

## Diastereoselective Ammonium-Directed Epoxidation in the

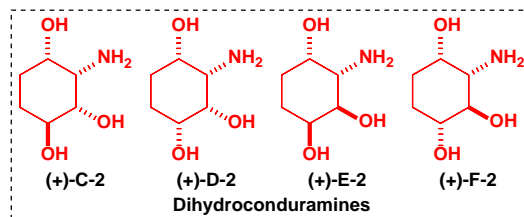
### Asymmetric Syntheses of Dihydroconduramines (+)-C-2, (-)-C-2, (+)-D-2, (+)-E-2, (+)-F-2 and (-)-F-2

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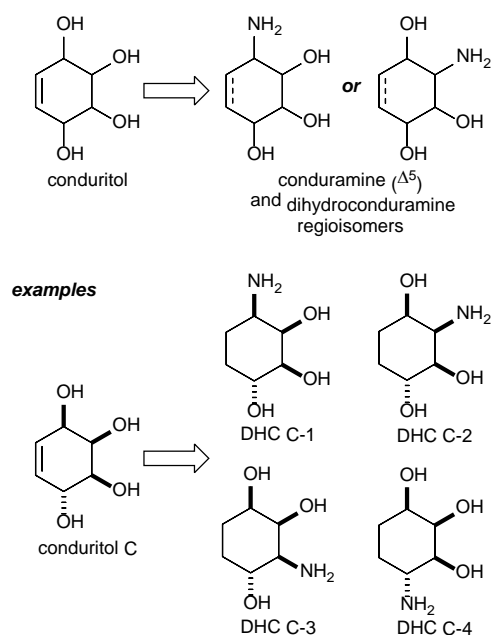
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Epoxidations (40% aq HBF<sub>4</sub> then *m*-CPBA) of racemic *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol and racemic *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol proceed with very high levels of diastereoselectivity (>95:5 dr). The latter is in direct contrast to the epoxidation of the corresponding *trans*-diastereoisomer (which proceeds with essentially no selectivity), showing that the relative configuration of the substrate dramatically influences the diastereoselectivity in these instances. Meanwhile, epoxidations of enantiopure (1*R*,2*S*, $\alpha$ *R*)-2-[(*N*- $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol and (1*S*,2*R*, $\alpha$ *R*)-2-[(*N*- $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol [surrogates for the enantiomers of *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol] proceed with complete diastereoselectivity (>95:5 dr) under the same conditions, showing that neither the presence of the  $\alpha$ -methyl group nor the relative configuration of the  $\alpha$ -methylbenzyl stereocenter have an effect upon the established level of diastereoselectivity in these cases. In contrast, epoxidations of enantiopure (1*R*,2*S*, $\alpha$ *R*)-2-[*N*-benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol and (1*S*,2*R*, $\alpha$ *R*)-2-[*N*-benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol [surrogates for the enantiomers of *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol] proceed with lower diastereoselectivity (~70:30 dr). Thus, the presence of the  $\alpha$ -methyl group has a detrimental effect on the established level of diastereoselectivity in these cases (although again the relative configuration of the  $\alpha$ -methylbenzyl stereocenter is unimportant). The diastereoselective epoxidation pathway is used to enable the asymmetric syntheses of six hitherto unknown, enantiopure dihydroconduramines (+)-C-2, (-)-C-2, (+)-D-2, (+)-E-2, (+)-F-2 and (-)-F-2 (>99% ee in each case).

## Introduction

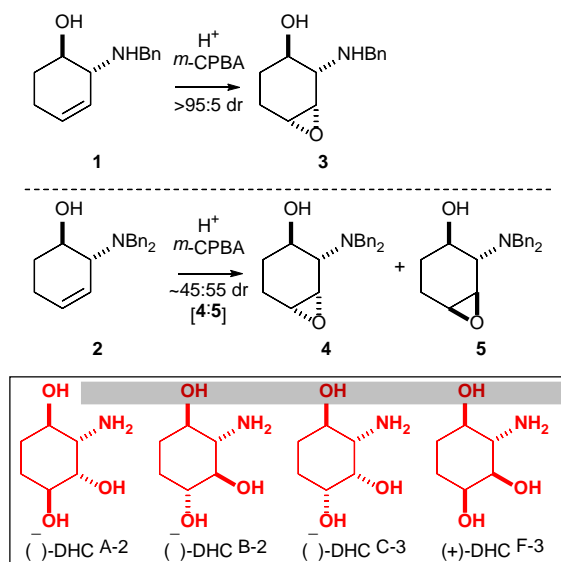
Molecules with the potential to act as sugar mimics are becoming increasingly popular as targets for laboratory syntheses.<sup>1</sup> This is because the progression of many diseases is linked to problems associated with carbohydrate-processing enzymes, and the identification of selective inhibitors of these enzymes is gaining attention as a potential therapeutic method. The conduramine and dihydroconduramine (DHC) families of aminocyclitols are two groups of carbocyclic aminosugar analogues which have attracted the interest of the synthetic community.<sup>2,3</sup> Both families can be thought of as derivatives of the parent conduritols (cyclohex-5-en-1,2,3,4-tetrols) in which the formal substitution of a hydroxyl group by an amino group has taken place. Thus, there are two possible regioisomeric forms of conduramines and dihydroconduramines: those based on a 3-aminocyclohex-5-en-1,2,4-triol scaffold and those based on a 4-aminocyclohex-5-en-1,2,3-triol (or the corresponding saturated derivatives). Aside from the IUPAC recommended names for these structures, conduramines and dihydroconduramines are also named after their parent conduritol, using the corresponding letter (A–F) to indicate the relative configuration and a number (1–4) to indicate the position of the amino functionality (Figure 1).



**FIGURE 1.** Gross structures of a conduritol (cyclohex-5-en-1,2,3,4-tetraol), a conduramine (4-aminocyclohex-5-en-1,2,3-triol or 3-aminocyclohex-5-en-1,2,4-triol), and a dihydroconduramine (4-aminocyclohexan-1,2,3-triol or 3-aminocyclohexan-1,2,4-triol).

Despite the interest in these compounds, until very recently the entire sub-family of X-2 and X-3 dihydroconduramines (comprising some sixteen stereoisomeric forms) was unknown. We have, however, reported preparations of enantiopure dihydroconduramines (–)-A-2, (–)-B-2, (–)-C-3 and (+)-F-3 using ammonium-directed epoxidation of enantiopure (1*R*,2*R*)-*trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol **1** as the key step,<sup>4</sup> which proceeded with complete diastereoselectivity (>95:5 dr) to give the intermediate epoxide **3**.<sup>5</sup> In fact, it was found that *N,N*-dibenzyl substitution on the amino group was not tolerated in this

diastereoselective epoxidation process: epoxidation of racemic *trans*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol **2** proceeded to give an ~45:55 mixture of the corresponding epoxides **4** and **5**.<sup>5</sup> This was ascribed to a predicted predilection of the substrate to form an intramolecular hydrogen bond between the ammonium ion (donor) and the hydroxyl group (acceptor); it was proposed that the presence of two N–H bonds on the ammonium ion derived from **1** circumvented this limitation and hence enabled an ammonium-directed epoxidation process (Figure 2).



**FIGURE 2.** Synthesis of dihydroconduramines (–)-A-2, (–)-B-2, (–)-C-3 and (+)-F-3 using ammonium-directed epoxidation of enantiopure (1*R*,2*R*)-*trans*-2-(*N*-benzylamino)cyclohex-3-en-1-ol **1** as the key step.

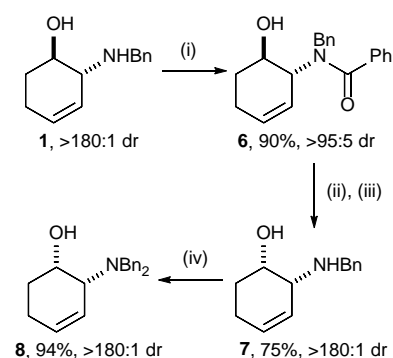
It was envisaged that the diastereoisomeric substrate *cis*-2-aminocyclohex-3-en-1-ol (or suitable *N*-substituted derivative) would act as a common precursor for the preparation of other (as yet unknown) stereoisomeric forms of the same sub-family of dihydroconduramine. Racemic *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol and *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol were thus prepared and evaluated as substrates for epoxidation. Interestingly both substrates were found to undergo highly diastereoselective epoxidation (in direct contrast to the behaviour of the corresponding *trans*-diastereoisomers **1** and **2**), revealing that the relative configuration of the substrate is in fact a key factor in determining the overall diastereoselectivity. With these observations in hand, the synthesis of appropriate enantiopure substrates was explored. Enantiopure (1*S*,2*R*, $\alpha$ *R*)-*cis*-2-[*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol and (1*R*,2*S*, $\alpha$ *R*)-*cis*-2-[*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol were found to be suitable surrogates for the enantiomeric forms of *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol, with neither the presence of the  $\alpha$ -methyl group nor the relative configuration of the  $\alpha$ -methylbenzyl stereocenter having a significant effect on the established reaction diastereoselectivity. Meanwhile, evaluation of the corresponding *N*-benzylated derivatives as proxies for the enantiomeric forms of *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol show a reduction in diastereoselectivity; the presence of the  $\alpha$ -methyl substituent is deleterious to the

established reaction diastereoselectivity in these cases. The results of these studies are fully delineated herein and culminate in the preparations of the requisite, enantiopure dihydroconduramines (+)-C-2, (-)-C-2, (+)-D-2, (+)-E-2, (+)-F-2 and (-)-F-2 (in >99% ee in each case).

## Results and Discussion

We have previously prepared **1** (in 53% overall yield and >180:1 dr) from 1,3-cyclohexadiene via monoepoxidation using AcOOH followed by regioselective and stereospecific epoxide ring-opening upon treatment with benzylamine in <sup>i</sup>PrOH at 80 °C.<sup>4</sup> A strategy based upon a neighbouring group participation reaction with inversion of configuration (previously reported in closely related systems)<sup>6</sup> was envisaged in order to access the corresponding *cis*-diastereoisomer **7**. Thus, treatment of **1** with benzoyl chloride gave benzamide **6** in 90% yield, and then treatment of **6** with SOCl<sub>2</sub> followed by K<sub>2</sub>CO<sub>3</sub> and MeOH gave **7** in 75% yield and >180:1 dr<sup>7</sup> (Scheme 1). The relative configuration within **7** was unambiguously established by single crystal X-ray diffraction analysis,<sup>8</sup> thus confirming that the reaction had proceeded with inversion of configuration. The mechanism of the transformation of **6** into **7** under these conditions most likely involves initial activation of the hydroxyl group followed by S<sub>N</sub>2-type displacement (with inversion of configuration) upon participation of the oxygen atom of the benzamido carbonyl functionality as a nucleophile; subsequent methanolysis then gives **7**. Treatment of **7** with BnBr, <sup>i</sup>Pr<sub>2</sub>NEt and DMAP resulted in chemoselective *N*-benzylation to give **8** in 94% yield and >180:1 dr<sup>9</sup> (Scheme 1).

**SCHEME 1. Preparation of Racemic Substrates **7** and **8**.<sup>a</sup>**



<sup>a</sup>Reagents and Conditions: (i) PhCOCl, Na<sub>2</sub>CO<sub>3</sub>, THF, rt, 24 h; (ii) SOCl<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 4 h; (iii) K<sub>2</sub>CO<sub>3</sub>, MeOH, rt, 16 h; (iv) BnBr, <sup>i</sup>Pr<sub>2</sub>NEt, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h.

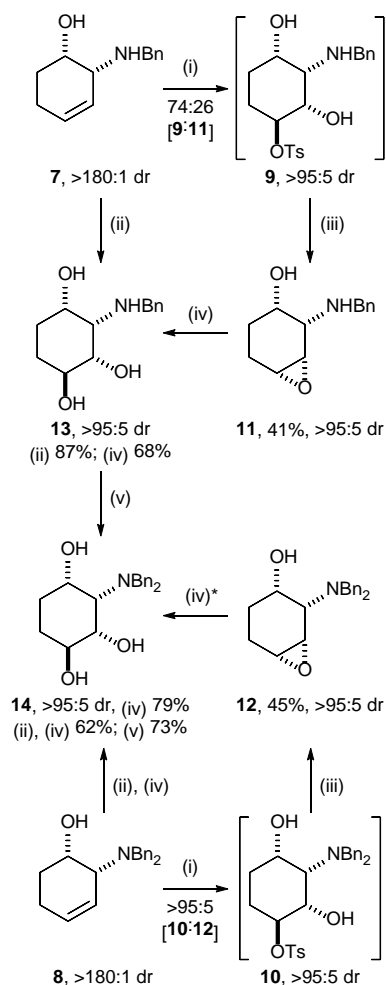
Treatment of *N*-benzyl substrate **7** with 5.0 equiv of 40% aq HBF<sub>4</sub> then 1.6 equiv of *m*-CPBA for 21 h gave complete conversion to triol **13** as a single diastereoisomer (>95:5 dr) which was isolated in 87% yield. Meanwhile, use of TsOH as the acid protecting agent in the epoxidation reaction gave a 74:26 mixture of tosylate **9** and epoxide **11**. The connectivity of **9** was apparent from <sup>1</sup>H-<sup>1</sup>H COSY analysis (the location of the CHOTs moiety was evidenced by characteristic chemical shift values at δ<sub>H</sub> ~4.6 ppm and δ<sub>C</sub> ~80 ppm). The relative configuration within **9** was then assigned on the basis of <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis,

assuming a chair conformation was favored in solution. Treatment of this mixture with DBU resulted in **11** only, which was isolated in 41% yield (from **7**), consistent with base induced ring-closure of **9** occurring to give **11**. The identity of and relative configuration within **11** were unambiguously established by single crystal X-ray diffraction analysis.<sup>8</sup> Finally, treatment of **11** with 40% aq HBF<sub>4</sub> gave complete conversion to triol **13** as a single diastereoisomer which was isolated in 68% yield. Chemoselective *N*-benzylation of **13** (BnBr, <sup>i</sup>Pr<sub>2</sub>NEt, DMAP) gave the corresponding *N,N*-dibenzyl derivative **14** in 73% yield (Scheme 2), whose identity and relative configuration were unambiguously established by single crystal X-ray diffraction analysis.<sup>8</sup> The identity of and relative configuration within **13** were therefore also unambiguously established. These results are entirely consistent with completely diastereoselective epoxidation to give **11** being followed by completely regioselective and stereospecific epoxide ring-opening upon attack of the conjugate base (TsO<sup>-</sup> or H<sub>2</sub>O) of the acid protecting agent (TsOH or 40% aq HBF<sub>4</sub>) at the carbon atom distal to the in situ formed ammonium moiety, forming either **9** or **13**, respectively. This regioselectivity of ring-opening is consistent with the regioselectivity that we have observed in other closely related systems (most notably in the epoxidation and subsequent ring-opening reactions of **1** and **2**),<sup>4</sup> and is presumably the result of the drive to minimise the destabilising, inductively electron-withdrawing influence of the ammonium moiety on the transition state of the reaction.

The analogous epoxidation reaction of *N,N*-dibenzyl substrate **8** (treatment with 40% aq HBF<sub>4</sub> then *m*-CPBA for 21 h) gave a 35:65 mixture of epoxide **12** and triol **14**. Subjection of this mixture to 40% aq HBF<sub>4</sub> resulted in convergence to **14** after 24 h, which was isolated in 62% yield from **8**. Repetition of the epoxidation reaction using TsOH in place of 40% aq HBF<sub>4</sub> gave >95% conversion to tosylate **10** as a single regio- and diastereoisomer.<sup>10</sup> The connectivity of **10** was again apparent from the <sup>1</sup>H-<sup>1</sup>H COSY analysis (as before, the characteristic chemical shift values of  $\delta_H \sim 4.6$  ppm and  $\delta_C \sim 80$  ppm indicated the location of the *CHOTs* moiety) and the relative configuration within **10** then followed from <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis, again assuming a chair conformation was favored in solution. Treatment of **10** with DBU gave epoxide **12**, which was isolated in 45% yield from **8**. Treatment of **12** with 40% aq HBF<sub>4</sub> for 24 h gave 85% conversion to triol **14** as a single diastereoisomer; resubjection to the reaction conditions then delivered **14** in quantitative conversion and 79% isolated yield (Scheme 2). Therefore, the epoxidation of **8** is completely diastereoselective under these conditions, in contrast to the epoxidation of the *trans*-diastereoisomer **2** under the same reaction conditions which gives an ~45:55 mixture of epoxides **4** and **5**.<sup>4</sup> The hydroxyl-bearing stereocenter is therefore far from a mere spectator to this reaction and the relative configuration of the substrate has significant bearing on the diastereoselectivity of the epoxidation. Ring-opening of epoxide **12** proceeds with complete regioselectivity (at the carbon atom distal to the in situ formed ammonium moiety)

and complete stereospecificity, to give either **10** (in the presence of TsOH) or **14** (in the presence of 40% aq HBF<sub>4</sub>), in parallel with the behaviour of epoxides **3–5** and **11**.

**SCHEME 2. Investigation of the Epoxidation of Racemic Substrates **7** and **8**.<sup>a</sup>**

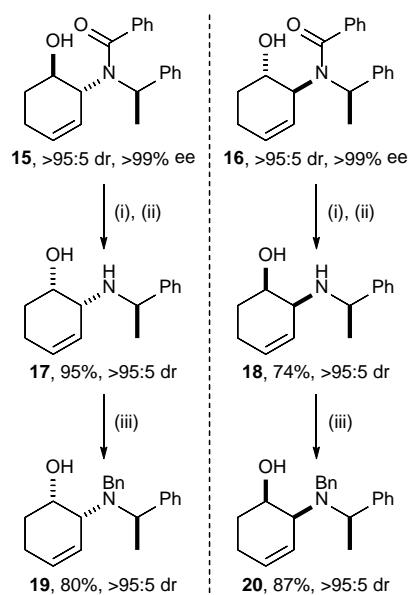


<sup>a</sup>Reagents and Conditions: (i) TsOH, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 21 h; (ii) 40% aq HBF<sub>4</sub>, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 21 h; (iii) DBU, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; (iv) 40% aq HBF<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; (v) BnBr, <sup>i</sup>Pr<sub>2</sub>NEt, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h. \* Resubjection to these reaction conditions was required to promote full conversion.

With these results in hand, the synthesis of appropriate enantiopure substrates for epoxidation was pursued. We have previously reported preparation of the enantiopure (>99% ee), diastereoisomeric amides **15** and **16** en route to the enantiomeric forms of **7**. Treatment of both **15** and **16** with SOCl<sub>2</sub> and then K<sub>2</sub>CO<sub>3</sub> in MeOH gave the corresponding amino alcohols **17** and **18** in 95% and 74% yield, respectively (Scheme 3). The identity of and relative configuration within **17** were unambiguously established by single crystal X-ray diffraction analysis,<sup>8</sup> with the absolute configuration being assigned from the known (*R*)-configuration of the α-methylbenzyl stereogenic center. This analysis also confirms that the reaction proceeds with inversion of configuration of the hydroxyl-bearing stereogenic center, as expected. The relative and absolute configurations of **18** were therefore assigned by direct analogy. Rather than effecting exchange of the *N*-α-methylbenzyl group within **17** and **18** for an *N*-benzyl group to give access to the enantiomers of **7** themselves, it was envisaged that both **17** and **18** might prove suitable enantiopure substrates for epoxidation

and thus act as surrogates for the enantiomers of **7**. By extension, it was also envisaged that the corresponding substrates **19** and **20** incorporating *N*-benzyl-*N*- $\alpha$ -methylbenzyl substitution would mimic the enantiomers of **8**. The chemoselective *N*-benzylation of **17** and **18** was therefore investigated and although it was found that treatment of **17** with BnBr in the presence of  $i\text{Pr}_2\text{NEt}$  and DMAP in  $\text{CH}_2\text{Cl}_2$  at rt provided only ~50% conversion to **19** after 24 h at rt, treatment of both **17** and **18** with BnBr in the presence of  $\text{K}_2\text{CO}_3$  in refluxing MeCN provided quantitative conversion to the corresponding diastereoisomers **19** and **20** within the same timeframe, and thus **19** and **20** were isolated in 80% and 87% yield, respectively (Scheme 3). The relative configuration within **19** was unambiguously confirmed by single crystal X-ray diffraction analysis,<sup>8</sup> with the absolute configuration being assigned from the known (*R*)-configuration of the  $\alpha$ -methylbenzyl stereogenic center. Both the relative and absolute configurations of **20** could thus also be confidently assigned.

**SCHEME 3. Preparation of Enantiopure Substrates 17–20.<sup>a</sup>**



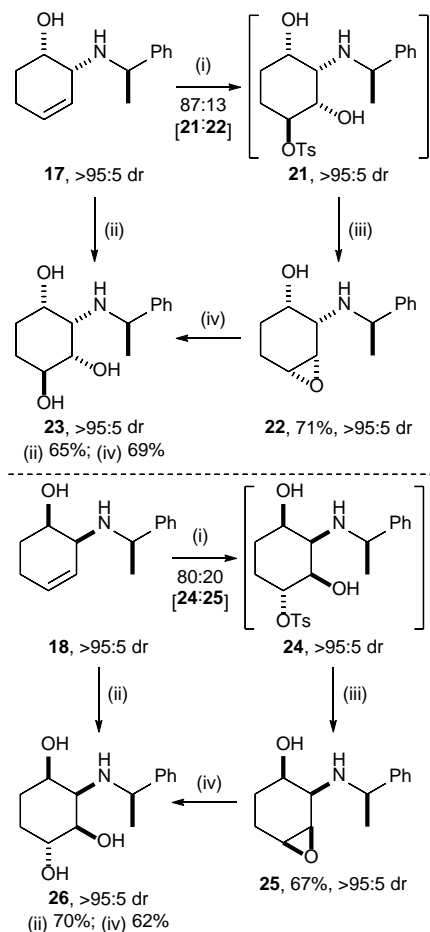
<sup>a</sup>Reagents and Conditions: (i)  $\text{SOCl}_2$ ,  $\text{CH}_2\text{Cl}_2$ , rt, 4 h; (ii)  $\text{K}_2\text{CO}_3$ , MeOH, rt, 16 h; (iii) BnBr,  $\text{K}_2\text{CO}_3$ , MeCN, reflux, 24 h.

Investigations into the diastereoselectivities of the epoxidations of **17–20** were now undertaken. In brief, the results of these studies showed that the *N*- $\alpha$ -methylbenzyl substrates **17** and **18** underwent completely diastereoselective epoxidation which was followed by completely regioselective and stereospecific ring-opening at the carbon atom distal to the in situ formed ammonium moiety to give the corresponding ring-opened products as single diastereoisomers. In contrast, the *N*-benzyl-*N*- $\alpha$ -methylbenzyl substrates **19** and **20** underwent epoxidation with poor levels of diastereoselectivity although the subsequent regioselectivity of ring-opening remained high and the ring-opening proceeded with complete stereospecificity to produce the corresponding mixture of products.

Treatment of *N*- $\alpha$ -methylbenzyl substrate **17** with 40% aq HBF<sub>4</sub> and then *m*-CPBA for 21 h resulted in complete consumption of starting material to form an ~10:90 mixture of epoxide **22** and triol **23**. When the reaction duration was extended to 30 h, quantitative formation of **23** was observed and it was isolated in 65% yield. Under identical conditions, *N*- $\alpha$ -methylbenzyl substrate **18** gave triol **26** as the only product, which was isolated in 70% yield. The identities of and relative configurations within **23** and **26** were unambiguously established by single crystal X-ray diffraction analyses,<sup>8</sup> with the absolute configuration being assigned from the known (*R*)-configurations of the  $\alpha$ -methylbenzyl stereogenic centers. Use of TsOH (rather than 40% aq HBF<sub>4</sub>) resulted in formation of an 87:13 mixture of tosylate **21** and epoxide **22** from **17** and an 80:20 mixture of tosylate **24** and epoxide **25** from **18**. The connectivities of **21** and **24** were apparent from <sup>1</sup>H-<sup>1</sup>H COSY analysis ( $\delta_{\text{H}}$  ~4.6 ppm,  $\delta_{\text{C}}$  ~80 ppm indicated the location of the *CHOTs* moiety) and the relative configuration therein then followed from <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis, assuming a chair conformation was favored in solution. Treatment of the 87:13 mixture of tosylate **21** and epoxide **22** with DBU gave **22** as the only product, which was isolated in 71% yield from **17**. Similarly, the 80:20 mixture of tosylate **24** and epoxide **25** converged on **25** upon treatment with DBU, and **25** was isolated in 67% yield. Treatment of the isolated epoxides **22** and **25** with 40% aq HBF<sub>4</sub> gave the corresponding triols **23** and **26** as single diastereoisomers in both cases and **23** and **26** were isolated in 69% and 62% yields, respectively. The analogous behaviour of the two diastereoisomers **17** and **18** shows that the relative configuration of the  $\alpha$ -methylbenzyl stereocenter has a negligible effect on the diastereoselectivity of the epoxidation in these cases, as may be reasonably expected (Scheme 4).



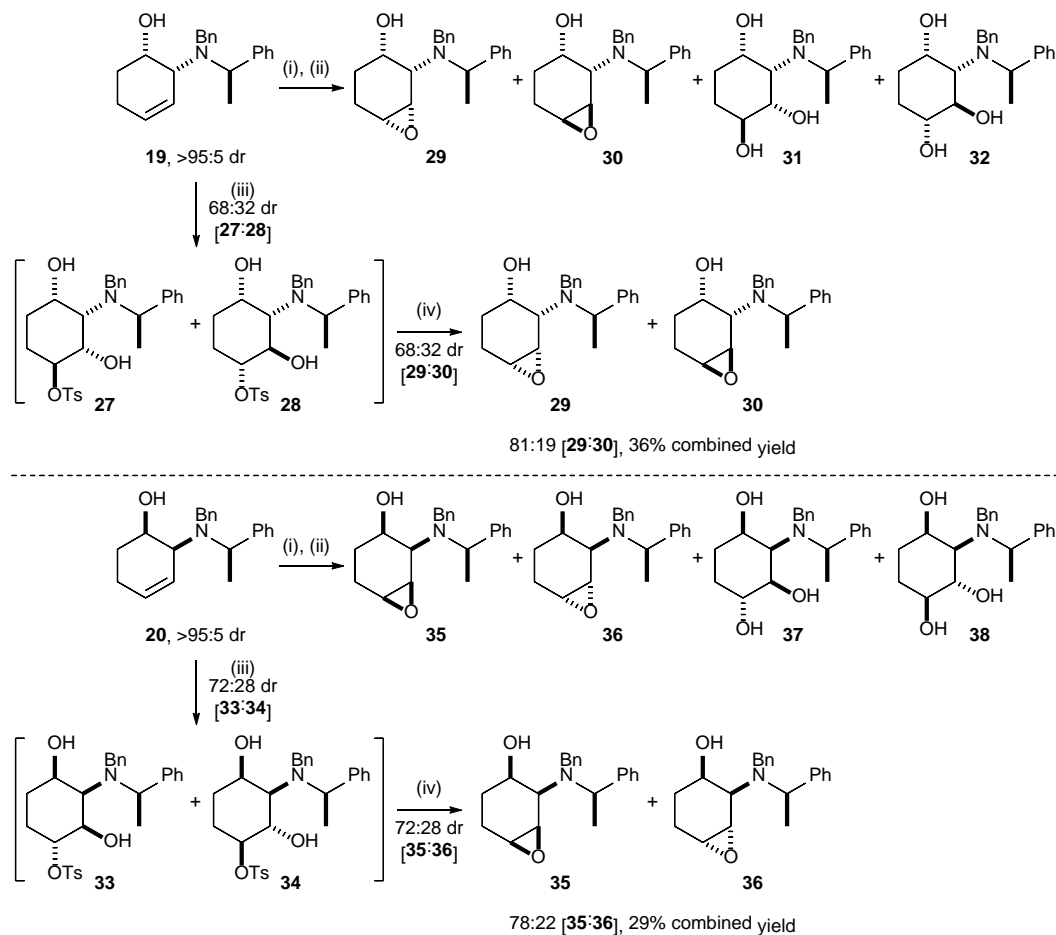
**SCHEME 4. Investigation of the Epoxidation of Enantiopure Substrates 17 and 18.<sup>a</sup>**



<sup>a</sup>Reagents and Conditions: (i) TsOH, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 21 h; (ii) 40% aq HBF<sub>4</sub>, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 30 h; (iii) DBU, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; (iv) 40% aq HBF<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h.

Epoxidation of *N*-benzyl-*N*- $\alpha$ -methylbenzyl substrate **19** (using 5.0 equiv of *m*-CPBA in the presence of 40% aq HBF<sub>4</sub> for 30 h) resulted in an ~1:1:1 mixture of **29**, **30** and **31**.<sup>11</sup> Treatment of this mixture with 40% aq HBF<sub>4</sub> for 24 h gave a 21:28:49:2 mixture of **29**, **30**, **31** and **32**, respectively, and after a further five days the mixture converged upon **31** and **32** only, in ~70:30 dr. Under identical conditions, *N*-benzyl-*N*- $\alpha$ -methylbenzyl substrate **20** gave a 48:31:21 mixture of **35**, **36** and **37**, respectively;<sup>12</sup> treatment of this mixture with 40% aq HBF<sub>4</sub> for 24 h gave a 21:23:53:3 mixture of **35**, **36**, **37** and **38**, respectively, and after a further five days the mixture converged upon **37** and **38** in ~70:30 dr. Use of TsOH (in place of 40% aq HBF<sub>4</sub>) resulted in formation of a 68:32 mixture of tosylates **27** and **28** from **19**, and a 72:28 mixture of tosylates **33** and **34** from **20**. Treatment of these mixtures with DBU gave the corresponding mixtures of epoxides: **29** and **30** were formed in 68:32 dr and isolated as an 81:19 mixture in 36% combined yield from **19**, whilst **35** and **36** were formed in 72:28 dr and isolated as a 78:22 mixture in 29% combined yield from **20**. From these results it is again apparent that the relative configuration of the  $\alpha$ -methylbenzyl stereocenter has a negligible effect on the diastereoselectivity of the epoxidation (Scheme 5).

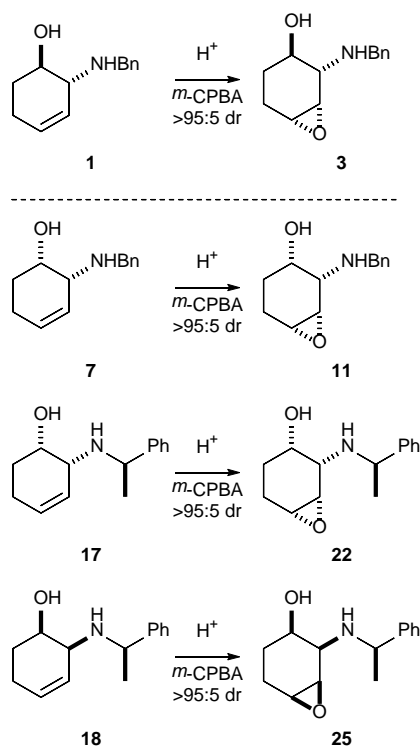
**SCHEME 5. Investigation of the Epoxidation of Enantiopure Substrates 19 and 20.<sup>a</sup>**



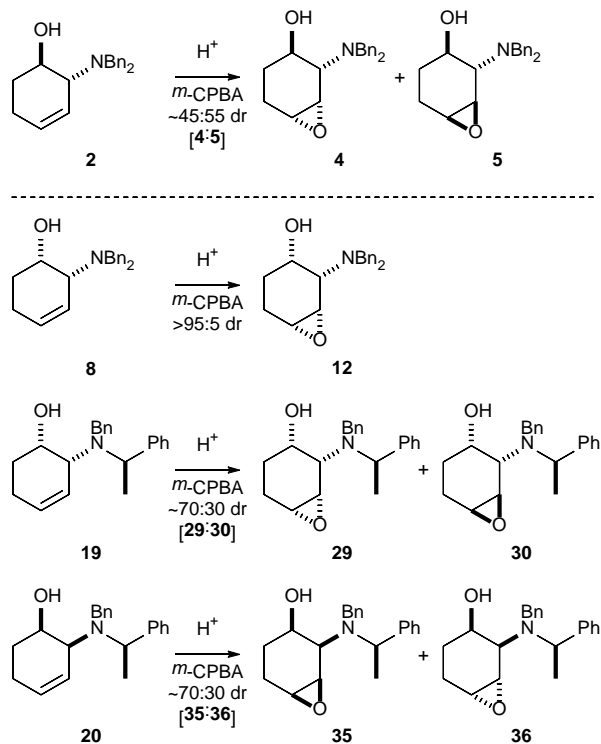
<sup>a</sup>Reagents and Conditions: (i) 40% aq HBF<sub>4</sub>, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 30 h; (ii) 40% aq HBF<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt [for time and product ratios for these steps, see text]; (iii) TsOH, *m*-CPBA, CH<sub>2</sub>Cl<sub>2</sub>, rt, 30 h; (iv) DBU, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h.

It can be concluded that the epoxidations (H<sup>+</sup>, *m*-CPBA) of the 2-aminocyclohex-3-en-1-ol derivatives **1**, **7**, **17** and **18**, in which the nitrogen atom bears either a single *N*-benzyl or *N*- $\alpha$ -methylbenzyl substituent proceed with very high levels (>95:5 dr) of diastereoselectivity in all cases to give the corresponding epoxides **3**, **11**, **22** and **25** in which epoxidation has selectively occurred on the face of the olefin that is *syn* to the amino substituent. This selectivity is independent of the relative configuration of the substrate, the presence of the  $\alpha$ -methyl group and the relative configuration of the  $\alpha$ -stereocenter (Figure 3). Meanwhile, 2-aminocyclohex-3-en-1-ol derivatives **2**, **8**, **19** and **20** in which the nitrogen atom bears either *N,N*-dibenzyl or *N*-benzyl-*N*- $\alpha$ -methylbenzyl substituents reveal more complicated behaviour in their epoxidation reactions (Figure 4). Epoxidation of *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol **8** is anomalous as it proceeds with complete diastereoselectivity (to give **12** in >95:5 dr); epoxidations of *trans*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol **2** and the *cis*-2-[*N*-benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol epimers **19** and **20** proceed with low levels of diastereoselectivity (**2** gives epoxides **4** and **5** in ~45:55 dr, **19** gives epoxides **29** and **30** in ~70:30 dr, and **20** gives epoxides **35** and **36** in ~70:30 dr). This indicates that the epoxidation diastereoselectivity is dependent on the relative configuration of the substrate and that the introduction of an  $\alpha$ -methyl group causes a reduction in the diastereoselectivity, irrespective of

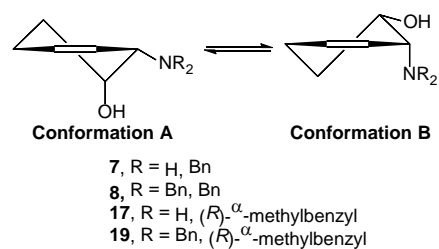
the relative configuration of the resultant  $\alpha$ -stereocenter. The cases which involve high diastereoselectivity (i.e., **1**, **7**, **8**, **17** and **18**) can all be rationalised by invoking the ability of the in situ formed ammonium moiety to direct the stereochemical course of the reaction by hydrogen-bonding, promoting delivery of the oxidant to the *syn* face of the olefin. It is noteworthy, however, that **7** and **17** show a preference for half-chair conformations **7A** and **17A** in the solid state (Figure 5). In these conformers the *N*-benzylamino substituent is in a pseudo-equatorial position and the hydroxyl group is in a pseudo-axial position. If these represent the reactive conformations in solution,<sup>13</sup> then direction by the hydroxyl group may contribute to the high diastereoselectivity.<sup>14</sup> An identical argument applies to the corresponding half-chair conformers of **8** and **18** (Figure 5) which may therefore provide a rationale for the anomalous level of diastereoselectivity observed for **8**. The cases which involve low diastereoselectivity (**2**, **19** and **20**) suggest an inability of the in situ formed ammonium moiety (or the hydroxyl group) to effect direction of the reaction. This effect may be due to a number of factors, including the intrinsic hydrogen-bonding ability of the ammonium moiety, steric effects, and the absolute configuration of the nitrogen atom (for ammonium moieties derived from tertiary amines bearing three different *N*-substituents, such as **19** and **20**). We have previously rationalised the inability of **2** to undergo diastereoselective epoxidation as the result of a predilection for formation of an intramolecular hydrogen bond<sup>4</sup> and it may be that the relative configuration of the substrate, as well as the identity of the nitrogen substituents, influences the strength of intramolecular hydrogen-bonding. By extension, the ability to form an intermolecular hydrogen-bond to the peracid and the relative strength of this interaction may also be influenced, especially by the identity of the *N*-substituents (the intermediate ammonium moiety derived from protonation of **19** and **20** has the nitrogen atom as a stereogenic center of unknown configuration) and the interplay of these factors may thus contribute to the variable levels of diastereoselectivity observed.



**FIGURE 3.** Summary of epoxidation diastereoselectivity ( $\text{H}^+$ ,  $m\text{-CPBA}$ ) for **1**, **7**, **17** and **18**.



**FIGURE 4.** Summary of epoxidation diastereoselectivity ( $\text{H}^+$ ,  $m\text{-CPBA}$ ) for **2**, **8**, **19** and **20**.



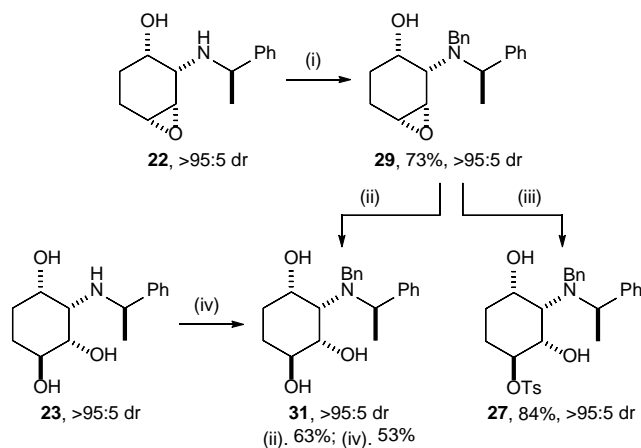
**FIGURE 5.** Half-chair conformations of **7**, **8**, **17** and **19**.

The structural and stereochemical assignments within both the  $N\text{-}\alpha\text{-methylbenzyl}$  series of compounds **21–26** and the  $N\text{-benzyl-}N\text{-}\alpha\text{-methylbenzyl}$  series of compounds **27–38** were further established

and secured by a series of chemical correlations and single-crystal X-ray diffraction analyses.<sup>8</sup> The studies concerning the derivatives of **17** and **19** are described below (those concerning the derivatives of **18** and **20**, which are directly analogous, are contained within the SI).

Chemoselective *N*-benzylation of both *N*- $\alpha$ -methylbenzyl epoxide **22** and triol **23** gave samples of the corresponding *N*-benzyl-*N*- $\alpha$ -methylbenzyl epoxide **29** and triol **31**. Treatment of epoxide **29** with either TsOH or 40% aq HBF<sub>4</sub> gave the corresponding ring-opened products, tosylate **27** and triol **31**, as single regio- and diastereoisomers in both cases, in 84% and 63% yield, respectively. These results establish that epoxide **29** undergoes completely regioselective and stereospecific ring-opening under both of these reaction conditions (Scheme 6). The relative configurations within **27**, **29** and **31** were thence unambiguously established by single-crystal X-ray diffraction analyses.<sup>8</sup> The absolute configurations could then be assigned from the known (*R*)-configuration of the  $\alpha$ -methylbenzyl stereocenter in each case. The connectivity of **27** was also apparent from <sup>1</sup>H-<sup>1</sup>H COSY analysis ( $\delta_{\text{H}}$  ~4.5 ppm,  $\delta_{\text{C}}$  ~86 ppm indicated location of the *CHOTs* moiety) and the relative configuration could be assigned from <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis, assuming a chair conformation was favored in solution; it is apparent that the favoured solid-state and solution phase (CDCl<sub>3</sub>) chair conformations of **27** are the same, with the bulky *N*-benzyl-*N*- $\alpha$ -methylbenzyl substituent occupying an equatorial position.

**SCHEME 6. Chemical Correlation Experiments.<sup>a</sup>**

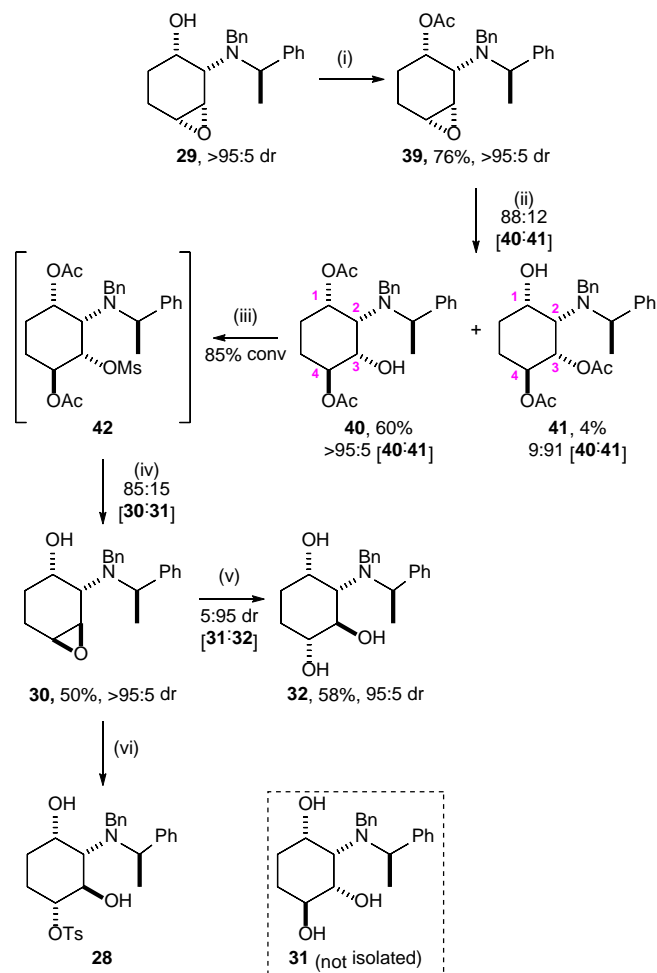


<sup>a</sup>Reagents and Conditions: (i) BnBr, K<sub>2</sub>CO<sub>3</sub>, MeCN, reflux, 24 h; (ii) 40% aq HBF<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; (iii) TsOH, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; (iv) BnBr, <sup>i</sup>Pr<sub>2</sub>NEt, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h.

An authentic sample of epoxide **30** was prepared from epoxide **29** by application of our previously reported epoxide inversion protocol.<sup>15</sup> Treatment of **29** with Ac<sub>2</sub>O gave **39** in 76% yield, with subsequent treatment of **39** with AcOH at 50 °C giving an 88:12 mixture of diacetates **40** and **41**. These species proved to be effectively separable by preparative tlc, with a sample enriched in **40** (>95%) being isolated in 60% yield and a sample enriched in **41** (>90%) being isolated in 4% yield. The regiochemistries of **40** and **41** were assigned by a combination of NMR spectroscopic methods (including <sup>1</sup>H-<sup>13</sup>C HMBC analyses to

secure the locations of the acetate functionalities, which were associated with signals in the  $^1\text{H}$  NMR spectrum having  $\delta_{\text{H}} > 4.8$  ppm). The relative configurations within **40** and **41** were thence assigned by  $^1\text{H}$  NMR  $^3J$  coupling constant analysis, assuming a chair conformation was favored in solution; this also suggested that the favoured conformers placed the *N*-benzyl-*N*- $\alpha$ -methylbenzyl group in an equatorial position, with the remainder of the substituents being sited in axial positions. The preference for this conformation explains the formation of a mixture of **40** and **41**, as the axial oxy functionalities at C(1) and C(3) are easily able to exchange the acyl group. Next, treatment of **40** with MsCl in pyridine gave ~85% conversion to mesylate **42** and treatment of this crude reaction mixture with  $\text{K}_2\text{CO}_3$  in MeOH resulted in formation of an ~85:15 mixture of epoxide **30** and triol **31**. Chromatography gave epoxide **30** in 50% yield, although triol **31** was not isolated. The formation of triol **31** as a product in this reaction sequence is simply the result of unreacted **40** undergoing methanolysis of both of the acetate ester functionalities (Scheme 7). With a pure sample of epoxide **30** in hand its identity and relative configuration was unambiguously established by single-crystal X-ray diffraction analysis,<sup>8</sup> with the absolute configuration following from the known (*R*)-configuration of the  $\alpha$ -methylbenzyl stereocenter. When epoxide **30** was treated with 40% aq  $\text{HBF}_4$  for 24 h, approximately 41% conversion to triol **32** was observed, establishing a somewhat slower rate of ring-opening than for the diastereoisomeric epoxide **29**,<sup>12</sup> although the ring-opening of **30** occurs with similarly high regioselectivity to that of **29** and with complete stereospecificity. In order to promote reaction conversion the ring-opening reaction was conducted at 40 °C, which gave quantitative conversion to a 5:95 mixture of triols **31** and **32** (i.e., **32** in 95:5 dr) that proved chromatographically inseparable and thus were isolated in 58% combined yield. Treatment of epoxide **30** with TsOH provided an authentic sample of tosylate **28**.<sup>16</sup> The connectivity of **28** was apparent from  $^1\text{H}$ - $^1\text{H}$  COSY analysis ( $\delta_{\text{H}}$  ~4.7 ppm,  $\delta_{\text{C}}$  ~81 ppm indicated location of the *CHOTs* moiety) and the relative configuration therein then followed from  $^1\text{H}$  NMR  $^3J$  coupling constant analysis, assuming a chair conformation was favored in solution (Scheme 7).

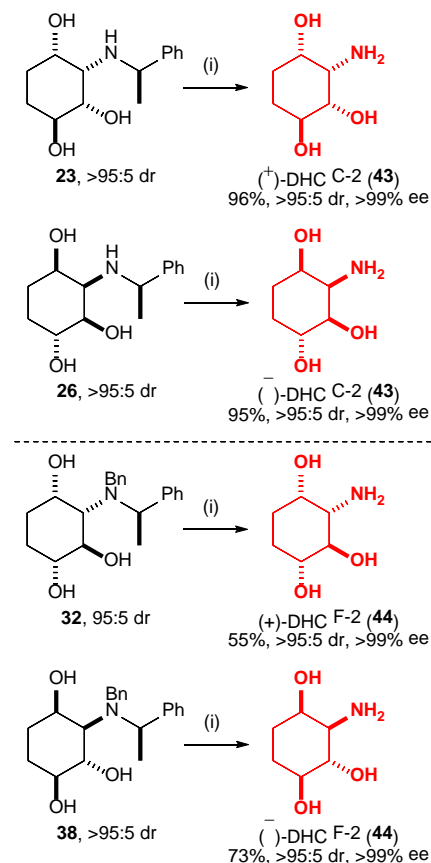
**SCHEME 7. Chemical Correlation Experiments.<sup>a</sup>**



<sup>a</sup>Reagents and Conditions: (i) Ac<sub>2</sub>O, DMAP, pyridine, rt, 24 h; (ii) AcOH, 50 °C, 36 h; (iii) MsCl, pyridine, rt, 16 h; (iv) K<sub>2</sub>CO<sub>3</sub>, MeOH, rt, 16 h; (v) 40% aq HBF<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 40 °C, 24 h; (vi) TsOH, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h.

At this stage, a series of hydrogenolytic *N*-debenzylation reactions was performed in order to access the enantiomeric forms of some of the target dihydroconduramines. Hydrogenolysis of triol **23** gave (+)-dihydroconduramine C-2 (**43**) { [ $\alpha$ ]<sub>D</sub><sup>25</sup> +25.9 (*c* 0.25 in MeOH)} in 96% yield and hydrogenolysis of triol **26** gave (–)-dihydroconduramine C-2 (**43**) { [ $\alpha$ ]<sub>D</sub><sup>25</sup> –23.4 (*c* 1.0 in MeOH)} in 95% yield. Given the known enantiopurities of the corresponding starting materials **17** and **18** (i.e., >99% ee in both cases) and that all synthetic intermediates possess multiple (at least three) stereogenic centers, the enantiopurities of the samples of (+)-dihydroconduramine C-2 (**43**) and (–)-dihydroconduramine C-2 (**43**), as well as all intermediates prepared en route, could be confidently inferred as >99% ee (Scheme 8). In addition, hydrogenolysis of triol **32** (95:5 dr) provided (+)-dihydroconduramine F-2 (**44**) { [ $\alpha$ ]<sub>D</sub><sup>25</sup> +33.2 (*c* 0.5 in MeOH)} in 55% yield and >95:5 dr, whilst hydrogenolysis of triol **38** (>95:5 dr) provided (–)-dihydroconduramine F-2 (**44**) { [ $\alpha$ ]<sub>D</sub><sup>25</sup> –31.0 (*c* 0.25 in MeOH)} in 73% yield and >95:5 dr. Again, the enantiopurities of these samples, as well as all intermediates prepared en route, could be confidently inferred as >99% ee (Scheme 8).

**SCHEME 8. Preparation of the Enantiomers of Dihydroconduramine C-2 and F-2.<sup>a</sup>**

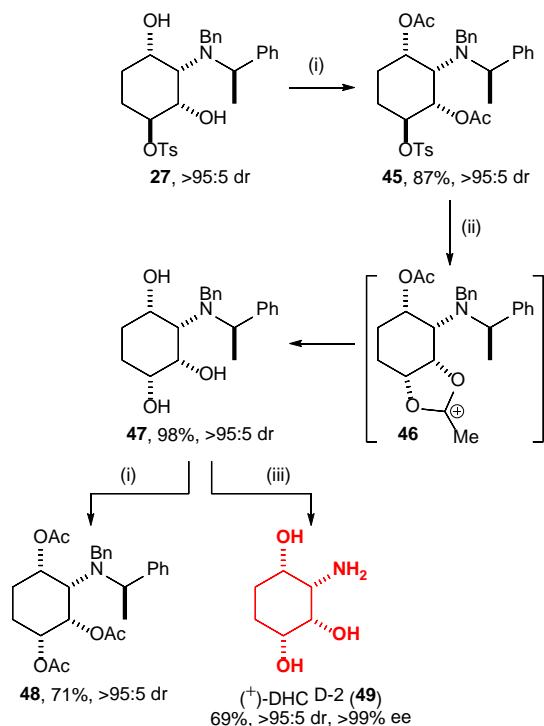


<sup>a</sup>Reagents and Conditions: (i) H<sub>2</sub>, Pd(OH)<sub>2</sub>/C, MeOH, rt, 24 h.

The synthesis of the remaining dihydroconduramines (D-2 and E-2) in one representative, enantiomeric series was also undertaken, with derivatives of **17** (rather than derivatives of **18**) being arbitrarily chosen as the starting materials for these studies. Treatment of tosylate **27** with excess Ac<sub>2</sub>O gave the corresponding diacetate derivative **45** in 87% yield, and then sequential treatment of **45** with KOAc in EtOH/H<sub>2</sub>O and then K<sub>2</sub>CO<sub>3</sub> in MeOH gave **47** in 98% yield. Although it was not possible to assign the relative configuration within **47** by <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis, peracetylation gave the corresponding triacetate **48** which proved amenable to this analysis (thus establishing the relative configurations of both **47** and **48**), assuming a chair conformation, with the bulky *N,N*-dibenzylamino group occupying an equatorial position. This result is therefore entirely consistent with a Winstein reaction occurring,<sup>17</sup> which involves displacement of the tosylate functionality of **45** upon participation of the proximal acetate functionality to give intermediate 1,3-dioxolan-2-ylum ion **46** that undergoes hydrolysis in situ to give an intermediate vicinal hydroxy acetate (possibly as a mixture of regioisomers); treatment of this (these) intermediate(s) with K<sub>2</sub>CO<sub>3</sub> in MeOH would result in transesterification of any acetate ester functionalities that are present to give the common amino triol **47**. Hydrogenolysis of **47** gave (+)-dihydroconduramine D-2 (**49**) { [ $\alpha$ ]<sub>D</sub><sup>25</sup> +10.4 (*c* 1.0 in MeOH)} in 69% yield, >95:5 dr and >99% ee<sup>18</sup> (Scheme 9).



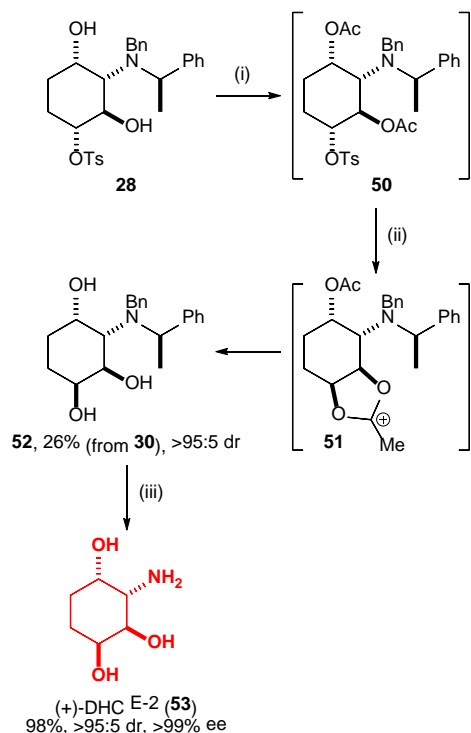
**SCHEME 9. Preparation of Dihydroconduramine D-2.<sup>a</sup>**



<sup>a</sup>Reagents and Conditions: (i) Ac<sub>2</sub>O, DMAP, pyridine, rt, 24 h; (ii) KOAc, EtOH, H<sub>2</sub>O, reflux, 72 h, then K<sub>2</sub>CO<sub>3</sub>, MeOH, rt, 24 h; (iii) H<sub>2</sub>, Pd(OH)<sub>2</sub>/C, MeOH, rt, 24 h.

In a directly analogous manner,<sup>19</sup> treatment of tosylate **28** with excess Ac<sub>2</sub>O gave the corresponding diacetate derivative **50** and sequential treatment of **50** with KOAc in EtOH/H<sub>2</sub>O then K<sub>2</sub>CO<sub>3</sub> in MeOH gave **52** in 26% yield (from epoxide **30**). In this case, the relative configuration within **52** was assigned by <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis, assuming a chair conformation was favoured in solution. The formation of **52** is therefore entirely consistent with a Winstein reaction occurring,<sup>17</sup> proceeding via the intermediacy of 1,3-dioxolan-2-ylum ion **51**. Finally, hydrogenolysis of **52** gave (+)-dihydroconduramine E-2 (**53**) {[α]<sub>D</sub><sup>25</sup> +89.3 (*c* 1.0 in MeOH)} in 98% yield, >95:5 dr and >99% ee<sup>18</sup> (Scheme 10).

**SCHEME 10. Preparation of Dihydroconduramine E-2.<sup>a</sup>**



<sup>a</sup>Reagents and Conditions: (i) Ac<sub>2</sub>O, DMAP, pyridine, rt, 24 h; (ii) KOAc, EtOH, H<sub>2</sub>O, reflux, 72 h, then K<sub>2</sub>CO<sub>3</sub>, MeOH, rt, 24 h; (iii) H<sub>2</sub>, Pd(OH)<sub>2</sub>/C, MeOH, rt, 24 h.

## Conclusion

In conclusion, epoxidations (40% aq HBF<sub>4</sub> then *m*-CPBA) of racemic *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol and racemic *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol proceed with very high levels of diastereoselectivity (>95:5 dr). In the latter case, the high diastereoselectivity of the process is in direct contrast to the epoxidation of the corresponding *trans*-diastereoisomer, which proceeded with essentially no selectivity. The relative configuration of the substrate therefore dramatically influences the epoxidation diastereoselectivity in these instances. The analogous epoxidations of enantiopure (1*R*,2*S*, $\alpha$ *R*)-2-(*N*- $\alpha$ -methylbenzyl)aminocyclohex-3-en-1-ol and (1*S*,2*R*, $\alpha$ *R*)-2-(*N*- $\alpha$ -methylbenzyl)aminocyclohex-3-en-1-ol, which were prepared as surrogates for the enantiomers of *cis*-2-(*N*-benzylamino)cyclohex-3-en-1-ol, also proceed with complete diastereoselectivity (>95:5 dr). This demonstrates that neither the presence of the  $\alpha$ -methyl group nor the relative configuration of the  $\alpha$ -methylbenzyl stereocenter have an effect upon the established level of diastereoselectivity in these cases. Meanwhile, epoxidations of enantiopure (1*R*,2*S*, $\alpha$ *R*)-2-[*N*-benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol and (1*S*,2*R*, $\alpha$ *R*)-2-[*N*-benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol, which were prepared as surrogates for the enantiomers of *cis*-2-(*N,N*-dibenzylamino)cyclohex-3-en-1-ol, proceed with lower levels of diastereoselectivity (~70:30 dr). Thus, the presence of the  $\alpha$ -methyl group has a detrimental effect on the established level of diastereoselectivity in these cases although again the relative configuration of the  $\alpha$ -

methylbenzyl stereocenter is unimportant. Together, the results demonstrate that the relative configuration of the substrate and the identity of the *N*-substituents can, in some cases dramatically, affect the diastereoselectivity of the epoxidation process in these systems. In all cases where high epoxidation diastereoselectivity is observed, the stereochemical outcome can be rationalised by invoking an ammonium-directed process. The intermediate epoxides undergo *in situ* ring-opening with complete regioselectivity and stereospecificity: attack of the conjugate base of the acid protecting agent occurs at the carbon atom that is distal to the ammonium moiety to give the corresponding functionalised products. This transformation is used to enable the asymmetric syntheses of the novel, enantiopure dihydroconduramines (+)-C-2, (-)-C-2, (+)-D-2, (+)-E-2, (+)-F-2 and (-)-F-2 (>99% 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.<sup>20</sup> Organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. Flash column chromatography was performed on Kieselgel 60 silica.

Melting points are uncorrected. Specific rotations are reported in 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup> and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in cm<sup>-1</sup>. NMR spectra were recorded in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. <sup>1</sup>H-<sup>1</sup>H COSY and <sup>1</sup>H-<sup>13</sup>C HMQC analyses were used to establish atom connectivity. Accurate mass analyses were performed using an ion trap analyzer.

**X-ray Crystal Structure Determination.**<sup>8</sup> Data were collected using graphite monochromated Cu-K $\alpha$  radiation via standard procedures at 150 K. The structures were solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealized positions. The structures were refined using CRYSTALS.<sup>21</sup>

**(1*RS*,2*RS*)-2-(*N*-Benzoyl-*N*-benzylamino)cyclohex-3-en-1-ol 6.** Benzoyl chloride (1.88 mL, 16.2 mmol) was added dropwise to a stirred solution of **1** (3.30 g, 16.2 mmol, >180:1 dr) and Na<sub>2</sub>CO<sub>3</sub> (3.44 g, 32.5 mmol) in THF (65 mL) at 0 °C. The resultant mixture was stirred at rt for 24 h and then H<sub>2</sub>O (30 mL) was added. The aqueous layer was extracted with Et<sub>2</sub>O (3  $\times$  40 mL) and the combined organics were washed with brine (100 mL), dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 3:1) gave **6** as a white solid (4.50 g, 90%, >95:5 dr); mp 126–129 °C;  $\nu_{\text{max}}$  3435, 3065, 3028, 2950, 2918, 1607, 1594;  $\delta_{\text{H}}$  (500 MHz, PhMe-*d*<sub>8</sub>, 363 K) 1.21–1.33 (1H, m, C(6)*H*<sub>A</sub>),

1.55–1.63 (1H, m, C(6)*H<sub>B</sub>*), 1.65–1.79 (2H, m, C(5)*H<sub>2</sub>*), 3.54–3.62 (1H, m, C(1)*H*), 4.28 (1H, d, *J* 15.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.64–4.78 (2H, m, C(2)*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 5.27–5.33 (1H, m, C(3)*H*), 5.43–5.50 (1H, m, C(4)*H*), 6.95–7.11 (6H, m, *Ph*), 7.24–7.30 (2H, m, *Ph*), 7.39–7.43 (2H, m, *Ph*);  $\delta_{\text{C}}$  (125 MHz, PhMe-*d*<sub>8</sub>, 363 K) 25.4 (C(5)), 31.5 (C(6)), 47.8 (NCH<sub>2</sub>Ph), 63.9 (C(2)), 69.8 (C(1)), 127.6, 127.8, 128.7, 129.5 (C(3), *o,m,p-Ph*), 131.2 (C(4)), 138.4, 140.6 (*i-Ph*), 174.0 (COPh); *m/z* (ESI<sup>+</sup>) 308 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>22</sub>NO<sub>2</sub><sup>+</sup> 308.1645; found 308.1644.

**(1*RS*,2*SR*)-2-(*N*-Benzylamino)cyclohex-3-en-1-ol 7.** SOCl<sub>2</sub> (250  $\mu$ L, 3.46 mmol) was added to a stirred solution of **6** (280 mg, 0.912 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.55 mL) at 0 °C. The resultant solution was stirred at rt for 4 h and then concentrated in vacuo. The residue was dissolved in MeOH (12.5 mL) and K<sub>2</sub>CO<sub>3</sub> (1.0 g, 7.2 mmol) was added. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. The residue was partitioned between H<sub>2</sub>O (20 mL) and CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  20 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 19:1) gave **7** as a white powder (140 mg, 75%, >180:1 dr);<sup>22</sup> mp 70.2–76.7 °C;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.53–1.68 (2H, m, C(6)*H<sub>2</sub>*), 1.87–1.98 (1H, m, C(5)*H<sub>A</sub>*), 2.05–2.16 (1H, m, C(5)*H<sub>B</sub>*), 3.08–3.13 (1H, m, C(2)*H*), 3.74 (1H, ddd, *J* 8.4, 4.8, 3.4, C(1)*H*), 3.81 (1H, d, *J* 13.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.85 (1H, d, *J* 13.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 5.54 (1H, app ddt, *J* 10.0, 3.5, 1.9, C(3)*H*), 5.72 (1H, app dtd, *J* 10.0, 3.7, 1.7, C(4)*H*), 7.17–7.31 (5H, m, *Ph*).

**(1*RS*,2*SR*)-2-(*N,N*-Dibenzylamino)cyclohex-3-en-1-ol 8.** <sup>i</sup>Pr<sub>2</sub>NEt (760  $\mu$ L, 4.37 mmol), BnBr (520  $\mu$ L, 4.37 mmol) and DMAP (3.6 mg, 29.1  $\mu$ mol) were added sequentially to a stirred solution of **7** (592 mg, 2.91 mmol, >180:1 dr) in CH<sub>2</sub>Cl<sub>2</sub> (8.4 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 9:1) gave **8** as a pale yellow oil (799 mg, 94%, >180:1 dr);  $\nu_{\text{max}}$  3427, 3084, 3061, 3025, 2921, 2838;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.61–1.71 (1H, m, C(6)*H<sub>A</sub>*), 1.81–1.91 (1H, m, C(6)*H<sub>B</sub>*), 1.97–2.10 (1H, m, C(5)*H<sub>A</sub>*), 2.15–2.26 (1H, m, C(5)*H<sub>B</sub>*), 3.52 (1H, app ddt, *J* 6.1, 4.1, 1.9, C(2)*H*), 3.61 (2H, d, *J* 14.0, N(CH<sub>A</sub>H<sub>B</sub>Ph)<sub>2</sub>), 3.74 (1H, ddd, *J* 10.7, 6.1, 4.1, C(1)*H*), 3.93 (2H, d, *J* 14.0, N(CH<sub>A</sub>H<sub>B</sub>Ph)<sub>2</sub>), 4.05 (1H, br s, OH), 5.75 (1H, dddd, *J* 10.0, 4.1, 2.4, 1.6, C(3)*H*), 5.98 (1H, app ddt, *J* 10.0, 4.7, 2.4, C(4)*H*), 7.23–7.38 (10H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 23.4 (C(5)), 28.3 (C(6)), 56.1 (C(2)), 56.5 (N(CH<sub>2</sub>Ph)<sub>2</sub>), 66.8 (C(1)), 124.0 (C(3)), 127.2, 128.5, 128.9 (*o,m,p-Ph*), 131.7 (C(4)), 139.3 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 294 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>24</sub>NO<sup>+</sup> 294.1852; found 294.1851.

**(1*RS*,2*RS*,3*RS*,4*SR*)-2-(*N*-Benzylamino)-3,4-epoxycyclohexan-1-ol 11.** *Step 1.* A solution of **7** (250 mg, 1.23 mmol, >180:1 dr) in CH<sub>2</sub>Cl<sub>2</sub> (3.4 mL) was added to anhydrous TsOH (1.06 g, 6.15 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (73% wt, 463 mg, 1.97 mmol) was added.

The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4 × 15 mL), dried and concentrated in vacuo to give a 74:26 mixture of **9** and **11**, respectively, as a yellow oil (380 mg). Data for **9**: δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) [selected peaks] 2.40 (3H, s, ArMe), 2.71–2.74 (1H, m, C(2)*H*), 3.90–3.94 (1H, m, C(3)*H*), 3.98–4.01 (1H, m, C(1)*H*), 4.56–4.60 (1H, m, C(4)*H*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) [selected peaks] 54.3 (C(2)), 67.2 (C(1)), 68.3 (C(3)), 79.6 (C(4)).

*Step 2.* DBU (150 μL, 1.05 mmol) was added to a stirred solution of the 74:26 mixture of **9** and **11**, from the previous step (380 mg) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 98:2) gave **11** as a pale yellow solid (111 mg, 41% from **7**, >95:5 dr); mp 64–69 °C; ν<sub>max</sub> 3416, 3416, 3026, 2997, 2936, 2851; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.36–1.55 (2H, m, C(6)*H*<sub>2</sub>), 1.87 (1H, dddd, *J* 15.4, 8.9, 6.2, 2.5, C(5)*H*<sub>A</sub>), 2.10–2.19 (1H, m, C(5)*H*<sub>B</sub>), 3.06 (1H, dd, *J* 5.6, 4.0, C(2)*H*), 3.28 (1H, app t, *J* 4.0, C(3)*H*), 3.30–3.33 (1H, m, C(4)*H*), 3.56 (1H, ddd, *J* 9.6, 5.6, 3.9, C(1)*H*), 3.94 (1H, d, *J* 13.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.02 (1H, d, *J* 13.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.24–7.43 (5H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 22.3 (C(5)), 24.6 (C(6)), 51.9 (NCH<sub>2</sub>Ph), 53.8 (C(2)), 54.5 (C(3)), 55.1 (C(4)), 66.4 (C(1)), 127.2, 128.2, 128.5 (*o,m,p-Ph*), 140.0 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 220 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>18</sub>NO<sub>2</sub><sup>+</sup> 220.1332; found 220.1331.

**(1RS,2RS,3RS,4SR)-2-(N,N-Dibenzylamino)-3,4-epoxycyclohexan-1-ol 12.** *Step 1.* A solution of **8** (250 mg, 0.853 mmol, >180:1 dr) in CH<sub>2</sub>Cl<sub>2</sub> (2.4 mL) was added to anhydrous TsOH (734 mg, 4.26 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (73% wt, 402 mg, 1.71 mmol) was added. The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4 × 15 mL), dried and concentrated in vacuo to give a >95:5 mixture of **10** and **12**, respectively, as a yellow oil (302 mg). Data for **10**: δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.48–1.63 (1H, m, C(5)*H*<sub>A</sub>), 1.79 (2H, dt, *J* 9.6, 3.3, C(6)*H*<sub>2</sub>), 2.04–2.15 (1H, m, C(5)*H*<sub>B</sub>), 2.45 (3H, s, ArMe), 2.86 (1H, t, *J* 2.6, C(2)*H*), 3.77 (2H, d, *J* 14.6, N(CH<sub>A</sub>H<sub>B</sub>Ph)<sub>2</sub>), 4.03 (2H, d, *J* 14.6, N(CH<sub>A</sub>H<sub>B</sub>Ph)<sub>2</sub>), 4.10–4.18 (2H, m, C(1)*H*, C(3)*H*), 4.69 (1H, app q, *J* 3.1, C(4)*H*), 7.21–7.36 (12H, m, *Ph*, *Ar*), 7.73–7.77 (2H, m, *Ar*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 19.0 (C(5)), 21.7 (ArMe), 25.7 (C(6)), 55.0 (N(CH<sub>2</sub>Ph)<sub>2</sub>), 59.6 (C(2)), 68.0 (C(1)), 68.8 (C(3)), 80.1 (C(4)), 127.2, 128.4, 128.6, 129.9, 139.9, 144.9 (*Ph*, *Ar*).

*Step 2.* DBU (103 μL, 0.678 mmol) was added to a stirred solution of the >95:5 mixture of **10** and **12** from the previous step (302 mg) in CH<sub>2</sub>Cl<sub>2</sub> (1.3 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **12** as a pale yellow oil (118 mg, 45% from **8**, >95:5 dr); ν<sub>max</sub> 3510, 3084, 3061, 3026, 3001, 2930, 2849, 2810; δ<sub>H</sub> (400

MHz, CDCl<sub>3</sub>) 1.34–1.45 (1H, m, C(5)*H*<sub>A</sub>), 1.78–1.95 (2H, m, C(5)*H*<sub>B</sub>, C(6)*H*<sub>A</sub>), 2.14 (1H, ddd, *J* 16.7, 10.5, 6.8, C(6)*H*<sub>B</sub>), 3.08 (1H, dd, *J* 3.9, 1.6, C(2)*H*), 3.29 (1H, app t, *J* 4.4, C(4)*H*), 3.41–3.47 (2H, m, C(3)*H*, *OH*), 4.01 (2H, d, *J* 14.1, N(CH<sub>A</sub>*H*<sub>B</sub>Ph)<sub>2</sub>), 4.11 (2H, d, *J* 14.1, N(CH<sub>A</sub>*H*<sub>B</sub>Ph)<sub>2</sub>), 4.17 (1H, app s, C(1)*H*), 7.21–7.26 (2H, m, *Ph*), 7.29–7.35 (4H, m, *Ph*), 7.38–7.44 (4H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 19.4 (C(6)), 28.3 (C(5)), 52.9 (C(4)), 55.2 (N(CH<sub>2</sub>Ph)<sub>2</sub>), 55.7 (C(2)), 56.9 (C(3)), 67.3 (C(1)), 126.9, 128.3, 128.6 (*o,m,p-Ph*), 140.2 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 310 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>24</sub>NO<sub>2</sub><sup>+</sup> 310.1802; found 310.1801.

**(1*RS*,2*RS*,3*RS*,4*RS*)-2-(*N*-Benzylamino)cyclohexane-1,3,4-triol 13.** *Method A. Epoxidation of 7.* HBF<sub>4</sub> (40% aq, 1.43 mL, 9.35 mmol) was added to a stirred solution of **7** (380 mg, 1.87 mmol, >180:1 dr) in CH<sub>2</sub>Cl<sub>2</sub> (5.2 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (75% wt, 686 mg, 2.99 mmol) was added. The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with 2.25 M aq NaOH (20 mL) and extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 30 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **13** as a colourless oil (380 mg, 87%, >95:5 dr); ν<sub>max</sub> 3300, 3090, 3042, 2929, 2876; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.34–1.44 (1H, m, C(5)*H*<sub>A</sub>), 1.61–1.72 (2H, m, C(6)*H*<sub>A</sub>), 1.77–1.87 (1H, m, C(6)*H*<sub>B</sub>), 1.95–2.06 (1H, m, C(5)*H*<sub>B</sub>), 2.70 (3H, br s, *OH*, *NH*), 2.98 (1H, app t, *J* 3.5, C(2)*H*), 3.64–3.69 (1H, m, C(3)*H*), 3.80–3.86 (1H, m, C(4)*H*), 3.92 (1H, app dt, *J* 7.3, 3.5, C(1)*H*), 3.95 (2H, s, NCH<sub>2</sub>Ph), 7.25–7.39 (5H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 26.3 (C(5)), C(6)), 52.6 (NCH<sub>2</sub>Ph), 57.5 (C(2)), 69.5 (C(1)), 70.3 (C(4)), 73.6 (C(3)), 127.4, 128.4, 128.6 (*o,m,p-Ph*), 139.6 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 238 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>20</sub>NO<sub>3</sub><sup>+</sup> 238.1438; found 238.1437.

*Method B. Ring-opening of 11.* HBF<sub>4</sub> (40% aq, 250 μL, 1.59 mmol) was added to a stirred solution of **11** (69.6 mg, 0.318 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.88 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (5 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 10 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **13** as a colourless oil (51 mg, 68%, >95:5 dr).

**(1*RS*,2*RS*,3*RS*,4*RS*)-2-(*N,N*-Dibenzylamino)cyclohexane-1,3,4-triol 14.** *Method A. Epoxidation of 8.* HBF<sub>4</sub> (40% aq, 530 μL, 3.36 mmol) was added to a stirred solution of **8** (197 mg, 0.672 mmol, >180:1 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.9 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (73% wt, 253 mg, 1.08 mmol) was added. The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with 2.25

M aq NaOH (10 mL) and extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 15 mL). The combined organic extracts were dried and concentrated in vacuo to give a 35:65 mixture of **12** and **14**, respectively (332 mg). HBF<sub>4</sub> (40% aq, 840 μL, 5.38 mmol) was added to a stirred solution of the 35:65 mixture of **12** and **14** (332 mg) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 19:1) gave **14** as a white solid (136 mg, 62%, >95:5 dr); mp 136–139 °C;  $\nu_{\text{max}}$  3280, 3027, 2930, 2893, 2808;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.43–1.58 (2H, m, C(5)*H*<sub>A</sub>, *OH*), 1.75–1.93 (2H, m, C(6)*H*<sub>2</sub>), 2.08–2.20 (1H, m, C(5)*H*<sub>B</sub>), 2.92–3.03 (2H, m, C(2)*H*, *OH*), 3.58–3.76 (1H, br s, *OH*), 3.92 (2H, d, *J* 14.4, N(CH<sub>A</sub>*H*<sub>B</sub>Ph)<sub>2</sub>), 4.03–4.15 (4H, m, C(3)*H*, C(4)*H*, N(CH<sub>A</sub>*H*<sub>B</sub>Ph)<sub>2</sub>), 4.17–4.21 (1H, m, C(1)*H*), 7.20–7.36 (10H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 21.6 (*C*(5)), 25.9 (*C*(6)), 54.9 (N(CH<sub>2</sub>Ph)<sub>2</sub>), 59.5 (*C*(2)), 68.5 (*C*(1)), 70.4 (*C*(4)), 71.8 (*C*(3)), 127.0, 128.5, 128.6 (*o,m,p-Ph*), 140.2 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 328 ([*M*+*H*]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [*M*+*H*]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>26</sub>NO<sub>3</sub><sup>+</sup> 328.1907; found 328.1903.

*Method B. Ring-opening of 12.* HBF<sub>4</sub> (40% aq, 270 μL, 1.72 mmol) was added to a stirred solution of **12** (107 mg, 0.344 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.96 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 15 mL). The combined organics were dried and concentrated in vacuo to give a 15:85 mixture of **12** and **14**, respectively (126 mg). HBF<sub>4</sub> (40% aq, 320 μL, 2.04 mmol) was added to a stirred solution of the 15:85 mixture of **12** and **14** (126 mg) in CH<sub>2</sub>Cl<sub>2</sub> (1.1 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **14** as a white solid (88.5 mg, 79%, >95:5 dr).

*Method C. N-Benzylolation of 13.* *i*Pr<sub>2</sub>NEt (90.0 μL, 0.506 mmol), BnBr (60.0 μL, 0.506 mmol) and DMAP (cat.) were added sequentially to a stirred solution of **13** (80.0 mg, 0.337 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.96 mL) at rt. The resultant mixture was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 19:1) gave **14** as a white solid (80.0 mg, 73%, >95:5 dr).

**(1*S*,2*R*, $\alpha$ *R*)-2-[*N*-( $\alpha$ -Methylbenzyl)amino]cyclohex-3-en-1-ol 17.** SOCl<sub>2</sub> (170 μL, 2.37 mmol) was added to a stirred solution of **15** (200 mg, 0.623 mmol, >95:5 dr, >99% ee) in CH<sub>2</sub>Cl<sub>2</sub> (0.75 mL) at 0 °C. The resultant mixture was stirred at rt for 4 h and then concentrated in vacuo. MeOH (8.2 mL) and K<sub>2</sub>CO<sub>3</sub> (700 mg) were then added sequentially. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. H<sub>2</sub>O (15 mL) was then added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography

(eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **17** as a white solid (130 mg, 95%, >95:5 dr); mp 50–51 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> –113.8 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3410, 3320, 3061, 3024, 2963, 2923, 2839;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.40 (3H, d, *J* 6.7, C( $\alpha$ )Me), 1.61–1.67 (2H, m, C(6)H<sub>2</sub>), 1.88–1.99 (1H, m, C(5)H<sub>A</sub>), 2.14 (1H, app dtd, *J* 18.0, 6.0, 3.9, 1.8, C(5)H<sub>B</sub>), 3.03–3.08 (1H, m, C(2)H), 3.76 (1H, app dt, *J* 7.0, 4.7, C(1)H), 3.90 (1H, q, *J* 6.7, C( $\alpha$ )H), 5.31 (1H, app ddt, *J* 10.0, 3.9, 2.1, C(3)H), 5.70 (1H, app dtd, *J* 10.0, 3.9, 1.8, C(4)H), 7.24–7.38 (5H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 22.5 (C(5)), 24.1 (C( $\alpha$ )Me), 27.0 (C(6)), 53.5 (C(2)), 56.5 (C( $\alpha$ )), 65.3 (C(1)), 126.3 (*o,m-Ph*), 127.2, 127.4 (C(3), *p-Ph*), 128.6 (*o,m-Ph*), 129.4 (C(4)), 145.7 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 218 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>20</sub>NO<sup>+</sup> 218.1539; found 218.1539.

**(1R,2S, $\alpha$ R)**-2-[N-( $\alpha$ -Methylbenzyl)amino]cyclohex-3-en-1-ol **18**. SOCl<sub>2</sub> (4.72 mL, 65.1 mmol) was added to a stirred solution of **16** (5.50 g, 17.1 mmol, >95:5 dr, >99% ee) in CH<sub>2</sub>Cl<sub>2</sub> (20.3 mL) at 0 °C. The resultant mixture was stirred at rt for 4 h and then concentrated in vacuo. MeOH (139 mL) and K<sub>2</sub>CO<sub>3</sub> (11.8 g) were then added sequentially. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. H<sub>2</sub>O (75 mL) was then added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  100 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **18** as an orange oil (2.76 g, 74%, >95:5 dr); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +250 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3421, 3061, 3023, 2961, 2923, 2838;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.40 (3H, d, *J* 6.5, C( $\alpha$ )Me), 1.47–1.58 (1H, m, C(6)H<sub>A</sub>), 1.66–1.75 (1H, m, C(6)H<sub>B</sub>), 1.93–2.04 (1H, m, C(5)H<sub>A</sub>), 2.10–2.21 (1H, m, C(5)H<sub>B</sub>), 2.96–3.01 (1H, m, C(2)H), 3.51 (1H, ddd, *J* 9.8, 5.2, 2.8, C(1)H), 4.04 (1H, q, *J* 6.5, C( $\alpha$ )H), 5.76–5.83 (2H, m, C(3)H, C(4)H), 7.22–7.38 (5H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 23.3 (C(5)), 25.0 (C( $\alpha$ )Me), 27.2 (C(6)), 53.0 (C(2)), 56.1 (C( $\alpha$ )), 66.4 (C(1)), 126.8 (*o,m-Ph*), 127.1 (C(3)), 127.2 (*p-Ph*), 128.5 (*o,m-Ph*), 129.5 (C(4)), 145.0 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 218 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>20</sub>NO<sup>+</sup> 218.1539; found 218.1537.

**(1S,2R, $\alpha$ R)**-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol **19**. K<sub>2</sub>CO<sub>3</sub> (3.21 g, 23.3 mmol) and BnBr (1.38 mL, 11.6 mmol) were added sequentially to a stirred solution of **17** (1.01 g, 4.65 mmol, >95:5 dr) in MeCN (7.4 mL) at rt. The resultant solution was heated at reflux for 24 h and then allowed to cool to rt and concentrated in vacuo. H<sub>2</sub>O (75 mL) was then added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  100 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **19** as a yellow solid (1.14 g, 80%, >95:5 dr); mp 62–70 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> –220 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3431, 3084, 3061, 3025, 2936, 2876, 2839;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.48 (3H, d, *J* 6.9, C( $\alpha$ )Me), 1.55–1.65 (2H, m, C(6)H<sub>A</sub>), 1.72–1.82 (1H, m, C(6)H<sub>B</sub>), 1.95–2.07 (1H, m, C(5)H<sub>A</sub>), 2.12–2.22 (1H, m, C(5)H<sub>B</sub>), 3.38 (1H, app dt, *J* 10.7, 5.1, C(1)H), 3.42–3.47 (1H, m, C(2)H), 3.68 (1H, s, OH), 3.74 (1H, d, *J* 14.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.00–4.09 (2H, m, C( $\alpha$ )H, NCH<sub>A</sub>H<sub>B</sub>Ph), 5.79



(1H, dddd, *J* 9.9, 4.2, 2.5, 1.5, C(3)*H*), 5.97 (1H, app ddt, *J* 9.9, 4.2, 2.2, C(4)*H*), 7.18–7.47 (10H, m, *Ph*);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) 12.0 (C( $\alpha$ )*Me*), 23.7 (C(5)), 27.8 (C(6)), 52.9 (C(2)), 54.2 (NCH<sub>2</sub>Ph), 57.0 (C( $\alpha$ )), 67.0 (C(1)), 126.6 (C(3)), 127.2, 127.3 (*p-Ph*), 127.9, 128.4, 128.5, 128.8 (*o,m-Ph*), 131.8 (C(4)), 140.9, 143.0 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 308 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>26</sub>NO<sup>+</sup> 308.2009; found 308.2009.

**(1*R*,2*S*, $\alpha$ *R*)-2-[*N*-Benzyl-*N*-( $\alpha$ -methylbenzyl)amino]cyclohex-3-en-1-ol 20.** K<sub>2</sub>CO<sub>3</sub> (2.80 g, 20.1 mmol) and BnBr (1.20 mL, 10.1 mmol) were added sequentially to a stirred solution of **18** (875 mg, 4.03 mmol, >95:5 dr) in MeCN (6.4 mL) at rt. The resultant solution was heated at reflux for 24 h and then allowed to cool to rt and concentrated in vacuo. H<sub>2</sub>O (50 mL) was then added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  75 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **20** as a yellow solid (1.08 g, 87%, >95:5 dr); mp 75–84 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +344 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3357, 3083, 3060, 3025, 2967, 2935, 2875, 2839;  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.39–1.54 (4H, m, C( $\alpha$ )*Me*, C(6)*H*<sub>A</sub>), 1.84–1.94 (1H, m, C(6)*H*<sub>B</sub>), 1.95–2.15 (2H, m, C(5)*H*<sub>2</sub>), 3.62 (1H, d, *J* 15.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.69–3.78 (1H, m, C(1)*H*), 3.79–3.84 (1H, m, C(2)*H*), 3.88–3.97 (2H, m, C( $\alpha$ )*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.48 (1H, s, OH), 4.77 (1H, dddd, *J* 9.8, 4.3, 2.5, 1.5, C(3)*H*), 5.73 (1H, ddd, *J* 9.8, 4.5, 2.0, C(4)*H*), 7.25–7.48 (10H, m, *Ph*);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) 19.6 (C( $\alpha$ )*Me*), 24.0 (C(5)), 28.2 (C(6)), 52.3 (C(2)), 54.2 (NCH<sub>2</sub>Ph), 57.5 (C( $\alpha$ )), 67.0 (C(1)), 125.8 (C(3)), 127.0, 127.5 (*p-Ph*), 128.2, 128.3, 128.6 (*o,m-Ph*), 131.5 (C(4)), 140.5, 140.6 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 308 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>26</sub>NO<sup>+</sup> 308.2009; found 308.2007.

**(1*S*,2*S*,3*S*,4*R*, $\alpha$ *R*)-2-[*N*-( $\alpha$ -Methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 22.** *Step 1.* A solution of **17** (3.10 g, 14.3 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (39.7 mL) was added to anhydrous TsOH (12.3 g, 71.4 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (68% wt, 5.78 g, 22.8 mmol) was added. The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and washed with 0.1 M aq NaHCO<sub>3</sub> (4  $\times$  50 mL), dried and concentrated in vacuo to give an 87:13 mixture of **21** and **22**, respectively, as a yellow oil (6.03 g). Data for **21**:  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) [selected peaks] 1.40 (3H, d, *J* 6.8, C( $\alpha$ )*Me*), 2.34 (3H, s, Ar*Me*), 2.65 (1H, app t, *J* 3.0, C(2)*H*), 3.63 (1H, app t, *J* 3.4, C(3)*H*), 3.96–4.07 (2H, m, C(1)*H*, C( $\alpha$ )*H*), 4.52 (1H, app d, *J* 3.4, C(4)*H*);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) [selected peaks] 21.6 (Ar*Me*), 22.4 (C( $\alpha$ )*Me*), 53.3 (C(2)), 55.8 (C( $\alpha$ )), 67.0 (C(1)), 69.2 (C(3)), 79.5 (C(4)).

*Step 2.* DBU (2.29 mL, 16.1 mmol) was added to a stirred solution of the 87:13 mixture of **21** and **22** from the previous step (6.03 g) in CH<sub>2</sub>Cl<sub>2</sub> (30.4 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave

**22** as a pale yellow solid (2.36 g, 71% from **17**, >95:5 dr); mp 50–52 °C;  $[\alpha]_{\text{D}}^{25}$  –58.2 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3387, 3053, 3061, 3020, 3000, 2953, 2920, 2873;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.31–1.40 (1H, m, *J* 13.1, 3.2, C(5)*H*<sub>A</sub>), 1.43 (3H, d, *J* 6.6, (C( $\alpha$ ))*Me*), 1.45–1.54 (1H, m, C(5)*H*<sub>B</sub>), 1.80 (1H, dddd, *J* 15.7, 8.8, 6.1, 2.8, C(6)*H*<sub>A</sub>), 2.04–2.13 (1H, m, C(6)*H*<sub>B</sub>), 2.84 (1H, app td, *J* 4.3, 0.8, C(2)*H*), 2.92 (1H, app t, *J* 4.3, C(3)*H*), 3.20 (1H, ddd, *J* 4.3, 2.8, 1.4, C(1)*H*), 3.50–3.59 (1H, m, C(4)*H*), 3.74 (1H, br s, *OH*), 3.95 (1H, q, *J* 6.6, C( $\alpha$ ))*H*), 7.24–7.29 (1H, m, *Ph*), 7.32–7.41 (4H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 21.8 (C(6)), 24.2 (C( $\alpha$ ))*Me*), 24.9 (C(5)), 52.6 (C(3)), 55.3 (C(4)), 55.6 (C(2)), 57.0 (C( $\alpha$ )), 66.1 (C(1)), 126.6, 127.2, 128.5 (*o,m,p-Ph*), 145.7 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 234 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>20</sub>NO<sub>2</sub><sup>+</sup> 234.1489; found 234.1489.

**(1*S*,2*S*,3*S*,4*S*, $\alpha$ *R*)-2-[(*N*-( $\alpha$ -Methylbenzyl)amino)cyclohexane-1,3,4-triol 23. Method A. Epoxidation of **17**.** HBF<sub>4</sub> (40% aq, 3.6 mL, 23 mmol) was added to a stirred solution of **17** (1.0 g, 4.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (13 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (75% wt, 1.9 g, 7.4 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with 2.25 M aq NaOH (75 mL) and extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 100 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **23** as a white solid (0.75 g, 65%, >95:5 dr); mp 138–145 °C;  $[\alpha]_{\text{D}}^{25}$  +53.1 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3336, 3063, 3028, 2929;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.32–1.43 (4H, m, C(5)*H*<sub>A</sub>, C( $\alpha$ ))*Me*), 1.64–1.86 (2H, m, C(6)*H*<sub>2</sub>), 1.93–2.04 (1H, m, C(5)*H*<sub>B</sub>), 2.84 (1H, app t, *J* 3.6, C(2)*H*), 3.41 (1H, app t, *J* 3.6, C(3)*H*), 3.78 (1H, app td, *J* 5.9, 3.6, C(4)*H*), 3.92 (1H, app dt, *J* 6.7, 3.6, C(1)*H*), 4.05 (1H, q, *J* 6.6, C( $\alpha$ ))*H*), 7.23–7.37 (5H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 23.1 (C(5)), 24.4 (C( $\alpha$ ))*Me*), 26.2 (C(6)), 55.1 (C(2)), 56.6 (C( $\alpha$ )), 69.7 (C(1)), 70.2 (C(4)), 74.3, (C(3)), 126.7, 127.3, 128.6 (*o,m,p-Ph*), 145.4 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 252 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>22</sub>NO<sub>3</sub><sup>+</sup> 252.1594; found 252.1594.

**Method B. Ring-opening of 22.** HBF<sub>4</sub> (40% aq, 443  $\mu$ L, 2.83 mmol) was added to a stirred solution of **22** (132 mg, 0.566 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.6 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 20 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **23** as a white solid (98 mg, 69%, >95:5 dr).

**(1*R*,2*R*,3*R*,4*S*, $\alpha$ *R*)-2-[(*N*-( $\alpha$ -Methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 25. Step 1.** A solution of **18** (810 mg, 3.73 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (10.4 mL) was added to anhydrous TsOH (3.21 g, 18.6 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (70% wt, 1.47 g, 5.97 mmol)

was added. The resultant solution was stirred at rt for 21 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (30 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4 × 30 mL), dried and concentrated in vacuo to give a 80:20 mixture of **24** and **25**, respectively, as a yellow oil (1.44 g). Data for **24**: δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) [selected peaks] 1.46 (3H, d, *J* 6.6, C(α)*Me*), 2.47 (3H, s, Ar*Me*), 2.66 (1H, app t, *J* 3.0, C(2)*H*), 3.78–3.82 (1H, m, C(1)*H*), 3.91–3.95 (1H, m, C(3)*H*), 4.00 (1H, q, *J* 6.6, C(α)*H*), 4.69 (1H, q, *J* 3.3, C(4)*H*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) [selected peaks] 21.7 (Ar*Me*), 24.1 (C(α)*Me*), 53.4 (C(2)), 56.1 (C(α)), 69.5 (C(3)), 69.6 (C(1)), 79.8 (C(4)).

*Step 2.* DBU (582 μL, 3.84 mmol) was added to a stirred solution of the 80:20 mixture of **24** and **25** from the previous step (1.44 mg) in CH<sub>2</sub>Cl<sub>2</sub> (7.2 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **25** as a pale yellow oil (586 mg, 67% from **18**, >95:5 dr); [α]<sub>D</sub><sup>25</sup> +159.5 (*c* 1.0 in CHCl<sub>3</sub>); ν<sub>max</sub> 3424, 3061, 3025, 2928; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.39–1.47 (5H, m, C(6)*H*<sub>2</sub>, C(α)*Me*), 1.83 (1H, dddd, *J* 15.6, 9.1, 6.8, 2.1, C(5)*H*<sub>A</sub>), 2.10–2.20 (1H, m, C(5)*H*<sub>B</sub>), 2.91 (1H, dd, *J* 5.9, 3.8, C(2)*H*), 3.30–3.41 (3H, m, C(1)*H*, C(3)*H*, C(4)*H*), 3.78 (1H, br s, OH), 4.16 (1H, q, *J* 6.5, C(α)*H*), 7.24–7.30 (1H, m, *Ph*), 7.31–7.39 (4H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 22.6 (C(6)), 24.4 (C(5)), 25.1 (C(α)*Me*), 51.1 (C(2)), 53.9 (C(4)), 55.1 (C(3)), 55.4 (C(α)), 66.7 (C(1)), 126.9, 127.3, 128.6 (*o,m,p-Ph*), 144.6 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 234 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>20</sub>NO<sub>2</sub><sup>+</sup> 234.1489; found 234.1489.

**(1R,2R,3R,4R,αR)-2-[N-(α-Methylbenzyl)amino]cyclohexane-1,3,4-triol** **26.** *Method A.*

*Epoxidation of 18.* HBF<sub>4</sub> (40% aq, 502 μL, 3.22 mmol) was added to a stirred solution of **18** (140 mg, 0.645 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.8 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (75%, 0.243 g, 1.03 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. 2.25 M aq NaOH (15 mL) was then added and the resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 30 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **26** as a white solid (113 mg, 70%, >95:5 dr); mp 149–157 °C; [α]<sub>D</sub><sup>25</sup> +26.0 (*c* 1.0 in CHCl<sub>3</sub>); ν<sub>max</sub> 3345, 3062, 3028, 2929, 2863; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.32–1.43 (4H, m, C(5)*H*<sub>A</sub>, C(α)*Me*), 1.53–1.64 (1H, m, C(6)*H*<sub>A</sub>), 1.69–1.79 (1H, m, C(6)*H*<sub>B</sub>), 1.94–2.04 (1H, m, C(5)*H*<sub>B</sub>), 2.85 (1H, app t, *J* 3.5, C(2)*H*), 3.67 (2H, m, C(1)*H*, C(3)*H*), 3.91 (1H, m, C(4)*H*), 4.04 (1H, q, *J* 6.6, C(α)*H*), 7.22–7.39 (5H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 23.1 (C(5)), 24.5 (C(α)*Me*), 26.1 (C(6)), 55.3 (C(2)), 56.9 (C(α)), 70.3 (C(4)), 70.5 (C(1)), 73.7 (C(3)), 126.7, 127.2, 128.6 (*o,m,p-Ph*), 145.6 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 252 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>14</sub>H<sub>22</sub>NO<sub>3</sub><sup>+</sup> 252.1594; found 252.1594.

*Method B. Ring-opening of 25.* HBF<sub>4</sub> (40% aq, 272  $\mu$ L, 1.73 mmol) was added to a stirred solution of **25** (81 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.96 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (5 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 180:20:1) gave **26** as a white solid (54 mg, 62%, >95:5 dr).

**(1*S*,2*S*,3*S*,4*S*, $\alpha$ *R*)-2-[*N*-Benzyl-*N*-( $\alpha$ -methylbenzyl)amino]-4-tosyloxycyclohexan-1,3-diol **27.****

*Ring-opening of 29.* A solution of **29** (472 mg, 1.46 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (4.1 mL) was added to anhydrous TsOH (1.26 g, 7.30 mmol) at rt. The resultant solution was stirred at rt for 24 h and then diluted with CH<sub>2</sub>Cl<sub>2</sub> (30 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4  $\times$  20 mL), dried and concentrated in vacuo to give **27** as a yellow solid (611 mg, 84%, >95:5 dr); mp 133–140  $^{\circ}$ C;  $[\alpha]_{\text{D}}^{25}$   $-40.2$  (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3453, 3061, 3028, 2936, 2836;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.37 (3H, d, *J* 6.9, C( $\alpha$ )*Me*), 1.48–1.81 (3H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>2</sub>), 2.00–2.13 (1H, m, C(5)*H*<sub>B</sub>), 2.18–2.23 (1H, m, *OH*), 2.46 (3H, s, *ArMe*), 2.84 (1H, app t, *J* 2.5, C(2)*H*), 3.29 (1H, d, *J* 15.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.78 (1H, app s, C(1)*H*), 4.11 (2H, m, C(3)*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.34 (1H, d, *J* 9.3, *OH*), 4.63 (1H, q, *J* 6.9, C( $\alpha$ )*H*), 4.70 (1H, app q, *J* 3.2, C(4)*H*), 7.00–7.05 (2H, m, *Ph*), 7.11–7.26 (4H, m, *Ph*), 7.33–7.39 (4H, m, *Ph*, *Ar*), 7.43–7.49 (2H, m, *Ph*), 7.80–7.86 (2H, m, *Ar*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 10.9 (C( $\alpha$ )*Me*), 18.9 (C(5)), 21.7 (*ArMe*), 24.7 (C(6)), 52.4 (NCH<sub>2</sub>Ph), 54.6 (C( $\alpha$ )), 60.2 (C(2)), 67.8 (C(1)), 68.6 (C(3)), 80.6 (C(4)), 126.6, 127.1, 127.8, 128.2, 128.7, 128.9, 130.0 (*o,m,p-Ph*, *Ar*), 142.8, 143.6, 145.0 (*i-Ph*, *Ar*); *m/z* (ESI<sup>+</sup>) 496 ([*M*+*H*]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [*M*+*H*]<sup>+</sup> Calcd for C<sub>28</sub>H<sub>34</sub>NO<sub>5</sub>S<sup>+</sup> 496.2152; found 496.2151.

**(1*S*,2*S*,3*S*,4*R*, $\alpha$ *R*)-2-[*N*-Benzyl-*N*-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol **29.****

*Benzylation of 22.* K<sub>2</sub>CO<sub>3</sub> (6.25 g, 45.2 mmol) and BnBr (2.69 mL, 22.6 mmol) were added sequentially to a stirred solution of **22** (2.11 mg, 9.05 mmol, >95:5 dr) in MeCN (14.4 mL) at rt. The resultant solution was heated at reflux for 24 h and then allowed to cool to rt and concentrated in vacuo. H<sub>2</sub>O (50 mL) was then added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  75 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **29** as a yellow solid (2.14 g, 73%, >95:5 dr); mp 85–92  $^{\circ}$ C;  $[\alpha]_{\text{D}}^{25}$   $-42.8$  (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3514, 3084, 3060, 3025, 3003, 2996, 2937, 2849;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.30–1.40 (1H, m, C(6)*H*<sub>A</sub>), 1.45 (3H, d, *J* 6.8, C( $\alpha$ )*Me*), 1.65–1.75 (1H, m, C(6)*H*<sub>B</sub>), 1.83 (1H, app ddt, *J* 15.8, 7.0, 4.2, C(5)*H*<sub>A</sub>), 2.09 (1H, ddd, *J* 15.8, 9.5, 6.4, C(5)*H*<sub>B</sub>), 3.07 (1H, dd, *J* 4.8, 2.0, C(2)*H*), 3.25 (1H, app t, *J* 4.2, C(4)*H*), 3.38–3.42 (1H, m, C(3)*H*), 3.49 (1H, d, *J* 8.9, *OH*), 3.55–3.63 (1H, m, C(1)*H*), 4.19–4.27 (2H, m, C( $\alpha$ )*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.36 (1H, d, *J* 14.6, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.18–7.40 (8H, m, *Ph*), 7.51–7.56 (2H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 15.3 (C( $\alpha$ )*Me*),

19.8 (C(5)), 28.1 (C(6)), 53.0 (C(4), NCH<sub>2</sub>Ph), 54.3 (C(2)), 56.8 (C(3)), 56.9 (C( $\alpha$ )), 69.4 (C(1)), 126.8, 126.9, 127.7, 128.2, 128.3, 128.5 (*o,m,p-Ph*), 141.8, 143.9 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 324 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>26</sub>NO<sub>2</sub><sup>+</sup> 324.1958; found 324.1959.

**(1*S*,2*S*,3*R*,4*S*, $\alpha$ *R*)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 30.** *Step 1.* MsCl (211  $\mu$ L, 2.73 mmol) was added to a stirred solution of **40** (387 mg, 0.910 mmol) in pyridine (9.1 mL) at 0 °C. The resultant solution was stirred at rt for 16 h and then concentrated in vacuo to give an ~15:85 mixture of **40** and **42**, respectively.

*Step 2.* K<sub>2</sub>CO<sub>3</sub> (1.28 g) was added to a stirred solution of the residue from the previous step in MeOH (12.8 mL) at rt. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. H<sub>2</sub>O (15 mL) was added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  20 mL). The combined organics were dried and concentrated in vacuo to give an 85:15 mixture of **30** and **31**, respectively. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **30** as an orange solid (148 mg, 50%, >95:5 dr); mp 123–130 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> –35.3 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3459, 3084, 3061, 3026, 2968, 2932, 2850;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.33–1.57 (5H, m, C(6)H<sub>2</sub>, C( $\alpha$ )Me), 1.84–1.93 (1H, m, C(5)H<sub>A</sub>), 2.05 (1H, dddd, *J* 15.4, 9.0, 6.2, 2.6, C(5)H<sub>B</sub>), 2.62 (1H, s, OH), 3.14 (1H, d, *J* 4.3, C(2)H), 3.26 (1H, m, C(4)H), 3.33 (1H, d, *J* 4.3, C(3)H), 3.35–3.41 (1H, m, C(1)H), 4.06–4.16 (2H, m, C( $\alpha$ )H, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.20 (1H, d, *J* 14.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.22–7.37 (6H, m, *Ph*), 7.37–7.44 (2H, m, *Ph*), 7.48–7.53 (2H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 12.1 (C( $\alpha$ )Me), 19.1 (C(5)), 23.1 (C(6)), 52.9 (C(4)), 53.2 (C(3)), 53.6 (NCH<sub>2</sub>Ph), 54.0 (C(2)), 57.0 (C( $\alpha$ )), 65.5 (C(1)), 127.2, 127.3, 127.8, 128.0, 128.3, 128.7 (*o,m,p-Ph*), 140.6, 142.9 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 324 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>26</sub>NO<sub>2</sub><sup>+</sup> 324.1958; found 324.1958.

**(1*S*,2*R*,3*S*,4*R*, $\alpha$ *R*)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 29 and (1*S*,2*S*,3*R*,4*S*, $\alpha$ *R*)-2-[N-benzyl-N-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 30.** *Step 1.* A solution of **19** (200 mg, 0.651 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.8 mL) was added to anhydrous TsOH (561 mg, 3.26 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (73% wt, 767 mg, 3.26 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4  $\times$  20 mL), dried and concentrated in vacuo to give a 68:32 mixture of **27** and **28**, respectively, as a yellow oil (240 mg).

*Step 2.* DBU (79  $\mu$ L, 0.52 mmol) was added to a stirred solution of a 68:32 mixture of **27** and **28** from the previous step (240 mg) in CH<sub>2</sub>Cl<sub>2</sub> (0.99 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo to give a 68:32 mixture of **29** and **30**, respectively. Purification via flash

column chromatography (eluent CHCl<sub>3</sub>) gave an 81:19 mixture of **29** and **30**, respectively, as a pale yellow oil (75 mg, 36%).

**(1S,2S,3S,4S,αR)-2-[N-Benzyl-N-(α-methylbenzyl)amino]cyclohexane-1,3,4-triol 31.** *Method A. N-Benzylation of 23.* <sup>i</sup>Pr<sub>2</sub>NEt (92 μL, 0.53 mmol), BnBr (62 μL, 0.53 mmol) and DMAP (280 μg, 23.3 μmol) were added sequentially to a stirred solution of **23** (88 mg, 0.35 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **31** as a white solid (63 mg, 53%, >95:5 dr); mp 146–153 °C; [α]<sub>D</sub><sup>25</sup> –26.4 (c 1.0 in CHCl<sub>3</sub>); ν<sub>max</sub> 3368, 3084, 3061, 3027, 2933, 2839; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.41–1.49 (4H, m, C(5)H<sub>A</sub>, C(α)Me), 1.61–1.86 (2H, m, C(6)H<sub>2</sub>), 2.10 (1H, tdd, *J* 14.3, 4.6, 2.1, C(5)H<sub>B</sub>), 2.38 (1H, s, OH), 2.94 (1H, app t, *J* 2.0, C(2)H), 3.43 (1H, d, *J* 15.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.80 (1H, s, C(1)H), 4.06–4.17 (4H, m, C(3)H, C(4)H, NCH<sub>A</sub>H<sub>B</sub>Ph, OH), 4.78 (1H, q, *J* 6.9, C(α)H), 7.06–7.29 (6H, m, *Ph*), 7.34–7.40 (2H, m, *Ph*), 7.52–7.56 (2H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 11.7 (C(α)Me), 21.2 (C(5)), 24.8 (C(6)), 52.6 (NCH<sub>2</sub>Ph), 54.7 (C(α)), 60.2 (C(2)), 68.6 (C(1)), 70.8, 71.5 (C(3), C(4)), 126.8 (*o,m-Ph*), 126.9, 126.9, 128.2, 128.6, 128.8 (*o,m,p-Ph*), 143.0, 143.9 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 342 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2061.

*Method B. Ring-opening of 29.* HBF<sub>4</sub> (40% aq, 400 μL, 2.55 mmol) was added to a stirred solution of **29** (165 mg, 0.511 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.4 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/<sup>i</sup>PrOH (3:1, v/v, 3 × 15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **31** as a white solid (110 mg, 63%, >95:5 dr).

**(1S,2S,3R,4R,αR)-2-[N-Benzyl-N-(α-methylbenzyl)amino]cyclohexane-1,3,4-triol 32.** *Ring-opening of 30.* HBF<sub>4</sub> (40% aq, 199 μL, 1.27 mmol) was added to a stirred solution of **30** (82.0 mg, 0.254 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.71 mL) at rt. The resultant solution was stirred at 40 °C for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/<sup>i</sup>PrOH (3:1, v/v, 3 × 20 mL). The combined organics were dried and concentrated in vacuo to give a 5:95 mixture of **31** and **32**, respectively. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 99:1) gave **32** as a white solid (50 mg, 58%, 95:5 dr); mp 133–136 °C; [α]<sub>D</sub><sup>25</sup> +115.6 (c 1.0 in CHCl<sub>3</sub>); ν<sub>max</sub> 3403, 3084, 3061, 3027, 2935; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.23–1.33 (1H, m, C(6)H<sub>A</sub>), 1.37 (3H, d, *J* 7.0, C(α)Me), 1.45–1.54 (1H, m, C(6)H<sub>B</sub>), 1.67–1.77 (2H, m, C(5)H<sub>2</sub>), 2.49 (1H, d, *J* 2.4, OH), 2.64 (1H, dd, *J* 10.6, 2.0, C(2)H), 3.24 (1H, app s, C(1)H), 3.48–3.56 (2H, m, C(4)H, OH), 3.76 (1H, dd, *J* 10.6, 8.3, C(3)H), 3.90 (1H, d, *J* 14.9, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.06 (1H, q, *J* 7.0, C(α)H), 4.43 (1H, d, *J* 14.9, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.28–7.45 (10H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 19.5 (C(α)Me), 25.4 (C(5)), 30.3 (C(6)), 51.9 (NCH<sub>2</sub>Ph), 56.8 (C(α)), 61.3 (C(2)), 67.9 (C(1)),

69.9 (C(3)), 75.4 (C(4)), 127.0, 127.4, 127.7, 128.4, 128.4, 128.6 (*o,m,p-Ph*), 140.9, 142.2 (*i-Ph*);  $m/z$  (ESI<sup>+</sup>) 342 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>)  $m/z$ : [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2062.

**(1S,2S,3S,4S, $\alpha$ R)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol 31 and (1S,2S,3R,4R, $\alpha$ R)-2-[N-benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol 32.** *via Epoxidation of 19.* **Step 1.** HBF<sub>4</sub> (40% aq, 510  $\mu$ L, 3.26 mmol) was added to a stirred solution of **19** (200 mg, 0.651 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.8 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (75% wt, 0.767 g, 3.26 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with 2.25 M aq NaOH (15 mL) and extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  30 mL). The combined organics were dried and concentrated in vacuo to give an ~1:1:1 mixture of **29**, **30** and **31** (310 mg).

**Step 2.** HBF<sub>4</sub> (40% aq, 750  $\mu$ L, 4.80 mmol) was added to a stirred solution of the ~1:1:1 mixture of **29**, **30** and **31** from the previous step (310 mg) in CH<sub>2</sub>Cl<sub>2</sub> (2.7 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organic extracts were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo to give a 21:28:49:2 mixture of **29**, **30**, **31** and **32**, respectively (211 mg).

**Step 3.** HBF<sub>4</sub> (40% aq, 512  $\mu$ L, 3.26 mmol) was added to a stirred solution of the 21:28:49:2 mixture of **29**, **30**, **31** and **32** from the previous step (211 mg) in CH<sub>2</sub>Cl<sub>2</sub> (1.8 mL) at rt. The resultant solution was stirred at rt for 5 days and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo to give a 70:30 mixture of **31** and **32**, respectively (144 mg).

**(1R,2R,3R,4R, $\alpha$ R)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]-4-tosyloxycyclohexan-1,3-diol 33.** A solution of **35** (99 mg, 0.31 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.85 mL) was added to anhydrous TsOH (263 mg, 1.53 mmol) at rt and the resultant solution was stirred at rt for 24 h. The resultant mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4  $\times$  15 mL), dried and concentrated in vacuo to **33** as a yellow oil (99 mg, 66%, >95:5 dr);  $[\alpha]_D^{25}$  +4.6 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3510, 3019, 2935;  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.48–1.59 (1H, m, C(5)*H*<sub>A</sub>, C( $\alpha$ )*Me*), 1.77–1.84 (2H, m, C(6)*H*<sub>2</sub>), 1.97–2.08 (1H, m, C(5)*H*<sub>B</sub>), 2.47 (3H, s, *ArMe*), 2.88 (1H, app t, *J* 2.5, C(2)*H*), 2.96 (1H, br s, *OH*), 3.31 (1H, br s, *OH*), 3.82 (2H, app s, NCH<sub>2</sub>Ph), 3.92–3.96 (1H, m, C(3)*H*), 4.15–4.19 (1H, m, C(1)*H*), 4.51–4.55 (1H, m, C(4)*H*), 4.66 (1H, q, *J* 7.0, C( $\alpha$ )*H*), 7.15–7.45 (12H, m, *Ph*, *Ar*), 7.69–7.73 (2H, m, *Ar*);  $\delta_C$  (101 MHz, CDCl<sub>3</sub>) 15.2 (C( $\alpha$ )*Me*), 19.0 (C(5)), 21.6 (*ArMe*), 26.3 (C(6)), 52.2 (NCH<sub>2</sub>Ph), 55.1 (C( $\alpha$ )), 59.8 (C(2)), 68.0 (C(1)), 69.3 (C(3)), 79.7 (C(4)), 126.8, 127.0, 127.0, 127.7, 128.1, 128.3, 128.9, 129.9, 133.4 (*o,m,p-Ph*, *Ar*), 142.8, 143.1, 144.8 (*i*-

*Ph*, *Ar*);  $m/z$  (ESI<sup>+</sup>) 496 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>)  $m/z$ : [M+H]<sup>+</sup> Calcd for C<sub>28</sub>H<sub>34</sub>NO<sub>5</sub>S<sup>+</sup> 496.2152; found 496.2147.

**(1*R*,2*R*,3*R*,4*S*, $\alpha$ *R*)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 35.** K<sub>2</sub>CO<sub>3</sub> (267 mg, 1.93 mmol) and BnBr (115 mL, 965  $\mu$ mol) were added sequentially to a stirred solution of **25** (90 mg, 0.39 mmol, >95:5 dr) in MeCN (0.61 mL) at rt. The resultant solution was heated at reflux for 24 h and then allowed to cool to and concentrated in vacuo. H<sub>2</sub>O (10 mL) was added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **35** as a yellow oil (57.9 mg, 49%, >95:5 dr); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +113.9 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3511, 3084, 3060, 3026, 3004, 2936, 2850;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.47 (3H, d, *J* 7.0, C( $\alpha$ )*Me*), 1.50–1.60 (1H, m, C(6)*H*<sub>A</sub>), 1.68–1.89 (2H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>B</sub>), 2.03–2.13 (1H, m, C(5)*H*<sub>B</sub>), 2.64 (1H, dd, *J* 4.1, 2.1, C(3)*H*), 3.08 (1H, app t, *J* 4.1, C(4)*H*), 3.32 (1H, dd, *J* 4.8, 2.1, C(2)*H*), 3.85 (1H, br s, *OH*), 3.91 (1H, br s, C(1)*H*), 4.10–4.22 (2H, m, NCH<sub>A</sub>H<sub>B</sub>Ph, C( $\alpha$ )*H*), 4.31 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.24–7.31 (2H, m, *Ph*), 7.33–7.44 (6H, m, *Ph*), 7.47–7.53 (2H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 17.7 (C( $\alpha$ )*Me*), 20.0 (C(5)), 28.2 (C(6)), 52.6 (C(4)), 53.0 (NCH<sub>2</sub>Ph), 53.7 (C(2)), 56.1 (C(3)), 56.2 (C( $\alpha$ )), 69.7 (C(1)), 126.8, 127.1, 127.7, 128.3, 128.3, 128.4 (*o,m,p-Ph*), 140.9, 142.5 (*i-Ph*);  $m/z$  (ESI<sup>+</sup>) 324 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>)  $m/z$ : [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>26</sub>NO<sub>2</sub><sup>+</sup> 324.1958; found 324.1954.

**(1*R*,2*R*,3*S*,4*R*, $\alpha$ *R*)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 36.** *Step 1.* MsCl (110  $\mu$ L, 1.43 mmol) was added to a stirred solution of **55** (202 mg, 0.475 mmol, >95:5 dr) in pyridine (4.75 mL) at 0 °C. The resultant solution was stirred at rt for 16 h and then concentrated in vacuo to give an ~10:90 mixture of **55** and **57**, respectively.

*Step 2.* K<sub>2</sub>CO<sub>3</sub> (640 mg) was added to a stirred solution of the residue from the previous step in MeOH (6.4 mL) at rt. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. H<sub>2</sub>O (15 mL) was added and the resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  20 mL). The combined organics were dried and concentrated in vacuo to give a 78:8:14 mixture of **36**, **37** and **58**, respectively. Purification via flash column chromatography (eluent CHCl<sub>3</sub>) gave **58** as a yellow oil (12 mg, 7%, >95:5 dr); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +11.6 (*c* 0.5 in CHCl<sub>3</sub>);  $\nu_{\max}$  (ATR) 3059, 3027, 2933, 2848, 1736;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.39 (3H, d, *J* 7.1, C( $\alpha$ )*Me*), 1.41–1.48 (1H, m, C(6)*H*<sub>A</sub>), 1.61 (3H, s, *COMe*), 1.64–1.83 (2H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>B</sub>), 1.87–1.95 (1H, m, C(5)*H*<sub>B</sub>), 2.67 (1H, dd, *J* 3.9, 1.5, C(3)*H*), 3.13–3.17 (1H, m, C(4)*H*), 3.38 (1H, d, *J* 4.6, C(2)*H*), 3.87 (1H, q, *J* 7.1, C( $\alpha$ )*H*), 3.95 (1H, d, *J* 15.8, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.18 (1H, d, *J* 15.8, NCH<sub>A</sub>H<sub>B</sub>Ph), 5.07 (1H, app tt, *J* 4.6, 1.5, C(1)*H*), 7.21–7.46 (10 H, m, *Ph*);  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>) 18.9 (C(5)), 20.1 (C( $\alpha$ )*Me*), 20.9 (*COMe*), 21.2 (C(6)), 52.2 (C(3)), 53.0 (C(4)), 53.6 (NCH<sub>2</sub>Ph), 54.0 (C(2)), 59.6 (C( $\alpha$ )), 72.2 (C(1)), 126.6, 126.9, 127.4, 127.7, 128.4 (*o,m,p-Ph*), 141.6, 142.0 (*i-Ph*), 170.6 (*COMe*);  $m/z$  (ESI<sup>+</sup>) 366 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>)



$m/z$ :  $[M+H]^+$  Calcd for  $C_{23}H_{28}NO_3^+$  366.2064; found 366.2061. Further elution gave **36** as a yellow oil (108 mg, 70%, >95:5 dr);  $[\alpha]_D^{25} +50.8$  ( $c$  1.0 in  $CHCl_3$ );  $\nu_{max}$  3443, 3060, 3026, 2933, 2848;  $\delta_H$  (400 MHz,  $CDCl_3$ ) 1.45–1.63 (5H, m,  $C(6)H_2$ ,  $C(\alpha)Me$ ), 1.85–2.04 (2H, m,  $C(5)H_2$ ), 2.53 (1H, app dd,  $J$  3.8, 1.0,  $C(3)H$ ), 3.02–3.06 (1H, m,  $C(4)H$ ), 3.12 (1H, d,  $J$  4.6,  $OH$ ), 3.59 (1H, app d,  $J$  4.9,  $C(2)H$ ), 3.79–3.86 (1H, m,  $C(1)H$ ), 3.90–4.00 (2H, m,  $C(\alpha)H$ ,  $NCH_AH_BPh$ ), 4.07 (1H, d,  $J$  15.4,  $NCH_AH_BPh$ ), 7.28–7.47 (10H, m,  $Ph$ );  $\delta_C$  (100 MHz,  $CDCl_3$ ) 19.2 ( $C(\alpha)Me$ ), 19.7 ( $C(5)$ ), 23.9 ( $C(6)$ ), 52.6 ( $C(4)$ ), 52.8 ( $C(3)$ ), 53.3 ( $NCH_2Ph$ ), 53.9 ( $C(2)$ ), 58.1 ( $C(\alpha)$ ), 65.6 ( $C(1)$ ), 127.2, 127.4, 127.6, 128.0, 128.5, 128.8 ( $o,m,p-Ph$ ), 140.2, 140.5 ( $i-Ph$ );  $m/z$  ( $ESI^+$ ) 324 ( $[M+H]^+$ , 100%); HRMS ( $ESI^+$ )  $m/z$ :  $[M+H]^+$  Calcd for  $C_{21}H_{26}NO_2^+$  324.1958; found 324.1954.

*Preparation of an authentic sample of 34 via ring-opening of 36.* A solution of **36** (40 mg, 0.124 mmol, >95:5 dr) in  $CH_2Cl_2$  (0.34 mL) was added to anhydrous TsOH (107 mg, 0.619 mmol) at rt and the resultant solution was stirred at rt for 24 h. The resultant mixture was diluted with  $CH_2Cl_2$  (5 mL), washed with 0.1 M aq  $NaHCO_3$  ( $4 \times 10$  mL), dried and concentrated in vacuo to give **34** as a yellow oil (34 mg);  $\delta_H$  (400 MHz,  $CDCl_3$ ) 1.32–1.55 (4H, m,  $C(6)H_A$ ,  $C(\alpha)Me$ ), 1.68–1.76 (1H, m,  $C(6)H_B$ ), 1.78–2.00 (2H, m,  $C(5)H_2$ ), 2.43–2.47 (4H, m,  $C(2)H$ ,  $ArMe$ ), 3.87–4.02 (2H, m,  $C(1)H$ ,  $NCH_AH_BPh$ ), 4.12–4.29 (4H, m,  $C(3)H$ ,  $C(4)H$ ,  $C(\alpha)H$ ,  $NCH_AH_BPh$ ), 7.19–7.39 (12H, m,  $Ph$ ,  $Ar$ ) 7.76–7.81 (2H, m,  $Ar$ );  $\delta_C$  (101 MHz,  $CDCl_3$ ) 15.1 ( $C(\alpha)Me$ ), 21.6 ( $ArMe$ ), 24.5 ( $C(5)$ ), 29.6 ( $C(6)$ ), 50.2 ( $NCH_2Ph$ ), 57.7 ( $C(\alpha)$ ), 63.1 ( $C(2)$ ), 67.3 ( $C(1)$ ), 69.0 ( $C(3)$ ), 85.7 ( $C(4)$ ), 127.0, 127.1, 127.7, 127.7, 128.4, 128.6, 129.5, 134.3 ( $o,m,p-Ph$ ,  $Ar$ ), 141.0, 143.4, 144.3 ( $i-Ph$ ,  $Ar$ ).

**(1R,2S,3R,4S,αR)-2-[N-Benzyl-N-(α-methylbenzyl)amino]-3,4-epoxycyclohexan-1-ol 35 and (1R,2R,3S,4R,αR)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3,4-epoxycyclohexane 36.** via *Epoxidation of 20.* *Step 1.* A solution of **20** (200 mg, 0.651 mmol, >95:5 dr) in  $CH_2Cl_2$  (1.8 mL) was added to anhydrous TsOH (561 mg, 3.26 mmol) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (73% wt, 767 mg, 3.26 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid  $Na_2SO_3$  was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with  $CH_2Cl_2$  (20 mL), washed with 0.1 M aq  $NaHCO_3$  ( $4 \times 20$  mL), dried and concentrated in vacuo to give a 72:28 mixture of **33** and **34**, respectively, as a yellow oil (270 mg).

*Step 2.* DBU (89  $\mu$ L, 0.52 mmol) was added to a stirred solution of the 72:28 mixture of **33** and **34** from the previous step (270 mg) in  $CH_2Cl_2$  (1.1 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo to give a 72:28 mixture of **35** and **36**, respectively. Purification via flash column chromatography (eluent  $CHCl_3$ ) gave a 78:22 mixture of **35** and **36**, respectively, as a pale yellow oil (61 mg, 29%).

**(1R,2R,3R,4R, $\alpha$ R)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol **37**. Method A.**

*N*-Benzylation of **26**.  $i$ Pr<sub>2</sub>NEt (104  $\mu$ L, 597  $\mu$ mol), BnBr (71  $\mu$ L, 0.60 mmol) and DMAP (320  $\mu$ g, 26.5  $\mu$ mol) were added sequentially to a stirred solution of **26** (100 mg, 0.398 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.1 mL) at rt. The resultant mixture was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **37** as a white solid (35.7 mg, 27%, >95:5 dr); mp 134–138 °C;  $[\alpha]_D^{25}$  –7.4 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3372, 3084, 3060, 3027, 2987, 2850;  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.41–1.51 (4H, m, C( $\alpha$ )Me, C(5)H<sub>A</sub>), 1.75–1.95 (2H, m, C(6)H<sub>2</sub>), 2.07 (1H, app tdd, *J* 14.1, 4.7, 2.8, C(5)H<sub>B</sub>), 2.96 (1H, app t, *J* 2.6, C(2)H), 2.96 (1H, br s, OH), 3.34 (1H, d, *J* 7.2, OH), 3.67–3.80 (2H, m, NCH<sub>A</sub>H<sub>B</sub>Ph, C(3)H), 3.93–4.03 (2H, m, NCH<sub>A</sub>H<sub>B</sub>Ph, C(4)H), 4.19–4.26 (1H, m, C(1)H), 4.74 (1H, q, *J* 6.9, C( $\alpha$ )H), 7.15–7.29 (6H, m, Ph), 7.34–7.40 (2H, m, Ph), 7.47–7.52 (2H, m, Ph);  $\delta_C$  (100 MHz, CDCl<sub>3</sub>) 13.8 (C( $\alpha$ )Me), 21.4 (C(5)), 26.6 (C(6)), 52.4 (NCH<sub>2</sub>Ph), 55.0 (C( $\alpha$ )), 60.0 (C(2)), 68.6 (C(1)), 69.6 (C(4)), 72.0 (C(3)), 126.8, 126.9, 126.9, 128.2, 128.4, 128.8 (*o,m,p*-Ph), 143.1, 143.7 (*i*-Ph); *m/z* (ESI<sup>+</sup>) 342 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2063.

*Method B. Ring-opening of 35*. HBF<sub>4</sub> (40% aq, 310  $\mu$ L, 1.98 mmol) was added to a stirred solution of **35** (128 mg, 0.396 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.1 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (2.25 M, 10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 49:1) gave **37** as a white solid (82 mg, 61%, >95:5 dr).

**(1R,2R,3S,4S, $\alpha$ R)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol **38**. Method A.**

*Step 1. Ring-opening of 36*. HBF<sub>4</sub> (40% aq, 188  $\mu$ L, 1.20 mmol) was added to a stirred solution of **36** (76 mg, 0.24 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (0.67 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  20 mL). The combined organics were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo to give an 85:15 mixture of **36** and **38**, respectively (76.5 mg).

*Step 2*. HBF<sub>4</sub> (40% aq, 185  $\mu$ L, 1.18 mmol) was added to a stirred solution of the 85:15 mixture of **36** and **38** from the previous step (76.5 mg, 0.237 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.66 mL) at rt. The resultant solution was stirred at 40 °C for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  20 mL). The combined organics were dried and concentrated in vacuo to give a 5:95 mixture of **37** and **38**, respectively. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 32:1) gave **38** as a white solid (30 mg, 37%, >95:5 dr); mp 185–196 °C;  $[\alpha]_D^{25}$  –38.5 (*c* 1.0 in 1:1 CHCl<sub>3</sub>/MeOH);  $\nu_{\max}$  3375, 3061, 3027, 2942, 2877, 2843;  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.42–1.56 (4H, m,

C(6)*H<sub>A</sub>*, C( $\alpha$ )*Me*), 1.64 (1H, s, OH) 1.70–1.79 (3H, m, C(5)*H<sub>2</sub>*, C(6)*H<sub>B</sub>*), 2.42 (1H, dd, *J* 10.6, 2.1, C(2)*H*), 2.49 (1H, s, OH), 2.91 (1H, s, OH), 3.19–3.28 (1H, m, C(4)*H*), 3.77 (1H, dd, *J* 10.6, 8.3, C(3)*H*), 3.94 (1H, d, *J* 14.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.24 (1H, q, *J* 6.9, C( $\alpha$ )*H*), 4.30 (1H, d, *J* 14.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.36–4.41 (1H, m, C(1)*H*), 7.18–7.39 (10H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 14.6 (C( $\alpha$ )*Me*), 25.2 (C(5)), 30.6 (C(6)), 50.9 (NCH<sub>2</sub>Ph), 56.1 (C( $\alpha$ )), 61.7 (C(2)), 69.8 (C(1)), 70.2 (C(3)), 75.4 (C(4)), 127.1, 127.2, 127.6, 128.5, 128.6, 128.8 (*o,m,p-Ph*), 140.7, 143.5 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 342 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2065.

**Method B. Ring-opening of 36.** HBF<sub>4</sub> (40% aq, 159  $\mu$ L, 1.01 mmol) was added to a stirred solution of **36** (65.6 mg, 0.203 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.56 mL) at rt. The resultant solution was stirred at 40 °C for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 32:1) gave **38** as a white solid (37 mg, 53%, 90:10 dr).

**(1*R*,2*R*,3*R*,4*R*, $\alpha$ *R*)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol 37 and (1*R*,2*R*,3*S*,4*S*, $\alpha$ *R*)-2-[N-benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol 38.** *via Epoxidation of 20.* **Step 1.** HBF<sub>4</sub> (40% aq, 510  $\mu$ L, 3.26 mmol) was added to a stirred solution of **20** (200 mg, 0.651 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.8 mL) at rt. The resultant solution was stirred at rt for 5 min and then *m*-CPBA (75% wt, 767 mg, 3.26 mmol) was added. The resultant solution was stirred at rt for 30 h and then solid Na<sub>2</sub>SO<sub>3</sub> was added until starch-iodide paper indicated that no *m*-CPBA was present. The resultant mixture was diluted with 2.25 M aq NaOH (2.25 M, 15 mL) and extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  30 mL). The combined organics were dried and concentrated in vacuo to give a 48:31:21 mixture of **35**, **36** and **37**, respectively (315 mg).

**Step 2.** HBF<sub>4</sub> (40% aq, 760  $\mu$ L, 4.87 mmol) was added to a stirred solution of the 48:31:21 mixture of **35**, **36** and **37** from the previous step (315 mg) in CH<sub>2</sub>Cl<sub>2</sub> (2.7 mL) at rt. The resultant solution was stirred at rt for 24 h and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo to give a 21:23:53:3 mixture of **35**, **36**, **37** and **38**, respectively (200 mg).

**Step 3.** HBF<sub>4</sub> (40% aq, 485  $\mu$ L, 3.09 mmol) was added to a stirred solution of the 21:23:53:3 mixture of **35**, **36**, **37** and **38** from the previous step (200 mg) in CH<sub>2</sub>Cl<sub>2</sub> (1.7 mL) at rt. The resultant solution was stirred at rt for 5 days and then 2.25 M aq NaOH (10 mL) was added. The resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  15 mL). The combined organics were dried and concentrated in vacuo to give an ~70:30 mixture of **37** and **38**, respectively (200 mg).

**(1S,2S,3S,4R,αR)-1-Acetoxy-2-[N-benzyl-N-(α-methylbenzyl)amino]-3,4-epoxycyclohexane 39.**

Ac<sub>2</sub>O (875 μL, 9.28 mmol) and DMAP (2.5 mg, 21 μmol) were added sequentially to a stirred solution of **29** (1.00 g, 3.09 mmol, >95:5 dr) in pyridine (12.9 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave **39** as a yellow oil (864 mg, 76%, >95:5 dr);  $[\alpha]_{\text{D}}^{25} +17.8$  (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3061, 3024, 2970, 2848, 1730;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.24 (1H, dddd, *J* 14.5, 12.1, 7.6, 2.3, C(6)*H*<sub>A</sub>), 1.44 (3H, d, *J* 6.8, C(α)*Me*), 1.67–1.86 (3H, m, C(5)*H*<sub>2</sub>, C(6)*H*<sub>B</sub>), 1.95 (3H, s, COMe), 3.06 (1H, dd, *J* 4.4, 2.0, C(2)*H*), 3.19–3.23 (1H, m, C(4)*H*), 3.28 (1H, m, C(3)*H*), 4.10 (1H, q, *J* 6.8, C(α)*H*), 4.21 (1H, d, *J* 15.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.45 (1H, d, *J* 15.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.88–4.92 (1H, m, C(1)*H*), 7.19–7.26 (2H, m, *Ph*), 7.30–7.37 (4H, m, *Ph*), 7.44–7.50 (4H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 14.5 (C(α)*Me*), 19.0 (C(5)), 21.5 (COMe), 25.9 (C(6)), 51.3 (C(4)), 52.6 (NCH<sub>2</sub>Ph), 54.1 (C(3)), 54.2 (C(2)), 56.7 (C(α)), 72.6 (C(1)), 126.6, 126.8, 127.6, 127.9, 128.2, 128.3 (*o,m,p-Ph*), 141.8, 144.0 (*i-Ph*), 171.3 (COMe); *m/z* (ESI<sup>+</sup>) 366 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 366.2064; found 366.2062.

**(1S,2R,3S,4S,αR)-1,4-Diacetoxy-2-[N-benzyl-N-(α-methylbenzyl)amino]cyclohexan-3-ol 40 and (1S,2S,3S,4S,αR)-3,4-diacetoxy-2-[N-benzyl-N-(α-methylbenzyl)amino]cyclohexan-1-ol 41.** A stirred solution of **39** (630 mg, 1.72 mmol, >95:5 dr) in AcOH (1.91 mL) was heated at 50 °C for 36 h and then allowed to cool to rt and diluted with 0.1 M aq NaHCO<sub>3</sub> (10 mL). The resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The combined organics were washed with 0.1 M aq NaHCO<sub>3</sub> (20 mL), dried and concentrated in vacuo to give an 88:12 mixture of **40** and **41**, respectively. Purification via preparative thin layer chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave a >95:5 mixture of **40** and **41** as a white solid (439 mg, 60%) and a 9:91 mixture of **40** and **41** as a yellow oil (28 mg, 4%). Data for **40**: *R*<sub>f</sub> = 0.57;  $\nu_{\text{max}}$  (ATR) 3485, 3024, 2925, 2850, 1734;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.39 (3H, d, *J* 6.8, C(α)*Me*), 1.49–1.60 (2H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>A</sub>), 1.73–1.82 (1H, m, C(6)*H*<sub>B</sub>), 1.86–1.98 (4H, m, COMe, C(5)*H*<sub>B</sub>), 2.02 (3H, s, COMe), 3.02 (1H, app t, *J* 2.6, C(2)*H*), 3.16 (1H, d, *J* 8.7, OH), 3.93 (1H, d, *J* 15.1, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.12–4.22 (2H, m, C(3)*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.33 (1H, q, *J* 6.8, C(α)*H*), 5.00–5.07 (2H, m, C(1)*H*, C(4)*H*), 7.15–7.29 (6H, m, *Ph*), 7.30–7.36 (2H, m, *Ph*), 7.38–7.43 (2H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 14.2 (C(α)*Me*), 18.9 (C(5)), 21.1, 21.3 (COMe), 24.9 (C(6)), 52.3 (NCH<sub>2</sub>Ph), 55.8 (C(2)), 56.8 (C(α)), 71.2 (C(3)), 72.7 (C(4)), 74.8 (C(1)), 126.6, 126.9, 127.6, 127.9, 128.2, 128.2 (*o,m,p-Ph*), 141.7, 143.8 (*i-Ph*), 169.2, 169.8 (COMe); *m/z* (ESI<sup>+</sup>) 426 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>25</sub>H<sub>32</sub>NO<sub>5</sub><sup>+</sup> 426.2275; found 426.2271. Data for **41**: *R*<sub>f</sub> = 0.50;  $\nu_{\text{max}}$  (ATR) 3468, 3060, 3027, 2924, 2850, 1740;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.39 (3H, d, *J* 6.9, C(α)*Me*), 1.53–1.72 (3H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>2</sub>), 1.89–1.98 (1H, m, C(5)*H*<sub>B</sub>), 2.01 (3H, s, C(3)(COMe)), 2.03 (3H, s, C(4)(COMe)), 2.51 (1H, d, *J* 7.1, OH), 3.15 (1H, app t, *J* 2.9, C(2)*H*), 3.84 (1H, m, C(1)*H*), 4.04

(1H, d, *J* 15.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.11 (1H, d, *J* 15.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.18 (1H, q, *J* 6.9, C( $\alpha$ )H), 4.99–5.03 (1H, m, C(4)H), 5.26–5.30 (1H, m, C(3)H), 7.16–7.38 (10H, m, *Ph*);  $\delta_C$  (100 MHz, CDCl<sub>3</sub>) 15.6 (C( $\alpha$ )Me), 19.4 (C(5)), 21.0, 27.8 (COMe), 29.7 (C(6)), 52.5 (NCH<sub>2</sub>Ph), 55.5 (C(2)), 57.0 (C( $\alpha$ )), 69.4 (C(1)), 69.8 (C(4)), 73.6 (C(3)), 126.7, 127.0, 127.7, 127.8, 128.2, 128.3 (*o,m,p-Ph*), 141.8, 143.4 (*i-Ph*), 169.4, 169.4 (COMe); *m/z* (ESI<sup>+</sup>) 426 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>25</sub>H<sub>32</sub>NO<sub>5</sub><sup>+</sup> 426.2275; found 426.2271.

**(1*S*,2*S*,3*S*,4*S*)-2-Aminocyclohexane-1,3,4-triol [(+)-Dihydroconduramine C-2] 43.** Pd(OH)<sub>2</sub>/C (39 mg) was added to a stirred degassed solution of **23** (78 mg, 0.31 mmol, >95:5 dr) in MeOH (2 mL) at rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo to give (+)-**43** as a white solid (44 mg, 96%, >95:5 dr, >99% ee); mp 153–163 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +25.9 (*c* 0.25 in MeOH);  $\nu_{\max}$  3310, 2953, 2928;  $\delta_H$  (400 MHz, MeOH-*d*<sub>4</sub>) 1.26–1.37 (1H, m, C(6)H<sub>A</sub>), 1.69–1.77 (2H, m, C(5)H<sub>2</sub>), 1.88–1.97 (1H, m, C(6)H<sub>B</sub>), 3.19 (1H, app t, *J* 3.4, C(2)H), 3.47 (1H, dd, *J* 7.3, 3.4, C(3)H), 3.75–3.82 (2H, m, C(1)H, C(4)H);  $\delta_C$  (100 MHz, MeOH-*d*<sub>4</sub>) 26.9 (C(5)), 27.4 (C(6)), 54.8 (C(2)), 70.5 (C(1)), 71.7 (C(4)), 76.0 (C(3)); *m/z* (ESI<sup>+</sup>) 148 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>3</sub><sup>+</sup> 148.0968; found 148.0968.

**(1*R*,2*R*,3*R*,4*R*)-2-Aminocyclohexane-1,3,4-triol [(–)-Dihydroconduramine C-2] 43.** Pd(OH)<sub>2</sub>/C (25 mg) was added to a stirred degassed solution of **26** (49 mg, 0.20 mmol, >95:5 dr) in MeOH (1.5 mL) at rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo to give (–)-**43** as a yellow solid (27 mg, 95%, >95:5 dr, >99% ee); mp 151–162 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> –23.4 (*c* 1.0 in MeOH).

**(1*S*,2*S*,3*R*,4*R*)-2-Aminocyclohexane-1,3,4-triol [(+)-Dihydroconduramine F-2] 44.** Pd(OH)<sub>2</sub>/C (25 mg) was added to a stirred degassed solution of **32** (48 mg, 0.141 mmol, 95:5 dr) in MeOH (1.5 mL) at rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 14:5:1) gave (+)-**44** as a yellow oil (11 mg, 55%, >95:5 dr, >99% ee); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +33.2 (*c* 0.5 in MeOH);  $\nu_{\max}$  3447, 2940, 2880, 2860;  $\delta_H$  (400 MHz, MeOH-*d*<sub>4</sub>) 1.47–1.58 (1H, m, C(6)H<sub>A</sub>), 1.67–1.85 (3H, m, C(5)H<sub>2</sub>, C(6)H<sub>B</sub>), 2.43–2.50 (1H, m, C(2)H), 3.32–3.38 (2H, m, C(3)H, C(4)H), 3.92–3.96 (1H, m, C(1)H);  $\delta_C$  (100 MHz, MeOH-*d*<sub>4</sub>) 28.1 (C(5)), 30.2 (C(6)), 58.6 (C(2)), 69.7 (C(1)), 74.8 (C(4)), 77.2 (C(3)); *m/z* (ESI<sup>+</sup>) 148 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>3</sub><sup>+</sup> 148.0968; found 148.0968.

**(1*R*,2*R*,3*S*,4*S*)-2-Aminocyclohexane-1,3,4-triol [(–)-Dihydroconduramine F-2] 44.** Pd(OH)<sub>2</sub>/C (10 mg) was added to a stirred degassed solution of **38** (20 mg, 0.059 mmol, >95:5 dr) in MeOH (1 mL) at

rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH/35% aq NH<sub>4</sub>OH, 5:4:1) gave (–)-**44** as a yellow oil (6.3 mg, 73%, >95:5 dr, >99% ee); [ $\alpha$ ]<sub>D</sub><sup>25</sup> –31.0 (c 0.25 in MeOH).

**(1S,2S,3S,4S,αR)-1,3-Diacetoxy-2-[N-benzyl-N-(α-methylbenzyl)amino]-4-tosyloxycyclohexane**

**45.** Ac<sub>2</sub>O (579 μL, 6.14 mmol) and DMAP (830 μg, 6.80 μmol) were added sequentially to a stirred solution of **27** (507 mg, 1.02 mmol, >95:5 dr) in pyridine (4.3 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave **45** as a yellow solid (515 mg, 87%, >95:5 dr); mp 60–62 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +45.4 (c 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3028, 2937, 2807, 1736;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.18 (3H, d, *J* 6.9, C(α)*Me*), 1.53–1.66 (3H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>2</sub>), 1.77–1.88 (1H, m, C(5)*H*<sub>B</sub>), 1.96 (3H, s, *COMe*), 1.97 (3H, s, *COMe*), 2.50 (3H, s, *ArMe*), 3.10 (1H, app t, *J* 2.8, C(2)*H*), 3.88 (1H, q, *J* 6.9, C(α)*H*), 3.97 (1H, d, *J* 14.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.12 (1H, d, *J* 14.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.67–4.71 (1H, m, C(4)*H*), 4.78–4.83 (1H, m, C(1)*H*), 5.21–5.24 (1H, m, C(3)*H*), 7.20–7.45 (12H, m, *Ph*, *Ar*), 7.81–7.87 (2H, m, *Ar*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 15.3 (C(α)*Me*), 20.7 (C(5)), 21.1, 21.4 (*COMe*), 21.7 (*ArMe*), 24.8 (C(6)), 50.8 (C(2)), 52.1 (NCH<sub>2</sub>Ph), 57.2 (C(α)), 73.4 (C(1)), 73.5 (C(3)), 77.0 (C(4)), 126.8, 127.1, 127.5, 127.8, 127.8, 128.3, 128.4, 129.9, 133.7 (*o,m,p-Ph*, *Ar*), 141.4, 142.8, 145.0 (*i-Ph*, *Ar*), 169.7, 170.4 (*COMe*); *m/z* (ESI<sup>+</sup>) 580 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>32</sub>H<sub>38</sub>NO<sub>7</sub>S<sup>+</sup> 580.2363; found 580.2357.

**(1S,2S,3S,4R,αR)-2-[N-Benzyl-N-(α-methylbenzyl)amino]cyclohexane-1,3,4-triol** **47.** *Step 1.*

KOAc (60 mg, 0.61 mmol) was added to a stirred solution of **45** (348 mg, 0.601 mmol, >95:5 dr) in EtOH/H<sub>2</sub>O (6:1, v/v, 13.1 mL) at rt. The resultant mixture was heated at reflux for 72 h and then allowed to cool to rt and concentrated in vacuo.

*Step 2.* K<sub>2</sub>CO<sub>3</sub> (1.34 g, 9.70 mmol) was added to a stirred solution of the residue from the previous step in MeOH (13.4 mL) at rt. The resultant mixture was stirred at rt for 24 h and then concentrated in vacuo. 2.25 M aq NaOH (20 mL) was added and the resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3 × 30 mL). The combined organics were dried and concentrated in vacuo. Purification via flash column chromatography (eluent CHCl<sub>3</sub>/MeOH, 99:1) gave **47** as a yellow oil (201 mg, 98%, >95:5 dr); [ $\alpha$ ]<sub>D</sub><sup>25</sup> –1.36 (c 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3366, 3084, 3060, 3027, 2938, 2874, 2840;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.25–1.37 (1H, m, C(5)*H*<sub>A</sub>), 1.45 (3H, d, *J* 6.9, C(α)*Me*), 1.63–1.88 (3H, m, C(5)*H*<sub>B</sub>, C(6)*H*<sub>2</sub>), 2.51 (2H, m, C(2)*H*, *OH*), 2.60 (1H, s, *OH*), 3.41 (1H, d, *J* 15.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.45–3.54 (1H, m, C(4)*H*), 3.75 (1H, m, C(1)*H*), 3.86 (1H, d, *J* 8.9, *OH*), 4.15 (1H, d, *J* 15.4, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.28 (1H, dd, *J* 8.6, 2.7, C(3)*H*), 4.81 (1H, q, *J* 6.9, C(α)*H*), 7.06–7.12 (2H, m, *Ph*), 7.12–7.29 (4H, m, *Ph*), 7.35–7.41 (2H, m, *Ph*), 7.51–7.57 (2H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz,

CDCl<sub>3</sub>) 11.7 (C( $\alpha$ )Me), 23.2 (C(6)), 27.8 (C(5)), 52.7 (NCH<sub>2</sub>Ph), 54.8 (C( $\alpha$ )), 64.5 (C(2)), 67.6 (C(1)), 71.4 (C(4)), 72.1 (C(3)), 126.7, 127.0, 128.2, 128.5, 128.8 (*o,m,p*-Ph), 142.8, 143.7 (*i*-Ph); *m/z* (ESI<sup>+</sup>) 342 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2059.

**(1S,2S,3S,4R, $\alpha$ R)-1,3,4-Triacetoxy-2-[N-benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane 48.** Ac<sub>2</sub>O (93  $\mu$ L, 0.98 mmol) and DMAP (86  $\mu$ g, 0.7  $\mu$ mol) were added sequentially to a stirred solution of **47** (37 mg, 0.11 mmol, >95:5 dr) in pyridine (0.45 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30-40 °C petroleum ether/EtOAc, 3:1) gave **48** as a yellow oil (36 mg, 71%, >95:5 dr); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +51.6 (c 1.0 in CHCl<sub>3</sub>);  $\nu_{\max}$  3062, 3028, 2966, 1736;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.21–1.31 (1H, m, C(6)H<sub>A</sub>), 1.38 (3H, d, *J* 6.9, C( $\alpha$ )Me), 1.45–1.52 (1H, m, C(5)H<sub>A</sub>), 1.80–1.95 (2H, m, C(5)H<sub>B</sub>, C(6)H<sub>B</sub>), 2.01 (3H, s, COMe), 2.02 (3H, s, COMe), 2.07 (3H, s, COMe), 2.74 (1H, app t, *J* 2.8, C(2)H), 3.89–3.99 (2H, m, NCH<sub>A</sub>H<sub>B</sub>Ph, C( $\alpha$ )H), 4.32 (1H, d, *J* 14.2, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.70 (1H, ddd, *J* 12.3, 4.4, 2.8, C(4)H), 4.88 (1H, app q, *J* 2.8, C(1)H), 5.76 (1H, app t, *J* 2.8, C(3)H), 7.29–7.39 (10H, m, Ph);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 14.3 (C( $\alpha$ )Me), 20.3 (C(5)), 20.9 (COMe), 21.2 (COMe), 21.5 (COMe), 27.3 (C(6)), 51.9 (NCH<sub>2</sub>Ph), 54.6 (C(2)), 56.8 (C( $\alpha$ )), 71.6 (C(4)), 73.2 (C(1)), 73.3 (C(3)), 126.8, 127.0, 127.5, 128.1, 128.3, 128.4 (*o,m,p*-Ph), 141.2, 143.0 (*i*-Ph), 170.2, 170.5, 170.6 (COMe); *m/z* (ESI<sup>+</sup>) 468 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>27</sub>H<sub>34</sub>NO<sub>6</sub><sup>+</sup> 468.2381; found 468.2379.

**(1S,2S,3S,4R)-2-Aminocyclohexane-1,3,4-triol [(+)-Dihydroconduramine D-2] 49.** Pd(OH)<sub>2</sub>/C (37 mg) was added to a stirred degassed solution of **47** (74 mg, 0.22 mmol, >95:5 dr) in MeOH (2 mL) at rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo to give (+)-**49** as a yellow oil (22 mg, 69%, >95:5 dr, >99% ee); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +10.4 (c 1.0 in MeOH);  $\nu_{\max}$  3345, 2936, 2873;  $\delta_{\text{H}}$  (400 MHz, MeOH-*d*<sub>4</sub>) 1.46–1.57 (2H, m, C(5)H<sub>A</sub>, C(6)H<sub>A</sub>), 1.79–1.92 (2H, m, C(5)H<sub>B</sub>, C(6)H<sub>B</sub>), 2.84 (1H, app s, C(2)H), 3.62–3.68 (1H, m, C(4)H), 3.71 (1H, app s, C(3)H), 3.77 (1H, app dt, *J* 6.2, 3.0, C(1)H);  $\delta_{\text{C}}$  (100 MHz, MeOH-*d*<sub>4</sub>) 25.2 (C(5)), 28\* (C(6)), 55.4 (C(2)), 71.5 (C(1)), 72.1 (C(4)), 75.0 (C(3));<sup>23</sup> *m/z* (ESI<sup>+</sup>) 148 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>3</sub><sup>+</sup> 148.0968; found 148.0968.

**(1S,2S,3R,4S, $\alpha$ R)-2-[N-Benzyl-N-( $\alpha$ -methylbenzyl)amino]cyclohexane-1,3,4-triol 52.** *Step 1.* A solution of **30** (145 mg, 0.449 mmol, >95:5 dr) in CH<sub>2</sub>Cl<sub>2</sub> (1.25 mL) was added to anhydrous TsOH (0.386 g, 2.24 mmol) at rt. The resultant solution was stirred at rt for 24 h and then diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL), washed with 0.1 M aq NaHCO<sub>3</sub> (4  $\times$  15 mL), dried and concentrated in vacuo to give **28** as a yellow solid (170 mg);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.13–1.26 (1H, m, C(6)H<sub>A</sub>), 1.36 (3H, d, *J* 7.0, C( $\alpha$ )Me), 1.42–1.53 (1H, m, C(6)H<sub>B</sub>), 1.78–1.99 (1H, m, C(5)H<sub>2</sub>), 2.46 (3H, s, ArMe), 2.66 (1H, dd, *J* 10.6, 2.1, C(2)H), 3.09–3.16 (1H,

m, C(1)*H*), 3.39 (1H, s, *OH*), 3.91 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.96–4.10 (2H, m, C(3)*H*, C( $\alpha$ )*H*), 4.31 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.52 (1H, ddd, *J* 11.5, 8.6, 5.5, C(4)*H*), 7.24–7.44 (12H, m, *Ph*, *Ar*), 7.84–7.89 (2H, m, *Ar*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 18.3 (C( $\alpha$ )*Me*), 21.7 (*ArMe*), 24.6 (C(5)), 29.6 (C(6)), 52.0 (NCH<sub>2</sub>Ph), 56.6 (C( $\alpha$ )), 61.0 (C(2)), 67.0 (C(3)), 68.0 (C(1)), 85.6 (C(4)), 127.1, 127.4, 127.7, 127.8, 128.4, 128.5, 128.6, 129.6 (*o,m,p-Ph*, *Ar*), 140.6, 142.4, 144.4 (*i-Ph*, *Ar*).

*Step 2.* Ac<sub>2</sub>O (194  $\mu$ L, 2.06 mmol) and DMAP (0.27 mg, 0.00229 mmol) were added sequentially to a stirred solution of the residue of **28** from the previous step (170 mg) in pyridine (1.4 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo to give **50** as a yellow oil (183 mg);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 0.99–1.11 (1H, m, C(6)*H<sub>A</sub>*), 1.29 (3H, d, *J* 6.9, C( $\alpha$ )*Me*), 1.63–1.81 (3H, m, C(5)*H<sub>2</sub>*, C(6)*H<sub>B</sub>*), 1.84 (3H, s, *COMe*), 2.11 (3H, s, *COMe*), 2.45 (3H, s, *ArMe*), 2.92 (1H, dd, *J* 11.2, 2.5, C(2)*H*), 3.88 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.96 (1H, q, *J* 6.9, C( $\alpha$ )*H*), 4.02 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.51 (1H, br app q, *J* 2.5, C(1)*H*), 4.58 (1H, ddd, *J* 11.4, 8.9, 5.6, C(4)*H*), 5.51 (1H, dd, *J* 11.2, 8.9, C(3)*H*), 7.21–7.37 (12H, m, *Ph*, *Ar*), 7.74–7.79 (2H, m, *Ar*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 15.5 (C( $\alpha$ )*Me*), 21.2 (*COMe*), 21.4 (*COMe*), 21.6 (*ArMe*), 25.5 (C(5)), 25.7 (C(6)), 51.8 (NCH<sub>2</sub>Ph), 56.1 (C( $\alpha$ )), 58.1 (C(2)), 69.5 (C(3)), 74.3 (C(1)), 82.0 (C(4)), 123.9, 127.2, 127.5, 127.8, 127.9, 128.3, 128.4, 129.8 (*o,m,p-Ph*, *Ar*), 140.8, 142.6 (*Ph*, *Ar*), 170.1 (*COMe*), 170.1 (*COMe*).

*Step 3.* KOAc (31.6 mg, 0.322 mmol) was added to a stirred solution of the residue of **50** from the previous step (183 mg) in EtOH/H<sub>2</sub>O (6:1, v/v, 6.87 mL) at rt. The resultant mixture was heated at reflux for 72 h and then allowed to cool to rt and concentrated in vacuo.

*Step 4.* K<sub>2</sub>CO<sub>3</sub> (266 mg, 1.92 mmol) was added to a stirred solution of the residue from the previous step in MeOH (5.3 mL) at rt. The resultant mixture was stirred at rt for 24 h and then concentrated in vacuo. 2.25 M aq NaOH (15 mL) was added and the resultant mixture was extracted with CHCl<sub>3</sub>/*i*PrOH (3:1, v/v, 3  $\times$  20 mL). The combined organics were dried and concentrated in vacuo. Purification via preparative thin layer chromatography (eluent CHCl<sub>3</sub>) gave **52** as a yellow oil (39.8 mg, 26% from **30**, >95:5 dr);  $[\alpha]_{\text{D}}^{25}$  +95.0 (*c* 1.0 in CHCl<sub>3</sub>);  $\nu_{\text{max}}$  3422, 3061, 3027, 2929;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 1.23–1.31 (1H, m, C(6)*H<sub>A</sub>*), 1.34–1.42 (3H, d, *J* 7.1, C( $\alpha$ )*Me*), 1.68–1.87 (3H, m, C(5)*H<sub>2</sub>*, C(6)*H<sub>B</sub>*), 2.63 (1H, s, *OH*), 3.17–3.22 (1H, m, C(1)*H*), 3.28 (1H, dd, *J* 10.6, 1.8, C(2)*H*), 3.83 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 3.95 (1H, dd, *J* 10.6, 3.0, C(3)*H*), 4.01 (1H, q, *J* 7.1, C( $\alpha$ )*H*), 4.23 (1H, app q, *J* 3.0, C(4)*H*), 4.42 (1H, d, *J* 14.7, NCH<sub>A</sub>H<sub>B</sub>Ph), 7.26–7.45 (10H, m, *Ph*);  $\delta_{\text{C}}$  (100 MHz, CDCl<sub>3</sub>) 19.9 (C( $\alpha$ )*Me*), 23.4 (C(5)), 28.7 (C(6)), 51.8 (NCH<sub>2</sub>Ph), 56.5 (C(2)), 56.6 (C( $\alpha$ )), 65.5 (C(3)), 68.5 (C(1)), 68.6 (C(4)), 127.0, 127.4, 127.8, 128.4, 128.5, 128.6 (*o,m,p-Ph*), 140.7, 141.8 (*i-Ph*); *m/z* (ESI<sup>+</sup>) 342 ([*M*+*H*]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [*M*+*H*]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 342.2064; found 342.2060.



**(1*S*,2*S*,3*R*,4*S*)-2-Aminocyclohexane-1,3,4-triol [(+)-Dihydroconduramine E-2] 53.** Pd(OH)<sub>2</sub>/C (36 mg) was added to a stirred degassed solution of **52** (71 mg, 0.21 mmol, >95:5 dr) in MeOH (2 mL) at rt. The resultant mixture was stirred at rt under H<sub>2</sub> (1 atm) for 24 h and then filtered through Celite® (eluent MeOH). The filtrate was concentrated in vacuo to give (+)-**53** as a yellow oil (30 mg, 98%, >95:5 dr, >99% ee); [α]<sub>D</sub><sup>25</sup> +89.3 (*c* 1.0 in MeOH); ν<sub>max</sub> 3355, 2930, 2900; δ<sub>H</sub> (400 MHz, MeOH-*d*<sub>4</sub>) 1.55–1.69 (2H, m, C(5)*H*<sub>A</sub>, C(6)*H*<sub>A</sub>), 1.80–1.91 (2H, m, C(5)*H*<sub>B</sub>, C(6)*H*<sub>B</sub>), 2.85 (1H, dd, *J* 9.7, 3.0, C(2)*H*), 3.52 (1H, dd, *J* 9.7, 2.8, C(3)*H*), 3.92–4.01 (2H, m, C(1)*H*, C(4)*H*); δ<sub>C</sub> (100 MHz, MeOH-*d*<sub>4</sub>) 26.7 (C(5)), 27.5 (C(6)), 54.6 (C(2)), 70.2 (C(1)), 70.7 (C(4)), 73.6 (C(3)); *m/z* (ESI<sup>+</sup>) 148 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>6</sub>H<sub>14</sub>NO<sub>3</sub><sup>+</sup> 148.0968; found 148.0968.

**(1*R*,2*R*,3*R*,4*S*,α*R*)-1-Acetoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-3,4-epoxycyclohexane 54.** Ac<sub>2</sub>O (579 μL, 6.14 mmol) and DMAP (1.7 mg, 14 μmmol) were added sequentially to a stirred solution of **35** (661 mg, 2.05 mmol, >95:5 dr) in pyridine (8.52 mL) at rt. The resultant solution was stirred at rt for 24 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave **54** as a yellow oil (570 mg, 76%, >95:5 dr); [α]<sub>D</sub><sup>25</sup> +73.7 (*c* 1.0 in CHCl<sub>3</sub>); ν<sub>max</sub> 3060, 3026, 2931, 2845, 1733; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.37 (3H, d, *J* 7.0, C(α)*Me*), 1.42–1.55 (1H, m, C(6)*H*<sub>A</sub>), 1.78–1.89 (6H, m, C(5)*H*<sub>2</sub>, C(6)*H*<sub>B</sub>, COMe), 2.50 (1H, ddd, *J* 4.4, 2.0, 1.1, C(3)*H*), 3.01–3.06 (1H, m, C(4)*H*), 3.36 (1H, dd, *J* 4.4, 2.0, C(2)*H*), 3.95–4.07 (2H, m, C(α)*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.57 (1H, d, *J* 15.6, NCH<sub>A</sub>H<sub>B</sub>Ph), 5.14–5.19 (1H, m, C(1)*H*), 7.21–7.29 (2H, m, *Ph*), 7.31–7.38 (6H, m, *Ph*), 7.43–7.47 (2H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 19.2 (C(5)), 19.4 (C(α)*Me*), 21.3 (COMe), 26.0 (C(6)), 50.9 (C(4)), 52.8 (C(3)), 52.9 (NCH<sub>2</sub>Ph), 53.5 (C(2)), 58.0 (C(α)), 73.7 (C(1)), 126.4, 127.2, 127.5, 127.5, 128.3, 128.4 (*o,m,p-Ph*), 142.0, 142.6 (*i-Ph*), 171.4 (COMe); *m/z* (ESI<sup>+</sup>) 366 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>28</sub>NO<sub>3</sub><sup>+</sup> 366.2064; found 366.2059.

**(1*R*,2*S*,3*R*,4*R*,α*R*)-1,4-Diacetoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]cyclohexan-3-ol 55 and (1*R*,2*R*,3*R*,4*R*,α*R*)-3,4-diacetoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]cyclohexan-1-ol 56.** A stirred solution of **54** (520 mg, 1.42 mmol, >95:5 dr) in AcOH (1.58 mL) was heated at 50 °C for 36 h, then allowed to cool to rt. 0.1 M aq NaHCO<sub>3</sub> (10 mL) was added and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The combined organics were washed with 0.1 M aq NaHCO<sub>3</sub> (20 mL), dried and concentrated in vacuo to give an 83:17 mixture of **55** and **56**, respectively. Purification via preparative thin layer chromatography (eluent 30–40 °C petroleum ether/EtOAc, 4:1) gave a >95:5 mixture of **55** and **56** as pale yellow oil (315 mg, 41%) and a 5:95 mixture of **55** and **56** as a yellow oil (64 mg, 11%). Data for **55**: *R*<sub>f</sub> = 0.53; ν<sub>max</sub> (ATR) 3483, 3028, 2934, 2841, 1734; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.43 (3H, d, *J* 6.9, C(α)*Me*), 1.49–1.56 (1H, m, C(5)*H*<sub>A</sub>), 1.68–1.78 (1H, m, C(6)*H*<sub>A</sub>), 1.82 (3H, s, COMe), 1.84–1.95 (2H, m, C(5)*H*<sub>B</sub>,

C(6)*H<sub>B</sub>*), 1.98 (3H, s, COMe), 2.87 (1H, d, *J* 8.4, OH), 2.98 (1H, app t, *J* 2.7, C(2)*H*), 3.78–3.84 (1H, m, C(3)*H*), 4.07 (1H, d, *J* 15.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.12 (1H, d, *J* 15.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.23 (1H, q, *J* 6.9, C(α)*H*), 4.89–4.94 (1H, m, C(4)*H*), 5.37–5.42 (1H, m, C(1)*H*), 7.19–7.38 (10H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 15.9 (C(α)Me), 19.1 (C(5)), 21.0, 21.4 (COMe), 25.3 (C(6)), 52.2 (NCH<sub>2</sub>Ph), 55.0 (C(2)), 56.5 (C(α)), 72.0 (C(3)), 72.4 (C(4)), 74.4 (C(1)), 126.7, 126.9, 127.7, 127.9, 128.1, 128.3 (*o,m,p-Ph*), 141.6, 143.3 (*i-Ph*), 169.7 (COMe); *m/z* (ESI<sup>+</sup>) 426 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>25</sub>H<sub>32</sub>NO<sub>5</sub><sup>+</sup> 426.2275; found 426.2270. Data for **56**: *R<sub>f</sub>* = 0.46; ν<sub>max</sub> (ATR) 3577, 3027, 2931, 2949, 1738; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.43 (3H, d, *J* 6.8, C(α)Me), 1.54–1.62 (1H, m, C(5)*H<sub>A</sub>*), 1.68–1.84 (5H, m, C(6)*H<sub>2</sub>*, COMe), 1.86–1.98 (4H, m, C(5)*H<sub>B</sub>*, COMe), 2.72 (1H, d, *J* 8.6, OH), 3.04 (1H, app t, *J* 2.7, C(2)*H*), 4.08 (1H, d, *J* 15.0, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.18–4.26 (2H, m, C(α)*H*, NCH<sub>A</sub>H<sub>B</sub>Ph), 4.28–4.35 (1H, m, C(1)*H*), 4.83–4.88 (1H, m, C(4)*H*), 4.95–4.98 (1H, m, C(3)*H*), 7.18–7.25 (2H, m, *Ph*), 7.28–7.36 (6H, m, *Ph*), 7.38–7.43 (2H, m, *Ph*); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 14.5 (C(α)Me), 19.0 (C(5)), 20.9, 21.1 (COMe), 28.5 (C(6)), 52.4 (NCH<sub>2</sub>Ph), 54.8 (C(2)), 56.8 (C(α)), 69.4 (C(4)), 70.5 (C(1)), 74.8 (C(3)), 126.7, 126.8, 127.9, 127.9, 128.1, 128.3 (*o,m,p-Ph*), 141.6, 143.5 (*i-Ph*), 168.9, 169.2 (COMe); *m/z* (ESI<sup>+</sup>) 426 ([M+H]<sup>+</sup>, 100%); HRMS (ESI<sup>+</sup>) *m/z*: [M+H]<sup>+</sup> Calcd for C<sub>25</sub>H<sub>32</sub>NO<sub>5</sub><sup>+</sup> 426.2275; found 426.2270.

**Supporting Information Available:** Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra, and crystallographic information file (for structures CCDC 1846210–1846221). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References and Notes

<sup>1</sup> For example, see: (a) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. Sugar-Mimic Glycosidase Inhibitors: Natural Occurrence, Biological Activity and Prospects for Therapeutic Application. *Tetrahedron: Asymmetry* **2000**, *11*, 1645–1680. (b) Asano, N. Sugar-Mimicking Glycosidase Inhibitors: Bioactivity and Application. *Cell. Mol. Life Sci.* **2009**, *66*, 1479–1492.

<sup>2</sup> For a review, see: Łysek, R.; Vogel, P. Synthesis of Amino- and Diaminoconduritols and Their Applications. *Tetrahedron* **2006**, *62*, 2733–2768.

<sup>3</sup> For selected examples of more recent synthetic investigations, see: (a) Kurbanoglu, I. N.; Besoluka, S.; Zenginb, M. Stereospecific Synthesis of N-Tosyl Derivatives of Dihydroconduramine E-2 and ent-F-2. *ARKIVOC* **2010**, (*x*), 77–85. (b) Lu, P.-H.; Yang, C.-S. Devendar, B. Liao, C.-C. Syntheses of Optically Pure Conduramines via the Strategy of Hetero Diels-Alder Reaction of Masked o-Benzoquinones with Homochiral Nitroso Dienophiles. *Org. Lett.* **2010**, *12*, 2642–2645. (c) Kuno, S.; Higaki, K.; Takahashi, A.;

Nanbab, E.; Ogawa, S. Potent Chemical Chaperone Compounds for GM1-Gangliosidosis: N-Substituted (+)-Conduramine F-4 Derivatives. *Med. Chem. Commun.* **2015**, *6*, 306–310. (d) Katakam, R.; Anugula, R.; Macha, L.; Batchu, V. R. Stereoselective Synthesis of N-Benzyl Conduramine F-1, N-Benzyl ent-Conduramine E-1, Dihydroconduramine F-1 and ent-Dihydroconduramine E-1. *Tetrahedron Lett.* **2017**, *58*, 559–562.

<sup>4</sup> Da Silva Pinto, S.; Davies, S. G.; Fletcher, A. M.; Roberts, P. M.; Thomson, J. E. Stereoselective Ammonium-Directed Epoxidation in the Asymmetric Syntheses of Dihydroconduramines (–)-A-2, (–)-B-2, (–)-C-3 and (+)-F-3. *Synthesis* **2018**, *50*, 64–83.

<sup>5</sup> Epoxides **3**, **4** and **5** underwent regioselective and stereospecific ring-opening under the reaction conditions, upon attack of the conjugate base of the Brønsted acid at the carbon atom distal to the in situ formed ammonium moiety, to give the corresponding ring-opened products.

<sup>6</sup> For example, see: (a) Schiffrers, I.; Rantanen, T.; Schmidt, F.; Bergmans, W.; Zani, L.; Bolm, C. Resolution of Racemic 2-Aminocyclohexanol Derivatives and Their Application as Ligands in Asymmetric Catalysis. *J. Org. Chem.* **2006**, *71*, 2320–2331. (b) Leathen, M. L.; Rosen, B. R.; Wolfe, J. P. New Strategy for the Synthesis of Substituted Morpholines. *J. Org. Chem.* **2009**, *74*, 5107–5110. (c) Hennessy, E. J.; Adam, A.; Aquila, B. M.; Castriotta, L. M.; Cook, D.; Hattersley, M.; Hird, A. W.; Huntington, C.; Kamhi, V. M.; Laing, N. M.; Li, D.; MacIntyre, T.; Omer, C. A.; Oza, V.; Patterson, T.; Repik, G.; Rooney, M. T.; Saeh, J. C.; Sha, L.; Vasbinder, M. M.; Wang, H.; Whitston, D. Discovery of a Novel Class of Dimeric Smac Mimetics as Potent IAP Antagonists Resulting in a Clinical Candidate for the Treatment of Cancer (AZD5582). *J. Med. Chem.* **2013**, *56*, 9897–9919.

<sup>7</sup> Claridge, T. D. W.; Davies, S. G.; Polywka, M. E. C.; Roberts, P. M.; Russell, A. J.; Savory, E. D.; Smith, A. D. “Pure by NMR”? *Org. Lett.* **2008**, *10*, 5433–5436.

<sup>8</sup> Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallography Data Centre as supplementary publication numbers CCDC 1846210–1846221. Copies of these data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

<sup>9</sup> The diastereoisomeric purity of **8** was assigned from the known diastereoisomeric purity of the precursor **7**, i.e., >180:1 dr.

<sup>10</sup> This reaction required use of 2.0 equiv of *m*-CPBA to effect completion of the reaction within 21 h; use of 1.6 equiv of *m*-CPBA for 21 h gave an 8:92 mixture of unreacted starting material **8** and tosylate **10**, respectively; although treatment of this mixture with DBU resulted in conversion to an 8:92 mixture of

unreacted starting material **8** and epoxide **12**, respectively, these proved to be inseparable by column chromatography.

<sup>11</sup> Epoxidation of **19** using only 1.6 equiv of *m*-CPBA under the same conditions gave a 19:21:27:33 mixture of unreacted starting material **19**, epoxide **29**, epoxide **30** and triol **31**, respectively. Similarly, epoxidation of **20** using only 1.6 equiv of *m*-CPBA under the same conditions gave a 5:5:14:76 mixture of unreacted starting material **20**, epoxide **35**, epoxide **36** and triol **37**, respectively.

<sup>12</sup> Ring-opening of epoxides **29** or **35** upon attack of the requisite nucleophile at C(4) presumably proceeds via a chairlike transition state which places the bulky *N*-benzyl-*N*- $\alpha$ -methylbenzyl group in a pseudoequatorial position. In contrast, ring-opening of epoxides **30** or **36** upon attack of the requisite nucleophile at C(4) must either traverse a higher energy chairlike transition state which places the bulky *N*-benzyl-*N*- $\alpha$ -methylbenzyl group in a pseudoaxial position, or a higher energy twistboatlike transition state. Taken together with other observations described herein, it is clear that the rate of epoxide ring-opening in these systems can be affected by both the presence of an  $\alpha$ -methyl substituent and the relative configuration of the  $\alpha$ -stereocenter, although the precise origin of this phenomenon is not immediately apparent.

<sup>13</sup> Interrogation of the favored conformations of **7** and **17** in CD<sub>2</sub>Cl<sub>2</sub> by <sup>1</sup>H NMR <sup>3</sup>*J* coupling constant analysis proved inconclusive.

<sup>14</sup> For selected examples concerning diastereoselective peracid epoxidation of cyclohex-3-en-1-ol and derivatives, see: (a) Ye, D.; Fringuelli, F.; Piermatti, O.; Pizzo, F. Highly Diastereoselective Epoxidation of Cycloalkenols with Monoperoxyphthalic Acid in Water. *J. Org. Chem.* **1997**, *62*, 3748–3750. (b) Boyd, D. R.; Sharma, N. D.; Kerley, N. A.; McConville, G.; Allen, C. C. R.; Blacker, A. J. Chemoenzymatic Synthesis of Enantiopure Dihydroxy-1,2,3,4-tetrahydronaphthalenes from Naphthalene and Dihydronaphthalene Precursors. *ARKIVOC* **2003**, (vii), 32–48. (c) Mehta, G.; Ramesh, S. S. Quest for Inosito-Inositols: Synthesis of Novel, Annulated and Conformationally Locked Inositols. *Tetrahedron Lett.* **2003**, *44*, 3105–3108.<sup>15</sup> Aciro, C.; Davies, S. G.; Roberts, P. M.; Russell, A. J.; Smith, A. D.; Thomson, J. E. Ammonium-Directed Dihydroxylation: Metal-Free Synthesis of the Diastereoisomers of 3-Aminocyclohexane-1,2-diol. *Org. Biomol. Chem.* **2008**, *6*, 3762–3770.

<sup>16</sup> Tosylate **28** was not purified and was characterised directly from the crude reaction mixture; it was subsequently transformed into triol **52** in three further steps.

<sup>17</sup> Roberts, J. D.; Young, W. G.; Winstein, S. The Role of Neighboring Groups in Replacement Reactions. V. The Effect of the Neighboring Acetoxy Group on the Course of the Replacement of the Tosylate Group of trans-2-Acetoxy-cyclohexyl p-Toluenesulfonate. *J. Am. Chem. Soc.* **1942**, *64*, 2796.

<sup>18</sup> The enantiopurities of (+)-DHC D-2 (**49**) and (+)-DHC E-2 (**53**) were assigned from the known enantiopurity of the starting material **17** (i.e., >99% ee) using the same rationale as for the other DHCs prepared in this study.

<sup>19</sup> Application of our previously employed protocol (see ref 4 and ref 15) to form **51**, viz. attempted Winstein reaction of the mesylate **42** followed by methanolysis, produced a complex mixture of products and **52** was not isolated after column chromatography.

<sup>20</sup> Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518–1520.

<sup>21</sup> Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, C. K.; Watkin, D. J. CRYSTALS Version 12: Software for Guided Crystal Structure Analysis *J. Appl. Crystallogr.* **2003**, *36*, 1487.

<sup>22</sup> Sabaté, M.; Llebaria, A.; Molins, E.; Miravittles, C.; Delgado, A. Iodocyclization of O-(3-Cyclohexenyl)thiocarbamides. An Unexpected Approach to Vicinal cis-Aminocyclohexenols. *J. Org. Chem.* **2000**, *65*, 4826–4829.

<sup>23</sup> A signal associated with C(6) was not evident in the <sup>13</sup>C NMR spectrum of (+)-DHC D-2 (**49**); the approximate peak position was obtained from the <sup>1</sup>H-<sup>13</sup>C HSQC NMR spectrum of this compound and is reported to the nearest integer (shown in italics and marked with an asterisk).