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Ammonium-Directed Olefinic Epoxidation: Kinetic and Mechanistic Insights

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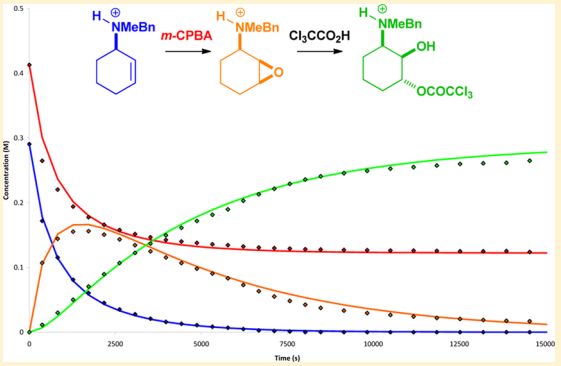
Supporting Information

ABSTRACT: The ammonium-directed olefinic epoxidations of a range of differentially N-substituted cyclic allylic and homoallylic amines (derived from cyclopentene, cyclohexene, and cycloheptene) have been investigated, and the reaction kinetics have been analyzed. The results of these studies suggest that both the ring size and the identity of the substituents on nitrogen are important in determining both the overall rate and the stereochemical outcome of the epoxidation reaction. In general, secondary amines or tertiary amines with nonsterically demanding substituents on nitrogen are superior to tertiary amines with sterically demanding substituents on nitrogen in their ability to promote the oxidation reaction. Furthermore, in all cases examined, the ability of the (in situ formed) ammonium substituent to direct the stereochemical course of the epoxidation reaction is either comparable or superior to that of the analogous hydroxyl substituent. Much slower rates of ring-opening of the intermediate epoxides are observed in cyclopentene-derived and cycloheptene-derived allylic amines as compared with their cyclohexene-derived allylic and homoallylic amine counterparts, allowing for isolation of these intermediates in both of the former cases.



INTRODUCTION

The stereochemical outcome of a reaction is of enormous importance in organic chemistry, and the ability to predict and direct stereoselectivity is invaluable in organic synthesis. Substrates equipped with functionality capable of precoordinating a reagent may result in subsequent intramolecular delivery of the reagent and, therefore, offer high levels of diastereoselectivity: such transformations have been termed substrate-directed reactions by Evans.[1] As part of an ongoing research program employing methods for the chemo- and diastereoselective electrophilic functionalization of unsaturated amines at the olefin,[2] we have previously developed an ammonium-directed olefinic epoxidation of allylic and homoallylic amines to facilitate the diastereoselective synthesis of amino diol units.[3,4] This protocol was utilized in the asymmetric syntheses of the imino sugars (+)-1-deoxynojirimycin and (+)-1-deoxyaltronojirimycin,[5] and a derivative of the amino sugar L-acosamine.[6] In the latter case, the diastereoselective conjugate addition of lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**1**[7] to *tert*-butyl sorbate **2** was followed by treatment of the resultant β-amino ester **3** with aq HBF_4 and then *m*-CPBA, which resulted in conversion to lactone **5**. This is consistent with a mechanism involving ammonium-directed epoxidation of the olefin via a transition state in which 1,3-allylic strain is minimized, resulting in formation of epoxide **4**. Ring-opening of **4** upon attack of H_2O at the oxirane carbon atom distal to the ammonium moiety [i.e., at C(5)], followed by lactonization under the acidic reaction conditions, then leads to **5**. A further four steps realized a concise and highly selective asymmetric synthesis of methyl *N*,*O*-diacetyl-α-L-acosaminide **6**[6] (Scheme 1).

This ammonium-directed olefinic epoxidation has thus been shown to be synthetically powerful and is general for primary, secondary, and tertiary amines.[4a,d,e] To obtain further insight into the origin of selectivity and reactivity in some of the conformationally constrained (cyclic) allylic and homoallylic amines studied so far (Figure 1),[4] the effect of variation of the substituents on nitrogen on the reaction diastereoselectivity, product distribution, and rate of reaction was explored, and the results of these investigations are delineated herein.

RESULTS AND DISCUSSION

Oxidation of N-Substituted 3-Aminocyclohex-1-enes.

A range of N-substituted 3-aminocyclohex-1-enes **9**−**12** were prepared via Wohl−Ziegler allylic bromination of cyclohexene

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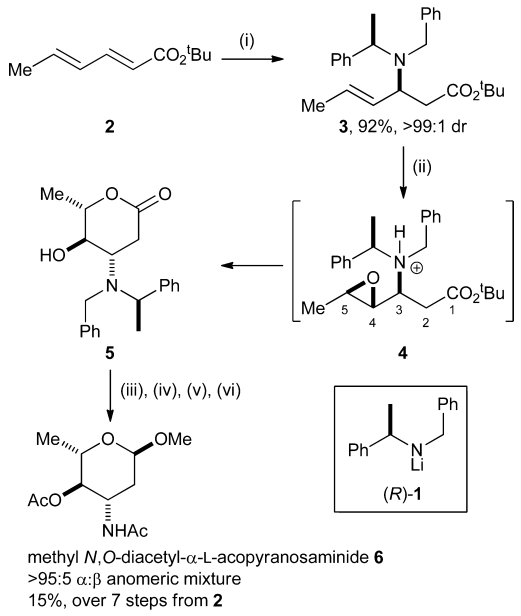
Scheme 1[a]



[a]Reagents and conditions: (i) lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**1**, THF, −78 °C, 2 h; (ii) HBF_4 (40% w/w in H_2O), *m*-CPBA (4 equiv), CH_2Cl_2, rt, 48 h; (iii) H_2 (5 atm), $Pd(OH)_2/C$ (50% w/w wrt substrate), EtOAc, rt, 48 h; (iv) DIBAL-H, CH_2Cl_2, −78 °C, 30 min; (v) MeOH, HCl (conc aq), rt, 16 h; (vi) Ac_2O, pyridine, DMAP, rt, 30 min.

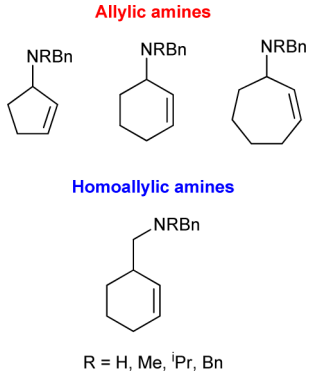
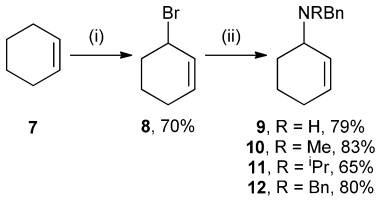


Figure 1. Allylic and homoallylic amine substrates (derived from cyclopentene, cyclohexene, and cycloheptene) for study into ammonium-directed epoxidation.

7 with NBS,[8] followed by displacement of the bromide within **8** by the requisite amine (Scheme 2).

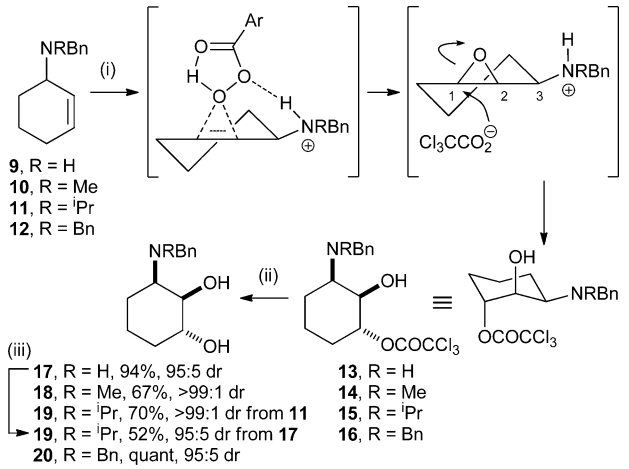
As previously reported,[4a] sequential treatment of 3-(*N*,*N*-dibenzylamino)cyclohex-1-ene **12** with 5 equiv of Cl_3CCO_2H and 1.6 equiv of *m*-CPBA[9] gave, on basic aqueous workup using $NaHCO_3$, trichloroacetate ester **16** in 95:5 dr and quantitative yield.[10] Transesterification of **16** upon treatment with K_2CO_3 in MeOH gave amino diol **20** in 95:5 dr (the minor diastereoisomer was the corresponding 1,2-*anti*-2,3-*anti*-diastereoisomer) and quantitative yield. Application of this protocol to **9**−**11**[11] gave, in each case, quantitative conversion to the corresponding trichloroacetate esters **13**−**15** in ≥95:5 dr.[10] Subsequent transesterification using K_2CO_3 in MeOH gave amino diols **17**−**19** in 67−94% isolated yield, and in ≥95:5 dr (in each case, the minor diastereoisomer was the corresponding 1,2-*anti*-2,3-*anti*-diastereoisomer). The relative configurations within **13**, **16**, **17**, and **20** have previously been unambiguously assigned.[4a] The relative configuration within **14** was established unambiguously via single-crystal X-ray diffraction analysis,[12] which, therefore, allowed the relative configuration within **18** to be unambiguously assigned. The relative configurations within **15** and **19** were determined by chemical correlation: reductive alkylation of **17** upon treatment with acetone in the presence of $NaB(OAc)_3H$ gave a sample of **19** in 52% yield, which was spectroscopically identical to the product obtained from the ammonium-directed oxidation of **11** (Scheme 3). We have

Scheme 2[a]



[a]Reagents and conditions: (i) NBS, $(PhCO_2)_2$, CCl_4, 90 °C, 1.5 h; (ii) HNRBn, K_2CO_3, THF, 50 °C, 16 h.

Scheme 3[a]



[a]Reagents and conditions: (i) Cl_3CCO_2H, *m*-CPBA, CH_2Cl_2, rt, 21 h, then $NaHCO_3$ (0.1 M aq); (ii) K_2CO_3, MeOH, rt, 16 h; (iii) acetone, $NaB(OAc)_3H$, AcOH, rt, 24 h.

previously rationalized the chemoselectivities of the oxidation reactions of allylic amines **9** and **12** as a result of temporary protection of the amine functionality from electrophilic reaction by protonation to give the corresponding ammonium ions. The diastereoselectivities of these reactions are then due to these ammonium ions being able to direct the *m*-CPBA to the *syn* face of the olefin by hydrogen-bonding[4a] (analogous to the proposals of Bartlett and Henbest[13] to explain the stereochemical outcome of the oxidation of the corresponding allylic alcohol).[14] Subsequent regioselective and stereospecific epoxide ring-opening upon attack of trichloroacetic acid is directed to the C(1)-oxirane carbon, where the destabilizing electron-withdrawing inductive effect of the ammonium moiety on the transition state is less pronounced; also, ring-opening at C(1) gives a chairlike transition state, resulting in the formation of the corresponding trichloroacetate esters **13** and **16**, respectively, and transesterification gives the corresponding diols **17** and **20**. Both the chemo- and diastereoselectivities of

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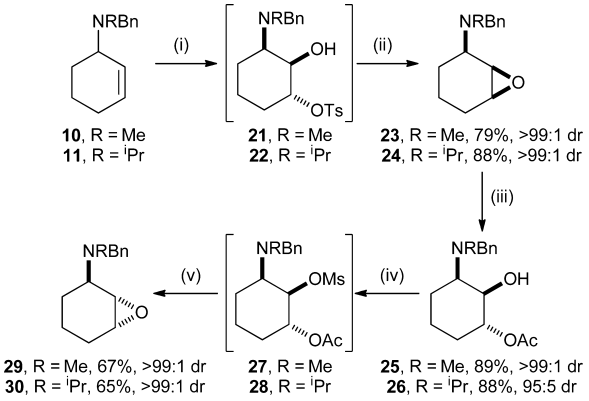
the dihydroxylations of allylic amines **10** and **11** under these conditions are also in accordance with this mechanistic rationale.

To facilitate subsequent analysis during rate studies, authentic samples of the intermediate epoxides and minor diastereoisomeric products arising from the oxidations of **10** and **11** were prepared. The use of 3 equiv of TsOH[11] in place of 5 equiv of Cl_3CCO_2H[11] as the Brønsted acid protecting agent for the oxidations of **10** and **11** (according to our previously reported procedure)[4a] gave hydroxy tosylates **21** and **22** (in >99:1 dr in each case) as the major products. Recrystallization of **21** gave an analytical sample and allowed its relative configuration to be unambiguously established by single-crystal X-ray diffraction analysis.[12] Meanwhile, treatment of the crude samples of **21** and **22** with DBU gave *syn*-epoxides **23** and **24** in 79% and 88% isolated yield, respectively (two steps), as single diastereoisomers (>99:1 dr) in each case. Treatment of **23** and **24** with AcOH gave hydroxy acetates **25** and **26** in ≥95:5 dr, which were then isolated in 89% and 88% yield as single diastereoisomers. The relative configuration within **25** was unambiguously established by single-crystal X-ray diffraction analysis.[12] Mesylation of the free hydroxyl groups within acetates **25** and **26** was followed by treatment of the intermediate mesylates **27** and **28** with K_2CO_3 in MeOH, which resulted in conversion to *anti*-epoxides **29** and **30** in 67% and 65% yield, as single diastereoisomers (Scheme 4). Upon

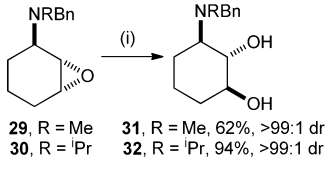
Scheme 4[a]



[a]Reagents and conditions: (i) TsOH, *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) DBU, CH_2Cl_2, rt, 24 h; (iii) AcOH, 50 °C, 24 h; (iv) MsCl, Et_3N, CH_2Cl_2, 0 °C, 1 h; (v) K_2CO_3, MeOH, rt, 16 h.

treatment of **29** and **30** with 3 M aq H_2SO_4, the corresponding amino diols **31** and **32** were formed, and isolated in 62% and 94% yield, and in >99:1 dr in each case (Scheme 5). The absence of amino diols **31** and **32** in the crude reaction mixtures produced from the ammonium-directed olefinic

Scheme 5[a]



[a]Reagents and conditions: (i) H_2SO_4 (3 M aq), 1,4-dioxane, 40 °C, 24 h.

oxidations of the corresponding allylic amines **10** and **11** (giving amino diols **18** and **19**, respectively, in >99:1 dr) confirmed the very high diastereoselectivities of these processes.

With these authentic samples in hand (from which authentic samples of the corresponding ammonium species could be derived simply by addition of Cl_3CCO_2H), the second-order rate constants for the olefinic oxidation of allylic amines **9**–**12** in CD_2Cl_2 solution were determined.[4a,15] In each case, the course of the reaction was monitored by 500 MHz ^{1}H NMR spectroscopy, with the concentrations of reactants and products being determined relative to 1,4-bis(trimethylsilyl)benzene as an (inert) internal standard, of known (unchanging) concentration: 1,4-bis(trimethylsilyl)benzene gives a characteristic singlet at δ_H 0.31 ppm, remote from any resonances associated with the various intermediate ammonium species formed throughout the course of this reaction. This procedure was first applied to *N*,*N*-dibenzyl-substituted amine **12**. Addition of Cl_3CCO_2H to a solution of **12** in CD_2Cl_2 gave ammonium **33**. Upon subsequent addition of *m*-CPBA, the consumption of ammonium **33** was monitored by calculation of the average integration of the peaks due to C(2)*H* (δ_H 5.86–5.97 ppm) and C(1)*H* (δ_H 6.31–6.39 ppm), while the consumption of *m*-CPBA was monitored by integration of the signals corresponding to two protons at δ_H 7.88–7.91 and 7.95–7.97 ppm. The formation of trichloroacetate ammonium **35** was monitored by calculation of the average integration of the signals due to C(3)*H* (δ_H 3.69–3.79 ppm) and C(1)*H* (δ_H 5.15–5.23 ppm). As previously noted,[4a] no significant accumulation of the epoxide ammonium intermediate **34** occurred in this reaction (Figure 2). A mass discrepancy was noted in the experimental data (0.32 M initial concentration of **33**; 0.31 M final concentration of **35**), but is likely associated with the competing direct formation of diol **20** (as the corresponding ammonium species) by ring-opening of epoxide ammonium **34** by H_2O (rather than Cl_3CCO_2H to give **35**), as well as the incomplete diastereoselectivity of this reaction (95:5 dr), resulting in formation of a minor diastereoisomeric epoxide and associated ring-opened products. Although operation of neither of these processes was monitored during this experiment, trace amounts of impurities (~5%) were evident at its conclusion. The rates of consumption of both *m*-CPBA and ammonium **33** were equal, indicating second-order rather than first-order kinetics.[15] Independent analysis of the concentration profiles of both *m*-CPBA and ammonium **33** using the integrated form of the second-order rate law allowed determination of the rate constant (at 298 K) as $k_1 = (7.3 \pm 0.5) \times 10^{-4}$ mol^{-1} dm^3 s^{-1}. This compares to $k_1 = 1.9 \times 10^{-3}$ mol^{-1} dm^3 s^{-1} obtained when this oxidation reaction was performed by us in $CDCl_3$.[4a] Numerical simulation using the finite difference method was employed to model the behavior of ammoniums **33**, **34**, and **35** under these reaction conditions, allowing estimation of a value for the second-order rate constant for the epoxide ring-opening reaction as $k_2 \approx (8 \pm 2.0) \times 10^{-4}$ mol^{-1} dm^3 s^{-1}.[16]

When this procedure was applied to *N*-benzyl-*N*-isopropyl-substituted allylic amine **11**, addition of 5 equiv of Cl_3CCO_2H to **11** to give ammonium **36** rendered the nitrogen atom a stereogenic center and gave rise to a mixture of two ammonium diastereoisomers (epimers at the nitrogen atom) in a ratio of ~1:1. This was particularly evident from the splitting of the resonances associated with C(1)*H*, and the diastereotopic NCH_2Ph and NCHMe_2 substituents. Treatment of a sample of

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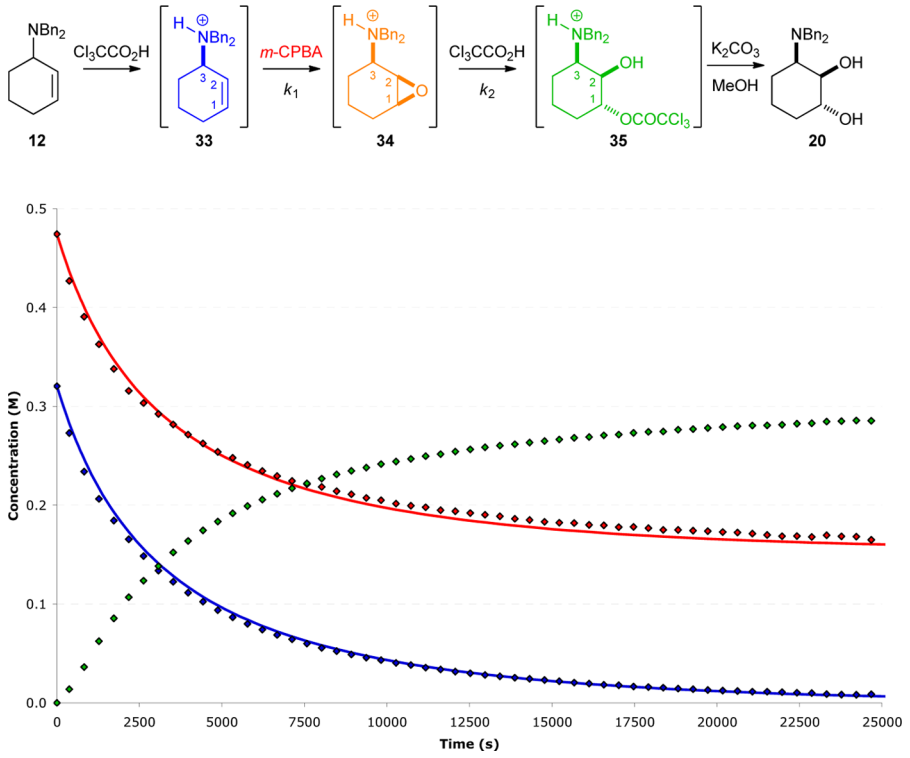

Figure 2. Real-time (^{1}H NMR data points) and simulated (continuous lines) concentration profiles for Cl_3CCO_2H (5 equiv) and *m*-CPBA (1.6 equiv) promoted oxidation of **12** at 298 K in CD_2Cl_2. [**33**], blue; [*m*-CPBA], red; [**35**], green (for brevity, for ammonium ions **33**–**35**, the $Cl_3CCO_2^-$ counterions are not shown).

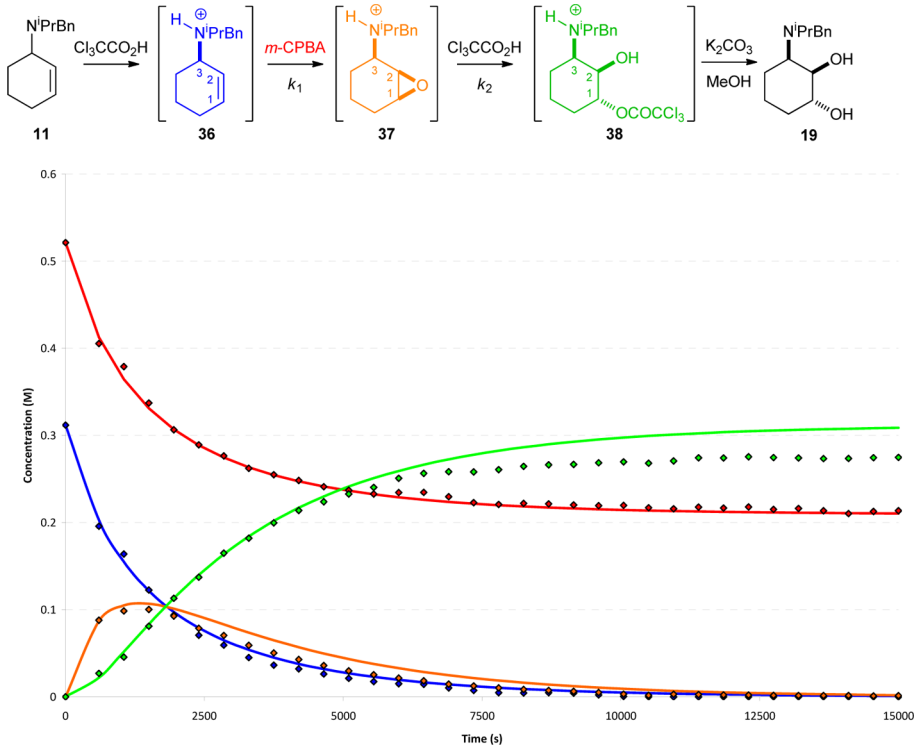

Figure 3. Real-time (^{1}H NMR data points) and simulated (continuous lines) concentration profiles for Cl_3CCO_2H (5 equiv) and *m*-CPBA (1.6 equiv) promoted oxidation of **11** at 298 K in CD_2Cl_2. [**36**], blue; [*m*-CPBA], red; [**37**], orange; [**38**], green (for brevity, for ammonium ions **36**–**38**, the $Cl_3CCO_2^-$ counterions are not shown; **36**–**38** were observed as mixtures of epimers at nitrogen).

epoxide **24** in CD_2Cl_2 (0.4 M) with 5 equiv of Cl_3CCO_2H gave an authentic sample of epoxide ammonium **37** (an ~1:1 mixture of epimers at the nitrogen atom), which underwent ring-opening to give an authentic sample of ammonium **38** (also as a mixture of epimers at the nitrogen atom). These species were confirmed as being epimeric at the nitrogen atom,

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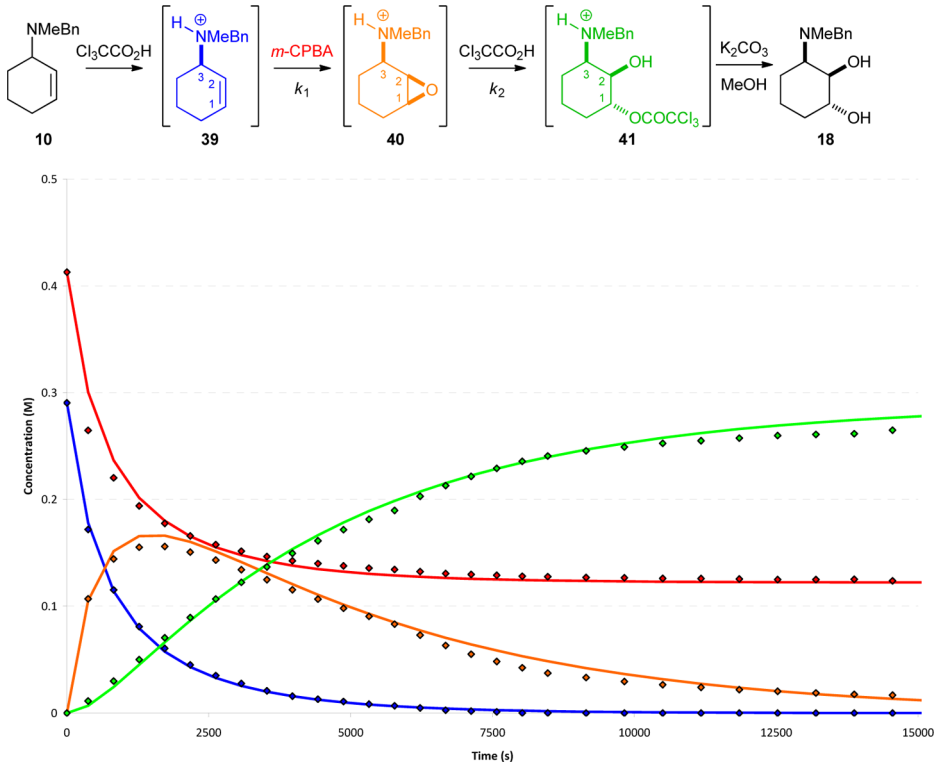

Figure 4. Real-time (^{1}H NMR data points) and simulated (continuous lines) concentration profiles for Cl_3CCO_2H (5 equiv) and *m*-CPBA (1.6 equiv) promoted oxidation of **10** at 298 K in CD_2Cl_2. [**39**], blue; [*m*-CPBA], red; [**40**], orange; [**41**], green (for brevity, for ammonium ions **39**–**41**, the $Cl_3CCO_2^-$ counterions are not shown; **39**–**41** were observed as mixtures of epimers at nitrogen).

since treatment of the sample with K_2CO_3 in MeOH resulted in conversion to diol **19** only. To follow the course of the epoxidation and ring-opening reactions, integration ranges were carefully chosen so as to include signals arising from *both* of the epimers of ammonium species **36**, **37**, and **38**. Hence, the consumption of ammonium **36** was monitored by calculation of the average integration of the peaks due to C(2)*H* (δ_H 5.77–5.84 and 5.89–5.98 ppm) and C(1)*H* (δ_H 6.23–6.34 ppm), with the consumption of *m*-CPBA again being monitored by the disappearance of the signals at δ_H 7.88–7.91 and 7.95–7.97 ppm. The formation of ammonium **38** was monitored by integration of the signal due to C(1)*H* (δ_H 5.15–5.20 and 5.29–5.34 ppm). Unlike during the olefinic oxidation of *N*,*N*-dibenzyl-substituted amine **12**, the formation and disappearance of an intermediate species (epoxide ammonium **37**) could be followed by integration of the peaks due to C(1)*H* rising and falling (at δ_H 3.43–3.47 and 3.50–3.54 ppm). The mass discrepancy in the experimental data (0.31 M initial concentration of **36**; 0.27 M final concentration of **38**) in this case is likely due to the formation of diol **19** (as the corresponding ammonium species) by ring-opening of epoxide **37** by H_2O (rather than Cl_3CCO_2H), which was evident at the end of the reaction (~5–10%). Independent analysis of the rate of loss of both *m*-CPBA and ammonium **36** using the integrated form of the second-order rate law allowed determination of the rate constant (at 298 K) as $k_1 = (1.6 \pm 0.2) \times 10^{-3}$ mol^{-1} dm^3 s^{-1}. Numerical simulation to model the behavior of ammoniums **36**, **37**, and **38** under these reaction conditions allowed determination of the second-order rate constant for the epoxide ring-opening reaction as $k_2 = (6.5 \pm 1.0) \times 10^{-4}$ mol^{-1} dm^3 s^{-1}; good correlation between the simulated concentration profiles and the experimental data was noted (Figure 3). The ~1:1 ratio of ammonium diastereoisomers **36** remained constant throughout the course of this reaction. As a result, no information regarding the relative rates of epoxidation of these species can be gleaned from these data, since this observation is consistent with either very similar rates of epoxidation of both ammonium diastereoisomers **36** or a system under Curtin–Hammett control (i.e., rapid equilibration of both diastereoisomers of **36**, but preferential reaction of only one). Similarly, the ~1:1 ratio of the two ammonium diastereoisomers **37** remained constant throughout the reaction, and so no conclusions as to the relative rate of ring-opening of these two species can be drawn.

In a similar manner, addition of 5 equiv of Cl_3CCO_2H to **10** gave ammonium **39** as a mixture of two ammonium diastereoisomers (epimers at the nitrogen atom) in a ratio of ~1:1. Authentic samples of ammonium species **40** and **41** (also mixtures of epimers at the nitrogen atom) were prepared upon addition of 5 equiv of Cl_3CCO_2H to a sample of epoxide **23** in CD_2Cl_2 (0.4 M), and the ring-opening process was monitored by ^{1}H NMR spectroscopy (over 12 h). Subsequent treatment with K_2CO_3 in MeOH gave diol **18** only. The oxidation of *N*-benzyl-*N*-methyl-substituted allylic amine **10** was then monitored by ^{1}H NMR spectroscopy,[17] and application of the integrated form of the second-order rate law to the experimental data so generated gave $k_1 = (3.7 \pm 0.2) \times 10^{-3}$ mol^{-1} dm^3 s^{-1} at 298 K. The ~1:1 ratios of ammonium epimers **39** and **40** did not change during the course of these studies. In this case, numerical simulation using the finite difference method gave $k_2 = (3.0 \pm 1.0) \times 10^{-4}$ mol^{-1} dm^3 s^{-1} (Figure 4). It is, therefore, apparent that the rates of ring-opening of epoxide ammonium species **34**, **37**, and **40** are similar.

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An attempt to apply the same procedure for the determination of the rate constant k_1 of the oxidation of *N*-benzyl-substituted amine **9** revealed complete consumption of starting material within 5 min. However, when the reaction was conducted at higher dilution (0.08 M wrt **9**), the rate constant was determined to be $k_1 = 3.6 \times 10^{-2}$ mol^{-1} dm^3 s^{-1}. Thus, the kinetic studies revealed the ammonium-directed epoxidation reactions of allylic amines **9**:**10**:**11**:**12** to have approximate relative rates of 49:5:2:1, respectively (Figure 5).

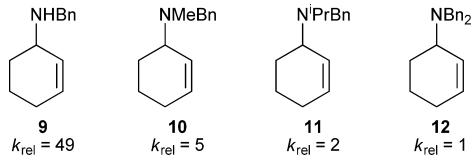


Figure 5. Approximate relative rates of oxidation of allylic amines **9**–**12** in CD_2Cl_2.

It has previously been shown by us that the relative rates of oxidation of 3-(*N*,*N*-dibenzylamino)cyclohex-1-ene **12**, *syn*-3-(*N*,*N*-dibenzylamino)-5-*tert*-butylcyclohex-1-ene **42**, and *anti*-3-(*N*,*N*-dibenzylamino)-5-*tert*-butylcyclohex-1-ene **43** are approximately 1:1:2[4a] (Figure 6). Molecular modeling implied that the

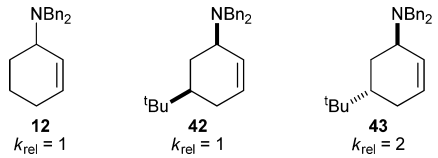


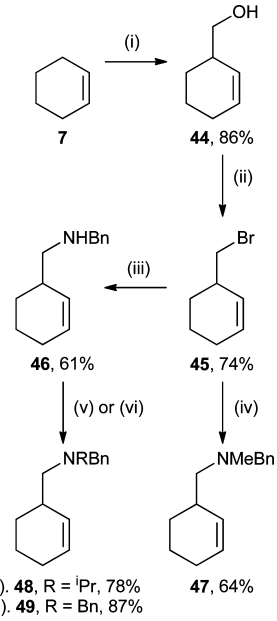
Figure 6. Approximate relative rates of oxidation of allylic amines **12**, **42**, and **43** in $CDCl_3$.

ammonium ions derived from protonation of both **12** and *syn*-**42** adopted essentially identical conformations, as expected, with the ammonium moiety occupying a pseudoequatorial site within a half-chair conformation. In the corresponding ammonium ion derived from *anti*-**43**, the minimum energy conformation was one in which the ammonium moiety lay midway between a pseudoaxial and pseudoequatorial position of a half-chair. It was postulated that the latter represented a better reactive geometry within the hydrogen-bonded transition state for olefinic oxidation, which, led to an increased rate of reaction.[4a] Reduction of the steric bulk of the ammonium moiety from RNHBn$_2^+$ (in **33**) or RNH^{i}PrBn$^+$ (in **36**) to RNHMeBn$^+$ (in **39**) to RNH$_2$Bn$^+$ (in the corresponding ammonium species derived from **9**) may allow more facile distortion of the half-chair ground-state conformation of the six-membered ring due to the reduced steric interactions that would be suffered by placing the ammonium moiety closer to a pseudoaxial orientation (i.e., less energy is required to achieve the optimum reactive conformation). Reaction with the ammonium moiety in a more favorable reactive geometry would manifest itself in an increased rate of reaction. The very large increase in rate on moving from tertiary amines **10**–**12** to secondary amine **9** suggests that the secondary amine is better able to form a hydrogen bond with the peracid: a closer association between oxidant and substrate is likely to stabilize the transition state for epoxidation, so increasing the rate of reaction. The presence of two potential hydrogen-bond donor sites for the ammonium ion derived from secondary amine **9** may also account for its increased reactivity. A combination of these factors may account for the very much greater rate of oxidation observed for **9** as compared with **10**–**12**.

To investigate this hypothesis further, secondary and tertiary 3-aminomethylcyclohex-1-enes bearing a range of substituents on nitrogen were selected for investigation. It was anticipated that the addition of a methylene group between the carbocyclic ring and the amino group would confer a greater degree of conformational flexibility to these substrates, even those containing a very sterically demanding amino moiety (i.e., *N*,*N*-dibenzyl- and *N*-benzyl-*N*-isopropyl-substituted amino groups), and so give more insight into their relative hydrogen-bond-directing ability.

Oxidation of N-Substituted 3-Aminomethylcyclohex-1-enes. N-Substituted 3-aminomethylcyclohex-1-enes **46**–**49** were prepared from the common intermediate bromide **45**.[4c,18] Substitution using benzylamine and *N*-benzyl-*N*-methylamine gave the corresponding amines **46** and **47** in 61% and 64% yield, respectively. Attempted substitution of bromide within **45** by *N*-benzyl-*N*-isopropylamine gave low levels of conversion to the desired tertiary amine **48** (<10%), even after extended reaction times, while displacement with dibenzylamine gave a sample of **49** that was difficult to purify. The requisite tertiary amines **48** and **49** were, therefore, prepared through N-alkylation of secondary amine **46**, upon treatment with acetone in the presence of NaB(OAc)$_3$H, and BnBr in the presence of ^{i}Pr$_2$NEt, respectively (Scheme 6).

Scheme 6[a]



[a]Reagents and conditions: (i) KO^{t}Bu, BuLi, 0 °C to rt, 18 h, then $(CH_2O)_n$, 60 °C, 3 h; (ii) NBS, PPh_3, CH_2Cl_2, 0 °C to rt, 17 h; (iii) $BnNH_2$, NaI, 50 °C, 20 h; (iv) HNMeBn, K_2CO_3, MeCN, 60 °C, 20 h; (v) Na(OAc)$_3$BH, AcOH, acetone, rt, 24 h; (vi) BnBr, ^{i}Pr$_2$NEt, CH_2Cl_2, 40 °C, 2 h.

Oxidation of secondary amine **46** and tertiary amines **47**–**49** upon treatment with 5 equiv of Cl_3CCO_2H and 1.6 equiv of *m*-CPBA was followed by transesterification with K_2CO_3 in MeOH and gave the corresponding amino diols **50**–**53** in ≥90:10 dr (in each case, the minor diastereoisomer was the corresponding 1,2-*anti*-2,3-*anti*-diastereoisomer). Chromatography allowed isolation of **50**–**53** in modest to good yield (55–

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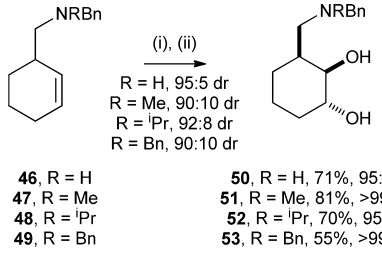
81%), and in ≥95:5 dr (Scheme 7). It is notable that, in all of the cases examined here, the directing ability of the (in situ

Scheme 7[a]

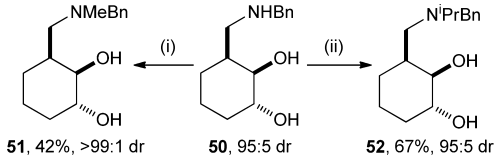


[a]Reagents and conditions: (i) Cl_3CCO_2H, *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) K_2CO_3, MeOH, rt, 16 h.

formed) ammonium substituent is greater than that offered by the corresponding hydroxyl substituent: we have previously reported that, under analogous conditions, dihydroxylation of cyclohexene-derived homoallylic alcohol **44** gave a 76:24 mixture of the corresponding 1,2-*anti*-2,3-*syn*- and 1,2-*anti*-2,3-*anti*-diastereoisomers of 3-hydroxymethylcyclohexane-1,2-diol.[4c]

The relative configurations within *N*-benzylamino diol **50** and *N*,*N*-dibenzylamino diol **53** have previously been established unambiguously.[4c] The relative configurations within **51** and **52** were unambiguously assigned by chemical correlation, through reductive alkylation of **50** with either paraformaldehyde or acetone, respectively (Scheme 8).

Scheme 8[a]

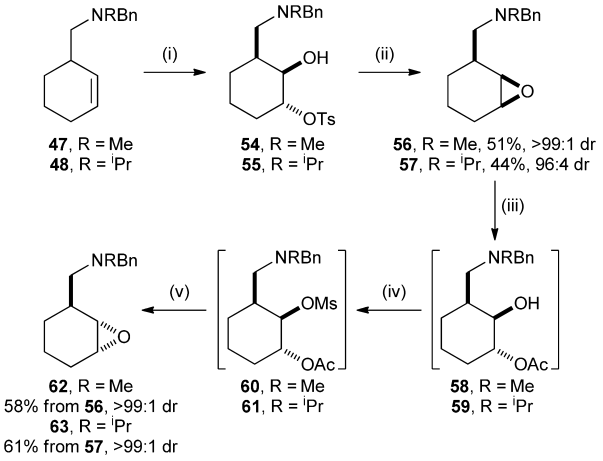


[a]Reagents and conditions: (i) $(CH_2O)_n$, $NaB(OAc)_3H$, AcOH, CH_2Cl_2, rt, 20 h; (ii) acetone, $NaB(OAc)_3H$, AcOH, rt, 24 h.

Next, authentic samples of the intermediate epoxides and minor diastereoisomeric products of these oxidation reactions were prepared. Ammonium-directed oxidation of **47** and **48** employing TsOH, followed by treatment of the crude reaction mixtures with DBU, gave *syn*-epoxides **56** (>99:1 dr) and **57** (96:4 dr). A three-step epoxide inversion strategy gave *anti*-epoxides **62** and **63** in >99:1 dr in both cases (Scheme 9).[19] Ring-opening of *anti*-epoxides **62** and **63** upon treatment with 3 M aq H_2SO_4 proceeded to give a mixture of diastereoisomers (R = Me, **51**:**64**, 31:69 dr; R = ^{i}Pr, **52**:**65**, 23:77 dr).[20,21] The major diastereoisomers **64** and **65** were isolated in 36% and 48% yield after chromatography, and in >99:1 dr and 95:5 dr, respectively. The relative configurations within **64** and **65** were assigned on the basis of ^{1}H NMR ^3J coupling constant analyses (Scheme 10).

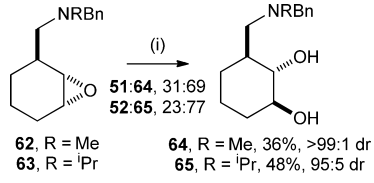
The oxidation reactions of homoallylic amines **46**–**49** in $CDCl_3$ solution were next followed by ^{1}H NMR spectroscopy, and from the data generated, application of the integrated form of the second-order rate law gave the second-order rate constants of $k = 9.5 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**46**), $k = 2.2 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**47**), $k = 2.1 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**48**), and $k = 1.3 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**49**). The relative rates of

Scheme 9[a]



[a]Reagents and conditions: (i) TsOH, *m*-CPBA, CH_2Cl_2, rt, 21 h; (ii) DBU, CH_2Cl_2, rt, 24 h; (iii) AcOH, 50 °C, 24 h; (iv) MsCl, Et_3N, CH_2Cl_2, 0 °C, 1 h; (v) K_2CO_3, MeOH, rt, 16 h.

Scheme 10[a]



[a]Reagents and conditions: (i) H_2SO_4 (3 M aq), 1,4-dioxane, 40 °C, 24 h.

epoxidation of **46**:**47**:**48**:**49** were, therefore, determined to be approximately 7:2:2:1 (Figure 7).

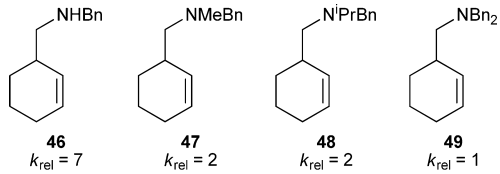


Figure 7. Approximate relative rates of oxidation of homoallylic amines **46**–**49** in $CDCl_3$.

In comparison to the parent *N*,*N*-dibenzyl-substituted allylic amine **12**, the rates of oxidation of all homoallylic amines **46**–**49** are faster. This is in accordance with the olefin being more nucleophilic, as the electron-withdrawing ammonium group is now located further from it. Furthermore, *N*-benzyl-*N*-methyl-substituted **47**, *N*-benzyl-*N*-isopropyl-substituted **48**, and *N*,*N*-dibenzyl-substituted **49** of the 3-aminomethylcyclohex-1-ene (homoallylic) series showed similar rates of reaction, which is consistent with the assertion that the incorporation of a methylene group between the carbocyclic ring and the amino group confers greater conformational flexibility to theses substrates: in each of these cases, the ammonium moiety may be more able to adopt a favorable geometry to promote efficient hydrogen-bond-directed oxidation, which is manifest in similar rates of reaction. It is also noteworthy that oxidation of *N*-benzyl-substituted secondary amine **46** is again somewhat faster than its tertiary amine counterparts **47**–**49**.

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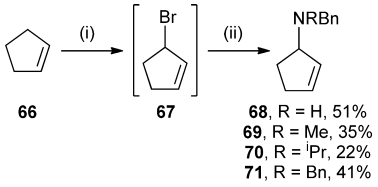
Oxidation of N-Substituted 3-Aminocyclopent-1-enes. The effect of varying the size of the carbocyclic ring on this reaction was next explored. N-Substituted 3-aminocyclopent-1-enes **68**–**71** were prepared from **67** by bromide displacement with the requisite amine (Scheme 11).

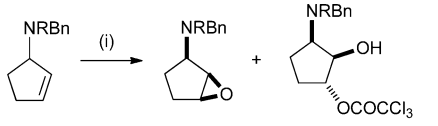
Scheme 11[a]



[a]Reagents and conditions: (i) NBS, AIBN, CCl_4, reflux, 1 h; (ii) HNRBn, rt, 1.5 h.

We have previously demonstrated that the epoxidation of cyclopentene-derived allylic amine **71** using 5 equiv of Cl_3CCO_2H and 1.05 equiv of *m*-CPBA is complete within 3.5 h at rt[4c] and (unlike its cyclohexene-derived allylic amine counterpart **12**) the corresponding epoxide was isolated rather than ring-opened product(s). The faster rate of ring-opening of cyclohexene oxide versus cyclopentene oxide by a range of nucleophiles[22] has previously been associated with the relief of torsional strain that occurs in the former case.[23] On the basis of these previous observations, it was anticipated that the rate of oxidation of each member of the cyclopentene-derived series of allylic amines **68**–**71** would be greater than that of their counterpart within the cyclohexene-derived series of allylic amines **9**–**12** and would result in formation of the corresponding *syn*-epoxide as the major product (rather than trichloroacetate esters resulting from ring-opening). Indeed, oxidation of **68**–**71** with 5 equiv of Cl_3CCO_2H and 1.05 equiv of *m*-CPBA gave, in all cases, a mixture comprising only the corresponding *syn*-epoxides **72**–**75** (>99:1 dr) as the major products (≥88%) and the corresponding trichloroacetate esters **76**–**79** (>99:1 dr) as the minor products (≤12%). Chromatographic purification allowed isolation of *syn*-epoxides **72**–**75** in 46–99% yield, and in >99:1 dr in each case (Scheme 12). The

Scheme 12[a]

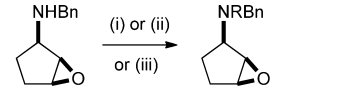


	R	ratio epoxide:ester	epoxide yield % (dr)
68	H	**72**:**76**, 88:12	59 (>99:1)
69	Me	**73**:**77**, 92:8	46 (>99:1)
70	^{i}Pr	**74**:**78**, 92:8	59 (>99:1)
71	Bn	**75**:**79**, >99:1	99 (>99:1)

[a]Reagents and conditions: (i) Cl_3CCO_2H, *m*-CPBA, CH_2Cl_2, rt, 3.5 h.

relative syn configurations within **72**–**74** were unambiguously established by chemical correlation to **75**, whose relative syn configuration has previously been established by single-crystal X-ray diffraction analysis.[4c] Treatment of **72** with BnBr/^{i}Pr$_2$NEt gave **75** in 70% yield, while N-alkylation of **72** upon treatment with MeI/^{i}Pr$_2$NEt or acetone/NaB(OAc)$_3$H gave **73** and **74**, respectively (Scheme 13). In addition, authentic samples of

Scheme 13[a]



72, >99:1 dr (i). **73**, R = Me, 45%, >99:1 dr
(ii). **74**, R = ^{i}Pr, 65%, >99:1 dr
(iii). **75**, R = Bn, 70%, >99:1 dr

[a]Reagents and conditions: (i) MeI, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 20 h; (ii) acetone, NaB(OAc)$_3$H, AcOH, rt, 24 h; (iii) BnBr, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 20 h.

trichloroacetate esters **76**–**79** were prepared upon treatment of *syn*-epoxides **72**–**75** with Cl_3CCO_2H (although it was not possible to isolate pure samples of **76**–**79** due to the lability of the trichloroacetate ester moiety), thus unambiguously confirming that **76**–**79** arise from in situ ring-opening of **72**–**75** and, therefore, that the oxidation reaction is completely diastereoselective in each case. As with the analogous oxidation of 3-hydroxycyclopentene (which has been reported to proceed with very high levels of syn diastereoselectivity),[1,24] this stereochemical outcome is consistent with the reaction being under hydrogen-bond control,[25] although several examples of syn-selective osmylation and epoxidation reactions of 3-substituted cyclopentenes, which proceed in the absence of any obvious associative interactions (e.g., hydrogen-bonding) in the transition state, have been reported.[26] In these cases, it has been proposed that the diastereoselectivity results from attack on the syn face being favored in order to minimize torsional strain in the transition state.[27]

The rates of oxidation of allylic amines **68**–**71** were next examined, and the second-order rate constants were determined as $k = 3.7 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**68**), $k = 2.6 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**69**), $k = 1.1 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**70**), and $k = 6.1 \times 10^{-3}$ mol^{-1} dm^3 s^{-1} (**71**). Thus, the relative rates of oxidation of **68**:**69**:**70**:**71** were determined to be approximately 6:4:2:1 (Figure 8).

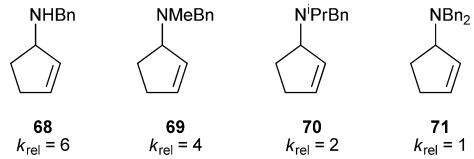


Figure 8. Approximate relative rates of oxidation of allylic amines **68**–**71** in $CDCl_3$.

These data reveal a decrease in epoxidation rate as the series **68** (R = H), **69** (R = Me), **70** (R = ^{i}Pr), and **71** (R = Bn) is traversed,[28] so following the same trend as that observed for the cyclohexene-derived allylic series **9**–**12** and homoallylic series **46**–**49**. As initially expected, the rates of oxidation of the cyclopentene-derived tertiary amines **69**–**71** are greater than those of their cyclohexene-derived allylic amine counterparts **10**–**12**. This is consistent with the previously reported greater rate of peracid epoxidation of cyclopentene as compared with that of cyclohexene,[29] but may also be indicative that, in the absence of the exceptional and unique conformational bias imparted by the six-membered ring in **10**–**12**, distortion of the ammonium moiety into a more optimal geometry for epoxidation is possible in all of these cyclopentene-derived systems, resulting in much similar rates of reaction. In contrast, however, the rates of oxidation of the cyclopentene-derived

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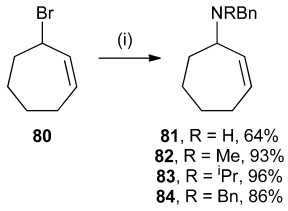
tertiary amines **69**–**71** are of a similar magnitude to those of their cyclohexene-derived homoallylic amine counterparts **46**–**49**. In the latter case, the electron-withdrawing ammonium group is located further from the olefin, which would be expected to render the olefin more nucleophilic, hence compensating for the expected inherent decrease in reactivity of the olefin toward epoxidation in the cyclohexene-derived homoallylic series compared to the cyclopentene-derived allylic series.

Oxidation of N-Substituted 3-Aminocyclohept-1-enes. Attention next turned to oxidation of the seven-membered ring system. A range of N-substituted 3-aminocyclohept-1-enes **81**–**84** were prepared upon bromide displacement within **80** by the requisite amines to give 3-aminocyclohept-1-enes **81**–**84** in 64–96% yield after chromatographic purification (Scheme 14).

Scheme 14[a]

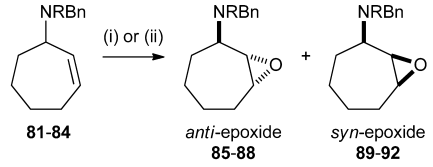


[a]Reagents and conditions: (i) HNRBn, K_2CO_3, THF, 50 °C, 16 h.

Oxidation of *N*,*N*-dibenzyl-substituted allylic amine **84** under our previously reported conditions (treatment with 5 equiv of Cl_3CCO_2H and 1.05 equiv of *m*-CPBA for 3.5 h)[4c] resulted in 88% conversion to a 94:6 mixture of the known epoxides *anti*-**88** and *syn*-**92**,[4c] and under the same conditions, oxidation of *N*-benzyl-*N*-isopropyl-substituted allylic amine **83** gave >95% conversion to a 93:7 mixture of *anti*-epoxide **87** and *syn*-epoxide **91**, respectively. However, the analogous oxidation of *N*-benzyl-*N*-methyl-substituted allylic amine **82** gave only 66% conversion to a 75:25 mixture of *anti*-epoxide **86** and *syn*-epoxide **90**, which suggested, somewhat surprisingly, that the rate of oxidation of **82** is slower than those of **83** and **84**. The oxidation reaction of **82** could be driven to >95% conversion within 7 h by increasing the amount of *m*-CPBA used to 1.6 equiv: a 75:25 mixture of *anti*-epoxide **86** and *syn*-epoxide **90** was thus produced, with only a small amount (~5%) of products resulting from ring-opening being present. Finally, oxidation of secondary amine **81** was investigated: using 2.5 equiv of *m*-CPBA in the presence of 5 equiv of Cl_3CCO_2H (optimized conditions) afforded a 15:85 mixture of *anti*-epoxide **85** and *syn*-epoxide **89** after 20 min. This result indicates a hitherto unprecedented *reversal* in the sense of epoxidation diastereofacial selectivity between secondary amine **81** and its tertiary amine counterparts **82**–**84**. Chromatographic purification gave a 15:85 mixture of **85** and **89** in 83% combined yield, while exhaustive purification allowed isolation of a diastereoisomerically pure sample of **85** in 51% yield (Scheme 15).

The configurations within *syn*-epoxides **89**–**92** were established by chemical correlation: N-alkylation of *syn*-epoxide **89** (the *major* product resulting from the oxidation of *N*-benzyl-substituted allylic amine **81**) upon treatment with MeI/^{i}Pr$_2$NEt, acetone/NaB(OAc)$_3$H, and BnBr/^{i}Pr$_2$NEt gave, in each case, a sample of the corresponding *syn*-epoxides **90**–**92** (Scheme 16), which were spectroscopically identical to the *minor* diastereoisomeric products resulting from oxidation of the corresponding tertiary allylic amines **82**–**84**. The relative syn configurations within epoxides **89**–**91** could, therefore, be unambiguously assigned from the known relative syn configuration within epoxide **92**.[4c] In addition, N-benzylation of the 15:85 mixture of **85**:**89** upon treatment with BnBr gave a 15:85 mixture of **88**:**92**, thus unambiguously confirming the relative *anti* configuration within **88**. These analyses also allowed the relative configurations within *anti*-epoxides **86** and **87** to be unambiguously assigned.

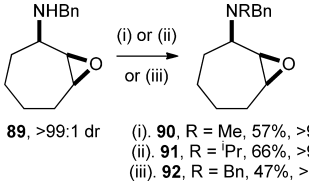
Scheme 15[a]



	R	Conditions	Conversion %	Epoxide ratio *anti*:*syn*	Yield *anti* % (dr)	Yield *syn* % (dr)
81	H	(i)	>99	**85:89**, 15:85	-	51 (>99:1)
82	Me	(ii)	66	**86:90**, 75:25	-	-
82	Me	(iii)	>95	**86:90**, 75:25	36 (>99:1)	4 (>99:1)
83	^{i}Pr	(ii)	>95	**87:91**, 93:7	46 (>99:1)	-
84	Bn	(ii)	88	**88:92**, 94:6	69 (>99:1)	4 (>99:1)

[a]Reagents and conditions: (i) Cl_3CCO_2H, *m*-CPBA (2.5 equiv), CH_2Cl_2, rt, 20 min; (ii) Cl_3CCO_2H, *m*-CPBA (1.05 equiv), CH_2Cl_2, rt, 3.5 h; (iii) Cl_3CCO_2H, *m*-CPBA (1.6 equiv), CH_2Cl_2, rt, 7 h.

Scheme 16[a]



[a]Reagents and conditions: (i) MeI, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 20 h; (ii) acetone, NaB(OAc)$_3$H, AcOH, rt, 24 h; (iii) BnBr, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 20 h.

Next, the rates of oxidation of allylic amines **81**–**84** were examined, and the second-order rate constants were determined to be $k = 1.8 \times 10^{-2}$ mol^{-1} dm^3 s^{-1} (**81**), $k = 7.0 \times 10^{-4}$ mol^{-1} dm^3 s^{-1} (**82**), $k = 1.4 \times 10^{-3}$ mol^{-1} dm^3 s^{-1} (**83**), and $k = 2.2 \times 10^{-3}$ mol^{-1} dm^3 s^{-1} (**84**). From these data, the approximate relative rates of oxidation of **81**:**82**:**83**:**84** were determined to be 26:1:2:3, with the *syn*:*anti* reaction diastereoselectivities being 85:15 (**81**), 25:75 (**82**), 7:93 (**83**), and 6:96 (**84**), respectively. Although secondary amine **81** undergoes the most rapid epoxidation in the cycloheptene-derived series of allylic amines, the observed rate order (and, indeed, reaction diastereoselectivity) for tertiary amines **82**–**84** does not follow the pattern that would be expected from the relative rate order in the cyclohexene-derived allylic amine series **9**–**12** and homoallylic amine series **46**–**49**, and cyclopentene-derived series **68**–**71** (Figure 9).

We have previously ascribed the high levels of *anti* diastereoselectivity in the oxidation of *N*,*N*-dibenzyl-substituted **84** to the ability of the amino group to play two distinct roles: the sterically demanding substituents on nitrogen may enforce a well-defined chair-type conformation on the otherwise conformationally labile cycloheptene ring,[30] such that hydrogen-bonding by the in situ formed ammonium moiety results in

dx.doi.org/10.1021/jo3010556 | J. Org. Chem. 2012, 77, 7241–7261

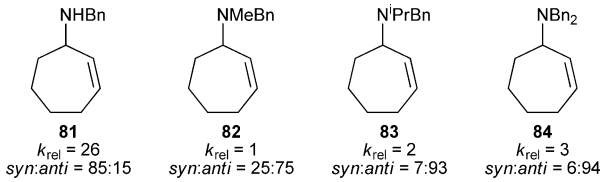


Figure 9. Approximate relative rates of oxidation of allylic amines **81**–**84** in $CDCl_3$, and *syn*:*anti* reaction diastereoselectivities.

efficient epoxidation on the (least hindered) *anti* face.[4c] With a reduction in steric bulk of the amino group, the cycloheptene ring presumably becomes less well conformationally defined, and reaction through multiple conformations can occur (potentially via both ammonium-directed and nondirected pathways) to give rise to a mixture of products. The situation then becomes comparable to the epoxidation of 3-hydroxycycloheptene, which has been reported to proceed with only low levels of *syn* diastereoselectivity (~2:1 dr) upon reaction with a range of peracids.[31] However, if the hydrogen-bonding ability of the ammonium species derived from secondary amine **81** is superior to that of the ammonium species derived from its tertiary amine counterparts **82**–**84** (as well as that of the hydroxyl group), then reaction *syn* to the amino group through one favorable conformation would result in a highly diastereoselective reaction.

CONCLUSION

The ammonium-directed olefinic epoxidations of a range of differentially N-substituted cyclic allylic and homoallylic amines (derived from cyclopentene, cyclohexene, and cycloheptene) have been investigated, and the reaction kinetics have been analyzed. The results of these studies suggest that both the ring size and the identity of the substituents on nitrogen are important in determining both the overall rate and the stereochemical outcome of the epoxidation reaction. Comparison of all of the relative rates (and diastereoselectivities) of the ammonium-directed epoxidation reactions (Figure 10) allows the following conclusions to be drawn: (i) Secondary amines or tertiary amines with nonsterically demanding substituents on nitrogen are generally superior to tertiary amines with sterically demanding substituents on nitrogen in their ability to promote the oxidation reaction. (ii) The ability of the (in situ formed) ammonium substituent to direct the stereochemical course of the epoxidation reaction is either comparable or superior to that of the analogous hydroxyl substituent. (iii) The relative rates of epoxidation of the allylic amines are generally all lower than that for the corresponding homoallylic amine (for example, **12**, **71**, and **84** compared to **49**). This suggests that the electron-withdrawing effect of the ammonium moiety is a key feature here. As previously noted, location of the electron-withdrawing ammonium moiety further from the olefin (i.e., in the homoallylic position rather than the allylic position) likely renders it more nucleophilic (regardless of the size of the ring system), and as a result, **49** reacts fastest within this series of cycloalkenyl amines. (iv) The increased rate of reaction for the cyclopentene-derived allylic amines versus their cyclohexene-derived allylic amine counterparts parallels that noted for the parent cycloalkenes (cyclopentene and cyclohexene) in a range of reactions;[32] this observation has often been attributed to relief of ring strain upon reaction in the former case. (iv) High levels of *syn* diastereoselectivity are observed in all cases with the exception of the cycloheptene-derived allylic amines **81**–**84**, which give either the corresponding *syn*- or *anti*-epoxide as the major diastereoisomer, depending on the nature of the amino substituent. (v) Much slower rates of ring-opening of the intermediate epoxides are observed in cyclopentene-derived and cycloheptene-derived allylic amines as compared with their cyclohexene-derived allylic and homoallylic amine counterparts, allowing for isolation of these intermediates in both of the former cases. Using the information garnered from these investigations, further studies of this ammonium-directed epoxidation reaction to both enhance our mechanistic understanding of the process and further exploit its synthetic utility are underway within our laboratory.

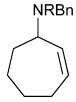
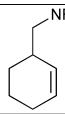
Substrate	H	Me	^{i}Pr	Bn
	**68** k_{rel} = 53 (>99:1)	**69** k_{rel} = 37 (>99:1)	**70** k_{rel} = 16 (>99:1)	**71** k_{rel} = 9 (>99:1)
	**9** k_{rel} = 51 (95:5)	**10** k_{rel} = 5 (>99:1)	**11** k_{rel} = 2 (>99:1)	**12** k_{rel} = 1 (95:5)
	**81** k_{rel} = 26 (85:15)	**82** k_{rel} = 1 (25:75)	**83** k_{rel} = 2 (7:93)	**84** k_{rel} = 3 (4:96)
	**46** k_{rel} = 136 (95:5)	**47** k_{rel} = 31 (>99:1)	**48** k_{rel} = 30 (95:5)	**49** k_{rel} = 19 (>99:1)

Figure 10. Approximate relative rates of epoxidation of allylic and homoallylic amines (*m*-CPBA, Cl_3CCO_2H, CH_2Cl_2).

EXPERIMENTAL SECTION

General Experimental Details. *m*-CPBA was supplied as a 70–77% slurry in water and titrated according to the procedure of Swern[33] immediately before use. Water was purified by an Elix UV-10 system. Organic solvents were used as supplied (analytical or HPLC grade) without prior purification. Thin-layer chromatography was performed on aluminum plates coated with 60 F_{254} silica. Plates were visualized using UV light (254 nm), iodine, 1% aqueous $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed either on Kieselgel 60 silica on a glass column or on an automated flash column chromatography platform.

Melting points are uncorrected. IR spectra were recorded as either a thin film on NaCl plates (film) or a KBr disk (KBr), as stated. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. $^1H-^1H$ COSY and $^1H-^{13}C$ HMQC analyses were used to establish atom connectivity. Accurate mass measurements were run on a MicroTOF instrument internally calibrated with polyalanine.

(*RS*)-3-Bromocyclohex-1-ene 8. Benzoyl peroxide (70% w/w, 842 mg, 2.43 mmol) and NBS (43.8 g, 246 mmol) were added sequentially to a stirred solution of **7** (40.0 g, 490 mol) in CCl_4 (200 mL). The resultant suspension was heated at 90 °C for 1.5 h, then allowed to cool to rt before being filtered through Celite (eluent CH_2Cl_2). The filtrate was washed with 0.1 M aq $NaHCO_3$ (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via reduced pressure distillation gave **8** as a yellow oil (27.6 g, 70%).[4a] bp 50–52 °C (14 mbar); δ_H (400 MHz, $CDCl_3$) 1.65–2.28 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 4.83–4.89 (1H, m, C(3)*H*), 5.80–5.86 (1H, m, C(1)*H*), 5.89–5.96 (1H, m, C(2)*H*).

(*RS*)-3-(*N*-Benzylamino)cyclohex-1-ene 9. A stirred mixture of **8** (0.20 mL, 1.62 mmol), benzylamine (0.44 mL, 4.06 mmol), and K_2CO_3 (268 mg, 1.94 mmol) in THF (2 mL) was heated at 50 °C for

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16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 30 → 50% Et_2O in 30−40 °C petrol) gave **9** as a pale yellow oil (240 mg, 79%).[4a] δ_H (400 MHz, $CDCl_3$) 1.35−2.06 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 3.21−3.29 (1H, m, C(3)H), 3.79−3.89 (2H, m, NCH_2Ph), 5.61−5.82 (2H, m, C(1)H, C(2)H), 7.21−7.49 (5H, m, *Ph*).

(*RS*)-3-(*N*-Benzyl-*N*-methylamino)cyclohex-1-ene 10. A stirred mixture of **8** (0.20 mL, 1.62 mmol), *N*-benzyl-*N*-methylamine (0.32 mL, 4.06 mmol), and K_2CO_3 (268 mg, 1.94 mmol) in THF (2 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2 → 20% Et_2O in 30−40 °C petrol) gave **10** as a pale yellow oil (270 mg, 83%).[34] δ_H (400 MHz, $CDCl_3$) 1.48−2.04 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.23 (3H, s, N*Me*), 3.20−3.41 (1H, m, C(3)H), 3.47 (1H, d, *J* 13.3, NCH_AH_BPh), 3.67 (1H, d, *J* 13.3, NCH_AH_BPh), 5.70−5.77 (1H, m, C(1)H), 5.81−5.88 (1H, m, C(2)H), 7.21−7.37 (5H, m, *Ph*).

(*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)cyclohex-1-ene 11. A stirred mixture of **8** (0.20 mL, 1.62 mmol), *N*-benzyl-*N*-isopropylamine (0.40 mL, 4.06 mmol), and K_2CO_3 (268 mg, 1.94 mmol) in THF (2 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2 → 10% Et_2O in 30−40 °C petrol) gave **11** as a pale yellow oil (243 mg, 65%). ν_{max} (film) 3083, 3061, 2960 (C−H), 1493 (C═C); δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.11 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.53−1.61 (2H, m, C(4)H_A, C(5)H_A), 1.81−1.91 (2H, m, C(4)H_B, C(5)H_B), 1.98−2.02 (2H, m, C(6)H_2), 3.04 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.49−3.55 (1H, m, C(3)H), 3.75 (2H, AB system, *J* 15.7, NCH_2Ph), 5.73−5.75 (1H, m, C(2)H), 5.80−5.83 (1H, m, C(1)H), 7.22−7.26 (1H, m, *Ph*), 7.33 (2H, t, *J* 7.4, *Ph*), 7.43 (2H, d, *J* 7.4, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.6, 21.3 (NCH*Me*$_2$), 22.3 (*C*(5)), 25.2 (*C*(6)), 28.2 (*C*(4)), 48.8 (NCHMe$_2$), 49.9 (NCH$_2$Ph), 53.8 (*C*(3)), 126.2 (*p-Ph*), 127.9, 128.0 (*o,m-Ph*), 129.4 (*C*(1)), 132.6 (*C*(2)), 143.0 (*i-Ph*); *m/z* (ESI$^+$) 230 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{24}N^+$ ([M + H]$^+$) requires 230.1903; found 230.1900.

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclohex-1-ene 12. A stirred mixture of **8** (0.20 mL, 1.62 mmol), dibenzylamine (0.78 mL, 4.06 mmol), and K_2CO_3 (268 mg, 1.94 mmol) in THF (2 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 2% Et_2O in 30−40 °C petrol) gave **12** as a pale yellow oil (359 mg, 80%).[4a] δ_H (400 MHz, $CDCl_3$) 1.44−1.63 (2H, m, C(5)H_2), 1.81−2.08 (4H, m, C(4)H_2, C(6)H_2), 3.39 (1H, app br s, C(3)H), 3.59 (2H, d, *J* 13.9, N(CH$_A$H$_B$Ph)$_2$), 3.79 (2H, d, *J* 13.9, N(CH$_A$H$_B$Ph)$_2$),), 5.75−5.88 (2H, m, C(1)H, C(2)H), 7.21−7.49 (10H, m, *Ph*).

(*RS*,*RS*,*RS*)-3-(*N*-Benzylamino)cyclohexane-1,2-diol 17. Step 1: Cl_3CCO_2H (4.37 g, 26.7 mmol) was added to a solution of **9** (1.01 g, 5.39 mmol) in CH_2Cl_2 (14.8 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (77%, 1.96 g, 8.62 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give **13** as a yellow oil that was used without purification.

Step 2: K_2CO_3 (7.43 g, 53.9 mmol) was added to a solution of **13** in MeOH (100 mL), and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (50 mL) was added, and the residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography on neutral alumina (gradient elution, 0 → 10% MeOH in CH_2Cl_2) gave **17** as a white solid (1.11 g, 94%, 95:5 dr).[4a] mp 150−151 °C; δ_H (400 MHz, MeOH-d_4) 1.45−1.90 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 3.25−3.39 (1H, m, C(3)H), 3.83−4.04 (2H, m, C(1)H, C(2)H), 4.05−4.15 (2H, m, NCH_2Ph), 7.31−7.42 (3H, m, *Ph*), 7.44−7.51 (2H, m, *Ph*).

(*RS*,*RS*,*RS*)-3-(*N*-Benzyl-*N*-methylamino)cyclohexane-1,2-diol 18. Step 1: Cl_3CCO_2H (1.62 g, 9.93 mmol) was added to a solution of **10** (400 mg, 1.99 mmol) in CH_2Cl_2 (4 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (69%, 796 mg, 3.18 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give **14** as a pale yellow solid that was used without purification. Recrystallization of an aliquot from 40−60 °C petrol/Et_2O (15:1) gave an analytical sample. $C_{16}H_{20}Cl_3NO_3$ requires C, 50.5; H, 5.3; N, 3.7%; found C, 50.4; H, 5.4; N, 3.6%; mp 92−95 °C; ν_{max} (KBr) 3395 (O−H), 3086, 3063, 3029, 2946 (C−H), 1764 (C═O); δ_H (400 MHz, $CDCl_3$) 1.51−2.00 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.24 (3H, s, N*Me*), 2.61−2.73 (1H, m, C(3)H), 3.50−3.80 (1H, br s, OH) overlapping 3.62 (1H, d, *J* 13.4, NCH_AH_BPh) and 3.70 (1H, d, *J* 13.4, NCH$_A$H$_B$Ph), 4.11−4.16 (1H, m, C(2)H), 5.31−5.35 (1H, m, C(1)H), 7.24−7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.1, 23.7, 23.8 (*C*(4), *C*(5), *C*(6)), 38.5 (N*Me*), 58.2 (NCH$_2$Ph), 60.4 (*C*(3)), 65.4 (*C*(2)), 77.2 (*C*(1)), 90.1 (CCl_3), 127.2 (*p-Ph*), 128.4, 129.0 (*o,m-Ph*), 138.5 (*i-Ph*), 160.9 (OCOCCl$_3$); *m/z* (ESI$^+$) 380 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{21}Cl_3NO_3^+$ ([M + H]$^+$) requires 380.0582; found 380.0571.

Step 2: K_2CO_3 (2.75 g, 19.9 mmol) was added to a solution of **14** in MeOH (7 mL), and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (50 mL) was added, and the residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 6 → 60% MeOH in EtOAc) gave **18** as a pale yellow oil (316 mg, 67%, >99:1 dr). $C_{14}H_{21}NO_2$ requires C, 71.5; H, 9.0; N, 5.95%; found C, 71.6; H, 9.0; N, 5.9%; ν_{max} (film) 3394 (O−H), 2938 (C−H); δ_H (400 MHz, $CDCl_3$) 1.51−1.92 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.20 (3H, s, N*Me*), 2.72 (1H, ddd, *J* 9.9, 4.7, 3.4, C(3)H), 3.60 (2H, AB system, *J* 13.3, NCH_2Ph), 3.95 (1H, app t, *J* 3.4, C(2)H), 4.12−4.18 (1H, m, C(1)H), 7.23−7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.0, 24.2, 27.5 (*C*(4), *C*(5), *C*(6)), 38.5 (N*Me*), 58.5 (NCH$_2$Ph), 60.6 (*C*(3)), 69.2, 69.4 (*C*(1), *C*(2)), 127.1 (*p-Ph*), 128.4, 128.9 (*o,m-Ph*), 139.2 (*i-Ph*); *m/z* (ESI$^+$) 236 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{14}H_{22}NO_2^+$ ([M + H]$^+$) requires 236.1645; found 236.1636.

(*RS*,*RS*,*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)cyclohexane-1,2-diol 19. From **11**, Step 1: Cl_3CCO_2H (817 mg, 5.00 mmol) was added to a solution of **11** (230 mg, 1.00 mmol) in CH_2Cl_2 (3.5 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (70%, 394 mg, 1.60 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give **15** as a pale yellow oil that was used without purification.

Step 2: K_2CO_3 (1.38 g, 10.0 mmol) was added to a solution of **15** in MeOH (7 mL), and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (50 mL) was added, and the residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution,

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50 → 100% EtOAc in 30−40 °C petrol) gave **19** as a pale yellow oil (185 mg, 70%, >99:1 dr). ν_{max} (film) 3416 (O−H), 3084, 3061, 2962 (C−H); δ_H (400 MHz, $CDCl_3$) 1.07 (3H, d, *J* 6.7, NCHMe_A), 1.09 (3H, d, *J* 6.7, NCHMe_B), 1.45−1.50 (1H, m, C(6)H_A), 1.54−1.70 (4H, m, C(4)H_2, C(5)H_2), 1.65−1.77 (1H, m, C(6)H_B), 3.05−3.10 (1H, m, C(3)*H*), 3.18 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.58−3.60 (1H, m, C(2)*H*), 3.62 (1H, d, *J* 15.4, NCH_AH_BPh), 3.86 (1H, d, *J* 15.4, NCH$_A$$H_B$Ph), 3.90−3.99 (1H, m, C(1)*H*), 7.23−7.33 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.0 (NCH*Me*$_2$), 20.0, 25.4, 28.2 (*C*(4), *C*(5), *C*(6)), 48.7 (NCHMe$_2$), 50.7 (NCH$_2$Ph), 57.2 (*C*(3)), 70.3 (*C*(1)), 71.5 (*C*(2)), 126.7 (*p-Ph*), 127.5, 128.5 (*o,m-Ph*), 142.4 (*i-Ph*); *m/z* (ESI$^+$) 264 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{26}NO_2^+$ ([M + H]$^+$) requires 264.1958; found 264.1950.

From **17**: NaB(OAc)$_3$H (251 mg, 3.95 mmol) was added to a stirred solution of **17** (207 mg, 0.79 mmol, 95:5 dr) and AcOH (45 μL, 0.79 mmol) in acetone (3 mL) at rt. The resultant mixture was stirred at rt for 24 h before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), and the resultant solution was washed sequentially with satd aq $NaHCO_3$ (3 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 40 → 80% EtOAc in 30−40 °C petrol) gave **19** as a pale yellow oil (112 mg, 52%, 95:5 dr).

(*RS*,*RS*,*RS*)-3-(*N*,*N*-Dibenzylamino)cyclohexane-1,2-diol 20. Step 1: Cl_3CCO_2H (29.5 g, 181 mmol) was added to a solution of **12** (10.0 g, 36.0 mmol) in CH_2Cl_2 (120 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (77%, 12.9 g, 57.6 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 200 mL) and brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo to give **16** as a yellow oil that was used without purification.

Step 2: K_2CO_3 (10.0 g, 72.4 mmol) was added to a solution of **16** in MeOH (500 mL), and the resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (100 mL) was added, and the residue was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with brine (150 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 100% EtOAc in 30−40 °C petrol) gave **20** as a pale yellow oil (11.4 g, quant, 95:5 dr).[4a] δ_H (400 MHz, $CDCl_3$) 1.43−1.89 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.14 (1H, br s, O*H*), 3.10−3.20 (1H, m, C(3)*H*), 3.69−3.78 (2H, d, *J* 14.4, N(CH_AH_BPh)$_2$), 3.81−3.91 (3H, m, C(2)*H*, N(CH$_A$$H_B$Ph)$_2$), 3.99−4.06 (1H, m, C(1)*H*), 7.22−7.38 (10H, m, *Ph*).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)-cyclohexane 23. Step 1: Anhydrous TsOH (7.69 g, 44.7 mmol) was added to a stirred solution of **10** (3.00 g, 14.9 mmol) in CH_2Cl_2 (30 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (69%, 5.60 g, 22.4 mmol) was added, and the mixture was stirred at rt for 21 h. The reaction mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and then basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The resultant mixture was extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic layers were washed sequentially with 0.1 M aq $NaHCO_3$ (6 × 100 mL) and brine (125 mL), dried ($MgSO_4$), and concentrated in vacuo to give **21** as a green solid (5.22 g) that was used without purification. Recrystallization of an aliquot from 40−60 °C petrol/Et_2O (10:1) gave an analytical sample. $C_{21}H_{27}NO_4S$ requires C, 64.75; H, 7.0; N, 3.6%; found C, 64.8; H, 7.0; N, 3.7%; mp 75−83 °C; ν_{max} (film) 3406 (O−H), 3062, 3029, 2947, 2869, 2797 (C−H); δ_H (400 MHz, $CDCl_3$) 1.37−1.83 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.14 (3H, s, N*Me*), 2.42 (3H, s, Ar*Me*), 2.61 (1H, ddd, *J* 11.9, 4.3, 2.8, C(3)*H*), 3.30−3.60 (1H, br s, O*H*) overlapping 3.48 (1H, d, *J* 13.4, NCH_AH_BPh), 3.60 (1H, d, *J* 13.4, NCH$_A$$H_B$Ph), 3.43−4.00 (1H, m, C(2)*H*), 4.76−4.83 (1H, m, C(1)*H*), 7.17−7.39 (7H, m, *Ar*, *Ph*), 7.79−7.84 (2H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 18.6, 21.6, 23.6, 24.7 (*C*(4), *C*(5), *C*(6), Ar*Me*), 38.2 (N*Me*), 58.1 (NCH$_2$Ph), 60.2 (*C*(3)), 65.8 (*C*(2)), 79.7 (*C*(1)), 127.2 (*p-Ph*), 127.8, 128.4, 128.8, 129.9 (*Ar*, *o,m-Ph*), 133.9, 138.7, 144.8 (*Ar*, *i-Ph*); *m/z* (ESI$^+$) 390 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{21}H_{27}NO_4S^+$ ([M + H]$^+$) requires 390.1734; found 390.1730.

Step 2: DBU (2.67 mL, 17.9 mmol) was added to a stirred solution of **21** (5.22 g) in CH_2Cl_2 (25 mL), and the resultant mixture was stirred at rt for 24 h. The mixture was diluted with H_2O (100 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 175 mL). The combined organic layers were washed sequentially with H_2O (3 × 200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Filtration through a pad of silica (eluent EtOAc/40−60 °C petrol, 7:3) gave **23** as a pale yellow oil (2.56 g, 79%, >99:1 dr). $C_{14}H_{19}NO$ requires C, 77.4; H, 8.8; N, 6.45%; found C, 77.5; H, 8.8; N, 6.4%; ν_{max} (film) 3086, 3064, 3026, 2985, 2938, 2861, 2784 (C−H); δ_H (400 MHz, $CDCl_3$) 1.17−1.32, 1.46−1.92 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.36 (3H, s, N*Me*), 3.00 (1H, ddd, *J* 10.9, 4.6, 1.3, C(3)*H*), 3.13 (1H, app t, *J* 4.3, C(1)*H*), 3.32 (1H, app d, *J* 4.6, C(2)*H*), 3.66 (1H, d, *J* 13.4, NCH_AH_BPh), 3.80 (1H, d, *J* 13.4, NCH$_A$$H_B$Ph), 7.20−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.9, 21.5, 23.1 (*C*(4), *C*(5), *C*(6)), 38.9 (N*Me*), 51.7 (*C*(1)), 54.6 (*C*(2)), 58.5 (NCH$_2$Ph), 60.5 (*C*(3)), 126.8 (*p-Ph*), 128.2, 128.8 (*o,m-Ph*), 140.0 (*i-Ph*); *m/z* (ESI$^+$) 218 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{14}H_{20}NO^+$ ([M + H]$^+$) requires 218.1539; found 218.1537.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-cyclohexane 24. Step 1: Anhydrous TsOH (675 mg, 3.92 mmol) was added to a stirred solution of **11** (300 mg, 1.31 mmol) in CH_2Cl_2 (2.6 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (77%, 437 mg, 1.96 mmol) was added, and the mixture was stirred at rt for 21 h. The reaction mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and then basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic extracts were washed sequentially with 0.1 M aq $NaHCO_3$ (3 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo to give **22** as a pale yellow oil that was used without purification.

Step 2: DBU (0.24 mL, 1.6 mmol) was added to a stirred solution of **22** in CH_2Cl_2 (2.2 mL), and the resultant mixture was stirred at rt for 24 h. The mixture was diluted with H_2O (100 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed sequentially with H_2O (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 15:1) gave **24** as a colorless oil (284 mg, 88%, >99:1 dr). ν_{max} (film) 2961 (C−H), 1494, 1453 (C═C); δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.7, NCHMe_A), 1.10 (3H, d, *J* 6.7, NCHMe_B), 1.10−1.84 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.98−3.05 (1H, m, C(3)*H*), 3.09 (1H, app t, *J* 4.4, C(1)*H*), 3.18−3.27 (2H, m, C(2)*H*, NC*H*Me$_2$), 3.84 (2H, AB system, *J* 14.7, NCH_2Ph), 7.18−7.43 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.9 (NCH*Me*$_2$), 22.1, 23.0, 23.1 (*C*(4), *C*(5), *C*(6)), 48.1 (NCHMe$_2$), 49.8 (NCH$_2$Ph), 52.2, 55.0, 56.3 (*C*(1), *C*(2), *C*(3)), 126.3 (*p-Ph*), 128.0, 128.1 (*o,m-Ph*), 142.4 (*i-Ph*); *m/z* (ESI$^+$) 246 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{24}NO^+$ ([M + H]$^+$) requires 246.1852; found 246.1850.

(*RS*,*RS*,*RS*)-1-Acetoxy-3-(*N*-benzyl-*N*-methylamino)-cyclohexan-2-ol 25. A stirred solution of **23** (12.2 g, 56.1 mmol) in AcOH (35 mL) was heated at 50 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (300 mL). The solution was basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (3 × 500 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 400 mL), washed sequentially with 0.1 M aq $NaHCO_3$ (3 × 400 mL) and brine (400 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via recrystallization from 40−60 °C petrol/Et_2O (9:1) gave **25** as a pale yellow solid (13.7 g, 89%, >99:1 dr); $C_{16}H_{23}NO_3$ requires C, 69.3; H, 8.4; N, 5.05%; found C, 69.3; H, 8.3; N, 5.1%; mp 89−91 °C; ν_{max} (KBr) 3458 (O−H), 3028, 2943, 2867, 2795 (C−H), 1735 (C═O); δ_H (400 MHz, $CDCl_3$) 1.46−1.90 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.08 (3H, s, CO*Me*), 2.20 (3H, s, N*Me*), 2.51−2.64 (1H, m, C(3)*H*), 3.43 (1H, br s, O*H*), 3.60 (2H, AB system, *J* 13.4, NCH_2Ph), 3.97−4.05 (1H, m, C(2)*H*), 5.15−5.23 (1H,

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m, C(1)*H*), 7.20−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3, 21.3, 23.9, 24.3 (*C*(4), *C*(5), *C*(6), CO*Me*), 38.5 (N*Me*), 58.2 (NCH_2Ph), 60.8 (*C*(3)), 66.1 (*C*(2)), 71.6 (*C*(1)), 127.0 (*p-Ph*), 128.3, 128.9 (*o,m-Ph*), 139.1 (*i-Ph*), 170.1 (COMe); *m/z* (ESI^+) 278 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{16}H_{24}NO_3^+$ ($[M + H]^+$) requires 278.1751; found 278.1757.

(*RS*,*RS*,*RS*)-1-Acetoxy-3-(*N*-benzyl-*N*-isopropylamino)-cyclohexan-2-ol 26. A stirred solution of **24** (326 mg, 1.33 mmol) in AcOH (0.83 mL) was heated at 50 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (10 mL). The solution was basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 10 mL), washed sequentially with 0.1 M aq $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give **26** as a colorless oil (355 mg, 88%, >95:5 dr). ν_{max} (film) 3411 (O−H), 2931 (C−H), 1732 (C═O); δ_H (400 MHz, $CDCl_3$) 1.07 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.10 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.46−1.70 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.06 (3H, s, CO*Me*), 2.90−2.94 (1H, m, C(3)*H*), 3.23 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.70−3.72 (1H, m, C(2)*H*), 3.78 (2H, AB system, *J* 13.4, NCH_2Ph), 5.00−5.13 (1H, m, C(1)*H*), 7.14−7.30 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.7, 19.3 (CH*Me*$_2$), 20.0, 21.3, 24.6, 24.7 (*C*(4), *C*(5), *C*(6), CO*Me*), 48.8 (NCHMe$_2$), 50.1 (NCH_2Ph), 58.2 (*C*(3)), 68.4 (*C*(2)), 72.2 (C(1)), 126.5 (*p-Ph*), 127.3, 128.5 (*o,m-Ph*), 142.9 (*i-Ph*), 170.1 (COMe); *m/z* (ESI^+) 306 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{18}H_{28}NO_3^+$ ($[M + H]^+$) requires 306.2064; found 306.2064.

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)-cyclohexane 29. Step 1: MsCl (5.70 mL, 73.9 mmol) was added to a stirred solution of **25** (13.7 g, 49.3 mmol) and Et_3N (23 mL, 165 mmol) in CH_2Cl_2 (270 mL) at 0 °C, and the resultant solution was stirred at 0 °C for 1 h. The reaction mixture was then allowed to warm to rt and washed with H_2O (350 mL). The aqueous layer was extracted with CH_2Cl_2 (350 mL). The combined organic extracts were washed sequentially with 10% aq $CuSO_4$ (3 × 500 mL) and brine (500 mL), dried ($MgSO_4$), and concentrated in vacuo to give **27** as a brown oil (17.3 g) that was used without purification. δ_H (400 MHz, $CDCl_3$) 1.46−1.84 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 1.93 (3H, s, CO*Me*), 2.36 (3H, s, N*Me*), 2.82−2.90 (1H, m, C(3)*H*), 3.13 (3H, s, OSO_2Me), 3.70 (2H, AB system, *J* 13.4, NCH_2Ph), 4.81−4.85 (1H, m, C(2)*H*), 5.12−5.18 (1H, m, C(1)*H*), 7.22−7.38 (5H, m, *Ph*).

Step 2: K_2CO_3 (18 g, 130 mmol) was added to a stirred solution of **27** (17.3 g) in MeOH (400 mL). The resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (400 mL) was added, and the mixture was extracted with CH_2Cl_2 (4 × 400 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 700 mL), washed sequentially with H_2O (2 × 500 mL) and brine (500 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 60% EtOAc in 40−60 °C petrol) gave **29** as a pale yellow oil (7.98 g, 67%, >99:1 dr). $C_{14}H_{19}NO$ requires C, 77.4; H, 8.8; N, 6.45%; found C, 77.4; H, 8.8; N, 6.4%; ν_{max} (film) 3062, 3027, 2978, 2843, 2792 (C−H); δ_H (400 MHz, $CDCl_3$) 1.18−1.36, 1.43−1.52, 1.61−1.76, 2.06−2.15 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.30 (3H, s, N*Me*), 2.89−2.97 (1H, m, C(3)*H*), 3.19−3.26 (2H, m, C(1)*H*, C(2)*H*), 3.69 (2H, AB system, *J* 13.3, NCH_2Ph), 7.23−7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.1, 22.1, 25.0 (*C*(4), *C*(5), *C*(6)), 38.3 (N*Me*), 53.2, 55.3 (C(1), C(2)), 58.4 (NCH_2Ph), 58.4 (C(3)), 127.0 (*p-Ph*), 128.3, 128.7 (*o,m-Ph*), 139.5 (*i-Ph*); *m/z* (ESI^+) 218 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{14}H_{20}NO^+$ ($[M + H]^+$) requires 218.1539; found 218.1541.

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-cyclohexane 30. Step 1: MsCl (0.13 mL, 1.65 mmol) was added to a stirred solution of **26** (336 mg, 1.10 mmol) and Et_3N (0.51 mL, 3.69 mmol) in CH_2Cl_2 (6.0 mL) at 0 °C, and the resultant solution was stirred at 0 °C for 1 h. The reaction mixture was then allowed to warm to rt and washed with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic extracts were washed sequentially with 10% aq $CuSO_4$ (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo to give **28** as a colorless oil (448 mg) that was used without purification. δ_H (400 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.10 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.66−1.98 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 1.93 (3H, s, CO*Me*), 2.82−2.90 (1H, m, C(3)*H*), 2.91 (3H, s, OSO_2Me), 3.00−3.15 (1H, m, NC*H*Me$_2$), 3.80 (2H, AB system, *J* 13.4, NCH_2Ph), 4.56−4.66 (1H, m, C(2)*H*), 5.22−5.28 (1H, m, C(1)*H*), 7.22−7.38 (5H, m, *Ph*).

Step 2: K_2CO_3 (402 mg, 2.91 mmol) was added to a stirred solution of **28** (448 mg) in MeOH (8.9 mL). The resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 15 mL), washed sequentially with H_2O (2 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 9:1) gave **30** as a colorless oil (174 mg, 65%, >99:1 dr). ν_{max} (film) 2935 (C−H), 1493, 1463 (C═C); δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.11 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.20−1.48 (4H, m, C(4)H_A, C(5)H_2, C(6)H_A), 1.58−1.75 (2H, m, C(4)H_B, C(6)H_B), 2.05−2.09 (1H, m, C(3)*H*), 3.02 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.12−3.15 (1H, m C(1)*H*), 3.18−3.21 (1H, m, C(2)*H*), 3.83 (2H, AB system, *J* 15.6, NCH_2Ph), 7.21−7.42 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.5, 20.7, 21.1, 24.9, 26.8 (*C*(4), *C*(5), *C*(6), NCH*Me*$_2$), 49.8 (NCHMe$_2$), 50.9 (NCH_2Ph), 52.7, 53.4, 56.7 (*C*(1), *C*(2), (C(3)), 126.5 (*p-Ph*), 127.7, 128.1 (*o,m-Ph*), 142.1 (*i-Ph*); *m/z* (ESI^+) 246 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{16}H_{24}NO^+$ ($[M + H]^+$) requires 246.1852; found 246.1845.

(1*RS*,2*RS*,3*SR*)-3-(*N*-Benzyl-*N*-methylamino)cyclohexane-1,2-diol 31. A solution of **29** (1.00 g, 4.60 mmol) in 1,4-dioxane (18 mL) and 3 M aq H_2SO_4 (6 mL) was stirred at 40 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (100 mL) and washed with satd aq $NaHCO_3$ (180 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 80 mL), and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (3 × 250 mL) and brine (250 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 12 → 100% Et_2O in 40−60 °C petrol) gave **31** as a pale yellow oil (668 mg, 62%, >99:1 dr). $C_{14}H_{21}NO_2$ requires C, 71.5; H, 9.0; N, 5.95%; found C, 71.5; H, 8.9; N, 5.9%; ν_{max} (film) 3418 (O−H), 2932, 2861, 2799 (C−H); δ_H (400 MHz, $CDCl_3$) 1.08−1.96 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.11 (3H, s, N*Me*), 2.29−2.45 (1H, m, C(3)*H*), 3.30 (1H, dd, *J* 10.1, 8.3, C(2)*H*), 3.39 (1H, d, *J* 13.0, NCH_AH$_B$Ph), 3.49 (1H, ddd, *J* 10.8, 8.3, 4.6, C(1)*H*), 3.65 (1H, d, *J* 13.0, NCH$_A$$H_B$Ph), 4.00−4.40 (2H, br s, O*H*), 7.12−7.32 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.1, 21.7, 31.8 (*C*(4), *C*(5), *C*(6)), 36.4 (N*Me*), 58.2 (NCH_2Ph), 66.1 (*C*(3)), 74.1 (*C*(1)), 75.1 (*C*(2)), 127.1 (*p-Ph*), 128.4, 128.8 (*o,m-Ph*), 139.0 (*i-Ph*); *m/z* (ESI^+) 236 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{14}H_{22}NO_2^+$ ($[M + H]^+$) requires 236.1645; found 236.1652.

(1*RS*,2*RS*,3*SR*)-3-(*N*-Benzyl-*N*-isopropylamino)cyclohexane-1,2-diol 32. A solution of **30** (101 mg, 0.41 mmol) in 1,4-dioxane (1.6 mL) and 3 M aq H_2SO_4 (0.54 mL) was stirred at 40 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (10 mL) and washed with satd aq $NaHCO_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (3 × 20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 8:2) gave **32** as a colorless oil (84.1 mg, 94%, >99:1 dr). ν_{max} (film) 3419 (O−H), 2936 (C−H); δ_H (400 MHz, $CDCl_3$) 1.10 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.11 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.25−1.96 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.41−2.47 (1H, m, C(3)*H*), 3.07 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.16 (1H, app t, *J* 9.7, C(2)*H*), 3.44−3.49 (1H, m, C(1)*H*), 3.50 (1H, d, *J* 13.0, NCH_AH$_B$Ph), 3.80 (1H, d, *J* 13.0, NCH$_A$$H_B$Ph), 7.21−7.38 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.0, 21.9, 22.7, 29.7, 31.5 (*C*(4), *C*(5), *C*(6), NCH*Me*$_2$), 48.1 (NCHMe$_2$), 49.3 (NCH_2Ph), 59.6 (*C*(3)), 74.6, 74.8 (*C*(1), *C*(2)), 127.1 (*p-Ph*), 128.4, 128.6 (*o,m-Ph*), 140.2 (*i-Ph*); *m/z* (ESI^+) 549 ($[2M + Na]^+$, 100%), 264 ($[M + H]^+$, 94%); HRMS (ESI^+) $C_{16}H_{26}NO_2^+$ ($[M + H]^+$) requires 264.1958; found 264.1958.

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(*RS*)-3-(*N,N*-Dibenzyl-ammonium)cyclohex-1-ene trichloroacetate 33. Cl_3CCO_2H (196 mg, 1.20 mmol) was added to a solution of **12** (66 mg, 0.24 mmol) in $CDCl_3$ (0.8 mL); δ_H (400 MHz, $CDCl_3$) 1.59−2.26 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 4.20 (1H, dd, *J* 13.4, 6.6, NCH_AH_BPh), 4.25−4.28 (1H, m, C(3)*H*), 4.32 (1H, dd, *J* 13.4, 5.6, NCH_AH_BPh), 4.40 (1H, dd, *J* 13.4, 6.1, NCH$_A$$H_B$Ph), 4.49 (1H, dd, *J* 13.4, 4.3, NCH$_A$$H_B$Ph), 5.85 (1H, app d, *J* 10.4, C(1)*H*), 6.21−6.33 (1H, m, C(2)*H*), 7.35−7.43 (10H, m, *Ph*), 8.45 (1H, br s, N*H*); δ_C (100 MHz, $CDCl_3$) 20.4, 22.6, 22.4 (*C*(4), *C*(5), *C*(6)), 55.0, 55.2 (NCH_2Ph), 60.2 (*C*(3)), 120.2 (*C*(1)), 128.6, 128.6 (*i-Ph*), 128.7, 129.6, 130.3, 130.5, 130.7 (*o,m,p-Ph*), 137.6 (*C*(2)).

(*RS*)-3-(*N*-Benzyl-*N*-isopropylammonium)cyclohex-1-ene trichloroacetate 36. Cl_3CCO_2H (196 mg, 1.20 mmol) was added to a solution of **11** (55 mg, 0.24 mmol) in $CDCl_3$ (0.8 mL). δ_H (400 MHz, $CDCl_3$) 1.45−1.52 (6H, m, CH*Me*$_2$), 1.62−2.29 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 3.85−3.89 (1H, m, NC*H*Me$_2$), 4.23−4.38 (2H, m, C(3)*H*, NCH_AH_BPh), 4.41−4.45 (1H, m, NCH$_A$$H_B$Ph), 5.77 (0.5H, app d, *J* 10.4, C(1)*H*), 5.90 (0.5H, app d, *J* 10.1, C(1)*H*), 6.21−6.24 (1H, m, C(2)*H*), 7.40−7.49 (5H, m, *Ph*), 7.60 (0.5H, m, N*H*), 7.68 (0.5H, m, N*H*); δ_C (100 MHz, $CDCl_3$) 18.7, 18.8, 18.9 (NCH*Me*$_2$), 19.6, 20.5, 23.7, 24.3, 24.4, 25.3 (*C*(4), *C*(5), *C*(6)), 51.2, 52.0 (NCH_2Ph), 56.3, 56.7 (NCH*Me*$_2$), 59.7, 60.5 (*C*(3)), 120.4, 120.7 (*C*(1)), 129.6, 129.7 (*i-Ph*), 129.7, 129.8, 130.1, 130.3, 130.4 (*o,m,p-Ph*), 136.9, 137.5 (*C*(2)).

(*RS*)-3-(*N*-Benzyl-*N*-methylammonium)cyclohex-1-ene trichloroacetate 39. Cl_3CCO_2H (196 mg, 1.20 mmol) was added to a solution of **10** (48 mg, 0.24 mmol) in $CDCl_3$ (0.8 mL). δ_H (400 MHz, $CDCl_3$) 1.65−2.22 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.77 (1.5H, d, *J* 5.1, N*Me*), 2.80 (1.5H, d, *J* 5.1, N*Me*), 4.14 (0.5H, dd, *J* 12.9, 7.5, NCH_ACH_BPh), 4.21 (1H, dd, *J* 13.0, 7.2, NCH_ACH_BPh), 4.23−4.30 (1H, m, C(3)*H*), 4.46 (0.5H, dd, *J* 13.0, 4.6, NCH$_A$CH_BPh), 4.50 (0.5H, dd, *J* 12.9, 4.1, NCH$_A$CH_BPh), 5.73 (0.5H, app d, *J* 10.4, C(1)*H*), 5.80 (0.5H, app d, *J* 10.4, C(1)*H*), 6.21−6.24 (0.5H, m, C(2)*H*), 6.30−6.33 (0.5H, m, C(2)*H*), 7.35−7.46 (5H, m, *Ph*), 8.68 (0.5H, br s, N*H*), 8.80 (0.5H, br s, N*H*); δ_C (100 MHz, $CDCl_3$) 20.1, 20.2, 21.1, 23.4, 24.4, 24.5 (*C*(4), *C*(5), *C*(6)), 35.3, 36.3 (N*Me*), 57.5, 57.8 (NCH_2Ph), 61.2, 61.4 (*C*(3)), 118.6, 120.9 (*C*(1)), 128.4, 128.6 (*i-Ph*), 129.7, 130.4, 130.5, 130.6 (*o,m,p-Ph*), 137.0, 138.3 (*C*(2)).

(*RS*)-3-(*N*-Benzylamino)methylcyclohex-1-ene 46. A stirred mixture of **45** (1.00 g, 5.71 mmol), benzylamine (5 mL, 45.7 mmol), and NaI (85 mg, 0.57 mmol) was heated at 50 °C for 20 h. The reaction mixture was cooled to rt and diluted with EtOAc (100 mL). The mixture was washed with 1 M aq NaOH (100 mL), and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 85:15) gave **46** as a yellow oil (700 mg, 61%).[35] δ_H (400 MHz, $CDCl_3$) 1.32−1.37 (1H, m, C(6)H_A), 1.52−1.58 (1H, m, C(5)H_A), 1.71−1.79 (1H, m, C(5)H_B), 1.80−1.86 (1H, m, C(6)H_B), 1.97−2.03 (2H, m, C(4)H_2), 2.30−2.36 (1H, m, C(3)*H*), 2.53−2.63 (2H, m, C(3)CH_2N), 3.79−3.86 (2H, m, NCH_2Ph), 5.60−5.63 (1H, m, C*H*═CH), 5.72−5.76 (1H, m, CH═C*H*), 7.25−7.35 (5H, m, *Ph*).

(*RS*)-3-(*N*-Benzyl-*N*-methylamino)methylcyclohex-1-ene 47. K_2CO_3 (943 mg, 6.84 mmol) and *N*-benzyl-*N*-methylamine (1.84 mL, 14.3 mmol) were added to a stirred solution of **45** (1.00 g, 5.71 mmol) in MeCN (3 mL) at rt, and the resultant solution was heated at 60 °C for 20 h before being allowed to cool to rt and concentrated in vacuo. The residue was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (2 × 40 mL) and brine (40 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 95:5) gave **47** as a pale yellow oil (768 mg, 64%). ν_{max} (film) 3085, 3062, 2960, 2927 (C−H), 1452 (C═C); δ_H (400 MHz, $CDCl_3$) 1.32−1.36 (1H, m, C(4)H_A), 1.55−1.65 (1H, m, C(5)H_A), 1.70−1.76 (1H, m, C(5)H_B), 1.81−1.96 (1H, m, C(4)H_B), 2.02−2.07 (2H, m, C(6)H_2), 2.23 (3H, s, N*Me*), 2.31−2.40 (2H, m, C(3)CH_2N), 2.39−2.41 (1H, m, C(3)*H*), 3.51 (2H, AB system, *J* 13.4, NCH_2Ph), 5.75−5.80 (2H, m, C(1)*H*, C(2)*H*), 7.26−7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.2 (C(5)), 25.6 (*C*(6)), 27.5 (*C*(4)), 33.5 (*C*(3)), 42.6 (N*Me*), 62.7 (C(3)CH_2N), 63.4 (NCH_2Ph), 126.8 (*p-Ph*), 127.5, 128.1 (*o,m-Ph*), 128.9, 130.3 (*C*(1), *C*(2)), 139.6 (*i-Ph*); *m*/*z* (ESI$^+$) 216 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}N^+$ ([M + H]$^+$) requires 216.1747; found 216.1744.

(*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)methylcyclohex-1-ene 48. $NaB(OAc)_3H$ (1.06 g, 5.00 mmol) was added to a stirred solution of **46** (201 mg, 1.00 mmol) and AcOH (57 μL, 1.00 mmol) in acetone (5 mL) at rt. The resultant mixture was stirred at rt for 24 h before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), and the resultant solution was washed sequentially with satd aq $NaHCO_3$ (3 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 98:2) gave **48** as a pale yellow oil (189 mg, 78%). ν_{max} (film) 3084, 3061, 2963, 2926 (C−H), 1493 (C═C); δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.6, NCH*Me*$_A$), 1.11 (3H, d, *J* 6.6, NCH*Me*$_B$), 1.25−1.33 (1H, m, C(4)H_A), 1.45−1.60 (1H, m, C(5)H_A), 1.67−1.70 (1H, m, C(5)H_B), 1.80−1.83 (1H, m, C(4)H_B), 1.98−2.03 (2H, m, C(6)H_2), 2.22−2.29 (1H, m, C(3)*H*), 2.29−2.38 (2H, m, C(3)CH_2N), 2.93 (1H, septet, *J* 6.6, NC*H*Me$_2$), 3.60 (2H, AB system, *J* 14.4, NCH_2Ph), 5.73−5.75 (2H, m, C(1)*H*, C(2)*H*), 7.23−7.42 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.0, 18.1 (NCH*Me*$_2$), 21.2 (*C*(5)), 25.7 (*C*(6)), 27.4 (*C*(4)), 34.0 (*C*(3)), 49.0 (NCHMe$_2$), 54.6 (C(3)CH_2N), 54.7 (NCH_2Ph), 126.4 (*p-Ph*), 127.2, 128.0 (*o,m-Ph*), 128.4, 130.7 (*C*(1)), (*C*(2)), 141.6 (*i-Ph*); *m*/*z* (ESI$^+$) 244 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{26}N^+$ ([M + H]$^+$) requires 244.2060; found 244.2055.

(*RS*)-3-(*N,N*-Dibenzylamino)methylcyclohex-1-ene 49. $^iPr_2NEt$ (1.1 mL, 6.26 mmol) and BnBr (0.74 mL, 6.26 mmol) were added sequentially to a stirred solution of **46** (840 mg, 4.17 mmol) in CH_2Cl_2 (10 mL) at rt. The resultant solution was heated to 40 °C for 2 h and allowed to cool to rt. The reaction mixture was diluted with 2 M aq KOH (20 mL) and extracted with Et_2O (2 × 20 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 98:2) gave **49** as a colorless oil (1.05 g, 87%).[4c] δ_H (400 MHz, $CDCl_3$) 1.28−1.35 (1H, m, C(6)H_A), 1.48−1.61 (2H, m, C(5)H_2), 1.86−1.90 (1H, m, C(6)H_B), 1.93−1.99 (2H, m, C(4)H_2), 2.32−2.37 (2H, m, C(3)CH_2N), 2.40−2.45 (1H, m, C(3)*H*), 3.51 (2H, d, *J* 13.6, N(C$H_A$$H_B$Ph)$_2$), 3.68 (2H, d, *J* 13.6, N(CH$_A$$H_B$Ph)$_2$), 5.69−5.74 (2H, m, C(1)*H*, C(2)*H*), 7.24−7.43 (10H, m, *Ph*).

(1*RS*,2*RS*,3*SR*)-3-(*N*-Benzylamino)methylcyclohexane-1,2-diol 50. Cl_3CCO_2H (486 mg, 2.98 mmol) was added to a solution of **46** (150 mg, 0.75 mmol) in CH_2Cl_2 (2.1 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 486 mg, 2.98 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present. MeOH (15 mL) and K_2CO_3 (1.02 g, 7.4 mmol) were then added, and the resultant suspension was stirred at rt for 16 h before being concentrated in vacuo. H_2O (50 mL) was then added, and the mixture was extracted with CH_2Cl_2 (4 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 50 → 100% EtOAc in 30−40 °C petrol) gave **50** as a yellow oil (124 mg, 71%, ∼95% purity, 95:5 dr).[4c] δ_H (500 MHz, $CDCl_3$) 1.22−1.40 (2H, m, C(4)H_A, C(5)H_A), 1.47−1.50 (1H, m, C(6)H_A), 1.55−1.57 (2H, m, C(5)H_B, C(6)H_B), 1.95−1.98 (1H, m, C(4)H_B), 2.23−2.27 (1H, m, C(1)*H*), 2.75 (1H, dd, *J* 14.5, 1.5, C(3)C$H_A$$H_B$N), 3.02 (1H, dd, *J* 14.5, 11.5, C(3)CH$_A$$H_B$N), 3.52 (1H, dd, *J* 8.2, 4.4, C(2)*H*), 3.64−3.68 (1H, m, C(3)*H*), 3.66 (1H, d, *J* 13.1, NC$H_A$$H_B$Ph), 3.81 (1H, d, *J* 13.1, NCH$_A$$H_B$Ph), 7.25−7.35 (5H, m, *Ph*).

(1*RS*,2*RS*,3*SR*)-3-(*N*-Benzyl-*N*-methylamino)-methylcyclohexane-1,2-diol 51. From **47**: Cl_3CCO_2H (817 mg, 5.00 mmol) was added to a solution of **47** (215 mg, 1.00 mmol) in CH_2Cl_2 (3.5 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (70%, 394 mg, 1.60 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present.

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MeOH (20 mL) and K_2CO_3 (1.38 g, 10.0 mmol) were then added, and the resultant suspension was stirred at rt for 16 h before being concentrated in vacuo. H_2O (50 mL) was then added, and the mixture was extracted with CH_2Cl_2 (4 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 50 → 100% EtOAc in 30−40 °C petrol) gave **51** as a pale yellow oil (190 mg, 81%, >99:1 dr). ν_{max} (film) 3405 (O−H), 3061, 2931 (C−H), 1494, 1453 (C═C); δ_H (400 MHz, $CDCl_3$) 1.19−1.27 (2H, m, C(6)H_A, C(5)H_A), 1.27−1.54 (3H, m, C(4)H_2, C(5)H_B), 1.93−1.98 (1H, m, C(6)H_B), 2.17 (1H, dd, *J* 12.6, 3.3, C(3)CH_AH$_B$N), 2.28 (3H, s, N*Me*), 2.52−2.58 (1H, m, C(3)*H*), 3.08 (1H, app t, *J* 12.6, C(3)CH$_A$$H_B$N), 3.30 (1H, d, *J* 12.9, NCH_AH$_B$Ph), 3.33−3.38 (1H, m, C(1)*H*), 3.42 (1H, dd, *J* 9.3, 4.8, C(2)*H*), 3.72 (1H, d, *J* 12.9, NCH$_A$$H_B$Ph), 7.27−7.36 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.0 (*C*(5)), 28.5 (*C*(4)), 31.9 (*C*(6)), 33.8 (*C*(3)), 42.4 (N*Me*), 58.9 (C(3)CH_2N), 62.9 (NCH_2Ph), 71.2 (*C*(1)), 78.9 (*C*(2)), 127.6, 128.4, 129.4 (*o,m,p-Ph*), 137.3 (*i-Ph*); *m/z* (ESI$^+$) 250 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{24}NO_2^+$ ([M + H]$^+$) requires 250.1802; found 250.1802.

From **50**: NaB(OAc)$_3$H (134 mg, 0.637 mmol), paraformaldehyde (20 mg, 0.67 mmol), and AcOH (15 μL, 0.212 mmol) were added to a stirred solution of **50** (50 mg, 0.212 mmol, 95:5 dr) in CH_2Cl_2 (1.0 mL) at rt, and the resultant solution was stirred for 20 h at rt before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL), and the resultant solution was washed with satd aq $NaHCO_3$ (3 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent EtOAc/30−40 °C petrol, 3:2) gave **51** as a pale yellow oil (22 mg, 42%, >99:1 dr).

(1*RS*,2*RS*,3*SR*)-3-(*N*-Benzyl-*N*-isopropylamino)-methylcyclohexane-1,2-diol 52. From **48**: Cl_3CCO_2H (187 mg, 1.13 mmol) was added to a solution of **48** (54 mg, 0.225 mmol) in CH_2Cl_2 (0.75 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (70%, 55 mg, 0.36 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present. MeOH (5 mL) and K_2CO_3 (310 mg, 2.25 mmol) were then added, and the resultant suspension was stirred at rt for 16 h before being concentrated in vacuo. H_2O (15 mL) was then added, and the mixture was extracted with CH_2Cl_2 (4 × 15 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 50 → 100% EtOAc in 30−40 °C petrol) gave **52** as a pale yellow oil (43 mg, 70%, 95:5 dr). ν_{max} (film) 3405 (O−H), 3061, 2931 (C−H), 1494, 1452 (C═C); δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.4, NCH*Me*$_A$), 1.14−1.18 (1H, m, C(6)H_A), 1.19 (3H, d, *J* 6.4, NCH*Me*$_B$), 1.25−1.30 (1H, m, C(5)H_A), 1.44−1.52 (3H, m, C(4)H_2, C(5)H_B), 1.85−1.90 (1H, m, C(6)H_B), 2.33 (1H, dd, *J* 13.2, 2.8, C(3)CH_AH$_B$N), 2.51−2.54 (1H, m, C(3)*H*), 2.99−3.14 (4H, m, C(2)*H*, C(3)CH$_A$$H_B$N, NC*H*Me$_2$, NC$H_AH_B$Ph), 3.35−3.39 (1H, m, C(1)*H*), 3.92 (1H, d, *J* 13.2, NCH$_A$$H_B$Ph), 7.30−7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.8, 20.0, 20.9 (*C*(5), NCH*Me*$_2$), 28.6 (*C*(4)), 31.8 (*C*(6)), 33.3 (*C*(3)), 48.4 (NCHMe$_2$), 50.2 (C(3)CH_2N), 53.7 (NCH_2Ph), 70.9 (*C*(2)), 78.9 (*C*(1)), 127.5 (*p-Ph*), 128.4, 129.0 (*o,m-Ph*), 138.3 (*i-Ph*); *m/z* (ESI$^+$) 278 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{28}NO_2^+$ ([M + H]$^+$) requires 278.2115; found 278.2114.

From **50**: NaB(OAc)$_3$H (91 mg, 0.43 mmol) was added to a stirred solution of **50** (50 mg, 0.215 mmol, 95:5 dr) and AcOH (15 μL, 0.212 mmol) in acetone (2 mL) at rt. The resultant mixture was stirred at rt for 24 h before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL), and the resultant solution was washed sequentially with satd aq $NaHCO_3$ (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 40 → 80% EtOAc in 30−40 °C petrol) gave **52** as a pale yellow oil (40 mg, 67%, 95:5 dr).

(1*RS*,2*RS*,3*SR*)-3-(*N*,*N*-Dibenzylamino)methylcyclohexane-1,2-diol 53. Cl_3CCO_2H (4.20 g, 25.7 mmol) was added to a solution of **49** (1.50 g, 5.15 mmol) in CH_2Cl_2 (14 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (70%, 1.90 g, 7.71 mmol) was added, and the mixture was stirred at rt for 21 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present. MeOH (80 mL) and K_2CO_3 (3.55 g, 25.7 mmol) were then added, and the resultant suspension was stirred at rt for 16 h before being concentrated in vacuo. H_2O (150 mL) was then added, and the mixture was extracted with CH_2Cl_2 (4 × 150 mL). The combined organic extracts were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via exhaustive flash column chromatography (gradient elution, 7 → 60% EtOAc in 30−40 °C petrol) gave **53** as a white solid (916 mg, 55%, >99:1 dr).[4c] δ_H (400 MHz, $CDCl_3$) 1.09−1.14 (2H, m, C(5)H_2), 1.26−1.29 (1H, m, C(6)H_A), 1.43−1.49 (2H, m, C(4)H_2), 1.71−1.78 (1H, m, C(6)H_B), 2.20−2.24 (1H, m, C(3)*H*), 2.55−2.60 (1H, br s, O*H*), 2.60−2.70 (2H, m, C(3)CH_2N), 3.07−3.15 (3H, m, C(1)*H*, N(CH_AH$_B$Ph)$_2$), 3.36−3.39 (1H, m, C(2)*H*), 4.05−4.09 (2H, m, N(CH$_A$$H_B$Ph)$_2$), 6.78−6.99 (1H, br s, O*H*), 7.27−7.42 (10H, m, *Ph*).

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)-methylcyclohexane 56. Step 1: Anhydrous TsOH (1.67 g, 9.69 mmol) was added to a stirred solution of **47** (647 mg, 3.23 mmol) in CH_2Cl_2 (6.4 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (77%, 1.08 g, 4.85 mmol) was added, and the mixture was stirred at rt for 21 h. The reaction mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and then basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The resultant mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed sequentially with 0.1 M aq $NaHCO_3$ (6 × 30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo to give **54** as a yellow oil (1.30 g) that was used without purification.

Step 2: DBU (0.58 mL, 3.89 mmol) was added to a stirred solution of **54** (1.30 g) in CH_2Cl_2 (5.4 mL), and the resultant mixture was stirred at rt for 24 h. The mixture was diluted with H_2O (10 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed sequentially with H_2O (3 × 30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo to give a 90:10 mixture of **56**:**62**. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 16:1) gave **56** as a colorless oil (379 mg, 51%, >99:1 dr). ν_{max} (film) 2935 (C−H), 1495, 1453 (C═C); δ_H (400 MHz, $CDCl_3$) 1.12−1.36 (2H, m, C(4)H_A, C(5)H_A), 1.32−1.45 (1H, m, C(4)H_B), 1.48−1.55 (1H, m, C(5)H_B), 1.72−1.89 (2H, m, C(6)H_2), 2.05−2.09 (1H, m, C(3)*H*), 2.22 (3H, s, N*Me*), 2.36 (1H, dd, *J* 12.4, 7.0, C(3)H_AH$_B$N), 2.61 (1H, dd, *J* 12.4, 7.0, C(3)CH$_A$$H_B$N), 3.20 (1H, app t, *J* 4.0, C(1)*H*), 3.26−3.28 (1H, m, C(2)*H*), 3.54 (2H, app s, NCH_2Ph), 7.20−7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.7, 23.4, 24.0 (*C*(4), *C*(5), *C*(6)), 33.5 (N*Me*), 43.6 (*C*(3)), 52.7, 54.8 (*C*(1), *C*(2)), 60.8, 62.8 (NCH_2Ph, C(3)CH_2N), 126.8 (*p-Ph*), 128.1, 128.8 (*o,m-Ph*), 139.4 (*i-Ph*); *m/z* (ESI$^+$) 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}NO^+$ ([M + H]$^+$) requires 232.1696; found 232.1696.

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-methylcyclohexane 57. Step 1: Anhydrous TsOH (615 mg, 3.57 mmol) was added to a stirred solution of **48** (290 mg, 0.51 mmol) in CH_2Cl_2 (2.36 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (77%, 398 mg, 1.79 mmol) was added, and the mixture was stirred at rt for 21 h. The reaction mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and then basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The resultant mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic layers were washed sequentially with 0.1 M aq $NaHCO_3$ (6 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo to give **55** as a yellow oil that was used without purification.

Step 2: DBU (0.21 mL, 1.41 mmol) was added to a stirred solution of **55** in CH_2Cl_2 (2.0 mL), and the resultant mixture was stirred at rt for 24 h. The mixture was diluted with H_2O (5 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed sequentially with H_2O (3 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo to give an 82:18 mixture of **57**:**63**. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 32:1) gave **57** as a colorless oil (136 mg, 44%, 96:4 dr). ν_{max} (film) 2964 (C−H), 1494, 1453 (C═C); δ_H

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(400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.04 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.08−1.56 (4H, m, C(4)H_2, C(5)H_2), 1.76−1.95 (3H, m, C(3)*H*, C(6)H_2), 2.36 (1H, dd, *J* 13.1, 6.6, C(3)CH_AH$_B$N), 2.61 (1H, dd, *J* 13.1, 8.0, C(3)CH$_A$*H*$_B$N), 2.91 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.17−3.19 (1H, m, OC*H*), 3.28−3.30 (1H, m, OC*H*), 3.64 (2H, AB system, *J* 14.6, NCH_2Ph), 7.19−7.42 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.3, 17.8 (NCH*Me*$_2$), 19.9, 23.3, 24.1 (*C*(4), *C*(5), *C*(6)), 34.3 (*C*(3)), 49.8, 52.3, 52.9, 54.9, 55.3 (*C*(1), *C*(2), C(3)*C*H$_2$N, NCH$_2$Ph, NCMe$_2$), 126.5 (*p-Ph*), 126.6, 128.1 (*o,m-Ph*), 141.4 (*i-Ph*); *m/z* (ESI$^+$) 260 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{26}NO^+$ ([M + H]$^+$) requires 260.2009; found 260.2006.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)-methylcyclohexane 62. Step 1: A stirred solution of **56** (116 mg, 0.72 mmol) in AcOH (0.45 mL) was heated at 50 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (5 mL). The solution was basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 10 mL), washed sequentially with 0.1 M aq $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give **58** as a yellow oil that was used without purification.

Step 2: MsCl (74 μL, 0.94 mmol) was added to a stirred solution of **58** and Et_3N (0.29 mL, 2.10 mmol) in CH_2Cl_2 (3.42 mL) at 0 °C, and the resultant solution was stirred at 0 °C for 1 h. The reaction mixture was then allowed to warm to rt and washed with H_2O (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed sequentially with 10% aq $CuSO_4$ (3 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo to give **60** as a yellow oil that was used without purification.

Step 3: K_2CO_3 (229 mg, 1.66 mmol) was added to a stirred solution of **60** in MeOH (5.08 mL). The resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 10 mL), washed sequentially with H_2O (2 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to give a 75:25 mixture of **62**:**56**. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 4:1) gave **62** as a colorless oil (84 mg, 58%, >99:1 dr). ν_{max} (film) 2932 (C−H), 1495, 1452 (C=C); δ_H (400 MHz, $CDCl_3$) 0.75−0.85 (1H, m, C(4)H_A), 1.34−1.40 (2H, m, C(5)H_2), 1.58−1.66 (2H, m, C(4)H_B, C(6)H_A), 2.01−2.20 (2H, m, C(3)*H*, C(6)H_B), 2.24 (3H, s, N*Me*), 2.29 (1H, dd, *J* 11.3, 6.9, C(3)CH_AH$_B$N), 2.41 (1H, dd, *J* 11.3, 9.4, C(3)CH$_A$*H*$_B$N), 3.12−3.14 (2H, m, C(1)*H*, C(2)*H*), 3.69 (2H, AB system, *J* 14.1, NCH_2Ph), 7.24−7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.8 (*C*(5)), 25.0 (*C*(6)), 26.1 (*C*(4)), 30.3 (*C*(3)), 42.6 (N*Me*), 52.5, 54.8 (*C*(1), *C*(2)), 60.7, 62.7 (C(3)*C*H$_2$N, NCH$_2$Ph), 126.9 (*p-Ph*), 127.9, 128.6 (*o,m-Ph*), 139.6 (*i-Ph*); *m/z* (ESI$^+$) 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}NO^+$ ([M + H]$^+$) requires 232.1696; found 232.1695.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-methylcyclohexane 63. Step 1: A stirred solution of **57** (147 mg, 0.57 mmol) in AcOH (0.36 mL) was heated at 50 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (5 mL). The solution was basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 10 mL), washed sequentially with 0.1 M aq $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give **59** as a yellow oil that was used without purification.

Step 2: MsCl (64 μL, 0.81 mmol) was added to a stirred solution of **59** and Et_3N (0.25 mL, 1.81 mmol) in CH_2Cl_2 (2.95 mL) at 0 °C, and the resultant solution was stirred at 0 °C for 1 h. The reaction mixture was then allowed to warm to rt and washed with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed sequentially with 10% aq $CuSO_4$ (3 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to give **61** as a yellow oil that was used without purification.

Step 3: K_2CO_3 (198 mg, 1.43 mmol) was added to a stirred solution of **61** in MeOH (4.40 mL). The resultant suspension was stirred at rt for 16 h, then concentrated in vacuo. H_2O (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic extracts were concentrated in vacuo (to a volume of approximately 10 mL), washed sequentially with H_2O (2 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo to give a 75:25 mixture of **63**:**57**. Purification via flash column chromatography (eluent 30−40 °C petrol/Et_2O, 9:1) gave **63** as a colorless oil (86 mg, 61%, >99:1 dr). ν_{max} (film) 2933 (C−H), 1494, 1452 (C=C); δ_H (400 MHz, $CDCl_3$) 0.75−0.85 (1H, m, C(4)H_A), 0.98 (3H, d, *J* 6.7, NCH*Me*$_A$), 1.05 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.10−1.38 (2H, m, C(5)H_A, C(6)H_A), 1.46−1.75 (2H, m, C(4)H_B, C(5)H_B), 1.95−2.09 (2H, m, C(3)*H*, C(6)H_B), 2.32−2.55 (2H, m, C(3)HCH_2N), 2.95 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.05−3.08 (2H, m, C(1)*H*, C(2)*H*), 3.73 (2H, AB system, *J* 15.6, NCH_2Ph), 7.11−7.46 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.5, 17.3, 18.5, 25.9, 26.0 (*C*(4), *C*(5), *C*(6), NCH*Me*$_2$), 32.8 (*C*(3)), 48.9 (NCHMe$_2$), 52.5 (NCH$_2$Ph), 52.7, 54.2 (*C*(1), *C*(2)), 55.0 (C(3)*C*H$_2$N), 126.6 (*p-Ph*), 128.1, 128.5 (*o,m-Ph*), 141.1 (*i-Ph*); *m/z* (ESI$^+$) 260 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{26}NO^+$ ([M + H]$^+$) requires 260.2009; found 260.2004.

(*RS*,*RS*,*RS*)-3-(*N*-Benzyl-*N*-methylamino)methylcyclohexane-1,2-diol 64. A solution of **62** (43 mg, 0.19 mmol) in 1,4-dioxane (0.72 mL) and 3 M aq H_2SO_4 (0.24 mL) was stirred at 40 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (5 mL) and washed with satd aq $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (3 × 15 mL) and brine (15 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 69:31 mixture of **64**:**51**. Purification via flash column chromatography (eluent 100% EtOAc) gave **64** as a colorless oil (17 mg, 36%, >99:1 dr). ν_{max} (film) 3393 (O−H), 2928, 2802 (C−H); δ_H (500 MHz, $CDCl_3$) 0.84−0.96 (1H, m, C(4)H_A), 1.25−1.78 (5H, m, C(4)H_B, C(5)H_2, C(6)H_A), 1.92−1.98 (1H, m, C(6)H_B), 2.24 (3H, s, N*Me*), 2.38 (1H, dd, *J* 12.4, 3.0, C(3)-CH_AH$_B$N), 2.62 (1H, app t, *J* 12.4, C(3)CH$_A$*H*$_B$N), 3.21 (1H, app t, *J* 9.1, C(2)*H*), 3.37 (1H, d, *J* 12.9, NCH_AH$_B$Ph), 3.44−3.50 (1H, m, C(1)*H*), 3.94 (1H, d, *J* 12.9, NCH$_A$*H*$_B$Ph), 7.16−7.36 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 23.0 (*C*(4)), 28.4 (*C*(5)), 31.1 (*C*(6)), 37.9 (C(3)), 42.3 (N*Me*), 63.0 (NCH$_2$Ph), 64.3 (C(3)CH$_2$N), 74.9 (C(1)), 82.6 (*C*(2)), 127.5 (*p-Ph*), 128.5, 129.1 (*o,m-Ph*), 137.1 (*i-Ph*); *m/z* (ESI$^+$) 250 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{24}NO_2^+$ ([M + H]$^+$) requires 250.1802; found 250.1796.

(*RS*,*RS*,*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)-methylcyclohexane-1,2-diol 65. A solution of **63** (56 mg, 0.23 mmol) in 1,4-dioxane (0.87 mL) and 3 M aq H_2SO_4 (0.29 mL) was stirred at 40 °C for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (5 mL) and washed with satd aq $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (3 × 5 mL) and brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 77:23 mixture of **65**:**52**. Purification via flash column chromatography (eluent EtOAc/30−40 °C petrol, 9:1) gave **65** as a colorless oil (29 mg, 48%, 95:5 dr). ν_{max} (film) 3410 (O−H), 2929, 2856 (C−H); δ_H (500 MHz, $CDCl_3$) 0.86−1.86 (6H, m, C(4)H_2, C(5)H_2, C(6)H_A, C(3)*H*) overlapping 0.98 (3H, d, *J* 6.7, NCH*Me*$_A$) and 1.15 (3H, d, *J* 6.7, NCH*Me*$_B$), 1.92−1.98 (1H, m, C(6)H_B), 2.39−2.42 (1H, m, C(3)CH_AH$_B$N), 2.45−2.58 (1H, m, C(3)CH$_A$*H*$_B$N), 3.03 (1H, septet, *J* 6.7, NC*H*Me$_2$), 3.11 (1H, app t, *J* 9.9, C(2)*H*), 3.23 (1H, d, *J* 14.5, NCH_AH$_B$Ph), 3.44−3.49 (1H, m, C(1)*H*), 3.94 (1H, d, *J* 14.5, NCH$_A$*H*$_B$Ph), 7.18−7.31 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 11.7, 19.7 (NCH*Me*$_2$), 22.1, 27.9, 30.1 (*C*(4), C(5), *C*(6)), 36.7 (*C*(3)), 47.4 (NCHMe$_2$), 53.4 (C(3)CH$_2$N), 53.6 (NCH$_2$Ph), 73.4 (*C*(1)), 80.2 (*C*(2)), 126.3 (*p-Ph*), 127.5, 128.4 (*o,m-Ph*), 137.4 (*i-Ph*); *m/z* (ESI$^+$) 278 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{28}NO_2^+$ ([M + H]$^+$) requires 278.2115; found 278.2114.

(*RS*)-3-(*N*-Benzylamino)cyclopent-1-ene 68. A mixture of **66** (5.00 g, 73.4 mmol), NBS (3.25 g, 18.4 mmol), and AIBN (cat. amt.) in CCl_4 (12.5 mL) was heated at reflux for 1 h. The reaction mixture was cooled to 0 °C, then filtered through a pad of Celite (eluent CCl_4)

to give a yellow solution of **67**. Benzylamine (10.0 mL, 91.7 mmol) was added to the solution of **67** at 0 °C, and the mixture was then warmed to rt and stirred for 1.5 h. The mixture was then filtered and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (150 mL), washed with satd aq $NaHCO_3$ (3 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 7 → 60% EtOAc in 30−40 °C petrol) gave **68** as a brown oil (1.63 g, 51%).[36] δ_H (400 MHz, $CDCl_3$) 1.44−1.67 (2H, m), 2.17−2.51 (3H, m), 3.83 (2H, AB system, *J* 13.0), 3.88−3.94 (1H, m), 5.82−5.92 (2H, m), 7.22−7.38 (5H, m).

(*RS*)-3-(*N*-Benzyl-*N*-methylamino)cyclopent-1-ene 69. A mixture of **66** (5.00 g, 73.4 mmol), NBS (3.25 g, 18.4 mmol), and AIBN (cat. amt.) in CCl_4 (12.5 mL) was heated at reflux for 1 h. The reaction mixture was cooled to 0 °C, then filtered through a pad of Celite (eluent CCl_4) to give a yellow solution of **67**. *N*-Benzyl-*N*-methylamine (11.8 mL, 91.7 mmol) was added to the solution of **67** at 0 °C, and the mixture was then warmed to rt and stirred for 1.5 h. The mixture was then filtered and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), washed sequentially with 10% aq citric acid (3 × 50 mL) and satd aq $NaHCO_3$ (3 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 10 → 25% EtOAc in 30−40 °C petrol) gave **69** as a light brown oil (1.21 g, 35%).[34] δ_H (400 MHz, $CDCl_3$) 1.78−2.00 (2H, m), 2.15 (3H, s), 2.24−2.47 (2H, m), 3.49−3.65 (2H, m), 3.93−4.02 (1H, m), 5.77−5.97 (2H, m), 7.21−7.37 (5H, m).

(*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)cyclopent-1-ene 70. A mixture of **66** (5.00 g, 73.4 mmol), NBS (3.25 g, 18.4 mmol), and AIBN (cat. amt.) in CCl_4 (12.5 mL) was heated at reflux for 1 h. The reaction mixture was cooled to 0 °C, then filtered through a pad of Celite (eluent CCl_4) to give a yellow solution of **67**. *N*-Benzyl-*N*-isopropylamine (15.1 mL, 91.7 mmol) was added to the solution of **67** at 0 °C, and the mixture was then warmed to rt and stirred for 1.5 h. The mixture was then filtered and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), washed sequentially with 10% aq citric acid (3 × 50 mL) and satd aq $NaHCO_3$ (3 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/EtOAc, 9:1) gave **70** as a light brown oil (881 mg, 22%). ν_{max} (film) 2962 (C−H), 1493, 1452 (C=C); δ_H (400 MHz, $CDCl_3$) 1.04 (6H, app t, *J* 6.4, NCHMe_2), 1.66−1.78 (1H, m, C(4)H_A), 1.94−2.07 (1H, m, C(4)H_B), 2.26 (1H, dd, *J* 6.5, 2.0, C(5)H_A), 2.31−2.43 (1H, m, C(5)H_B), 2.92 (1H, septet, *J* 6.4, NC*H*Me_2), 3.59 (2H, t, *J* 16.6, NCH_2Ph), 4.18−4.20 (1H, m, C(3)*H*), 5.70−5.76 (1H, m, C(1)*H*), 5.83−5.85 (1H, m, C(2)*H*), 7.17−7.24 (1H, m, *Ph*), 7.30 (2H, t, *J* 7.5, *Ph*), 7.33−7.40 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.0, 20.3 (NCHMe_2), 27.5 (*C*(4)), 31.6 (*C*(5)), 49.3 (NCHMe_2), 49.5 (NCH_2Ph), 63.6 (*C*(3)), 126.2 (*p-Ph*), 127.9, 128.0 (*o,m-Ph*), 132.2 (*C*(1)), 134.3 (*C*(2)), 142.3 (*i-Ph*); *m/z* (ESI$^+$) 216 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}N^+$ ([M + H]$^+$) requires 216.1747; found 216.1746.

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclopent-1-ene 71. A mixture of **66** (5.00 g, 73.4 mmol), NBS (3.25 g, 18.4 mmol), and AIBN (cat. amt.) in CCl_4 (12.5 mL) was heated at reflux for 1 h. The reaction mixture was cooled to 0 °C, then filtered through a pad of Celite (eluent CCl_4) to give a yellow solution of **67**. Dibenzylamine (17.6 mL, 91.7 mmol) was added to the solution of **67** at 0 °C, and the mixture was then warmed to rt and stirred for 1.5 h. The mixture was then filtered and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), washed sequentially with 10% aq citric acid (3 × 50 mL) and satd aq $NaHCO_3$ (3 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1 → 5% Et_2O in 30−40 °C petrol) gave **71** as a pale yellow oil (1.99 g, 41%).[4c] δ_H (400 MHz, $CDCl_3$) 1.92−2.09 (2H, m, C(4)H_2), 2.34−2.58 (2H, m, C(5)H_2), 3.59 (2H, d, *J* 14.0, N(CH_AH$_B$Ph)$_2$), 3.81 (2H, d, *J* 14.0, N(CH$_A$H$_B$Ph)$_2$), 4.17−4.25 (1H, m, C(3)*H*), 5.88−5.95 (1H, m, C(1)*H*), 5.99−6.05 (1H, m, C(2)*H*), 7.32−7.58 (10H, m, *Ph*).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzylamino)cyclopentane 72. Cl_3CCO_2H (2.36 g, 14.4 mmol) was added to a solution of **68** (500 mg, 2.89 mmol) in CH_2Cl_2 (10 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 720 mg, 3.03 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give an 88:12 mixture of **72**:**76**. Purification via flash column chromatography (eluent 5 → 20% EtOAc in 30−40 °C petrol) gave **72** as a pale brown oil (315 mg, 59%, >99:1 dr). ν_{max} (film) 2027 (C−H), 1453 (C=C); δ_H (400 MHz, $CDCl_3$) 1.15 (1H, m, C(5)H_A), 1.57−1.68 (1H, m, C(4)H_A), 1.87 (1H, dt, *J* 13.2, 8.2, C(5)H_B), 2.08 (1H, dd, *J* 13.2, 8.2, C(4)H_B), 3.23 (1H, t, *J* 8.2, C(3)*H*), 3.45−3.55 (2H, m, C(1)*H*, C(2)*H*), 3.92 (2H, AB system, *J* 13.1, NCH_2Ph), 7.23−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.6 (*C*(4)), 26.3 (*C*(5)), 52.3 (NCH_2Ph), 56.4, 57.5 (*C*(1), *C*(2)), 59.0 (*C*(3)), 127.0 (*p-Ph*), 128.2, 128.5 (*o,m-Ph*), 140.3 (*i-Ph*); *m/z* (ESI$^+$) 212 ([M + Na]$^+$, 30%), 190 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{12}H_{16}NO^+$ ([M + H]$^+$) requires 190.1226; found 190.1225.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)cyclopentane 73. From **69**: Cl_3CCO_2H (2.19 g, 13.4 mmol) was added to a solution of **69** (500 mg, 2.67 mmol) in CH_2Cl_2 (9.0 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 653 mg, 2.80 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 40 mL) and brine (40 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 92:8 mixture of **73**:**77**. Purification via flash column chromatography (eluent 20 → 40% EtOAc in 30−40 °C petrol) gave **73** as a pale yellow oil (256 mg, 46%, >99:1 dr). ν_{max} (film) 3027, 2952 (C−H), 1494, 1453 (C=C); δ_H (400 MHz, $CDCl_3$) 1.40−1.53 (1H, m, C(4)H_A), 1.53−1.68 (2H, m, C(5)H_A, C(4)H_B), 2.03−2.14 (1H, m, C(5)H_B), 2.33 (3H, s, N*Me*), 3.10 (1H, app dd, *J* 9.0, 7.5, C(3)*H*), 3.40 (1H, app d, *J* 2.5, C(2)*H*), 3.49−3.54 (1H, m, C(1)*H*), 3.64−3.70 (2H, m, NCH_2Ph), 7.22−7.29 (3H, m, *Ph*), 7.29−7.39 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.1 (*C*(4)), 26.0 (*C*(5)), 39.6 (N*Me*), 54.3 (*C*(2)), 56.3 (*C*(1)), 59.9 (NCH_2Ph), 65.3 (*C*(3)), 126.9 (*p-Ph*), 128.2, 128.9 (*o,m-Ph*), 139.2 (*i-Ph*); *m/z* (ESI$^+$) 204 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{18}NO^+$ ([M + H]$^+$) requires 204.1383; found 204.1384.

From **72**: MeI (164 mg, 1.15 mmol) was added to a stirred solution of **72** (218 mg, 1.15 mmol) and $^iPr_2NEt$ (0.30 mL, 1.73 mmol) in CH_2Cl_2 (3 mL) at rt. The resultant mixture was stirred for 20 h before being diluted with CH_2Cl_2 (30 mL), washed sequentially with satd aq Na_2CO_3 (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and then concentrated in vacuo. Purification via flash column chromatography (gradient elution, 20 → 40% EtOAc in 30−40 °C petrol) gave **73** as a pale yellow oil (105 mg, 45%, >99:1 dr).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)cyclopentane 74. From **70**: Cl_3CCO_2H (1.90 g, 11.6 mmol) was added to a solution of **70** (500 mg, 2.32 mmol) in CH_2Cl_2 (7.8 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 567 mg, 2.44 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 40 mL) and brine (40 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 92:8 mixture of **74**:**78**. Purification via flash column chromatography (eluent 10 → 20% EtOAc in 30−40 °C petrol) gave **74** as a pale yellow oil (318 mg, 59%, >99:1 dr). ν_{max} (film) 3026, 2964 (C−H); δ_H (400 MHz, $CDCl_3$) 1.09 (3H, d, *J* 6.7, NCHMe_A), 1.11 (3H, d, *J* 6.7, NCHMe_B), 1.35−1.61 (3H, m, C(4)H_2, C(5)H_A), 2.01 (1H, dd, *J* 13.1, 7.6, C(5)H_B), 3.13 (1H, septet, *J* 6.7, NC*H*Me_2), 3.26−3.31 (1H, m, C(3)*H*), 3.31−3.38 (2H, m, C(1)*H*, C(2)*H*), 3.78−3.93 (2H, m, NCH_2Ph), 7.19−7.27 (1H, m, *Ph*), 7.31 (2H, t, *J* 7.6, *Ph*), 7.42 (2H, d, *J* 7.6, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.5, 20.2 (NCHMe_2), 21.8 (*C*(4)), 25.6 (*C*(5)), 48.9 (NCHMe_2), 50.3 (NCH_2Ph), 54.1, 57.7 (*C*(1), *C*(2)),

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59.6 (C(3)), 126.3 (*p-Ph*), 127.9, 128.0 (*o,m-Ph*), 142.4 (*i-Ph*); *m/z* (ESI$^+$) 254 ([M + Na]$^+$, 60%), 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}NO^+$ ([M + H]$^+$) requires 232.1696; found 232.1699.

From **72**: $NaB(OAc)_3H$ (136 mg, 0.64 mmol) was added to a stirred solution of **72** (81 mg, 0.43 mmol) and AcOH (25 μL, 0.43 mmol) in acetone (2 mL) at rt. The resultant mixture was stirred at rt for 24 h before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL), and the resultant solution was washed sequentially with satd aq $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 10 → 30% Et_2O in 30−40 °C petrol) gave **74** as a colorless oil (64 mg, 65%, >99:1 dr).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*,*N*-dibenzylamino)-cyclopentane 75. From **71**: Cl_3CCO_2H (31.0 g, 190 mmol) was added to a solution of **71** (10.0 g, 38.0 mmol) in CH_2Cl_2 (127 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (73%, 9.43 g, 39.9 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of 0.1 M aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were washed with 0.1 M aq $NaHCO_3$ (4 × 200 mL) and brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1 → 8% EtOAc in 40−60 °C petrol) gave **75** as a colorless oil that solidified on standing to a white crystalline solid (10.5 g, 99%, >99:1 dr). δ_H (400 MHz, $CDCl_3$) 1.45−1.59 (3H, m, C(4)H_A, C(5)H_2), 2.00−2.11 (1H, m, C(4)H_B), 3.25−3.31 (1H, m, C(3)*H*), 3.34 (1H, app d, *J* 2.7, OC*H*), 3.47 (1H, app d, *J* 2.7, OC*H*), 3.74 (2H, d, *J* 14.3, N(C$H_A$$H_B$Ph)$_2$), 3.86 (2H, d, *J* 14.3, N(C$H_A$$H_B$Ph)$_2$), 7.22−7.46 (10H, m, *Ph*).

From **72**: BnBr (106 mg, 0.62 mmol) was added to a stirred solution of **72** (78 mg, 0.412 mmol) and ^{i}Pr$_2$NEt (0.10 mL, 0.62 mmol) in CH_2Cl_2 (1 mL) at rt. The resultant mixture was stirred for 20 h before being diluted with CH_2Cl_2 (20 mL), washed sequentially with water (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and then concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5 → 20% Et_2O in 30−40 °C petrol) gave **75** as a colorless oil (80 mg, 70%, >99:1 dr).

(*RS*)-3-(*N*-Benzylamino)cyclohept-1-ene 81. A stirred mixture of **80** (1.00 g, 5.7 mmol), benzylamine (1.56 mL, 14.3 mmol), and K_2CO_3 (0.95 g, 6.90 mmol) in THF (15 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **81** as a yellow oil (731 mg, 64%).[37] δ_H (400 MHz, $CDCl_3$) 1.24−1.39 (1H, m), 1.43−1.72 (3H, m), 1.75−1.83 (1H, m), 1.97 (1H, m), 2.02−2.12 (1H, m), 2.13−2.24 (1H, m), 3.41 (1H, dd, *J* 1.5, 10.1), 3.81 (2H, dd, *J* 13.0, 10.2), 5.71−5.77 (1H, m), 5.80−5.88 (1H, m), 7.22−7.36 (5H, m).

(*RS*)-3-(*N*-Benzyl-*N*-methylamino)cyclohept-1-ene 82. A stirred mixture of **80** (1.00 g, 5.7 mmol), *N*-benzyl-*N*-methylamine (1.84 mL, 14.3 mmol), and K_2CO_3 (0.95 g, 6.9 mmol) in THF (15 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **82** as a yellow oil (1.14 g, 93%).[34] δ_H (400 MHz, $CDCl_3$) 1.29−1.40 (1H, m), 1.42−1.58 (2H, m), 1.65−1.76 (1H, m), 1.91−2.10 (3H, m), 2.16−2.21 (1H, m), 2.22 (3H, s), 3.37 (1H, d, *J* 8.9), 3.57 (2H, dd, *J* 13.0, 23.2), 5.86 (1H, m), 5.88−5.94 (1H, m), 7.22−7.38 (5H, m).

(*RS*)-3-(*N*-Benzyl-*N*-isopropylamino)cyclohept-1-ene 83. A stirred mixture of **80** (1.35 g, 7.72 mmol), *N*-benzyl-*N*-isopropylamine (3.18 mL, 19.3 mmol), and K_2CO_3 (1.28 g, 9.25 mmol) in THF (20 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **83** as a colorless oil (3.70 g, 96%). ν_{max} (film) 2924 (C−H), 1493, 1451 (C=C); δ_H (400 MHz, $CDCl_3$) 1.06 (6H, app t, *J* 6.4, NCH*Me*$_2$), 1.22−1.35 (1H, m, C(5)H_A), 1.41−1.55 (2H, m, C(4)H_2), 1.61−1.76 (1H, m, C(6)H_A), 1.94 (2H, m, C(5)H_B, C(7)H_A), 2.01−2.08 (1H, m, C(6)H_B), 2.12−2.25 (1H, m, C(7)H_B), 3.02 (1H, septet, *J* 6.4, NC*H*Me$_2$), 3.49 (1H, app d, *J* 7.1, C(3)*H*), 3.74 (2H, AB system, *J* 15.4, NCH_2Ph), 5.70−5.79 (1H, m, C(1)*H*), 5.83−5.93 (1H, m, C(2)*H*), 7.18−7.25 (1H, m, *Ph*), 7.31 (2H, t, *J* 7.6, *Ph*), 7.41 (2H, d, *J* 7.6, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.1 (NCH*Me*$_2$), 26.8 (C(6)), 28.5, 28.8 (C(4), C(7)), 32.4 (C(5)), 49.1 (NCHMe$_2$), 50.3 (NCH$_2$Ph), 58.6 (C(3)), 126.2 (*p-Ph*), 127.9, 128.0 (*o,m-Ph*), 129.7 (C(2)), 138.2 (C(1)), 142.8 (*i-Ph*); *m/z* (ESI$^+$) 244 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{26}N^+$ ([M + H]$^+$) requires 244.2060; found 244.2058.

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclohept-1-ene 84. A stirred mixture of **80** (1.00 g, 5.7 mmol), dibenzylamine (2.75 mL, 14.3 mmol), and K_2CO_3 (0.95 g, 6.9 mmol) in THF (15 mL) was heated at 50 °C for 16 h. The resultant mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated and washed with satd aq $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **84** as a yellow oil (1.43 g, 86%). δ_H (400 MHz, $CDCl_3$) 1.26−2.23 (8H, m, C(4)H_2, C(5)H_2, C(6)H_2, C(7)H_2), 3.35 (1H, app d, *J* 10.4, C(3)*H*), 3.59 (2H, d, *J* 14.2, N(C$H_A$$H_B$Ph)$_2$), 3.74 (2H, d, *J* 14.2, N(C$H_A$$H_B$Ph)$_2$), 5.80−5.89 (1H, m, C(1)*H*), 5.93−6.00 (1H, m, C(2)*H*), 7.20−7.42 (10H, m, *Ph*).

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)-cycloheptane 86. Cl_3CCO_2H (3.79 g, 23.2 mmol) was added to a solution of **82** (1.00 g, 4.64 mmol) in CH_2Cl_2 (15.5 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 1.73 g, 7.42 mmol) was added, and the mixture was stirred at rt for 7 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of satd aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with satd aq $NaHCO_3$ (4 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 75:25 mixture of **86**:**90**. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **90** as a yellow oil (46 mg, 4%, >99:1 dr). R_f 0.5 (30−40 °C petrol/EtOAc, 4:1); ν_{max} (film) 2928 (C−H), 1494, 1453 (C=C); δ_H (400 MHz, $CDCl_3$) 0.76 (1H, app q, *J* 12.4, C(5)H_A), 1.29−1.61 (3H, m, C(4)H_A, C(6)H_2), 1.68 (1H, m, C(7)H_A), 1.72−1.86 (2H, m, C(4)H_B, C(5)H_B), 2.26−2.30 (1H, m, C(7)H_B), 2.32 (3H, s, N*Me*), 2.93 (1H, dd, *J* 11.5, 2.2, C(3)*H*), 3.10 (1H, app t, *J* 5.2, C(1)*H*), 3.30 (1H, app d, *J* 5.2, C(2)*H*), 3.57 (1H, d, *J* 13.4, NC$H_A$$H_B$Ph), 3.79 (1H, d, *J* 13.4, NCH$_A$$H_B$Ph), 7.21−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.2 (C(4)), 24.1 (C(6)), 27.3 (C(5)), 28.1 (C(7)), 38.2 (N*Me*), 53.2 (C(1)), 58.0 (NCH$_2$Ph), 60.1 (C(2)), 63.6 (C(3)), 126.8 (*p-Ph*), 128.2, 128.7 (*o,m-Ph*), 139.9 (*i-Ph*); *m/z* (ESI$^+$) 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}NO^+$ ([M + H]$^+$) requires 232.1696; found 232.1696. Further elution gave **86** as a yellow oil (357 mg, 36%, >99:1 dr). R_f 0.2 (30−40 °C petrol/EtOAc, 4:1); ν_{max} (film) 2927 (C−H), 1494, 1454 (C=C); δ_H (400 MHz, $CDCl_3$) 1.17−1.43 (3H, m, C(5)H_A, C(6)H_A, C(7)H_A), 1.55−1.67 (1H, m, C(4)H_A), 1.67−1.78 (1H, m, C(6)H_B), 1.88−2.01 (2H, m, C(4)H_B, C(5)H_B), 2.24−2.34 (1H, m, C(7)H_B), 2.30 (3H, s, N*Me*), 2.54 (1H, app dd, *J* 10.2, 7.5, C(3)*H*), 3.04 (1H, app dd, *J* 8.1, 5.4, C(1)*H*), 3.17 (1H, dd, *J* 7.5, 5.4, C(2)*H*), 3.72−3.78 (2H, m, NCH_2Ph), 7.21−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.1 (C(6)), 28.9 (C(5)), 29.2 (C(7)), 30.8 (C(4)), 38.2 (N*Me*), 53.2 (C(1)), 55.6 (C(2)), 58.5 (NCH$_2$Ph), 65.9 (C(3)), 127.0 (*p-Ph*), 128.2, 129.1 (*o,m-Ph*), 139.0 (*i-Ph*); *m/z* (ESI$^+$) 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $C_{15}H_{22}NO^+$ ([M + H]$^+$) requires 232.1696; found 232.1696.

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-cycloheptane 87. Cl_3CCO_2H (187 mg, 1.13 mmol) was added to a solution of **83** (55 mg, 0.23 mmol) in CH_2Cl_2 (0.76 mL), and the

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resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 57 mg, 0.24 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of satd aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed with satd aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 93:7 mixture of **87**:**91**. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **87** as a yellow oil (28 mg, 46%, >99:1 dr). ν_{max} (film) 2928 (C−H), 1457 (C═C); δ_H (400 MHz, $CDCl_3$) 1.06 (3H, d, *J* 6.6, NCHMe_A), 1.10 (3H, d, *J* 6.6, NCHMe_B), 1.26−1.33 (3H, m, C(4)H_A, C(5)H_A, C(6)H_A), 1.53−1.64 (1H, m, C(7)H_A), 1.64−1.73 (1H, m, C(5)H_B), 1.80 (1H, d, *J* 14.7, C(7)H_B), 1.83−1.91 (1H, m, C(6)H_B), 2.22−2.32 (1H, m, C(4)H_B), 2.75 (1H, app dd, *J* 10.0, 7.2, C(1)*H*), 3.00−3.05 (1H, m, C(3)*H*), 3.05−3.18 (2H, m, C(2)*H*, NC*H*Me_2), 3.82 (2H, AB system, *J* 15.7, NCH_2Ph), 7.18−7.44 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.0, 20.4 (NCHMe_2), 24.2 (*C*(5)), 29.3 (*C*(6)), 30.0 (*C*(4)), 32.7 (*C*(7)), 49.7 (NCHMe_2), 49.8 (NCH_2Ph), 54.6 (*C*(3)), 58.1 (*C*(2)), 60.3 (*C*(1)), 126.4 (*p-Ph*), 127.7, 128.1 (*o,m-Ph*), 142.6 (*i-Ph*); *m*/*z* (ESI^+) 260 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{17}H_{26}NO^+$ ($[M + H]^+$) requires 260.2009; found 260.2008.

(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-(*N*,*N*-dibenzylamino)-cycloheptane 88. Cl_3CCO_2H (5.74 g, 35.2 mmol) was added to a stirred solution of **84** (2.05 g, 7.03 mmol) in CH_2Cl_2 (23 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (74%, 1.72 g, 7.38 mmol) was added, and the mixture was stirred at rt for 3.5 h. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of satd aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed with satd aq $NaHCO_3$ (4 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 94:6 mixture of **88**:**92**. Purification via flash column chromatography (gradient elution, 2 → 20% Et_2O in 40−60 °C petrol) gave **92** as a colorless oil that solidified on standing to a white crystalline solid (94 mg, 4%, ∼95% purity, >99:1 dr).[4c] δ_H (400 MHz, $CDCl_3$) 0.59−2.31 (8H, m, C(4)H_2, C(5)H_2, C(6)H_2, C(7)H_2), 2.89 (1H, app dd, *J* 11.6, 2.8, C(1)*H*), 3.06 (1H, app t, *J* 5.3, C(3)*H*), 3.35 (1H, dd, *J* 4.8, 1.0, C(2)*H*), 3.59 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.90 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 7.21−7.42 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.4, 24.1, 27.1, 28.0 (*C*(4), *C*(5), *C*(6), *C*(7)), 53.3 (*C*(3)), 54.3 (N(CH_2Ph)$_2$), 58.4 (*C*(1)), 60.7 (*C*(2)), 126.7 (*p-Ph*), 128.1, 128.5 (*o*, *m-Ph*), 140.4 (*i-Ph*). Further elution gave **88** as a colorless oil that solidified on standing to a white crystalline solid (1.49 g, 69%, >99:1 dr).[4c] δ_H (400 MHz, $CDCl_3$) 1.02−2.25 (8H, m, C(4)H_2, C(5)H_2, C(6)H_2, C(7)H_2), 2.66 (1H, app dd, *J* 10.4, 7.5, C(3)*H*), 3.00 (1H, ddd, *J* 8.0, 6.5, 5.0, C(1)*H*), 3.24 (1H, dd, *J* 7.5, 5.0, C(2)*H*), 3.77 (4H, AB system, *J* 13.9, N(CH_2Ph)$_2$), 7.21−7.46 (10H, m, *Ph*).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzylamino)cycloheptane 89. Cl_3CCO_2H (4.07 g, 25.0 mmol) was added to a solution of **81** (1.00 g, 5.00 mmol) in CH_2Cl_2 (16.7 mL), and the resultant solution was stirred at rt for 5 min. *m*-CPBA (70%, 3.08 g, 12.5 mmol) was added, and the mixture was stirred at rt for 20 min. The mixture was quenched with satd aq Na_2SO_3 until starch-iodide paper indicated that *m*-CPBA was not present, and basified to pH 9 by the addition of satd aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with satd aq $NaHCO_3$ (4 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo to give a 15:85 mixture of **85**:**89**. Purification via flash column chromatography (gradient elution, 0 → 50% EtOAc in 30−40 °C petrol) gave **89** as a pale orange solid (550 mg, 51%, >99:1 dr). mp 24−26 °C; ν_{max} (film) 2928 (C−H), 1494, 1453 (C═C); δ_H (400 MHz, $CDCl_3$) 0.83−0.97 (1H, m, C(5)H_A), 1.24−1.61 (3H, m, C(4)H_A, C(6)H_2), 1.68−1.84 (3H, m, C(4)H_B, C(5)H_B, C(7)H_A), 2.22−2.35 (1H, m, C(7)H_B), 3.00 (1H, app dd, *J* 10.9, 2.5, C(3)*H*), 3.13 (1H, app t, *J* 5.0, C(1)*H*), 3.24 (1H, app d, *J* 5.0, C(2)*H*), 3.94 (1H, td, *J* 13.1, 6.1, NCH_2Ph), 7.18−7.48 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.2 (*C*(6)), 26.7 (*C*(5)), 28.3 (*C*(7)), 30.9 (*C*(4)), 51.1 (NCH_2Ph), 54.9 (*C*(1)), 57.6 (*C*(3)), 60.4 (*C*(2)), 126.9 (*p-Ph*), 128.1, 128.4 (*o,m-Ph*), 140.6 (*i-Ph*); *m*/*z* (ESI^+) 218 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{14}H_{20}NO^+$ ($[M + H]^+$) requires 218.1539; found 218.1539.

(1*RS*,2*SR*,3*SR*)-3-(*N*-Benzyl-*N*-methylamino)cycloheptane 90. MeI (28 μL, 0.46 mmol) was added to a stirred solution of **89** (100 mg, 0.46 mmol) and $^iPr_2NEt$ (0.12 mL, 0.69 mmol) in CH_2Cl_2 (0.9 mL) at rt. The resultant mixture was stirred for 20 h before being diluted with CH_2Cl_2 (10 mL), washed sequentially with satd aq Na_2CO_3 (3 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 20 → 40% EtOAc in 30−40 °C petrol) gave **90** as a pale yellow oil (61 mg, 57%, >99:1 dr).

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-isopropylamino)-cycloheptane 91. $NaB(OAc)_3H$ (64 mg, 0.303 mmol) was added to a stirred solution of **89** (47 mg, 0.216 mmol) and AcOH (14 μL, 0.216 mmol) in acetone (1.5 mL) at rt. The resultant mixture was stirred at rt for 24 h before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL), and the resultant solution was washed sequentially with satd aq $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 0 → 20% EtOAc in 30−40 °C petrol) gave **91** as a pale yellow oil (36 mg, 66%, >99:1 dr). ν_{max} (film) 2927 (C−H), 1452 (C═C); δ_H (400 MHz, $CDCl_3$) 0.60−0.74 (1H, m, C(5)H_A), 1.05 (3H, d, *J* 6.6, NCHMe_A), 1.08 (3H, d, *J* 6.6, NCHMe_B), 1.24−1.38 (1H, m, C(6)H_A), 1.41−1.67 (3H, m, C(4)H_A, C(6)H_B, C(7)H_A), 1.69−1.82 (2H, m, C(4)H_B, C(5)H_B), 2.21−2.33 (1H, m, C(7)H_B), 2.93 (1H, app dd, *J* 11.6, 2.4, C(3)*H*), 3.02 (1H, app t, *J* 4.5, C(1)*H*), 3.22 (1H, app d, *J* 4.5, C(2)*H*), 3.27 (1H, septet, *J* 6.6, NC*H*Me_2), 3.81 (2H, AB system, *J* 14.0, NCH_2Ph), 7.23−7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.8, 22.1 (NCHMe_2), 24.1 (*C*(6)), 27.3 (*C*(4)), 27.5 (*C*(5)), 28.2 (*C*(7)), 48.3 (NCHMe_2), 49.6 (NCH_2Ph), 53.6 (*C*(1)), 58.6 (*C*(3)), 61.5 (*C*(2)), 126.4 (*p-Ph*), 128.0, 128.1 (*o,m-Ph*), 142.1 (*i-Ph*); *m*/*z* (ESI^+) 282 ($[M + Na]^+$, 50%) 260 ($[M + H]^+$, 100%); HRMS (ESI^+) $C_{17}H_{26}NO^+$ ($[M + H]^+$) requires 260.2009; found 260.2008.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*,*N*-dibenzylamino)-cycloheptane 92. BnBr (79 μL, 0.67 mmol) was added to a stirred solution of **89** (100 mg, 0.46 mmol) and $^iPr_2NEt$ (0.12 mL, 0.67 mmol) in CH_2Cl_2 (0.5 mL) at rt. The resultant mixture was stirred for 20 h before being diluted with CH_2Cl_2 (10 mL), washed sequentially with water (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/EtOAc, 4:1) gave **92** as a colorless oil that solidified on standing to a white crystalline solid (65 mg, 47%, ∼95% purity, >99:1 dr).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR spectra, and crystallographic information files (for structures CCDC 839524−839526). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(10) Small amounts (typically <5%) of the corresponding amino diol **17**−**20** was frequently observed in the crude samples of trichloroacetate esters **13**−**16**, arising from hydrolysis of the labile trichloroacetate ester functionality.

(11) Following our previously reported procedure to determine the number of equivalents of acid required for effective N-protection by protonation (see ref 4a), the formation of the corresponding ammonium species from **9**−**11** in the presence of Cl_3CCO_2H and TsOH was examined by ^1H NMR spectroscopy. The requisite acid was added in 1 equiv portions to a solution of the requisite amines **9**−**11** in $CDCl_3$, and it was concluded that 5 equiv of Cl_3CCO_2H or 3 equiv of TsOH would be sufficient to enable efficient ammonium-directed oxidation of allylic amines **9**−**11**.

(12) Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 839524 (**14**), CCDC 839525 (**21**), and CCDC 839526 (**25**).

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(17) The consumption of ammonium **39** was monitored by calculation of the average integration of the peaks due to C(2)*H* (δ_H 5.73−5.90 ppm) and C(1)*H* (δ_H 6.24−6.42 ppm), whereas the consumption of *m*-CPBA was monitored by calculation of the integration of the peak at δ_H 7.87−7.93 and 7.95−8.00 ppm. The formation of ammonium **41** was monitored by integration of the signal due to N*Me* (δ_H 3.07−3.11 ppm). The intermediate epoxide ammonium **40** was observed in the ^1H NMR spectrum at δ_H 3.64−3.72 ppm; an authentic sample was prepared upon addition of Cl_3CCO_2H (5 equiv) to a solution of **23** in CD_2Cl_2.

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(20) For a discussion concerning the regioselectivity of the ring-opening of the diastereoisomers of 1,2-epoxy-3-hydroxymethylcyclohexane, see ref 4c and references cited therein. Presumably, the regioselectivity of the ring-opening of *syn*-epoxides **56** and **57**, and *anti*-epoxides **62** and **63**, is governed by similar factors.

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