4) and then *m*-CPBA proceeded with high diastereoselectivity (>95:5 dr) and was followed by *in situ* ring-opening in a completely regioselective and stereospecific manner upon attack of the conjugate base of the acid. This ammonium-directed epoxidation process was employed as a key synthetic step to facilitate the asymmetric syntheses of enantiopure dihydroconduramines (−)-A-2, (−)-B-2, (−)-C-3 and (+)-F-3 in >98% ee in each case.

Experimental Section

General Experimental Details. Reactions involving moisture-sensitive reagents were carried out under a nitrogen atmosphere using standard vacuum line techniques and glassware that was flame-dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[34] *m*-CPBA was supplied as a 70-77% slurry in water and titrated according to the procedure of Swern[35] immediately before use.

Organic layers were dried over Na_2SO_4. Flash column chromatography was performed on Kieselgel 60 silica. Melting points are uncorrected. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. ^1H–^1H COSY and ^1H–^{13}C HMQC analyses were used to establish atom connectivity. Accurate mass measurements were run on a MicroTOF instrument internally calibrated with polyalanine.

X-ray Crystal Structure Determination.[9] Data were collected using either graphite monochromated Cu-Kα radiation (for **15**·HCl, **16**, **16**·HCl, **17**, **24**, **26**, **38** and **40**) or graphite monochromated Mo-Kα radiation (for **25** and **29**) via standard procedures at 150 K. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[36]

(*RS*,*RS*)-2-(*N*-Benzylamino)cyclohex-3-en-1-ol (±)-15. *Step 1*. AcOOH (39% in AcOH, 31.2 mL, 125 mmol) was added dropwise to a stirred suspension of **13** (10.0 g, 125 mmol) and Na_2CO_3 (119 g, 1.12 mol) in CH_2Cl_2 (350 mL) at 0 °C and the resultant suspension was stirred at 0 °C for 3.5 h. H_2O (200 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organics were washed with satd aq Na_2SO_3 (in 500 mL portions) until starch-iodide paper indicated that no peroxide was present, then dried and concentrated in vacuo at 0 °C to give **14** as a colourless oil (11.5 g); δ_H (400 MHz, $CDCl_3$) 1.57–1.67 (1H, m, C(6)H_A), 1.95–2.14 (2H, m, C(5)H_A, C(6)H_B), 2.21–2.29 (1H, m, C(5)H_B), 3.22–3.28 (1H, m, C(1)*H*), 3.50–3.55 (1H, m, C(2)*H*), 5.89–6.01 (2H, m, C(3)*H*, C(4)*H*).

Step 2. Benzylamine (13.6 mL, 125 mmol) was added to a stirred solution of the residue from the previous step (11.5 g) in ^{i}PrOH (125 mL) at rt and the resultant solution was heated at 80 °C for 4 h, then allowed to cool to rt and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 95:5:0.5) gave (±)-**15** as an orange solid (13.4 g, 53% from **13**, >180:1 dr); mp 53–56 °C; ν_{max} 3300, 3100, 2901, 2830, 1666; δ_H (500 MHz, $CDCl_3$) 1.49–1.60 (1H, m, C(6)H_A), 1.90–1.98 (1H, m, C(6)H_B), 2.06–2.11 (2H, m, C(5)H_2), 3.00 (1H, app dt, *J* 8.1, 2.8, C(2)*H*), 3.43 (1H, ddd,

J 11.5, 8.1, 3.5, C(1)*H*), 3.70 (1H, d, *J* 13.0, NC*H*$_A$H$_B$Ph), 3.89 (1H, d, *J* 13.0, NCH$_A$*H*$_B$Ph), 5.61–5.68 (2H, m, C(3)*H*, C(4)*H*), 7.16–7.31 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 24.7 (*C*(5)), 28.8 (*C*(6)), 50.5 (N*C*H$_2$Ph), 61.0 (*C*(2)), 71.0 (*C*(1)), 126.7 (*C*(3)), 127.1, 128.2, 128.5 (*o,m,p-Ph*), 128.5 (*C*(4)), 140.4 (*i-Ph*); *m/z* (ESI$^+$) 204 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{18}NO^+$ ([M+H]$^+$) requires 204.1383; found 204.1382.

Analysis of (±)-**15** by chiral HPLC [Chiralpak AD-H, mobile phase: hexane/^{i}PrOH (v/v, 95:5), flow rate: 1 mL/min, 10 μL injection] gave complete resolution of enantiomers [(1*R*,2*R*)-**15** t_R = 13.6 min; (1*S*,2*S*)-**15** t_R = 15.3 min].

(1*R*,2*R*)-2-(*N*-Benzylamino)cyclohex-3-en-1-ol (1*R*,2*R*)-15. $LiAlH_4$ (2.4 M in THF, 3.4 mL, 8.2 mmol) was added dropwise via syringe to a stirred solution of (1*R*,2*R*)-**31** (500 mg, 2.04 mmol, >95:5 dr) in THF (40 mL) at 0 °C and the resultant solution was heated at 60 °C for 16 h, then allowed to cool to rt and then cooled to 0 °C. 2 M aq NaOH (5 mL) was then added dropwise and the resultant mixture was heated at 60 °C for 3 h. The resultant mixture was allowed to cool to rt, filtered through a plug of Celite® (eluent CH_2Cl_2), and the filtrate was concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 97:3:0.5) gave (1*R*,2*R*)-**15** as a yellow oil (340 mg, 82%, >180:1 dr, 99.3% ee); $[\alpha]_D^{25}$ −123.1 (*c* 1.0 in $CHCl_3$).

Analysis of (1*R*,2*R*)-**15** by chiral HPLC [Chiralpak AD-H, mobile phase: hexane/^{i}PrOH (v/v, 95:5), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*R*,2*R*)-**15** to be assessed as 99.3% ee [(1*R*,2*R*)-**15** t_R = 14.3 min].

(1*S*,2*S*)-2-(*N*-Benzylamino)cyclohex-3-en-1-ol (1*S*,2*S*)-15. $LiAlH_4$ (2.4 M in THF, 3.4 mL, 8.2 mmol) was added dropwise via syringe to a stirred solution of (1*S*,2*S*)-**31** (500 mg, 2.04 mmol, >95:5 dr) in THF (40 mL) at 0 °C and the resultant solution was heated at 60 °C for 16 h, then allowed to cool to rt and then cooled to 0 °C. 2 M aq NaOH (5 mL) was then added dropwise and the resultant mixture was heated at 60 °C for 3 h. The resultant mixture was allowed to cool to rt, filtered through a plug of Celite® (eluent CH_2Cl_2), and the filtrate was concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 97:3:0.5) gave (1*S*,2*S*)-**15** as a yellow oil (300 mg, 73%, >180:1 dr, 99.1% ee); $[\alpha]_D^{25}$ +124.9 (*c* 1.0 in $CHCl_3$).

Analysis of (1*S*,2*S*)-**15** by chiral HPLC [Chiralpak AD-H, mobile phase: hexane/^{i}PrOH (v/v, 95:5), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*S*,2*S*)-**15** to be assessed as 99.1% ee [(1*S*,2*S*)-**15** t_R = 15.8 min].

(*RS*,*RS*)-2-(*N*,*N*-Dibenzylamino)cyclohex-3-en-1-ol (±)-16. BnBr (7.00 mL, 59.1 mmol), ^{i}Pr$_2$NEt (10.3 mL, 59.1 mmol) and DMAP (48 mg, 0.394 mmol) were added sequentially to a stirred solution of (±)-**15** (8.00 g, 39.4 mmol, >180:1 dr) in CH_2Cl_2 (113 mL) at rt and the resultant solution was stirred at rt for 24

h, then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 95:5) gave (±)-**16** as a white solid (10.0 g, 86%, >180:1 dr); mp 60–63 °C; ν_{max} 3100, 2830, 1660; δ_H (500 MHz, $CDCl_3$) 1.40–1.53 (1H, m, C(6)H_A), 1.93–2.00 (1H, m, C(6)H_B), 2.05–2.13 (2H, m, C(5)H_2), 2.91 (1H, s, O*H*), 3.11–3.18 (1H, m, C(2)*H*), 3.46 (2H, d, *J* 13.3, N(CH_AH$_B$Ph)$_2$), 3.67 (1H, ddd, *J* 11.9, 8.7, 3.7, C(1)*H*), 3.80 (2H, d, *J* 13.3, N(CH$_A$$H_B$Ph)$_2$), 5.70–5.84 (2H, m, C(3)*H*, C(4)*H*), 7.17–7.33 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 24.9 (*C*(5)), 28.9 (*C*(6)), 54.5 (N(*C*H$_2$Ph)$_2$), 63.1 (*C*(2)), 67.7 (*C*(1)), 123.3 (*C*(3)), 127.2, 128.4, 128.9 (*o*,*m*,*p*-*Ph*), 130.4 (*C*(4)), 139.6 (*i*-*Ph*); *m/z* (ESI$^+$) 294 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{24}NO^+$ ([M+H]$^+$) requires 294.1852; found 294.1848.

(1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*-Benzylamino)-4-tosyloxycyxlohexan-1,3-diol (±)-17. Anhydrous TsOH (25.4 g, 148 mmol) was added to a stirred solution of (±)-**15** (6.00 g, 29.5 mmol, >180:1 dr) in CH_2Cl_2 (82 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (72% wt, 11.3 g, 47.3 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant suspension was diluted with CH_2Cl_2 (50 mL), washed with 0.1 M aq $NaHCO_3$ (4 × 50 mL), dried and concentrated in vacuo to give (±)-**17** as a beige solid (10.2 g, 88%, >95:5 dr); mp 136–140 °C; ν_{max} 3323, 3033, 2942; δ_H (400 MHz, $CDCl_3$) 1.53–1.93 (4H, m, C(6)H_2, C(5)H_2), 2.46 (3H, s, Ar*Me*), 2.74 (1H, dd, *J* 10.0, 3.2, C(2)*H*), 3.59 (1H, app td, *J* 10.0, 4.4, C(1)*H*), 3.66 (1H, d, *J* 13.2, NCH_AH$_B$Ph), 3.80 (1H, d, *J* 13.2, NCH$_A$$H_B$Ph), 3.96–4.00 (1H, m, C(3)*H*), 4.68–4.73 (1H, m, C(4)*H*), 7.25–7.40 (7H, m, *Ar*, *Ph*), 7.77–7.83 (2H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 21.7 (*Me*), 24.1 (*C*(5)), 27.5 (*C*(6)), 50.8 (N*C*H$_2$Ph), 61.5 (*C*(2)), 66.7 (*C*(3)), 68.2 (*C*(1)), 78.8 (*C*(4)), 127.3, 127.7, 128.1, 128.6, 129.9, 133.7, 139.6, 144.9 (*Ar*, *Ph*); *m/z* (ESI$^+$) 392 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_5S^+$ ([M+H]$^+$) requires 392.1526; found 392.1522.

(1*R*,2*S*,3*S*,4*S*)-2-(*N*-Benzylamino)-4-tosyloxycyclohexan-1,3-diol (1*R*,2*S*,3*S*,4*S*)-17. Anhydrous TsOH (380 mg, 2.22 mmol) was added to a stirred solution of (1*R*,2*R*)-**15** (90 mg, 0.44 mmol, >180:1 dr) in CH_2Cl_2 (1.2 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 160 mg, 0.709 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant suspension was diluted with CH_2Cl_2 (10 mL), washed with 0.1 M aq $NaHCO_3$ (4 × 10 mL), dried and concentrated in vacuo to give (1*R*,2*S*,3*S*,4*S*)-**17** as a white powder (120 mg, 70%, >95:5 dr); mp 138–140 °C; $[\alpha]_D^{25}$ −26.7 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*RS*)-2-(*N*-Benzylamino)-3,4-epoxycyclohexan-1-ol (±)-18. DBU (280 μL, 1.93 mmol) was added to a stirred solution of (±)-**17** (700 mg, 1.79 mmol, >95:5 dr) in CH_2Cl_2 (5.2 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column

chromatography (eluent $CHCl_3$/MeOH, 95:5) gave (±)-**18** as a colourless oil (390 mg, 99%, >99:1 dr); ν_{max} 3320, 2981, 2939, 2890; δ_H (400 MHz, $CDCl_3$) 1.37 (1H, dtd, *J* 11.3, 13.0, 7.0, C(6)H_A), 1.73–1.82 (1H, m, C(6)H_B), 1.90–2.00 (1H, m, C(5)H_A), 2.02–2.11 (1H, m, C(5)H_B), 2.72 (1H, dd, *J* 8.1, 2.0, C(2)*H*), 3.31 (1H, app t, *J* 4.4, C(4)*H*), 3.39–3.42 (1H, m, C(3)*H*), 3.51 (1H, ddd, *J* 11.3, 8.1, 3.2, C(1)*H*), 3.90 (1H, d, *J* 13.1, NCH_AH$_B$Ph), 4.11 (1H, d, 13.1, NCH$_A$$H_B$Ph), 7.25–7.41 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 22.3 (*C*(5)), 28.0 (*C*(6)), 50.8 (N*C*H$_2$Ph), 54.5 (*C*(4)), 54.5 (*C*(3)), 61.0 (*C*(2)), 68.1 (*C*(1)), 127.2, 128.1, 128.5 (*o*,*m*,*p-Ph*), 140.1 (*i-Ph*); *m/z* (CI^+) 220 ([M+H]$^+$, 100%); HRMS (CI^+) $C_{13}H_{18}NO_2^+$ ([M+H]$^+$) requires 220.1332; found 220.1332.

(1*R*,2*S*,3*S*,4*R*)-2-(*N*-Benzylamino)-3,4-epoxycyclohexan-1-ol (1*R*,2*S*,3*S*,4*R*)-18. DBU (300 μL, 1.99 mmol) was added to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**17** (720 mg, 1.84 mmol, >95:5 dr) in CH_2Cl_2 (3.8 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH 95:5) gave (1*R*,2*S*,3*S*,4*R*)-**18** as a colourless oil (300 mg, 74%, >99:1 dr); $[\alpha]_D^{25}$ −136.2 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*-Benzylamino)cyclohexane-1,3,4-triol (±)-20. *Method A. Epoxidation of (±)-***15** *in the presence of Cl_3CCO_2H. Step 1.* Anhydrous Cl_3CCO_2H (1.00 g, 6.15 mmol) was added to a stirred solution of (±)-**15** (250 mg, 1.23 mmol, >180:1 dr) in CH_2Cl_2 (3.4 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 452 mg, 1.97 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant suspension was diluted with CH_2Cl_2 (30 mL), washed with 0.1 M aq $NaHCO_3$ (4 × 20 mL), dried and concentrated in vacuo to give (±)-**19** as a beige solid (370 mg, >95:5 dr); δ_H (400 MHz, $CDCl_3$) 1.49–1.91 (4H, m, C(6)H_2, C(5)H_2), 2.82 (1H, dd, *J* 9.5, 2.9, C(2)*H*), 3.74–3.84 (1H, m, C(1)*H*), 3.92 (1H, d, *J* 13.2, NCH_AH$_B$Ph), 4.01 (1H, m, *J* 13.2, NCH$_A$$H_B$Ph), 4.10–4.16 (1H, m, C(3)*H*), 5.09–5.17 (1H, m, C(4)*H*), 7.23–7.42 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 22.9 (*C*(5)), 27.8 (*C*(6)), 50.7 (N*C*H$_2$Ph), 61.3 (*C*(2)), 65.7 (*C*(3)), 67.8 (*C*(1)), 76.4 (*C*(4)), 89.7 (*C*Cl_3), 128.1, 128.3, 128.6 (*o*,*m*,*p-Ph*), 138.4 (*i-Ph*), 160.8 (*C*OCCl_3).

Step 2. K_2CO_3 (296 mg) was added to a stirred solution of the residue from the previous step (370 mg) in MeOH (15 mL) at rt and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. 2 M aq NaOH (30 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 50 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (±)-**20** as a pale yellow powder (166 mg, 57%, >99:1 dr); mp 136–138 °C; ν_{max} 3180, 2918, 2872; δ_H (500 MHz, $CDCl_3$) 1.67–1.75 (2H, m, C(5)H_A, C(6)H_A), 1.77–1.84 (1H, m, C(5)H_B), 1.87–1.95 (1H, m, C(6)H_B), 2.85 (1H, dd,

J 8.2, 3.5, C(2)*H*), 3.69–3.74 (1H, m, C(3)*H*), 3.76 (1H, d, *J* 13.1, NC*H*$_A$H$_B$Ph), 3.87 (1H, d, *J* 13.1, NCH$_A$*H*$_B$Ph), 3.89–3.93 (1H, m, C(1)*H*), 3.96–3.99 (1H, m, C(4)*H*), 7.27–7.36 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 26.1 (*C*(5)), 27.4 (*C*(6)), 51.3 (N*C*H$_2$Ph), 62.0 (*C*(2)), 68.8 (*C*(3)), 69.3 (*C*(4)), 69.7 (*C*(1)), 127.2, 128.1, 128.5 (*o,m,p-Ph*), 140.1 (*i-Ph*); *m/z* (ESI$^+$) 238 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{20}NO_3^+$ ([M+H]$^+$) requires 238.1438; found 238.1441.

*Method B. Epoxidation of (±)-**15** in the presence of aq HBF$_4$.* HBF_4 (40% aq, 960 μL, 6.15 mmol) was added to a stirred solution of (±)-**15** (250 mg, 1.23 mmol, >180:1 dr) in CH_2Cl_2 (3.4 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 452 mg, 1.97 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. 2 M aq NaOH (20 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 30 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (±)-**20** as a pale yellow powder (220 mg, 75%, >99:1 dr).

*Method C. Ring-opening of epoxide (±)-**18** by aq HBF$_4$.* HBF_4 (40% aq, 0.46 mL, 2.97 mmol) was added to a stirred solution of (±)-**18** (130 mg, 0.593 mmol, >99:1 dr) in CH_2Cl_2 (1.6 mL) at rt and the resultant mixture was stirred at rt for 21 h. 2 M aq NaOH (5 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 30 mL). The combined organic extracts were dried and concentrated in vacuo to give a (±)-**20** as a yellow pale solid (70 mg, 50%, >99:1 dr).

*Method D. Ring-opening of epoxide (±)-**18** by Cl$_3$CCO$_2$H.* Anhydrous Cl_3CCO_2H (490 mg, 2.97 mmol) was added to a stirred solution of (±)-**18** (130 mg, 0.593 mmol, >99:1 dr) in CH_2Cl_2 (1.6 mL) at rt and the resultant solution was stirred at rt for 21 h. MeOH (8.2 mL) and K_2CO_3 (160 mg) were then added and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. 2 M aq NaOH (3 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 5 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (±)-**20** as a pale yellow powder (91 mg, 65%, >99:1 dr).

(1*R*,2*S*,3*S*,4*S*)-2-(*N*-Benzylamino)cyclohexane-1,3,4-triol (1*R*,2*S*,3*S*,4*S*)-20. HBF_4 (40% aq, 640 μL, 4.92 mmol) was added to a stirred solution of (1*R*,2*R*)-**15** (200 mg, 0.985 mmol, >180:1 dr) in CH_2Cl_2 (2.7 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 360 mg, 1.58 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. 2 M aq NaOH (20 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 30 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent

$CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (1*R*,2*S*,3*S*,4*S*)-**20** as a white powder (130 mg, 56%, >99:1 dr); mp 139–143 °C; $[\alpha]_D^{25}$ −14.8 (*c* 0.75 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*,*N*-Dibenzylamino)-4-tosyloxycyxlohexan-1,3-diol (±)-21. Anhydrous TsOH (445 mg, 2.59 mmol) was added to a stirred solution of (±)-**23** (160 mg, 0.517 mmol, >99:1 dr) in CH_2Cl_2 (1.4 mL) at rt and the resultant solution was stirred at rt for 21. The resultant solution was washed with 0.1 M aq $NaHCO_3$ (5 × 15 mL), dried and concentrated in vacuo to give (±)-**21** as a beige solid (180 mg, 72%, >95:5 dr); mp 133–135 °C; ν_{max} 3381, 3062, 3028, 2942; δ_H (400 MHz, $CDCl_3$) 1.24–1.42 (1H, m, C(6)H_A), 1.51–1.61 (1H, m, C(5)H_A), 1.71–1.75 (1H, m, O*H*), 1.84–1.96 (2H, m, C(5)H_B, C(6)H_B) 2.47 (3H, s, Ar*Me*), 2.79 (1H, dd, *J* 10.6, 1.9, C(2)*H*), 3.38 (1H, s, O*H*), 3.61 (2H, d, *J* 13.6, N(C$H_A$$H_B$Ph)$_2$), 4.03 (1H, app td, *J* 10.6, 4.3, C(1)*H*), 4.12 (2H, d, *J* 13.6, N(CH_AH_BPh)$_2$), 4.54–4.64 (2H, m, C(3)*H*, C(4)*H*), 7.22–7.39 (12H, m, *Ar*, *Ph*), 7.69–7.75 (2H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 21.6 (*Me*), 23.2 (*C*(5)), 27.8 (*C*(6)), 54.5 (N(*C*H_2Ph)$_2$), 60.4 (*C*(2)), 63.0 (*C*(3)), 67.0 (*C*(1)), 79.6 (*C*(4)), 127.2, 127.5, 128.5, 129.0, 129.8, 133.7, 139.3, 144.9 (*Ar*, *Ph*); *m/z* (ESI^+) 482 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{27}H_{32}NO_5S^+$ ($[M+H]^+$) requires 482.1996; found 485.1995.

(1*R*,2*S*,3*S*,4*S*)-2-(*N*,*N*-Dibenzylamino)-4-tosyloxycyxlohexan-1,3-diol (1*R*,2*S*,3*S*,4*S*)-21. *Method A. From (1R,2S,3S,4S)-**17**. Step 1.* BnBr (170 μL, 1.53 mmol), $^iPr_2NEt$ (270 μL, 1.53 mmol) and DMAP (1.2 mg, 0.01 mmol) were added sequentially to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**17** (400 mg, 1.02 mmol, >95:5 dr) in CH_2Cl_2 (2.9 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1), gave a 70:30 mixture of (1*R*,2*S*,3*S*,4*S*)-**21** and (1*R*,2*S*,3*S*,4*R*)-**23**, respectively, as a white solid (270 mg).

Step 2. Anhydrous TsOH (167 mg, 0.970 mmol) was added to a stirred solution of the residue from the previous step (270 mg) in CH_2Cl_2 (1.4 mL) at rt and the resultant solution was stirred at rt for 21 h. The resultant solution was washed with 0.1 M aq $NaHCO_3$ (5 × 20 mL), dried and concentrated in vacuo to give (1*R*,2*S*,3*S*,4*S*)-**21** as a yellow pale solid (251 mg, 51%, >95:5 dr).

*Method B. From (1R,2S,3S,4R)-**23**.* Anhydrous TsOH (292 mg, 1.70 mmol) was added to a stirred solution of (1*R*,2*S*,3*S*,4*R*)-**23** (105 mg, 0.340 mmol, >99:1 dr) in CH_2Cl_2 (0.94 mL) at rt and the resultant solution was stirred at rt for 21 h. The resultant solution was washed with 0.1 M aq $NaHCO_3$ (5 × 10 mL), dried and concentrated in vacuo to give (1*R*,2*S*,3*S*,4*S*)-**21** as a pale yellow solid (110 mg, 67%, >95:5 dr); mp 144–151 °C; $[\alpha]_D^{25}$ −58.5 (*c* 0.75 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*RS*)-2-(*N*,*N*-Dibenzylamino)-3,4-epoxycyclohexan-1-ol (±)-23 and (1*RS*,2*SR*,3*RS*,4*SR*)-2-(*N*,*N*-dibenzylamino)-3,4-epoxycyclohexan-1-ol (±)-24. *Step 1.* Anhydrous TsOH (2.26 g, 12.8 mmol) was added to a stirred solution of (±)-**16** (750 mg, 2.56 mmol, >180:1 dr) in CH_2Cl_2 (7.1

mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 2.93 g, 12.8 mmol) was then added and the resultant solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant suspension was diluted with CH_2Cl_2 (20 mL), washed with 0.1 M aq $NaHCO_3$ (4 × 30 mL), dried and concentrated in vacuo. Filtration through a plug of silica gel (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave a 47:53 mixture of (±)-**21** and (±)-**22**, respectively, as an orange oil (500 mg); ν_{max} 3385, 3028; *m/z* (ESI^+) 482 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{27}H_{32}NO_5S^+$ ($[M+H]^+$) requires 482.1996; found 482.1987. Data for (±)-**21**: δ_H (400 MHz, $CDCl_3$) [selected peaks][37] 1.24–1.48 (1H, m, C(6)H_A), 1.52–1.59 (1H, m, C(5)H_A) 1.84–2.00 (2H, m, C(5)H_B, C(6)H_B), 2.79 (1H, dd, *J* 10.5, 2.0, C(2)*H*), 3.61 (2H, d, *J* 13.7, N(C$H_A$$H_B$Ph)$_2$), 4.07 (1H, app dt, *J* 10.5, 4.2, C(1)*H*), 3.13 (2H, d, *J* 13.7, N(C$H_A$$H_B$Ph)$_2$), 4.59–4.66 (2H, m, C(3)*H*, C(4)*H*); δ_C (100 MHz, $CDCl_3$) 21.6 (*Me*), 23.2 (*C*(5)), 27.8 (*C*(6)), 52.0 (N(*C*H_2Ph)$_2$), 60.4 (*C*(2)), 62.9 (*C*(1)), 67.0 (*C*(3)), 79.6 (*C*(4)). Data for (±)-**22**: δ_H (400 MHz, $CDCl_3$) [selected peaks][37] 1.04–1.17 (1H, m, C(6)H_A), 1.24–1.48 (1H, m, C(5)H_A), 1.84–2.00 (2H, m, C(5)H_B, C(6)H_B), 2.45 (1H, app t, *J* 10.4, C(2)*H*), 3.38 (1H, app dt, *J* 10.4, 4.4, C(1)*H*), 3.86–3.94 (5H, m, C(3)*H*, N(CH_2Ph)$_2$), 4.40 (1H, ddd, *J* 11.6, 8.6, 5.0, C(4)*H*); δ_C (100 MHz, $CDCl_3$) 21.6 (*Me*), 26.5 (*C*(5)), 28.4 (*C*(6)), 54.4 (N(*C*H_2Ph)$_2$), 65.5 (*C*(2)), 66.9 (*C*(1)), 72.3 (*C*(3)), 85.0 (*C*(4)).

Step 2. DBU (170 μL, 1.12 mmol) was added to a stirred solution of the residue from the previous step (500 mg) in CH_2Cl_2 (2.1 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave a 47:53 mixture of (±)-**23** and (±)-**24**, respectively, as a yellow oil (300 mg, 38%); ν_{max} 3479, 3027, 2940, 2841; *m/z* (ESI^+) 310 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{20}H_{24}NO_2^+$ ($[M+H]^+$) requires 310.1802; found 310.1799.

(1*RS*,2*SR*,3*SR*,4*RS*)-2-(*N*,*N*-Dibenzylamino)-3,4-epoxycyclohexan-1-ol (±)-23. BnBr (3.25 mL, 27.4 mmol), $^iPr_2NEt$ (4.80 mL, 27.4 mmol) and DMAP (22.3 mg, 0.183 mmol) were added sequentially to a stirred solution of (±)-**18** (4.00 g, 18.3 mmol, >99:1 dr) in CH_2Cl_2 (52 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave (±)-**23** as a colourless oil (6.60 g, quant, >99:1 dr); ν_{max} 3487, 2981, 2890; δ_H (400 MHz, $CDCl_3$) 1.19–1.31 (1H, m, C(6)H_A), 1.79–2.06 (3H, m, C(5)H_2, C(6)H_B), 2.80 (1H, dd, *J* 9.3, 1.1, C(2)*H*), 3.07 (1H, s, O*H*), 3.18 (1H, app t, *J* 4.2, C(4)*H*), 3.43 (1H, dd, *J* 4.2, 1.1, C(3)*H*), 3.62 (2H, d, *J* 13.7, N(C$H_A$$H_B$Ph)$_2$), 3.82 (1H, ddd, *J* 12.5, 9.3, 3.4, C(1)*H*), 4.13 (2H, d, 13.7, N(C$H_A$$H_B$Ph)$_2$), 7.24–7.37 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 22.5 (*C*(5)), 29.1 (*C*(6)), 51.5 (*C*(4)), 52.0 (*C*(3)), 54.8 (N(*C*H_2Ph)$_2$), 62.8 (*C*(2)), 63.9 (*C*(1)), 127.3, 128.5, 128.9 (*o*,*m*,*p*-*Ph*), 139.1 (*i*-*Ph*); *m/z* (ESI^+) 310 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{20}H_{24}NO_2^+$ ($[M+H]^+$) requires 310.1802; found 310.1801.

(1*R*,2*S*,3*S*,4*R*)-2-(*N*,*N*-Dibenzylamino)-3,4-epoxycyclohexan-1-ol (1*R*,2*S*,3*S*,4*R*)-23. BnBr (320 μL, 2.67 mmol), $^{i}Pr_2NEt$ (470 μL, 2.67 mmol) and DMAP (2.2 mg, 0.018 mmol) were added sequentially to a stirred solution of (1*R*,2*S*,3*S*,4*R*)-**18** (350 mg, 1.78 mmol, >99:1 dr) in CH_2Cl_2 (5.1 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave (1*R*,2*S*,3*S*,4*R*)-**23** as a colourless oil (470 mg, 95%, >99:1 dr); $[\alpha]_D^{25}$ −149.3 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*SR*,3*RS*,4*SR*)-2-(*N*,*N*-Dibenzylamino)-3,4-epoxycyclohexan-1-ol (±)-24, (1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*,*N*-dibenzylamino)cyclohexane-1,3,4-triol (±)-25, and (1*RS*,2*SR*,3*RS*,4*RS*)-2-(*N*,*N*-dibenzylamino)cyclohexane-1,3,4-triol (±)-26. Anhydrous Cl_3CCO_2H (1.40 g, 8.53 mmol) was added to a stirred solution of (±)-**16** (500 mg, 1.71 mmol, >180:1 dr) in CH_2Cl_2 (4.7 mL) at rt and the resultant solution was stirred at rt for 5 min. *m*-CPBA (75% wt, 1.95 g, 8.53 mmol) was then added and the solution was stirred at rt for 21 h. Solid Na_2SO_3 was added until starch-iodide paper indicated that no *m*-CPBA was present. MeOH (23.7 mL) and K_2CO_3 (470 mg) were then added and the resultant suspension was stirred at rt for 48 h, then concentrated in vacuo. 2 M aq NaOH (30 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 30 mL). The combined organic extracts were dried and concentrated in vacuo to give incomplete conversion to a 28:43:29 mixture of (±)-**24**, (±)-**25** and (±)-**26**, respectively. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 95:5:0.5) gave a mixture of (±)-**16**, (±)-**24** and (±)-**26**, respectively (346 mg). Further elution gave (±)-**25** as a white solid (200 mg, 36%, >99:1 dr); mp 193–197 °C; ν_{max} 3265, 3028, 2937, 2848; δ_H (400 MHz, $CDCl_3$) 1.43–1.67 (2H, m, C(5)H_A, C(6)H_A), 1.88–2.00 (2H, m, C(5)H_B, C(6)H_B), 2.87 (1H, dd, *J* 10.3, 1.5, C(2)*H*), 3.67 (2H, d, *J* 13.8, N(CH_AH$_B$Ph)$_2$), 3.86–3.92 (1H, m, C(4)*H*), 4.07 (1H, app dt, *J* 10.5, 4.4, C(1)*H*), 4.13 (2H, d, *J* 13.8, N(CH$_A$$H_B$Ph)$_2$), 4.31–4.36 (1H, m, C(3)*H*), 7.21–7.37 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*(5)), 27.9 (*C*(6)), 54.7 (N(*C*H$_2$Ph)$_2$), 60.9 (*C*(2)), 63.8 (*C*(1)), 69.6 (*C*(3)), 71.3 (*C*(4)), 127.2, 128.5, 128.9 (*o*,*m*,*p*-*Ph*), 139.6 (*i*-*Ph*); *m/z* (ESI$^+$) 328 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_3^+$ ([M+H]$^+$) requires 328.1907; found 328.1906. Further purification of the mixture of (±)-**16**, (±)-**24** and (±)-**26** via flash column chromatography (eluent $CHCl_3$/35% aq NH_4OH 100:0.5) gave (±)-**16** as a white solid (20 mg, 4%, >99:1 dr). Further elution gave (±)-**24** as a white solid (58 mg, 11%, >99:1 dr); mp 108–112 °C; ν_{max} 3532, 2911, 2806; δ_H (400 MHz, $CDCl_3$) 1.19 (1H, app qd, *J* 12.5, 4.6, C(6)H_A), 1.52–1.61 (1H, m, C(6)H_B), 1.67–1.78 (1H, m, C(5)H_A), 2.03–2.12 (1H, m, C(5)H_B), 2.69 (1H, d, *J* 9.5, C(2)*H*), 3.08–3.13 (2H, m, C(3)*H*, C(4)*H*), 3.38–3.48 (1H, m, C(1)*H*), 3.59 (2H, d, *J* 13.5, N(CH_AH$_B$Ph)$_2$), 3.86 (2H, d, 13.5, N(CH$_A$$H_B$Ph)$_2$), 7.14–7.30 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.3 (*C*(5)), 23.5 (*C*(6)), 50.6 (*C*(3)), 52.9 (*C*(4)), 54.7 (N(*C*H$_2$Ph)$_2$), 62.6 (*C*(2)), 67.2 (*C*(1)), 127.4, 128.5, 128.9 (*o*,*m*,*p*-*Ph*), 138.8

(*i-Ph*); *m/z* (ESI$^+$) 310 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{24}NO_2^+$ ([M+H]$^+$) requires 310.1802; found 310.1800. Further elution gave an impure sample of (±)-**26** as a yellow oil (106 mg, ~18%, >95:5 dr).

(1*R*,2*S*,3*R*,4*S*)-2-(*N*,*N*-Dibenzylamino)-3,4-epoxycyclohexan-1-ol (1*R*,2*S*,3*R*,4*S*)-24. *Step 1.* MsCl (200 μL, 2.48 mmol) was added to a stirred solution of (1*R*,2*R*,3*S*,4*S*)-**34** (340 mg, 0.827 mmol, >99:1 dr) in pyridine (8.2 mL) at 0 °C and the resultant solution was stirred at rt for 16 h, then concentrated in vacuo to give a 10:90 mixture of (1*R*,2*R*,3*S*,4*S*)-**34** and (1*R*,2*S*,3*S*,4*S*)-**35**, respectively.

Step 2. K_2CO_3 (1.5 g) was added to a stirred solution of the residue from the previous step in MeOH (15 mL) and the resultant suspension was stirred at rt for 16 h then concentrated in vacuo. H_2O (15 mL) was added and the resultant mixture was extracted with CH_2Cl_2 (3 ×20 mL). The combined organic extracts were dried and concentrated in vacuo to give a 90:10 mixture of (1*R*,2*S*,3*R*,4*S*)-**24** and (1*R*,2*S*,3*S*,4*S*)-**25**, respectively. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (1*R*,2*S*,3*R*,4*S*)-**24** as an orange solid (190 mg, 74%, >99:1 dr); mp 76–80 °C; $[\alpha]_D^{25}$ −98.0 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*SR*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (±)-25. Anhydrous Cl_3CCO_2H (159 mg, 0.970 mmol) was added to a stirred solution of (±)-**23** (60.0 mg, 0.194 mmol, >99:1 dr) in CH_2Cl_2 (540 μL) at rt and the resultant solution was stirred at rt for 21 h. MeOH (2 mL) and K_2CO_3 (40 mg) were then added and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. 2 M aq NaOH (1.5 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 1.5 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (±)-**25** as a white solid (30 mg, 47%, >99:1 dr).

Analysis of (±)-**25** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 92:8), flow rate: 1 mL/min, 10 μL injection] gave complete resolution of enantiomers [(1*R*,2*S*,3*S*,4*S*)-**25** t_R = 13.9 min; (1*S*,2*R*,3*R*,4*R*)- t_R = 20.8 min].

(1*R*,2*S*,3*S*,4*S*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (1*R*,2*S*,3*S*,4*S*)-25. BnBr (56 μL, 0.47 mmol), ^{i}Pr$_2$NEt (83 μL, 0.47 mmol) and DMAP (0.4 mg, 0.003 mmol) were added sequentially to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**20** (75 mg, 0.32 mmol, >99:1 dr) in CH_2Cl_2 (0.90 mL) at rt and the resultant solution was stirred at rt for 24 h, then concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 90:10:0.5) gave (1*R*,2*S*,3*S*,4*S*)-**25** as a white solid (74 mg, 72%, >99:1 dr, 99.5% ee); mp 203–204 °C; $[\alpha]_D^{25}$ −90.7 (*c* 1.0 in $CHCl_3$).

Analysis of (1*R*,2*S*,3*S*,4*S*)-**25** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 92:8), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*R*,2*S*,3*S*,4*S*)-**25** to be assessed as 99.5% ee [(1*R*,2*S*,3*S*,4*S*)-**25** t_R = 14.2 min].

(1*RS*,2*SR*,3*RS*,4*RS*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (±)-26. *Method A. Ring-opening of epoxide (±)-**24** by aq HBF₄.* HBF_4 (40% aq, 30 μL, 1.3 mmol) was added to a stirred solution of (±)-**24** (80 mg, 0.26 mmol, >99:1 dr) in CH_2Cl_2 (0.72 mL) at rt and the resultant solution was stirred at 40 °C for 24 h. 2 M aq NaOH (10 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 15 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (±)-**26** as a white solid (60 mg, 71%, >99:1 dr); mp 158–166 °C; ν_{max} 3403, 3062, 3028, 2934, 2868; δ_H (400 MHz, $CDCl_3$) 1.16–1.38 (2H, m, C(5)H_A, C(6)H_A), 1.85–2.02 (2H, m, C(5)H_B, C(6)H_B), 2.29 (1H, br s, O*H*), 2.43 (1H, app t, *J* 10.2, C(2)*H*), 2.85 (1H, br s, O*H*), 3.03 (1H, br s, O*H*), 3.41 (1H, app td, *J* 9.4, 8.6, 4.5, C(4)*H*), 3.52 (1H, dd, *J* 10.2, 8.6, C(3)*H*), 4.62 (1H, app td, *J* 10.2, 4.5, C(1)*H*), 4.93 (4H, app s, N(CH_2Ph)$_2$), 7.12–7.46 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 28.5 (*C*(5)), 30.0 (*C*(6)), *55** (N(*C*H_2Ph)$_2$), 65.4 (*C*(2)), 68.6 (*C*(1)), 74.4 (*C*(4)), 74.8 (*C*(3)), 127.3, 128.5, 129.3 (*o*,*m*,*p-Ph*), 139.5 (*i-Ph*);[39] *m/z* (ESI$^+$) 328 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_3^+$ ([M+H]$^+$) requires 328.1907; found 328.1910.

Analysis of (±)-**26** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 90:10), flow rate: 1 mL/min, 10 μL injection] gave complete resolution of enantiomers [(1*S*,2*R*,3*S*,4*S*)-**26** t_R = 11.7 min; (1*R*,2*S*,3*R*,4*R*)-**26** t_R = 18.6 min].

*Method B. Ring-opening of epoxide (±)-**24** by Cl_3CCO_2H.* Anhydrous Cl_3CCO_2H (251 mg, 1.54 mmol) was added to a stirred solution of **24** (95.1 mg, 0.307 mmol, >99:1 dr) in CH_2Cl_2 (0.85 mL) at rt and the resultant solution was stirred at rt for 21 h. MeOH (4.3 mL) and K_2CO_3 (85 mg) were then added and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. 2 M aq NaOH (5 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 10 mL). The combined organic extracts were dried and concentrated in vacuo to give a 4:96 mixture of **25** and **26** as a white solid (71 mg, 71%).

(1*R*,2*S*,3*R*,4*R*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (1*R*,2*S*,3*R*,4*R*)-26. HBF_4 (40% aq, 60 μL, 2.3 mmol) was added to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**24** (0.14 g, 0.45 mmol, >99:1 dr) in CH_2Cl_2 (1.25 mL) at rt and the resultant solution was stirred at 40 °C for 24 h. 2 M aq NaOH (10 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 15 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (1*R*,2*S*,3*R*,4*R*)-**26** as a colourless oil (110 mg, 74%, >99:1 dr, 98.2% ee); $[\alpha]_D^{25}$ −44.7 (*c* 1.0 in $CHCl_3$).

Analysis of (1*R*,2*S*,3*R*,4*R*)-**26** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 90:10), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*R*,2*S*,3*R*,4*R*)-**26** to be assessed as 98.2% ee [(1*R*,2*S*,3*R*,4*R*)-**26** t_R = 19.0 min].

(1*R*,2*R*,α*R*)-2-[(*N*-(α-Methylbenzyl)amino]cyclohex-3-en-1-ol 27 and (1*S*,2*S*,α*R*)-2-[(*N*-(α-methylbenzyl)amino]cyclohex-3-en-1-ol 28. *Step 1*. AcOOH (39% in AcOH, 31.2 mL, 125 mmol) was added dropwise to a stirred suspension of **13** (10.0 g, 125 mmol) and Na_2CO_3 (119 g, 1.12 mol) in CH_2Cl_2 (350 mL) at 0 °C and the resultant suspension was stirred at 0 °C for 3.5 h. H_2O (200 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organics were washed with satd aq Na_2SO_3 (in 500 mL portions) until starch-iodide paper indicated that no peroxide was present, then dried and concentrated in vacuo at 0 °C to give **14** as a colourless oil (13.0 g).

Step 2. (*R*)-α-Methylbenzylamine (16.1 mL, 125 mmol) was added to a stirred solution of the residue from the previous step (13.0 g) in ^{i}PrOH (125 mL) at rt and the resultant solution was heated at 80 °C for 4 h, then allowed to cool to rt and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH 98:2:0.5) gave a 50:50 mixture of **27** and **28**, respectively, as a beige solid (14.5 g, 53% from **13**).[26] Data for **27**: δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.6, C(α)*Me*), 1.60–1.69 (1H, m, C(6)H_A), 1.91–2.04 (1H, m, C(6)H_B), 2.08–2.15 (2H, m, C(5)H_2), 3.05–3.11 (1H, m, C(2)*H*), 3.35–3.44 (1H, m, C(1)*H*), 3.98 (1H, q, *J* 6.6, C(α)*H*), 5.41–5.46 (1H, m, C(3)*H*), 5.60–5.70 (1H, m, C(4)*H*), 7.22–7.38 (5H, m, *Ph*). Data for **28**: δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.6, C(α)*Me*), 1.41–1.52 (1H, m, C(6)H_A), 1.91–2.04 (1H, m, C(6)H_B), 2.08–2.15 (2H, m, C(5)H_2), 2.71–2.77 (1H, m, C(2)*H*), 3.35–3.44 (1H, m, C(1)*H*), 4.05 (1H, q, *J* 6.6, C(α)*H*), 5.60–5.70 (1H, m, C(4)*H*), 5.73–5.78 (1H, m, C(3)*H*), 7.22–7.38 (5H, m, *Ph*).

(1*R*,2*R*,α*R*)-2-[(*N*-Benzoyl-*N*-α-methylbenzyl)amino]cyclohex-3-en-1-ol 29 and (1*S*,2*S*,α*R*)-2-[(*N*-benzoyl-*N*-α-methylbenzyl)amino]cyclohex-3-en-1-ol 30. Na_2CO_3 (4.40 g, 41.4 mmol) and benzoyl chloride (2.40 mL, 20.7 mmol) were added sequentially to a stirred solution of a 50:50 mixture of **27** and **28** (4.50 g, 20.7 mmol) in THF (100 mL) at 0 °C and the resultant solution was stirred at rt for 24 h. H_2O (50 mL) was then added and the aqueous layer was extracted with Et_2O (3 × 60 mL). The combined organic layers were washed with brine (300 mL), then dried, filtered and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave **29** as a pale yellow solid (2.50 g, 38%, >95:5 dr); mp 148–150 °C; $[\alpha]_D^{25}$ −69.9 (*c* 1.0 in $CHCl_3$); ν_{max} 3393, 3059, 3026, 2939, 1616; δ_H (500 MHz, d_8-PhMe, 363 K) 1.08–1.18 (1H, m, C(6)H_A), 1.50–1.56 (1H, m, C(6)H_B), 1.60–1.80 (5H, m, C(5)H_2, C(α)*Me*), 3.69–3.78 (1H, m, C(1)*H*), 4.18–4.24 (1H, m, C(2)*H*), 4.52–4.60 (1H, m, C(α)*H*),

5.36–5.42 (1H, m, C(3)*H*), 5.45–5.51 (1H, m, C(4)*H*), 6.90–7.12 (6H, m, *Ph*), 7.27–7.33 (2H, m, *Ph*), 7.42–7.49 (2H, m, *Ph*); δ_C (125 MHz, d_8-PhMe, 363 K) 20.5[38] (C(α)*Me*), 25.1 (*C*(5)), 31.2 (*C*(6)), 56.2 (*C*(α)), 64.3 (*C*(2)), 69.0 (*C*(1)), 127.3 (*C*(3)), 127.3, 128.2,[38] 128.4, 128.8[38] (*Ph*), 130.7 (*C*(4)), 139.7, 144.0 (*Ph*), 172.6 (*C*OPh); *m/z* (ESI$^+$) 322 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{21}H_{24}NO_2^+$ ([M+H]$^+$) requires 322.1802; found 322.1801. Further elution gave **30** as a pale yellow powder (2.50 g, 38%, >95:5 dr); mp 68–72 °C; $[\alpha]_D^{25}$ +163.9 (*c* 1.0 in $CHCl_3$); ν_{max} 3393, 3029, 2937, 1614; δ_H (500 MHz, d_8-PhMe, 363 K) 1.21–1.35 (1H, m, C(6)H_A), 1.63–1.79 (5H, m, C(6)H_B, C(5)H_A, C(α)*Me*) 1.83–1.96 (1H, m, C(5)H_B), 3.99–4.14 (2H, m, C(1)*H*, C(2)*H*), 4.80–4.92 (1H, m, C(α)*H*), 5.19–5.30 (1H, m, C(3)*H*), 5.32–5.43 (1H, m, C(4)*H*), 6.93–7.16 (6H, m, *Ph*), 7.29–7.41 (4H, m, *Ph*); δ_C (125 MHz, d_8-PhMe, 363 K) 19.0 (C(α)*Me*), 25.2 (*C*(5)), 32.2 (*C*(6)), 56.0 (*C*(α)), 62.8 (*C*(1)), 68.4 (*C*(2)), 127.3 (*C*(4)), 127.5, 128.2 (*Ph*), 128.5 (*C*(3)), 128.6, 128.9,[38] 139.7, 142.6 (*Ph*), 171.7 (*C*OPh); *m/z* (ESI$^+$) 322 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{21}H_{24}NO_2^+$ ([M+H]$^+$) requires 322.1802; found 322.1801.

(1*R*,2*R*)-1-Formyloxy-2-(*N*-benzoylamino)cyclohex-3-ene (1*R*,2*R*)-31. A stirred solution of **29** (6.50 g, 20.2 mmol, >95:5 dr) in HCO_2H (90% aq, 195 mL) was heated at 60 °C for 18 h, then allowed to cool to rt and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/acetone, 9:1) gave (1*R*,2*R*)-**31** as a pale yellow solid (4.70 g, 94%, >95:5 dr); mp 139–145 °C; $[\alpha]_D^{25}$ −126.2 (*c* 1.0 in $CHCl_3$); ν_{max} 3270, 2921, 1712, 1640; δ_H (400 MHz, $CDCl_3$) 1.97–2.05 (2H, m, C(6)H_2), 2.24–2.31 (2H, m, C(5)H_2), 4.84–4.92 (1H, m, C(2)*H*), 5.14–5.22 (1H, m, C(1)*H*), 5.59–5.65 (1H, m, C(3)*H*), 5.85–5.92 (1H, m, C(4)*H*), 6.20–6.29 (1H, m, N*H*), 7.42–7.47 (2H, m, *Ph*), 7.49–7.54 (1H, m, *Ph*), 7.74–7.78 (2H, m, *Ph*), 8.12 (1H, s, C*H*O); δ_C (100 MHz, $CDCl_3$) 23.7 (*C*(5)), 26.2 (*C*(6)), 50.6 (*C*(2)), 72.1 (*C*(1)), 126.1 (*C*(3)), 126.9, 128.5 (*Ph*), 129.4 (*C*(4)), 131.5, 134.0 (*Ph*), 161.1 (*C*HO), 167.1 (N*C*OPh); *m/z* (ESI$^+$) 268 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{14}H_{16}NO_3^+$ ([M+H]$^+$) requires 246.1125; found 246.1127.

(1*S*,2*S*)-1-Formyloxy-2-(*N*-benzoylamino)cyclohex-3-ene (1*S*,2*S*)-31. A stirred solution of **30** (1.00 g, 3.11 mmol, >95:5 dr) in HCO_2H (90% aq, 15 mL) was heated at 60 °C for 18 h, then allowed to cool to rt and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/acetone, 9:1) gave (1*S*,2*S*)-**31** as a pale yellow solid (530 mg, 69%, >95:5 dr); mp 140–146 °C; $[\alpha]_D^{25}$ +130.6 (*c* 1.0 in $CHCl_3$).

(1*R*,2*S*,3*S*,4*S*)-2-Aminocyclohexane-1,3,4-triol [(−)-Dihydroconduramine A-2] 32. $Pd(OH)_2$/C (50% wt of substrate, 45 mg) was added to a stirred degassed solution of (1*R*,2*S*,3*S*,4*S*)-**20** (90 mg, 0.38 mmol, >99:1 dr) in MeOH (1 mL) and the resultant suspension was stirred under H_2 (1 atm) at rt for 24 h. The resultant suspension was then filtered through Celite® (eluent MeOH), and the filtrate was concentrated in vacuo to give **32** as a yellow oil (47 mg, 85%, >99:1 dr, 99.5% ee);[29] $[\alpha]_D^{25}$ −25.8 (*c* 1.0 in MeOH); ν_{max}

3348, 2981, 2971, 2933; δ_H (400 MHz, d_4-MeOH) 1.54–1.73 (3H, m, C(5)H_A, C(6)H_2), 1.76–1.88 (1H, m, C(5)H_B), 2.75 (1H, dd, *J* 8.8, 2.7, C(2)*H*), 3.50 (1H, app dt, *J* 9.6, 4.7, C(1)*H*), 3.75–3.81 (2H, m, C(3)*H*, C(4)*H*); δ_C (100 MHz, d_4-MeOH) 27.2 (*C*(5)), 28.7 (*C*(6)), 56.4 (*C*(2)), 70.9 (*C*(4)), 72.0 (*C*(1)), 74.2 (*C*(3)); *m/z* (ESI$^+$) 148 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_6H_{14}NO_3^+$ ([M+H]$^+$) requires 148.0968; found 148.0968.

(1*RS*,2*SR*,3*SR*,4*RS*)-1-Acetoxy-2-(*N*,*N*-dibenzylamino)-3,4-epoxycyclohexane (±)-**33.** Ac_2O (6.00 mL, 64.0 mmol) and DMAP (26.0 mg, 0.213 mmol) were added sequentially to a stirred solution of (±)-**23** (6.60 g, 21.3 mmol, >99:1 dr) in pyridine (89 mL) at rt and the resultant solution was stirred at rt for 24 h. The resultant solution was diluted with CH_2Cl_2 (80 mL) and washed sequentially with H_2O (70 mL), satd aq Na_2CO_3 (70 mL) and brine (50 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave (±)-**33** as a yellow oil (6.8 g, 91%, >99:1 dr); ν_{max} 3027, 2943, 2808, 1739; δ_H (400 MHz, $CDCl_3$) 1.30–1.42 (1H, m, C(6)H_A), 1.71–1.79 (1H, m, C(6)H_B), 1.90–1.97 (2H, m, C(5)H_2), 2.12 (3H, s, CO*Me*), 3.07 (1H, dd, *J* 8.6, 1.7, C(2)*H*), 3.10–3.13 (1H, m, C(4)*H*), 3.40 (1H, dd, *J* 3.9, 1.7, C(3)*H*) 3.81 (2H, d, *J* 13.7, N(CH_AH$_B$Ph)$_2$), 3.90 (2H, d, *J* 13.7, N(CH$_A$$H_B$Ph)$_2$), 5.24 (1H, ddd, *J* 10.5, 8.6, 3.7, C(1)*H*), 7.18–7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.5 (CO*Me*), 22.2 (*C*(5)), 27.9 (*C*(6)), 51.1 (*C*(4)), 54.9 (*C*(3)), 54.9 (N(*C*H$_2$Ph)$_2$), 58.4 (*C*(2)), 68.5 (*C*(1)), 126.8, 128.1, 128.8 (*o*,*m*,*p*-*Ph*), 140.0 (*i*-*Ph*), 170.2 (*C*OMe); *m/z* (ESI$^+$) 352 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{26}NO_3^+$ ([M+H]$^+$) requires 352.1907; found 352.1909.

(1*R*,2*S*,3*S*,4*R*)-1-Acetoxy-2-(*N*,*N*-dibenzylamino)-3,4-epoxycyclohexane (1*R*,2*S*,3*S*,4*R*)-33. Ac_2O (300 μL, 3.12 mmol) and DMAP (1.2 mg, 0.01 mmol) were added sequentially to a stirred solution of (1*R*,2*S*,3*S*,4*R*)-**23** (320 mg, 1.04 mmol, >99:1 dr) in pyridine (4.3 mL) at rt and the resultant solution was stirred at rt for 24 h. The resultant solution was diluted with CH_2Cl_2 (10 mL) and washed sequentially with H_2O (10 mL), satd aq Na_2CO_3 (10 mL) and brine (10 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave (1*R*,2*S*,3*S*,4*R*)-**33** as a colourless oil (310 mg, 85%, >99:1 dr); $[\alpha]_D^{25}$ −24.0 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*RS*,3*SR*,4*SR*)-1,4-Diacetoxy-2-(*N*,*N*-dibenzylamino)cyclohexan-3-ol (±)-34. A stirred solution of (±)-**33** (6.77 g, 19.3 mmol, >99:1 dr) in AcOH (20 mL) was heated at 50 °C for 36 h, then allowed to cool to rt. 0.1 M aq $NaHCO_3$ (50 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were washed with 0.1 M aq $NaHCO_3$ (50 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave (±)-**34** as a pale orange oil (6.5 g, 82%, >99:1 dr); ν_{max} 3499, 3028, 2949, 1734; δ_H (400 MHz, $CDCl_3$) 1.43–1.60 (1H, m, C(5)H_A, C(6)H_A) 1.67 (3H, s, CO*Me*), 1.89–2.00 (2H, m, C(5)H_B, C(6)H_B), 2.15 (3H, s, CO*Me*), 2.95 (1H, dd, *J* 10.8, 2.7, C(2)*H*), 3.74 (2H, d, *J* 13.7, N(CH_AH$_B$Ph)$_2$), 3.98

(2H, d, *J* 13.7, N(CH$_A$*H*$_B$Ph)$_2$), 4.06–4.12 (1H, m, C(3)*H*), 4.69–4.74 (1H, m, C(4)*H*), 5.38–5.47 (1H, m, C(1)*H*), 7.15–7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.8, 21.7 (CO*Me*), 22.8 (*C*(5)), 26.7 (*C*(6)), 56.0 (N(*C*H$_2$Ph)$_2$), 57.3 (*C*(2)), 70.1 (*C*(1)), 71.9 (*C*(3)), 72.2 (*C*(4)), 126.7, 128.2, 128.5 (*o,m,p-Ph*), 140.4 (*i-Ph*), 170.2, 170.4 (*C*OMe); *m/z* (ESI$^+$) 412 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{30}NO_5^+$ ([M+H]$^+$) requires 412.2118; found 412.2118.

(1*R*,2*R*,3*S*,4*S*)-1,4-Diacetoxy-2-(*N*,*N*-dibenzylamino)cyclohexan-3-ol (1*R*,2*R*,3*S*,4*S*)-34. A stirred solution of (1*R*,2*S*,3*S*,4*R*)-**33** (310 mg, 0.854 mmol, >99:1 dr) in AcOH (1 mL) was heated at 50 °C for 36 h, then allowed to cool to rt. 0.1 M aq $NaHCO_3$ (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then washed with 0.1 M aq $NaHCO_3$ (10 mL), dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave (1*R*,2*R*,3*S*,4*S*)-**34** as a colourless oil (260 mg, 72%, >99:1 dr); $[\alpha]_D^{25}$ +23.0 (*c* 1.0 in $CHCl_3$).

(1*R*,2*S*,3*R*,4*R*)-2-Aminocyclohexane-1,3,4-triol [(−)-Dihydroconduramine B-2] 36. $Pd(OH)_2$/C (50% wt of substrate, 38 mg) was added to a stirred degassed solution of (1*R*,2*S*,3*R*,4*R*)-**26** (75 mg, 0.23 mmol, >99:1 dr) in MeOH (1.5 mL) and the resultant suspension was stirred under H_2 (1 atm) at rt for 24 h. The resultant suspension was then filtered through Celite® (eluent MeOH), and the filtrate was concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/35% aq NH_4OH, 14:5:1) gave **36** as a white solid (22 mg, 65%, >99:1 dr, 98.2% ee);[29] mp 168–178 °C; $[\alpha]_D^{25}$ −19.9 (*c* 1.0 in MeOH); ν_{max} 3358, 3308, 2935, 2900, 2865; δ_H (400 MHz, d_4-MeOH) 1.27–1.47 (2H, m, C(5)H_A, C(6)H_A), 1.85–1.94 (2H, m, C(5)H_B, C(6)H_B), 2.48 (1H, t, *J* 9.5, C(2)*H*), 3.02 (1H, app t, *J* 9.5, C(3)*H*), 3.23–3.40 (1H, m, C(1)*H*, C(4)*H*); δ_C (100 MHz, d_4-MeOH) 30.2 (*C*(5)), 31.5 (*C*(6)), 61.2 (*C*(2)), 73.7 (*C*(1)), 74.3 (*C*(4)), 78.9 (*C*(3)); *m/z* (ESI$^+$) 148 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_6H_{14}NO_3^+$ ([M+H]$^+$) requires 148.09682; found 148.09676.

(1*RS*,2*SR*,3*SR*,4*SR*)-1,3-Diacetoxy-2-(*N*,*N*-dibenzylamino)-4-tosyloxycyxlohexane (±)-37. Ac_2O (100 μL, 1.06 mmol) and DMAP (0.4 mg, 0.003 mmol) were added sequentially to a stirred solution of (±)-**21** (170 mg, 0.353 mmol, >95:5 dr) in pyridine/CH_2Cl_2 (1:1, v:v, 7.6 mL) at rt and the resultant solution was stirred at rt for 24 h. The resultant solution was diluted with CH_2Cl_2 (15 mL) and washed sequentially with H_2O (15 mL), satd aq Na_2CO_3 (15 mL) and brine (15 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 7:3) gave (±)-**37** as a yellow oil (200 mg, quant, >95:5 dr); mp 141–146 °C; ν_{max} 3029, 2954, 1748; δ_H (400 MHz, $CDCl_3$) 1.61–1.94 (6H, m, CO*Me*, C(5)H_2, C(6)H_A), 1.95–2.04 (1H, m, C(6)H_B), 2.19 (3H, s, CO*Me*), 2.50 (3H, s, Ar*Me*), 3.23 (1H, dd, *J* 11.0, 2.8, C(2)*H*), 3.70 (2H, d, *J* 14.0, N(CH_AH$_B$Ph)$_2$), 3.78 (2H, d, *J* 14.0, N(CH$_A$*H*$_B$Ph)$_2$), 4.49 (1H, q,

J 3.0, C(4)*H*), 5.00–5.10 (1H, m, C(3)*H*), 5.36 (1H, td, *J* 11.0, 4.7, C(1)*H*), 7.17–7.39 (12H, m, *Ar*, *Ph*), 7.54–7.62 (2H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 20.9, 21.5 (CO*Me*), 21.7 (Ar*Me*), 24.5 (*C*(5)), 25.4 (*C*(6)), 55.7 (*C*(2)), 55.7 (N(*C*H_2Ph)$_2$), 69.5 (*C*(1)), 73.5 (*C*(3)), 75.2 (*C*(4)), 126.9, 127.7, 128.3, 129.7, 133.2, 139.6, 144.8 (*Ar*, *Ph*), 169.4, 170.3 (*C*OMe); *m/z* (ESI$^+$) 566 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{31}H_{36}NO_7S^+$ ([M+H]$^+$) requires 566.2207; found 566.2209.

(1*R*,2*S*,3*S*,4*S*)-1,3-Diacetoxy-2-(*N*,*N*-dibenzylamino)-4-tosyloxycyxlohexane (1*R*,2*S*,3*S*,4*S*)-37. Ac_2O (60 μL, 0.62 mmol) and DMAP (0.3 mg, 0.002 mmol) were added sequentially to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**21** (100 mg, 0.208 mmol, >95:5 dr) in pyridine/CH_2Cl_2 (1:1, v:v, 4.4 mL) at rt and the resultant solution was stirred at rt for 24 h. The resultant solution was diluted with CH_2Cl_2 (15 mL) and washed sequentially with H_2O (15 mL), satd aq Na_2CO_3 (15 mL) and brine (15 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc 7:3) gave (1*R*,2*S*,3*S*,4*S*)-**37** as a yellow oil (100 mg, 85%, >95:5 dr); $[\alpha]_D^{25}$ −2.4 (*c* 1.0 in $CHCl_3$).

(1*RS*,2*SR*,3*SR*,4*RS*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (±)-38. *Step 1.* KOAc (35.4 mg, 0.361 mmol) was added to a stirred solution of (±)-**37** (200 mg, 0.354 mmol, >95:5 dr) in EtOH/H_2O (6:1, v:v, 7.45 mL) and the resultant suspension was heated at reflux for 72 h, then allowed to cool to rt and concentrated in vacuo. H_2O (20 mL) was added and the resultant mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo.

Step 2. K_2CO_3 (172 mg, 1.24 mmol) was added to a stirred solution of the residue from the previous step in MeOH (17 mL) at rt and the resultant suspension was stirred at rt for 24 h, then concentrated in vacuo. 2 M aq NaOH (20 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (±)-**38** as a yellow solid (99 mg, 86%, >99:1 dr); mp 137–139 °C; ν_{max} 3398, 3028, 2940, 2862; δ_H (400 MHz, $CDCl_3$) 1.02–1.16 (1H, m, C(6)H_A), 1.57–1.84 (3H, m, C(5)H_2, O*H*), 2.08 (1H, dq, *J* 12.5, 3.9, C(6)H_B), 2.26 (1H, br s, O*H*), 2.32 (1H, dd, *J* 10.5, 1.9, C(2)*H*), 3.52 (1H, ddd, *J* 11.4, 5.0, 2.7, C(4)*H*), 3.65 (2H, d, *J* 13.9, N(CH_AH$_B$Ph)$_2$), 4.07 (1H, app td, *J* 10.5, 4.8, C(1)*H*), 4.18 (2H, d, *J* 13.9, N(CH$_A$$H_B$Ph)$_2$), 4.39–4.47 (1H, m, C(3)*H*), 7.21–7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 26.2 (*C*(5)), 29.7 (*C*(6)), 54.6 (N(*C*H_2Ph)$_2$), 63.0 (*C*(1)), 63.5 (*C*(2)), 68.6 (*C*(3)), 71.6 (*C*(4)), 127.2, 128.5, 128.8 (*o*,*m*,*p*-*Ph*), 139.5 (*i*-*Ph*); *m/z* (ESI$^+$) 328 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_3^+$ ([M+H]$^+$) requires 328.1907; found 328.1903.

Analysis of (±)-**38** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 92:8), flow rate: 1 mL/min, 10 μL injection] gave complete resolution of enantiomers [(1*R*,2*S*,3*S*,4*R*)-**38** t_R = 13.8 min; (1*S*,2*R*,3*R*,4*S*)-**38** t_R = 17.0 min].

(1*R*,2*S*,3*S*,4*R*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (1*R*,2*S*,3*S*,4*R*)-38. *Step 1.* KOAc (37.2 mg, 0.379 mmol) was added to a stirred solution of (1*R*,2*S*,3*S*,4*S*)-**37** (210 mg, 0.372 mmol, >95:5 dr) in EtOH/H_2O (6:1, v:v, 8.80 mL) and the resultant suspension was heated at reflux for 72 h, then allowed to cool to rt and concentrated in vacuo. H_2O (20 mL) was added and the resultant mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo.

Step 2. K_2CO_3 (180 mg, 1.30 mmol) was added to a stirred solution of the residue from the previous step in MeOH (18 mL) at rt and the resultant suspension was stirred at rt for 24 h, then concentrated in vacuo. 2 M aq NaOH (20 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (1*R*,2*S*,3*S*,4*R*)-**38** as a yellow oil (90 mg, 74%, >99:1 dr, 99.5% ee); $[\alpha]_D^{25}$ −102.6 (*c* 1.0 in $CHCl_3$).

Analysis of (1*R*,2*S*,3*S*,4*R*)-**38** by chiral HPLC [Chiralpak OD-H, mobile phase: hexane/^{i}PrOH (v/v, 92:8), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*R*,2*S*,3*S*,4*R*)-**38** to be assessed as 99.5% ee [(1*R*,2*S*,3*S*,4*R*)-**38** t_R = 13.5 min].

(1*R*,2*S*,3*S*,4*R*)-2-Aminocyclohexane-1,3,4-triol [(−)-Dihydroconduramine C-3] 39. $Pd(OH)_2$/C (50% wt of substrate, 38 mg) was added to a stirred degassed solution of (1*R*,2*S*,3*S*,4*R*)-**38** (75 mg, 0.23 mmol, >99:1 dr) in MeOH (1.5 mL) and the resultant suspension was stirred under H_2 (1 atm) at rt for 24 h. The resultant suspension was then filtered through Celite® (eluent MeOH), and the filtrate was concentrated in vacuo to give **39** as a yellow oil (25 mg, 74%, >99:1 dr, 99.5% ee);[29] $[\alpha]_D^{25}$ −31.3 (*c* 1.0 in MeOH); ν_{max} 3349, 2955, 2849; δ_H (400 MHz, d_4-MeOH) 1.31 (1H, app tdd, *J* 13.2, 11.2, 3.9, C(6)H_A), 1.62–1.70 (1H, m, C(5)H_A), 1.77 (1H, app tdd, *J* 13.2, 11.2, 3.9, C(5)H_B), 1.87–1.96 (1H, m, C(6)H_B), 2.70 (1H, dd, *J* 9.8, 2.8, C(2)*H*), 3.58–3.70 (2H, m, C(1)*H*, C(4)*H*), 3.98 (1H, *J* 2.8, 1.2, C(3)*H*); δ_C (100 MHz, d_4-MeOH) 27.3 (*C*(5)), 31.3 (*C*(6)), 59.0 (*C*(2)), 69.5 (*C*(1)), 71.9 (*C*(4)), 72.5 (*C*(3)); *m/z* (ESI^+) 148 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_6H_{14}NO_3^+$ ($[M+H]^+$) requires 148.0968; found 148.0966.

(1*RS*,2*SR*,3*RS*,4*SR*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (±)-40. *Step 1.* MsCl (110 μL, 1.39 mmol) was added to a stirred solution of (±)-**34** (190 mg, 0.462 mmol, >99:1 dr) in pyridine (2.9 mL) at 0 °C and the resultant solution was stirred at rt for 16 h, then concentrated in vacuo to give a 10:90 mixture of (±)-**34** and (±)-**35**, respectively, as a brown oil.

Step 2. KOAc (100 mg, 1.04 mmol) was added to a stirred solution of the residue from the previous step in EtOH/H_2O (6:1, v:v, 22.2 mL) and the resultant suspension was heated at reflux for 72 h, then allowed to cool to rt and concentrated in vacuo. H_2O (20 mL) was added and the resultant mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo.

Step 3. K_2CO_3 (440 mg, 3.18 mmol) was added to a stirred solution of the residue from the previous step in MeOH (44 mL) at rt and the resultant suspension was stirred at rt for 24 h, then concentrated in vacuo. 2 M aq NaOH (20 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH (3:1, v/v, 3 × 20 mL). The combined organic extracts were dried and concentrated in vacuo to give a 90:10 mixture of (±)-**40** and (±)-**25**, respectively. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (±)-**40** as a white solid (80 mg, 53%, >99:1 dr); mp 147–157 °C; ν_{max} 3323, 3083, 3060, 3023, 2943, 2916, 2856; δ_H (400 MHz, $CDCl_3$) 1.35–1.45 (1H, m, C(5)H_A), 1.63–1.83 (2H, m, C(6)H_2), 1.88 (1H, dd, *J* 14.6, 3.4, C(5)H_B), 2.07 (1H, br s, O*H*), 2.16 (1H, br d, *J* 3.5, O*H*), 2.86 (1H, app t, *J* 10.3, C(2)*H*), 3.16 (1H, br s, O*H*), 3.53 (1H, dd, *J* 10.3, 3.0, C(3)*H*), 3.75 (1H, td, *J* 10.5, 3.2, C(1)*H*), 3.92 (4H, app s, N($CH_2Ph)_2$), 4.01–4.06 (1H, m, C(4)*H*), 7.17–7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 26.5 (*C*(5)), 28.7 (*C*(6)), *56** (N(*C*$H_2Ph)_2$), 62.7 (*C*(2)), 68.4 (*C*(1)), 70.2 (*C*(3)), 70.9 (*C*(4)), 127.2, 128.5, 129.3 (*o*,*m*,*p*-*Ph*), 139.6 (*i*-*Ph*);[39] *m/z* (ESI$^+$) 328 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_3^+$ ([M+H]$^+$) requires 328.1907; found 328.1908. Further elution (eluent $CHCl_3$/MeOH, 95:5) gave an impure sample of (±)-**25** as a yellow oil (30 mg).

Analysis of (±)-**40** by chiral HPLC [Chiralpak AD-H, mobile phase: hexane/^{i}PrOH (v/v, 90:10), flow rate: 1 mL/min, 10 μL injection] gave complete resolution of enantiomers [(1*R*,2*S*,3*R*,4*S*)-**40** t_R = 13.3 min; (1*S*,2*R*,3*S*,4*R*)-**40** t_R = 16.4 min].

(1*R*,2*S*,3*R*,4*S*)-2-(*N*,*N*-Dibenzylamino)cyclohexane-1,3,4-triol (1*R*,2*S*,3*R*,4*S*)-40. *Step 1.* MsCl (190 μL, 2.41 mmol) was added to a stirred solution of (1*R*,2*R*,3*S*,4*S*)-**34** (330 mg, 0.803 mmol, >99:1 dr) in pyridine (8.0 mL) at 0 °C and the resultant solution was stirred at rt for 16 h, then concentrated in vacuo to give a 10:90 mixture of (1*R*,2*R*,3*S*,4*S*)-**34** and (1*R*,2*S*,3*S*,4*S*)-**35**, respectively, as a brown oil (500 mg).

Step 2. KOAc (200 mg, 2.08 mmol) was added to a stirred solution of the residue from the previous step (500 mg) in EtOH/H_2O (6:1, v:v, 44.4 mL) and the resultant suspension was heated at reflux for 72 h, then allowed to cool to rt and concentrated in vacuo. H_2O (40 mL) was added and the resultant mixture was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were dried and concentrated in vacuo.

Step 3. K_2CO_3 (880 mg, 6.37 mmol) was added to a stirred solution of the residue from the previous step in MeOH (88 mL) at rt and the resultant suspension was stirred at rt for 24 h, then concentrated in vacuo. 2 M aq NaOH (40 mL) was then added and the resultant mixture was extracted with $CHCl_3$/^{i}PrOH

(3:1, v/v, 3 × 40 mL). The combined organic extracts were dried and concentrated in vacuo to give a 90:10 mixture of (1*R*,2*S*,3*R*,4*S*)-**40** and (1*R*,2*S*,3*S*,4*S*)-**25**, respectively. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 97:3) gave (1*R*,2*S*,3*R*,4*S*)-**40** as a white solid (145 mg, 55%, >99:1 dr, 98.5% ee); mp 159–162 °C; $[\alpha]_D^{25}$ +11.7 (*c* 1.0 in $CHCl_3$). Further elution (eluent $CHCl_3$/MeOH, 95:5) gave an impure sample of (1*R*,2*S*,3*S*,4*S*)-**25** as a yellow oil (21 mg).

Analysis of (1*R*,2*S*,3*R*,4*S*)-**40** by chiral HPLC [Chiralpak AD-H, mobile phase: hexane/^{i}PrOH (v/v, 90:10), flow rate: 1 mL/min, 10 μL injection] and comparison to the racemic standard allowed (1*R*,2*S*,3*R*,4*S*)-**40** to be assessed as 98.5% ee [(1*R*,2*S*,3*R*,4*S*)-**40** t_R = 13.3 min].

(1*R*,2*S*,3*R*,4*S*)-2-Aminocyclohexane-1,3,4-triol [(+)-Dihydroconduramine F-3] 41. $Pd(OH)_2$/C (50% wt of substrate, 40 mg) was added to a stirred degassed solution of (1*R*,2*S*,3*R*,4*S*)-**40** (80 mg, 0.24 mmol, >99:1 dr) in MeOH (1.5 mL) and the resultant suspension was stirred under H_2 (1 atm) at rt for 24 h. The resultant suspension was then filtered through Celite® (eluent MeOH), and the filtrate was concentrated in vacuo to give **41** as a yellow oil (27 mg, 75%, >99:1 dr, 98.5% ee);[29] $[\alpha]_D^{25}$ +26.7 (*c* 1.0 in MeOH); ν_{max} 3354, 2938, 2875; δ_H (400 MHz, d_4-MeOH) 1.48 (1H, tdd, *J* 13.6, 4.4, 2.7, C(5)H_A), 1.59–1.86 (3H, m, C(6)H_2, C(5)H_B), 2.87 (1H, app t, *J* 9.7, C(2)*H*), 3.18–3.30 (2H, m, C(1)*H*, C(3)*H*), 3.88 (1H, app q, 2.7, C(4)*H*); δ_C (100 MHz, d_4-MeOH) 28.4 (*C*(6)), 28.5 (*C*(5)), 57.7 (*C*(2)), 70.1 (*C*(4)), 74.3 (*C*(1)), 76.1 (*C*(3)); *m/z* (ESI^+) 148 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_6H_{14}NO_3^+$ ($[M+H]^+$) requires 148.0968; found 148.0967.

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra, chiral HPLC traces, and crystallographic information files (for structures CCDC 1572458–1572467). This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] Due to the volatility of epoxide **14**, the conversion was judged by determining the ratio of unreacted dibenzylamine to ring-opened product (±)-**16**.

[11] The diastereoisomeric purity of (±)-**16** was assigned from the known diastereoisomeric purity of the precursor (±)-**15**, i.e., >180:1 dr.

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[28] Chemoselective *N*-benzylation of (1*R*,2*S*,3*S*,4*S*)-**20** (treatment with $BnBr/^iPr_2NEt$/DMAP) gave a sample of enantiopure (1*R*,2*S*,3*S*,4*S*)-**25**. The enantiomeric excess of (1*R*,2*S*,3*S*,4*S*)-**25** was determined by chiral HPLC analysis (and comparison with the corresponding authentic racemic standard), for which the authors would like to thank Professor Darren J. Dixon and Mr Sam R. Ellis.

[29] The enantiomeric excesses of dihydroconduramines A-2 (**32**), B-2 (**36**), C-3 (**39**) and F-3 (**41**) were assigned from the known enantiomeric excesses of the corresponding precursors (1*R*,2*S*,3*S*,4*S*)-**20**, (1*R*,2*S*,3*R*,4*R*)-**26**, (1*R*,2*S*,3*S*,4*R*)-**38** and (1*R*,2*S*,3*R*,4*S*)-**40**, respectively.

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[37] Other signals associated with the aromatic rings within **21** and **22** (which could not be unambiguously assigned to their respective diastereoisomer) were observed: δ_H (400 MHz, $CDCl_3$) 2.46 (3H, s, Ar*Me*), 2.48 (3H, s, Ar*Me*), 7.22–7.88 (28H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 127.1, 127.2, 127.5, 127.7, 128.4, 129.0, 129.3, 129.8, 129.9, 133.6, 133.7, 139.2, 129.3, 144.8, 145.1 (*Ar*, *Ph*).

[38] This signal was partly obscured by the signal associated with the d_8-PhMe solvent; other signals in these regions could not be discerned.

[39] The signal associated with $N(CH_2Ph)_2$ was very broad and of low intensity; the approximate peak position (to the nearest integer) is shown in italics and marked with an asterisk.