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Diastereodivergent Hydroxyfluorination of Cyclic and Acyclic Allylic Amines: Synthesis of 4-Deoxy-4-fluorophytosphingosines

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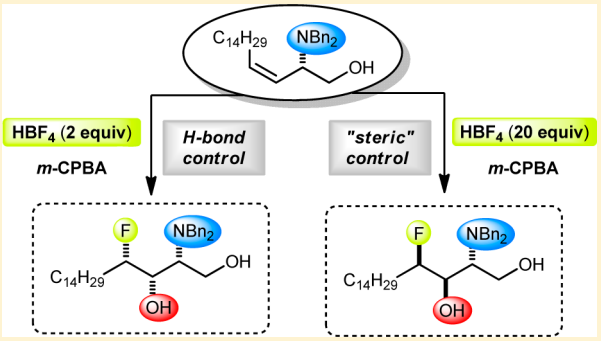
Supporting Information

ABSTRACT: A diastereodivergent hydroxyfluorination protocol enabling the direct conversion of some conformationally biased allylic amines to the corresponding diastereoisomeric amino fluorohydrins has been developed. Sequential treatment of a conformationally biased allylic amine with 2 equiv of $HBF_4{\cdot}OEt_2$ followed by *m*-CPBA promotes epoxidation of the olefin on the face proximal to the amino group under hydrogen-bonded direction from the in situ formed ammonium ion. Regioselective and stereospecific epoxide ring-opening by transfer of fluoride from a BF_4^- ion (an S_N2-type process at the carbon atom distal to the ammonium moiety) then occurs in situ to give the corresponding amino fluorohydrin. Alternatively, an analogous reaction using 20 equiv of $HBF_4{\cdot}OEt_2$ results in preferential epoxidation of the opposite face of the olefin, which is followed by regioselective and stereospecific epoxide ring-opening by transfer of fluoride from a BF_4^- ion (an S_N2-type process at the carbon atom distal to the ammonium moiety). The synthetic utility of this methodology is demonstrated via its application to a synthesis of 4-deoxy-4-fluoro-L-xylo-phytosphingosine and 4-deoxy-4-fluoro-L-lyxo-phytosphingosine, each in five steps from Garner's aldehyde.



INTRODUCTION

The unique physical, chemical, and biological characteristics of organofluorine compounds have long fascinated the chemical community, and the range of beneficial properties that fluorine can confer on designer molecules[1] has led to myriad applications across medicinal chemistry,[2] agrochemistry,[3] and materials science.[4] Around 30−40% of agrochemicals and 20% of pharmaceuticals on the market in 2006 contained at least one fluorine atom,[5] as did 10 of the leading 30 blockbuster drugs by sale in the USA in 2008.[6] Although much attention has been lavished on the beneficial effects that fluorine can confer on rationally designed molecules, there has also been considerable activity in the preparation and biological evaluation of fluorinated analogues of naturally occurring amino compounds,[7] including α- and β-amino acids,[8] amino-sugars,[9] iminosugars,[10] amino- and diaminocyclitols,[11] and sphingoid bases and ceramides.[12] To meet the ever-increasing demand for stereodefined, fluorinated organic compounds,[5] a number of nucleophilic and electrophilic fluorination methods have been developed,[13] including asymmetric protocols.[14] Unfortunately, many of these approaches suffer from economic or practical setbacks, which often relate to the fluorinating agents themselves. In contrast, $BF_3{\cdot}OEt_2$ and $HBF_4{\cdot}OEt_2$ are inexpensive and easily handled, and we have initiated a research program to examine the potential of these reagents as nucleophilic fluorinating agents.[15,16] For instance, treatment of enantiopure 2,3-epoxy amine **1** with $HBF_4{\cdot}OEt_2$ gave the corresponding amino fluorohydrin **2** in 79% yield as a single diastereoisomer. The stereochemical outcome of this process is consistent with an S_N2-type epoxide ring-opening by transfer of fluoride from a BF_4^- ion, resulting in inversion of configuration. A sequence of four further manipulations gave (*S*,*S*)-3-deoxy-3-fluorosafingol **3**[16] (Scheme 1).

We became interested in the possibility of harnessing both our diastereoselective ammonium-directed olefinic oxidation reaction[17] and regioselective and stereospecific ring-opening fluorination reaction[16] for the development of a one-pot process for the direct conversion of an allylic amine to the corresponding amino fluorohydrin. Herein, an efficient, practical and scalable protocol for the hydroxyfluorination of an allylic amine upon sequential treatment with $HBF_4{\cdot}OEt_2$ followed by *m*-CPBA is delineated.[18] The diastereofacial selectivity of the hydroxyfluorination process can be controlled in certain cases by adjusting the stoicheometry of $HBF_4{\cdot}OEt_2$ employed in the reaction, and the synthetic utility of this diastereodivergent hydroxyfluorination protocol is exemplified by application to the synthesis of 4-deoxy-4-fluoro-L-*xylo*-phytosphingosine and 4-deoxy-4-fluoro-L-*lyxo*-phytosphingosine, each in five steps from Garner's aldehyde.

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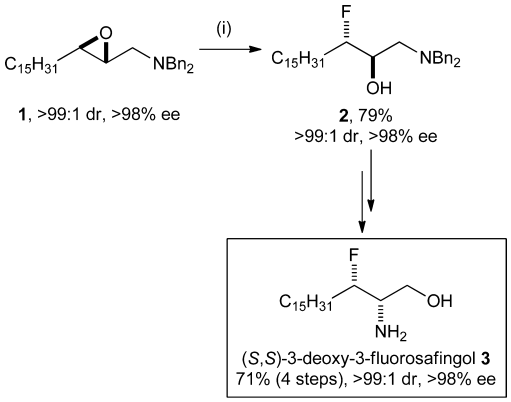
Scheme 1[a]

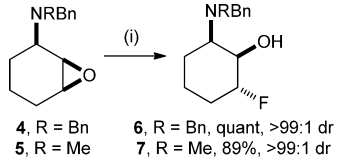


[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2, 0 °C, 5 min.

RESULTS AND DISCUSSION

Ring-opening fluorination of 2,3-epoxy amine **4** with $HBF_4{\cdot}OEt_2$ gave amino fluorohydrin **6** as a single diastereoisomer which was isolated in quantitative yield, with the analogous reaction of 2,3-epoxy amine **5** giving the corresponding amino fluorohydrin **7** in 89% yield, as previously reported (Scheme 2).[16] A plausible mechanistic rationale for

Scheme 2[a]

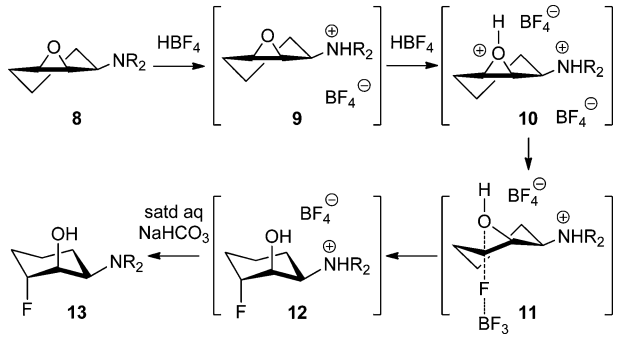


[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2, rt, 5 min.

the stereochemical outcome of this ring-opening fluorination process involves initial *N*-protonation of a 2,3-epoxy amine substrate **8** by HBF_4[19] to give ammonium species **9**. The oxirane moiety within **9** may then be activated to nucleophilic attack through *O*-protonation to form the dicationic species **10**.[20] Transfer of fluoride from a BF_4^- ion[21] to the activated oxirane **10** at the carbon atom distal to the ammonium group (where its destabilizing inductive electron-withdrawing influence on the transition state **11** is less pronounced)[22] results in conversion to **12**, via an S_N2-type pathway. Subsequent basic aqueous workup gives the amino fluorohydrin **13** (Scheme 3).

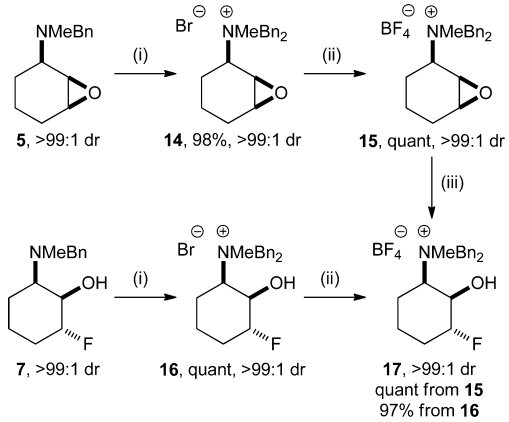
In order to verify the requirement for oxirane activation, tetraalkylammonium tetrafluoroborate salt **15** was synthesized as a model for the intermediate 2,3-epoxy ammonium species **9**. Thus, 2,3-epoxy amine **5** was treated with BnBr in MeCN to give tetraalkylammonium bromide salt **14**, and subsequent anion exchange by treatment with $Ag(MeCN)_4BF_4$ in CH_2Cl_2[23] gave tetraalkylammonium tetrafluoroborate salt **15** in 98% yield and >99:1 dr over two steps. A solution of **15** in CD_2Cl_2 was allowed to stand at rt and was monitored by ^1H and ^{19}F NMR spectroscopy. No ring-opening of the epoxide by the BF_4^- ion was observed even after several days, suggesting in this case that oxirane activation is a prerequisite to fluorination. Addition of 1 equiv of *N*,*N*-dibenzyl-*N*-cyclohexylammonium tetrafluoroborate to the solution of **15** resulted in no reaction,

Scheme 3



implying that ring-opening is unlikely to be assisted by another (N−H) ammonium species acting as a hydrogen-bond donor. In a separate experiment, however, addition of 1 equiv of $HBF_4{\cdot}OEt_2$ to the solution of **15** followed by immediate ^1H and ^{19}F NMR spectroscopic analyses revealed that complete consumption of the epoxide had occurred, and fluorohydrin **17** was isolated in quantitative yield and >99:1 dr after aqueous workup with satd aq $NaBF_4$. An authentic sample of **17** was prepared upon sequential *N*-benzylation of amino fluorohydrin **7** and anion exchange of **16** with $Ag(MeCN)_4BF_4$ (Scheme 4).

Scheme 4[a]



[a]Reagents and conditions: (i) BnBr, MeCN, reflux, 22 h; (ii) $Ag(MeCN)_4BF_4$, CH_2Cl_2, rt; (iii) $HBF_4{\cdot}OEt_2$ (1 equiv), rt, then satd aq $NaBF_4$.

The generality of our ring-opening fluorination reaction with $HBF_4{\cdot}OEt_2$ was assessed by application to a range of 5-, 6-, and 7-membered carbocyclic 2,3-epoxy amines **18**−**22**,[24] which allowed for evaluation of the effects of both ring size and the relative stereochemistry between the oxirane and the amino group on the carbocyclic scaffold on the outcome of the reaction. The ring-opening fluorination reactions of **18**,[16] **19**,[16] **20**, and **22** proceeded to give the corresponding amino fluorohydrins **23**,[16] **24**,[16] **25**, and **27** as single diastereoisomers (>99:1 dr) in all cases, which were isolated in good yield (Scheme 5). The relative configurations within amino fluorohydrins **23**−**25** and **27** were unambiguously established, in each case, via single-crystal X-ray diffraction analyses.[25] The stereochemical outcomes of these ring-opening fluorination reactions are therefore consistent with a reaction pathway involving an S_N2-type epoxide opening by transfer of fluoride from a BF_4^- ion, resulting in inversion of configuration at the

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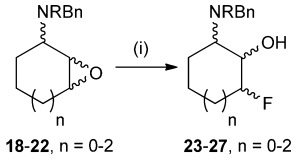
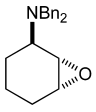
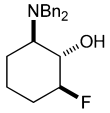
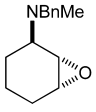
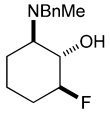
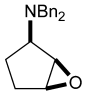
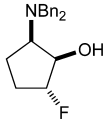
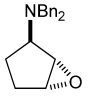
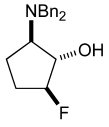
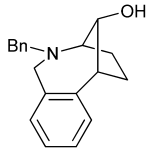
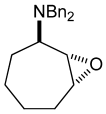
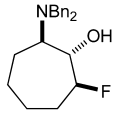
Scheme 5[a]



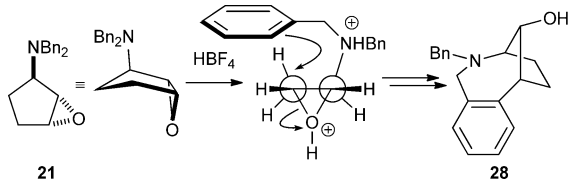
18-22, n = 0-2 **23-27**, n = 0-2

2,3-Epoxy Amine	Amino Fluorohydrin Product	Other Product(s)
		
18, >99:1 dr	**23**, 73%, >99:1 dr	
		
19, >99:1 dr	**24**, 71%, >99:1 dr	
		
20, >99:1 dr	**25**, 78%, >99:1 dr	
		
21, >99:1 dr	**26**, 35%, >99:1 dr	**28**, 55%, >99:1 dr
		
22, >99:1 dr	**27**, 75%, >99:1 dr	

[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2, rt, 5 min.

carbon atom distal to the amino group. For 2,3-epoxy amine **21**,[24] however, a competitive intramolecular electrophilic aromatic substitution reaction occurred that resulted in the formation of bicycle **28** as the major product, thus somewhat compromising the yield of amino fluorohydrin **26** (Scheme 5). The relative configuration within amino fluorohydrin **26** was assigned on the basis of a mechanism of formation involving an S_N2-type epoxide ring-opening, while the relative configuration within bicycle **28** was unambiguously established via single-crystal X-ray diffraction analysis.[25] Examination of the single-crystal X-ray diffraction structure of 2,3-epoxy amine **21**[25] reveals a solid-state conformation in which the bicyclic system adopts a boatlike conformation[26] with a pseudoaxial *N*,*N*-dibenzylamino group. If maintained in solution, this conformation would provide ideal positioning of the *N*,*N*-dibenzylamino group for the intramolecular cyclization reaction leading to bicycle **28** (Scheme 6).

Scheme 6



21 **28**

The 2,3-epoxy amine substrates **4**, **5**, and **18**−**22** for these reactions were all prepared from the corresponding cyclic allylic amines using our protocol for ammonium-directed olefinic oxidation as the key step,[17] which relies upon the in situ protection of an allylic amine from *N*-oxidation by conversion to the corresponding ammonium species on treatment with a strong Brønsted acid, prior to treatment with *m*-CPBA. Therefore, the possibility of employing $HBF_4{\cdot}OEt_2$ as the acid protecting agent in these reactions was next assessed, in order to circumvent the need for isolation of the epoxide intermediate and so develop a direct ("one-pot") hydroxyfluorination protocol. Treatment of allylic amine **29** with either 1 or 1.5 equiv of $HBF_4{\cdot}OEt_2$ followed by *m*-CPBA (2 equiv) led to the formation of complex mixtures of products. However, the use of 2 equiv of $HBF_4{\cdot}OEt_2$ in this reaction gave a 67:12:21 mixture of amino fluorohydrins **6** and **23**, and *m*-CBA ester **30**, respectively. The relative configuration within *m*-CBA ester **30** was established unambiguously through treatment of the 67:12:21 mixture of **6**:**23**:**30** with K_2CO_3 in MeOH, which resulted in transesterification of **30** to the corresponding known diol **31**,[17a] while leaving amino fluorohydrins **6** and **23** unchanged. Increasing the amount of $HBF_4{\cdot}OEt_2$ led to increasing amounts of amino fluorohydrin **23** being produced in the reaction, until a plateau was reached beyond 30 equiv, when the ratio of amino fluorohydrins **6**:**23** was 10:90. A rate enhancement was also noted at high equivalents of $HBF_4{\cdot}OEt_2$: when the course of the hydroxyfluorination reactions of allylic amine **29** were monitored by ^1H NMR spectroscopy, complete consumption of starting material occurred after 2 h when using 20 equiv of $HBF_4{\cdot}OEt_2$, while starting material remained even after 7 h when using 2 equiv of $HBF_4{\cdot}OEt_2$. The rate acceleration of epoxidation of isolated alkenes by peracids in the presence of strong Brønsted acids has been documented and is postulated to be a result of protonation of the peracid generating a more electrophilic, and hence more reactive, oxidizing agent[27] (Scheme 7).

Amino fluorohydrin **6** and *m*-CBA ester **30** presumably arise from epoxidation of the olefin on the face *syn* to the ammonium group (forming epoxide **4** in protonated form), followed by regioselective and stereospecific ring-opening by either transfer of fluoride from a BF_4^- ion to, or attack of *m*-CBA at, the oxirane carbon distal to the ammonium group. Amino fluorohydrin **23** meanwhile, is consistent with epoxidation on the face of the olefin *anti* to the ammonium group (forming epoxide **18** in protonated form), followed by regioselective and stereospecific ring-opening by transfer of fluoride from a BF_4^- ion to the oxirane carbon distal to the ammonium group. The product distributions of these reactions presumably reflect the relative rate of the former epoxidation process over the latter. When using 2 equiv of $HBF_4{\cdot}OEt_2$, epoxidation of allylic amine **29** on the face *syn* to the amino group is favored, presumably as a result of hydrogen bonding of the peracid to the in situ formed ammonium ion.[28] Increasing the amount of $HBF_4{\cdot}OEt_2$ to 20 equiv promotes protonation of the *m*-CPBA,[27] and this

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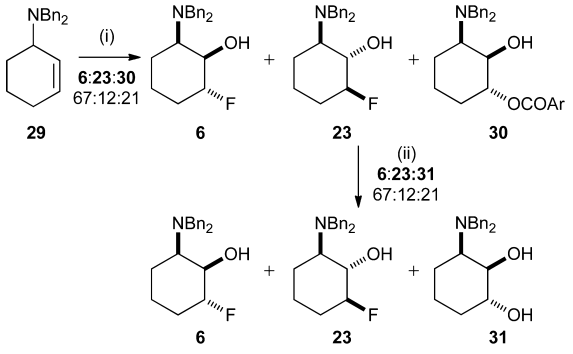
Scheme 7[a]



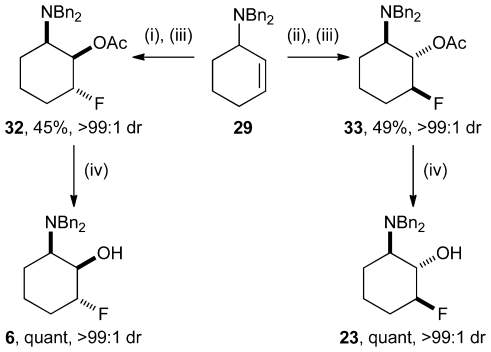
HBF_4·OEt_2 (equiv)	Ratio 6:23:30
2	67:12:21
5	43:48:9
10	26:70:4
20	16:84:0
30	10:90:0
40	10:90:0

[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) K_2CO_3, MeOH, rt, 1 h. Ar = *m*-ClC_6H_4.

may serve to decrease the hydrogen-bond acceptor ability of the peracid, as well as introduce electrostatic repulsive interactions between the protonated peracid and the ammonium group. Non-hydrogen-bond-directed epoxidation, presumably occurring preferentially on the face of the olefin *anti* to the ammonium ion due to minimization of unfavorable steric interactions and/or electronic interactions (minimization of dipoles),[29] may therefore predominate due to activation of the *m*-CPBA as a more potent electrophilic oxidant by protonation,[27] thus resulting in a reversal of the sense of diastereofacial selectivity of epoxidation (Scheme 8).

Unfortunately, attempted separation of the product mixtures from these hydroxyfluorination reactions proved unsuccessful. However, treatment of the crude product mixtures with Ac_2O in pyridine facilitated the isolation of diastereoisomerically pure samples of acetates **32** and **33**. Thus, hydroxyfluorination of **29** with 2 equiv of HBF_4·OEt_2 and 2 equiv of *m*-CPBA followed by acetylation of the crude product mixture allowed isolation of acetate **32** in 45% yield and >99:1 dr, while hydroxyfluorination of **29** with 20 equiv of HBF_4·OEt_2 and 2 equiv of *m*-CPBA followed by acetylation of the crude product mixture allowed for the isolation of acetate **33** in 49% yield and >99:1 dr. The relative configurations within acetates **32** and **33** were unambiguously established through transesterification (treatment with K_2CO_3 in MeOH) which gave the corresponding amino fluorohydrins **6** and **23** in quantitative yield in each case (Scheme 9).

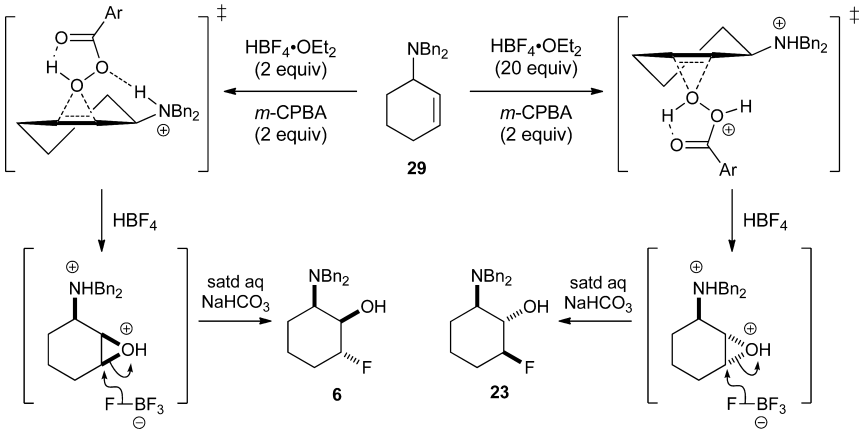
Scheme 9[a]



[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) HBF_4·OEt_2 (20 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (iii) Ac_2O, pyridine, rt, 20 h; (iv) K_2CO_3, MeOH, rt, 3 h.

The generality of this hydroxyfluorination procedure for other cyclic allylic amines was next investigated. Hydroxyfluorination of tertiary allylic amine **34** using 2 equiv of HBF_4·OEt_2 and 2 equiv of *m*-CPBA gave an 85:3:12 mixture of amino fluorohydrins **7** and **24** and *m*-CBA ester **35**, respectively. Treatment of the crude product mixture with K_2CO_3 in MeOH to effect transesterification of *m*-CBA ester **35** to the corresponding known diol **36**[17i] (while leaving fluorohydrins **7** and **24** unaffected) enabled chromatographic separation of the mixture and thus allowed isolation of fluorohydrin **7** in 73% yield as a single diastereoisomer. This compares to an overall yield of 70% for the two-step conversion of tertiary allylic amine **34** into fluorohydrin **7** when employing sequential epoxidation[17i] and ring-opening fluorination[16] steps (Scheme 10). Under analogous conditions, hydroxyfluorination of secondary allylic amine **37** gave a 90:10 mixture of amino fluorohydrin **38** and *m*-CBA ester **40**, respectively. Treatment

Scheme 8



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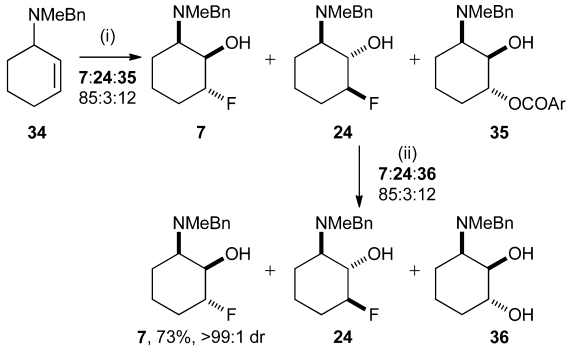
Scheme 10[a]

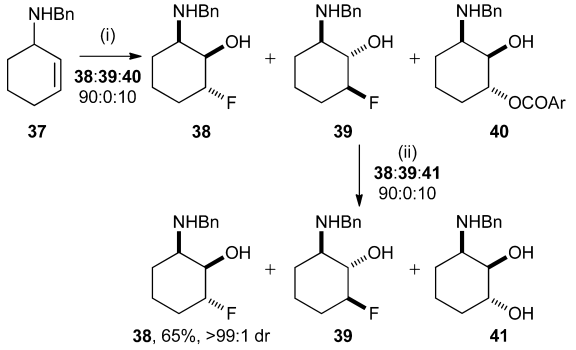


HBF_4·OEt_2 (equiv)	Ratio 7:24:35
2	85:3:12
5	68:25:7
10	46:50:4
20	35:63:2

[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv) CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) K_2CO_3, MeOH, rt, 1 h. Ar = *m*-ClC_6H_4.

of this mixture with K_2CO_3 in MeOH to effect transesterification of *m*-CBA ester **40** to the corresponding known diol **41**,[17a] followed by chromatography, gave fluorohydrin **38** in 65% yield as a single diastereoisomer (Scheme 11). The

Scheme 11[a]



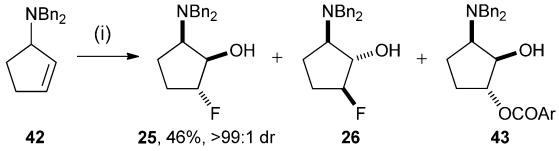
HBF_4·OEt_2 (equiv)	Ratio 38:39:40
2	90:0:10
5	86:5:9
10	82:11:7
20	77:17:6

[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) K_2CO_3, MeOH, rt, 1 h. Ar = *m*-ClC_6H_4.

relative configuration within **38** was unambiguously established via single-crystal X-ray diffraction analysis.[25] The effect of increasing the number of equivalents of HBF_4·OEt_2 on the diastereoselectivities of these hydroxyfluorination reactions was next studied. For both tertiary amine **34** and secondary amine **37**, increasing the amount of HBF_4·OEt_2 used in the hydroxyfluorination reaction increased the amount of the corresponding amino fluorohydrins **24** and **39** arising from epoxidation on the face of the olefin *anti* to the in situ formed ammonium ion. This resulted in a reversal of the reaction diastereoselectivity for tertiary amine **34** when using 20 equiv of HBF_4·OEt_2 (Scheme 10), although a more subtle effect was noted for hydroxyfluorination of secondary amine **37**, and amino fluorohydrin **38** remained the major product even when using 20 equiv of HBF_4·OEt_2: a second fluorinated species which appeared in the crude reaction mixture upon increasing equiv of HBF_4 was tentatively assigned as amino fluorohydrin **39** by analogy to the cases of hydroxyfluorination of tertiary amines **29** and **34**, where the configurations within each of the corresponding fluorohydrin products **6**, **7**, **23**, and **24** were unambiguously established (Scheme 11). It is noteworthy that the rates of ammonium-directed olefinic oxidation of allylic amines **29**, **34**, and **37** increase in the order **29** < **34** < **37**.[17i] Presumably, the increased ability of the in situ formed ammonium ion derived from secondary amine **37** to promote rapid hydrogen-bond directed epoxidation (leading to amino fluorohydrin **38**) means that, even at high concentrations of HBF_4·OEt_2, the rate of the non-hydrogen-bond directed reaction (leading to amino fluorohydrin **39**) is not able to outpace it.

Hydroxyfluorination of cyclopentene-derived tertiary allylic amine **42** (Scheme 12) and cycloheptene-derived tertiary allylic

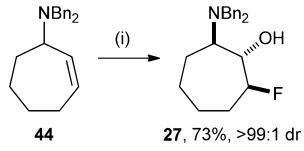
Scheme 12[a]



HBF_4·OEt_2 (equiv)	Ratio 25:26:43
2	74:0:26
5	71:4:25
10	73:9:18
20	71:16:13

[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h. Ar = *m*-ClC_6H_4.

Scheme 13[a]



[a]Reagents and conditions: (i) HBF_4·OEt_2 (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h.

amine **44** (Scheme 13) upon treatment with 2 equiv of HBF_4·OEt_2 and 2 equiv of *m*-CPBA proceeded to give the corresponding amino fluorohydrins **25** and **27** as the major products which, after treatment of the crude reaction mixture with K_2CO_3 in MeOH,[30] were isolated in 46 and 73% yield, respectively. In comparison, the overall yields for the corresponding two-step conversions of tertiary allylic amines **42** and **44** into fluorohydrins **25** and **27** (employing sequential epoxidation[17c,i] and ring-opening fluorination steps) are 77 and 52%, respectively. The stereochemical outcome of the hydroxyfluorination reaction of cyclopentene-derived allylic

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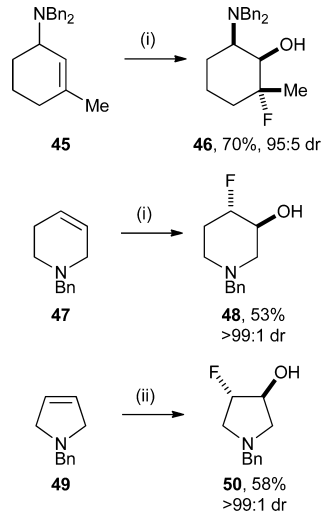
amine **42** is consistent with initial epoxidation occurring on the face of the olefin *syn* to the in situ formed ammonium ion, followed by regioselective and stereospecific S_N2-type epoxide ring-opening occurring upon transfer of fluoride from a BF_4^- ion to the oxirane carbon distal to the ammonium group. Meanwhile, the stereochemical outcome of the hydroxyfluorination reaction of cycloheptene-derived allylic amine **44** is consistent with initial epoxidation occurring on the face of the olefin *anti* to the in situ formed ammonium ion, followed by regioselective and stereospecific S_N2-type epoxide ring-opening occurring upon transfer of fluoride from a BF_4^- ion to the oxirane carbon distal to the ammonium group. In both cases, the diastereoselectivity of the epoxidation reaction and the regioselectivity of the ring-opening step are entirely consistent with that previously observed by us during the ammonium-directed oxidation of these substrates using *m*-CPBA in the presence of Cl_3CCO_2H.[17c,i] In both cases, we have rationalized the selectivity of the epoxidation step as being the result of hydrogen-bonded delivery of the *m*-CPBA by the in situ formed ammonium ion, although in the case of cyclopentene-derived allylic amine **42**, attack on the face of the olefin *syn* to the in situ formed ammonium moiety may be inherently favored due to minimization of developing torsional strain in the transition state.[31] When 20 equiv of $HBF_4{\cdot}OEt_2$ in the hydroxyfluorination of cyclopentene-derived allylic amine **42** was used, a reduction in the reaction diastereoselectivity was apparent, although a complete reversal in the sense of facial selectivity was not observed (Scheme 12). Analogous reaction of cycloheptene-derived allylic amine **44** resulted in the formation of a complex mixture of products, of which the major component was amino fluorohydrin **27**. The observations that the selectivities of the hydroxyfluorinations of 5-membered ring substrate **42** and 7-membered ring substrate **44** do not reverse when using 20 equiv of $HBF_4{\cdot}OEt_2$ is consistent with the much faster rates of ammonium-directed epoxidation of both cyclopentene-derived **42** and cycloheptene-derived **44** under these conditions, as compared to that of their cyclohexene-derived counterpart **29**[17i] (i.e., the hydrogen-bond directed epoxidation would be expected to be the dominant pathway in both of the former cases). This does not, however, discount the possibility that epoxidation *syn* to the ammonium moiety formed in situ from **42** is inherently favored.[31]

Trisubstitution on the olefin was also tolerated by this reaction, with the hydroxyfluorination of allylic amine **45** giving amino fluorohydrin **46** in 95:5 dr, which was isolated in 70% yield and 95:5 dr after purification. The relative configuration within **46** was assigned on the basis of $^1H-^1H$ and $^1H-^{19}F$ NMR ^3J coupling constant and $^1H-^{19}F$ NMR HOESY analyses (Scheme 14). Tetrahydropyridine **47** and dihydropyrrole **49** were also investigated as substrates for this reaction. In the former case, reaction of **47** gave the corresponding 4-fluoropiperidin-3-ol **48** in 53% yield as a single diastereoisomer.[32] In the latter case, 10 equiv of $HBF_4{\cdot}OEt_2$ proved optimal to ensure complete ring-opening of the epoxide, and this enabled the isolation of 4-fluoropyrrolidin-3-ol **50** in 58% yield as a single diastereoisomer.[32] The regiochemistry within **48** was assigned by $^1H-^1H$ NMR COSY analysis, and the relative configurations within both **48** and **50** were assigned on the basis of the reaction proceeding via an S_N2-type epoxide ring-opening step[33] (Scheme 14).

The hydroxyfluorination of acyclic allylic and homoallylic amines was also investigated. Under our optimized conditions,

Scheme 14[a]



[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) $HBF_4{\cdot}OEt_2$ (10 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h.

treatment of tertiary alkenyl amines **51**–**58** with 2 equiv of $HBF_4{\cdot}OEt_2$ and 2 equiv of *m*-CPBA gave the corresponding amino fluorohydrins **60**–**67** as single diastereoisomers (>99:1 dr), which were isolated after chromatography in modest to good yield.[32] We have previously unambiguously established the relative configurations within **60**, **62**, and **67** through single-crystal X-ray diffraction analyses,[25] and therefore, the relative configurations within the remaining amino fluorohydrin products of these reactions were assigned on the basis of our mechanistic proposal for this hydroxyfluorination process. Under analogous conditions, hydroxyfluorination of allylic amine **59** gave a mixture of products containing an 88:12 mixture of amino fluorohydrins **68**:**69**, from which the major product **68** was isolated in 28% yield and >99:1 dr and the minor product **69** in 7% yield and >99:1 dr. The relative configuration within **68** was unambiguously established via single-crystal X-ray diffraction analysis,[25] which therefore allowed the relative configuration within **69** to be assigned (on the basis of a stereospecific S_N2-type epoxide ring-opening). The expected higher level of 1,3-allylic strain[34] associated with allylic amines **57** and **58** as compared to **59** is thus consistent with the higher reaction diastereoselectivity for the former two processes over the latter (Scheme 15).

The synthetic utility of this methodology was next demonstrated by application to the synthesis of 4-deoxy-4-fluoro-L-*xylo*-phytosphingosine and 4-deoxy-4-fluoro-L-*lyxo*-phytosphingosine; fluorinated analogues of the sphingoid bases L-*xylo*-phytosphingosine and L-*lyxo*-phytosphingosine, respectively.[35] The allylic amine substrate required for these reactions was prepared from Garner's aldehyde **70**. Wittig olefination of **70** upon treatment with $[C_{15}H_{31}PPh_3]^+Br^-$ and NaHMDS gave a mixture of olefin isomers (*Z*)-**71** and (*E*)-**72**, although peak overlap in the ^1H NMR spectrum of the crude reaction mixture precluded determination of the (*E*):(*Z*) ratio. Chromatography allowed separation of (*Z*)-**71** and (*E*)-**72**, which were isolated in 77 and 7% yield, respectively. Treatment of (*Z*)-**71** with $HBF_4{\cdot}OEt_2$ (either 2 equiv or 20 equiv) followed by *m*-CPBA (2 equiv) was investigated in the hope of achieving a one-pot sequential *N*-deprotection, ammonium-

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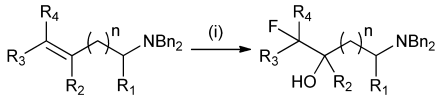
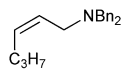
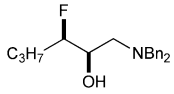
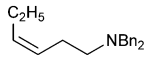
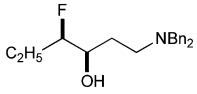
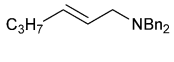
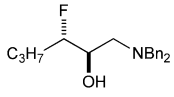
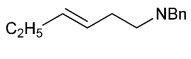
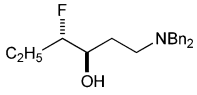
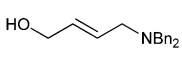
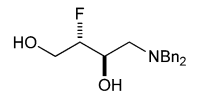
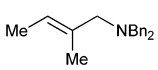
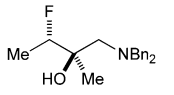
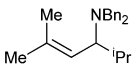
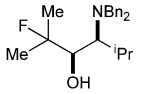
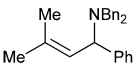
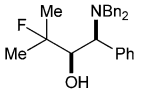
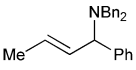
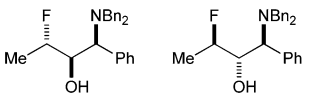
Scheme 15[a]



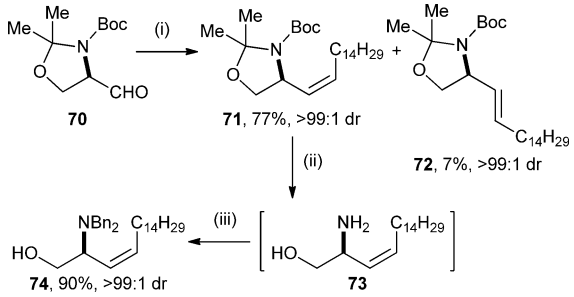
51-59, n = 0 or 1 **60-69**, n = 0 or 1

Alkenyl Amine	Amino Fluorohydrin Product(s)
	
51, >99:1 dr	**60**, 57%, >99:1 dr
	
52, >99:1 dr	**61**, 24%, >99:1 dr
	
53, >99:1 dr	**62**, 53%, >99:1 dr
	
54, >99:1 dr	**63**, 48%, >99:1 dr
	
55, >99:1 dr[b]	**64**, 32%, >99:1 dr[b]
	
56, >99:1 dr	**65**, 56%, >99:1 dr
	
57[c]	**66**, 82% (98%),[c] >99:1 dr[d]
	
58	**67**, 76% (61%),[c] >99:1 dr
	
59, >99:1 dr[d]	**68**, 28%, >99:1 dr[e] **69**, 7%, >99:1 dr[e]

[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h. [b]Reaction was run with 10 equiv of $HBF_4{\cdot}OEt_2$. [c]Yields in parentheses are for the corresponding two-step (sequential epoxidation[17e] and ring-opening fluorination[16]) processes. [d]Reaction was run for 30 min. [e]Reaction produced an 88:12 diastereoisomeric mixture of amino fluorohydrins **68**:**69**.

directed epoxidation, and ring-opening fluorination, but unfortunately, only a complex mixture of products was furnished in both cases. Therefore, in order to provide an alternative substrate for evaluation, hydrolysis of the *N*,*O*-acetonide and *N*-Boc protecting groups within (*Z*)-**71** was achieved using methanolic HCl, and was followed by treatment with BnBr in the presence of K_2CO_3 to give **74** in 90% yield (Scheme 16).

Scheme 16[a]



70 **71**, 77%, >99:1 dr **72**, 7%, >99:1 dr

74, 90%, >99:1 dr **73**

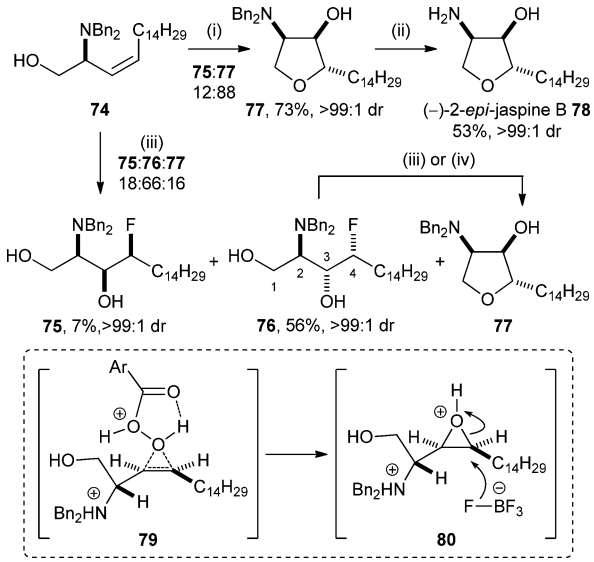
[a]Reagents and conditions: (i) $[C_{15}H_{31}PPh_3]^+Br^-$, NaHMDS, THF, hexane, −78 °C to rt, 42 h; (ii) HCl (conc aq), MeOH, reflux, 17 h; (iii) BnBr, K_2CO_3, EtOH, reflux, 4 h.

Hydroxyfluorination of **74** upon treatment with $HBF_4{\cdot}OEt_2$ (20 equiv) and *m*-CPBA (2 equiv) for 18 h gave a 12:88 mixture of amino fluorohydrin **75** and the functionalized tetrahydrofuran **77**. Chromatography allowed isolation of **77** in 73% yield as a single diastereoisomer. The relative configuration within **77** was established through hydrogenolysis, which gave (−)-2-*epi*-jaspine B [(−)-2-*epi*-pachasstrissamine] **78**[36] in 53% yield. Optimization of the reaction conditions revealed that the use of 4 equiv of *m*-CPBA and a reaction time of 30 min resulted in >95% conversion of starting material to give an 18:66:16 mixture of amino fluorohydrins **75** and **76** and functionalized tetrahydrofuran **77**, respectively. Chromatographic separation gave amino fluorohydrin **76** in 56% isolated yield and >99:1 dr. Resubjection of the authentic sample of **76** to the reaction conditions resulted in formation of tetrahydrofuran **77** as the only product. Thus, the C(2)−C(3) relative configuration within **76** could be unambiguously assigned, and is consistent with the epoxidation step proceeding preferentially via transition-state model **79**, in which 1,3-allylic strain is minimized and the epoxidation proceeds on the face of the olefin *anti* to the ammonium group to give epoxide **80** as the major product. Subsequent in situ regioselective and stereospecific S_N2-type ring-opening of **80** by transfer of fluoride from a BF_4^- ion to the oxirane carbon atom distal to the ammonium moiety leads to amino fluorohydrin **76**, with BF_3 assisted[37] S_N2-type (5-*exo*-*tet*)[38] cyclization of **76** under the reaction conditions leading to tetrahydrofuran **77**. In support of this assertion, treatment of amino fluorohydrin **76** with 2 equiv of $HBF_4{\cdot}OEt_2$ led only to the return of unreacted starting material after 18 h, while sequential treatment with 1 equiv of $HBF_4{\cdot}OEt_2$ followed by 1 equiv of $BF_3{\cdot}OEt_2$ for 18 h gave complete conversion to tetrahydrofuran **77** (quantitative isolated yield). From these combined data, it can be deduced that the intermediate epoxide **80** is formed in 82:18 dr under these reaction conditions (Scheme 17).

Allylic amine **74** was next treated with 2 equiv of $HBF_4{\cdot}OEt_2$ followed by 2 equiv of *m*-CPBA and, after a reaction time of 18 h, gave a 67:16:18 mixture of amino fluorohydrins **75** and **76**, and the functionalized tetrahydrofuran **81**, respectively. The observation of amino fluorohydrin **75** as the major product in this reaction indicates opposite sense of diastereofacial selectivity as compared to the analogous reaction using 20 equiv of $HBF_4{\cdot}OEt_2$. Purification allowed the isolation of amino

dx.doi.org/10.1021/jo301056r | J. Org. Chem. 2012, 77, 7262−7281

Scheme 17[a]

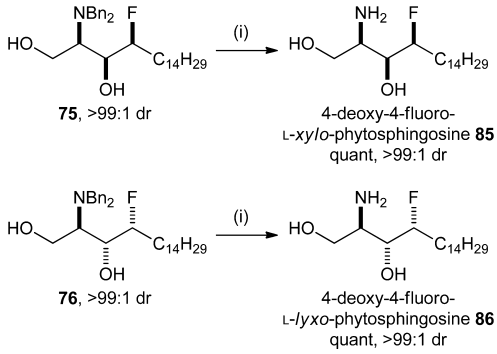


[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (20 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) H_2 (1 atm), $Pd(OH)_2/C$, MeOH, rt, 24 h; (iii) $HBF_4{\cdot}OEt_2$ (20 equiv), CH_2Cl_2 then *m*-CPBA (4 equiv), rt, 30 min; (iv) $HBF_4{\cdot}OEt_2$ (1 equiv), $BF_3{\cdot}OEt_2$ (1 equiv), CH_2Cl_2, rt, 18 h. Ar = *m*-ClC_6H_4.

fluorohydrin **75** in 47% yield and tetrahydrofuran **81** in 14% yield. The relative configuration within amino fluorohydrin **75** was assigned on the basis of an ammonium-directed epoxidation of **74** (via transition state model **83** in which 1,3-allylic strain is minimized) to give the corresponding protonated epoxide **84**, which undergoes in situ regioselective S_N2-type ring-opening by transfer of fluoride from a BF_4^- ion to the oxirane carbon atom distal to the ammonium group. The relative configuration within tetrahydrofuran **81** was unambiguously established through hydrogenolysis, which gave (+)-4-*epi*-jaspine B [(+)-4-*epi*-pachastrissamine] **82**[39] in 92% yield. A plausible mechanism for the production of **81** under the conditions of the hydroxyfluorination reaction would involve direct cyclization of the terminal hydroxy group onto the epoxide functionality within **84**.[40] Furthermore, resubjection of amino fluorohydrin **75** to the reaction conditions led only to the recovery of starting material (i.e., **75**), indicating that tetrahydrofuran **81** does not arise from the in situ cyclization of **75**. From these combined data it can be deduced that the intermediate epoxide **84** is formed in 84:16 dr under these reaction conditions (Scheme 18).

Hydrogenolytic *N*-debenzylation of **75** completed the synthesis of 4-deoxy-4-fluoro-L-*xylo*-phytosphingosine **85**, in five steps and 33% overall yield from Garner's aldehyde **70**, while an analogous procedure applied to amino fluorohydrin **76** gave 4-deoxy-4-fluoro-L-*lyxo*-phytosphingosine **86**, in five steps and 39% overall yield from Garner's aldehyde **70** (Scheme 19).

Scheme 19[a]

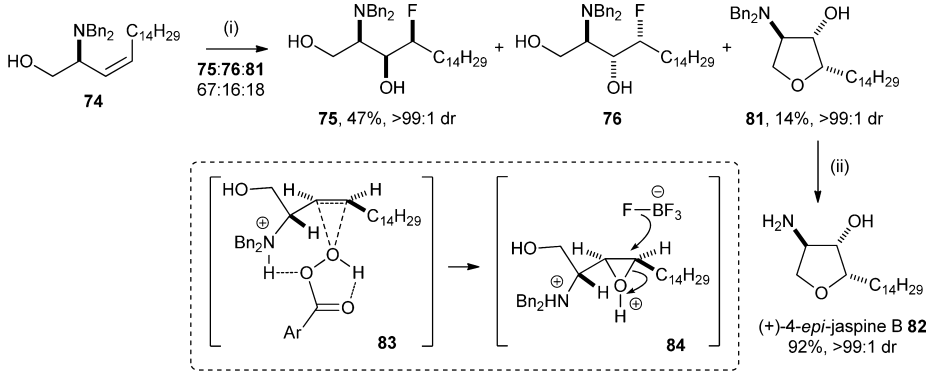


[a]Reagents and conditions: (i) H_2 (1 atm), $Pd(OH)_2/C$, MeOH, rt, 24 h.

CONCLUSION

In conclusion, a diastereodivergent hydroxyfluorination protocol enabling the direct conversion of conformationally biased allylic amines to the corresponding diastereoisomeric amino fluorohydrins has been developed. Sequential treatment of a conformationally biased allylic amine with 2 equiv of $HBF_4{\cdot}OEt_2$ followed by *m*-CPBA promotes epoxidation of the olefin on the face proximal to the amino group, under hydrogen-bonded direction from the in situ formed ammonium ion. Regioselective and stereospecific epoxide ring-opening by transfer of fluoride from a BF_4^- ion (an S_N2-type process at the carbon atom distal to the ammonium moiety) then occurs in situ to give the corresponding amino fluorohydrin. Alternatively, an analogous reaction using 20 equiv of $HBF_4{\cdot}OEt_2$ results in preferential epoxidation of the opposite face of the olefin, which is followed by regioselective and stereospecific

Scheme 18[a]



[a]Reagents and conditions: (i) $HBF_4{\cdot}OEt_2$ (2 equiv), CH_2Cl_2 then *m*-CPBA (2 equiv), rt, 18 h; (ii) H_2 (5 atm), $Pd(OH)_2/C$, EtOAc, rt, 4.5 h. Ar = *m*-ClC_6H_4.

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epoxide ring-opening by transfer of fluoride from a BF_4^- ion (an S_N2-type process at the carbon atom distal to the ammonium moiety). The synthetic utility of this methodology is demonstrated via its application to a synthesis of 4-deoxy-4-fluoro-L-*xylo*-phytosphingosine and 4-deoxy-4-fluoro-L-*lyxo*-phytosphingosine, each in five steps from Garner's aldehyde.

EXPERIMENTAL SECTION

General Experimental Details. Reactions involving moisture-sensitive reagents were carried out under a nitrogen atmosphere using standard vacuum line techniques and glassware that was flame-dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[41] *m*-CPBA was supplied as a 70−77% slurry in water and titrated according to the procedure of Swern[42] before use. Dry 0.5 M solutions of *m*-CPBA were freshly prepared by treating a solution of titrated *m*-CPBA (70−77% with H_2O) in CH_2Cl_2 with $MgSO_4$, followed by filtration of the supernatant solution through a Pasteur pipet (packed to half depth with $MgSO_4$) into a volumetric flask, and addition of further CH_2Cl_2 as necessary. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminum plates coated with 60 F_{254} silica. 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. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. $^1H-^1H$ COSY and $^1H-^{13}C$ HMQC analyses were used to establish atom connectivity. Accurate mass measurements were run on a MicroTOF instrument internally calibrated with polyalanine.

General Procedure 1 for Ring-Opening Fluorination of Epoxy Amines with HBF_4·OEt_2. HBF_4·OEt_2 (2 equiv) was added in one portion to a stirred solution of the requisite epoxy amine (1 equiv, 0.25 M in CH_2Cl_2) at rt, and the reaction mixture was stirred at this temperature for 5 min. Satd aq $NaHCO_3$ was then added, and the layers were separated. The organic layer was washed twice with satd aq $NaHCO_3$, and the combined aqueous layers were extracted twice with CH_2Cl_2. The combined organic layers were then dried and concentrated in vacuo.

General Procedure 2 for Hydroxyfluorination of Alkenyl Amines with HBF_4·OEt_2 and *m*-CPBA. HBF_4·OEt_2 was added to a stirred solution of the requisite alkenyl amine (1 equiv in CH_2Cl_2)[43] at rt and the resultant mixture was stirred at this temperature for 5 min. A predried solution of *m*-CPBA (2 equiv, 0.5 M in CH_2Cl_2) was added, and the resultant mixture was stirred at rt for the time stated. Satd aq Na_2SO_3 was then added until starch−iodide paper indicated no remaining oxidant. Satd aq $NaHCO_3$ was added, and the layers were separated. The organic layer was washed twice with satd aq $NaHCO_3$, and the combined aqueous layers were extracted twice with CH_2Cl_2. The combined organic layers were then dried and concentrated in vacuo.

(*RS*,*RS*,*RS*)-2-(*N*,*N*-Dibenzylamino)-6-fluorocyclohexan-1-ol (6). Following general procedure 1, **4**[17a] (108 mg, 0.37 mmol, >99:1 dr) in CH_2Cl_2 (1.5 mL) was treated with HBF_4·OEt_2 (100 μL, 0.74 mmol). Purification via flash column chromatography (gradient elution, 5→40% EtOAc in 30−40 °C petroleum ether) gave **6** as a colorless syrup which solidified on standing to a white crystalline solid (117 mg, quant, >99:1 dr):[16] R_f 0.46 (30−40 °C petroleum ether/EtOAc, 4:1); mp 74−77 °C; δ_H (400 MHz, $CDCl_3$) 1.43−1.87 (6H, m, C(3)H_2, C(4)H_2, C(5)H_2), 2.95 (1H, br s, O*H*), 3.01−3.09 (1H, m, C(2)*H*), 3.82 (4H, A_2, N(CH_2Ph)$_2$), 4.17−4.24 (1H, app dt, *J* 6.3, 3.3, C(1)*H*), 4.84 (1H, app dq, *J* 45.5, 3.0, C(6)*H*), 7.22−7.37 (10H, m, *Ph*).

(*RS*,*RS*,*RS*)-2-(*N*-Benzyl-*N*-methylamino)-6-fluorocyclohexan-1-ol (7). From **5**: Following general procedure 1, **5**[17i] (217 mg, 1.00 mmol, >99:1 dr) in CH_2Cl_2 (4.0 mL) was treated with HBF_4·OEt_2 (0.27 mL, 2.0 mmol). Purification via flash column chromatography on neutralized silica gel (gradient elution, 7→60% EtOAc in 30−40 °C petroleum ether) gave **7** as a yellow oil (211 mg, 89%, >99:1 dr):[16] R_f 0.28 (30−40 °C petroleum ether/EtOAc, 7:3; neutralized silica gel); δ_H (400 MHz, $CDCl_3$) 1.44−1.93 (6H, m, C(3)H_2, C(4)H_2, C(5)H_2), 2.21 (3H, s, N*Me*), 2.63 (1H, dddd, *J* 11.6, 4.7, 2.9, 2.6, C(2)*H*), 3.43 (1H, br s, O*H*), 3.56 (1H, d, *J* 13.4, NCH_A), 3.74 (1H, d, *J* 13.4, NCH_B), 4.20 (1H, app dt, *J* 6.1, 3.1, C(1)*H*), 4.93 (1H, app dq, *J* 45.4, 3.1, C(6)*H*), 7.24−7.38 (5H, m, *Ph*).

From **34**: Following general procedure 2, **34** (161 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h to give an 85:3:12 mixture of **7**:**24**:**35**. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo to give an 85:3:12 mixture of **7**:**24**:**36**. Purification via flash column chromatography (gradient elution, 7→60% EtOAc in 30−40 °C petroleum ether) gave **7** as a yellow oil (139 mg, 73%, >99:1 dr).

(1*RS*,2*RS*,3*SR*)-1-(*N*,*N*-Dibenzyl-*N*-methylammonio)-2,3-epoxycyclohexane Tetrafluoroborate (15). Step 1: BnBr (0.36 mL, 3.0 mmol) was added to a stirred solution of **5**[17i] (652 mg, 3.00 mmol, >99:1 dr) in MeCN (15 mL), and the resultant mixture was heated at reflux for 22 h and then was allowed to cool to rt and concentrated in vacuo. The residue was triturated with Et_2O, and the precipitate was collected by filtration and washed with Et_2O to give **14** as a hygroscopic pale orange solid (1.14 g, 98%, >99:1 dr): ν_{max} 3004, 2924 (C−H), 1497, 752, 703; δ_H (400 MHz, $CDCl_3$) 1.27−1.42 (1H, m, C(5)H_A), 1.67−1.91 (3H, m, C(4)H_2, C(5)H_B), 1.98−2.11 (1H, m, C(6)H_A), 2.18−2.30 (1H, m, C(6)H_B), 3.02 (3H, s, N*Me*), 3.30−3.38 (1H, m, C(3)*H*), 3.84 (1H, app d, *J* 4.0, C(2)*H*), 4.04−4.13 (1H, m, C(1)*H*), 4.60 (1H, d, *J* 13.3, N($CH_AH_BPh)_A$), 4.90 (1H, d, *J* 12.9, N($CH_AH_BPh)_B$), 5.21 (1H, d, *J* 12.9, N($CH_AH_BPh)_B$), 5.40 (1H, d, *J* 13.3, N($CH_AH_BPh)_A$), 7.34−7.73 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.2 (*C*(5)), 20.9 (*C*(6)), 21.7 (*C*(4)), 46.3 (N*Me*), 49.5 (*C*(2)), 54.4 (*C*(3)), 64.1 (N($CH_2Ph)_A$), 64.5 (N($CH_2Ph)_B$), 68.3 (*C*(1)), 127.3, 129.4, 130.7, 130.8, 133.2, 133.6 (*Ph*); *m*/*z* (ESI$^+$) 308 ([M]$^+$, 100); HRMS (ESI$^+$) $C_{21}H_{26}NO^+$ ([M]$^+$) requires 308.2009, found 308.2001.

Step 2: MeCN (82 μL, 1.6 mmol) and CH_2Cl_2 (2.5 mL) were added sequentially to $AgBF_4$ (68.1 mg, 0.35 mmol), and the resultant solution was added to a stirred solution of **14** (136 mg, 0.35 mmol, >99:1 dr) in CH_2Cl_2 (1.0 mL). The resultant mixture was stirred at rt for 5 min and then filtered and concentrated in vacuo to give **15** as a hygroscopic white solid (138 mg, quant, >99:1 dr): ν_{max} 3036, 2956 (C−H), 1050, 1030, 754, 727, 703; δ_H (400 MHz, $CDCl_3$) 1.30−1.44 (1H, m, C(5)H_A), 1.71−1.94 (3H, m, C(4)H_2, C(5)H_B) 1.99−2.19 (2H, m, C(6)H_2), 2.93 (3H, s, N*Me*), 3.34−3.39 (1H, m, C(3)*H*), 3.65 (1H, app d, *J* 4.0, C(2)*H*), 3.81 (1H, app dd, *J* 9.1, 5.6, C(1)*H*), 4.36 (1H, d, *J* 13.4, N($CH_AH_BPh)_A$), 4.54 (1H, d, *J* 12.9, N($CH_AH_BPh)_B$), 4.82−4.93 (2H, m, N($CH_AH_BPh)_A$, N($CH_AH_BPh)_B$), 7.38−7.56 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.7 (*C*(6)), 20.3 (*C*(5)), 21.6 (*C*(4)), 46.0 (N*Me*), 48.9 (*C*(2)), 54.4 (*C*(3)), 64.0 (N($CH_2Ph)_A$), 64.5 (N($CH_2Ph)_B$), 68.2 (*C*(1)), 126.7, 129.5, 130.9, 131.0, 132.9, 133.4 (*Ph*); δ_F (377 MHz, $CDCl_3$) −151.2 (s); *m*/*z* (ESI$^+$) 308 ([M]$^+$, 100); HRMS (ESI$^+$) $C_{21}H_{26}NO^+$ ([M]$^+$) requires 308.2009, found 308.2003.

(*RS*,*RS*,*RS*)-1-(*N*,*N*-Dibenzyl-*N*-methylammonio)-3-fluorocyclohexan-2-ol Tetrafluoroborate (17). From **7**: Step 1: BnBr (172 μL, 1.45 mmol) was added to a stirred solution of **7** (344 mg, 1.45 mmol, >99:1 dr) in MeCN (7.2 mL), and the resultant mixture was heated at reflux for 22 h, allowed to cool to rt, and concentrated in vacuo. The residue was triturated with Et_2O, and the precipitate was collected by filtration and washed with Et_2O to give **16** as a hygroscopic pale brown solid (592 mg, quant, >99:1 dr): δ_H (400 MHz, $CDCl_3$) 1.50−1.95 (4H, m, C(4)H_2, C(5)H_2), 2.30−2.55 (2H, m, C(6)H_2), 3.02 (3H, s, N*Me*), 3.36 (1H, app d, *J* 12.1, C(1)*H*), 4.37

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(1H, d, *J* 13.1, N(C$H_A$$H_B$Ph)$_A$), 4.53 (1H, d, *J* 13.0, N(C$H_A$$H_B$Ph)$_B$), 4.65−4.88 (2H, m, C(2)*H*, C(3)*H*), 4.97 (1H, d, *J* 13.1, N(CH$_A$$H_B$Ph)$_A$), 5.60 (1H, d, *J* 13.0, N(CH$_A$$H_B$Ph)$_B$), 6.08 (1H, d, *J* 6.8, O*H*), 7.27−7.51 (8H, m, *Ph*), 7.76−7.84 (2H, m, *Ph*).

Step 2: MeCN (71 μL, 1.4 mmol) and CH_2Cl_2 (2.0 mL) were added sequentially to $AgBF_4$ (58.4 mg, 0.30 mmol), the resultant solution was added to a stirred solution of **16** (123 mg, 0.30 mmol, >99:1 dr) in CH_2Cl_2 (1.0 mL), and the mixture was stirred at rt for 5 min, filtered, and concentrated in vacuo to give **17** as a hygroscopic white solid (121 mg, 97%, >99:1 dr): ν_{max} 3500 (O−H), 3036, 2953, 2876 (C−H), 1057, 1033, 1009, 750, 726, 703; δ_H (400 MHz, $CDCl_3$) 1.50−1.95 (4H, m, C(4)H_2, C(5)H_2), 2.26−2.45 (2H, m, C(6)H_2), 2.83 (3H, s, N*Me*), 3.39 (1H, d, *J* 11.9, C(1)*H*), 4.28 (1H, d, *J* 13.4, N(C$H_A$$H_B$Ph)$_A$), 4.37−4.47 (2H, m, N(C$H_A$$H_B$Ph)$_B$, O*H*), 4.63−4.83 (3H, m, C(2)*H*, C(3)*H*, N(CH$_A$$H_B$Ph)$_A$), 5.32 (1H, d, *J* 12.9, N(CH$_A$$H_B$Ph)$_B$), 7.23−7.60 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.6 (d, *J* 32.8, *C*(4)), 24.1 (d, *J* 20.0, *C*(5)), 29.7 (*C*(6)), 45.4 (N*Me*), 64.1, 64.7, 64.8, 65.1 (*C*(2), N(CH_2Ph)$_2$), 67.3 (*C*(1)), 91.3 (d, *J* 175, *C*(3)), 126.6, 127.0, 129.3, 129.5, 130.8, 131.1, 132.6, 133.6 (*Ph*); δ_F (377 MHz, $CDCl_3$) −187.2 (m), −150.9 (s, BF_4^-); *m*/*z* (ESI$^+$) 328 ([M]$^+$, 100); HRMS (ESI$^+$) $C_{21}H_{27}FNO^+$ ([M]$^+$) requires 328.2071, found 328.2069.

From **15**: HBF_4·OEt_2 (8.6 μL, 0.06 mmol) was added to a stirred solution of **15** (25.0 mg, 0.06 mmol, >99:1 dr) in CD_2Cl_2 (0.25 mL) at rt, and the resultant mixture was stirred at rt for 5 min. Satd aq $NaBF_4$ (10 mL) and CH_2Cl_2 (10 mL) were added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried ($NaBF_4$) and concentrated in vacuo to give **17** as a colorless oil (26.3 mg, quant, >99:1 dr).

(1*RS*,2*SR*,6*RS*)-2-(*N*,*N*-Dibenzylamino)-6-fluorocyclohexan-1-ol (23). Following general procedure 1, **18**[17b] (402 mg, 1.37 mmol, >99:1 dr) in CH_2Cl_2 (5.5 mL) was treated with HBF_4·OEt_2 (0.37 mL, 2.7 mmol). Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **23** as a colorless oil which solidified on standing to a white crystalline solid (314 mg, 73%, >99:1 dr):[16] R_f 0.26 (30−40 °C petroleum ether/Et_2O, 4:1); mp 77−79 °C; δ_H (400 MHz, $CDCl_3$) 1.08−1.22 (1H, m, C(4)H_A), 1.29 (1H, app qd, *J* 12.6, 3.3, C(3)H_A), 1.40−1.54 (1H, m, C(5)H_A), 1.80−1.90 (1H, m, C(4)H_B), 1.90−1.98 (1H, m, C(3)H_B), 2.03−2.13 (1H, m, C(5)H_B), 2.37−2.47 (1H, app td, *J* 11.0, 2.8, C(2)*H*), 3.40 (2H, d, *J* 13.1, N(C$H_A$$H_B$Ph)$_2$), 3.62 (1H, ddd, *J* 13.0, 10.0, 8.4, C(1)*H*), 3.76 (1H, br s, O*H*), 3.90 (2H, d, *J* 13.1, N(CH$_A$$H_B$Ph)$_2$), 4.23 (1H, dddd, *J* 51.5, 11.3, 8.4, 5.2, C(6)*H*), 7.24−7.38 (10H, m, *Ph*).

(1*RS*,2*SR*,6*RS*)-2-(*N*-Benzyl-*N*-methylamino)-6-fluorocyclohexan-1-ol (24). Following general procedure 1, **19**[17i] (217 mg, 1.00 mmol, >99:1 dr) in CH_2Cl_2 (4.0 mL) was treated with HBF_4·OEt_2 (0.27 mL, 2.0 mmol). Purification via flash column chromatography on neutralized silica gel (gradient elution, 2→20% EtOAc in 30−40 °C petroleum ether) gave **24** as a colorless oil which solidified on standing to a white crystalline solid (169 mg, 71%, >99:1 dr):[16] R_f 0.13 (30−40 °C petroleum ether/EtOAc, 9:1; neutralized silica gel); mp 77−79 °C; δ_H (400 MHz, $CDCl_3$) 1.15−1.32 (2H, m, C(3)H_A, C(4)H_A), 1.40−1.56 (1H, m, C(5)H_A), 1.76−1.94 (2H, m, C(3)H_B, C(4)H_B), 2.07−2.17 (1H, m, C(5)H_B), 2.22 (3H, s, N*Me*), 2.35−2.45 (1H, m, C(2)*H*), 3.47 (1H, d, *J* 13.0, NCH_A), 3.55 (1H, ddd, *J* 12.8, 10.2, 8.3, C(1)*H*), 3.74 (1H, d, *J* 13.0, NCH_B), 4.37 (1H, dddd, *J* 51.5, 11.2, 8.3, 5.2, C(6)*H*), 7.24−7.37 (5H, m, *Ph*).

(*RS*,*RS*,*RS*)-2-(*N*,*N*-Dibenzylamino)-5-fluorocyclopentan-1-ol (25). From **20**: Following general procedure 1, **20**[17c] (140 mg, 0.50 mmol, >99:1 dr) in CH_2Cl_2 (2.0 mL) was treated with HBF_4·OEt_2 (136 μL, 1.00 mmol). Purification via flash column chromatography (gradient elution, 2→20% EtOAc in 30−40 °C petroleum ether) gave **25** as a white crystalline solid (118 mg, 78%, >99:1 dr): R_f 0.31 (30−40 °C petroleum ether/EtOAc, 9:1); mp 68−71 °C; ν_{max} 3457 (O−H), 3085, 3063, 3029, 2967, 2942, 2919, 2847 (C−H), 1494, 1453, 1046; δ_H (400 MHz, $CDCl_3$) 1.67−1.91 (2H, m, C(3)H_A, C(4)H_A), 1.95−2.07 (1H, m, C(4)H_B), 2.21−2.41 (1H, m, C(3)H_B), 3.27−3.37 (1H, m, C(2)*H*), 3.50 (1H, br s, O*H*), 3.74 (4H, A_2 system, N(CH_2Ph)$_2$), 4.16 (1H, dd, *J* 10.2, 4.1, C(1)*H*), 4.95 (1H, app ddd, *J* 50.9, 6.5, 1.7, C(5)*H*), 7.24−7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 26.9 (*C*(3)), 29.5 (d, *J* 22.4, *C*(4)), 55.7 (N(CH_2Ph)$_2$), 65.5 (*C*(2)), 74.1 (d, *J* 30.4, *C*(1)), 97.3 (d, *J* 174, *C*(5)), 127.3 (*p*-*Ph*), 128.5, 129.0 (*o*,*m*-*Ph*), 138.2 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −176.8 (m); *m*/*z* (ESI$^+$) 300 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{19}H_{23}FNO^+$ ([M + H]$^+$) requires 300.1758, found 300.1756. Anal. Calcd for $C_{19}H_{22}FNO$: C, 76.2; H, 7.4; N, 4.7. Found: C, 76.4; H, 7.4; N, 4.6.

From **42**: Following general procedure 2, **42** (211 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h to give a 74:26 mixture of **25**:**43**. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% EtOAc in 30−40 °C petroleum ether) gave **25** as a white crystalline solid (110 mg, 46%, >99:1 dr).

(1*RS*,2*SR*,5*RS*)-2-(*N*,*N*-Dibenzylamino)-5-fluorocyclopentan-1-ol (26) and (*RS*,*RS*,*RS*)-*N*(2)-Benzyl-4,5-benzo-2-azabicyclo-[4.2.1]nonan-9-ol (28). Following general procedure 1, **21**[17c] (140 mg, 0.50 mmol, >99:1 dr) in CH_2Cl_2 (2.0 mL) was treated with HBF_4·OEt_2 (136 μL, 1.00 mmol) to give a 35:65 mixture of **26**:**28**. Purification via flash column chromatography (gradient elution, 5→40% EtOAc in 30−40 °C petroleum ether) gave **26** as a white crystalline solid (52.2 mg, 35%, >99:1 dr): R_f 0.28 (30−40 °C petroleum ether/EtOAc, 4:1); mp 79−81 °C; ν_{max} 3419 (O−H), 3085, 3062, 3028, 3004, 2962, 2882, 2836, 2805 (C−H), 1494, 1454, 1365, 1075, 1056, 1028; δ_H (400 MHz, $CDCl_3$) 1.73−2.26 (5H, m, C(3)H_2, C(4)H_2, O*H*), 3.02 (1H, app dd, *J* 8.9, 8.0, C(2)*H*), 3.58 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.82 (2H, d, *J* 13.9, N(CH$_A$$H_B$Ph)$_2$), 4.21 (1H, ddd, *J* 23.2, 8.0, 3.8, C(1)*H*), 4.66−4.86 (1H, m, C(5)*H*), 7.22−7.42 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.9 (*C*(3)), 27.7 (d, *J* 22.4, *C*(4)), 54.9 (N(CH_2Ph)$_2$), 65.9 (*C*(2)), 77.9 (d, *J* 24.0, *C*(1)), 98.1 (d, *J* 179, *C*(5)), 127.1 (*p*-*Ph*), 128.4, 128.6 (*o*,*m*-*Ph*), 139.7 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −180.5 (m); *m*/*z* (ESI$^+$) 621 ([2M + Na]$^+$, 100), 322 ([M + Na]$^+$, 92), 300 ([M + H]$^+$, 86); HRMS (ESI$^+$) $C_{19}H_{23}FNO^+$ ([M + H]$^+$) requires 300.1758, found 300.1756. Further elution gave **28** as a white crystalline solid (77.4 mg, 55%, >99:1 dr): R_f 0.08 (30−40 °C petroleum ether/EtOAc, 4:1); mp 139−143 °C; ν_{max} 3385 (O−H), 3062, 3027, 2923 (C−H), 1493, 1452, 1028; δ_H (400 MHz, $CDCl_3$) 1.65 (1H, br s, O*H*), 1.96−2.15 (2H, m, C(7)H_A, C(8)H_A), 2.31−2.43 (1H, m, C(7)H_B), 2.43−2.55 (1H, m, C(8)H_B), 3.24 (1H, app d, *J* 9.4, C(1)*H*), 3.35 (1H, d, *J* 15.9, C(3)H_A), 3.54 (1H, app d, *J* 6.6, C(6)*H*), 3.62 (1H, d, *J* 13.4, NC$H_A$$H_B$Ph), 3.74 (1H, d, *J* 13.4, NCH$_A$$H_B$Ph), 4.20 (1H, d, *J* 15.9, C(3)H_B), 4.26 (1H, s, C(9)*H*), 6.94 (1H, app d, *J* 7.3, *Ar*), 7.06−7.14 (1H, m, *Ar*), 7.19 (2H, app d, *J* 4.0, *Ar*), 7.24−7.41 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 28.7 (*C*(7)), 29.5 (*C*(8)), 51.2 (*C*(3)), 54.5 (*C*(1)), 57.2 (NCH_2Ph), 71.5 (*C*(6)), 76.9 (*C*(9)), 126.0, 127.1, 127.4, 128.4, 129.0, 129.1, 130.8, 138.2, 139.3, 143.2 (*Ar*, *Ph*); *m*/*z* (ESI$^+$) 280 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{19}H_{22}NO^+$ ([M + H]$^+$) requires 280.1696, found 280.1694. Anal. Calcd for $C_{19}H_{21}NO$: C, 81.7; H, 7.6; N, 5.0. Found: C, 81.8; H, 7.4; N, 4.9.

(1*RS*,2*SR*,7*RS*)-2-(*N*,*N*-Dibenzylamino)-7-fluorocycloheptan-1-ol (27). From **22**: Following general procedure 1, **22**[17c] (307 mg, 1.00 mmol, >99:1 dr) in CH_2Cl_2 (4.0 mL) was treated with HBF_4·OEt_2 (0.27 mL, 2.0 mmol). Purification via flash column chromatography (gradient elution, 5→40% EtOAc in 30−40 °C petroleum ether) gave **27** as a colorless oil which solidified on standing to a white crystalline solid (247 mg, 75%, >99:1 dr): R_f 0.36 (30−40 °C petroleum ether/EtOAc, 9:1); mp 81−82 °C ($CHCl_3$/heptane); ν_{max} 3375 (O−H), 3105, 3086, 3062, 3028, 3006, 2937, 2863, 2813 (C−H), 1495, 1454; δ_H (400 MHz, $CDCl_3$) 1.25−1.50 (3H, m, C(3)H_A, C(4)H_A, C(5)H_A), 1.56−1.93 (4H, m, C(4)H_B, C(5)H_B, C(6)H_2), 1.99−2.11 (1H, m, C(3)H_B), 2.46 (1H, app t, *J* 10.0, C(2)*H*), 3.34 (2H, d, *J* 13.3, N(C$H_A$$H_B$Ph)$_2$), 3.73 (1H, ddd, *J* 19.3, 9.9, 6.1, C(1)*H*), 3.86 (2H, d, *J* 13.3, N(CH$_A$$H_B$Ph)$_2$), 4.35 (1H, dddd, *J* 47.2,

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8.8, 6.1, 3.4, C(7)*H*), 4.72 (1H, s, O*H*), 7.23−7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.0 (d, *J* 9.6, *C*(5)), 21.9 (*C*(3)), 25.4 (*C*(4)), 29.0 (d, *J* 21.6, *C*(6)), 53.1 ($N(CH_2Ph)_2$), 58.7 (d, *J* 10.4, *C*(2)), 74.5 (d, *J* 22.4, *C*(1)), 97.6 (d, *J* 169, *C*(7)), 127.5 (*p-Ph*), 128.6, 129.2 (*o,m-Ph*), 138.4 (*i-Ph*); δ_F (377 MHz, $CDCl_3$) −171.2 (m); *m*/*z* (ESI^+) 677 ($[2M + Na]^+$, 100), 328 ($[M + H]^+$, 96); HRMS (ESI^+) $C_{21}H_{27}FNO^+$ ($[M + H]^+$) requires 328.2071, found 328.2067. Anal. Calcd for $C_{21}H_{26}FNO$: C, 77.0; H, 8.0; N, 4.3. Found: C, 76.8; H, 7.9; N, 4.2.

From **44**: Following general procedure 2, **44** (175 mg, 0.60 mmol) in CH_2Cl_2 (3.4 mL) was treated with $HBF_4{\cdot}OEt_2$ (165 μL, 1.21 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.4 mL, 1.2 mmol) for 18 h. K_2CO_3 (8.3 mg, 0.06 mmol) and MeOH (1.5 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% EtOAc in 30−40 °C petroleum ether) gave **27** as a white crystalline solid (144 mg, 73%, >99:1 dr).

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclohex-1-ene (29). Dibenzylamine (18 mL, 94 mmol) was added to 3-bromocyclohex-1-ene (6.00 g, 37.3 mmol) at 0 °C, and the resultant mixture was allowed to warm to rt and then heated at 60 °C for 30 min. The residue was allowed to cool to rt and was partitioned between CH_2Cl_2 (400 mL) and H_2O (400 mL). The organic layer was separated and washed sequentially with 10% aq citric acid (3 × 200 mL) and satd aq $NaHCO_3$ (3 × 200 mL) and then dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **29** as a colorless syrup which solidified on standing to a white crystalline solid (7.08 g, 68%):[17a,i] mp 35−36 °C; δ_H (400 MHz, $CDCl_3$) 1.78−1.99 (2H, m, C(5)H_2), 2.19−2.49 (4H, m, C(4)H_2, C(6)H_2), 3.41 (2H, d, *J* 13.9, $N(CH_AH_BPh)_2$), (2H, d, *J* 13.9, $N(CH_AH_BPh)_2$), 3.98−4.13 (1H, m, C(3)*H*), 5.65−5.85 (2H, m, C(1)*H*, C(2)*H*), 7.11−7.49 (10H, m, *Ph*).

(*RS*,*RS*,*RS*)-1-Acetoxy-2-(*N*,*N*-dibenzylamino)-6-fluorocyclohexane (32). Following general procedure 2, **29** (166 mg, 0.60 mmol) in CH_2Cl_2 (3.4 mL) was treated with $HBF_4{\cdot}OEt_2$ (165 μL, 1.21 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.4 mL, 1.2 mmol) for 18 h to give a 67:12:21 mixture of **6**:**23**:**30**. Pyridine (1.0 mL) and Ac_2O (0.57 mL, 6.0 mmol) were added to the residue and the resultant mixture was stirred at rt for 20 h and then concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **32** as a colorless oil which solidified on standing to a white crystalline solid (95.2 mg, 45%, >99:1 dr); R_f 0.42 (30−40 °C petroleum ether/Et_2O, 4:1): mp 87−89 °C; ν_{max} 3085, 3063, 3027, 2943, 2871, 2835, 2804 (C−H), 1743 (C═O), 1229, 747, 736; δ_H (400 MHz, $CDCl_3$) 1.49−1.72 (3H, m, C(4)H_2, C(5)H_A), 1.75−1.92 (3H, m, C(3)H_2, C(5)H_B), 2.04 (3H, s, CO*Me*), 3.04 (1H, app dq, *J* 12.1, 3.4, C(2)*H*), 3.75 (4H, A_2 system, $N(CH_2Ph)_2$), 4.58−4.75 (1H, m, C(6)*H*), 5.42−5.47 (1H, m, C(1)*H*), 7.19−7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.7 (*C*(4)), 21.3 (CO*Me*), 23.0 (*C*(3)), 26.1 (d, *J* 20.8, *C*(5)), 53.9 (*C*(2)), 55.1 ($N(CH_2Ph)_2$), 71.2 (d, *J* 29.6, *C*(1)), 88.1 (d, *J* 173, *C*(6)), 126.8 (*p-Ph*), 128.2, 128.3 (*o,m-Ph*), 140.3 (*i-Ph*), 170.0 (*C*OMe); δ_F (377 MHz, $CDCl_3$) −188.8 (m); *m*/*z* (ESI^+) 378 ($[M + Na]^+$, 89), 356 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{22}H_{27}FNO_2^+$ ($[M + H]^+$) requires 356.2020, found 356.2012.

K_2CO_3 (82.9 mg, 0.60 mmol) and MeOH (1.5 mL) were added to **32** (95.2 mg, 0.27 mmol, >99:1 dr), and the resultant mixture was stirred at rt for 3 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo to give **6** as a white, crystalline solid (83.9 mg, quant, >99:1 dr).

(1*RS*,2*SR*,6*RS*)-1-Acetoxy-2-(*N*,*N*-dibenzylamino)-6-fluorocyclohexane (33). Following general procedure 2, **29** (166 mg, 0.60 mmol) in CH_2Cl_2 (2.0 mL) was treated with $HBF_4{\cdot}OEt_2$ (1.6 mL, 12 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.4 mL, 1.2 mmol) for 18 h to give a 16:84 mixture of **6**:**23**. Pyridine (1.0 mL) and Ac_2O (0.57 μL, 6.0 mmol) were added to the residue, and the resultant mixture was stirred at rt for 20 h then concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **33** as a colorless oil which solidified on standing to a white crystalline solid (105 mg, 49%, >99:1 dr): R_f 0.37 (30−40 °C petroleum ether/Et_2O, 4:1); mp 109−111 °C; ν_{max} 3086, 3064, 3030, 2951, 2854, 2810 (C−H), 1733 (C═O), 1367, 1234, 1039, 1028, 747, 733, 696; δ_H (400 MHz, $CDCl_3$) 1.04−1.18 (1H, m, C(4)H_A), 1.40 (1H, app qd, *J* 12.8, 3.7, C(3)H_A), 1.44−1.58 (1H, m, C(5)H_A), 1.77−1.88 (1H, m, C(4)H_B), 1.95−2.05 (1H, m, C(5)H_B), 2.08−2.17 (1H, m, C(3)H_B), 2.25 (3H, s, CO*Me*), 2.62−2.71 (1H, m, C(2)*H*), 3.47 (2H, d, *J* 13.6, $N(CH_AH_BPh)_2$), 3.85 (2H, d, *J* 13.6, $N(CH_AH_BPh)_2$), 4.27 (1H, dddd, *J* 50.6, 11.6, 8.8, 5.2, C(6)*H*), 5.26 (1H, ddd, *J* 12.3, 10.7, 8.8, C(1)*H*), 7.19−7.35 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.1 (d, *J* 12.8, *C*(4)), 21.4 (CO*Me*), 23.6 (d, *J* 1.6, *C*(3)), 30.6 (d, *J* 17.6, *C*(5)), 53.7 ($N(CH_2Ph)_2$), 58.8 (d, *J* 8.0, *C*(2)), 73.9 (d, *J* 16.0, *C*(1)), 93.1 (d, *J* 181, *C*(6)), 126.9 (*p-Ph*), 128.2, 128.7 (*o,m-Ph*), 139.7 (*i-Ph*), 170.4 (COMe); δ_F (377 MHz, $CDCl_3$) −180.5 (app d, *J* 50.6); *m*/*z* (ESI^+) 733 ($[2M + Na]^+$, 100), 378 ($[M + Na]^+$, 85), 356 ($[M + H]^+$, 87), 336 ($[M - F]^+$, 71); HRMS (ESI^+) $C_{22}H_{27}FNO_2^+$ ($[M + H]^+$) requires 356.2020, found 356.2013.

K_2CO_3 (82.9 mg, 0.60 mmol) and MeOH (1.50 mL) were added to **33** (105 mg, 0.30 mmol, >99:1 dr), and the resultant mixture was stirred at rt for 3 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo to give **23** as a white, crystalline solid (92.6 mg, quant, >99:1 dr).

(*RS*)-3-(*N*-Benzyl-*N*-methylamino)cyclohex-1-ene (34). A stirred mixture of 3-bromocyclohex-1-ene (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 (2.0 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) and then dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **34** as a pale yellow oil (270 mg, 83%):[44] δ_H (400 MHz, $CDCl_3$) 1.48−1.60, 1.77−1.90, 1.96−2.04 (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_A), 3.67 (1H, d, *J* 13.3, NCH_B), 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*-Benzylamino)cyclohex-1-ene (37). Benzylamine (6.6 mL, 60 mmol) was added to 3-bromocyclohex-1-ene (3.90 g, 24.2 mmol) at 0 °C, and the resultant mixture was allowed to warm to rt and was then heated at 60 °C for 30 min. The residue was allowed to cool to rt and was partitioned between CH_2Cl_2 (100 mL) and satd aq $NaHCO_3$ (100 mL). The organic layer was separated and washed with satd aq $NaHCO_3$ (2 × 100 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petroleum ether/EtOAc, 4:1; neutralized silica gel) gave **37** as a yellow oil (3.46 g, 76%):[17a] δ_H (400 MHz, $CDCl_3$) 1.35−1.61 (2H, m), 1.71−1.81 (1H, m), 1.85−2.06 (3H, m), 3.21−3.29 (1H, m, C(3)*H*), 3.79−3.89 (2H, m, NCH_2), 5.61−5.82 (2H, m, C(1)*H*, C(2)*H*), 7.21−7.49 (5H, m, *Ph*).

(*RS*,*RS*,*RS*)-2-(*N*-Benzylamino)-6-fluorocyclohexan-1-ol (38). Following general procedure 2, **37** (150 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with $HBF_4{\cdot}OEt_2$ (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h to give a 90:10 mixture of **38**:**40**. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo

to give a 90:10 mixture of **38**:**41**. Purification via flash column chromatography (gradient elution, 7→60% EtOAc in 30−40 °C petroleum ether) gave **38** as a white crystalline solid (116 mg, 65%, >99:1 dr): R_f 0.16 (30−40 °C petroleum ether/EtOAc, 7:3); mp 82−83 °C; ν_{max} 3329 (O−H), 3087, 3063, 3029, 2941, 2867 (C−H), 1455, 1073, 699; δ_H (400 MHz, $CDCl_3$) 1.39−1.51 (1H, m, C(3)H_A), 1.54−1.77 (4H, m, C(3)H_B, C(4)H_2, C(5)H_A), 1.79−1.98 (1H, m, C(5)H_B), 2.43 (1H, br s, O*H*), 2.98−3.07 (1H, m, C(2)*H*), 3.78 (2H, AB system, NCH_2Ph), 3.82−3.88 (1H, m, C(1)*H*), 4.77 (1H, dtd, *J* 48.0, 5.7, 3.3, C(6)*H*), 7.24−7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.2 (d, *J* 4.8, *C*(4)), 26.4 (*C*(3)), 27.2 (d, *J* 19.2, *C*(5)), 51.1 (NCH_2Ph), 55.8 (*C*(2)), 68.9 (d, *J* 27.2, *C*(1)), 91.5 (d, *J* 168, *C*(6)), 127.2 (*p-Ph*), 128.1, 128.6 (*o,m-Ph*), 140.1 (*i-Ph*); δ_F (377 MHz, $CDCl_3$) −191.8 (m); *m*/*z* (FI^+) 223 ($[M]^+$, 100); HRMS (FI^+) $C_{13}H_{18}FNO^+$ ($[M]^+$) requires 223.1367, found 223.1367. Anal. Calcd for $C_{13}H_{18}FNO$: C, 69.9; H, 8.1; N, 6.3. Found: C, 70.1; H, 8.1; N, 6.2.

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclopent-1-ene (42). A mixture of cyclopentene (119 mL, 1.35 mol), NBS (60.0 g, 337 mmol), and benzoyl peroxide (70% with H_2O, 1.17 g, 3.37 mmol) in CCl_4 (216 mL) was heated at reflux for 1 h. The reaction mixture was then cooled to 0 °C and filtered through a pad of Celite (eluent CCl_4) to give a yellow solution. Dibenzylamine (162 mL, 843 mmol) was immediately added dropwise at 0 °C, and the resultant mixture was allowed to warm to rt and was stirred for 30 min. The reaction mixture was then filtered, heated to 40 °C, and stirred at this temperature for 1 h and then filtered and stirred at rt for 12 h. The mixture was then filtered and concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (1 L) and washed sequentially with 10% aq citric acid (3 × 500 mL) and satd aq $NaHCO_3$ (3 × 500 mL) then concentrated in vacuo. The residue was dissolved in 1 M aq HCl (1 L) and washed with Et_2O (3 × 200 mL). The aqueous layer was then slowly basified by the portionwise addition of solid $NaHCO_3$ and then extracted with CH_2Cl_2 (3 × 300 mL). The combined organic extracts were dried, filtered, and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1%→5% Et_2O in 40−60 °C petroleum ether) gave **42** as a pale yellow oil (36.3 g, 41%):[17c,i] 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(C$H_A$$H_B$Ph)$_2$), 3.81 (2H, d, *J* 14.0, N(CH$_A$$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*).

(*RS*)-3-(*N*,*N*-Dibenzylamino)cyclohept-1-ene (44). A mixture of 3-bromocyclohept-1-ene (16.0 g, 91.4 mmol), dibenzylamine (44 mL, 230 mmol), and K_2CO_3 (15.2 g, 110 mmol) was stirred at 60 °C for 35 h. The mixture was then diluted with H_2O (1 L) and CH_2Cl_2 (1 L). The organic layer was separated and washed sequentially with 10% aq citric acid (3 × 500 mL) and satd aq $NaHCO_3$ (500 mL) and then dried and concentrated in vacuo. Purification via recrystallization (^{i}PrOH) gave **44** as a white crystalline solid (21.6 g, 81%):[17c,i] mp 54−55 °C; δ_H (400 MHz, $CDCl_3$) 1.26−2.33 (8H, m, C(4)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$$H_B$Ph)$_2$), 3.74 (2H, d, *J* 14.2, N(CH$_A$$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*).

(*RS*)-3-(*N*,*N*-Dibenzylamino)-1-methylcyclohex-1-ene (45). Step 1: MeMgCl (3.0 M in THF, 50 mL, 150 mmol) was added dropwise to a stirred solution of cyclohex-2-enone (9.7 mL, 100 mmol) in THF (350 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 18 h. Satd aq NH_4Cl (150 mL) was then added, and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 150 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via distillation at reduced pressure (1.2 mmHg) gave (*RS*)-1-methylcyclohex-2-enol as a colorless oil (7.54 g, 67%):[45] bp 24−26 °C (1.2 mmHg); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, s, *Me*), 1.51 (1H, br s, O*H*), 1.59−1.80 (4H, m, C(5)H_2, C(6)H_2), 1.88−2.09 (2H, m, C(4)H_2), 5.61−5.67 (1H, m, C(2)*H*), 5.76 (1H, app dt, *J* 9.9, 3.8, C(3)*H*).

Step 2: A solution of (*RS*)-1-methylcyclohex-2-enol (5.00 g, 44.6 mmol) in Et_2O (25 mL) was added dropwise to a stirred suspension of KH (268 mg, 6.69 mmol) in Et_2O (30 mL) at 0 °C, and the resultant mixture was stirred at this temperature for 30 min. This mixture was then added dropwise via cannula to a stirred solution of Cl_3CCN (4.5 mL, 45 mmol) in Et_2O (50 mL), and the resultant mixture was stirred at rt for 44 h. Satd aq NH_4Cl (10 mL) was then added, and the resultant mixture was dried, filtered through a pad of silica gel (eluent Et_2O), and concentrated in vacuo. Purification via recrystallization from 30−40 °C petroleum ether gave (*RS*)-3-trichloroacetamido-1-methylcyclohex-1-ene as a white crystalline solid (6.07 g, 53%):[45] mp 71−73 °C; δ_H (400 MHz, $CDCl_3$) 1.55−1.74 (4H, m, C(4)H_2, C(5)H_2) overlapping 1.72 (3H, s, *Me*), 1.84−2.01 (2H, m, C(6)H_2), 4.42 (1H, app s, C(3)*H*), 5.34−5.40 (1H, m, C(2)*H*), 6.56 (1H, br s, N*H*).

Step 3: Aqueous NaOH (10 M, 12 mL) was added dropwise to a stirred solution of (*RS*)-3-trichloroacetamido-1-methylcyclohex-1-ene (6.07 g, 23.7 mmol) in EtOH (34 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 17 h. The mixture was then extracted with Et_2O/30−40 °C petroleum ether (4:1 v/v, 3 × 50 mL), and the combined organic layers were washed with H_2O (2 × 50 mL), dried, and concentrated in vacuo. BnBr (1.2 mL, 10.3 mmol), K_2CO_3 (2.13 g, 15.4 mmol), and MeCN (26 mL) were added to the residue, and the resultant mixture was heated at reflux for 18 h and then concentrated in vacuo. The residue was partitioned between EtOAc (30 mL) and H_2O (30 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 30 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **45** as a colorless oil (1.13 g, 16%): R_f 0.37 (30−40 °C petroleum ether/Et_2O, 19:1); ν_{max} 3104, 3084, 3062, 3026, 3003, 2962, 2928, 2859, 2830, 2799, 2723, 1494, 1453, 743, 697; δ_H (400 MHz, $CDCl_3$) 1.38−1.53 (2H, m, C(4)H_A, C(5)H_A), 1.70 (3H, s, C(1)*Me*), 1.76−2.05 (4H, m, C(4)H_B, C(5)H_B, C(6)H_2), 3.34 (1H, br s, C(3)*H*), 3.55 (2H, d, *J* 14.1, N(C$H_A$$H_B$Ph)$_2$), 3.77 (2H, d, *J* 14.1, N(CH$_A$$H_B$Ph)$_2$), 5.49 (1H, br s, C(2)*H*), 7.19−7.48 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 22.0, 22.8 (*C*(4), *C*(5)), 23.8 (C(1)*Me*), 30.3 (*C*(6)), 53.8 (N(CH_2Ph)$_2$), 54.9 (*C*(3)), 125.0 (*C*(2)), 126.5 (*p-Ph*), 128.1, 128.5 (*o,m-Ph*), 137.4, 141.1 (*i-Ph*, *C*(1)); *m*/*z* (ESI^+) 292 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{21}H_{26}N^+$ ($[M + H]^+$) requires 292.2060, found 292.2059.

(*RS*,*RS*,*RS*)-2-(*N*,*N*-Dibenzylamino)-6-fluoro-6-methylcyclohexan-1-ol (46). Following general procedure 2, **45** (233 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.60 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo to give **46** in 95:5 dr. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **46** as a colorless oil which solidified on standing to a white crystalline solid (184 mg, 70%, 95:5 dr): R_f 0.32 (30−40 °C petroleum ether/Et_2O, 4:1); mp 55−59 °C; ν_{max} 3457, 3085, 3062, 3028, 2937, 2870, 1494, 1453, 1374, 1152, 1072, 1058, 1029, 747, 737, 699; δ_H (400 MHz, $CDCl_3$) 1.25−1.39 (1H, m, C(3)H_A), 1.45 (3H, d, *J* 23.0, C(6)*Me*), 1.50−1.78 (5H, m, C(3)H_B, C(4)H_2, C(5)H_2), 3.12 (1H, ddd, *J* 12.5, 6.7, 3.2, C(2)*H*), 3.78 (2H, d, *J* 14.6, N(C$H_A$$H_B$Ph)$_2$), 3.87 (2H, d, *J* 14.6, N(CH$_A$$H_B$Ph)$_2$), 3.89−3.93 (1H, m, C(1)*H*), 7.21−7.37 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.9 (d, *J* 1.6, *C*(4)), 23.5 (*C*(3)), 25.2 (d, *J* 22.4, C(6)*Me*), 31.0 (d, *J* 21.6, *C*(5)), 54.5 (N(CH_2Ph)$_2$), 60.4 (*C*(2)), 70.9 (d, *J* 32.8, *C*(1)), 95.9 (d, *J* 165, *C*(6)), 126.9 (*p-Ph*), 128.4, 128.5 (*o,m-Ph*), 140.0 (*i-Ph*); δ_F (377 MHz, $CDCl_3$) −156.7 (m); *m*/*z* (ESI^+) 677 ($[2M + Na]^+$, 100), 350 ($[M + Na]^+$, 59), 328 ($[M + H]^+$, 89); HRMS (ESI^+) $C_{21}H_{27}FNO^+$ ($[M + H]^+$) requires 328.2071, found 328.2070. Data for minor diastereoisomer: δ_H (400 MHz, $CDCl_3$) [selected peaks] 1.14 (3H, d, *J* 23.4, C(6)*Me*), 2.36−2.45 (1H, m, C(2)*H*), 3.38 (2H, d, *J* 13.3, N(C$H_A$$H_B$Ph)$_2$); δ_F (377 MHz, $CDCl_3$) −133.0 (m).

***N*(1)-Benzyl-1,2,3,6-tetrahydropyridine (47).** MsCl (11 mL, 140 mmol) was added dropwise to a stirred solution of *N*(1)-benzyl-4-hydroxypiperidine (24.0 g, 125 mmol) and Et_3N (19 mL, 140 mmol) in PhMe (300 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 1.5 h. H_2O (75 mL) was then added, and the layers

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were separated. The organic layer was washed with H_2O (75 mL) and then dried. The resultant solution was diluted with PhMe (150 mL) and *N*,*N*-dimethylacetamide (100 mL), ^tBuOK (18.3 g, 163 mmol) was added, and the resultant mixture was stirred at rt for 5 days. H_2O (150 mL) was added, and the layers were separated. The organic layer was washed with H_2O (2 × 150 mL), dried, and concentrated in vacuo. Purification via distillation at reduced pressure (1.1 mmHg) gave **47** as a colorless oil (17.6 g, 81%):[46] bp 75−78 °C (1.1 mmHg); δ_H (400 MHz, $CDCl_3$) 2.15−2.22 (2H, m, C(3)H_2), 2.58 (2H, t, *J* 5.6, C(2)H_2), 2.97−3.01 (2H, m, C(6)H_2), 3.60 (2H, s, NCH_2Ph), 5.65−5.71 (1H, m, C(4)*H*), 5.74−5.81 (1H, m, C(5)*H*), 7.24−7.40 (5H, m, *Ph*).

(*RS*,*RS*)-*N*(1)-Benzyl-4-fluoropiperidin-3-ol (48). Following general procedure 2, **47** (200 mg, 1.15 mmol) in CH_2Cl_2 (6.6 mL) was treated with $HBF_4{\cdot}OEt_2$ (0.32 mL, 2.4 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 4.6 mL, 2.3 mmol) for 18 h. K_2CO_3 (16.0 mg, 0.12 mmol) and MeOH (2.9 mL) were then added to the residuem and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 12→100% EtOAc in 30−40 °C petroleum ether) gave **48** as a pale yellow oil (130 mg, 53%, >99:1 dr): R_f 0.43 (30−40 °C petroleum ether/EtOAc, 1:1); ν_{max} 3385 (O−H), 3087, 3062, 3029, 2951, 2935, 2807 (C−H), 1454, 1060, 1026, 748, 700; δ_H (400 MHz, $CDCl_3$) 1.77−1.91 (1H, m, C(5)H_A), 1.98−2.14 (1H, m, C(5)H_B), 2.30−2.46 (2H, m, C(2)H_A, C(6)H_A), 2.53−2.64 (1H, m, C(6)H_B), 2.80 (1H, app dt, *J* 11.8, 4.3, C(2)H_B), 3.02 (1H, br s, O*H*), 3.54 (2H, app s, NCH_2Ph), 3.78−3.86 (1H, m, C(3)*H*), 4.38−4.58 (1H, m, C(4)*H*), 7.24−7.37 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 28.2 (d, *J* 19.1, C(5)), 49.4 (d, *J* 5.7, C(6)), 55.8 (*C*(2)), 62.3 (NCH_2Ph), 68.4 (d, *J* 20.0, *C*(3)), 91.8 (d, *J* 177, *C*(4)), 127.3 (*p*-*Ph*), 128.4, 129.1 (*o*,*m*-*Ph*), 137.7 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −188.1 (m); *m*/*z* (FI^+) 209 ($[M]^+$, 100); HRMS (FI^+) $C_{12}H_{16}FNO^+$ ($[M]^+$) requires 209.1210, found 209.1213. Anal. Calcd for $C_{12}H_{16}FNO$: C, 68.9; H, 7.7; N, 6.7. Found: C, 69.0; H, 7.6; N, 6.6.

(*RS*,*RS*)-*N*(1)-Benzyl-4-fluoropyrrolidin-3-ol (50). Following general procedure 2, **49** (421 mg, 2.64 mmol) in CH_2Cl_2 (12 mL) was treated with $HBF_4{\cdot}OEt_2$ (3.6 mL, 26 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 10.6 mL, 5.29 mmol) for 18 h. K_2CO_3 (36.5 mg, 0.26 mmol) and MeOH (6.6 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 10→80% EtOAc in 30−40 °C petroleum ether) gave **50** as a pale yellow oil (297 mg, 58%, >99:1 dr): R_f 0.26 (30−40 °C petroleum ether/EtOAc, 3:2); ν_{max} 3375 (O−H), 3088, 3063, 3030, 2961, 2932, 2804 (C−H), 1454, 1096, 1029, 757, 701; δ_H (400 MHz, $CDCl_3$) 2.56 (1H, dd, *J* 10.2, 3.2, C(2)H_A), 2.69 (1H, dd, *J* 29.0, 11.6, C(5)H_A), 2.92 (1H, dd, *J* 10.2, 5.3, C(2)H_B), 3.08 (1H, dddd, *J* 26.8, 11.6, 5.6, 3.2, C(5)H_B), 3.68 (2H, AB system, J_{AB} 12.9, NCH_2Ph), 4.31 (1H, app dt, *J* 18.4, 4.1, C(3)*H*), 4.90 (1H, app dd, *J* 52.8, 5.3, C(4)*H*), 7.25−7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 58.2 (d, *J* 24.0, C(5)), 59.6 (C(2)), 59.8 (NCH_2Ph), 75.7 (d, *J* 27.2, C(3)), 98.3 (d, *J* 181, C(4)), 127.3 (*p*-*Ph*), 128.4, 128.8 (*o*,*m*-*Ph*), 137.9 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −177.0 (m); *m*/*z* (FI^+) 195 ($[M]^+$, 100); HRMS (FI^+) $C_{11}H_{14}FNO^+$ ($[M]^+$) requires 195.1054, found 195.1056. Anal. Calcd for $C_{11}H_{14}FNO$: C, 67.7; H, 7.2; N, 7.2. Found C, 67.8; H, 7.3; N, 7.1.

(*Z*)-1-(*N*,*N*-Dibenzylamino)hex-2-ene (51). NBS (1.78 g, 10.0 mmol) was added portionwise to a stirred solution of (*Z*)-hex-2-en-1-ol (1.00 g, 10.0 mmol) and PPh_3 (2.62 g, 10.0 mmol) in THF (20 mL) at 0 °C, and the resultant mixture was stirred at this temperature for 1 h. Dibenzylamine (3.9 mL, 20 mmol) was then added, and the resultant mixture was allowed to warm to rt over 24 h. Et_2O (50 mL) was then added, and the resultant mixture was stirred for 10 min, filtered through a pad of Celite (eluent Et_2O), and concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (50 mL) and satd aq $NaHCO_3$ (50 mL), and the layers were separated. The organic layer was washed with satd aq $NaHCO_3$ (50 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **51** as a colorless oil (2.23 g, 80%, >99:1 dr): R_f 0.33 (30−40 °C petroleum ether/Et_2O, 19:1); ν_{max} 3085, 3063, 3026, 2958, 2871, 2822, 2792, 2710, 1494, 1454, 740, 696; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.5, C(6)H_3), 1.38 (2H, app sextet, *J* 7.4, C(5)H_2), 1.99 (2H, app q, *J* 6.8, C(4)H_2), 3.09 (2H, d, *J* 5.1, C(1)H_2), 3.60 (4H, s, N(CH_2Ph)$_2$), 5.53−5.65 (2H, m, C(2)*H*, C(3)*H*), 7.22−7.44 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 13.8 (*C*(6)), 22.8 (*C*(5)), 29.6 (*C*(4)), 50.1 (*C*(1)), 58.0 (N(CH_2Ph)$_2$), 126.8 (*p*-*Ph*), 127.1 (*C*(3)), 128.1, 128.8 (*o*,*m*-*Ph*), 132.9 (*C*(2)), 139.9 (*i*-*Ph*); *m*/*z* (ESI^+) 280 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{20}H_{26}N^+$ ($[M + H]^+$) requires 280.2060, found 280.2058.

(*Z*)-1-(*N*,*N*-Dibenzylamino)hex-3-ene (52). Et_3N (5.6 mL, 40 mmol) and MsCl (2.3 mL, 30 mmol) were added sequentially to a stirred solution of (*Z*)-hex-3-en-1-ol (2.4 mL, 20 mmol) in CH_2Cl_2 (33 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 1 h. Aqueous HCl (1 M, 50 mL) was then added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried and concentrated in vacuo. The residue was dissolved in EtOH (50 mL), and dibenzylamine (9.6 mL, 50 mmol) was added. The resultant mixture was stirred and heated at 70 °C for 16 h, allowed to cool to rt, and concentrated in vacuo. The residue was partitioned between satd aq $NaHCO_3$ (100 mL) and CH_2Cl_2 (100 mL), and the layers were separated. The organic layer was washed sequentially with 10% aq citric acid (3 × 100 mL) and satd aq $NaHCO_3$ (100 mL), dried, and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **52** as a colorless oil (3.28 g, 59%, >99:1 dr): R_f 0.38 (30−40 °C petroleum ether/Et_2O, 19:1); ν_{max} 3085, 3063, 3027, 3007, 2962, 2932, 2873, 2795 (C−H), 1494, 1453, 1366, 1126, 1072, 1028, 743, 698; δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.6, C(6)H_3), 2.02 (2H, app quintet, *J* 7.33 C(5)H_2), 2.25−2.33 (2H, app q, *J* 7.2, C(2)H_2), 2.50 (2H, t, *J* 7.8, C(1)H_2), 3.62 (4H, s, N(CH_2Ph)$_2$), 5.27−5.36 (1H, m, C(3)*H*), 5.37−5.45 (1H, m, C(4)*H*), 7.22−7.44 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.3 (*C*(6)), 20.6 (*C*(5)), 24.9 (*C*(2)), 53.3 (*C*(1)), 58.2 (N(CH_2Ph)$_2$), 126.75 (*p*-*Ph*), 126.81 (*C*(3)), 128.1, 128.8 (*o*,*m*-*Ph*), 132.5 (*C*(4)), 139.9 (*i*-*Ph*); *m*/*z* (ESI^+) 280 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{20}H_{26}N^+$ ($[M + H]^+$) requires 280.2060, found 280.2058.

(*E*)-1-(*N*,*N*-Dibenzylamino)hex-2-ene (53). Step 1: Diethyl azodicarboxylate (1.4 mL, 8.9 mmol) was added dropwise to a stirred solution of (*E*)-hex-2-en-1-ol (888 mg, 8.86 mmol, >99:1 dr), *N*-benzyl-2,4-dinitrobenzenesulfonamide (2.30 g, 6.82 mmol), and PPh_3 (2.32 g, 8.86 mmol) in THF (8.0 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 19 h and was then concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave (*E*)-*N*-benzyl-*N*-(hex-2-enyl)-2′,4′-dinitrobenzenesulfonamide as a yellow solid (2.86 g, quant, >99:1 dr):[47] R_f 0.25 (30−40 °C petroleum ether/EtOAc, 4:1); mp 68−69 °C; δ_H (400 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.3, C(6)H_3), 1.31 (2H, app sextet, *J* 7.3, C(5)H_2), 1.90−1.98 (2H, m, C(4)H_2), 3.87 (2H, d, *J* 6.6, C(1)H_2), 4.53 (2H, s, NCH_2Ph), 5.23 (1H, dtd, *J* 15.2, 6.6, 1.5, C(2)*H*), 5.52 (1H, dt, *J* 15.2, 6.9, C(3)*H*), 7.21−7.33 (5H, m, *Ph*), 8.13 (1H, d, *J* 8.5, *Ar*), 8.39 (1H, dd, *J* 8.5, 2.2, *Ar*), 8.48 (1H, d, *J* 2.2, *Ar*).

Step 2: 2-Mercaptoacetic acid (0.71 mL, 10 mmol) was added to a stirred solution of (*E*)-*N*-benzyl-*N*-(hex-2-enyl)-2′,4′-dinitrobenzenesulfonamide (2.86 g, 6.82 mmol, >99:1 dr) and Et_3N (1.9 mL, 14 mmol) in CH_2Cl_2 (34 mL) and the resultant solution was stirred at rt for 1 h and then concentrated in vacuo. The residue was dissolved in EtOAc (40 mL), washed with 5% aq NaOH (3 × 40 mL), dried, and concentrated in vacuo to give (*E*)-1-(*N*-benzylamino)hex-2-ene as an orange oil (1.17 g, 91%):[47] δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, C(6)H_3), 1.40 (2H, app sextet, *J* 7.4, C(5)H_2), 1.51 (1H, br s, N*H*),

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1.97−2.06 (2H, m, C(4)H_2), 3.23 (2H, d, J 5.1, C(1)H_2), 3.79 (2H, s, NCH_2Ph), 5.51−5.66 (2H, m, C(2)H, C(3)H), 7.23−7.39 (5H, m, Ph).

Step 3: BnBr (0.59 mL, 5.0 mmol) was added to a stirred solution of (*E*)-1-(*N*-benzylamino)hex-2-ene (945 mg, 4.99 mmol, >99:1 dr) and K_2CO_3 (2.07 g, 15.0 mmol) in MeCN (25 mL) and the resultant mixture was heated at reflux for 20 h then allowed to cool to rt, filtered (eluent Et_2O) and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **53** as a colorless oil (1.21 g, 87%, >99:1 dr): R_f 0.34 (30−40 °C petroleum ether/Et_2O, 19:1); ν_{max} 3085, 3062, 3027, 2957, 2926, 2872, 2792, 2711, 1494, 1454, 970, 732, 696; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, J 7.3, C(6)H_3), 1.41 (2H, app sextet, J 7.3, C(5)H_2), 2.03 (2H, app q, J 6.7, C(4)H_2), 3.03 (2H, d, J 5.8, C(1)H_2), 3.58 (4H, s, N(CH_2Ph)$_2$), 5.49−5.65 (2H, m, C(2)H, C(3)H), 7.21−7.43 (10H, m, Ph); δ_C (100 MHz, $CDCl_3$) 13.7 (*C*(6)), 22.5 (*C*(5)), 34.6 (*C*(4)), 55.5 (*C*(1)), 57.6 (N(*C*H_2Ph)$_2$), 126.7 (*p*-*Ph*), 127.3 (*C*(3)), 128.1, 128.8 (*o*,*m*-*Ph*), 134.0 (*C*(2)), 139.9 (*i*-*Ph*); m/z (ESI$^+$) 280 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{20}H_{26}N^+$ ([M + H]$^+$) requires 280.2060, found 280.2055.

(*E*)-1-(*N*,*N*-Dibenzylamino)hex-3-ene(54). Et_3N (5.6 mL, 40.0 mmol) and MsCl (2.3 mL, 30 mmol) were added sequentially to a stirred solution of (*E*)-hex-3-en-1-ol (2.3 mL, 20 mmol) in CH_2Cl_2 (33 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 1 h; 1 M aq HCl (50 mL) was then added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried and concentrated in vacuo. The residue was dissolved in EtOH (50 mL) and dibenzylamine (9.6 mL, 50 mmol) was added. The resultant mixture was stirred and heated at 70 °C for 16 h then was allowed to cool to rt and was concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (100 mL) and satd aq $NaHCO_3$ (100 mL) and the layers were separated. The organic layer was washed sequentially with 10% aq citric acid (3 × 100 mL) and satd aq $NaHCO_3$ (100 mL) and then dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **54** as a colorless oil (3.11 g, 56%, >99:1 dr): R_f 0.38 (30−40 °C petroleum ether/Et_2O, 24:1); ν_{max} 3085, 3063, 3027, 2961, 2932, 2873, 2845, 2795 (C−H), 1494, 1453, 1367, 1127, 1073, 1028, 966, 743, 698; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, t, J 7.5, C(6)H_3), 1.98−2.07 (2H, m, C(5)H_2), 2.21−2.30 (2H, app q, J 7.1, C(2)H_2), 2.52 (2H, t, J 7.6, C(1)H), 3.61 (4H, s, N(CH_2Ph)$_2$), 5.32−5.42 (1H, m, C(3)H), 5.45−5.54 (1H, m, C(4)H), 7.22−7.44 (10H, m, Ph); δ_C (100 MHz, $CDCl_3$) 13.8 (*C*(6)), 25.6 (*C*(5)), 30.4 (*C*(2)), 53.5 (*C*(1)), 58.2 (N(*C*H_2Ph)$_2$), 126.7 (*p*-*Ph*), 127.2 (*C*(3)), 128.1, 128.8 (*o*,*m*-*Ph*), 133.0 (*C*(4)), 140.0 (*i*-*Ph*); m/z (ESI$^+$) 280 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{20}H_{26}N^+$ ([M + H]$^+$) requires 280.2060, found 280.2059.

(*E*)-4-(*N*,*N*-Dibenzylamino)but-2-en-1-ol (55). Step 1: Dibenzylamine (6.4 mL, 33 mmol) was added to a stirred solution of methyl 4-bromocrotonate (85%, 4.2 mL, 30 mmol) and K_2CO_3 (12.4 g, 90.0 mmol) in MeCN (150 mL) and the resultant mixture was heated at reflux for 21 h and then concentrated in vacuo. The residue was partitioned between EtOAc (100 mL) and H_2O (100 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL) and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave methyl (*E*)-4-(*N*,*N*-dibenzylamino)but-2-enoate as a pale yellow oil (7.00 g, 79%, >99:1 dr): R_f 0.24 (30−40 °C petroleum ether/Et_2O, 9:1); ν_{max} 3085, 3062, 3028, 2949, 2924, 2796, 2713 (C−H), 1721 (C═O), 1269, 1169, 737, 697; δ_H (400 MHz, $CDCl_3$) 3.23 (2H, app dd, J 5.8, 1.0, C(4)H_2), 3.62 (4H, s, N(CH_2Ph)$_2$), 3.76 (3H, s, OMe), 6.10 (1H, d, J 15.8, C(2)H), 7.05 (1H, dt, J 15.8, 5.8, C(3)H), 7.23−7.45 (10H, m, Ph); δ_C (100 MHz, $CDCl_3$) 51.5 (O*Me*), 54.1 (*C*(4)), 61.8 (N(*C*H_2Ph)$_2$), 122.4 (*C*(2)), 127.1 (*p*-*Ph*), 128.3, 128.7 (*o*,*m*-*Ph*), 139.0 (*i*-*Ph*), 146.8 (*C*(3)), 166.8 (*C*(1)); m/z (ESI$^+$) 296 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{19}H_{22}NO_2^+$ ([M + H]$^+$) requires 296.1645, found 296.1642.

Step 2: DIBAL-H (1.0 M in hexanes, 48 mL, 48 mmol) was added dropwise to a stirred solution of methyl (*E*)-4-(*N*,*N*-dibenzylamino)-but-2-enoate (6.35 g, 21.5 mmol) in CH_2Cl_2 (50 mL) at 0 °C, and the resultant solution was allowed to warm to rt and was stirred at this temperature for 18 h. The mixture was then cooled to 0 °C, satd aq Rochelle's salt (100 mL) was added dropwise (*cautiously!*), and the resultant mixture was stirred vigorously at rt for 23 h. The mixture was then filtered through a pad of Celite (eluent Et_2O) and the layers were separated. The aqueous phase was extracted with Et_2O (3 × 100 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 10→80% EtOAc in 30−40 °C petroleum ether) gave **55** as a colorless oil (5.72 g, 99%, >99:1 dr): R_f 0.13 (30−40 °C petroleum ether/EtOAc, 4:1); ν_{max} 3328 (O−H), 3085, 3062, 3027, 2921, 2794, 2712 (C−H), 971, 733, 696; δ_H (400 MHz, $CDCl_3$) 1.64 (1H, br s, OH), 3.11 (2H, d, J 4.3, C(4)H_2), 3.62 (4H, s, N(CH_2Ph)$_2$), 4.12 (2H, d, J 3.8, C(1)H_2), 5.73−5.86 (2H, m, C(2)H, C(3)H), 7.23−7.44 (10H, m, Ph); δ_C (100 MHz, $CDCl_3$) 55.2 (*C*(4)), 58.1 (N(*C*H_2Ph)$_2$), 63.3 (*C*(1)), 126.9 (*p*-*Ph*), 128.2, 128.8 (*o*,*m*-*Ph*), 129.7, 131.9 (*C*(2), *C*(3)), 139.6 (*i*-*Ph*); m/z (ESI$^+$) 268 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{18}H_{22}NO^+$ ([M + H]$^+$) requires 268.1696, found 268.1694.

(*E*)-1-(*N*,*N*-Dibenzylamino)-2-methylbut-2-ene (56). Dibenzylamine (2.9 mL, 15 mmol) and $NaBH(OAc)_3$ (4.45 g, 21.0 mmol) were added sequentially to a stirred solution of tiglic aldehyde (1.5 mL, 15 mmol) in THF (100 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 4 h. Satd aq $NaHCO_3$ (200 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 1→8% Et_2O in 30−40 °C petroleum ether) gave **56** as a colorless oil (2.14 g, 54%, >99:1 dr): R_f 0.51 (30−40 °C petroleum ether/Et_2O, 19:1); ν_{max} 3085, 3062, 3027, 2977, 2919, 2878, 2792, 2709, 1495, 1453, 744, 697; δ_H (400 MHz, $CDCl_3$) 1.63−1.68 (3H, m, C(4)H_3), 1.71−1.75 (3H, m, C(2)Me), 2.94 (2H, s, C(1)H_2), 3.54 (4H, s, N(CH_2Ph)$_2$), 5.44−5.46 (1H, m, C(3)H), 7.23−7.48 (10H, m, Ph); δ_C (100 MHz, $CDCl_3$) 13.4, 14.6 (C(2)*Me*, *C*(4)), 57.9 (*C*(1)), 62.8 (N(*C*H_2Ph)$_2$), 121.9 (*C*(3)), 126.7 (*p*-*Ph*), 128.2, 128.8 (*o*,*m*-*Ph*), 134.2 (*C*(2)), 140.2 (*i*-*Ph*); m/z (ESI$^+$) 266 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{19}H_{24}N^+$ ([M + H]$^+$) requires 266.1903, found 266.1904.

(*RS*)-2,5-Dimethyl-4-(*N*,*N*-dibenzylamino)hex-3-ene (57). 2-Methyl-1-propenylmagnesium bromide (0.5 M in THF, 15 mL, 7.5 mmol) was added to a stirred solution of (*RS*)-1-[α-(*N*,*N*-dibenzylamino)-β-methylpropyl]benzotriazole[48] (1.85 g, 5.00 mmol) in PhMe (25 mL) at rt. The resultant suspension was stirred at 50 °C for 2 h then was allowed to cool to rt followed by dropwise addition of satd aq NH_4Cl (10 mL). The resultant mixture was diluted with Et_2O (50 mL) and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed sequentially with 1 M aq NaOH (100 mL) and brine (100 mL), dried, and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petroleum ether) gave **57** as a white solid (1.35 g, 88%):[48] δ_H (400 MHz, $CDCl_3$) 0.85 (3H, d, J 6.6, C(5)Me_A), 1.27 (3H, d, J 6.6, C(5)Me_B), 1.56 (3H, s, C(2)Me_A), 1.88−1.93 (1H, m, C(5)H), 1.96 (3H, s, C(2)Me_B), 2.93 (1H, app t, J 10.4, C(4)H), 3.42 (2H, d, J 14.2, N(CH_AH$_B$Ph)$_2$), 3.95 (2H, d, J 14.2, N(CH$_A$H$_B$Ph)$_2$), 5.29 (1H, d, J 10.6, C(3)H), 7.30−7.33 (2H, m, Ph), 7.41 (4H, app t, J 7.5, Ph), 7.55 (4H, app d, J 7.5, Ph).

(*RS*)-1-(*N*,*N*-Dibenzylamino)-1-phenyl-3-methylbut-2-ene (58). 2-Methyl-1-propenylmagnesium bromide (0.5 M in THF, 15 mL, 7.5 mmol) was added to a stirred solution of (*RS*)-1-[α-(*N*,*N*-dibenzylamino)benzyl]benzotriazole[48] (2.02 g, 5.00 mmol) in PhMe (25 mL) at rt. The resultant suspension was stirred at 50 °C for 2 h then was allowed to cool to rt followed by dropwise addition of satd aq NH_4Cl (10 mL). The resultant mixture was diluted with Et_2O (50 mL), and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed sequentially with 1 M aq NaOH (100 mL) and brine (100 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petroleum ether/Et_2O, 99:1) gave **58** as a pale yellow oil (1.59 g,

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93%):[48] δ_H (400 MHz, $CDCl_3$) 1.54 (3H, s, C(3)Me_A), 1.94 (3H, s, C(3)Me_B), 3.57 (2H, d, *J* 13.8, N(CH_AH_BPh)$_2$), 3.77 (2H, d, *J* 13.8, N(CH_AH_BPh)$_2$), 4.58 (1H, d, *J* 9.8, C(1)*H*), 5.60 (1H, d, *J* 9.8, C(2)*H*), 7.25−7.28 (3H, m, *Ph*), 7.34−7.41 (6H, m, *Ph*), 7.47 (4H, d, *J* 7.6, *Ph*), 7.61 (2H, app d, *J* 7.3, *Ph*).

(*RS*,*E*)-1-(*N*,*N*-Dibenzylamino)-1-phenylbut-2-ene (59). ^{t}BuLi (1.7 M in pentane, 8.8 mL, 15 mmol) was added to a stirred solution of (*E*)-1-bromoprop-1-ene (0.64 mL, 7.5 mmol) in Et_2O (30 mL) at −78 °C, and the resultant mixture was stirred for 1 h at −78 °C. Solid $MgBr_2$·OEt_2 (1.55 g, 6.00 mmol) was then added, and the reaction mixture was allowed to warm to 0 °C over 30 min and was then added to a solution of (*RS*)-1-[α-(*N*,*N*-dibenzylamino)benzyl]-benzotriazole[48] (2.02 g, 5.0 mmol) in PhMe (30 mL) at 0 °C via cannula. The resultant mixture was stirred at 0 °C for 2 h then satd aq NH_4Cl (20 mL) was added. The aqueous layer was extracted with Et_2O (3 × 20 mL), and the combined organic layers were washed with 1 M aq NaOH (30 mL) and brine (30 mL), then dried and concentrated in vacuo. Purification by flash column chromatography (eluent 30−40 °C petroleum ether/Et_2O, 99:1) gave **59** as a white solid (621 mg, 38%, >99:1 dr):[48] δ_H (400 MHz, $CDCl_3$) 1.97 (3H, d, *J* 7.1, C(4)H_3), 3.65 (2H, d, *J* 13.7, N(CH_AH_BPh)$_2$), 3.81 (2H, d, *J* 13.7, N(CH_AH_BPh)$_2$), 4.37 (1H, d, *J* 8.6, C(1)*H*), 5.70−5.79 (1H, m, C(3)*H*), 5.84−5.90 (1H, m, C(2)*H*), 7.34 (3H, app q, *J* 7.0, *Ph*), 7.42−7.47 (6H, m, *Ph*), 7.55 (4H, d, *J* 7.1, *Ph*), 7.66 (2H, d, *J* 7.8, *Ph*).

(*RS*,*RS*)-1-(*N*,*N*-Dibenzylamino)-3-fluorohexan-2-ol (60). Following general procedure 2, **51** (224 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **60** as a pale yellow oil (145 mg, 57%, >99:1 dr): R_f 0.28 (30−40 °C petroleum ether/Et_2O, 4:1); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, app t, *J* 7.1, C(6)H_3), 1.31−1.57 (3H, m, C(4)H_2, C(5)H_A), 1.64−1.80 (1H, m, C(5)H_B), 2.53 (1H, dd, *J* 12.6, 3.7, C(1)H_A), 2.75 (1H, dd, *J* 12.6, 9.8, C(1)H_B), 3.18 (1H, br s, O*H*), 3.50 (2H, d, *J* 13.5, N(CH_AH_BPh)$_2$), 3.69 (1H, dddd, *J* 21.5, 9.8, 3.7, 3.5, C(2)*H*), 3.84 (2H, d, *J* 13.5, N(CH_AH_BPh)$_2$), 4.33 (1H, dddd, *J* 48.5, 9.0, 3.5, 3.4, C(3)*H*), 7.22−7.42 (10H, m, *Ph*).

(*RS*,*RS*)-1-(*N*,*N*-Dibenzylamino)-4-fluorohexan-3-ol (61). Following general procedure 2, **52** (200 mg, 0.72 mmol, >99:1 dr) in CH_2Cl_2 (4.1 mL) was treated with HBF_4·OEt_2 (195 μL, 1.43 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.9 mL, 1.5 mmol) for 18 h. K_2CO_3 (9.7 mg, 0.07 mmol) and MeOH (1.8 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **61** as a colorless oil (55 mg, 24%, >99:1 dr): R_f 0.23 (30−40 °C petroleum ether/Et_2O, 4:1); δ_H (400 MHz, $CDCl_3$) 0.98 (3H, app t, *J* 7.4, C(6)H_3), 1.47−1.78 (3H, m, C(2)H_A, C(5)H_2), 1.94 (1H, app dtd, *J* 14.4, 10.5, 3.9, C(2)H_B), 2.62 (1H, app dt, *J* 12.9, 4.3, C(1)H_A), 2.76−2.85 (1H, m, C(1)H_B), 3.29 (2H, d, *J* 13.1, N(CH_AH_BPh)$_2$), 3.64 (1H, dddd, *J* 20.7, 10.0, 3.8, 2.6, C(3)*H*), 3.89 (2H, d, *J* 13.1, N(CH_AH_BPh)$_2$), 4.16 (1H, app ddt, *J* 48.1, 8.4, 4.1, C(4)*H*), 5.59 (1H, br s, O*H*), 7.25−7.39 (10H, m, *Ph*).

(*RS*,*SR*)-1-(*N*,*N*-Dibenzylamino)-3-fluorohexan-2-ol (62). Following general procedure 2, **53** (224 mg, 0.80 mmol, >99:1 dr) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **62** as a colorless oil (134 mg, 53%, >99:1 dr):[16] R_f 0.28 (30−40 °C petroleum ether/Et_2O, 4:1); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, app t, *J* 7.2, C(6)H_3), 1.27−1.69 (4H, m, C(4)H_2, C(5)H_2), 2.58−2.76 (2H, m, C(1)H_2), 3.36 (1H, br s, O*H*), 3.49 (2H, d, *J* 13.4, N(CH_AH_BPh)$_2$), 3.72 (1H, dddd, *J* 11.5, 9.6, 5.8, 3.8, C(2)*H*), 3.83 (2H, d, *J* 13.4, N(CH_AH_BPh)$_2$), 4.29 (1H, dddd, *J* 48.5, 8.1, 5.8, 3.6, C(3)*H*), 7.23−7.43 (10H, m, *Ph*).

(*RS*,*SR*)-1-(*N*,*N*-Dibenzylamino)-4-fluorohexan-3-ol (63). Following general procedure 2, **54** (200 mg, 0.72 mmol, >99:1 dr) in CH_2Cl_2 (4.1 mL) was treated with HBF_4·OEt_2 (195 μL, 1.43 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.9 mL, 1.5 mmol) for 18 h. K_2CO_3 (9.7 mg, 0.07 mmol) and MeOH (1.8 mL) were then added to the residue and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **63** as a colorless oil (109 mg, 48%, >99:1 dr):[16] R_f 0.33 (30−40 °C petroleum ether/Et_2O, 4:1); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, app t, *J* 7.5, C(6)H_3), 1.49−1.87 (4H, m, C(2)H_2, C(5)H_2), 2.68−2.81 (2H, m, C(1)H_2), 3.46 (2H, d, *J* 13.1, N(CH_AH_BPh)$_2$), 3.54−3.64 (1H, m, C(3)*H*), 3.72 (2H, d, *J* 13.1, N(CH_AH_BPh)$_2$), 3.84−4.05 (1H, m, C(4)*H*), 6.17 (1H, br s, O*H*), 7.22−7.44 (10H, m, *Ph*).

(*RS*,*SR*)-2-Fluoro-4-(*N*,*N*-dibenzylamino)butane-1,3-diol (64). Following general procedure 2, **55** (160 mg, 0.60 mmol, >99:1 dr) in CH_2Cl_2 (2.8 mL) was treated with HBF_4·OEt_2 (0.82 mL, 6.0 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 2.4 mL, 1.2 mmol) for 18 h. K_2CO_3 (8.3 mg, 0.06 mmol) and MeOH (1.5 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 10→80% EtOAc in 30−40 °C petroleum ether) gave **64** as a colorless oil (58.3 mg, 32%, >99:1 dr): R_f 0.23 (30−40 °C petroleum ether/EtOAc, 3:2); ν_{max} 3394 (O−H), 3086, 3062, 3028, 2933, 2837, 2808, 1494, 1452, 1028, 739, 698; δ_H (400 MHz, $CDCl_3$) 2.64 (1H, dd, *J* 12.9, 9.6, C(4)H_A), 2.76 (1H, dd, *J* 12.9, 3.7, C(4)H_B), 2.81 (2H, br s, O*H*), 3.49 (2H, d, *J* 13.4, N(CH_AH_BPh)$_2$), 3.71−3.96 (5H, m, C(1)H_2, C(3)*H*, N(CH_AH_BPh)$_2$), 4.18−4.36 (1H, m, C(2)*H*), 7.23−7.43 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 55.7 (d, *J* 4.0, *C*(4)), 58.6 (N(*C*H_2Ph)$_2$), 62.3 (d, *J* 21.6, *C*(1)), 66.3 (d, *J* 25.6, *C*(3)), 94.5 (d, *J* 172, *C*(2)), 127.5 (*p*-*Ph*), 128.6, 129.1 (*o*,*m*-*Ph*), 138.1 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −200.0 (m); *m*/*z* (ESI$^+$) 304 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{18}H_{23}FNO_2^+$ ([M + H]$^+$) requires 304.1707, found 304.1700.

(*RS*,*SR*)-1-(*N*,*N*-Dibenzylamino)-2-methyl-3-fluorobutan-2-ol (65). Following general procedure 2, **56** (212 mg, 0.80 mmol, >99:1 dr) in CH_2Cl_2 (4.6 mL) was treated with HBF_4·OEt_2 (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% EtOAc in 30−40 °C petroleum ether) gave **65** as a colorless oil (135 mg, 56%, >99:1 dr): R_f 0.33 (30−40 °C petroleum ether/EtOAc, 9:1); ν_{max} 3453 (O−H), 3086, 3063, 3028, 2983, 2937, 2804, 1064, 744; δ_H (400 MHz, $CDCl_3$) 1.05 (3H, d, *J* 1.5, C(2)*Me*), 1.26 (3H, dd, *J* 24.8, 6.3, C(4)H_3), 2.57 (1H, dd, *J* 14.1, 1.3, C(1)H_A), 2.91 (1H, dd, *J* 14.1, 1.8, C(1)H_B), 2.99 (1H, br s, O*H*), 3.62 (2H, d, *J* 13.6, N(CH_AH_BPh)$_2$), 3.85 (2H, d, *J* 13.6, N(CH_AH_BPh)$_2$), 4.42 (1H, app

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dq, *J* 47.7, 6.3, C(3)*H*), 7.26−7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.7 (d, *J* 22.4, *C*(4)), 20.1 (C(2)*Me*), 59.5 (d, *J* 1.6, *C*(1)), 60.4 ($N(CH_2Ph)_2$), 71.8 (d, *J* 21.6, *C*(2)), 92.7 (d, *J* 172.6, *C*(3)), 127.4 (*p*-*Ph*), 128.5, 129.1 (*o*-, *m*-*Ph*), 138.9 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −180.6 (dq, *J* 47.7, 24.1); *m*/*z* (ESI^+) 324 ($[M + Na]^+$, 62), 302 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{19}H_{25}FNO^+$ ($[M + H]^+$) requires 302.1915, found 302.1903.

(*RS*,*SR*)-2-Fluoro-2,5-dimethyl-4-(*N*,*N*-dibenzylamino)hexan-3-ol (66). Following general procedure 2, **57** (123 mg, 0.40 mmol) in CH_2Cl_2 (2.3 mL) was treated with $HBF_4{\cdot}OEt_2$ (110 μL, 0.81 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 1.6 mL, 0.80 mmol) for 30 min. K_2CO_3 (5.5 mg, 0.04 mmol) and MeOH (1.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **66** as a colorless oil (112 mg, 82%, >99:1 dr):[16] R_f 0.38 (30−40 °C petroleum ether/Et_2O, 9:1); δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 21.5, C(2)Me_A), 1.12 (3H, dd, *J* 7.3, 0.5, C(5)Me_A), 1.17 (3H, dd, *J* 7.1, 0.8, C(5)Me_B), 1.45 (3H, d, *J* 23.0, C(2)Me_B), 2.34 (1H, app septet d, *J* 7.3, 2.3, C(5)*H*), 2.77 (1H, dd, *J* 8.3, 2.3, C(4)*H*), 3.54 (2H, d, *J* 12.9, $N(CH_AH_BPh)_2$), 3.74 (1H, dd, *J* 8.3, 3.0, C(3)*H*), 3.96 (2H, d, *J* 12.9, $N(CH_AH_BPh)_2$), 5.40 (1H, br s, O*H*), 7.23−7.36 (10H, m, *Ph*).

(*RS*,*SR*)-1-(*N*,*N*-Dibenzylamino)-1-phenyl-3-fluoro-3-methylbutan-2-ol (67). Following general procedure 2, **58** (273 mg, 0.80 mmol) in CH_2Cl_2 (4.6 mL) was treated with $HBF_4{\cdot}OEt_2$ (220 μL, 1.62 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 3.2 mL, 1.6 mmol) for 18 h. K_2CO_3 (11.1 mg, 0.08 mmol) and MeOH (2.0 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **67** as a white solid (229 mg, 76%, >99:1 dr):[16] R_f 0.23 (30−40 °C petroleum ether/Et_2O, 9:1); mp 114−120 °C; δ_H (400 MHz, $CDCl_3$) 0.97 (3H, d, *J* 22.0, C(3)Me_A), 1.11 (3H, d, *J* 22.2, C(3)Me_B), 3.04 (2H, d, *J* 13.1, $N(CH_AH_BPh)_2$), 3.81 (1H, d, *J* 10.1, C(1)*H*), 3.96 (2H, d, *J* 13.1, $N(CH_AH_BPh)_2$), 4.27 (1H, app t, *J* 10.1, C(2)*H*), 5.41 (1H, br s, O*H*), 7.24−7.50 (15H, m, *Ph*).

(1*RS*,2*SR*,3*RS*)-1-(*N*,*N*-Dibenzylamino)-1-phenyl-3-fluorobutan-2-ol (68) and (1*RS*,2*RS*,3*SR*)-1-(*N*,*N*-Dibenzylamino)-1-phenyl-3-fluorobutan-2-ol (69). Following general procedure 2, **59** (100 mg, 0.31 mmol, >99:1 dr) in CH_2Cl_2 (1.8 mL) was treated with $HBF_4{\cdot}OEt_2$ (83 μL, 0.61 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 1.2 mL, 0.60 mmol) for 18 h. K_2CO_3 (4.2 mg, 0.03 mmol) and MeOH (0.8 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (10 mL) and CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried and concentrated in vacuo to give a mixture of products containing an 88:12 mixture of **68**:**69**. Purification via flash column chromatography (gradient elution, 5→40% Et_2O in 30−40 °C petroleum ether) gave **68** as a colorless oil which solidified on standing to a white crystalline solid (30.9 mg, 28%, >99:1 dr): R_f 0.38 (30−40 °C petroleum ether/Et_2O, 4:1); mp 111−113 °C; ν_{max} 3496 (O−H), 3086, 3059, 3028, 2984, 2956, 2919, 2848 (C−H), 749, 699; δ_H (400 MHz, $CDCl_3$) 1.03 (3H, dd, *J* 24.8, 6.3, C(4)H_3), 3.06 (2H, d, *J* 13.3, $N(CH_AH_BPh)_2$), 3.54 (1H, dd, *J* 10.8, 0.5, C(1)*H*), 3.98 (2H, d, *J* 13.3, $N(CH_AH_BPh)_2$), 4.29 (1H, app dqd, *J* 46.2, 6.3, 2.9, C(3)*H*), 4.53 (1H, ddd, *J* 15.4, 10.8, 2.9, C(2)*H*), 4.58 (1H, s, O*H*), 7.22−7.50 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.2 (d, *J* 23.2, *C*(4)), 53.4 ($N(CH_2Ph)_2$), 63.4 (d, *J* 9.6, *C*(1)), 69.6 (d, *J* 20.8, *C*(2)), 91.4 (d, *J* 169, *C*(3)), 127.5, 128.4, 128.6, 128.7, 129.1, 129.8, 133.1, 138.2 (*Ph*); δ_F (377 MHz, $CDCl_3$) −178.2 (m); *m*/*z* (ESI^+) 749 ($[2M + Na]^+$, 30), 386 ($[M + Na]^+$, 80), 364 ($[M + H]^+$, 100); HRMS (ESI^+) $C_{24}H_{27}FNO^+$ ($[M + H]^+$) requires 364.2071, found 364.2060. Further elution gave **69** as a colorless oil which solidified on standing to a white crystalline solid (7.8 mg, 7%, >99:1 dr): R_f 0.23 (30−40 °C petroleum ether/Et_2O, 4:1); mp 108−110 °C; ν_{max} 3458 (O−H), 3086, 3063, 3029, 3004, 2935, 2838 (C−H), 748, 698; δ_H (400 MHz, $CDCl_3$) 1.04 (3H, dd, *J* 25.3, 6.1, C(4)H_3), 1.66 (1H, br s, O*H*), 3.10 (2H, d, *J* 13.5, $N(CH_AH_BPh)_2$), 3.66 (1H, d, *J* 9.7, C(1)*H*), 3.88 (2H, d, *J* 13.5, $N(CH_AH_BPh)_2$), 4.66 (1H, ddd, *J* 14.0, 9.7, 2.9, C(2)*H*), 5.25 (1H, app dqd, *J* 46.7, 6.3, 2.9, C(3)*H*), 7.24−7.53 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 13.2 (d, *J* 22.4, *C*(4)), 54.6 ($N(CH_2Ph)_2$), 64.2 (d, *J* 8.0, *C*(1)), 71.7 (d, *J* 21.6, *C*(2)), 91.7 (d, *J* 164, *C*(3)), 127.3, 128.0, 128.4, 128.5, 129.1, 130.0, 134.2 (*Ph*); δ_F (377 MHz, $CDCl_3$) −180.7 (m); *m*/*z* (ESI^+) 749 ($[2M + Na]^+$, 99), 386 ($[M + Na]^+$, 95), 364 ($[M + H]^+$, 100), 344 ($[M - F]^+$, 47); HRMS (ESI^+) $C_{24}H_{27}FNO^+$ ($[M + H]^+$) requires 364.2071, found 364.2058.

***tert*-Butyl (*S*,*Z*)-2,2-Dimethyl-4-(hexadec-1′-en-1′-yl)-oxazolidine-3-carboxylate (71) and *tert*-Butyl (*S*,*E*)-2,2-Dimethyl-4-(hexadec-1′-en-1′-yl)oxazolidine-3-carboxylate (72).** NaHMDS (1.0 M in THF, 28 mL, 28 mmol) was added dropwise to a stirred suspension of (*n*-pentadecyl)triphenylphosphonium bromide (16.7 g, 30.2 mmol) in THF (300 mL) at 0 °C, and the resultant mixture was allowed to warm to rt over 30 min. The mixture was cooled to −78 °C and *n*-hexane (450 mL) was added, followed by the dropwise addition of a solution of **70** (3.01 g, 13.1 mmol) in THF (150 mL). The resultant mixture was then allowed to warm to rt with stirring over 42 h. The reaction was quenched by addition of satd aq NH_4Cl (20 mL) and concentrated in vacuo. The residue was partitioned between Et_2O (200 mL) and H_2O (100 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **71** as a colorless oil (4.26 g, 77%, >99:1 dr):[49] R_f 0.38 (30−40 °C petroleum ether/Et_2O, 9:1); $[\alpha]_D^{20}$ −41.9 (*c* 1.0 in $CHCl_3$); {lit.[49a] for enantiomer $[\alpha]_D^{26}$ +53.5 (*c* 1.0 in $CHCl_3$)}; lit.[49b] for enantiomer $[\alpha]_D^{21}$ +50.7 (*c* 0.9 in $CHCl_3$)]; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, app t, *J* 6.8, C(16′)H_3), 1.20−1.64 (24H, m, C(4′)H_2-C(15′)H_2), 1.93−2.25 (2H, br m, C(3′)H_2), 3.64 (1H, dd, *J* 8.7, 3.2, C(5)H_A), 4.06 (1H, dd, *J* 8.7, 6.2, C(5)H_B), 4.49−4.78 (1H, br m, C(4)*H*), 5.33−5.57 (2H, br m, C(1′)*H*, C(2′)*H*). Further elution gave **72** as a white semisolid (378 mg, 7%, >99:1 dr):[49] R_f 0.28 (30−40 °C petroleum ether/Et_2O, 9:1); $[\alpha]_D^{20}$ +3.5 (*c* 1.0 in $CHCl_3$); {lit.[49b] for enantiomer $[\alpha]_D^{21}$ −5.7 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, app t, *J* 6.8, C(16′)H_3), 1.22−1.66 (24H, m, C(4′)H_2-C(15′)H_2), 1.98−2.06 (2H, m, C(3′)H_2), 3.71 (1H, dd, *J* 8.7, 2.0, C(5)H_A), 4.01 (1H, dd, *J* 8.7, 6.0, C(5)H_B), 4.14−4.50 (1H, br m, C(4)*H*), 5.34−5.72 (2H, m, C(1′)*H*, C(2′)*H*).

(*S*,*Z*)-2-(*N*,*N*-Dibenzylamino)octadec-3-en-1-ol (74). Concentrated aq HCl (1.7 mL) was added to a stirred solution of **71** (4.26 g, 10.1 mmol, >99:1 dr) in MeOH (32 mL), and the resultant mixture was heated at reflux for 17 h and then concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (100 mL) and 1 M aq NaOH (100 mL), and the layers were separated. The organic layer was washed with 1 M aq NaOH (2 × 50 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were then dried and concentrated in vacuo. BnBr (2.6 mL, 22 mmol), K_2CO_3 (4.17 g, 30.2 mmol), and EtOH (50 mL) were added to the residue, and the resultant mixture was heated at reflux for 4 h and then concentrated in vacuo. The residue was partitioned between Et_2O (100 mL) and H_2O (100 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **74** as a colorless oil (4.21 g, 90%, >99:1 dr): R_f 0.28 (30−40 °C petroleum ether/Et_2O, 9:1); $[\alpha]_D^{20}$ +7.9 (*c* 1.0 in $CHCl_3$); ν_{max} 3461 (O−H), 3086, 3063, 3028, 3005, 2922, 2852 (C−H), 1029, 744, 729; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, app t, *J* 6.8, C(18)H_3), 1.19−1.45 (24H, m, C(6)H_2-C(17)H_2), 1.87−2.04 (2H, m, C(5)H_2), 3.33 (1H, dd, *J* 10.4, 5.2,

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C(1)H_A), 3.36 (2H, d, *J* 13.5, N(C$H_A$$H_B$Ph)$_2$), 3.60 (1H, app t, *J* 10.4, C(1)H_B), 3.65−3.73 (1H, app td, *J* 10.1, 5.2, C(2)*H*), 3.91 (2H, d, *J* 13.5, N(C$H_A$$H_B$Ph)$_2$), 5.38−5.46 (1H, m, C(3)*H*), 5.80 (1H, app dt, *J* 11.0, 7.5, C(4)*H*), 7.23−7.35 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*(18)), 22.7, 28.1, 29.37, 29.39, 29.5, 29.6, 29.66, 29.70, 30.0, 31.9 (*C*(5)-*C*(17)), 53.5 (N(CH_2Ph)$_2$), 56.8 (*C*(2)), 61.2 (*C*(1)), 122.1 (*C*(4)), 127.2 (*p*-*Ph*), 128.5, 128.8 (*o*,*m*-*Ph*), 137.3 (*C*(3)), 139.3 (*i*-*Ph*); *m*/*z* (ESI$^+$) 464 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{32}H_{50}NO^+$ ([M + H]$^+$) requires 464.3887, found 464.3871.

(2*R*,3*S*,4*S*)-2-(*N*,*N*-Dibenzylamino)-4-fluorooctadecane-1,3-diol (75) and (2*S*,3*S*,4*R*)-2-Tetradecyl-4-(*N*,*N*-dibenzylamino)-tetrahydrofuran-3-ol (81). Following general procedure 2, **74** (2.78 g, 6.00 mmol, >99:1 dr) in CH_2Cl_2 (34 mL) was treated with HBF_4·OEt_2 (1.6 mL, 12 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 24 mL, 12 mmol) for 18 h. K_2CO_3 (82.9 mg, 0.60 mmol) and MeOH (15 mL) were then added to the residue, and the resultant mixture was stirred at rt for 1 h and then concentrated in vacuo. The residue was partitioned between H_2O (100 mL) and CH_2Cl_2 (100 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried and concentrated in vacuo to give a 67:16:18 mixture of **75**:**76**:**81**. Purification via flash column chromatography (gradient elution, 5→40% EtOAc in 30−40 °C petroleum ether) gave **81** as a colorless oil which solidified on standing to a white solid (397 mg, 14%, >99:1 dr): R_f 0.54 (30−40 °C petroleum ether/EtOAc, 4:1); mp 44−45 °C; $[\alpha]_D^{20}$ +1.9 (*c* 1.0 in $CHCl_3$); ν_{max} 3455, 3381 (O−H), 3086, 3062, 3028, 2917, 2850 (C−H), 1067, 1028, 747, 732, 697; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, app t, *J* 6.7, C(14′)H_3), 1.13−1.65 (26H, m, C(1′)H_2-C(13′)H_2), 3.37 (1H, app td, *J* 7.5, 1.6, C(4)*H*), 3.57−3.67 (3H, m, C(5)H_A, N(C$H_A$$H_B$Ph)$_2$), 3.68−3.74 (1H, m, C(2)*H*), 3.79 (2H, d, *J* 14.2, N(C$H_A$$H_B$Ph)$_2$), 4.07 (1H, app t, *J* 8.6, C(5)H_B), 4.27−4.33 (1H, br m, C(3)*H*), 7.21−7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*(14′)), 22.7, 26.3, 28.6, 29.4, 29.56, 29.58, 29.7, 29.8, 31.9 (*C*(1′)-*C*(13′)), 55.7 (N(CH_2Ph)$_2$), 68.4 (*C*(5)), 71.1 (*C*(4)), 74.0 (*C*(3)), 82.9 (*C*(2)), 127.1 (*p*-*Ph*), 128.3, 128.7 (*o*,*m*-*Ph*), 139.2 (*i*-*Ph*); *m*/*z* (ESI$^+$) 480 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{32}H_{50}NO_2^+$ ([M + H]$^+$) requires 480.3836, found 480.3814. Further elution gave **75** as a colorless oil which solidified on standing to an oily, white solid (1.42 g, 47%, >99:1 dr): R_f 0.27 (30−40 °C petroleum ether/EtOAc, 4:1); mp 34−36 °C; $[\alpha]_D^{20}$ −17.2 (*c* 1.0 in $CHCl_3$); ν_{max} 3383 (O−H), 3085, 3062, 3027, 2953, 2916, 2849 (C−H), 746, 723, 697; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, app t, *J* 6.8, C(18)H_3), 1.19−1.58 (25H, m, C(5)H_A, C(6)H_2-C(17)H_2), 1.66−1.81 (1H, m, C(5)H_B), 1.89 (1H, br s, O*H*), 3.05 (1H, app dt, *J* 9.0, 5.4, C(2)*H*), 3.65−3.78 (3H, m, C(3)*H*, N(C$H_A$$H_B$Ph)$_2$), 3.88−3.97 (2H, m, C(1)H_2), 4.01 (2H, d, *J* 13.4, N(C$H_A$$H_B$Ph)$_2$), 4.43−4.61 (1H, m, C(4)*H*), 7.23−7.36 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*(18)), 22.7, 25.5 (d, *J* 4.0), 29.35, 29.43, 29.5, 29.6, 29.65, 29.69, 30.8 (d, *J* 20.8), 31.9 (*C*(5)-*C*(17)), 54.7 (N(CH_2Ph)$_2$), 59.1 (*C*(1)), 59.4 (d, *J* 4.0, *C*(2)), 69.8 (d, *J* 20.8, *C*(3)), 93.4 (d, *J* 173, *C*(4)), 127.4 (*p*-*Ph*), 128.6, 129.1 (*o*,*m*-*Ph*), 138.9 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −197.9 (m); *m*/*z* (ESI$^+$) 500 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{32}H_{51}FNO_2^+$ ([M + H]$^+$) requires 500.3898, found 500.3892.

(*R*,*R*,*R*)-2-(*N*,*N*-Dibenzylamino)-4-fluorooctadecane-1,3-diol (76). HBF_4·OEt_2 (2.6 mL, 19 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 7.7 mL, 3.9 mmol) were sequentially added to **74** (446 mg, 0.96 mmol, >99:1 dr), and the resultant mixture was stirred at rt for 30 min. The reaction mixture was then added dropwise to a stirred mixture of satd aq Na_2SO_3 (20 mL) and satd aq $NaHCO_3$ (80 mL). EtOAc (100 mL) was then added, and the resultant mixture was stirred vigorously for 10 min. The layers were separated, the organic layer was washed with satd aq $NaHCO_3$ (2 × 50 mL), and the combined aqueous layers were extracted with EtOAc (2 × 50 mL). The combined organic layers were then dried and concentrated in vacuo to give a 18:66:16 mixture of **75**:**76**:**77**. Purification via flash column chromatography (gradient elution, 7→60% EtOAc in 30−40 °C petroleum ether) gave **75** as a yellow oil (33.1 mg, 7%, >99:1 dr): R_f 0.49 (30−40 °C petroleum ether/EtOAc, 7:3). Further elution gave **76** as a yellow oil which solidified on standing to a pale yellow wax (267 mg, 56%, >99:1 dr): R_f 0.26 (30−40 °C petroleum ether/EtOAc, 7:3); $[\alpha]_D^{20}$ +13.3 (*c* 1.0 in $CHCl_3$); ν_{max} 3376 (O−H), 3085, 3029, 2952, 2919, 2850 (C−H), 1113, 1022, 744, 698; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, app t, *J* 6.8, C(18)H_3), 1.19−1.78 (26H, m, C(5)H_2-C(17)H_2), 2.67 (1H, br s, O*H*), 2.89 (1H, app q, *J* 6.2, C(2)*H*), 3.73 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.80−3.91 (4H, m, C(1)H_A, C(3)*H*, N-(C$H_A$$H_B$Ph)$_2$), 3.95 (1H, dd, *J* 11.4, 6.6, C(1)H_B), 4.64 (1H, app ddt, *J* 48.3, 8.6, 4.2, C(4)*H*), 7.22−7.36 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*(18)), 22.7, 25.1 (d, *J* 4.8), 29.4, 29.5, 29.6, 29.66, 29.70, 31.2 (d, *J* 20.8), 31.9 (*C*(5)-*C*(17)), 54.6 (N(CH_2Ph)$_2$), 59.0 (*C*(1)), 59.3 (d, *J* 3.2, *C*(2)), 71.8 (d, *J* 19.2, *C*(3)), 93.9 (d, *J* 170, *C*(4)), 127.2 (*p*-*Ph*), 128.4, 128.9 (*o*,*m*-*Ph*), 139.3 (*i*-*Ph*); δ_F (377 MHz, $CDCl_3$) −196.3 (m); *m*/*z* (ESI$^+$) 500 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{32}H_{51}FNO_2^+$ ([M + H]$^+$) requires 500.3898, found 500.3883.

(2*S*,3*R*,4*R*)-2-Tetradecyl-4-(*N*,*N*-dibenzylamino)-tetrahydrofuran-3-ol (77). Following general procedure 2, **74** (139 mg, 0.30 mmol, >99:1 dr) in CH_2Cl_2 (1.0 mL) was treated with HBF_4·OEt_2 (0.82 mL, 6.0 mmol) and *m*-CPBA (0.5 M in CH_2Cl_2, 1.2 mL, 0.6 mmol) for 18 h to give a 12:88 mixture of **75**:**77**. Purification via flash column chromatography (gradient elution, 2→20% Et_2O in 30−40 °C petroleum ether) gave **77** as a colorless oil (105 mg, 73%, >99:1 dr): R_f 0.17 (30−40 °C petroleum ether/Et_2O, 9:1); $[\alpha]_D^{20}$ −19.1 (*c* 1.0 in $CHCl_3$); ν_{max} 3423 (O−H), 3086, 3063, 3028, 2923, 2853 (C−H), 749, 698; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, app t, *J* 6.8, C(14′)H_3), 1.20−1.54 (26H, m, C(1′)H_2-C(13′)H_2), 3.25−3.33 (1H, m, C(4)*H*), 3.64 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.68−3.74 (1H, m, C(5)H_A), 3.74 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.82 (1H, dd, *J* 5.3, 1.8, C(3)*H*), 3.90−3.96 (2H, m, C(2)*H*, C(5)H_B), 3.99 (1H, br s, O*H*), 7.25−7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*(14′)), 22.7, 25.8, 29.4, 29.6, 29.66, 29.69, 31.9, 34.3 (*C*(1′)-*C*(13′)), 56.0 (N(CH_2Ph)$_2$), 65.4 (*C*(4)), 68.2 (*C*(5)), 73.7 (*C*(3)), 86.6 (*C*(2)), 127.5 (*p*-*Ph*), 128.5, 129.0 (*o*,*m*-*Ph*), 137.6 (*i*-*Ph*); *m*/*z* (FI$^+$) 479 ([M]$^+$, 100); HRMS (FI$^+$) $C_{32}H_{49}NO_2^+$ ([M]$^+$) requires 479.3758, found 479.3771.

(2*S*,3*R*,4*R*)-2-Tetradecyl-4-aminotetrahydrofuran-3-ol [(−)-2-*epi*-Jaspine B] (78). Pd(OH)$_2$/C (47.3 mg, 50% w/w with respect to **77**) was added to a vigorously stirred solution of **77** (94.6 mg, 0.20 mmol, >99:1 dr) in degassed EtOAc (1.0 mL), and the resultant suspension was stirred at rt under H_2 (5 atm) for 4.5 h. The reaction mixture was then filtered through a pad of Celite (eluent EtOAc) and concentrated in vacuo to give **78** as a white solid (31.9 mg, 53%, >99:1 dr):[36] mp 94−96 °C; {lit.[36b] mp 106−108 °C}; $[\alpha]_D^{20}$ −13.3 (*c* 1.0 in MeOH); {lit.[36b] for enantiomer $[\alpha]_D^{25}$ +16.4 (*c* 0.85 in MeOH)}; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, app t, *J* 6.8, C(14′)H_3), 1.18−1.65 (26H, m, C(1′)H_2-C(13′)H_2), 2.21 (3H, br s, O*H*, NH_2), 3.40 (1H, dd, *J* 8.6, 6.8, C(5)H_A), 3.43−3.50 (1H, m, C(2)*H*), 3.58−3.66 (2H, m, C(3)*H*, C(4)*H*), 4.12 (1H, dd, *J* 8.6, 6.3, C(5)H_B).

(2*S*,3*S*,4*R*)-2-Tetradecyl-4-aminotetrahydrofuran-3-ol [(+)-4-*epi*-Jaspine B] (82). Pd(OH)$_2$/C (47.3 mg, 50% w/w with respect to **81**) was added to a vigorously stirred solution of **81** (94.6 mg, 0.20 mmol, >99:1 dr) in degassed MeOH (1.0 mL) and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The reaction mixture was then filtered through a pad of Celite (eluent MeOH) and concentrated in vacuo to give **82** as a white solid (54.3 mg, 92%, >99:1 dr):[39] mp 83−85 °C; $[\alpha]_D^{20}$ +1.4 (*c* 1.0 in MeOH); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, app t, *J* 6.7, C(14′)H_3), 1.17−1.70 (26H, m, C(1′)H_2-C(13′)H_2), 1.92 (3H, br s, O*H*, NH_2), 3.41 (1H, dd, *J* 9.2, 3.4, C(5)H_A), 3.45−3.52 (1H, m, C(2)*H*), 3.80−3.85 (1H, m, C(3)*H*), 3.87−3.94 (1H, m, C(4)*H*), 4.22 (1H, dd, *J* 9.2, 6.0, C(5)H_B).

(2*R*,3*S*,4*S*)-2-Amino-4-fluorooctadecane-1,3-diol [4-Deoxy-4-fluoro-L-*xylo*-phytosphingosine] (85). Pd(OH)$_2$/C (624 mg, 50% w/w with respect to **75**) was added to a vigorously stirred solution of **75** (1.25 g, 2.50 mmol, >99:1 dr) in degassed MeOH (25 mL), and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The reaction mixture was then filtered through a pad of Celite (eluent MeOH) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), and the resultant solution was washed with satd aq $NaHCO_3$ (50 mL), then dried and concentrated in vacuo to give **85** as a white solid (799 mg, quant, >99:1 dr): mp 97−98 °C; $[\alpha]_D^{20}$ −6.7 (*c* 1.0 in MeOH); ν_{max} 3376, 3324 (O−H, N−H), 2916, 2850 (C−H), 1470, 1115, 1035, 748; δ_H (400 MHz, MeOH-d_4) 0.91

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(3H, app t, *J* 6.9, C(18)H_3), 1.22−1.86 (26H, m, C(5)H_2-C(17)H_2), 2.90 (1H, app q, *J* 5.3, C(2)*H*), 3.46−3.58 (2H, m, C(1)H_A, C(3)*H*), 3.64 (1H, dd, *J* 10.9, 5.3, C(1)H_B), 4.58 (1H, app ddt, *J* 48.5, 8.8, 3.7, C(4)*H*); δ_C (100 MHz, MeOH-d_4) 13.5 (*C*(18)), 22.7, 25.2 (d, *J* 4.8), 29.5, 29.68, 29.70, 29.72, 29.72, 29.78, 29.80, 31.4 (d, *J* 20.8), 32.1 (*C*(5)-*C*(17)), 54.4 (d, *J* 4.0, *C*(2)), 63.4 (*C*(1)), 72.3 (d, *J* 18.4, *C*(3)), 94.9 (d, *J* 171, *C*(4)); δ_F (377 MHz, MeOH-d_4) −198.5 (m); *m*/*z* (ESI$^+$) 342 ([M + Na]$^+$, 45), 320 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{18}H_{39}FNO_2^+$ ([M + H]$^+$) requires 320.2959, found 320.2949.

(*R*,*R*,*R*)-2-Amino-4-fluorooctadecane-1,3-diol [4-Deoxy-4-fluoro-L-*lyxo*-phytosphingosine] (86). Pd(OH)$_2$/C (65.3 mg, 50% w/w with respect to **76**) was added to a vigorously stirred solution of **76** (131 mg, 0.26 mmol, >99:1 dr) in degassed MeOH (2.6 mL), and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The reaction mixture was then filtered through a pad of Celite (eluent MeOH) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), and the resultant solution was washed with satd aq $NaHCO_3$ (50 mL), then dried and concentrated in vacuo to give **86** as a white solid (83.1 mg, quant, >99:1 dr): mp 96−98 °C; $[\alpha]_D^{20}$+5.2 (*c* 1.0 in MeOH); ν_{max} 3353, 3287 (O−H, N−H), 2914, 2848 (C−H), 1469, 1077, 1055, 1042, 880; δ_H (400 MHz, MeOH-d_4) 0.92 (3H, app t, *J* 6.9, C(18)H_3), 1.13−1.71 (25H, m, C(5)H_A, C(6)H_2-C(17)H_2), 1.78−1.91 (1H, m, C(5)H_B), 2.96 (1H, br s, C(2)*H*), 3.41 (1H, app dd, *J* 28.1, 6.3, C(3)*H*), 3.53−3.61 (1H, m, C(1)H_A), 3.81 (1H, app d, *J* 8.2, C(1)H_B), 4.64−4.80 (1H, m, C(4)H); δ_C (100 MHz, MeOH-d_4) 14.5 (*C*(18)), 23.8, 26.4 (d, *J* 4.8), 30.5, 30.68, 30.73, 30.76, 30.81, 30.82, 30.84, 32.3 (d, *J* 21.0), 33.1 (*C*(5)-*C*(17)), 55.0 (*C*(2)), 64.6 (*C*(1)), 74.3 (d, *J* 18.1, *C*(3)), 94.4 (d, *J* 172, *C*(4)); δ_F (377 MHz, MeOH-d_4) −200.4 (m); *m*/*z* (ESI$^+$) 342 ([M + Na]$^+$, 59), 320 ([M + H]$^+$, 100); HRMS (ESI$^+$) $C_{18}H_{39}FNO_2^+$ ([M + H]$^+$) requires 320.2959, found 320.2951.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra and CIFs (for structures CCDC 879943−879947). 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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(25) Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 733896 (**21**) (see ref 17c), 810177 (**23**) (see ref 16), 810178 (**24**) (see ref 16), 879943 (**25**·HBF_4), 879944 (**27**), 879945 (**28**), 879946 (**38**), 810180 (*p*-nitrobenzoate ester derivative of **60**) (see ref 16), 810181 (*p*-nitrobenzoate ester derivative of **62**) (see ref 16), 810179 (**67**) (see ref 16), and 879947 (**68**).

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