Application of Electrocyclic Ring-opening and Desymmetrizing Nucleophilic Trappings of *meso*-6,6-Dibromobicyclo[3.1.0]hexanes to Total Syntheses of Crinine and Haemanthamine Alkaloids

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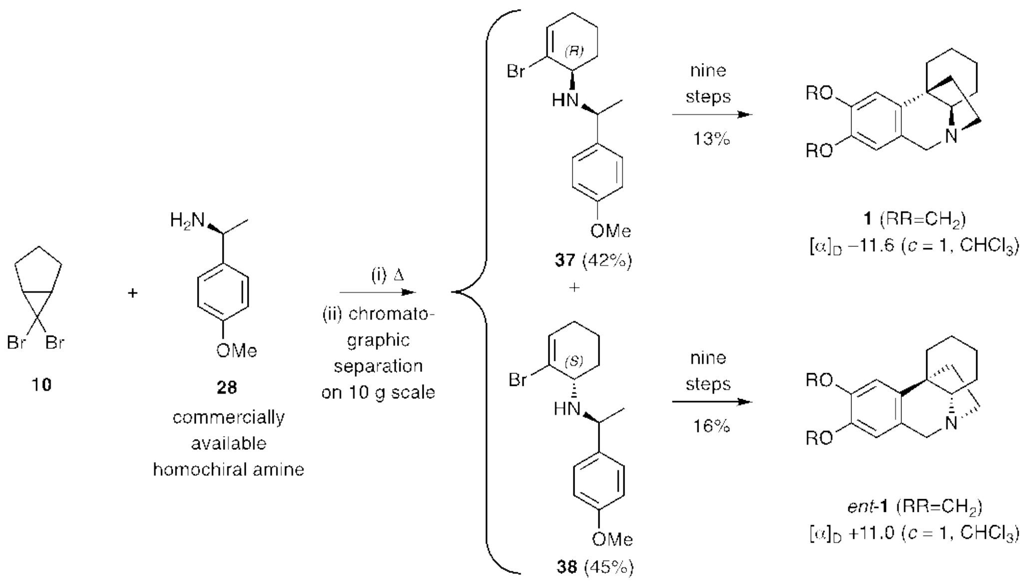
The thermally-induced electrocyclic ring-opening of C_2-symmetric (*meso*) 6,6-dibromobicyclo[3.1.0]hexanes such as **10** in the presence of the chiral, non-racemic 1°-amine **28** afforded a *ca*. 1:1 mixture of the diastereoisomeric and chromatographically separable 1-amino-2-bromo-2-cyclohexenes **37** and **38**. Each of these was elaborated, over nine steps including Suzuki-Miyaura cross-coupling, radical cyclization and Pictet-Spengler reactions, into (–)- or (+)-crinine (**1** or *ent*-**1**, respectively). Variations on these protocols have been applied to the total syntheses of (+)- and (–)-11-hydroxyvattitine [(+)- and (–)-**3**], (+)- and (–)-bulbispermine [(+)- and (–)-**4**], (+)- and (–)-haemanthidine [(+)- and (–)-**5**], (+)- and (–)-pretazettine [(+)- and (–)-**6**] and (+)- and (–)-tazettine [(+)- and (–)-**7**] as well as (±)-hamayne [(±)-**8**] and (±)-apohaemanthamine [(±)-**9**]. A number of these alkaloids have been synthesized for the first time.



INTRODUCTION

Within the vast collection of compounds isolated from the *Amaryllidaceae* family of herbaceous, perennial and bulbous flowering plants[1] those embodying the 2,3,4,4a-tetrahydro-1*H*,6*H*-β-5,10b-ethanophenanthridine skeleton **1** (Figure 1) or its α-5,10b-ethano-bridged enantiomer (*ent*-**1**) are defined as crinine or haemanthamine-type alkaloids, respectively.[1,2]

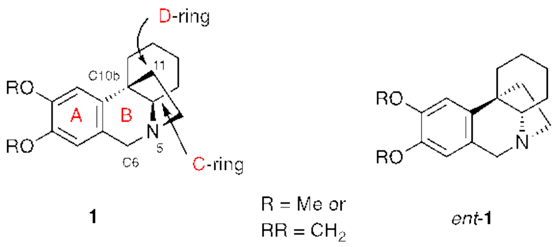


Figure 1: The 2,3,4,4a-tetrahydro-1*H*,6*H*-β-5,10b-ethanophenanthridine framework (**1**), the labeling of the associated rings and its α-5,10b-ethano-bridged enantiomer (*ent*-**1**)

So, for example, as shown in Figure 2, (–)-buphanisine [(–)-**2**] (isolated from the Central African plant *Boöphane fischeri*)[3] is a member of the former class while its optical antipode (+)-buphanisine [(+)-**2**] (isolated from the widely distributed plant *Sternbergia sicula*)[4] belongs to the haemanthamine group of alkaloids.

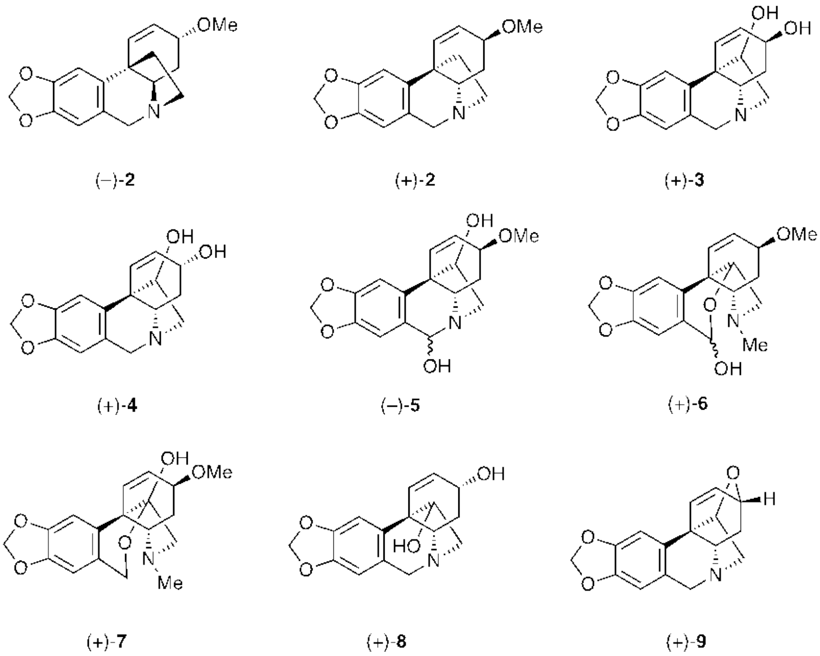


Figure 2: Representative members, (–)-**2**, (+)-**2**, (+)-**3**, (+)-**4**, (–)-**5**, (+)-**6**, (+)-**7**, (+)-**8**, and (+)-**9**, of the crinane and haemanthamine classes of alkaloids

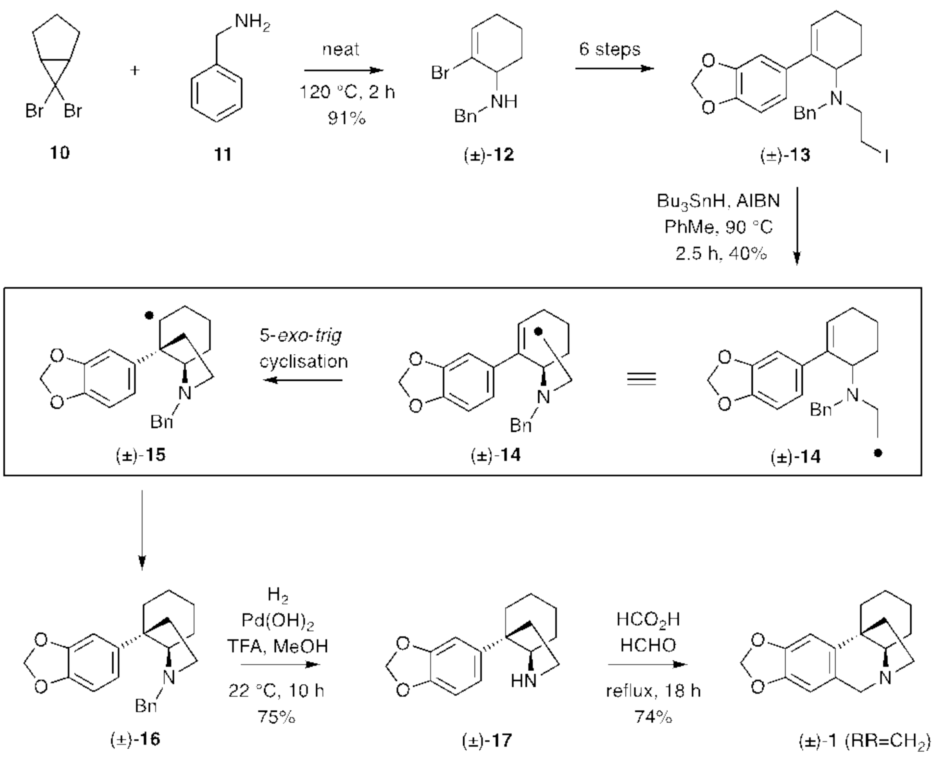
Other examples of such alkaloids relevant to the present discussion include the diastereisomerically-related compounds (+)-11-hydroxyvattitine [(+)-**3**][5] and (+)-bulbispermine [(+)-**4**][6] as well as (–)-haemanthidine [(–)-**5**][7,8] incorporating a hydroxy group in the B-ring and an established precursor to the alkaloids (+)-pretazettine [(+)-**6**] and (+)-tazettine [(+)-**7**].[9] (+)-Hamayne [(+)-**8**][10] as well as the structurally related ether (+)-apohaemanthamine [(+)-**9**][11] are further examples with the latter being both naturally occurring[11] and formed on treating crinamine with hot mineral acid.[12]

The title alkaloids exert manifold biological effects[13,14] including antimalarial, antiplasmodial, apoptosis-inducing, antibacterial, antiviral, neuroprotective and antiproliferative ones. This situation has prompted a range of productive studies on analogues.[15] Furthermore, it is also clear that certain of these natural products can serve as synthetic as well as biogenetic precursors to other classes of alkaloids.[16]

Such diverse properties have prompted extensive effects to develop total syntheses of the crinane and haemanthamine alkaloids. A range of approaches has been devised over the past four to five decades.[9,17,18] A particularly effective one has involved the formation of C3a-arylated perhydroindoles that embody the A-, C- and D-rings of the target framework **1** or *ent*-**1** and the subjection of such compounds to a Pictet-Spengler reaction and thus establishing the required B-ring and so completing the assembly these alkaloids.[18g,19] Two key challenges associated with such implementing protocols more broadly are, (i), the limited capacities currently available for introducing functionality (oxygenation) at C11 within the ethano-bridge of alkaloids such as (+)-**4**, (+)-**5**, (+)-**6**, (–)-**7**, (+)-**8** and (+)-**9** and, (ii), the restrictions on generating such systems in enantiomerically pure form.

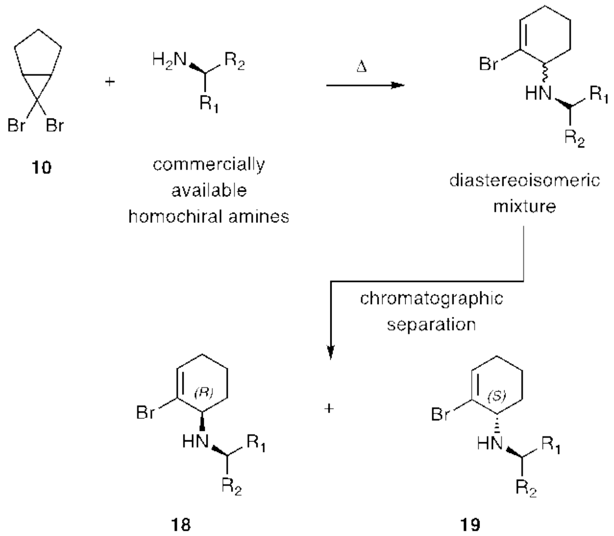
As an initial part of efforts to address the first of these deficiencies, we recently[18g] disclosed a total synthesis of the racemic modification of the crinane [*viz*. (±)-**1**]. The key elements of the approach are shown in Scheme 1 and involve, in the opening stages, the thermally-induced electrocyclic ring-opening of the ring-fused cyclopropane **10**[20] with the ensuing and C_2-symmetric π-allyl cation being intercepted by added benzylamine (**11**) and thereby delivering compound (±)-**12**. Over six steps allylic amine (±)-**12** was converted into the iodide (±)-**13** that upon exposure to *n*-Bu_3SnH resulted in the formation of the corresponding 1°-radical (±)-**14** and this then engaged in a 5-*exo*-trig radical cyclization to afford the isomeric radical (±)-**15** that upon hydrogen abstraction afforded the C3a-arylated perhydroindole (±)-**16**. This last compound embodies the ACD-ring system of the target framework and over two steps involving hydrogenolytic removal of the *N*-benzyl group, to give 2°-amine (±)-**17**, and reaction with formic acid and formaldehyde to effect a Pictet-Spengler reaction and so form the B-ring, (±)-crinane was obtained.

Scheme 1: A synthesis of (±)-crinane [(±)-**1** (R,R=CH_2)] from the C_2-symmetric ring-fused *gem*-dibromocyclopropane **10**



The C_2-symmetric nature of cyclopropane **10** and the π-allyl cation derived from its electrocyclic ring-opening means that carrying out such processes in the presence of chiral 1°-amines would be expected to result, as shown in Scheme 2, in the formation of mixtures diastereoisomeric allylic amines. These should be capable of chromatographic separation under conventional conditions and so affording the *R*- and *S*-configured products **18** and **19**, respectively. Given that heating at elevated temperatures will almost certainly be required to effect the desired conversions little if any diastereoselectivity would be expected. That said, if the diastereiosmers **18** and **19** could be formed and separated at scale then useful routes to both crinine or haemanthamine-type alkaloids could be realized.

Scheme 2: A possible pathway for preparing enantiomerically pure crinane alkaloid D-ring synthons of the general form **18** and **19** from cyclopropane **10** and homochiral 1°-amines.



The recent emergence of a significant suite of homochiral primary and secondary amines through the refinement of biocatalytic processes[21] resulted in our first efforts being directed at using these for the purposes of examining the stereochemical outcomes of the associated desymmetrizing reactions shown immediately above. As is detailed below, certain of these proved very successful and enabled the development of total syntheses, in enantiomerically pure form, of various of the alkaloids shown in Figure 2. Certain of these have been synthesized for the first time.

RESULTS AND DISCUSSION

(i) Electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (10) in the presence of homochiral primary and secondary amines – formation of enantiopure 1-amino-2-bromo-2-cyclohexenes of defined absolute configuration.

The suite of homochiral primary and secondary amines employed in examining the outcomes of the type of electrocyclic ring-opening/nucleophilic sequence proposed above are shown in Figure 3. Two distinct sets of conditions were used in effecting these processes, namely a microwave-promoted reaction of a THF solution of these reactants at 150 °C for 1.5 h (Method A) and the more conventional heating of a neat mixture of the same at 55 °C for 8 h (Method B). In each instance a four-fold excess of the relevant *S*-configured amine was used and a mixture of the diastereoisomeric 1-amino-2-bromo-2-cyclohexene derivatives **18** and **19** was thus produced. In 15 of the 19 cases (see Table 1) these could be separated from one another by flash chromatography (ΔR_f approx. 0.05) and, in all but one instance (see entry 17), the more mobile diastereoisomer had the more negative or less positive specific rotation. This trend was reversed when the *R*-configured amine *ent*-**28** was employed but not when *ent*-**23** served as the trapping nucleophile. With some exceptions, in the ^{1}H NMR spectra of the suites of compounds of the general forms **18** and **19** the resonance due to H-1 appeared at lower field in the chromatographically more mobile isomer while the reverse was so for the resonances due to the olefinic proton H-3 (the integrations of which were used to determine the diastereoisomeric ratio). The chromatographically less mobile and crystalline product derived from reaction of cyclopropane **10** with amine **30** was subjected to single-crystal X-ray analysis [see Supporting Information (SI) for details] and thus established to be compound **36** (Figure 4) possessing the *R*-configuration at C-1.

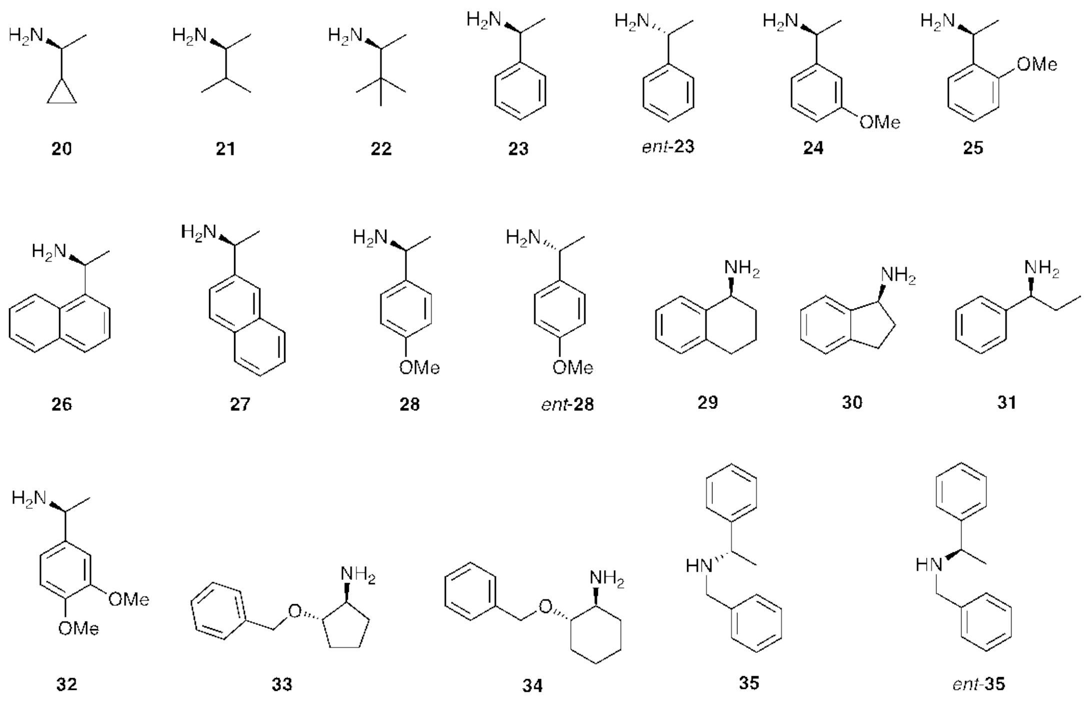


Figure 3: The commercially available amines **20-23**, *ent*-**23**, **23-28**, *ent*-**28**, **28-35** and *ent*-**35** used to trap the π-allyl cation derived from thermally-induced electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**).

Table 1: Outcomes of the reaction of cyclopropane **10** with amines **20-23**, *ent*-**23**, **23-28**, *ent*-**28**, **28-35** and *ent*-**35** under two distinct reaction conditions

Entry	Amine	Ratio[a] 18/19 Method A[b]	Ratio[a] 18/19 Method B[c]	Combined Yield (ex. Method A)	[α]D of more mobile diastere-oisomer[d]	[α]D of less mobile diastere-oisomer[d]
1	**20**	0.96:1	0.95:1	93%	No separation	No separation
2	**21**	1:1	1:1	95%	–92.2	+52.3
3	**22**	1:1	1:1	95%	–11.0	+70.8
4	**23**	1:1	1:1	94%	–92.7	–18.4
5	*ent*-**23**	1:1	1:1	89%	+96.5	+21.4
6	**24**	1:1	1:1	93%	–96.9	–23.6
7	**25**	1:1	0.95:1	94%	–90.6	–27.7
8	**26**	0.93:1	1:1	94%	–87.5	+13.6
9	**27**	0.94:1	0.95:1	91%	–86.0	–20.7
10	**28**	1:1	1:1	88%	–93.5	–20.8
11	*ent*-**28**	1:1	1:1	84%	+95.5	+18.5
12	**29**	0.82:1	0.95:1	84%	–42.2	+33.6
13	**30**	0.9:1	0.9:1	88%	–23.9	+40.0
14	**31**	0.9:1	0.9:1	88%	–93.1	–22.7
15	**32**	1:1	1:1	96%	No separation	No separation
16	**33**	0.95:1	0.95:1	96%	+10.2	+64.4
17	**34**	1:1	1:1	89%	+90.2	+21.1
18	**35**	0.74:1	NR	61%	No separation	No separation
19	*ent*-**35**	0.73:1	NR	50%	No separation	No separation

[a]ratio determined by ^{1}H NMR spectroscopy (see text); [b]Method A: microwave reaction conducted in THF at 150 °C and 80 psi for 1.5 h; [c]Method B: conventional reaction conducted with neat substrates at 55 °C for 8 h; [d]optical rotations were recorded in chloroform at 20 °C (*c* = 1 in most instances).

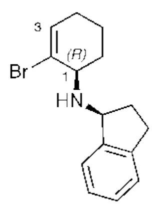


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Figure 4: The structure **36** (as established by single-crystal X-ray analysis) of the chromatographically less mobile product arising from the reaction of cyclopropane **10** with homochiral amine **30** using Method A

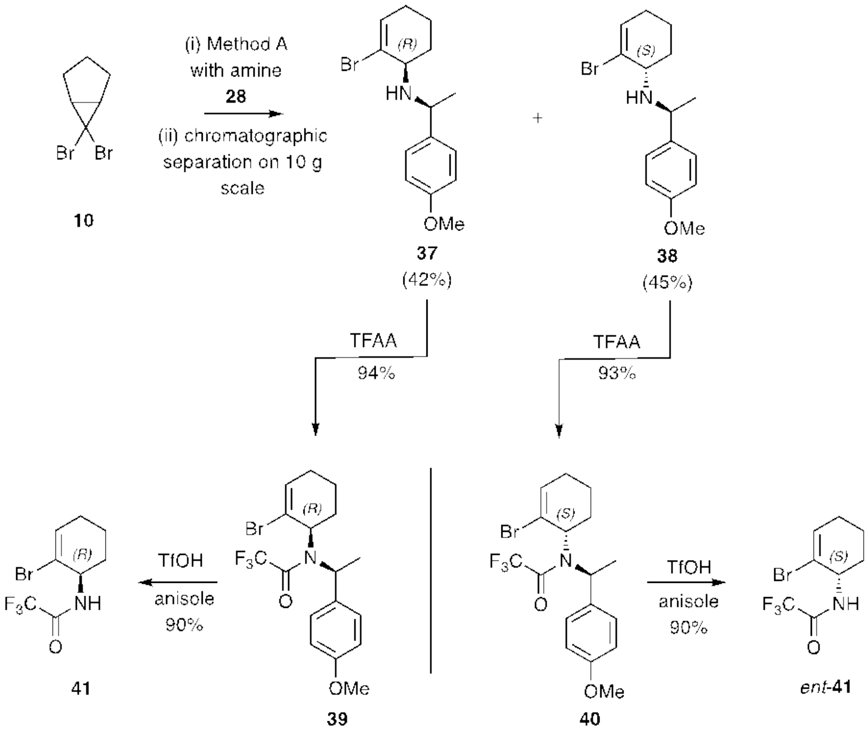
The various spectroscopic trends defined above, when considered in conjunction with the outcomes of other single-crystal X-ray analyses undertaken (as delineated below), led to the conclusion that the less mobile diastereoisomers likely possess the *R*-configuration at C-1 while the more mobile ones are *S*-configured at the same center. Whether or not the products of the reaction of compound **10** with amine **34** (entry 17, Table 1) conform to this "rule of thumb" remains to be determined.

Clearly the diastereoselectivities associated with the desymmetrizing electrocyclic ring-opening/nucleophilic trapping processes shown in Scheme 2 are very low and all efforts to improve upon these by varying the reaction conditions proved unsuccessful. However, this situation was offset to some extent, at least, by the ease with which certain of the products could be separated from one another, including at multi-gram-scale, using conventional flash chromatographic techniques. As such, sufficient quantities of various of the product 1-amino-2-bromo-2-cyclohexenes were available to explore their utility as building blocks for the assembly of the title alkaloids. Initial studies of this type, which are detailed in the following section, were focused on developing the means for generating the parent systems **1** (R,R=CH_2**)** and *ent*-**1** (R,R=CH_2), which, while not natural products themselves, have previously been targets for chemical synthesis.[18g]

(ii) Elaboration of 1-amino-2-bromo-2-cyclohexenes 37 and 38 into compounds 1(R,R=CH₂) and **ent-***1(R,R=CH₂)*

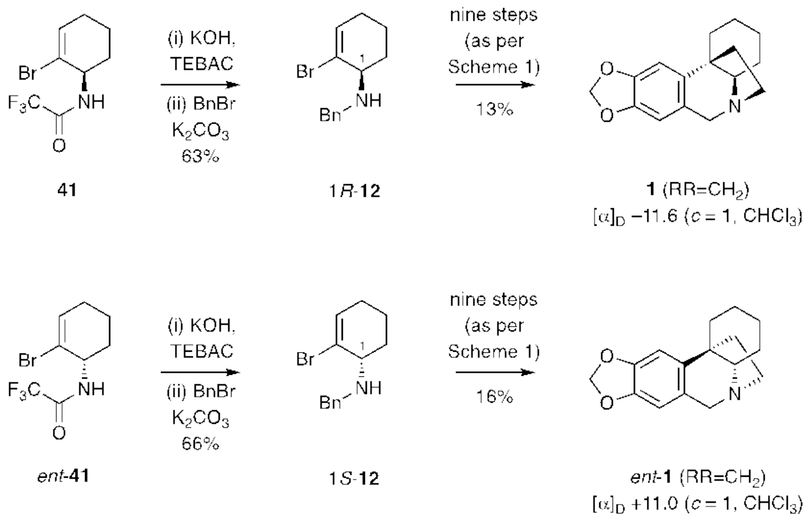
The opening stages of the reaction sequences used for the elaboration of the chromatographically separable 1-amino-2-bromo-2-cyclohexenes **37** and **38** (derived from the reaction of amine **28** with cyclopropane **10**) into (–)-crinane [**1** (R,R=CH_2)] and haemanthamine [aka (+)-crinane, *ent*-**1** (R,R=CH_2)], respectively, are shown in Scheme 3. The initial focus of our studies was on the removal of the chiral auxiliary at nitrogen in compounds **37** and **38**. Ultimately a two-step cleavage process proved necessary, the first being their high-yielding conversions, under standard conditions, into the corresponding trifluoroacetamides, **39** and **40**, respectively. Independent treatment of the latter pair of compounds with triflic acid (TfOH) in the presence of the anisole (serving as a benzyl cation scavenger) then afforded the enantiomerically related and crystalline trifluoroacetamides **41** (90%) and *ent*-**41** (90%), respectively, the structures, including absolute configurations, of which were confirmed by single-crystal X-ray analyses (see SI for details).

Scheme 3: Reaction of the C_2-symmetric *gem*-dibromocyclopropane **10** with amine **28** and elaboration of the diastereoisomeric adducts **37** and **38** to the homochiral trifluoroacetamides **41** and *ent*-**41**



The straightforward means by which trifluoroacetamides **41** (90%) and *ent*-**41** (90%) were elaborated to targets **1** (RR=CH_2) and *ent*-**1** (RR=CH_2) are shown in Scheme 4. Thus, sequential treatment of a dichloromethane solution of the former amide with aqueous potassium hydroxide in the presence of the phase transfer catalyst triethylbenzyl ammonium bromide (TEBAC) followed by immediate reaction of the resulting 1°-amine with benzyl bromide (BnBr) in the presence of potassium carbonate. This gave the *R*-configured form of compound **12** (63%), the racemic modification of which has been converted over nine steps into (±)-crinane (viz. (±)-**1** [R,R=CH_2]). Accordingly, the 2°-amine 1*R*-**12** was subjected to the same reaction sequence [see the Experimental Section for details], including the pivotal 5-*exo*-trig radical cyclization process, as shown in Scheme 1 and thus affording, in 13% overall yield, compound 1*R*-**1** (RR=CH_2). The specific rotation determined for this material was $[\alpha]_D$ = –11.6 (c = 1, $CHCl_3$). An analogous sequence allowed for the conversion of compound *ent*-**41**, via 2°-amine 1*S*-**12** (66%), into the 2,3,4,4a-tetrahydro-1*H*,6*H*-β-5,10b-ethanophenanthridine *ent*-**1** (R,R=CH_2) (16%), the specific rotation for which {$[\alpha]_D$ = +11.0 (c = 1, $CHCl_3$)} was a good match for that recently reported by others[17h] {$[\alpha]_D$ = +8.20 (c = 1, $CHCl_3$)}.

Scheme 4: Elaboration of Compound **41** and its Enantiomer to (–)- and (+)-Crinane



(iii) Developing protocols for the formation of enantiomerically pure and oxygenated 1-amino-2-bromo-2-cyclohexenes

Any efforts to adapt the protocols delineated immediately above to natural products such as those shown in Figure 1 require a capacity to introduce both unsaturation and oxygenation within the D-ring as well as, in most cases, oxygen (normally at C11) in the C-ring. While the radical cyclisation protocols detailed above do not allow this, suitable modifications to our previously reported synthesis of (±)-hamayne[18d] could do so. Accordingly, we set out to explore such possibilities by examining the relevant behaviors of the known, oxygenated, ring-fused and C_2-symmetric *gem*-dibromocyclopropanes **42** (Scheme 5), each diastereoisomeric form of which would be expected to undergo electrocyclic ring-opening to give a common *π*-allyl cation. In principle, the interception of such a cation by added homochiral amines could lead to four diastereoisomeric products but in practice, as revealed below, only the *trans*-forms **43** and **44**, were generated in significant amounts. The outcomes of conducting the appropriate suite of ring-opening experiments on compounds **42** and using the homochiral amines **20-23**, *ent*-**23**, **23-28**, *ent*-**28**, **28**-**35** and *ent*-**35** as trapping nucleophiles **(**under the same pair of reaction conditions as employed previously – See Table 1) are summarized in Table 2. As was observed in the non-oxygenated series, where the diastereoisomeric products **43** and **44** could be separated from one another (Table 2), the chromatographically more mobile one had the more negative or less positive specific rotation, save for those cases (entries 5 and 11, Table 2) where the enantiomeric form of the trapping amine was employed.

Scheme 5: A possible pathway for preparing enantiomerically pure and oxygenated crinane alkaloid D-ring synthons of the general form **43** and **44** from cyclopropane **42** and homochiral 1°-amines.

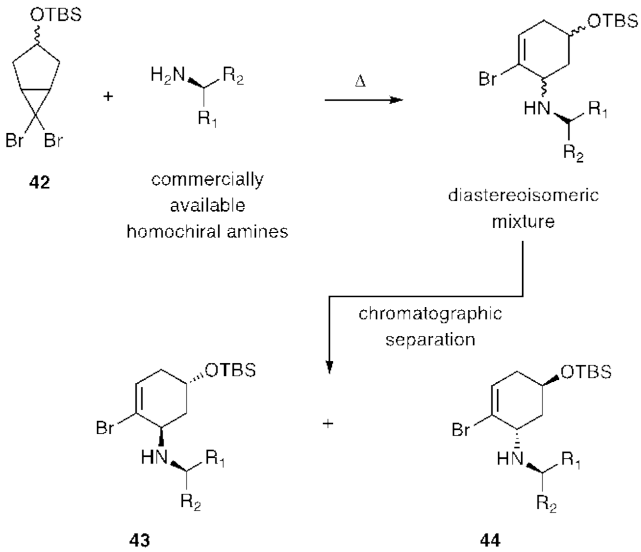


Table 2: Outcomes of the reaction of cyclopropanes **42** with amines **20-23**, *ent*-**23**, **23-28**, *ent*-**28**, **28-35** and *ent*-**35** under two distinct reaction conditions

Entry	Amine	Ratio[a] 43/44 Method A[b]	Ratio[a] 43/44 Method B[c]	Combined Yield (ex. Method A)	[α]D of more mobile diastere-oisomer[d]	[α]D of less mobile diastere-oisomer[d]
1	**20**	1:1	1:1	88%	No separation	No separation
2	**21**	1:1	1:1	87%	–15.2	+42.9
3	**22**	1:1	1:1	84%	–24.5	+53.8
4	**23**	0.87:1	0.80:1	88%	–70.4	–10.2
5	*ent*-**23**	0.87:1	0.80:1	89%	+64.3	+5.8
6	**24**	1:1	1:1	86%	–69.5	–19.1
7	**25**	1:1	1:1	83%	–41.5	–16.1
8	**26**	0.88:1	0.82:1	81%	–65.3	+10.3
9	**27**	0.88:1	0.82:1	84%	–67.1	–27.2
10	**28**	0.84:1	0.81:1	89%	–93.9	–11.5
11	*ent*-**28**	0.85:1	0.84:1	93%	+85.9	+17.2
12	**29**	1:1	1:1	85%	No separation	No separation
13	**30**	1:1	1:1	90%	–69.7	+54.4
14	**31**	0.88:1	0.88:1	89%	–64.6	–15.3
15	**32**	1:1	0.84:1	85%	–87.0	–35.2
16	**33**	1:1	1:1	88%	No separation	No separation
17	**34**	1:1	1:1	91%	No separation	No separation
18	**35**	0.74:1	NR	59%	No separation	No separation
19	*ent*-**35**	0.71:1	NR	61%	No separation	No separation

[a]ratio determined by ^{1}H NMR spectroscopy (see text); [b]Method A: microwave reaction conducted in THF at 150 °C and 80 psi for 1.5 h; [c]Method B: conventional reaction conducted with neat substrates at 55 °C for 8 h; [d]optical rotations were recorded in chloroform at 20 °C (c = 1 in most instances).

On the basis of the foregoing and given that a single-crystal X-ray analysis of the less mobile product from π-allyl trapping with amine **30** (see Experimental Section and Supporting Information for details) reveals that this is compound **45** (Figure 5), then the *R*-configuration is provisionally assigned to the new stereogenic center in the similarly less mobile products arising from the reactions shown in Table 2, except entries 5 and 11 (where the enantiomeric amines where used in the trapping reactions).

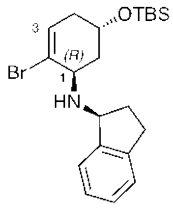


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Figure 5: The structure **45** (as established by single-crystal X-ray analysis) of the chromatographically less mobile product arising from the reaction of cyclopropane **42** with homochiral amine **30**.

With the conclusion of the methodological studies detailed above, attention turned to their exploitation in the total synthesis of key members of the title families of alkaloids. The successful outcomes of such studies are detailed in the following sections and these also serve to reinforce the structural assignments made above.

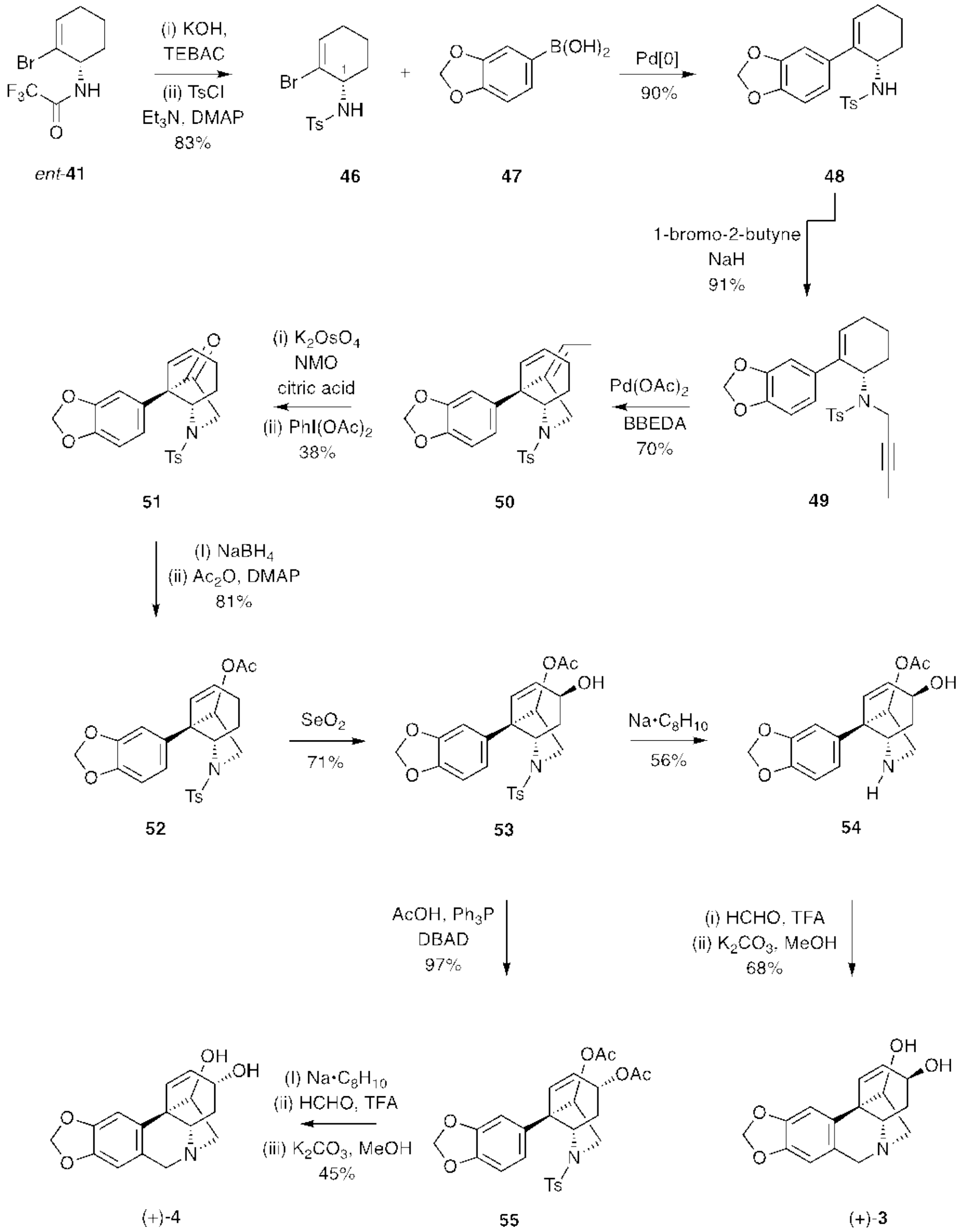
(iv) ***Total syntheses of (+)-11-hydroxyvattitine [(+)-3] and (+)-bulbispermine [(+)-4]***

The synthetic sequences leading to alkaloids (+)-**3** and (+)-**4** are shown in Scheme 6 and start with the two-step conversion of compound *ent*-**21** into the sulfonamide **46** (83%) that was subjected to Suzuki-Miyaura cross-coupling with the commercially available arylboronic acid **47** and thus forming the expected product **48** (90%). In keeping with earlier studies in the racemic series,[18b,d,e,f] *N*-propargylation of the last compound using 1-bromo-2-butyne in the presence of sodium hydride gave 1,6-enyne **49** (91%) that engaged in a palladium-catalyzed Alder ene reaction and so affording the C3a-arylated hexahydroindole **50** (70%). This pivotal transformation introduces both D-ring unsaturation and C-ring functionality as required in constructing targets (+)-**3** and (+)-**4**. The oxidative cleavage of the exocyclic double-bond within compound **50** was accomplished by treating with a combination of *N*-methylmorpholine *N*-oxide (NMO) and K_2OsO_4•$2H_2O$ in the presence of citric acid.[18f] The resulting diols were immediately cleaved oxidatively using $PhI(OAc)_2$ and so affording the ketone **51** albeit in just 38% yield, presumably because of competing dihydroxylation at the endo-cyclic double-bond in the substrate. Reduction of ketone **51** with sodium borohydride gave a single alcohol that upon acetylation afforded ester **52** in 81% yield. Treatment of this last compound with selenium dioxide afforded the allylic alcohol **53** stereoselectively in 71% yield and the structure of which was confirmed by single-crystal X-ray analysis (see SI for details). The associated tosyl group was cleaved using sodium naphthalenide[22] and the resulting secondary amine **54** (56%) subjected to a Pictet-Spengler reaction using formaldehyde in the presence of trifluoroacetic acid

(TFA). Treatment of the ensuing pentacyclic diacetate with potassium carbonate in methanol then gave (+)-11-hydroxyvattitine [(+)-**3**]. The spectral data acquired on this compound matched those reported for the natural product. A comparison of the relevant sets of ^{13}C NMR data are presented in the SI. Furthermore, the specific rotation of the synthetic material {$[\alpha]_D$ = +11.3 (*c* = 0.88, methanol)} compared favorably with the value observed[5] for the natural product {$[\alpha]_D$ = +11.0 (*c* = 0.88, methanol)}.

Engagement of compound **53** in a Mitsunobu reaction using acetic acid as the nucleophile and a combination of Ph_3P and DBAD for alcohol activation afforded diacetate **55** (97%), the structure of which was confirmed by single-crystal X-ray analysis (see SI for details). Subjection of this diester to the same three steps employed in completing the synthesis of the previous target then delivered (+)-bulbispermine [(+)-**4**] in 45% yield. Once again, all the NMR spectral data acquired on this product matched those reported for the racemate we had obtained earlier while the specific rotation of the synthetically-derived and enantiomerically pure material was in good agreement with that reported for the natural product {$[\alpha]_D$ = +108.9 (*c* 1.0, methanol); lit.[23] $[\alpha]_D$ = +106.7 (*c* 1.02, methanol)}.

Scheme 6: Syntheses of (+)-11-hydroxyvattitine [(+)-**3**] and (+)-bulbispermine [(+)-**4**] from trifluoroacetamide *ent*-**41**



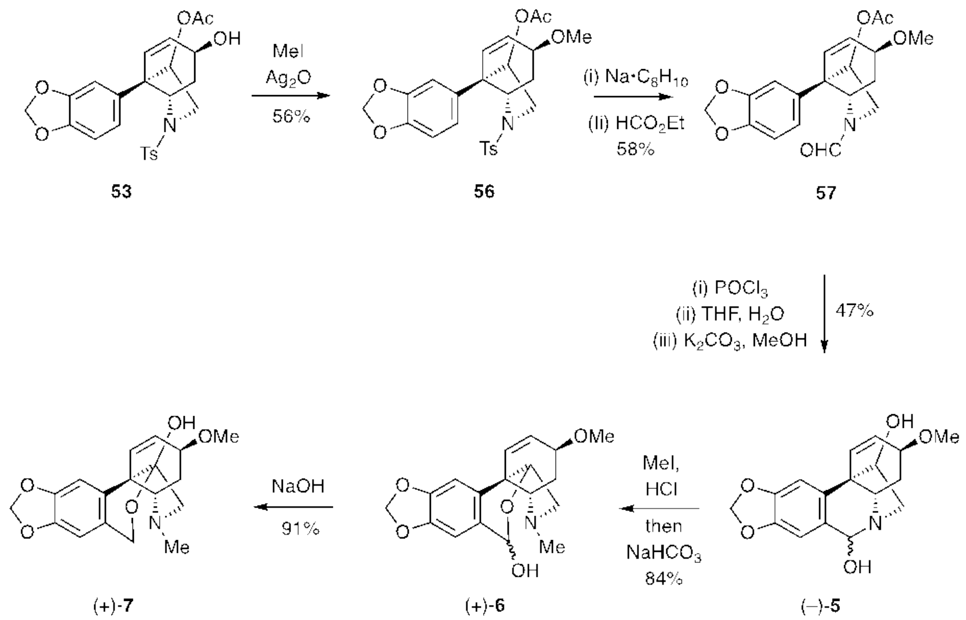
(v) *Total syntheses of (–)-11-hydroxyvattitine [(–)-3] and (–)-bulbispermine [(–)-4]*

A series of reactions analogous to those shown in Scheme 6 but now starting with homochiral allylic amine **41** allowed for the syntheses of alkaloids (–)-**3** and (–)-**4**. Full details of these conversions are presented in the Experimental Section. All of the spectra obtained on the final products matched those recorded for their enantiomers while the specific rotations of each were of similar magnitude but opposite sign to those of their optical antipodes. Furthermore, the structure of compound (–)-**3** was confirmed through a single-crystal X-ray analysis of its picrate salt.

(vi) ***Total syntheses of (–)-haemanthidine [(–)-5], (+)-pretazettine [(+)-6] and (+)-tazettine [(+)-7]***

Alkaloids (–)-**5**, (+)-**6** and (+)-**7** were readily prepared from the homochiral intermediate **53** using the reaction sequence shown in Scheme 7. Thus, Purdie-Irvine *O*-methylation of alcohol **53** afforded ether **56** (56%) and the structure of the latter was confirmed through the single-crystal X-ray analysis on the racemate obtained during preliminary studies. The tosyl group associated with compound **56** was cleaved with sodium naphthalenide to give the corresponding secondary amine. Treatment of this with ethyl formate then afforded the formamide **57** (58% over two steps) that on exposure to $POCl_3$ engaged in an intramolecular Vilsmaier-Haack-type formylation reaction to deliver, after exposure of the initially-formed cyclization product to aqueous THF then potassium carbonate, (–)-haemanthidine [(–)-**5**] in 47% yield. Treatment of compound (–)-**5** with methyl iodide, HCl then sodium bicarbonate afforded (+)-pretazzetine [(+)-**6**],[9] as a single anomer, in 84% yield. Finally, exposure of acetal (+)-**6** to sodium hydroxide afforded (+)-tazettine [(+)-**7**][9] in 91% yield and the structure of which was confirmed through an X-ray analysis of the readily picrate salt of the racemate obtained during preliminary studies. All the spectral data acquired on compounds (–)-**5,** (+)-**6** and (+)-**7** were in complete accord with the assigned structures and matched those reported previously (see SI for details). Relevant comparisons of the ^{13}C NMR data sets are also provided in the SI.

Scheme 7: Total syntheses of (–)-haemanthidine [(–)-**5**], (+)-pretazettine [(+)-**6**] and (+)-tazettine [(+)-**7**] from the C3a-arylated hexahydroindole **53**



(vii) ***Total syntheses of (+)-haemanthidine [(+)-5], (–)-pretazettine [(–)-6] and (–)-tazettine [(–)-7]***

Starting from amide **41**, compound *ent*-**53** (Figure 6) could be prepared using the early steps associated reaction sequence shown in Scheme 6 and this sulfonamide (the structure of which was confirmed by single-crystal X-ray analysis) could then be converted, using the same reaction steps as shown in Scheme 7, into the title compounds (+)-**5**, (–)-**6** and (–)-**7**. Once again, all the spectral data derived from this trio of hitherto unreported compounds accorded with the assigned structures and compared favorably with those detailed previously for their optical antipodes. Relevant comparisons are provided in the SI.

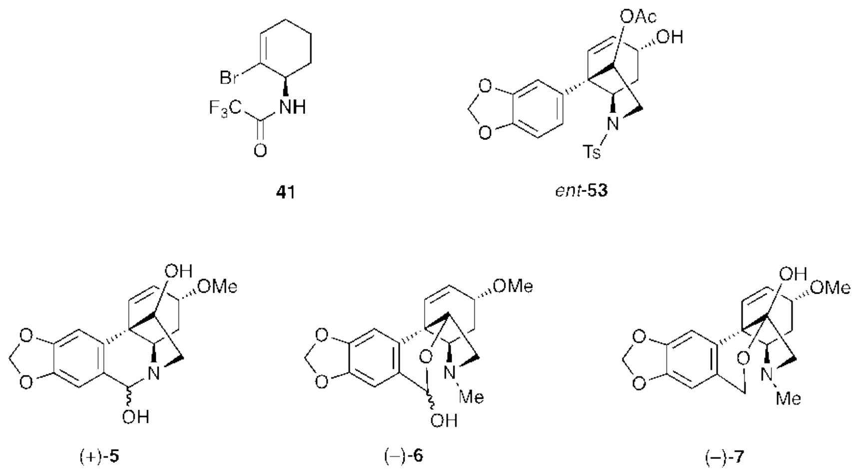


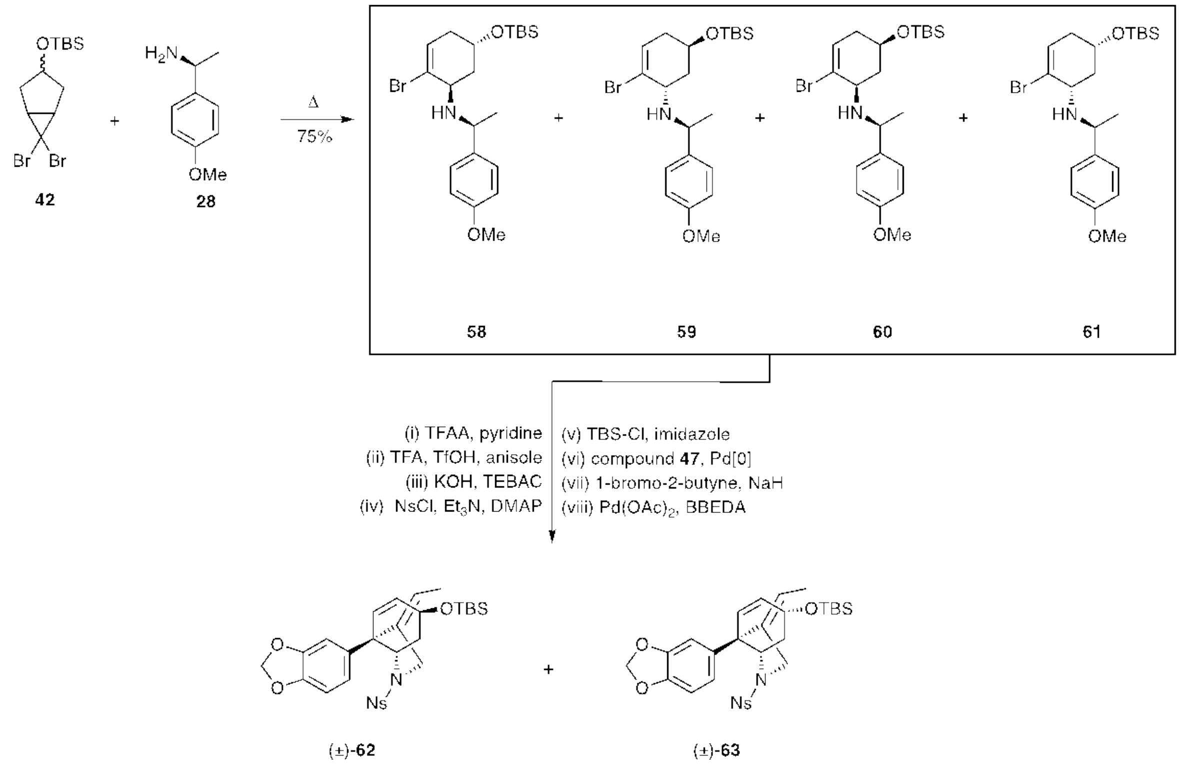
Figure 6: The structures of compounds **41**, *ent*-**53**, (+)-**5**, (–)-**6** and (–)-**7**

(viii) ***Total syntheses of (±)-hamayne [(±)-8] and (±)-apohaemanthamine [(±)-9]***

Total syntheses of alkaloids (±)-**8** and (±)-**9** were accomplished using the ring opening/nucleophilic trapping products derived from reaction of the oxygenated cyclopropane **42** and amine **28** (Scheme 8). Thus, using Method B a mixture of the four possible trapping products, **58**-**61**, and comprising the relevant pairs of *cis*- and *trans*-isomers, was obtained. Since these could not be separated from one another by normal flash chromatographic methods, this four-component mixture was carried through the illustrated eight steps and thereby affording the epimeric and chromatographically separable nosylates (±)-**62** and (±)-**63**. So, following the protocols defined in Scheme 3 and the early parts of Scheme 4, the mixture **58-61** was treated with TFAA and pyridine and thereby forming the corresponding mixture of trifluoroacetamides (90% combined yield) that also failed to separate under flash chromatographic conditions. Treatment of these amides with TFA/TfOH in the presence of anisole resulted in cleavage of the chiral auxiliaries and the resulting *cis*/*trans* pair of amides (67% combined yield) was treated with potassium hydroxide in the presence of triethylbenzylammonium chloride (TEBAC) and so affording the corresponding amino-alcohols and these were converted into the corresponding nosylates on reaction with nosyl chloride in the presence of triethylamine and DMAP. Treatment of these sulfonamides with TBS-Cl in the presence of imidazole resulted in the re-instatement of the silyl ether cleaved in a preceding step. The diastereoisomeric mixture of sulfonamide/ethers so-obtained (in 60% yield over three steps) were engaged in a Suzuki-Miyaura cross-coupling with the aryl boronic acid **47** under conditions similar to those employed in the conversion **46** + **47** $\rightarrow$ **48** (Scheme 6) and so afforded the expected product mixture (85%), the sulfonamide nitrogen of which was propargylated using 1-bromo-2-butyne in the presence of sodium hydride.

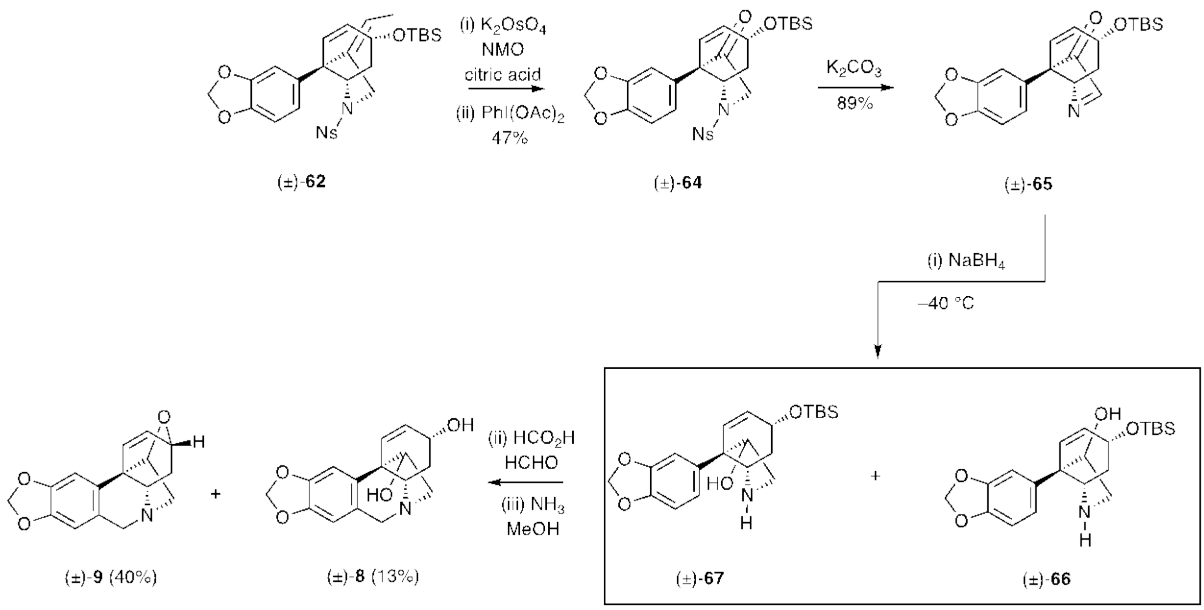
This mixture of product 1,6-enynes (88%) was then engaged in a palladium-catalyzed intramolecular Alder-ene reaction analogous the the conversion **49** → **50** (Scheme 6) and so affording the now chromatographically separable C3a-arylated hexahydroindoles (±)-**62** (9%) and (±)-**63** (56%).

Scheme 8: The reaction of cyclopropane **42** with homochiral 1°-amine **28** and the elaboration of products **58**-**61** to C3a-arylated hexahydroindoles (±)-**62** and (±)-**63**



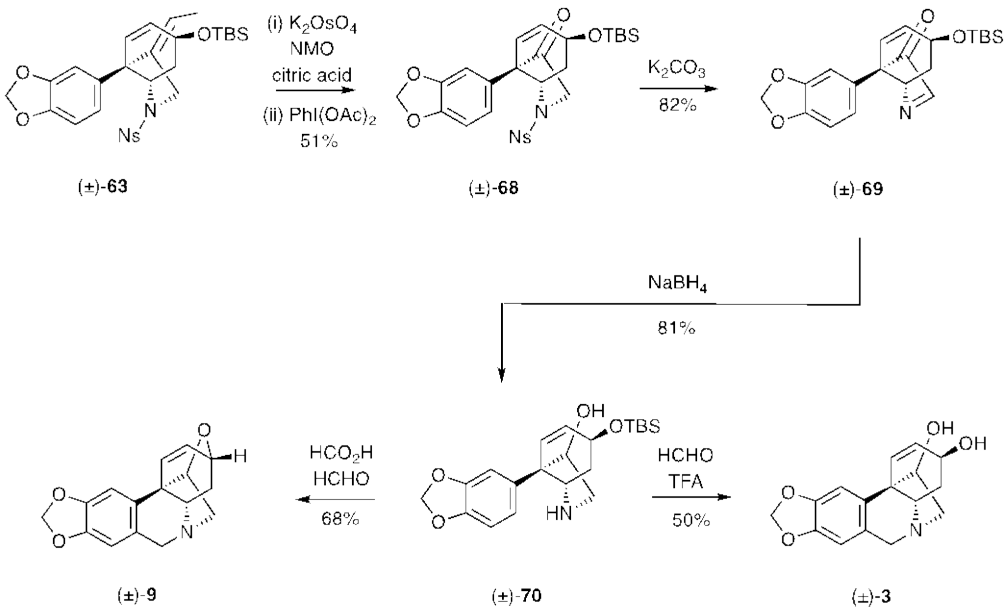
Of course, the less-than-desirable consequence of employing this reaction sequence was that cleavage of the chiral amine-based residue occurred prior to any chromatographic separation of the relevant diastereoisomers and so delivering racemates. Nevertheless, these could be exploited in developing routes to the title compounds (±)-**8** and (±)-**9**, the latter having not been the subject of previously successful total synthesis. So, for example compound (±)-**62** was converted (Scheme 9), through a three-step process and via intermediate (±)-**64**, into the ketone-conjugated imine (±)-**65**. Reduction of this last compound with sodium borohydride at –40 °C followed by immediate treatment of the resulting epimeric mixture of alcohols (±)-**66** and (±)-**67** with formaldehyde in formic acid afforded, after a work-up using ammonia-saturated methanol, a chromatographically separable mixture of (±)-hamayne [(±)-**8**] (13%) and apohaemanthamine [(±)-**9**] (40%). The structure of compound (±)-**9** was confirmed by single-crystal X-ray analysis (see SI for details). The spectral data derived from these final products were in accord with the assigned structures and matched those reported previously (see the SI for relevant comparisons of spectral data). Furthermore, a single crystal X-ray analysis of apohaemanthamine [(±)-**9**] was secured (see SI for details).

Scheme 9: Elaboration of C3a-arylated hexahydroindole (±)-**62** to (±)-hamayne [(±)-**8**] and (±)-apohaemanthamine [(±)-**9**]



A somewhat more efficient route to apohaemanthamine [(±)-**9**] arose from analogous manipulations of substrate (±)-**63** as shown in Scheme 10. So, when the by now standard two-step oxidation cleavage protocol was applied to this starting material then ketone (±)-**68** (51%) was obtained and on treating this K_2CO_3 and E1cb reaction took place and so delivering the □-azaenone (±)-**69** (82%). Reduction of this last compound took place stereoselectively and so affording alcohol (±)-**70** (81%) that when treated with formaldehyde in hot formic acid gave apohaemanthamine [(±)-**9**] in 68% yield. In contrast, on treating alcohol (±)-**70** with formaldehyde and trifluoroacetic acid (TFA) at 60 °C then a Pictet-Spengler reaction took place and this was accompanied by silyl ether cleavage and thus affording (±)-11-hydroxyvattitine [(±)-**3**] in 50% yield. The ^{1}H and ^{13}C NMR spectral data derived from this material matched those obtained for its enantiomerically pure counterpart and its structure was confirmed by single-crystal X-ray analysis (see Experimental Sction and SI for details).

Scheme 10: Elaboration of C3a-arylated hexahydroindole (±)-**63** to (±)-11-hydroxyvattitine [(±)-**3**] and (±)-apohaemanthamine [(±)-**9**]



CONCLUSION

The thermally-induced electrocyclic ring-opening of the *meso*-cyclopropanes **10** and **42** and the *in situ* nucleophilic trapping of the resulting π-allyl cations using commercially available, chiral, non-racemic amines has allowed for the formation of diastereoisomeric pairs of 2-bromocyclohex-2-en-1-amines. Various of these can be separated at multi-gram scale by conventional chromatographic methods and the individual isomers then manipulated so as to afford homochiral 2-bromocyclohex-2-en-1-amines. Manipulation of simple derivatives of these using a range of protocols, most notably palladium-catalyzed intramolecular Alder-ene reactions, then allows for their conversion into either crinine or haemanthamine-type alkaloids. Given the broad synthetic utility of the electrocyclic ring-opening/nucleophilic trapping reactions of ring-fused *gem*-dihalocyclopropanes in the synthesis of biologically relevant motifs,[18] the protocols defined here should find application in a wide range of settings, including for the purposes of establishing syntheses of enantiomerically pure forms of various erythrina[24] and aeruginosin-type[25] alkaloids.

EXPERIMENTAL SECTION

General Experimental Protocols

Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at room temperature in base-filtered $CDCl_3$ on a Varian spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei. For ^{1}H NMR spectra, signals arising from the residual protio-forms of the solvent were used as the internal standards. ^{1}H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) *J* (Hz), relative integral] where multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. The signal due to residual $CHCl_3$ appearing at δ_H 7.26 and the central resonance of the $CDCl_3$ "triplet" appearing at δ_C 77.0 were used to reference ^{1}H and ^{13}C NMR spectra, respectively. The signal due to residual CH_3OH appearing at δ_H 3.31 and the central resonance of the CD_3OD "multiplet" appearing at δ_C 49.0 were used to reference ^{1}H and ^{13}C NMR spectra, respectively. Infrared spectra (λ_{max}) were recorded on a Perkin–Elmer 1800 Series FTIR Spectrometer. Samples were analyzed as thin films on KBr plates. Low-resolution ESI mass spectra were recorded on a single quadrupole liquid chromatograph-mass spectrometer, while high-resolution measurements were conducted on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic-sector machine. Melting points were measured on an Optimelt automated melting point system and are uncorrected. Analytical thin layer chromatography (TLC) was performed on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates as supplied by Merck while silica gel 60 (40–63 μm) was used for the column chromatography. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid : ceric sulfate : sulfuric acid (conc.) : water (37.5 g : 7.5 g : 37.5 g : 720 mL) or potassium permanganate : potassium carbonate : 5% sodium hydroxide aqueous solution : water (3 g : 20 g: 5 mL : 300 mL). Flash chromatographic separations were carried out following protocols defined by Still *et al*.[26] with silica gel 60 (40–63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials and reagents were generally available from the Sigma–Aldrich, Merck, TCI, Strem or Lancaster Chemical Companies and were used as supplied. Drying agents and other inorganic salts were purchased from the AJAX, BDH or Unilab Chemical Companies. Tetrahydrofuran (THF), diethyl ether, methanol and dichloromethane were dried using a Glass Contour solvent purification system that is based upon a technology originally described by Grubbs *et al*.[27] Where necessary, reactions were performed under an nitrogen atmosphere.

Specific Experimental Protocols

Electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (10) in the presence of homochiral primary and secondary amines 20-23, *ent*-23, 23-28, *ent*-28, 28-35 and *ent*-35

Method A:

A solution of *gem*-dibromocyclopropane **10** (1.0 mmol, 1 equiv) in THF (2 mL) was treated with the relevant homochiral primary or secondary amine **20-35** (4 equiv) and the ensuing mixture subjected to microwave irradiation (200 W, 150 °C, 80 psi) for 1.5 h in a CEM Discover microwave reactor. The cooled reaction mixture was diluted with ethyl acetate (20 mL) and the resulting solution then washed with water (1 x 20 mL) and brine (1 x 20 mL) before dried (Na_2SO_4), filtered and concentrated under reduced pressure. The generally light-yellow oil thus obtained was subjected to flash chromatography (silica, 10:1 v/v hexane/ethyl acetate elution) to afford, in the majority of cases, two fractions with a ΔR_f of approximately 0.05. In all instances except that involving compound **36**, the products were isolated as clear, colorless oils.

Method B:

The *gem*-dibromocyclopropane **10** (0.3 mmol, 1 equiv) was treated with the relevant homochiral primary or secondary amines **20-35** (4 equiv) and the ensuing mixture stirred at 55 °C (bath temperature) for 8 h. A portion of the cooled mixture was dissolved in $CDCl_3$ and the resulting solution subjected to ^{1}H NMR spectroscopic analysis. The diastereoisomeric ratio of products **18** and **19** was established by integration of the relevant resonances, normally those due to the olefinic or allylic protons, *viz*. H-3 or H-1 respectively.

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **20**.* Inseparable diastereoisomers (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate).^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of diastereoisomers) 6.09 (m, 2H), 3.36 (s, 0.5H), 3.37 (s, 0.5H), 2.10−1.96 (complex m, 3H), 1.81−1.76 (complex m, 1H), 1.75−1.65 (complex m, 2H), 1.64−1.55 (complex m, 2H), 1.16 (d, *J* = 8.4 Hz, 1.5H), 1.13 (d, *J* = 4.8 Hz, 1.5H), 0.78−0.69 (complex m, 1H), 0.49−0.38 (complex m, 1.5H), 0.32−0.26 (complex m, 0.5H), 0.17−0.15 (complex m, 0.5H), 0.12−0.05 (complex m, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of diastereoisomers) 131.5, 131.4, 126.4, 126.3, 58.3, 57.0, 56.9, 56.5, 31.6, 30.2, 27.8(2), 27.8(0), 21.5, 20.6, 18.4, 18.1, 17.2, 16.9, 4.3, 4.2, 2.4, 1.9; IR (KBr): ν_{max} 3343, 3075, 2999, 2933, 2864, 1642, 1446, 1129, 1017, 986, 871 cm^{-1}; MS (EI, 70 eV): *m/z* 245 and 243 ($M^{+\bullet}$, 100 and 95%); HRMS $M^{+\bullet}$ Calcd for $C_{11}H_{18}{}^{79}BrN$: 243.0623, Found: 243.0623; Calcd for $C_{11}H_{18}{}^{81}BrN$: 245.0602, Found: 245.0606.

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **21**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (t, *J* = 4.0 Hz, 1H), 3.24 (m, 1H), 2.38 (m, 1H), 2.08−2.01 (complex m, 2H), 1.79−1.71 (complex m, 2H), 1.66 (m, 1H), 1.59−1.51 (complex m, 2H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.89 (t, *J* = 6.4 Hz, 6H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.7, 126.3, 56.7, 56.5, 33.6, 30.1, 28.0, 19.09, 18.2, 16.7, 16.5; IR (KBr): ν_{max} 3331, 3039, 2956, 2871, 1643, 1465, 1450, 1372, 1160, 1118, 1097, 1066, 981, 741 cm^{-1}; MS (EI, 70 eV): *m/z* 247 and 245 ($M^{+\bullet}$, both 20%), 232 and 230 [(M−Me•)$^+$, 97 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{11}H_{20}{}^{79}BrN$: 245.0779, Found: 245.0771; Calcd for $C_{11}H_{20}{}^{81}BrN$: 247.0759, Found: 247.0743; $[\alpha]_D^{20}$ = −92.2 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (t, *J* = 4.0 Hz, 1H), 3.24 (broad s, 1H), 2.61 (m, 1H), 2.08−2.00 (complex m, 2H), 1.81−1.77 (complex m, 2H), 1.72−1.66 (complex m, 2H), 1.59−1.53 (complex m, 1H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.4, 126.5, 56.9, 56.6, 31.2, 30.7, 27.9, 19.6, 17.2, 17.1, 16.4; IR (KBr): ν_{max} 3339, 3038, 2957, 2871, 1641, 1465, 1445, 1385, 1373, 1115, 982, 742 cm^{-1}; MS (EI, 70 eV): *m/z* 247 and 245 ($M^{+\bullet}$, both 20%), 232 and 230 [(M−Me•)$^+$, 98 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{11}H_{20}{}^{79}BrN$: 245.0779, Found: 245.0785; Calcd for $C_{11}H_{20}{}^{81}BrN$: 247.0759, Found: 247.0766; $[\alpha]_D^{20}$ = +52.3 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **22**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (s, 1H), 3.21 (s, 1H), 2.14 (m, 1H), 2.06−2.02 (complex m, 2H), 1.82−1.76 (complex m, 2H), 1.59−1.49 (complex m, 2H), 1.05 (d, *J* = 7.8 Hz, 3H), 0.89 (s, 9H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 126.0, 59.8, 57.0, 34.3, 29.6, 26.6, 26.5, 16.3, 14.6; IR (KBr): ν_{max} 3331, 3040, 2954, 2867, 1644, 1463, 1373, 1105, 981 cm^{-1}; MS (ESI, +ve): *m/z* 262 and 260 [(M+H)$^+$, 98 and 100%]; HRMS [M+H]$^+$ Calcd for $C_{12}H_{23}{}^{79}BrN$: 260.1014, Found: 260.1012; Calcd for $C_{12}H_{23}{}^{81}BrN$: 262.0993, Found: 262.0996; $[\alpha]_D^{20}$ = −11.0 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (t, *J* = 4.0 Hz, 1H), 3.19 (s, 1H), 2.40 (q, *J* = 6.4 Hz, 1H), 2.09−2.01 (complex m, 2H), 1.80−1.64 (complex m, 2H), 1.60−1.54 (complex m, 2H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.93 (s, 9H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 131.3, 126.6, 61.8, 59.4, 35.3, 31.4, 27.9, 26.6, 17.7, 16.9; IR (KBr): ν_{max} 3372, 3048, 2954, 2866, 1641, 1479, 1452, 1372, 1128, 1115, 985 cm^{-1}; MS (EI, 70 eV): *m/z* 261 and 259 ($M^{+•}$, both 10%), 246 and 244 $[(M-Me•)^+$, 98 and 100]; HRMS $M^{+•}$ Calcd for $C_{12}H_{22}{}^{79}BrN$: 259.0936, Found: 259.0927; Calcd for $C_{12}H_{22}{}^{81}BrN$: 261.0915, Found: 261.0919; $[\alpha]_D^{20}$ = +70.8 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **23**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.23 (m, 2H), 7.15 (m, 1H), 6.02 (t, *J* = 6.4 Hz, 1H), 3.97 (q, *J* = 8.8 Hz, 1H), 3.16 (broad s, 1H), 2.01−1.84 (complex m, 2H), 1.56−1.52 (complex m, 1H), 1.49−1.45 (complex m, 2H), 1.38 (m, 1H), 1.30 (d, *J* = 8.0 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 131.5, 128.2, 126.8, 126.7, 126.3, 58.1, 58.0, 31.4, 27.8, 24.5, 17.2; IR (KBr): ν_{max} 3344, 3026, 2957, 2928, 1640, 1450, 1270, 1112, 996, 977, 762, 741, 701 cm^{-1}; MS (EI, 70 eV): *m/z* 281 and 279 ($M^{+•}$, 5 and 4%), 266 and 264 ($[M-Me•]^+$, 99 and 100); HRMS $M^{+•}$ Calcd for $C_{14}H_{18}{}^{79}BrN$: 279.0623, Found: 279.0627; Calcd for $C_{14}H_{18}{}^{81}BrN$: 281.0602, Found: 281.0614; $[\alpha]_D^{20}$ = −92.7 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.16 (complex m, 5H), 6.05 (t, *J* = 4.0 Hz, 1H), 3.83 (q, *J* = 8.6 Hz, 1H), 3.03 (m, 1H), 1.99−1.92 (complex m, 2H), 1.77−1.70 (complex m, 2H), 1.64−1.57 (complex m, 2H), 1.58−1.48 (complex m, 1H),1.30 (d, *J* = 8.0 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 131.9, 128.4, 126.9, 126.7, 126.3, 55.5, 54.8, 28.8, 27.9, 25.3, 17.5; IR (KBr): ν_{max} 3401, 3026, 2928, 2860, 1642, 1450, 1267, 1114, 908, 733, 701 cm^{-1}; MS (EI, 70 eV): *m/z* 281 and 279 ($M^{+•}$, both 5 and 4 %), 266 and 264 ($[M-Me•]^+$, both 98 and 100); HRMS $M^{+•}$ Calcd for $C_{14}H_{18}{}^{79}BrN$: 279.0623, Found: 279.0622; Calcd for $C_{14}H_{18}{}^{81}Br$ N: 281.0602, Found: 281.0592; $[\alpha]_D^{20}$ = −18.4 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **ent-23**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.80 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2H), 7.30 (m, 2H), 7.23 (m, 1H), 6.09 (broad s, 1H), 4.06 (m, 1H), 3.23 (broad s, 1H), 2.08−1.92 (complex m, 2H), 1.66−1.63 (complex m, 1H), 1.57−1.53 (complex m, 2H), 1.47−1.43 (complex m, 1H), 1.38 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 131.6, 128.3, 126.9, 126.8, 126.2, 58.1, 58.0, 31.4, 27.8, 24.5, 17.3; IR (KBr): ν_{max} 3344, 3026, 2928, 1640, 1450, 1369, 1350, 1271, 1112, 995, 977, 762 cm^{-1}; MS (EI, 70 eV): *m/z* 281 and 279 ($M^{+•}$, both 5%), 266 and 264 ([M−Me•]$^+$, both 100); HRMS $M^{+•}$ Calcd for $C_{14}H_{18}{}^{79}BrN$: 279.0623, Found: 279.0623; Calcd for $C_{14}H_{18}{}^{81}BrN$: 281.0602, Found: 281.0601; $[\alpha]_D^{20}$ = +96.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (complex m, 5H), 6.12 (t, *J* = 4.0 Hz, 1H), 3.90 (q, *J* = 6.8 Hz, 1H), 3.06 (broad s, 1H), 2.10−1.95 (complex m, 2H), 1.91−1.77 (complex m, 2H), 1.72−1.64 (complex m, 2H), 1.55−1.49 (complex m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 132.0, 128.4, 126.9, 126.7, 126.2, 55.4, 54.8, 28.8, 27.9, 25.2, 17.5; IR (KBr): ν_{max} 3332, 3024, 2929, 1642, 1450, 1368, 1352, 1268, 1115, 978, 805, 762, 700 cm^{-1}; MS (EI, 70 eV): *m/z* 281 and 279 ($M^{+•}$, both 5%), 266 and 264 ([M−Me•]$^+$, both 100); HRMS $M^{+•}$ Calcd for $C_{14}H_{18}{}^{79}BrN$: 279.0623, Found: 279.0623; Calcd for $C_{14}H_{18}{}^{81}BrN$: 281.0602, Found: 281.0599; $[\alpha]_D^{20}$ = +21.4 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **24**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 1H), 6.97 (broad s, 2H), 6.76 (m, 1H), 6.09 (t, *J* = 4.0 Hz, 1H), 4.00 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.22 (broad s, 1H), 2.02−1.93 (complex m, 2H), 1.56−1.50 (complex m, 1H), 1.49−1.46 (complex m, 2H), 1.46−1.42 (complex m, 1H), 1.36 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 148.3, 131.6, 129.2, 126.3, 119.3, 112.3, 112.2, 58.2, 58.1, 55.2, 31.5, 27.8, 24.6, 17.3; IR (KBr): ν_{max} 3344, 2995, 2934, 2833, 1600, 1585, 1485, 1466, 1274, 1254, 1115, 1046, 781 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+•}$, both 30%), 296 and 294 [(M−Me•]$^+$, both 100]; HRMS $M^{+•}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0725; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0707; $[\alpha]_D^{20}$ = −96.9 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 1H), 6.97 (broad s, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.78 (m, 1H), 6.13 (t, *J* = 4.4 Hz, 1H), 3.90 (q, *J* = 6.4 Hz, 1H), 3.82 (s, 3H), 3.08 (m, 1H), 2.11−1.97 (complex m, 2H), 1.81 (m, 1H), 1.71−1.66 (complex m, 2H), 1.53 (m, 1H), 1.36 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 146.8, 132.0, 129.3, 126.3, 119.2, 112.6, 111.8, 55.4, 55.2, 54.7, 28.7, 27.9, 25.3, 17.5; IR (KBr): ν_{max} 3333, 2995, 2936, 2860, 2833, 1642, 1599, 1485, 1466, 1452, 1435, 1273, 1253, 1172, 1116, 1045, 979, 873, 743 cm^{-1}; MS (EI, 70 eV): *m/z* 310 and 308 [M–H•)$^+$, 95 and 64%], 296 and 294 [(M−Me•]$^+$, both 100]; HRMS $M^{+•}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$:

309.0728, Found: 309.0727; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0703; $[\alpha]_D^{20}$ = −23.6 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **25**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.20 (m, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.09 (t, J = 4.0 Hz, 1H), 4.32 (q, J = 6.8 Hz, 1H), 3.84 (s, 3H), 3.26 (broad s, 1H), 2.05−2.00 (complex m, 2H), 1.66 (broad s m, 1H), 1.62−1.56 (complex m, 2H), 1.50−1.46 (complex m, 1H), 1.37 (d, J = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 135.0, 134.3, 131.4, 126.7, 126.6, 120.5, 110.4, 57.8, 55.2, 51.7, 30.8, 27.8, 22.1, 17.4; IR (KBr): ν_{max} 3347, 3032, 2934, 2863, 2834, 1641, 1599, 1586, 1489, 1464, 1237, 1092, 1031 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+\bullet}$, 9 and 10%), 296 and 294 $[(M-Me\bullet)]^+$, 97 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0728; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0707; $[\alpha]_D^{20}$ = −90.6 (c 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 1H), 7.19 m, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.12 (m, 1H), 4.16 (m, 1H), 3.84 (s, 3H), 2.99 (m, 1H), 2.12−2.06 (complex m, 2H), 1.99 (m, 1H), 1.84−1.65 (complex m, 2H), 1.49 (m, 1H), 1.40 (d, J = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 132.0, 131.9, 127.9, 127.6, 126.3, 120.5, 110.4, 55.5, 55.2, 50.3, 28.7, 28.0, 23.0, 17.6; IR (KBr): ν_{max} 3334, 2935, 2861, 1642, 1598, 1489, 1464, 1438, 1237, 1119, 1092, 1048, 1030, 753 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+\bullet}$, 9 and 10%), 296 and 294 $[(M-Me\bullet)]^+$, 98 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0728; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0708; $[\alpha]_D^{20}$ = −27.7 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **26**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.4 Hz, 1H), 7.88 (m, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.54 (m, 1H), 7.49−7.46 (complex m, 2H), 6.12 (t, J = 4.0 Hz, 1H), 4.90 (q, J = 6.8 Hz, 1H), 3.33 (broad s, 1H), 2.10−2.04 (complex m, 2H), 2.03−1.94 (complex m, 1H), 1.70−1.63 (complex m, 2H), 1.53 (d, J = 6.8 Hz, 3H), 1.48−1.43 (complex m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 133.9, 131.6, 131.1, 128.8, 127.1, 126.2, 125.6(0), 125.5(5), 125.2, 123.7, 123.2, 58.3, 53.8, 31.2, 27.8, 23.8, 17.3; IR (KBr): ν_{max} 3335, 3047, 2927, 2860, 1641, 1444, 1176, 1115, 799, 778 cm^{-1}; MS (EI, 70 eV): *m/z*

331 and 329 ($M^{+\bullet}$, 98 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{20}{}^{79}BrN$: 329.0779, Found: 329.0778; Calcd for $C_{18}H_{20}{}^{81}BrN$: 331.0759, Found: 331.0756; $[\alpha]_D^{20}$ = −87.5 (*c* = 1, $CHCl_3$).
Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.6 Hz, 1H), 7.91 (m, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.56 (m, 1H), 7.52−7.48 (complex m, 2H), 6.18 (t, *J* = 4.0 Hz, 1H), 4.85 (q, *J* = 6.4 Hz, 1H), 3.23 (broad s, 1H), 2.03−1.98 (complex m, 2H), 1.86 (m, 1H), 1.70−1.66 (complex m, 2H), 1.64 (m, 1H), 1.53 (d, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 133.9, 132.1, 131.3, 129.0, 127.1, 126.3, 125.7(4), 125.7(0), 125.2, 123.4, 122.7, 55.6, 49.6, 29.1, 27.9, 24.9, 17.6; IR (KBr): ν_{max} 3344, 3047, 2928, 2862, 2831, 1641, 1595, 1510, 1444, 1177, 1113, 799, 778 cm^{-1}; MS (EI, 70 eV): *m/z* 331 and 329 ($M^{+\bullet}$, 98 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{20}{}^{79}BrN$: 329.0779, Found: 329.0780; Calcd for $C_{18}H_{20}{}^{81}BrN$: 331.0759, Found: 331.0761; $[\alpha]_D^{20}$ = +13.6 (*c* = 1, $CHCl_3$).
*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **27**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.84−7.81 (complex m, 4H), 7.58 (m, 1H), 7.49−7.42 (complex m, 2H), 6.11 (t, *J* = 4.0 Hz, 1H), 4.23 (q, *J* = 6.4 Hz, 1H), 3.29 (broad s, 1H), 2.09−1.93 (complex m, 2H), 1.71−1.61 (complex m, 2H), 1.57−1.51 (complex m, 2H), 1.46 (d, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 133.4, 132.8, 131.6, 128.0, 127.7, 127.6, 126.3, 125.9, 125.4, 125.3, 58.5, 58.2, 31.6, 27.8, 24.6, 17.3 (one signal obscured or overlapping); IR (KBr): ν_{max} 3344, 3053, 2927, 2861, 1600, 1442, 1130, 1112, 997, 979, 856, 819, 747 cm^{-1}; MS (EI, 70 eV): *m/z* 331 and 329 ($M^{+\bullet}$, both 5%), 316 and 314 $[(M-Me\bullet)]^+$, 98 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{20}{}^{79}BrN$: 329.0779, Found: 329.0781; Calcd for $C_{18}H_{20}{}^{81}BrN$: 331.0759, Found: 331.0753; $[\alpha]_D^{20}$ = −86.0 (*c* = 1, $CHCl_3$).
Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.87−7.80 (complex m, 4H), 7.57 (m, 1H), 7.46−7.45 (complex m, 2H), 6.15 (t, *J* = 4.0 Hz, 1H), 4.14 (q, *J* = 6.4 Hz, 1H), 3.12 (broad s, 1H), 2.07 (m, 1H), 2.02−1.84 (complex m, 2H), 1.73−1.67 (complex m, 2H), 1.54 (m, 1H), 1.47 (d, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 133.4, 132.0, 128.3, 127.7(1), 127.6(8), 126.3, 125.9, 125.5, 125.4, 124.9, 55.6, 54.9, 28.8, 27.9, 25.3, 17.6 (one signal obscured or overlapping); IR (KBr): ν_{max} 3334, 3052, 2928, 2860, 1680, 1443, 1129, 1115, 978, 856, 819, 746 cm^{-1}; MS (EI, 70 eV): *m/z* 331 and 329 ($M^{+\bullet}$, both 5%), 316

and 314 [(M−Me•)$^+$, 98 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{20}{}^{79}BrN$: 329.0779, Found: 329.0776; Calcd for $C_{18}H_{20}{}^{81}BrN$: 331.0759, Found: 331.0753; $[\alpha]_D^{20}$ = −20.7 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **28**.* Separable diastereoisomers. More mobile diastereoisomer **38** (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.09 (t, *J* = 4.0 Hz, 1H), 4.07 (q, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 3.21 (t, *J* = 4.0 Hz, 1H), 2.02−1.93 (complex m, 2H), 1.53 (m, 1H), 1.49−1.46 (complex m, 2H), 1.44 (m, 1H), 1.33 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 138.5, 131.5, 127.9, 126.4, 113.6, 57.9, 57.4, 55.2, 31.5, 27.8, 24.5, 17.3; IR (KBr): ν_{max} 3343, 2995, 2930, 2861, 1611, 1510, 1464, 1441, 1242, 1171, 1109, 1037, 830 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+\bullet}$, 97 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0727; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0706; $[\alpha]_D^{20}$ = −93.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer **37** (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.11 (broad s, 1H), 3.86 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.04 (m, 1H), 2.04−1.96 (complex m, 2H), 1.81 (m, 1H), 1.75−1.65 (complex m, 2H), 1.53 (m, 1H), 1.35 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 137.1, 131.9, 127.7, 126.4, 113.8, 55.4, 55.2, 54.3, 28.8, 27.9, 25.3, 17.5; IR (KBr): ν_{max} 3333, 2932, 2833, 1611, 1511, 1464, 1442, 1243, 1176, 1111, 1037, 978, 831, 809 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+\bullet}$, both 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0728; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0710; $[\alpha]_D^{20}$ = −20.8 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **ent-28**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.08 (t, *J* = 4.0 Hz, 1H), 4.00 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.21 (t, *J* = 4.4 Hz, 1H), 2.04−1.94 (complex m, 2H), 1.62 (m, 1H), 1.55−1.52 (complex m, 2H), 1.45 (m, 1H), 1.34 (d, *J* = 8.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 138.5, 131.5, 127.9, 126.4, 113.6, 57.9, 57.4, 55.2, 31.5, 27.8, 24.5, 17.3; IR (KBr): ν_{max} 3335, 2995, 2932, 1611, 1511, 1464, 1243, 1175, 1111, 1037, 830 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309 ($M^{+\bullet}$, 97 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0728; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0704; $[\alpha]_D^{20}$ = +95.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.11 (t, *J* = 4.0 Hz, 1H), 3.86 (q, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 3.05 (broad s, 1H), 2.09−1.97 (complex m, 2H), 1.80 (m, 1H), 1.73−1.63 (complex m, 2H), 1.52 (m, 1H), 1.34 (d, *J* = 6.4 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 137.0, 131.9, 127.7, 126.3, 113.7, 55.4, 55.2, 54.2, 28.8, 27.9, 25.3, 17.5; IR (KBr): ν_{max} 3342, 2996, 2931, 1611, 1511, 1464, 1442, 1301, 1243, 1172, 1110, 1038, 831 cm^{-1}; MS (EI, 70 eV): *m/z* 311 and 309.0 ($M^{+\bullet}$, 97 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrNO$: 309.0728, Found: 309.0725; Calcd for $C_{15}H_{20}{}^{81}BrNO$: 311.0708, Found: 311.0706; $[\alpha]_D^{20}$ = +18.5 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **29**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.6 Hz, 1H), 7.17−7.11 (complex m, 3H), 6.14 (t, *J* = 4.0 Hz, 1H), 3.76 (t, *J* = 3.6 Hz, 1H), 3.48 (s, 1H), 2.87−2.69 (complex m, 2H), 2.13−2.00 (complex m, 4H), 1.94−1.84 (complex m, 3H), 1.84−1.72 (complex m, 2H), 1.69−1.62 (m, 1H), 1.52 (broad s, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 137.5, 132.0, 128.8, 126.5, 125.8, 56.1, 52.7, 29.4, 28.0, 27.7, 19.0, 16.6 (three signals obscured or overlapping); IR (KBr): ν_{max} 3338, 3016, 2932, 1642, 1452, 1331, 1095, 1064, 983, 739 cm^{-1}; MS (EI, 70 eV): *m/z* 307 and 305 ($M^{+\bullet}$, 55 and 60%), 306 and 304 $[(M–H\bullet)^+$, 100 and 90]; HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{20}{}^{79}BrN$: 305.0779, Found: 305.0778; Calcd for $C_{16}H_{20}{}^{81}BrN$: 307.0759, Found: 307.0764; $[\alpha]_D^{20}$ = −42.2 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 1H), 7.18−7.12 (complex m, 3H), 6.10 (t, *J* = 4.0 Hz, 1H), 4.01 (t, *J* = 4.0 Hz, 1H), 3.45 (m, 1H), 2.83 (complex m, 1H), 2.73 (complex m, 1H), 2.11−2.02 (complex m, 4H), 1.89−1.83 (complex m, 4H), 1.76−1.68 (complex m, 2H), 1.63−1.58 (complex m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 137.2, 131.4, 129.1, 128.9, 126.8, 125.8, 58.5, 55.9, 32.6, 29.6, 29.3, 27.8, 18.1, 17.3 (one signal obscured or overlapping); IR (KBr): ν_{max} 3335, 3016, 2930, 1463, 1312, 1174, 1124 766, 745 cm^{-1}; MS (EI, 70 eV): *m/z* 307 and 305 ($M^{+\bullet}$, 55 and 57%), 306 and 304 $[(M–H\bullet)^+$, 100 and 91]; HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{20}{}^{79}BrN$: 305.0779, Found: 305.0779; Calcd for $C_{16}H_{20}{}^{81}BrN$: 307.0759, Found: 307.0756; $[\alpha]_D^{20}$ = +33.6 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **30**.* Separable diastereoisomers. More mobile diastereoisomer **S1** (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (m, 1H), 7.23−7.19 (complex m, 3H), 6.16 (t, *J* = 4.4 Hz, 1H), 4.31 (t, *J* = 6.8 Hz, 1H), 3.52 (broad s, 1H), 3.03 (m, 1H), 2.81 (m, 1H), 2.50 (m, 1H), 2.17−2.05 (complex m, 2H), 1.97 (m, 1H), 1.90−1.81 (complex m, 3H), 1.61 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 143.4, 132.3, 127.3, 126.3, 125.8, 124.5, 124.4, 60.9, 57.0, 34.1, 30.2, 29.7, 28.0, 17.1; IR (KBr): ν_{max} 3321, 3068, 3022, 2937, 2856, 1643, 1459, 1331, 1119, 1100, 1066, 985, 753 cm^{-1}; MS (EI, 70 eV): *m/z* 293 and 291 ($M^{+\bullet}$, 57 and 59%), 292 and 290 [(M–H•)$^+$, 100 and 95]; HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{18}{}^{79}BrN$: 291.0623, Found: 291.0622; Calcd for $C_{15}H_{18}{}^{81}BrN$: 293.0602, Found: 293.0593; $[\alpha]_D^{20}$ = −23.9 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer **36** (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (m, 1H), 7.28−7.19 (complex m, 3H), 6.16 (t, *J* = 4.0 Hz, 1H), 4.35 (t, *J* = 6.8 Hz, 1H), 3.54 (broad s, 1H), 3.02 (m, 1H), 2.84−2.76 (complex m, 1H), 2.45−2.40 (complex m, 1H), 2.12−2.07 (complex m, 2H), 1.97−1.84 (complex m, 1H), 1.82−1.77 (complex m, 3H), 1.61 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.3, 131.9, 127.3, 126.4, 126.3, 124.7, 123.9, 62.7, 58.6, 35.6, 31.5, 30.4, 27.8, 17.6; IR (KBr): ν_{max} 3330, 3023, 2957, 2932, 1643, 1455, 1328, 1176, 1126, 986, 771, 756, 740 cm^{-1}; MS (EI, 70 eV): *m/z* 293 and 291 ($M^{+\bullet}$, 59 and 61%), 292 and 290 [(M–H•)$^+$, 100 and 95]; HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{18}{}^{79}BrN$: 291.0623, Found: 291.0624; Calcd for $C_{15}H_{18}{}^{81}BrN$: 293.0602, Found: 293.0603; $[\alpha]_D^{20}$ = +40.0 (*c* = 1, $CHCl_3$); m.p. = 74−75 °C (recrystallised from methanol/dichloromethane).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **31**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.21 (complex m, 5H), 6.01 (t, *J* = 4.0 Hz, 1H), 3.68 (t, *J* = 7.6 Hz, 1H), 3.11 (broad s, 1H), 1.99−1.84 (complex m, 2H), 1.71−1.49 (complex m, 4H), 1.42−1.32 (complex m, 2H), 0.78 (t, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 131.5, 128.0, 127.5, 126.7, 126.3, 65.4, 58.5, 31.7, 31.4, 27.8, 17.3, 10.8; IR (KBr): ν_{max} 3351, 3026, 2959, 2872, 2858, 1641, 1491, 1452, 1331, 1109 cm^{-1}; MS (EI, 70 eV): *m/z* 295 and 293 ($M^{+\bullet}$, both 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrN$: 293.0779, Found: 293.0777; Calcd for $C_{15}H_{20}{}^{81}BrN$: 295.0759, Found: 295.0754; $[\alpha]_D^{20}$ = −93.1 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.32 (complex m, 5H), 6.12 (t, *J* = 4.0 Hz, 1H), 3.60 (t, *J* = 7.6 Hz, 1H), 3.04 (broad s, 1H), 2.01−1.84 (complex m, 2H), 1.83−1.71 (complex m, 4H), 1.53−1.50 (complex m, 2H), 0.83 (t, *J* = 6.8 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 142.4, 131.9, 128.2, 127.4, 126.9, 126.2, 61.5, 55.2, 31.6, 28.5, 27.9, 17.3, 11.1; IR (KBr): ν_{max} 3326, 3025, 2957, 1642, 1491, 1452, 1331, 1113 cm^{-1}; MS (EI, 70 eV): *m/z* 295 and 293 ($M^{+\bullet}$, 98 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{20}{}^{79}BrN$: 293.0779, Found: 293.0775; Calcd for $C_{15}H_{20}{}^{81}BrN$: 295.0759, Found: 295.0752; $[\alpha]_D{}^{20}$ = −22.7 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **32**.* Inseparable diastereoisomers. R_f 0.70 in 10:1 *v/v* hexane/ethyl acetate. ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 0.5H), 6.98 (s, 0.5H), 6.88 (complex m, 0.5H), 6.85 (complex m, 0.5H), 6.79 (complex m, 1H), 6.11 (t, *J* = 4.0 Hz, 0.5H), 6.07 (t, *J* = 4.0 Hz, 0.5H), 4.00 (q, *J* = 5.2 Hz, 1H), 3.90 (s, 1.5H), 3.88 (s, 1.5H), 3.86 (s, 3H), 3.20 (s, 0.5H), 3.05 (s, 0.5H), 2.06−1.96 (complex m, 2H), 1.84−1.80 (complex m, 0.5H), 1.68−1.62 (complex m, 2H), 1.55−1.50 (complex m, 1.5H), 1.34 (d, *J* = 7.5 Hz, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 148.9, 147.9, 147.8, 139.1, 137.7, 131.6, 131.5, 126.3, 126.2, 119.0, 118.9, 110.8, 109.8, 109.3, 58.2, 58.1, 55.9, 55.4, 54.4, 31.5, 28.5, 27.9, 27.8, 25.6, 24.9, 17.4, 17.3 (two signals obscured or overlapping); IR (KBr): ν_{max} 3333, 2995, 2933, 2832, 1592, 1516, 1508, 1464, 1259, 1233, 1167, 1139 1029, cm^{-1}; MS (EI, 70 eV): *m/z* 341 and 339 ($M^{+\bullet}$, 9 and 10%), 326 and 324 [(M−Me•)$^+$, 98 and 100]; HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{22}{}^{79}BrNO_2$: 339.0834, Found: 339.0837; Calcd for $C_{16}H_{22}{}^{81}BrNO_2$: 341.0813, Found: 341.0819.

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **33**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.24 (complex m, 5H), 6.12 (t, *J* = 4.0 Hz, 1H), 4.55 (q, *J* = 12.0 Hz, 2H), 3.71 (m, 1H), 3.28 (broad s, 1H), 3.19 (m, 1H), 2.05−2.00 (complex m, 2H), 1.99−1.93 (complex m, 2H), 1.89−1.84 (complex m, 2H), 1.76−1.72 (complex m, 4H), 1.59−1.37 (complex m, 2H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 131.7, 128.3, 127.6, 127.4, 126.2, 86.4, 71.3, 63.0, 57.6, 30.8, 30.3, 29.9, 27.9, 21.3, 17.1; IR (KBr): ν_{max} 3339, 3030, 2939, 1642, 1453, 1351, 1111, 1068, 982, 8734, 696 cm^{-1}; MS (EI, 70 eV): *m/z* 351 and 349 ($M^{+\bullet}$, both 50%), 350 and 348 (100 and 98); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{24}{}^{79}BrNO$: 349.1041. Found: 349.1042. Calcd for $C_{18}H_{24}{}^{81}BrNO$: 351.1021. Found: 351.1037; $[\alpha]_D{}^{20}$ = +10.2 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.75 in 10:1 *v/v* hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (complex m, 5H), 6.13 (t, *J* = 4.0 Hz, 1H), 4.53 (q, *J* = 11.6 Hz, 2H), 3.78 (m, 1H), 3.35 (broad s, 1H), 3.18 (m, 1H), 2.05−1.99 (complex m, 2H), 1.96−1.93

(complex m, 2H), 1.87−1.84 (complex m, 2H), 1.75−1.71 (complex m, 4H), 1.55−1.34 (complex m, 2H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 131.8, 128.3, 127.7, 127.4(4), 126.3(6), 86.0, 71.3, 62.8, 57.6, 32.2, 30.2, 30.0, 27.9, 21.6, 17.4; IR (KBr): ν_{max} 3332, 3030, 2938, 1642, 1453, 1351, 1112, 1068, 981, 734, 697 cm^{-1}; MS (EI, 70 eV): *m/z* 351 and 349 ($M^{+\bullet}$, both 50%), 350 and 348 (100 and 98); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{24}{}^{79}BrNO$: 349.1041, Found: 349.1042; Calcd for $C_{18}H_{24}{}^{81}BrNO$: 351.1021, Found: 351.1037; $[\alpha]_D^{20}$ = +64.0 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **34**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.30 (complex m, 4H), 7.27−7.24 (complex m, 1H), 6.09 (t, *J* = 4.0 Hz, 1H), 4.58 (q, *J* = 11.6 Hz, 2H), 3.29−3.23 (complex m, 2H), 2.54 (m, 1H), 2.15 (broad s, 1H), 2.06−2.02 (complex m, 3H), 1.96−1.91 (complex m, 2H), 1.68−1.64 (complex m, 2H), 1.56−1.53 (complex m, 2H), 1.29−1.22 (complex m, 4H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 131.1, 128.2, 127.3(2), 127.2(9), 126.8, 81.9, 70.7, 59.2, 56.1, 31.0, 30.0, 28.9, 27.8, 24.2, 24.1, 16.5; IR (KBr): ν_{max} 3341, 3030, 2931, 2858, 1641, 1452, 1097, 1072, 986, 733, 696 cm^{-1}; MS (EI, 70 eV): *m/z* 365 and 363 ($M^{+\bullet}$, both 100%); HRMS $M^{+\bullet}$ Calcd for $C_{19}H_{26}{}^{79}BrNO$: 363.1198, Found: 363.1201; Calcd for $C_{19}H_{26}{}^{81}BrNO$: 365.1177, Found: 365.1176; $[\alpha]_D^{20}$ = +90.2 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.23 (complex, 5H), 6.10 (m, 1H), 4.60 (q, *J* = 11.6 Hz, 2H), 3.34 (broad s, 1H), 3.23 (m, 1H), 2.76 (m, 1H), 2.16−2.12 (complex m, 2H), 2.06−1.96 (complex m, 4H), 1.80−1.76 (complex m, 2H), 1.68−1.64 (complex m, 2H), 1.33−1.22 (complex m, 4H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 131.5, 128.2, 127.5, 127.3, 126.0, 82.2, 70.5, 61.3, 57.6, 32.6, 32.3, 29.7, 27.8, 24.1(4), 24.1(1), 17.1; IR (KBr): ν_{max} 3332, 3030, 2930, 1643, 1452, 1356, 1097, 1073, 849, 733, 696 cm^{-1}; MS (EI, 70 eV): *m/z* 365 and 363 ($M^{+\bullet}$, 98 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{19}H_{26}{}^{79}BrNO$: 363.1195. Found: 363.1195. Calcd for $C_{19}H_{26}{}^{81}BrNO$: 365.1177. Found: 365.1176; $[\alpha]_D^{20}$ = +21.1 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **35**.* Inseparable diastereoisomers (R_f = 0.85 in 10:1 *v/v* hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-715 (complex m, 10H), 6.19 (m, 1H), 4.31 (m, 0.5H), 3.97−3.40 (complex m, 3.5H), 1.97−1.85 (complex m, 2H), 1.83−1.32

(complex m, 4H), 1.27 (d, J = 8.0 Hz, 1.5H), 1.20 (d, J = 8.0 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.7, 142.5, 141.7, 134.2, 133.6, 128.5, 128.4, 128.2, 128.1, 128.0(6), 129.9(9), 127.6(4), 127.5(7), 127.4, 126.8, 126.6, 126.4, 59.1, 59.0, 58.6, 58.4, 52.1, 50.5, 30.8, 27.6(1), 27.5(7), 22.6, 21.3, 20.9(8), 20.9(5), 19.1 (two signals obscured or overlapping); IR (KBr): ν_{max} 3060, 2932, 2836, 1635, 1601, 1452, 1373, 1205, 1123, 1027, 984, 958, 699 cm^{-1}; MS (EI, 70 eV): *m/z* 371 and 369 ($M^{+\bullet}$, 99 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{24}{}^{79}BrN$: 369.1092, Found: 369.1092; Calcd for $C_{21}H_{24}{}^{81}BrN$: 371.1072, Found: 371.1072.

*Products obtained from the electrocyclic ring-opening of 6,6-dibromobicyclo[3.1.0]hexane (**10**) in the presence of amine **ent-35**.* Inseparable diastereoisomers (R_f = 0.85 in 10:1 *v/v* hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.55-715 (complex m, 10H), 6.19 (m, 1H), 4.31 (m, 0.5H), 3.97−3.40 (complex m, 3.5H), 1.97−1.85 (complex m, 2H), 1.83−1.32 (complex m, 4H), 1.27 (d, J = 8.0 Hz, 1.5H), 1.20 (d, J = 8.0 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.7, 142.5, 141.7, 134.2, 133.6, 128.7, 128.5, 128.4, 128.2, 128.1(2), 128.0(9), 128.0(5), 127.9(9), 127.6, 127.4, 126.8, 126.6, 126.4, 59.1, 59.0, 58.6, 58.4, 52.1, 50.5, 30.8, 27.6, 27.5, 25.7, 21.3, 20.9(8), 20.9(4), 19.1 (one signal obscured or overlapping); IR (KBr): ν_{max} 3060, 3025, 2932, 1635, 1492, 1451, 1372, 1205, 1122, 1027, 698 cm^{-1}; MS (EI, 70 eV): *m/z* 371 and 369 ($M^{+\bullet}$, both 27%), 356 and 354.1 [(M−Me•)$^+$, 100 and 98]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{24}{}^{79}BrN$: 369.1092, Found: 369.1103; Calcd for $C_{21}H_{24}{}^{81}BrN$: 371.1072, Found: 371.1087.

Elaboration of 1-amino-2-bromo-2-cyclohexenes 37 and 38 into compounds 1 (R,R = CH_2) and *ent*-1 (R,R=CH_2)

Total synthesis of compound 1 (R,R=CH_2)

N-*((R)-2-Bromocyclohex-2-en-1-yl)-2,2,2-trifluoro*-N-*((*S*)-1-(4-methoxyphenyl)ethyl) Acetamide* (***39***). A magnetically stirred solution of amine **37** (1.50 g, 4.84 mmol) in dry pyridine (20 mL) was treated with trifluoroacetic anhydride (3.30 mL, 24.2 mmol) and the ensuing mixture stirred at 22 °C for 2 h before being quenched with HCl (20 mL of a 10% w/v aqueous solution) then diluted with ethyl acetate (50 mL). The separated aqueous layer was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers washed with brine (1 × 40 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:10 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.8), acetamide **39** (1.85 g, 94%) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major rotamer) 7.20 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.14 (m, 1H), 5.21 (q, J = 6.8 Hz, 1H), 3.75 (s, 3H), 3.67 (broad s, 1H), 2.06−1.97 (complex m, 1H), 1.92−1.81 (complex m, 2H), 1.69 (d, J = 6.9 Hz, 3H), 1.46 (m, 1H), 1.22−1.14 (complex m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major rotamer) 159.5, 155.0 (q, $J_{C\text{-}F}$ = 35 Hz), 133.1, 129.6 , 127.3, 120.9, 116.3 (q, $J_{C\text{-}F}$ = 287 Hz), 113.9, 57.4, 55.2, 54.8, 27.0, 26.9, 21.6, 17.4; IR (KBr): ν_{max} 2940, 2838, 1690, 1514, 1447, 1254, 1135, 1032, 833 cm^{-1}; MS (EI, 70 eV): *m/z* 407 and 405 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}{}^{79}BrF_3NO_2$: 405.0551, Found: 405.0551; Calcd for $C_{17}H_{19}{}^{81}BrF_3NO_2$: 407.0531, Found: 407.0529; $[\alpha]_D^{20}$ = +26.0 (c = 1, $CHCl_3$).

*(*R*)*-N-*(2-Bromocyclohex-2-en-1-yl)-2,2,2-trifluoroacetamide* ***(41)***. A magnetically stirred solution of acetamide **39** (1.80 g, 4.43 mmol) in dry CH_2Cl_2 (30 mL) maintained at 22 °C was treated with anisole (4.80 mL, 44.3 mmol) and trifluoromethanesulfonic acid (2.00 mL, 22.7 mmol) and the ensuing mixture, which developed a red coloration within few minutes, was stirred at 22 °C for 3 h then quenched with $NaHCO_3$ solution (40 mL of a saturated aqueous solution). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (dichloromethane) of the resulting solid, compound **41** (1.08 g, 90%) as a white, crystalline solid, m.p. = 121−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (broad s, 1H), 6.37 (t, J = 4.0 Hz, 1H), 4.65 (m, 1H), 2.20−2.11 (complex m, 2H), 2.04 (m, 1H), 1.93−1.85 (complex m, 1H), 1.77−1.70 (complex m, 1H), 1.64−1.63 (complex m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4 (q, $J_{C\text{-}F}$ = 37 Hz), 135.5, 119.5, 113.4 (q, $J_{C\text{-}F}$ = 286 Hz), 51.4, 30.2, 27.3, 17.8; IR (KBr): ν_{max} 3283, 3090, 1698, 1552, 1207, 1167, 979, 876 cm^{-1}; MS (EI, 70 eV): *m/z* 273 and 271 ($M^{+\bullet}$, 90 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_8H_9{}^{79}BrF_3NO$: 270.9820, Found: 270.9820; Calcd for $C_8H_9{}^{81}BrF_3NO$: 272.9799, Found: 272.9799; $[\alpha]_D^{20}$ = +78.0 (c = 1, $CHCl_3$).

*(*R*)*-N-*Benzyl-2-bromocyclohex-2-en-1-amine (1R-**12**)*. *Step i:* A magnetically stirred solution of compound **41** (1.00 g, 3.68 mmol) and triethylbenzylammonium chloride (83 mg, 0.37 mmol) in dichloromethane (30 mL) was treated with KOH (25 mL of a 20% w/v solution). The ensuing mixture was stirred at 22 °C for 8 h then the separated aqueous layer was extracted with dichloromethane (1 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow oil. *Step ii:* A solution of the yellow oil from step i was dissolved in acetonitrile (10 mL) and the resulting solution treated with K_2CO_3 (1.20 g, 7.4 mmol) and benzyl bromide (440 μL, 3.68 mmol). The ensuing mixture was stirred at 22 °C for 10 h before being poured into water (30 mL),

and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure and the residue so obtained subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), amine *(1R)*-**12** (650 mg, 66%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.23 (complex m, 5H), 6.21 (t, *J* = 4.0 Hz, 1H), 3.86 (d, *J* = 13.0 Hz, 1H), 3.76 (d, *J* = 13.0 Hz, 1H), 3.36 (m, 1H), 2.14−2.01 (complex m, 2H), 1.90−1.83 (complex m, 3H), 1.63−1.57 (complex m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 132.4, 128.3, 128.2, 126.9, 126.4, 58.1, 50.8, 29.2, 27.9, 18.3; IR (KBr): ν_{max} 3326, 3028, 2932, 1605, 1508, 1496, 1453, 1246, 1177, 1030 cm^{-1}; MS (EI, 70 eV): *m/z* 267 and 265 ($M^{+\bullet}$, 98 and 100%); HRMS $M^{+\bullet}$ Calcd for $C_{13}H_{16}{}^{79}BrN$: 265.0466, Found: 265.0464. Calcd for $C_{13}H_{16}{}^{81}BrN$: 267.0446, Found: 267.0442; $[\alpha]_D^{20}$ = +23.8 (*c* = 1, $CHCl_3$).

tert-*Butyl (*R*)-Benzyl(2-bromocyclohex-2-en-1-yl)carbamate.* A mixture of amine *(1R)*-**12** (650 mg, 2.44 mmol) and di-*tert*-butylcarbonate (620 mg, 2.9 mmol) was stirred at 22 °C for 4 h then subjected to flash chromatography (1:9 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.8) and recrystallization (ethyl acetate/hexane) of the resulting solid, *tert*-butyl (*R*)-benzyl(2-bromocyclohex-2-en-1-yl)carbamate (850 mg, 96%) as a white, crystalline solid, m.p. = 66−68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of carbamate rotamers) 7.31−7.20 (complex m, 5H), 6.32−6.22 (complex m, 1H), 5.00 (broad s, 1H), 4.60 (d, *J* = 16.6 Hz, 1H), 4.00 (broad d, *J* = 16.6 Hz, 1H), 2.02−2.01 (complex m, 4H), 1.65 (complex m, 2H), 1.52 (s, 3H), 1.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of carbamates rotamers) 155.8, 140.0, 134.2, 128.2, 128.0, 126.6, 126.3, 126.1, 124.4, 85.1, 79.8, 57.3, 48.0, 29.8, 28.3, 28.0, 27.3, 27.2, 20.9; IR (KBr): ν_{max} 2974, 2933, 1696, 1495, 1452, 1402, 1365, 1167, 1118, 987 cm^{-1}; MS (ESI, +ve): *m/z* 390 and 388 [(M+Na)$^+$, both 100%]; HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{24}{}^{79}BrNO_2Na$: 388.0888, Found: 388.0888; Calcd for $C_{18}H_{24}{}^{81}BrNO_2Na$: 390.0868, Found: 390.0869; $[\alpha]_D^{20}$ = +27.5 (*c* = 1, $CHCl_3$).

tert-*Butyl (*R*)-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)carbamate).* A magnetically stirred solution of *tert*-butyl (*R*)-benzyl(2-bromocyclohex-2-en-1-yl)carbamate (830 mg, 2.26 mmol), benzo[*d*][1,3]dioxol-5-yl-boronic acid **(47)** (750 mg, 4.53 mmol), $PdCl_2dppf\bullet CH_2Cl_2$ (130 mg, 0.16 mmol) and triethylamine (2.4 mL) in THF/water (10 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.25 h then heated under reflux for 2 h before being cooled, poured into water (50 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (1 × 30 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing yellow oil was subjected to flash chromatography (1:9 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), *tert*-butyl (*R*)-(2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)carbamate) (830 mg, 90%) as a clear, colourless foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of carbamate rotamers) 7.25−7.19 (complex m, 2H), 7.16−7.14 (complex m, 1H), 7.05−7.03 (complex m, 2H), 6.86−6.83 (complex m, 2H), 6.76−6.72 (complex m, 1H), 6.09 (broad s, 1H), 5.93 (m, 2H), 5.46 (broad s, 1H), 3.96 (d, *J* = 16.6 Hz, 1H), 3.83 (d, *J* = 16.6 Hz, 1H), 2.13−2.05 (complex m, 4H), 1.67−1.63 (complex m, 2H), 1.53 (s, 3H), 1.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of carbamate rotamers)156.2, 147.4, 146.4, 140.3, 138.9, 134.8, 130.3, 127.8, 126.0, 119.5, 107.9, 106.8, 100.9, 79.4, 53.0, 47.1, 29.4, 28.5, 28.1, 25.6, 21.1; IR (KBr): ν_{max} 3063, 2974, 2932, 1686, 1488, 1444, 1404, 1245, 1166, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 407 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{25}H_{29}NO_4$: 407.2097, Found: 407.2096; $[\alpha]_D^{20}$ = +66.7 (*c* = 1, $CHCl_3$).

*(*R*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine.* A magnetically stirred solution of *tert*-butyl (*R*)-(2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)-carbamate) (800 mg, 1.97 mmol) in anhydrous dichloromethane (20 mL) maintained at 22 °C under a nitrogen atmosphere was treated with trifluoroacetic acid (2.0 mL) and the resulting solution stirred for 1.25 h. NaOH (4 M aqueous solution) was then added to the reaction mixture until the pH reached 14 and at this point the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic phases were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:3 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), (*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine (540 mg, 90%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.21 (complex m, 5H), 6.80 (m, 1H), 6.76−6.71 (complex m, 2H), 5.97 (t, *J* = 4.0 Hz, 1H), 5.94 (s, 2H), 3.84 (d, *J* = 13.1 Hz, 1H), 3.67 (d, *J* = 13.1 Hz, 1H), 3.63 (m, 1H), 2.19−2.10 (complex m, 2H), 1.99 (m, 1H), 1.80 (m, 1H), 1.73−1.58 (complex m, 2H), 1.43 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.4, 140.4, 139.1, 135.5, 128.3, 128.1, 127.6, 126.8, 119.4, 108.0, 106.8, 100.8, 52.1, 51.4, 27.3, 26.1, 17.7; IR (KBr): ν_{max} 3434, 3025, 2931, 1605, 1502, 1488, 1439, 1243, 1217, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 307 ($M^{+\bullet}$, 70%), 306 $[(M−H\bullet)^+$, 100]; HRMS $[(M−H\bullet)^+]$ Calcd for $C_{20}H_{20}NO_2$ 306.1494, Found: 306.1493; $[\alpha]_D^{20}$ = +132.8 (*c* = 1, $CHCl_3$).

*(*R*)-2-((2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)amino)ethan-1-ol.* A magnet -ically stirred solution of (*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine

(500 mg, 1.63 mmol) in methanol (5 mL) contained in a sealable pressure tube and maintained at 0 °C was treated with ethylene oxide (4 mL). The reaction vessel was sealed and this then heated at 45 °C for 8 h. The reaction vessel was then re-cooled to 0 °C before being unsealed and the contents allowed to warm to 22 °C over 18 h. The residue was dissolved in a minimum volume of ethyl acetate and solution thus obtained concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:3 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), (*R*)-2-((2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)-amino)ethan-1-ol (540 mg, 95%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (complex m, 3H), 7.02−7.00 (complex m, 2H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.61−6.57 (complex m, 2H), 6.04 (m, 1H), 5.95 (dd, *J* = 10.0 and 1.3 Hz, 2H), 3.83 (broad s, 1H), 3.75 (d, *J* = 13.0 Hz, 1H), 3.51 (m, 1H), 3.40 (d, *J* = 13.0 Hz, 1H), 3.22 (m, 1H), 2.71 (m, 1H), 2.58 (m, 1H), 2.21−2.13 (complex m, 2H), 2.01−1.90 (complex m, 1H), 1.83−1.76 (complex m, 2H), 1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 146.2, 139.6, 139.2, 135.6, 130.4, 129.2, 128.1, 127.1, 120.0, 107.7, 107.5, 100.8, 58.3, 54.8, 53.5, 50.8, 25.9, 21.6, 21.0; IR (KBr): ν_{max} 3462, 3025, 2932, 1604, 1502, 1488, 1438, 1244, 1222, 1039, 935 cm^{-1}; MS (EI, 70 eV): *m/z* 351 ($M^{+\bullet}$, 10%), 320 (100), 201 (80), 120 (83), 91 (75); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{25}NO_3$: 351.1834, Found: 351.1837; $[\alpha]_D^{20}$ = +55.8 (*c* = 1, $CHCl_3$).

*(*R*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-benzyl-*N*-(2-iodoethyl)cyclohex-2-en-1-amine* (***13***). *Step i:* A magnetically stirred solution of (*R*)-2-((2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)-amino)ethan-1-ol (520 mg, 1.48 mmol) in anhydrous THF (10 mL) maintained at 22 °C under a nitrogen atmosphere was treated with triethylamine (270 μL, 1.92 mmol) and methanesulfonyl chloride (200 μL, 1.92 mmol). The reaction mixture thus obtained was stirred for 2 h then filtered through a pad of Celite™ that was washed with Et_2O (50 mL). The combined filtrates were then concentrated under reduced pressure to give a light-yellow oil. *Step ii:* A magnetically stirred solution of the yellow oil obtained from step i in acetone (20 mL) maintained at 22 °C under a nitrogen atmosphere was treated with sodium iodide (1.10 g, 7.33 mmol) and the ensuing mixture stirred for 3 h then filtered through a pad of Celite™ that was washed with ethyl acetate (2 × 20 mL). The combined filtrates were concentrated under reduced pressure and the residue thus obtained dissolved in ethyl acetate (50 mL). The resulting solution was washed with $Na_2S_2O_3$ (1 × 20 mL of a 5 % w/v aqueous solution) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford iodide **13** (580 mg, 85%) as a clear, pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.20

(complex m, 3H), 7.02 (m, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.72−6.68 (complex m, 2H), 6.02 (m, 1H), 5.98 (s, 2H), 3.80 (m, 1H), 3.67 (d, *J* = 13.5 Hz, 1H), 3.53 (d, *J* = 13.5 Hz, 1H), 2.88−2.74 (complex m, 3H), 2.39 (m, 1H), 2.18−2.13 (complex m, 2H), 1.99 (m, 1H), 1.84−1.68 (complex m, 2H), 1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 146.1, 140.0, 139.8, 136.2, 130.1, 128.8, 128.0, 127.0, 120.3, 107.9, 107.5, 100.8, 57.0, 55.0, 53.9, 25.9, 23.1, 21.0, 5.7; IR (KBr): ν_{max} 3024, 2930, 1604, 1502, 1487, 1437, 1243, 1222, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 461 ($M^{+\bullet}$, 10%), 433 (100); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{24}{}^{127}INO_2$: 461.0852, Found: 461.0847; $[\alpha]_D^{20}$ = +50.4 (*c* = 1, $CHCl_3$).

*(3a*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-benzyloctahydro-1*H*-indole (**16**).* A magnetically stirred solution of iodide **13** (0.54 g, 1.17 mmol) in anhydrous toluene (130 mL) maintained at 80 °C under an atmosphere of nitrogen was treated with AIBN (78 mg, 0.48 mmol, added in 3 equal aliquots over 2 h) and, dropwise over 2.5 h, tri-*n*-butyltin hydride (520 μL, 1.94 mmol) as a solution in anhydrous toluene (50 mL). After addition was complete, the solvent was removed under reduced pressure and the ensuing residue dissolved in ethyl acetate (50 mL). The resulting, magnetically stirred solution was treated with KF (20 mL of a 1 M aqueous solution) and stirring continued at 22 °C for 0.66 h. The ensuing suspension was then filtered through a pad of Celite™ into a separating funnel, the contents of which were diluted with ethyl acetate (50 mL). The solution so formed was washed with brine (1 × 50 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The light-yellow oil thus obtained was subjected to flash chromatography (1:7 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), compound **16** (150 mg, 38%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.4 Hz, 2H), 7.32 (m, 2H), 7.25 (m, 1H), 6.91 (d, *J* = 1.3 Hz, 1H), 6.84 (m, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.94 (s, 2H), 4.14 (d, *J* = 13.3 Hz, 1H), 3.19 (d, *J* = 13.3 Hz, 1H), 3.05 (m, 1H), 2.95 (broad s, 1H), 2.29 (m, 1H), 2.03 (m, 1H), 1.91−1.82 (complex m, 2H), 1.82−1.74 (complex m, 3H), 1.63 (m, 1H), 1.53 (m, 1H), 1.37 (m, 1H), 1.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.0, 141.5, 140.5, 128.4, 128.0, 126.5, 119.6, 107.6(8), 107.6(5), 100.7, 66.0, 57.8, 51.0, 47.6, 40.7, 35.0, 24.1, 23.0, 20.5; IR (KBr): ν_{max} 3026, 2931, 1607, 1505, 1487, 1451, 1233, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 335 ($M^{+\bullet}$, 85%), 334 (100); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{25}NO_2$: 335.1885, Found: 335.1879; $[\alpha]_D^{20}$ = −122.4 (*c* = 1, $CHCl_3$).

*(3a*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)octahydro-1*H*-indole (**17**).* A round-bottomed flask flask was charged with compound **16** (103 mg, 0.39 mmol), $Pd(OH)_2$ (50 mg of a 20% mixture with carbon), TFA (1.0 mL, 13 mmol) and MeOH (5 mL). The atmosphere was flushed with hydrogen, and a balloon full of hydrogen then attached. The contents of the flask

were stirred magnetically at 22 °C and after 10 h the suspension was concentrated under reduced pressure and the residue made basic with methanol/NaOH (20% w/w aqueous solution) before being filtered and the filtrate then concentrated under reduced pressure. The residue so formed was partitioned between water (10 mL) and chloroform (10 mL). The separated aqueous layer was extracted with chloroform (2 × 10 mL) and the combined organic phases then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:10 *v/v* ammonia-saturated methanol/chloroform elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), compound **17** (78 mg, 85%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 1.8 Hz, 1H), 6.80 (dd, *J* = 8.1 and 1.8 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 5.90 (s, 2H), 4.55 (broad s, 1H), 3.51 (t, *J* = 4.1 Hz, 1H), 3.22 (m, 1H), 3.06 (m, 1H), 2.01 (m, 1H), 1.90 (m, 1H), 1.80−1.73 (complex m, 3H), 1.69 (m, 1H), 1.64−1.58 (complex m, 1H), 1.49−1.42 (complex m, 2H), 1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 145.4, 139.9, 119.2, 107.8, 107.3, 100.8, 60.9, 47.7, 42.6, 41.0, 33.4, 25.7, 21.8, 20.7; IR (KBr): ν_{max} 3347, 2929, 1610, 1506, 1488, 1432, 1234, 1038, 934 cm^{-1}; MS (EI, 70 eV): *m/z* 245 ($M^{+\bullet}$, 100%), 244 $[(M–H\bullet)^+$, 97]; HRMS $M^{+\bullet}$ Calcd for $C_{15}H_{19}NO_2$: 245.1416. Found: 245.1413. Calcd for $C_{15}H_{18}NO_2$: 244.1338. Found: 244.1337; $[\alpha]_D^{20}$ = +12.5 (*c* = 1, $CHCl_3$).

*(−)-Crinane [**1**,* (R,R = CH_2)]. A magnetically stirred solution of compound **17** (70 mg, 0.29 mmol) in formic acid (5 mL) maintained at 22 °C under a nitrogen atmosphere was treated with paraformaldehyde (100 mg) and the resulting solution heated under reflux for 18 h. The cooled reaction mixture was concentrated under reduced pressure and the ensuing residue dissolved in chloroform (20 mL). The solution thus formed was adjusted to pH 14 with NaOH (20% w/w aqueous solution) then extracted with chloroform (2 × 5 mL). The combined organic phases were dried (Na_2SO_4), filtered then concentrated under reduced pressure. The resulting yellow oil was subjected to flash chromatography (1:10 *v/v* ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.4), compound **1** (R,R=CH_2) (57 mg, 78%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 1H), 6.41 (s, 1H), 5.83 (s, 2H), 4.34 (d, *J* = 16.6 Hz, 1H), 3.73 (d, *J* = 16.6 Hz, 1H), 3.36 (m, 1H), 2.86−2.75 (complex m, 2H), 2.29 (m, 1H), 2.19 (m, 1H), 1.80−1.72 (complex m, 4H), 1.57 (m, 1H), 1.47 (m, 1H), 1.27−1.13 (complex m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 145.5, 141.6, 125.1, 106.1, 103.1, 100.6, 67.3, 61.6, 51.7, 42.7, 37.4, 28.7, 27.1, 24.1, 21.5; IR (KBr): ν_{max} 2931, 2855, 1503, 1481, 1310, 1232, 1094, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 257 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{19}NO_2$: 257.1416, Found: 257.1417; $[\alpha]_D^{20}$ = −11.6 (*c* = 1, $CHCl_3$).

Total synthesis of compound *ent*-1 (R,R=CH_2)

N-*((*S*)-2-Bromocyclohex-2-en-1-yl)-2,2,2-trifluoro*-N-*((*S*)-1-(4-methoxyphenyl)ethyl) Acetamide (**40**).* A magnetically stirred solution of amine **38** (3.00 g, 9.68 mmol) in dry pyridine (40 mL) was treated with trifluoroacetic anhydride (6.70 mL, 48.4 mmol) and the ensuing mixture stirred at 22 °C for 2 h before being quenched with HCl (20 mL of a 10% w/v aqueous solution) then diluted with ethyl acetate (50 mL). The separated aqueous layer was extracted with ethyl acetate (3 × 20 mL) and the combined organic phases washed with brine (1 × 40 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.8), acetamide **40** (3.65 g, 93%) as a clear, pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major rotamer) 7.34 (d, *J* = 7.2 Hz, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.04 (broad s, 1H), 5.34 (q, *J* = 6.4 Hz, 1H), 3.89 (broad s, 1H), 3.79 (s, 3H), 2.45 (m, 1H), 2.15−2.12 (complex m, 2H), 2.02−1.96 (complex m, 2H), 1.87 (m, 1H), 1.63 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major rotamer) 159.6, 155.0 (q, *J* = 35 Hz), 137.3, 131.8, 130.5, 128.1, 116.3 (q, *J* = 287 Hz), 113.4, 55.9, 55.5, 55.1, 28.4, 26.7, 21.7, 19.1; IR (KBr): ν_{max} 2940, 2838, 1690, 1514, 1447, 1254, 1200, 1135. 1032, 833 cm^{-1}; MS (EI, 70 eV): *m/z* 407 and 405 ($M^{+\bullet}$, 100 and 99%); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}{}^{79}BrF_3NO_2$: 405.0551, Found: 405.0551; Calcd for $C_{17}H_{19}{}^{81}BrF_3NO_2$: 407.0531, Found: 407.0529; $[\alpha]_D^{20}$ = −46.7 (*c* = 1, $CHCl_3$).

*(*S*)*-N-*(2-Bromocyclohex-2-en-1-yl)-2,2,2-trifluoroacetamide (**ent-41**).* A magnetically stirred solution of acetamide **40** (3.5 g, 8.62 mmol) in dry dichloromethane (50 mL) was treated with anisole (9.40 mL, 86.2 mmol) then trifluoromethanesulfonic acid (3.80 mL, 43.1 mmol). The ensuing mixture, which developed a red coloration within few minutes, was stirred at 22 °C for 3 h then quenched with $NaHCO_3$ solution (50 mL of a saturated aqueous solution). The separated aqueous layer was extracted with dichloromethane (3 × 30 mL) and the combined organic layers washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (dichloromethane) of the resulting solid, compound ***ent*-41** (2.10 g, 90%) as white, crystalline masses, m.p. = 121−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (broad s, 1H), 6.35 (t, *J* = 3.9 Hz, 1H), 4.65 (m, 1H), 2.19−1.99 (complex m, 3H), 1.89 (m, 1H), 1.72 (m, 1H), 1.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4 (q, $J_{C\text{-}H}$ = 37 Hz), 135.5, 119.5, 113.4 (q, $J_{C\text{-}H}$ = 286 Hz), 51.5, 30.2, 27.3, 17.8; IR (KBr): ν_{max} 3343, 2932, 2833, 1716, 1611, 1511, 1464, 1442, 1301, 1243, 1171, 1110, 1038

cm^{-1}; MS (EI, 70 eV): *m/z* 273 and 271 (100 and 97%), 272 and 270 ($M^{+\bullet}$, 85 and 35); HRMS $M^{+\bullet}$ Calcd for $C_8H_9{}^{79}BrF_3NO$: 270.9820, Found: 270.9821; Calcd for $C_8H_9{}^{79}BrF_3NO$: 272.9799, Found: 272.9799; $[\alpha]_D^{20} = -73.5$ (*c* = 1, $CHCl_3$).

*(*S*)-*N*-Benzyl-2-bromocyclohex-2-en-1-amine (1*S*-**12**). Step i:* A magnetically stirred solution of acetamide ***ent*-41** (2.00 g, 7.35 mmol) and triethylbenzylammonium chloride (166 mg, 0.74 mmol) in dichloromethane (50 mL) was treated with KOH (50 mL of a 20% w/w aqueous solution). The ensuing mixture was stirred at 22 °C for 8 h then the separated aqueous layer extracted with dichloromethane (50 mL). The combined organic layers were dried (Na_2SO_4), filtered then concentrated under reduced pressure to give a light-yellow oil. *Step ii:* A magnetically stirred solution of the yellow oil obtained from step i in acetonitrile (30 mL) maintained at 22 °C was treated with K_2CO_3 (2.40 g, 14.7 mmol) and benzyl bromide (870 μL, 7.35 mmol). After 10 h the reaction mixture was poured into water (50 mL) then extracted with ethyl acetate (3 × 30 mL), and the combined organic phases dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.2), amine 1*S*-**12** (1.20 g, 63%) as a clear, white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.26 (complex m, 5H), 6.21 (t, *J* = 4.0 Hz, 1H), 3.86 (d, *J* = 12.9 Hz, 1H), 3.76 (d, *J* = 12.9 Hz, 1H), 3.36 (m, 1H), 2.17−2.01 (complex m, 2H), 1.90−1.73 (complex m, 3H), 1.60 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 132.4, 128.3, 128.2, 126.9, 126.4, 58.1, 50.7, 29.2, 27.9, 18.3; IR (KBr): ν_{max} 3337, 3026, 2934, 2832, 1640, 1494, 1452, 1331, 1106, 1064, 1028, 987 cm^{-1}; MS (EI, 70 eV): *m/z* 267 and 265 ($M^{+\bullet}$, 9 and 10%), 239 and 237 (both 50), 91 (100); HRMS $M^{+\bullet}$ Calcd for $C_{13}H_{16}{}^{79}BrN$: 265.0466, Found: 265.0466; Calcd for $C_{13}H_{16}{}^{79}BrN$: 267.0446, Found: 267.0451; $[\alpha]_D^{20} = -25.2$ (*c* = 1, $CHCl_3$).

tert-*Butyl (*S*)-Benzyl(2-bromocyclohex-2-en-1-yl)carbamate.* A mixture of amine 1*S*-**12** (1.10 g, 4.14 mmol) and di-*tert*-butyl carbonate (1.08 g, 5.0 mmol) in dry THF (40 mL) was stirred magnetically at 22 °C for 4 h then concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (1:9 *v/v* ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.4) and recrystallization (ethyl acetate/hexane) of the resulting solid afforded *tert*-butyl (*S*)-benzyl(2-bromocyclohex-2-en-1-yl)carbamate (1.00 g, 67%) as a white, crystalline solid, m.p. = 69−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of carbamate rotamers) 7.31−7.21 (complex m, 5H), 6.33 (m, 1H), 5.00 (broad s, 1H), 4.59 (d, *J* = 16.7 Hz, 1H), 4.00 (broadened d, *J* = 16.7 Hz, 1H), 2.02 (broad s, 4H), 1.64 (broad s, 2H), 1.51 (s, 3H), 1.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of carbamate rotamers) 159.7, 140.1, 134.4, 134.2, 128.2, 128.1, 126.7, 126.6, 126.4, 126.2, 124.5, 80.3, 80.0, 57.4, 30.0, 29.9, 28.6, 28.4, 28.2, 27.3, 21.0; IR (KBr): ν_{max} 2974, 2932, 1695, 1495, 1452, 1402, 1365, 1251, 1166 cm^{-1}; MS (ESI, +ve): *m/z* 390 and 388 [$(M+Na)^+$, 99 and 100%]; HRMS $[M+Na]^+$ Calcd for $C_{18}H_{24}{}^{79}BrNO_2Na$: 388.0888, Found: 388.0888; Calcd for $C_{18}H_{24}{}^{81}BrNO_2Na$: 390.0868, Found: 390.0870; $[\alpha]_D^{20} = -29.5$ (*c* = 1, $CHCl_3$).

tert-*Butyl (*S*)-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)carbamate*. A magnet -ically stirred solution of carbamate *tert*-butyl (*S*)-benzyl(2-bromocyclohex-2-en-1-yl)carbamate (1.00 g, 2.73 mmol), benzo[*d*][1,3]dioxol-5-yl-boronic acid (900 mg, 5.46 mmol), $PdCl_2dppf{\bullet}CH_2Cl_2$ (160 mg, 0.19 mmol) and triethylamine (3.00 mL) in THF/water (10 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.25 h then heated under reflux for 2 h before being cooled, poured into water (50 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (1 × 30 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:9 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), *tert*-butyl (*S*)-(2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)carbamate (1.00 g, 90%) as a clear, colourless foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of carbamates rotamers) 7.25−7.19 (complex m, 2H), 7.16−7.13 (complex m, 1H), 7.06−7.03 (complex m, 2H), 6.85 (m, 2H), 6.74 (m, 1H), 6.09 (broad s, 1H), 5.94−5.91 (complex m, 2H), 5.47 (broad s, 1H), 3.96 (d, *J* = 16.5 Hz, 1H), 3.83 (d, *J* = 16.5 Hz, 1H), 2.13−2.04 (complex m, 4H), 1.68−1.66 (complex m, 2H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of carbamates rotamers) 156.2, 147.4, 146.4, 140.3, 138.9, 134.9, 130.2, 127.8, 126.0, 119.5, 107.9, 106.9, 100.8, 79.4, 52.9, 47.0, 29.4, 28.1, 28.0, 25.6, 25.5, 21.1; IR (KBr): ν_{max} 2931, 1686, 1504, 1488, 1452, 1403, 1365, 1245, 1165, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 407 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{25}H_{29}NO_4$: 407.2097, Found: 407.2090; $[\alpha]_D^{20} = -64.8$ (*c* = 1, $CHCl_3$).

*(*S*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine.* A magnetically stirred solution of *tert*-butyl (*S*)-(2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)carbamate (1.00 g, 2.45 mmol) in anhydrous dichloromethane (20 mL) maintained at 22 °C under a nitrogen atmosphere was treated with trifluoroacetic acid (2.5 mL). The resulting solution was stirred for 1.25 h, treated with NaOH (4 M aqueous solution) until pH 14 was attained then the separated aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic phases were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (1:3 *v/v* ethyl

acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.42), (*S*)-2-(benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine (660 mg, 88%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.20 (complex m, 5H), 6.80 (m, 1H), 6.73 (m, 2H), 5.96 (t, *J* = 4.0 Hz, 1H), 5.93 (s, 2H), 3.84 (d, *J* = 13.2 Hz, 1H), 3.67 (d, *J* = 13.2 Hz, 1H), 3.61 (broad s, 1H), 2.23−2.12 (complex m, 2H), 1.99 (m, 1H), 1.79 (m, 1H), 1.72−1.59 (complex m, 2H), 1.46 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.5, 140.4, 139.1, 135.5, 128.2(3), 128.2(1), 127.6, 126.8, 119.4, 108.0, 106.9, 100.9, 52.1, 51.4, 27.3, 26.1, 17.7; IR (KBr): ν_{max} 3338, 3026, 2931, 1604, 1502, 1488, 1439, 1243, 1217, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 307 ($M^{+\bullet}$, 61%), 306 [(M–H•)$^+$, 100]; HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{21}NO_2$: 307.1572, Found: 307.1570; $[\alpha]_D^{20} = -136.2$ (*c* = 1, $CHCl_3$).

(S)-2-((2-(Benzo[d][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)amino)ethan-1-ol. A magnet-ically stirred solution of (*S*)-2-(benzo[*d*][1,3]dioxol-5-yl)-*N*-benzylcyclohex-2-en-1-amine (650 mg, 2.11 mmol) in methanol (5 mL) contained in a sealable pressure vessel was cooled to 0 °C then treated with ethylene oxide (4 mL). The reaction vessel was sealed then heated at 45 °C for 8 h. After this time, the vessel was re-cooled to 0 °C, unsealed and the contents allowed to warm to 22 °C and stand at this temperature for 18 h. The residue thus obtained was transferred into a round-bottomed flask using ethyl acetate and the resulting solution concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:3 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), (*S*)-2-((2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)amino)ethan-1-ol (720 mg, 97%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.24 (complex m, 3H), 7.01 (m, 2H), 6.74 (d, *J* = 8 Hz, 1H), 6.59 (m, 2H), 6.06 (broad s, 1H), 5.95 (m, 2H), 3.83 (broad s, 1H), 3.75 (d, *J* = 13.0 Hz, 1H), 3.51 (m, 1H), 3.40 (d, *J* = 13.0 Hz, 1H), 3.25 (m, 1H), 2.71 (m, 1H), 2.58 (m, 1H), 2.18−2.13 (complex m, 2H), 1.99−1.77 (complex m, 3H), 1.63 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 146.2, 139.6, 139.3, 135.6, 130.4, 129.2, 128.1, 127.1, 120.0, 107.7, 107.5, 100.8, 58.3, 54.8, 53.5, 50.8, 25.9, 21.6, 21.0; IR (KBr): ν_{max} 3468, 3025, 2932, 2882, 1604, 1502, 1487, 1438, 1244, 1222, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 351 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{25}NO_3$: 351.1834, Found: 351.1844; $[\alpha]_D^{20} = -53.6$ (*c* = 1, $CHCl_3$).

(S)-2-(Benzo[d][1,3]dioxol-5-yl)-N-benzyl-N-(2-iodoethyl)cyclohex-2-en-1-amine (***ent*-13**). *Step i:* A magnetically stirred solution of (*S*)-2-((2-(benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)(benzyl)amino)ethan-1-ol (720 mg, 2.05 mmol) in anhydrous THF (10 mL) maintained at 22 °C under a nitrogen atmosphere was treated with triethylamine (530 μL, 3.84 mmol) and

methanesulfonyl chloride (400 μL, 3.84 mmol). The resulting mixture stirred for 2 h at 22 °C then filtered through a pad of Celite™ that was washed with diethyl ether (50 mL). The combined filtrates were concentrated under reduced pressure to give a light-yellow oil. *Step ii:* A magnetically stirred solution of the yellow oil obtained from step i in acetone (20 mL) maintained at 22 °C under a nitrogen atmosphere was treated with sodium iodide (2.00 g, 13.3 mmol) and the ensuing mixture stirred for 3 h before being filtered through a pad of Celite™ that was washed with ethyl acetate (2 × 20 mL). The combined filtrates were concentrated under reduced pressure and the residue thus obtained dissolved in ethyl acetate (50 mL). The resulting solution was washed with $Na_2S_2O_3$ (1 × 20 mL of a 5 % w/v aqueous solution), dried (Na_2SO_4) then filtered and concentrated under reduced pressure to afford, after concentration of the appropriate fractions (R_f = 0.75), iodide ***ent*-13** (840 mg, 88%) as a clear, pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 3H), 7.03 (m, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.71 (m, 2H), 6.01 (broad s, 1H), 5.98 (q, *J* = 13.8 Hz, 2H), 3.81−3.80 (complex m, 1H), 3.67 (d, *J* = 13.5 Hz, 1H), 3.54 (d, *J* = 13.5 Hz, 1H), 2.89−2.74 (complex m, 3H), 2.36 (m, 1H), 2.17−2.15 (complex m, 2H), 1.99 (m, 1H), 1.82−1.69 (complex m, 2H), 1.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 146.0, 140.1, 139.8, 136.1, 130.0, 128.8, 127.9, 126.9, 120.3, 107.9, 107.5, 100.7, 56.9, 54.9, 53.9, 25.8, 23.0, 21.0, 5.7; IR (KBr): ν_{max} 3061, 3025, 2930, 2833, 1604, 1502, 1487, 1436, 1370, 1243, 1222, 1159, 1125, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 461 ($M^{+\bullet}$, 10%), 433 (100); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{24}INO_2$: 461.0852, Found: 461.0847; $[\alpha]_D^{20}$ = −53.0 (*c* = 1, $CHCl_3$).

*(3a*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-benzyloctahydro-1*H*-indole (**ent-16**).* A magnetic -ally stirred solution of iodide ***ent*-13** (820 mg, 1.82 mmol) in anhydrous toluene (130 mL), maintained at 80 °C under an atmosphere of nitrogen was treated with AIBN (117 mg, 0.71 mmol, added in 3 aliquots over 2 h) and tri-*n*-butyltin hydride [780 μL, 2.92 mmol as a solution in anhydrous toluene (50 mL) that was added dropwise over 2.5 h]. After addition was complete, the reaction mixture was cooled and then concentrated under reduced pressure. The ensuing residue was dissolved in ethyl acetate (50 mL) and the solution thus obtained was stirred with KF (20 mL of a 1.0 M aqueous solution) for 0.66 h. The resulting suspension was filtered through a pad of Celite™ into a separating funnel, the contents of which were diluted with ethyl acetate (1 × 50 mL). The combined organic phases were washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:7 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.5),

compound ***ent*-16** (240 mg, 40%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.35−7.32 (complex m, 2H), 7.25 (m, 1H), 6.92 (m, 1H), 6.89 (m, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.94 (s, 2H), 4.15 (d, *J* = 13.3 Hz, 1H), 3.19 (d, *J* = 13.3 Hz, 1H), 3.05 (m, 1H), 2.96 (broad s, 1H), 2.30 (m, 1H), 2.07 (m, 1H), 1.93−1.86 (complex m, 2H), 1.84−1.75 (complex m, 3H), 1.65 (m, 1H), 1.55 (m, 1H), 1.39 (m, 1H), 1.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.0, 141.4, 140.5, 128.4, 128.1, 126.5, 119.6, 107.7, 107.6, 100.7, 66.0, 57.8, 51.0, 47.6, 40.6, 35.0, 24.1, 23.0, 20.5; IR (KBr): ν_{max} 3026, 2930, 1607, 1505, 1487, 1451, 1233, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 335 ($M^{+•}$, 82%), 334 [(M–H•)$^{+}$, 100]; HRMS $M^{+•}$ Calcd for $C_{22}H_{25}NO_2$: 335.1885, Found: 335.1882; $[\alpha]_D^{20}$ = +126.6 (*c* = 1, $CHCl_3$).

*(3a*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)octahydro-1*H*-indole (**ent-17**)*. A flask was charged with compound ***ent*-16** (220 mg, 0.66 mmol), $Pd(OH)_2$ (75 mg, 20% w/w mixture with carbon), TFA (1.50 mL, 19.5 mmol) and methanol (10 mL). The atmosphere above the resulting solution was purged with hydrogen and a balloon of hydrogen then attached. After 10 h the magnetically stirred reaction mixture, which had been maintained at 22 °C, was concentrated under reduced pressure and the residue made basic with NaOH (20% w/w aqueous solution) in methanol then filtered before being concentrated under reduced pressure. The residue thus obtained was partitioned between water (10 mL) and chloroform (10 mL) and the separated aqueous phase extracted with chloroform (2 × 50 mL) then the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:10 v/v ammonia-saturated methanol/ chloroform elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), amine ***ent*-17** (150 mg, 94%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (broad s, 1H), 6.80 (m, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 5.90 (s, 2H), 3.43 (t, *J* = 4.3 Hz, 1H), 3.33 (broad s, 1H), 3.13 (m, 1H), 3.00 (m, 1H), 1.99 (m, 1H), 1.88 (m, 1H), 1.81−1.73 (complex m, 3H), 1.67 (m, 1H), 1.54 (m, 1H), 1.47−1.42 (complex m, 2H), 1.22 (complex m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 145.2, 140.6, 119.3, 107.7, 107.4, 100.8, 60.9, 47.8, 42.8, 41.2, 33.7, 26.1, 22.0, 20.9; IR (KBr): ν_{max} 2928, 2859, 1610, 1506, 1488, 1432, 1233, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 245 ($M^{+•}$, 100%), 244 [(M–H•)$^{+}$, 93]; HRMS $M^{+•}$ Calcd for $C_{15}H_{19}NO_2$: 245.1416, Found: 245.1416; Calcd for $[M-H•]^{+}$ $C_{15}H_{18}NO_2$: 244.1338, Found: 244.1335; $[\alpha]_D^{20}$ = −11.3 (*c* = 1, $CHCl_3$).

*(+)-Crinane [**ent-1**(R,R=CH_2)]*. A magnetically stirred solution of amine ***ent*-17** (50 mg, 0.20 mmol) in formic acid (5 mL) maintained at 22 °C under a nitrogen atmosphere was treated with paraformaldehyde (90 mg) and the resulting mixture heated under reflux for 18 h then

cooled and concentrated under reduced pressure. The residue thus obtained was dissolved in chloroform (20 mL) and the solution so formed treated with sufficient NaOH (20% w/w aqueous solution) so as to achieve pH 14 then the separated aqueous phase was extracted with chloroform (2 × 50 mL) before the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:10 *v/v* ammonia-saturated methanol/chloroform elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), ***ent*-1** (R,R=CH_2) (39 mg, 77%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (s, 1H), 6.45 (s, 1H), 5.88 (s, 2H), 4.48 (d, J = 16.4 Hz, 1H), 3.88 (d, J = 16.4 Hz, 1H), 3.59 (m, 1H), 3.05−2.89 (complex m, 2H), 2.34−2.27 (complex m, 2H), 2.03 (m, 1H), 1.81−1.73 (complex m, 3H), 1.59 (m, 1H), 1.48 (m, 1H), 1.31−1.16 (complex m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 146.1, 140.3, 122.6, 106.2, 103.3, 100.9, 67.6, 60.6, 51.5, 43.1, 36.5, 28.5, 26.3, 23.6, 21.2; IR (KBr): ν_{max} 2931, 1503, 1482, 1243, 1231, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* 257 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{19}NO_2$: 257.1416. Found: 257.1415; $[\alpha]_D^{20}$ = +11.0 (c = 1, $CHCl_3$).

Electrocyclic ring-opening of cyclopropane (42) in the presence of homochiral primary and secondary amines 20-23, *ent*-23, 23-28, *ent*-28, 28-35 and *ent*-35

Method A:

A solution of cyclopropane **42**[18d] (1.0 mmol, 1 equiv) in THF (2 mL) was treated with the relevant homochiral primary or secondary amine **20-35** (4 equiv) and the resulting solution subjected to microwave irradiation (200 W, 150 °C, 80 psi) for 1.5 h in a CEM Discover microwave reactor. The cooled reaction mixture was diluted with ethyl acetate (20 mL) and the resulting solution washed with water (1 × 20 mL) then brine (1 × 20 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The light-yellow oil thus obtained was subjected to flash chromatography (silica, 10:1 *v/v* hexane/ethyl acetate elution) to afford, in most instances, two fractions with a ΔR_f of approx. 0.05. In all cases except that involving compound **45**, the products were isolated as clear, colorless oils.

Method B:

The cyclopropane **42** (0.3 mmol, 1 equiv) was treated with the relevant homochiral primary or secondary amines **20-35** (4 equiv) and the ensuing mixture stirred at 55 °C (bath temperature) for 8 h. A fraction of the cooled reaction mixture was dissolved in $CDCl_3$ and the resulting solution subjected to ^{1}H NMR analysis with the ratio of the co-produced diastereoisomeric being established by integration of the relevant resonances, normally those due to the olefinic or allylic protons, *viz*. H-3 or H-1 respectively.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **20**.* Inseparable diastereoisomers (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) 5.93 (m, 1H), 4.06 (m, 1H), 3.56 (m, 0.5H), 3.39 (m, 0.5H), 2.30 (m, 1H), 2.06−1.89 (complex m, 3H), 1.74 (m, 1H), 1.40 (broad s, 1H), 1.08 (m, 3H), 0.81 (s, 9H), 0.66 (m, 1H), 0.38 (m, 2H), 0.23 (m, 0.5H), 0.13 (m, 0.5H), 0.06 (m, 1H), 0.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.8(6), 128.8(5), 125.4, 125.2(5), 63.6, 63.4, 58.1, 57.9, 57.8. 57.1, 39.9, 39.2, 37.4, 37.3, 25.8, 21.7, 20.4, 18.4, 18.1, 17.9, 4.6, 4.3, 2.5, 1.6, −4.6(7), −4.7(2); IR (KBr): ν_{max} 3343, 2956, 2928, 2885, 2856, 1642, 1471, 1251, 1111, 1073, 869, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 375 and 373 ($M^{+\bullet}$, 100 and 97%); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{32}{}^{79}BrNOSi$: 373.1437, Found: 373.1435; Calcd for $C_{17}H_{32}{}^{81}BrNOSi$: 375.1416, Found: 375.1413.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **21**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (dd, *J* = 5.1 and 2.6 Hz, 1H), 4.17 (m, 1H), 3.38 (broad s, 1H), 2.42 (m, 1H), 2.32 (dt, *J* = 17.2 and 5.2 Hz, 1H), 2.01 (m, 1H), 1.92 (m, 1H), 1.66 (m, 1H), 1.58 (m, 1H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.0 Hz, 3H), 0.89 (d, *J* = 6.0 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.3, 118.0, 63.3, 58.1, 56.6, 40.0, 37.5, 33.7, 25.8, 19.0, 18.3, 18.1, 16.2, −4.6 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2956, 2928, 2857, 1642, 1471, 1463, 1250, 1108, 1077, 870, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 377 and 375 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{34}{}^{79}BrNOSi$: 375.1593, Found: 375.1594; Calcd for $C_{17}H_{34}{}^{81}BrNOSi$: 377.1573, Found: 377.1587; $[\alpha]_D^{20}$ = −15.2 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.78 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (dd, *J* = 5.2 and 2.6 Hz, 1H), 4.10 (m, 1H), 3.39 (broad s, 1H), 2.63 (m, 1H), 2.30 (dt, *J* = 17.2 and 5.2 Hz, 1H), 2.01 (m, 1H), 1.94 (m, 1H), 1.82−1.72 (complex m, 2H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 7.2 Hz, 3H), 0.83 (s, 9H), 0.81 (m, 3H), 0.07 (s, 3H), 0.06 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.0, 125.2, 63.4. 58.1, 56.7, 39.5, 37.4, 30.8, 25.9, 19.6, 18.2, 16.7, 16.1, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2957, 2928, 2857, 1642, 1471, 1463, 1386, 1256, 1108, 1076, 868, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 377 and 375 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{34}{}^{79}BrNOSi$: 375.1593, Found: 375.1599; Calcd for $C_{17}H_{34}{}^{81}BrNOSi$: 377.1573, Found: 377.1582; $[\alpha]_D^{20}$ = +42.9 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **22*** Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.8 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (m, 1H), 4.13 (m, 1H), 3.33 (broad s, 1H), 2.32 (dt, *J* = 17.2 and 5.2 Hz, 1H), 2.16 (q, *J* = 6.4 Hz, 1H), 2.01 (m, 1H), 1.92 (m, 1H), 1.60 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.04 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.5, 124.9, 63.2, 59.8, 58.4, 38.7, 37.7, 34.3, 26.6, 25.8, 18.0, 14.2, −4.5(6), −4.6(0); IR (KBr): ν_{max} 2955, 2928, 2857, 1642, 1473, 1463, 1375, 1250, 1110, 1094, 871, 859, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 391 and 389 ($M^{+\bullet}$, both 7%), 376 and 374 [(M−Me•)$^+$, both 100]; HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{36}{}^{79}BrNOSi$: 389.1750, Found: 389.1754; Calcd for $C_{18}H_{36}{}^{81}BrNOSi$: 391.1729, Found: 391.1743; $[\alpha]_D^{20}$ = −24.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.78 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (m, 1H), 4.08 (m, 1H), 3.32 (broad s, 1H), 2.44 (q, *J* = 6.4 Hz, 1H), 2.32 (m, 1H), 2.01 (m, 1H), 1.95 (m, 1H), 1.77 (m, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.7, 125.4, 63.4, 62.4, 60.3, 41.0, 37.5, 35.1, 26.5, 25.8, 18.1, 17.2, −4.6 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2928, 2857, 1640, 1471, 1462, 1251, 1110, 1073, 869, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 391 and 389 ($M^{+\bullet}$, both 10%), 376 and 374 [(M−Me•)$^+$, 100 and 95]; HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{36}{}^{79}BrNOSi$: 389.1750, Found: 389.1744; Calcd for $C_{18}H_{36}{}^{81}BrNOSi$: 391.1729, Found: 391.1723; $[\alpha]_D^{20}$ = +53.8 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **23*** Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.22 (complex m, 5H), 5.92 (m, 1H), 4.03−3.96 (complex m, 2H), 3.36 (m, 1H), 2.28 (m, 1H), 1.95 (m, 1H), 1.65 (m, 1H), 1.55 (m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H), 0.82 (s, 9H), 0.01 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 128.8, 128.3, 126.9(6), 126.9(2), 125.1, 63.5, 58.9, 58.6, 40.1, 37.3, 25.8, 24.1, 18.1, −4.7, −4.8; IR (KBr): ν_{max} 2956, 2927, 2854, 1471, 1463, 1258, 1098 cm^{-1}; MS (EI, 70 eV): *m/z* 411 and 409 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{32}{}^{79}BrNOSi$: 409.1437, Found: 409.1444; Calcd for $C_{20}H_{32}{}^{81}BrNOSi$: 411.1416, Found: 411.1420; $[\alpha]_D^{20}$ = −70.4 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.30 (complex m, 4H), 7.24−7.21 (complex m, 1H), 5.94 (m, 1H), 4.10 (m, 1H), 3.86 (m, 1H), 3.17 (m, 1H), 2.29 (m, 1H), 2.00−1.94 (complex m, 2H), 1.72 (broad s, 1H), 1.60 (m, 1H), 1.37 (d, J = 6.4 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 129.3, 128.4, 127.0, 126.6, 124.8, 63.5, 56.5, 55.3, 37.4, 37.3, 25.8, 25.0, 18.2, −4.8; IR (KBr): ν_{max} 3332, 2955, 2927, 2856, 1642, 1471, 1252, 1098, 1075, 1005, 968, 869, 836, 775, 699 cm^{-1}; MS (EI, 70 eV): m/z 411 and 409 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{32}{}^{79}Br$ NOSi: 409.1437, Found: 409.1440; Calcd for $C_{20}H_{32}{}^{81}BrNOSi$: 411.1416, Found: 411.1422; $[\alpha]_D^{20}$ = −10.2 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **ent-23*** Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 v/v hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.20 (complex m, 5H), 5.92 (m, 1H), 4.04−3.98 (complex m, 2H), 3.36 (broad s, 1H), 2.27 (m, 1H), 1.95 (m, 1H), 1.66 (m, 1H), 1.56 (m, 1H), 1.36 (d, J = 6.4 Hz, 3H), 0.82 (s, 9H), 0.01 (s, 3H), −0.02 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 128.8, 128.3, 126.9(3), 126.8(9), 125.2, 63.5, 59.0, 58.6, 40.1, 37.3, 25.8, 24.2, 18.0, −4.7(5), −4.7(9); IR (KBr): ν_{max} 2955, 2927, 2855, 1641, 1471, 1251, 1100, 1075, 868, 775, 700 cm^{-1}; MS (EI, 70 eV): m/z 411 and 409 ($M^{+\bullet}$, 100 and 99%); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{32}{}^{79}BrNOSi$: 409.1437, Found: 409.1437; Calcd for $C_{20}H_{32}{}^{81}BrNOSi$: 411.1416, Found: 411.1429; $[\alpha]_D^{20}$ = +64.3 (c = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 v/v]hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.31 (complex m, 4H), 7.22 (complex m, 1H), 5.95 (m, 1H), 4.12 (m, 1H), 3.88 (q, J = 6.8 Hz, 1H), 3.17 (m, 1H), 2.27 (dt, J = 17.2 and 5.2 Hz, 1H), 1.98 (m, 2H), 1.75 (broad s, 1H), 1.61 (m, 1H), 1.37 (d, J = 9.2 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 129.3, 128.4, 127.0, 126.6, 124.9, 63.5, 56.5, 55.3, 37.4, 37.3, 25.8, 25.0, 18.2, −4.8; IR (KBr): ν_{max} 2955, 2927, 2856, 1641, 1471, 1251, 1100, 869, 830, 775, 699 cm^{-1}; MS (EI, 70 eV): m/z 411 and 409 ($M^{+\bullet}$, 100 and 97%); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{32}{}^{79}BrNOSi$: 409.1437, Found: 409.1433; Calcd for $C_{20}H_{32}{}^{81}BrNOSi$: 411.1416, Found: 411.1408; $[\alpha]_D^{20}$ = +5.8 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **24**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 v/v hexane/ethyl acetate): ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, J = 8.0 and 5.6 Hz, 1H), 6.97 (m, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.80 (m, 1H), 5.95 (m, 1H), 4.03 (m, 2H), 3.84 (s, 3H), 3.38 (m, 1H), 2.27 (m, 1H), 1.98 (m, 1H), 1.72 (m, 1H), 1.62 (m, 1H), 1.36 (d, J = 6.8 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 147.9, 129.3, 128.7, 125.2, 119.3, 112.5, 112.1, 63.6, 58.6, 55.1, 40.2, 37.3, 26.0, 25.8, 24.2, 18.0, −4.7, −4.8; IR (KBr): ν_{max} 2954, 2927, 2856, 1601, 1586, 1486, 1471, 1463, 1255, 1099, 86, 836 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+•}$, 100 and 95%), 426 and 424 [(M−Me•)$^+$, 98 and 95]; HRMS $M^{+•}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1555; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1525; $[\alpha]_D^{20}$ = −69.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 1H), 6.91 (m, 2H), 6.79 (m, 1H), 5.98 (m, 1H), 4.13 (m, 1H), 3.89 (q, *J* = 6.4 Hz, 1H), 3.83 (s, 3H), 3.22 (m, 1H), 2.31 (dt, *J* = 17.2 and 4.8 Hz, 1H), 2.02 (m, 2H), 1.75 (broad s, 1H), 1.64 (m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 146.5, 129.3(9), 129.3(7), 124.8, 119.1, 112.6, 111.8, 63.5, 56.5, 55.2, 37.4, 37.2, 25.8, 25.0, 18.2, −4.7 (resonances due to two carbons obscured or overlapping); IR (KBr): ν_{max} 2954, 2928, 2856, 1599, 1470, 1255, 1099, 1072, 867 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+•}$, 100 and 97%), 426 and 424 ([M−Me•]$^+$, 80 and 77); HRMS $M^{+•}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1533; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1510; $[\alpha]_D^{20}$ = −19.1 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **25**.* Separable diastereoisomers.More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 6.93 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 5.92 (m, 1H), 4.33 (q, *J* = 6.0 Hz, 1H), 4.04 (m, 1H), 3.83 (s, 3H), 3.40 (broad s, 1H), 2.27 (dt, *J* = 17.6 and 5.2 Hz, 1H), 1.96 (m, 1H), 1.89 (m, 1H), 1.64 (m, 1H), 1.36 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 9H), −0.00 (s, 3H), −0.03 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 128.6, 127.7, 127.5, 120.6, 110.4, 63.5, 58.5, 55.2, 52.2, 39.6, 37.3, 25.8, 22.0, 18.0, −4.7(8), −4.8(1) (resonances due to two carbons obscured or overlapping); IR (KBr): ν_{max} 2954, 2928, 2856, 1516, 1490, 1463, 1251, 1238, 1099, 867, 836, 775, 753 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+•}$, 70 and 68%), 426 and 424 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+•}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1553; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1523; $[\alpha]_D^{20}$ = −41.5 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.20 (complex m, 2H), 6.93 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 5.96 (m, 1H), 4.15 (m, 2H), 3.83 (s, 3H), 3.11 (broad s, 1H), 2.32 (m, 1H), 2.00 (m, 2H), 1.60 (m, 1H), 1.43 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 129.5, 128.1, 128.0, 120.5, 110.4, 63.4, 56.6, 55.1, 51.1, 37.4, 36.8, 25.8, 22.6, 18.2, −4.8 (resonances due to three carbons obscured or overlapping); IR (KBr): ν_{max} 2954, 2928, 2856, 1599, 1490, 1471, 1463, 1250, 1099. 1072, 871, 835, 775, 752 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+•}$, 62 and 60%), 426 and 424 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+•}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1552; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1526; $[\alpha]_D^{20}$ = −16.1 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **26**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H), 7.87 (m, 1H), 7.76 (m, 2H), 7.53−7.44 (complex m, 3H), 5.94 (m, 1H), 4.88 (q, *J* = 9.3 Hz, 1H), 404 (m, 1H), 3.45 (broad s, 1H), 2.30 (m, 1H), 1.96 (m, 1H), 1.80 (m, 1H), 1.61 (m, 1H), 1.53 (d, *J* = 6.8 Hz, 3H), 0.78 (s, 9H), −0.02 (s, 3H), −0.09 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0, 131.1, 128.9, 128.8, 127.3, 125.7, 125.6, 125.2, 124.0, 123.3, 63.5, 59.3, 54.6, 40.2, 37.4, 25.7, 23.9, 17.9, −4.8 (resonances due to three carbons obscured or overlapping); IR (KBr): ν_{max} 3048, 2955, 2927, 2855, 1641, 1596, 1471, 1462, 1251, 1099, 1077, 1004, 863, 836, cm^{-1}; MS (EI, 70 eV): *m/z* 461 and 459 ($M^{+•}$, 53 and 51%), 446 and 444 [(M−Me•)$^+$, 100 and 98]; HRMS $M^{+•}$ Calcd for $C_{24}H_{34}{}^{79}BrNOSi$: 459.1593, Found: 459.1588; Calcd for $C_{24}H_{34}{}^{81}BrNOSi$: 461.1573, Found: 461.1556; $[\alpha]_D^{20}$ = −65.3 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.77 (m, 2H), 7.55−7.46 (complex m, 3H), 6.00 (m, 1H), 4.84 (q, *J* = 7.6 Hz, 1H), 4.14 (m, 1H), 3.34 (m, 1H), 2.33 (dt, *J* = 17.4 and 5.8 Hz, 1H), 2.01 (m, 2H), 1.64 (m, 1H), 1.52 (d, *J* = 8.4 Hz, 3H), 0.87 (s, 9H), −0.06 (s, 3H), −0.03 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.9, 131.3, 129.4, 129.0, 127.2, 125.9, 125.7, 125.3, 124.9, 123.3, 122.6, 63.6, 56.7, 50.1, 37.8, 37.4, 25.8, 24.7, 18.2, −4.8 (resonances due to two carbons obscured or overlapping); IR (KBr): ν_{max} 3049, 2954, 2927, 2855, 1640, 1510, 1471, 1251, 1099, 1073, 867, 835, cm^{-1}; MS (EI, 70 eV): *m/z* 461 and 459 ($M^{+•}$, 55 and 53%), 446 and 444 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+•}$ Calcd for $C_{24}H_{34}{}^{79}BrNOSi$: 459.1593, Found: 459.1595; Calcd for $C_{24}H_{34}{}^{81}BrNOSi$: 461.1573, Found: 461.1581; $[\alpha]_D^{20}$ = +10.3 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **27**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.78 (complex m, 4H), 7.57 (m, 1H), 7.44 (m, 2H), 5.93 (m, 1H), 4.17 (q, *J* = 6.8 Hz, 1H), 4.02 (m, 1H), 3.40 (m, 1H), 2.29 (m, 1H), 1.94 (m, 1H), 1.67 (m, 1H), 1.53 (m, 1H), 1.47 (d, *J* = 7.4 Hz, 3H), 0.77 (s, 9H),

−0.01 (s, 3H), −0.09 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 133.4, 132.9, 128.8, 128.1, 127.7, 127.6, 125.8, 125.5, 125.4, 125.4, 63.6, 59.0, 58.9, 40.4, 37.3, 29.7, 25.7, 24.2, 18.0, −4.7, −4.8; IR (KBr): ν_{max} 3054, 2955, 2926, 2855, 1601, 1507, 1471, 1461, 1374, 1250, 1099, 1072, 858, 835, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 461 and 459 ($M^{+\bullet}$, 55 and 53%), 446 and 444 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{34}{}^{79}BrNOSi$: 459.1593, Found: 459.1591; Calcd for $C_{24}H_{34}{}^{81}BrNOSi$: 461.1573, Found: 461.1578; $[\alpha]_D^{20}$ = −67.1 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.81 (complex m, 4H), 7.53 (m, 1H), 7.45 (m, 2H), 5.97 (m, 1H), 4.14 (m, 1H), 4.06 (q, *J* = 7.8 Hz, 1H), 3.22 (m, 1H), 2.30 (m, 1H), 2.06−1.96 (complex m, 2H), 1.65 (m, 1H), 1.47 (d, *J* = 7.6 Hz, 3H), 0.88 (s, 9H), −0.09 (s, 3H), −0.08 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 133.3, 132.8, 129.4, 128.3, 127.7, 127.6, 126.0, 125.5(3), 125.4(9), 124.6, 63.5, 56.6, 55.3, 37.4, 37.3, 25.9, 25.8, 24.9, 18.2, −4.7, −4.8; IR (KBr): ν_{max} 3052, 2953, 2926, 2855, 1600, 1506, 1470, 1461, 1250, 1097, 1072, 856, 835, 816, 774, 744 cm^{-1}; MS (EI, 70 eV): *m/z* 461 and 459 ($M^{+\bullet}$, 55 and 53%), 446 and 444 [(M−Me•)$^+$, 100 and 98)]; HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{34}{}^{79}BrNOSi$: 459.1593, Found: 459.1596; Calcd for $C_{24}H_{34}{}^{81}BrNOSi$: 461.1573, Found: 461.1563; $[\alpha]_D^{20}$ = −27.2 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **28**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.90 (m, 1H), 4.03 (m, 1H), 3.94 (q, *J* = 5.6 Hz, 1H), 3.84 (s, 3H), 3.34 (m, 1H), 2.27 (m, 1H), 1.95 (m, 1H), 1.67 (m, 1H), 1.56 (m, 1H), 1.35 (d, *J* = 6.4 Hz, 3H), 0.83 (s, 9H), 0.01(9) (s, 3H), 0.01(5) (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 138.1, 128.7, 128.0, 125.2, 113.7, 63.6, 58.8, 57.9, 55.2, 40.1, 37.3, 25.8, 24.2, 18.0, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2955, 2927, 2855, 1641, 1611, 1512, 1470, 1463, 1255, 1100, 1071, 1039, 867, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+\bullet}$, 100 and 97%), 426 and 424 [(M−Me•)$^+$, 88 and 86]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1531; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1521; $[\alpha]_D^{20}$ = −93.9 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.99 (m, 1H), 4.15 (m, 1H), 3.94 (q, *J* = 6.4 Hz, 1H), 3.83 (s, 3H), 3.21 (m, 1H), 2.35 (m, 1H), 2.08−1.98 (complex m, 2H), 1.67 (m, 1H), 1.39 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 136.7, 129.2, 127.6, 124.9, 113.8, 63.5, 56.5, 55.2, 54.7, 37.4, 37.3, 25.8, 25.0, 18.2, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2955, 2928, 2856, 1641, 1611, 1512, 1463, 1255, 1098, 1072, 868, 832, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+\bullet}$, 100 and 97%), 426 and 424 [(M−Me•)$^+$, 75 and 71]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1545; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1519; $[\alpha]_D^{20}$ = −11.5 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **ent-28**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 5.91 (m, 1H), 4.03 (m, 1H), 3.95 (q, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 3.34 (broad s, 1H), 2.27 (m, 1H), 1.96 (m, 1H), 1.66 (m, 1H), 1.57 (m, 1H), 1.35 (d, *J* = 6.4 Hz, 3H), 0.83 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 138.1, 128.7, 127.9, 125.3, 113.7, 63.5, 58.8, 57.9, 55.2, 40.2, 37.3, 25.8, 24.2, 18.0, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2955, 2927, 2855, 1611, 1512, 1470, 1463, 1255, 1100, 1070, 867, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+\bullet}$, 65 and 62%), 426 and 424 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1543; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1522; $[\alpha]_D^{20}$ = +85.9 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 5.99 (m, 1H), 4.15 (m, 1H), 3.88 (q, *J* = 6.4 Hz, 1H), 3.83 (s, 3H), 3.21 (broad s, 1H), 2.35 (m, 1H), 2.06−1.98 (complex m, 2H), 1.68 (m, 1H), 1.39 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 136.7, 129.2, 127.6, 124.9, 113.7, 63.5, 56.4, 55.2, 54.6, 37.4, 37.3, 25.8, 25.0, 18.2, −4.7(8), −4.7(9); IR (KBr): ν_{max} 2954, 2928, 2856, 1611, 1512, 1470, 1463, 1255, 1176, 1098 1073, 1040, 869, 832, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 441 and 439 ($M^{+\bullet}$, 60 and 58%), 426 and 424 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNO_2Si$: 439.1542, Found: 439.1549; Calcd for $C_{21}H_{34}{}^{81}BrNO_2Si$: 441.1522, Found: 441.1528; $[\alpha]_D^{20}$ = +17.2 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **29**.* Inseparable diastereoisomers (R_f = 0.85 in 10:1 *v/v* hexane/ethyl acetate).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 1H), 7.18−7.13 (complex m, 3H), 5.98 (m, 0.5H), 5.91 (m, 0.5H), 4.27 (m, 0.5H), 4.08 (m, 0.5H), 3.97 (m, 0.5H), 3.77 (m, 0.5H), 3.61 (m, 0.5H), 3.56 (m, 0.5H), 2.84 (m, 1H), 2.73 (m, 1H), 2.39−2.26 (complex m, 1H), 2.14−2.08 (complex m, 1H), 2.06−1.98 (complex m, 2H), 1.90−1.86 (complex m, 2H), 1.80−1.74 (complex m, 2H), 0.93 (s, 4.5H), 0.89 (s, 4.5H), 0.14 (s, 1.5H), 0.12 (s, 1.5H), 0.08 (s, 1.5H) 0.06 (s, 1.5H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 137.4(2), 137.3(5), 129.6, 129.5, 129.1(0), 129.0(7), 128.9(2), 128.8(5), 128.7, 126.9, 126.6, 125.8, 125.7(3), 125.6(5), 124.4, 63.5, 63.3, 60.1, 57.6, 56.5, 52.9, 41.6, 38.5, 37.6, 37.3, 29.3(9), 29.3(0), 29.2, 27.4, 25.9, 25.8, 19.1, 18.1(3), 18.0(9), 17.6, −4.5(6), −4.5(8), −4.6, −4.7; IR (KBr): ν_{max} 3017, 2928, 2856, 1642, 1471, 1461, 1447, 1251, 1122, 1086, 864, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 437 and 435 ($M^{+\bullet}$, 100 and 97%); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{34}{}^{79}BrNOSi$: 435.1593, Found: 435.1587; Calcd for $C_{22}H_{34}{}^{81}BrNOSi$: 437.1573, Found: 437.1568.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **30**.* Separable diastereoisomers. More mobile diastereoisomer (R_f =0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 1H), 7.23−7.20 (complex m, 3H), 6.00 (m, 1H), 4.31−4.30 (complex m, 2H), 3.61 (broad s, 1H), 3.03 (m, 1H), 2.82 (m, 1H), 2.50 (m, 1H), 2.23 (m, 1H), 2.14−2.02 (complex m, 2H), 1.88−1.74 (complex m, 2H), 0.92 (s, 9H), 0.12(4) (s, 3H), 0.12(0) (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 143.4, 129.9, 127.4, 126.3, 124.6, 124.5, 124.3, 63.5, 61.1, 58.4, 38.2, 37.5, 33.9, 30.1, 25.9, 18.2, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 3024, 2952, 2927, 2855, 1643, 1471, 1461, 1250, 1105, 1079, 869, 862 835, 775, 750 cm^{-1}; MS (EI, 70 eV): *m/z* 423 and 421 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{32}{}^{79}BrNOSi$: 421.1437. Found: 421.1432. Calcd for $C_{21}H_{32}{}^{81}BrNOSi$: 423.1416. Found: 423.1423; $[\alpha]_D^{20}$ = −69.7 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (**45**) (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (m, 1H), 7.28−7.22 (complex m, 3H), 6.01 (m, 1H), 4.33 (t, *J* = 4.0 Hz, 1H), 4.18 (m, 1H), 3.73 (broad s, 1H), 3.04 (m, 1H), 2.83 (m, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.12−2.06 (complex m, 2H), 1.96−1.89 (complex m, 2H), 1.75 (broad s, 1H), 0.94 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.3, 129.2, 127.4, 126.3, 125.0, 124.8, 123.8, 63.4, 62.9, 59.6, 39.9, 37.3, 35.7, 30.3, 25.8, 18.1, −4.6 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 3342, 2954, 2926, 2854, 1644, 1461, 1255, 1124, 869, 835, 774 cm^{-1}; MS (EI, 70 eV): *m/z* 423 and 421 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{32}{}^{79}BrNOSi$: 421.1437, Found: 421.1438; Calcd for $C_{21}H_{32}{}^{81}BrNOSi$: 423.1416, Found: 423.1419; $[\alpha]_D^{20}$ = +54.4 (*c* = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **31**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.19 (complex m, 5H), 5.90 (m, 1H), 3.99 (m, 1H), 3.69 (t, J = 6.8 Hz, 1H), 3.31 (broad s, 1H), 2.23 (m, 1H), 1.93 (m, 1H), 1.78−1.46 (complex m, 4H), 0.84 (t, J = 7.6 Hz, 3H), 0.82 (s, 9H), −0.01 (s, 3H), −0.06 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 128.7, 128.2, 127.6, 126.9, 125.2, 66.0, 63.5, 59.4, 40.4, 37.3, 31.2, 25.8, 18.0, 10.8, −4.7(7), −4.8(2); IR (KBr): ν_{max} 2956, 2927, 2855, 1641, 1471, 1461, 1453, 1251, 1111, 869, 836, 775, 701 cm^{-1}; MS (EI, 70 eV): *m/z* 425 and 423 ($M^{+\bullet}$, 27 and 25%), 396 and 394 [(M−Et•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNOSi$: 423.1593, Found: 423.1591; Calcd for $C_{21}H_{34}{}^{81}BrNOSi$: 425.1573, Found: 425.1586; $[\alpha]_D^{20}$ = −64.6 (c = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.23 (complex m, 5H), 5.95 (m, 1H), 4.13 (m, 1H), 3.57 (t, J = 6.4 Hz, 1H), 3.15 (broad s, 1H), 2.31 (dt, J = 17.6 and 5.2 Hz, 1H), 1.99 (m, 2H), 1.77−1.55 (complex m, 3H), 0.88 (s, 9H), 0.87 (m, 3H), 0.08 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 129.4, 128.2, 127.7, 127.0, 124.9, 63.5, 61.9, 56.4, 37.6, 37.1, 31.6, 25.9, 18.3, 11.4, −4.6 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 3328, 2956, 2928, 2856, 1643, 1471, 1462, 1251, 1105, 1080, 861, 836, 775, 700 cm^{-1}; MS (EI, 70 eV): *m/z* 425 and 423 ($M^{+\bullet}$, 23 and 21%), 396 and 394 [(M−Et•)$^+$, 100 and 98]; HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{34}{}^{79}BrNOSi$: 423.1593, Found: 423.1591; Calcd for $C_{21}H_{34}{}^{81}BrNOSi$: 425.1573, Found: 425.1586; $[\alpha]_D^{20}$ = −15.3 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **32**.* Separable diastereoisomers. More mobile diastereoisomer (R_f = 0.7 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, J = 1.9 Hz, 1H), 6.89 (dd, J = 8.0 and 1.9 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 5.90 (m, 1H), 3.96 (m, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 3.34 (m, 1H), 2.28 (m, 1H), 1.94 (m, 1H), 1.67 (m, 1H), 1.58 (m, 1H), 1.34 (d, J = 4.0 Hz, 3H), 0.81 (s, 9H), 0.00 (s, 3H), −0.03 (s, 3H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 147.9, 138.7, 128.6, 125.3, 119.0, 110.8, 109.8, 63.6, 58.4, 58.3, 55.8, 55.7, 40.4, 37.3, 25.7, 24.3, 18.0, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2954, 2928, 2855, 1640, 1516, 1463, 1250, 1233, 1168, 1139, 1111, 1098, 1031, 866, 836 cm^{-1}; MS (EI, 70 eV): *m/z* 471 and 469 ($M^{+\bullet}$, 20 and 18%), 456 and 454 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{36}{}^{79}BrNO_3Si$: 469.1648, Found: 469.1645; Calcd for $C_{22}H_{36}{}^{81}BrNO_3Si$: 471.1627, Found: 471.1626; $[\alpha]_D^{20}$ = −87.0 (c = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65 in 10:1 *v/v* hexane/ethyl acetate): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (m, 1H), 6.80 (m, 2H), 5.95 (m, 1H), 4.10 (m, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.81 (m, 1H), 3.18 (broad s, 1H), 2.30 (dt, J = 15.2 and 3.6 Hz, 1H), 2.03−1.96 (complex m, 2H), 1.63 (broad s, 1H), 1.59 (m, 1H), 1.35 (d, J = 6.0 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 147.9, 137.3, 129.3, 125.0, 119.0, 110.7, 109.1, 63.5, 56.5, 55.8, 54.9, 37.4, 37.2, 25.9, 25.8, 25.3, 18.2, −4.7 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 2954, 2928, 2856, 1641, 1517, 1464, 1250, 1233, 1098, 1030, 867, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 471 and 469 ($M^{+\bullet}$, 23 and 21%), 456 and 454 [(M−Me•)$^+$, 100 and 98]; HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{36}{}^{79}BrNO_3Si$: 469.1648, Found: 469.1643; Calcd for $C_{22}H_{36}{}^{81}BrNO_3Si$: 471.1627, Found: 471.1617; $[\alpha]_D^{20}$ = −35.2 (c = 1, $CHCl_3$).

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **33**.* Inseparable diastereoisomers (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.25 (complex m, 5H), 5.95 (m, 1H), 4.56−4.45 (complex m, 2H), 4.04 (m, 1H), 3.72 (m, 1H), 3.49 (m, 0.5H), 3.39 (m, 0.5H), 3.20 (m, 0.5H), 3.13 (m, 0.5H), 2.31 (m, 0.5H), 2.26 (m, 0.5H), 2.06−1.91 (complex m, 4H), 1.79−1.66 (complex m, 5H), 1.46−1.32 (complex m, 1H), 0.88 (s, 4.5H), 0.87 (s, 4.5H), 0.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 129.2, 129.0, 128.3(1), 128.2(6), 127.6(4), 127.5(5), 127.4(6), 127.3(6), 125.0, 86.1, 85.9, 71.2, 63.5, 63.4, 63.0, 62.9, 58.8, 58.7, 38.8, 38.7, 37.4, 32.1, 30.4, 30.1, 29.9, 25.8(3), 25.8(1), 21.5, 21.2, 18.1, 18.0, −4.6(7), −4.7(4); IR (KBr): ν_{max} 3337, 3030, 2930, 2856, 1642, 1471, 1462, 1455, 1381, 1360, 1251, 1097, 1072, 962, 867, 776, 734, 696 cm^{-1}; MS (EI, 70 eV): *m/z* 481 and 479 ($M^{+\bullet}$, 100 and 97%); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{38}{}^{79}BrNO_2Si$: 479.1855, Found: 479.1862; Calcd for $C_{24}H_{38}{}^{81}BrNO_2Si$: 481.1835, Found: 481.1841.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **34**.* Inseparable diastereoisomers (R_f = 0.70 in 10:1 *v/v* hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 1H), 7.32−7.29 (complex m, 3H), 7.23 (m, 1H), 5.91 (m, 1H), 4.65 (m, 1H), 4.48 (m, 1H), 4.04 (m, 0.5H), 3.98 (m, 0.5H), 3.47 (broad s, 0.5H), 3.40 (broad s, 0.5H), 3.23 (m, 0.5H), 3.21 (m, 0.5H), 2.71 (m, 0.5H), 2.61 (m, 0.5H), 2.31 (m, 1H), 2.14−1.89 (complex m, 4H), 1.79−1.65 (complex m, 5H), 1.33−1.16 (complex m, 3H), 0.88 (s, 4.5H), 0.82 (s, 4.5H), 0.06(2) (s, 1,5H), 0.05(9) (s, 1.5H), 0.03(6) (s, 1.5H), 0.04(9) (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 138.8, 128.8, 128.5, 128.3, 127.6, 127.3(1), 127.3(0), 125.9, 124.9, 82.1, 81.5, 70.6, 70.4, 63.5, 63.2, 61.4, 59.1, 58.5, 56.9, 41.4, 37.9, 37.4, 37.3, 32.3, 29.9, 29.5(3), 29.5(1), 25.8, 25.7, 24.0(4), 24.0(2), 23.8, 23.7, 18.1, 18.0, −4.6, −4.7, −4.9; IR (KBr): ν_{max} 3338, 3030, 2929, 2856, 1642, 1471, 1462, 1453, 1251, 1097, 1072, 865, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 495 and 493 ($M^{+\bullet}$, 100 and 97%);

HRMS $M^{+\bullet}$ Calcd for $C_{25}H_{40}{}^{79}BrNO_2Si$: 493.2012. Found: 493.2016. Calcd for $C_{25}H_{40}{}^{81}BrNO_2Si$: 495.1991. Found: 495.1986.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **35**.* Inseparable diastereoisomers (R_f = 0.85 in 10:1 *v/v* hexane/ethyl acetate).^{1}H NMR (400 MHz, $CDCl_3$) δ (major diastereoisomers) 7.62 (m, 2H), 7.56 (m, 1H), 7.47 (m, 1H), 7.37−7.30 (complex m, 5H), 7.24 (complex m, 1H), 6.08 (m, 1H), 4.81 (m, 0.5H), 4.37 (m, 0.5H), 4.04−3.82 (complex m, 2.5H), 3.64 (m, 0.5H), 2.52 (m, 0.5H), 2.39 (m, 0.5H), 2.25−2.17 (complex m, 2H), 1.89 (m, 1H), 1.39 (d, *J* = 7.6 Hz, 1.5H), 1.28 (d, *J* = 7.6 Hz, 1.5H), 0.90 (s, 9H), 0.11 (s, 6H) (resonance due to one proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of diastereoisomers) 146.3, 145.2, 144.0, 142.7, 129.6, 129.5, 129.4, 129.3, 129.0, 128.9, 128.6, 128.5, 128.3, 128.2, 128.1(2), 128.0(5), 1279, 127.2, 68.6, 66.6(3), 66.6(0), 64.7, 60.7, 57.8, 53.9, 52.4, 51.7, 44.0, 38.7, 36.0, 27.4, 27.3, 21.9, 20.6, 19.8, 19.6, 19.5, –3.1(8), –3.2(1), –3.2(9), –3.3(0); IR (KBr): ν_{max} 2954, 2928, 2856, 1632, 1601, 1493, 1471, 1462, 1381, 1361, 1252, 1181, 1122, 1026, 1005, 968, 861 cm^{-1}; MS (EI, 70 eV): *m/z* 501 and 499 ($M^{+\bullet}$, both 2%), 486 and 484 [(M−Me•)$^+$, 52 and 48], 105 (100), 91 (73); HRMS $M^{+\bullet}$ Calcd for $C_{27}H_{38}{}^{79}BrNOSi$: 499.1906, Found: 499.1919; Calcd for $C_{27}H_{38}{}^{81}BrNOSi$: 501.1886s, Found: 501.1869.

*Products obtained from the electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **ent-35**.* Inseparable diastereoisomers (R_f = 0.85 in 10:1 *v/v* hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ (major diastereoisomers) 7.61 (m, 2H), 7.55 (m, 1H), 7.45 (m, 1H), 7.38−7.22 (complex m, 6H), 6.08 (m, 1H), 4.38 (m, 1H), 3.95 (m, 1H), 3.83 (m, 1H), 3.61 (m, 1H), 2.40 (m, 0.5H), 2.24−2.19 (complex m, 1.5H), 1.91 (m, 2H), 1.39 (d, *J* = 7.6 Hz, 1.5H), 1.28 (d, *J* = 7.6 Hz, 1.5H), 0.81 (s, 4.5H), 0.78 (s, 4.5H), −0.02 (s, 3H), −0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of diastereoisomers) 144.7, 143.6, 142.5, 141.1, 132.1, 128.1, 127.4, 126.7, 126.4, 121.8, 65.0(4), 65.0(2), 63.1, 57.6, 56.3, 53.4, 52.4, 50.9, 42.5, 37.3, 36.5, 34.4, 29.0, 25.7, 20.3, 19.0, 18.1, 18.0, 11.4, –4.7(4), –4.7(7), –4.8(2), –4.8(9); IR (KBr): ν_{max} 3061, 3027, 2953, 2928, 2855, 1634, 1493, 1471, 1461, 1452, 1252, 1122, 1027, 1005, 965, 861, 836, 775 cm^{-1}; MS (EI, 70 eV): *m/z* 501 and 499 ($M^{+\bullet}$, both 5%), 486 and 484 [(M−Me•)$^+$, 100 and 97]; HRMS $M^{+\bullet}$ Calcd for $C_{27}H_{38}{}^{79}BrNOSi$: 499.1906, Found: 499.1917; Calcd for $C_{27}H_{38}{}^{81}BrNOSi$: 501.1886, Found: 501.1867.

Total syntheses of (+)-11-hydroxyvattitine [(+)-3] and (+)-bulbispermine [(+)-4]

*(S)-*N*-(2-Bromocyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (**46**). Step i:* A magnetically stirred mixture of acetamide ***ent*-41** (3.00 g, 11.0 mmol) and triethylbenzylammonium chloride (250 mg, 1.1 mmol) in dichloromethane (50 mL) was

treated with KOH (50 mL of a 20% w/w aqueous solution). The ensuing mixture was stirred at 22 °C for 8 h, the separated aqueous layer extracted with dichloromethane (1 × 50 mL) and the combined organic phases dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing light-yellow oil was subjected directly to step ii. *Step ii:* A solution of the oil obtained from step i in dichloromethane (30 mL) was treated with triethylamine (2.3 mL, 16.5 mmol), *p*-TsCl (2.10 g, 11.0 mmol) and DMAP (130 mg, 1.1 mmol). The ensuing mixture was stirred at 22 °C for 1 h then treated with HCl (20 mL of a 2 M aqueous solution). The separated aqueous phase was extracted with dichloromethane (3 × 20 mL) and the combined organic phases then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (hexane/ethyl acetate) of the resulting solid, sulfonamide **46** (3.00 g, 83%) as white needles, m.p. = 100−101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 6.14 (t, *J* = 4.1 Hz, 1H), 5.19 (d, *J* = 7.1 Hz, 1H), 3.80 (m, 1H), 2.39 (s, 3H), 2.08−1.95 (complex m, 3H), 1.77 (m, 1H), 1.62−1.57 (complex m, 2H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.1, 135.0, 129.3, 127.3, 120.1, 55.0, 31.5, 27.3, 21.4, 16.4; IR (KBr): ν_{max} 3276, 2934, 2869, 1641, 1598, 1495, 1445, 1426, 1330, 1157, 1087, 1008 cm^{-1}; MS (ESI, +ve): *m/z* 354 and 352 [(M+Na)$^+$, both 100%], 332 and 330 [(M+H)$^+$, both 20]; HRMS [M+Na]$^+$ Calcd for $C_{13}H_{16}{}^{79}BrNO_2SNa$: 351.9983, Found: 351.9985; Calcd for $C_{13}H_{16}{}^{81}BrNO_2SNa$: 353.9962, Found: 353.9963; $[\alpha]_D^{20}$ = −26.0 (*c* = 1, $CHCl_3$).

*(*S*)-*N*-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (**48**).* A magnetically stirred mixture of sulfonamide **46** (3.00 g, 9.1 mmol) in benzene (100 mL) and Na_2CO_3 (30 mL of a 2 M aqueous solution) was treated with benzo[*d*][1,3]dioxol-5-yl-boronic acid (**47**) (2.20 g, 13.7 mmol), $Pd(Ph_3P)_4$ (530 mg, 0.46 mmol). The ensuing mixture was deoxygenated for 0.5 h using nitrogen then heated under reflux for 14 h before being cooled then poured into water (100 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic phases were washed with $NaHCO_3$ (50 mL of a saturated aqueous solution) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.35) and recrystallization (hexane/ethyl acetate) of the resulting solid, compound **48** (3.03 g, 90%) as a white, crystalline solid, m.p. = 161−161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.48 (d, *J* = 8.1 Hz, 1H), 6.40 (dd, *J* = 8.1 and 1.8 Hz, 1H), 6.33 (d, *J*

= 1.8 Hz, 1H), 5.92 (m, 1H), 5.88 (m, 2H), 4.52 (d, *J* = 6.0 Hz, 1H), 4.09 (m, 1H), 2.41 (s, 3H), 2.19−2.06 (complex m, 3H), 1.69−1.62 (complex m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 146.6, 143.0, 137.0, 136.0, 133.7, 130.4, 129.3, 127.0, 119.8, 107.9, 106.7, 100.8, 49.7, 30.0, 25.5, 21.5, 16.4; IR (KBr): ν_{max} 3291, 2930,1598, 1503, 1489, 1437, 1329, 1244, 1156, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 371 ($M^{+\bullet}$, 20%), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{21}NO_4S$: 371.1191, Found: 371.1192; $[\alpha]_D^{20}$ = −141.6 (*c* =1, $CHCl_3$).

*(*S*)-*N*-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)-*N*-(but-2-yn-1-yl)-4-methyl benzene-sulfonamide (**49**).* A magnetically stirred mixture of sulfonamide **48** (3.00 g, 8.1 mmol) in dry DMF (30 mL) was treated with NaH (490 mg, 12.2 mmol) and the ensuing mixture stirred at 0 °C for 0.5 h before treated with 1-bromo-2-butyne (1.00 mL, 12.2 mmol). The resulting solution was stirred at 22 °C for 1.5 h then poured into water (100 mL – CAUTION POSSIBILITY OF HYDROGEN EVOLUTION) and extracted with ethyl acetate (3 × 40 mL). The combined organic phases were washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), compound **49** (3.10 g, 91%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 6.71 (m, 2H), 6.63 (d, *J* = 8.5 Hz, 1H), 6.08 (m, 1H), 5.90 (s, 2H), 5.01 (m, 1H), 3.85 (m, 1H), 3.54 (m, 1H), 2.40 (s, 3H), 2.14 (m, 2H), 2.00 (m, 1H), 1.84−1.77 (complex m, 2H), 1.62-1.54 (complex m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 146.4, 142.8, 138.3, 136.7, 134.2, 132.6, 128.9, 127.7, 120.1, 107.7, 107.3, 100.8, 80.0, 75.3, 55.2, 33.7, 28.7, 25.4, 21.4, 20.1, 3.3; IR (KBr): ν_{max} 3026, 2919, 1598, 1503, 1489, 1438, 1335, 1244, 1224, 1156, 1095, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 423 ($M^{+\bullet}$, 10%), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_4S$: 423.1504, Found: 423.1505; $[\alpha]_D^{20}$ = −28.0 (*c* = 1, $CHCl_3$).

*(3a*R*,7a*S*,Z)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-3-ethylidene-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indole (**50**).*A magnetically stirred solution of compound **49** (470 mg, 1.1 mmol) in benzene (10 mL) was treated with BBEDA (50 mg, 0.22 mmol) and $Pd(OAc)_2$ (50 mg, 0.22 mmol). The ensuing solution was deoxygenated for 0.33 h using nitrogen then heated under reflux for 13 h before being cooled then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), diene **50** (330 mg, 70%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.50 (d, *J* = 8.1 Hz, 1H), 6.44 (dd, *J* = 8.1 and 1.4 Hz, 1H), 6.30 (broad s, 1H), 5.88 (q, *J* = 3.3 Hz, 2H), 5.84 (m, 1H), 5.42 (broad d, *J* = 9.9 Hz, 1H), 5.16 (m, 1H), 4.20 (d, *J* = 14.4 Hz,

1H), 3.92 (d, *J* = 14.4 Hz, 1H), 3.72 (m, 1H), 2.40 (s, 3H), 2.28 (m, 1H), 2.11 (m, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.62 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 146.1, 143.0, 141.2, 138.4, 134.2, 130.3, 129.2, 127.2, 126.8, 121.2, 120.4, 108.2, 107.5, 100.9, 67.4, 55.3, 49.6, 25.7, 21.9, 21.4, 14.5; IR (KBr): ν_{max} 2918, 1598, 1503, 1484, 1433, 1342, 1240, 1160, 1096, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 423 ($M^{+\bullet}$, 70%), 268 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_4S$: 423.1504. Found: 423.1502; $[\alpha]_D^{20}$ = +180 (*c* = 1, $CHCl_3$).

*(3a*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-tosyl-1,2,3a,6,7,7a-hexahydro-3*H*-indol-3-one (**51**). Step i:* A magnetically stirred mixture of diene **50** (300 mg, 0.71 mmol) in acetonitrile/water (2.5 mL of a 4:1 v/v mixture) was treated with citric acid (420 mg, 2.13 mmol), *N*-methylmorpholine-*N*-oxide (250 mg, 1.42 mmol) and potassium osmate dihydrate (27 mg, 0.071 mmol). The resulting mixture was stirred at 22 °C for 72 h then diluted with ethyl acetate (20 mL) and HCl (10 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with ethyl acetate (2 × 10 mL) and the combined organic phases were washed with brine (1 × 20 mL) before being dried (Na_2SO_4), filtered through a short plug of TLC-grade silica gel and then concentrated under reduced pressure. The ensuing brown oil was subjected to the step ii. *Step ii:* A magnetically stirred solution of the brown oil obtained from step i in dichloromethane (20 mL) was treated with iodobenzene diacetate (200 mg, 0.62 mmol). The ensuing solution was stirred at 22 °C for 2 h before being concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.2), ketone **51** (110 mg, 38%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.63 (d, *J* = 8.1 Hz, 1H), 6.36 (dd, *J* = 8.1 and 1.7 Hz, 1H), 6.26 (d, *J* = 1.7 Hz, 1H), 6.22 (m, 1H), 5.90 (s, 2H), 5.41 (d, *J* = 9.9 Hz, 1H), 4.07 (d, *J* = 18.3 Hz, 1H), 3.82 (m, 1H), 3.65 (d, *J* = 18.3 Hz, 1H), 2.45 (m, 1H), 2.44 (s, 3H), 2.28 (m, 1H), 2.14 (m, 1H), 1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 147.8, 147.0, 144.3, 133.2, 133.1, 132.5, 129.9, 127.6, 123.4, 121.3, 108.2, 108.0, 101.2, 64.9, 60.4, 54.5, 22.9, 21.5, 20.6; IR (KBr): ν_{max} 2915, 1756, 1597, 1504, 1488, 1436, 1348, 1244, 1158, 1090, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 411 ($M^{+\bullet}$, 10%), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{21}NO_5S$: 411.1140, Found: 411.1152; $[\alpha]_D^{20}$ = −6.5 (*c* = 1, $CHCl_3$).

*(3*R*,3a*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**52**). Step i:* A magnetically stirred mixture of ketone **51** (400 mg, 0.97 mmol) in THF/methanol (8 mL of a 1:1 v/v mixture) maintained at −78 °C was treated with $NaBH_4$ (110 mg, 2.92 mmol) and the reaction mixture then allowed to warm to 22 °C and stirred at this temperature for 10 h before being concentrated under reduced pressure. The residue thus

obtained was dissolved in ethyl acetate (30 mL) and the solution thus obtained washed with NH_4Cl (1 × 10 mL of a saturated aqueous solution) before being dried (Na_2SO_4) then filtered through a short plug of TLC-grade silica gel and the filtrate concentrated under reduced pressure. The white foam thus obtained was subjected to the step ii. *Step ii:* A solution of the white foam obtained from step i in pyridine (10 mL) was treated with Ac_2O (460 μL, 4.84 mmol) and DMAP (12 mg, 0.1 mmol). The ensuing solution was stirred at 22 °C for 4 h before being concentrated under reduced pressure and the yellow oil thus obtained subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.15) gave acetate **52** (350 mg, 80%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 6.61 (d, *J* = 8.1 Hz, 1H), 6.44 (dd, *J* = 8.1 and 1.5 Hz, 1H), 6.35 (d, *J* = 1.5 Hz, 1H), 6.16 (m, 1H), 5.75 (m, 2H), 5.65 (d, *J* = 10.4 Hz, 1H), 4.89 (t, *J* = 7.9 Hz, 1H), 3.95 (m, 1H), 3.62 (broad s, 1H), 3.24 (dd, *J* = 11.4 and 6.8 Hz, 1H), 2.48 (s, 3H), 2.34 (m, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.93 (s, 3H), 1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 147.8, 146.5, 143.9, 134.6, 134.0, 131.4, 129.8, 127.5, 125.0, 120.3, 107.8, 107.1, 101.1, 74.4, 64.4, 51.6, 50.4, 23.3, 21.5, 20.6, 20.4; IR (KBr): ν_{max} 3031, 2921, 1742, 1597, 1505, 1488, 1436, 1346, 1238, 1158, 1091, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 455 ($M^{+\bullet}$, 30%), 395 (35), 240 (83), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_6S$: 455.1403. Found: 455.1402; $[\alpha]_D^{20}$ = +149.0 (*c* = 1, $CHCl_3$).

*(3*R*,3a*S*,6*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-hydroxy-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**53**).* A magnetically stirred solution of acetate **52** (270 mg, 0.59 mmol) in dioxane (13 mL) was treated with SeO_2 (260 mg, 2.36 mmol) and the resulting mixture heated under reflux for 20 h before being cooled then concentrated under reduced pressure. The residue so obtained was subjected to flash chromatography (1:3 v/v ethyl acetate/toluene elution) to afford two fractions, A and B.

Concentration of fraction A (R_f = 0.4) gave, after recrystallization (chloroform/ methanol) of the resulting solid, alcohol **53** (200 mg, 71%) as a white, crystalline solid, m.p. = 178−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 6.60 (d, *J* = 8.2 Hz, 1H), 6.46 (d, *J* = 8.2 Hz, 1H), 6.31 (m, 1H), 6.20 (d, *J* = 10.3 Hz, 1H), 5.91 (m, 2H), 5.71 (d, *J* = 10.3 Hz, 1H), 4.87 (t, *J* = 7.5 Hz, 1H), 4.61 (m, 1H), 3.96 (m, 1H), 3.70 (m, 1H), 3.20 (m, 1H), 2.51 (complex m, 1H), 2.48 (s, 3H), 1.94 (s, 3H), 1.78 (broad s, 1H), 1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 148.0, 146.8, 144.2, 134.6, 133.6, 133.4, 129.9, 127.6, 126.8, 120.4, 108.0, 107.1, 101.2, 74.3, 63.9, 63.4, 51.9, 50.6, 33.0, 21.6, 20.7; IR (KBr): ν_{max} 3503, 2895, 1743, 1597, 1505, 1488, 1436, 1346, 1239, 1158, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 471 ($M^{+\bullet}$, 20%), 401(33), 316 (87), 256 (100), 91 (85);

HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_7S$: 471.1352. Found: 471.1353; $[\alpha]_D^{20}$ = +132.0 (*c* = 1, $CHCl_3$). These spectroscopic data match those reported previously,[29] although the stereochemistry at C-3 was assigned incorrectly in this earlier work.

Concentration of fraction B (R_f = 0.8) afforded the starting acetate **52** (50 mg) that was identical, in all respects, with an authentic sample.

*(3*R*,3a*S*,6*S*,7a*S*)-3a-(benzo[*d*][1,3]dioxol-5-yl)-6-hydroxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**54**).* A magnetically stirred mixture of alcohol **53** (0.17 g, 0.36 mmol) in THF (5 mL) maintained at −100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[6] in THF until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (1 mL of a saturated aqueous solution), $NaHCO_3$ (500 mg) and Na_2SO_4 (500 mg) were then added to the reaction mixture that was allowed to warm to 22 °C then stirred at this temperature for 12 h before being filtered and the solids thus retained rinsed with dichloromethane (3 × 20 mL). The combined filtrates were concentrated under reduced pressure and the ensuing light-yellow oil subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), compound **54** (62 mg, 56%) as a clear, colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, *J* = 1.4 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.73 (m, 1H), 6.07 (d, *J* = 10.4, 1H), 5.92 (s, 2H), 5.75 (d, *J* = 10.4 Hz, 1H), 5.54 (t, *J* = 6.1 Hz, 1H), 4.46 (m, 1H), 3.47 (broad s, 1H), 3.40 (m, 1H), 2.88 (m, 1H), 2.35−2.29 (complex m, 2H), 2.09 (m, 1H), 2.00 (s, 3H), 1.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 147.9, 146.3, 136.7, 132.7, 128.5, 119.9, 108.0, 107.4, 101.1, 80.1, 63.4, 62.5, 52.4, 50.7, 33.1, 21.0; IR (KBr): ν_{max} 3306, 3024, 2887, 1732, 1504, 1487, 1435, 1374, 1241, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 317 ($M^{+\bullet}$, 20%), 257 (40), 201 (50), 56 (100); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}NO_5$: 317.1263, Found: 317.1267; $[\alpha]_D^{20}$ = +60.7 (*c* = 1.3, $CHCl_3$).

*(+)-11-Hydroxyvattitine [(+)-**3**]. Step i:* A magnetically stirred solution of acetate **54** (62 mg, 0.20 mmol) in 1,2-dichloroethane (5 mL) was treated with paraformaldehyde (32 mg) then trifluoroacetic acid (320 μL, 4.15 mmol). The resulting solution was heated at 60 °C for 18 h before being cooled then concentrated under reduced pressure. The ensuing yellow oil was subjected to step ii. *Step ii:* A solution of the yellow oil obtained from step i in methanol (5 mL) was treated with anhydrous potassium carbonate (56 mg, 0.40 mmol) and the ensuing mixture stirred at 22 °C for 1 h before being concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform elution) to afford, after concentration of the appropriate fractions (R_f =

0.6), (+)-11-hydroxyvattitine [(+)-**3**] (38 mg, 68%) as a white foam. ^{1}H NMR (400 MHz, CD_3OD) δ 6.94 (s, 1H), 6.56 (s, 1H), 6.43 (d, *J* = 10.1 Hz, 1H), 6.18 (dd, *J* = 10.1 and 5.1 Hz, 1H), 5.89 (s, 2H), 4.34 (d, *J* = 16.6 Hz, 1H), 4.29 (m, 1H), 3.98 (m, 1H), 3.80 (d, *J* = 16.6 Hz, 1H), 3.46 (m, 1H), 3.44 (m, 1H), 3.18 (dd, *J* = 13.9 and 3.3 Hz, 1H), 2.27 (m, 1H), 1.83 (dd, *J* = 13.3 and 4.6 Hz, 1H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, CD_3OD) δ 148.2, 147.7, 137.0, 132.9, 127.9, 126.7, 107.8, 104.3, 102.2, 80.9, 64.7, 63.8, 61.6, 51.3, 33.0 (signal due to one carbon obscured or overlapping); IR (KBr): ν_{max} 3369, 2914, 1640, 1501, 1484, 1326, 1240, 1093, 1035 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 90%), 243 (81), 227 (90), 224 (64), 56 (100); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158. Found: 287.1158; $[\alpha]_D^{20}$ = +11.0 (*c* = 0.88, methanol) {lit[5] $[\alpha]_D^{25}$ = +11.3 (*c* 0.88, methanol)}.

*(3*R*,3a*S*,6*R*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indole-3,6-diyl Diacetate (**55**).* A magnetically stirred mixture of alcohol **53** (180 mg, 0.38 mmol) in THF (10 mL) was treated with acetic acid (33 mg, 0.57 mmol), triphenyl phosphine (150 mg, 0.57 mmol) and di-*tert*-butyl azodicarboxylate (130 mg, 0.57 mmol). The resulting solution was stirred at 22 °C for 1 h before being concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (1:3 v/v ethyl acetate/hexane eltuion) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (methanol/chloroform) of the resulting solid, diacetate **55** (190 mg, 97%) as a white, crystalline solid, m.p.= 160−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 6.50 (dd, *J* = 8.2 and 1.2 Hz, 1H), 6.32−6.28 (complex m, 2H), 6.00 (dd, *J* = 10.3 and 3.0 Hz, 1H), 5.90 (s, 2H), 5.72 (dt, *J* = 10.3 and 1.5 Hz, 1H), 5.40 (m, 1H), 5.26 (t, *J* = 5.0 Hz, 1H), 3.90 (m, 1H), 3.74 (m, 1H), 3.47 (m, 1H), 2.42 (s, 3H), 2.38 (cm, 1H), 2.25 (m, 1H), 2.09 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.0, 148.0, 146.7, 143.7, 134.0(3), 134.0(1), 129.8, 129.6, 129.1, 127.2, 119.6, 108.0, 106.9, 101.2, 75.3, 66.1, 62.9, 53.2, 51.4, 31.7, 21.5, 21.2, 20.9; IR (KBr): ν_{max} 2891, 1736, 1489, 1436, 1347, 1239, 1162, 1036 cm^{-1}; MS (EI, 70 eV): *m/z* 513 ($M^{+\bullet}$, 20%), 453 (27), 238 (80), 198 (100); HRMS $M^{+\bullet}$ Calcd for $C_{26}H_{27}NO_8S$: 513.1457, Found: 513.1453; $[\alpha]_D^{20}$ = +333.1 (*c* = 1.3, $CHCl_3$).

*(+)-Bulbispermine [(+)-**4**]. Step i:* A magnetically stirred mixture of diacetate **55** (190 mg, 0.37 mmol) in THF (5 mL) maintained at −100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[22] until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (1 mL of a saturated aqueous solution), $NaHCO_3$ (500 mg) and Na_2SO_4 (500 mg) were then added to the reaction mixture that was allowed to warm to 22 °C, stirred at this temperature for 12 h then filtered with the solids thus retained being rinsed with dichloromethane (3 × 20 mL). The

combined filtrates were concentrated under reduced pressure and the ensuing light-yellow oil was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform elution) to afford a light-yellow oil. *Step ii:* A magnetically stirred solution of the oil obtained from step i in 1,2-dichloroethane (5 mL) was treated with paraformaldehyde (64 mg) and trifluoroacetic acid (64 μL, 8.3 mmol) and the resulting solution heated at 60 °C for 18 h then cooled and concentrated under reduced pressure to give a light-yellow oil. *Step iii:* A solution of yellow oil obtained from step ii in methanol (5 mL) was treated with anhydrous potassium carbonate (150 mg, 1.1 mmol) and the ensuing mixture stirred at 22 °C for 1 h before being concentrated under reduced pressure. The light-yellow oil thus obtained was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform elution) to afford, after concentration of the appropriate fractions (R_f = 0.6) and recrystallization (methanol/chloroform) of the resulting solid, *(+)-bulbispermine [(+)-**4**]*[30] (48 mg, 45% over 3 steps) as a white, crystalline solid, m.p. = 130.5−132.5 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 6.84 (s, 1H), 6.50 (s, 1H), 6.22 (dd, *J* = 10.4 and 2.3 Hz, 1H), 6.02 (d, *J* = 10.3 Hz, 1H), 5.86 (s, 2H), 4.30 (m, 1H), 4.23 (d, *J* = 16.8 Hz, 1H), 3.93 (m, 1H), 3.69 (d, *J* = 16.8 Hz, 1H), 3.41 (m, 1H), 3.20 (m, 2H), 2.09 (m, 1H), 1.95 (m, 1H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, CD_3OD) δ 148.5, 148.0, 137.7, 137.5, 127.0, 125.1, 108.1, 104.5, 102.5, 81.3, 68.7, 67.8, 64.0, 61.8, 51.8, 34.7; IR (KBr): ν_{max} 3351, 2913, 1646, 1501, 1483, 1312, 1240, 1066, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 1%), 269 [$(M-H_2O)^{+\bullet}$, 100], 268 (48), 240 (45), 181 (56); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158. Found: 287.1161; $[\alpha]_D^{20}$ = +108.9 (*c* = 1.02, MeOH) {lit[23] $[\alpha]_D^{20}$ = +106.7 (*c* = 1.02, MeOH)}.

Total syntheses of (−)-11-hydroxyvattitine [(−)-3] and (−)-bulbispermine [(−)-4]

*(*R*)-*N*-(2-Bromocyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (**ent-46**).* *Step i:* A magnetically stirred solution of acetamide **41** (4.00 g, 14.7 mmol) and triethylbenzylammonium chloride (250 mg, 1.1 mmol) in dichloromethane (100 mL) was treated with KOH (80 mL of a 20% w/w aqueous solution) and the ensuing mixture stirred at 22 °C for 8 h. The separated aqueous layer was extracted with dichloromethane (1 × 50 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing yellow oil was immediately subjected to the next step ii. *Step ii:* A solution of the yellow oil obtained from step i in dichloromethane (30 mL) was treated with Et_3N (2.5 mL, 17.6 mmol), *p*-TsCl (3.40 g, 17.6 mmol) and DMAP (180 mg, 1.5 mmol). then stirred at 22 °C for 1 h before being treated with HCl (20 mL of a 2 M aqueous solution). The separated aqueous phase was extracted with dichloromethane (3 × 30 mL) and the

combined organic phases then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane) to afford, after concentration of the appropriate fractions (R_f = 0.6) and recrystallization (hexane/ethyl acetate) of the ensuing solid, sulfonamide ***ent*-46** (3.80 g, 78%) as white needles, m.p. 100−101°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.18 (t, *J* = 4.1 Hz, 1H), 4.86 (broad d, *J* = 7.1 Hz, 1H), 3.80 (m, 1H), 2.41 (s, 3H), 2.11−1.99 (complex m, 3H), 1.81 (m, 1H), 1.65−1.59 (complex m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 137.0, 135.2, 129.5, 127.5, 120.2, 55.1, 31.6, 27.4, 21.5, 16.5; IR (KBr): ν_{max} 3275, 2942, 2868, 1641, 1597, 1495, 1445, 1426, 1330, 1157, 1087, cm^{-1}; MS (ESI, +ve): *m/z* 354 and 352 [$(M+Na)^+$, both 100%], 332 and 330 [$(M+H)^+$, both 20]; HRMS $[M+Na]^+$ Calcd for $C_{13}H_{16}{}^{79}BrNO_2SNa$: 351.9983, Found: 351.9985; Calcd for $C_{13}H_{16}{}^{81}BrNO_2SNa$: 353.9962, Found: 353.9963; $[\alpha]_D^{20}$ = +30.0 (*c* = 1, $CHCl_3$).

*(*R*)-*N*-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (**ent-48**).* A magnetically stirred mixture of sulfonamide ***ent*-46** (3.8 g, 11.5 mmol) in benzene (100 mL) and Na_2CO_3 (30 mL of a 2 M aqueous solution) was treated with benzo[*d*][1,3]dioxol-5-yl-boronic acid (**47**) (2.80 g, 17.3 mmol and $Pd(Ph_3P)_4$ (660 mg, 0.58 mmol). The ensuing mixture was deoxygenated with nitrogen for 0.5 h then heated under reflux for 14 h before being cooled and poured into water (100 mL) then extracted with ethyl acetate (3 × 30 mL). The combined organic phases were washed with $NaHCO_3$ (1 × 50 mL of a saturated aqueous solution) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (hexane/ethyl acetate) of the resulting solid, compound ***ent*-48** (3.50 g, 82%) as a white, crystalline solid, m.p. = 163–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.49 (d, *J* = 8.0 Hz, 1H), 6.40 (dd, *J* = 8.0 and 1.8 Hz, 1H), 6.33 (d, *J* = 1.8 Hz, 1H), 5.94 (t, *J* = 4.6 Hz, 1H), 5.88 (m, 2H), 4.42 (broad d, *J* = 6.0 Hz, 1H), 4.08 (broad s, 1H), 2.42 (s, 3H), 2.20−2.07 (complex m, 3H), 1.69−1.62 (complex m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 146.7, 143.1, 137.0, 136.0, 133.7, 130.4, 129.3, 127.0, 119.8, 107.9, 106.6, 100.9, 49.7, 30.0, 25.5, 21.5, 16.5; IR (KBr): ν_{max} 3345, 2930, 1598, 1503, 1489, 1435, 1406, 1329, 1244, 1155, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 371 ($M^{+\bullet}$, 20%), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{20}H_{21}NO_4S$: 371.1191, Found: 371.1187; $[\alpha]_D^{20}$ = +137.5 (*c* = 1, $CHCl_3$).

*(*R*)-*N*-(2-(Benzo[*d*][1,3]dioxol-5-yl)cyclohex-2-en-1-yl)-*N*-(but-2-yn-1-yl)-4-methyl Benzene -sulfonamide (**ent-49**).* A magnetically stirred solution of sulfonamide ***ent*-48** (3.5 g, 9.4

mmol) in dry DMF (30 mL) was treated with NaH (560 mg, 14.1 mmol), the ensuing mixture was stirred at 0 °C for 0.5 h before treated with 1-bromo-2-butyne (1.20 mL, 14.1 mmol). The resulting solution was stirred at 22 °C for 1.5 h then poured into water (100 mL) (CAUTION POSSIBILITY OF HYDROGEN EVOLUTION) and extracted with ethyl acetate (3 × 40 mL). The combined organic phases were washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), compound ***ent*-49** (3.70 g, 93%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 6.73 (m, 2H), 6.64 (d, *J* = 8.5 Hz, 1H), 6.08 (m, 1H), 5.92 (s, 2H), 5.02 (m, 1H), 3.85 (dd, *J* = 18.3 and 2.3 Hz, 1H), 3.54 (dd, *J* = 18.3 and 2.3 Hz, 1H), 2.41 (s, 3H), 2.13 (m, 2H), 2.00 (m, 1H), 1.82−1.77 (complex m, 2H), 1.58 (t, *J* = 2.4 Hz, 3H), 1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 146.5, 142.8, 138.4, 136.8, 134.3, 132.7, 128.9, 127.8, 120.2, 107.8, 107.4, 100.8, 80.1, 75.3, 55.3, 33.8, 28.8, 25.5, 21.5, 20.2, 3.4; IR (KBr): ν_{max} 2918, 1598, 1504, 1489, 1436, 1334, 1244, 1155, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* 423 ($M^{+\bullet}$, 10%), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_4S$: 423.1504, Found: 423.1505; $[\alpha]_D^{20}$ = +37.2 (*c* = 1, $CHCl_3$).

*(3a*S*,7a*R*,Z)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-3-ethylidene-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indole (**ent**-50).* A magnetically stirred mixture of compound ***ent*-49** (2.5 g, 5.9 mmol) in benzene (50 mL) was treated with BBEDA (250 mg, 1.1 mmol) and $Pd(OAc)_2$ (250 mg, 1.1 mmol). The ensuing solution was deoxygenated with nitrogen for 0.33 h then heated under reflux for 13 h before being cooled then concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), diene ***ent*-50** (1.70 g, 68%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.50 (d, *J* = 8.1 Hz, 1H), 6.44 (dd, *J* = 8.1 and 1.4 Hz, 1H), 6.30 (broad s, 1H), 5.88 (m, 2H), 5.84 (m, 1H), 5.42 (broad d, *J* = 9.9 Hz, 1H), 5.17 (m, 1H), 4.20 (d, *J* = 14.4 Hz, 1H), 3.92 (d, *J* = 14.4 Hz, 1H), 3.72 (m, 1H), 2.40 (s, 3H), 2.27 (m, 1H), 2.11 (m, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.62 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 146.1, 143.1, 141.2, 138.5, 134.2, 130.4, 129.3, 127.2, 126.8, 121.2, 120.4, 108.3, 107.5, 100.9, 67.4, 55.3, 49.6, 25.8, 21.9, 21.4, 14.5; IR (KBr): ν_{max} 2918, 1598, 1503, 1484, 1433, 1342, 1240, 1160, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 423 ($M^{+\bullet}$, 70%), 268 (100), 200 (60); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_4S$: 423.1504, Found: 423.1503; $[\alpha]_D^{20}$ = −165.7 (*c* = 1, $CHCl_3$).

*(3aR,7aR)-3a-(Benzo[d][1,3]dioxol-5-yl)-1-tosyl-1,2,3a,6,7,7a-hexahydro-3H-indol-3-one (**ent-51**).* *Step i:* A magnetically stirred mixture of diene ***ent*-50** (1.60 g, 3.77 mmol) in acetonitrile/water (12.5 mL of a 4:1 v/v mixture) was treated with citric acid (2.10 g, 10.9 mmol), *N*-methylmorpholine-*N*-oxide (1.30 g, 11.1 mmol) then potassium osmate dihydrate (100 mg, 0.27 mmol). The resulting solution was stirred at 22 °C for 72 h before being diluted with ethyl acetate (40 mL) and HCl (30 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with ethyl acetate (2 × 30 mL) and the combined organic phases were washed with brine (1 × 40 mL) then dried (Na_2SO_4) before being filtered through a short plug of TLC-grade silica gel and the filtrate concentrated under reduced pressure. The ensuing brown oil was subjected to step i. *Step ii:* A solution of brown oil from step i in dichloromethane (20 mL) was treated with iodobenzene diacetate (2.50 g, 7.5 mmol) and the ensuing solution stirred at 22 °C for 2 h then concentrated under reduced pressure. The light-yellow oil so-obtained was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), ketone ***ent*-51** (600 mg, 39%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 6.63 (d, *J* = 8.1 Hz, 1H), 6.37 (dd, *J* = 8.1 and 1.7 Hz, 1H), 6.26 (d, *J* = 1.7 Hz, 1H), 6.22 (m, 1H), 5.91 (s, 2H), 5.43 (d, *J* = 9.9 Hz, 1H), 4.07 (d, *J* = 18.3 Hz, 1H), 3.82 (m, 1H), 3.65 (d, *J* = 18.3 Hz, 1H), 2.45 (m, 1H), 2.44 (s, 3H), 2.29 (m, 1H), 2.14 (m, 1H), 1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 147.9, 147.1, 144.3, 133.2, 133.1, 132.5, 129.9, 127.7, 123.4, 121.4, 108.2, 108.1, 101.2, 65.0, 60.5, 54.5, 22.9, 21.6, 20.6; IR (KBr): ν_{max} 2916, 1756, 1597, 1504, 1488, 1436, 1348, 1244, 1159, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 411 ($M^{+\bullet}$, 10%), 269 (50), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{22}H_{21}NO_5S$: 411.1140. Found: 411.1141; $[\alpha]_D^{20}$ = +5.1 (*c* = 1, $CHCl_3$).

*(3S,3aR,7aR)-3a-(Benzo[d][1,3]dioxol-5-yl)-1-tosyl-2,3,3a,6,7,7a-hexahydro-1H-indol-3-yl Acetate (**ent**-52).* *Step i:* A magnetically stirred solution of ketone ***ent*-51** (600 mg, 1.46 mmol) in THF/methanol (20 mL of a 1:1 v/v mixture) maintained at −78 °C was treated with $NaBH_4$ (170 mg, 4.38 mmol) then allowed to warm to 22 °C and maintained at this temperature 10 h before being concentrated under reduced pressure. The residue so-obtained was dissolved in ethyl acetate (40 mL) and the resulting solution washed with NH_4Cl (10 mL of a saturated aqueous solution) before being dried (Na_2SO_4) then filtered through a short plug of TLC-grade silica gel. The filtrate was concentrated under reduced pressure and the ensuing white foam subjected to step i. *Step ii:* A solution of the white foam from step i in pyridine (10 mL) was treated with Ac_2O (690 μL, 7.3 mmol) and DMAP (18 mg, 0.15 mmol) then stirred magnetically at 22 °C for 4 h before being concentrated under reduced pressure.

The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.2), acetate ***ent*-52** (550 mg, 82%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 6.61 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 8.2 and 1.5 Hz, 1H), 6.35 (d, *J* = 1.5 Hz, 1H), 6.16 (m, 1H), 5.91 (m, 2H), 5.65 (d, *J* = 10.4 Hz, 1H), 4.89 (t, *J* = 7.9 Hz, 1H), 3.95 (m, 1H), 3.62 (m, 1H), 3.24 (dd, *J* = 11.4 and 6.8 Hz, 1H), 2.48 (s, 3H), 2.34 (m, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.93 (s, 3H), 1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 147.9, 146.6, 144.0, 134.7, 134.1, 131.5, 129.9, 127.6, 125.1, 120.4, 107.9, 107.2, 101.1, 74.5, 64.5, 51.7, 50.5, 23.3, 21.6, 20.7, 20.5; IR (KBr): ν_{max} 3032, 2917, 1742, 1597, 1505, 1488, 1436, 1346, 1237, 1163, 1091, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 455 ($M^{+\bullet}$, 30%), 395 (23), 240 (70), 200 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_6S$: 455.1403, Found: 455.1403; $[\alpha]_D^{20} = -152.0$ (*c* = 1, $CHCl_3$).

*(3*S*,3a*R*,6*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-hydroxy-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**ent-53**).* A magnetically stirred solution of acetate ***ent*-52** (540 mg, 1.18 mmol) in dioxane (15 mL) was treated with SeO_2 (660 mg, 5.92 mmol). The ensuing mixture was heated under reflux for 20 h then cooled and concentrated under reduced pressure. The resulting yellow oil was subjected to flash chromatography (1:3 v/v ethyl acetate/toluene) to afford two fractions, A and B.

Concentration of fraction A (R_f = 0.4) gave, after recrystallization (methanol/chloroform) of the ensuing solid, alcohol ***ent*-53** (360 mg, 64%) as white, crystalline masses, m.p. = 178-181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 6.60 (d, *J* = 8.2 Hz, 1H), 6.45 (d, *J* = 8.2 Hz, 1H), 6.31 (m, 1H), 6.20 (d, *J* = 10.4 Hz, 1H), 5.91 (m, 2H), 5.72 (d, *J* = 10.4 Hz, 1H), 4.88 (t, *J* = 7.5 Hz, 1H), 4.61 (m, 1H), 3.96 (m, 1H), 3.70 (m, 1H), 3.20 (dd, *J* = 11.4 and 6.8 Hz, 1H), 2.51 (m, 1H), 2.48 (s, 3H), 1.94 (s, 3H), 1.62 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 148.0, 146.8, 144.2, 134.6, 133.6, 133.4, 129.9, 127.6, 126.7, 120.4, 108.0, 107.0, 101.2, 74.3, 63.9, 63.4, 51.9, 50.6, 33.0, 21.6, 20.7; IR (KBr): ν_{max} 3509, 2895, 1744, 1597, 1505, 1489, 1437, 1346, 1240, 1163, 1108, 1090, 1061 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 471 ($M^{+\bullet}$, 20%), 401 (30), 316 (90), 256 (100); HRMS $M^{+\bullet}$ Calcd for $C_{24}H_{25}NO_7S$: 471.1352, Found: 471.1356; $[\alpha]_D^{20} = -135.2$ (*c* = 1, $CHCl_3$).

Concentration of fraction B (R_f = 0.8) afforded the starting acetate ***ent*-52** (110 mg) that was identical, in all respects, with an authentic sample.

*(3*S*,3a*R*,6*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-hydroxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**ent-54**).* A magnetically stirred mixture of alcohol ***ent*-53** (180 mg, 0.38

mmol) in THF (5 mL) maintained at −100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[22] until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (1 mL of a saturated aqueous solution), $NaHCO_3$ (500 mg) and Na_2SO_4 (500 mg) were then added to the reaction mixture that was allowed to warm to 22 °C, stirred at this temperature for 12 h before being filtered and the solids thus retained rinsed with dichloromethane (3 × 20 mL). The combined filtrates were concentrated under reduced pressure and the resulting yellow oil was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.7), compound ***ent*-54** (85 mg, 71%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, *J* = 1.4 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.07 (dd, *J* = 10.4 and 1.4 Hz, 1H), 5.92 (s, 2H), 5.75 (d, *J* = 10.4 Hz, 1H), 5.54 (t, *J* = 6.1 Hz, 1H), 4.48 (m, 1H), 3.46 (m, 1H), 3.40 (m, 1H), 2.87 (dd, *J* = 11.7 and 6.7 Hz, 1H), 2.31 (broad s, 2H), 2.09 (m, 1H), 2.00 (s, 3H), 1.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 147.9, 146.3, 136.6, 132.7, 128.5, 120.0, 108.1, 107.4, 101.1, 80.1, 63.4, 62.5, 52.4, 50.6, 33.1, 21.0; IR (KBr): ν_{max} 3324, 3028, 2923, 2885, 1732, 1505, 1488, 1435, 1374, 1242, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 317 ($M^{+\bullet}$, 20%), 257 (30), 201 (40), 56 (100); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}NO_5$: 317.1263, Found: 317.1262; $[\alpha]_D^{20}$ = −67.9 (*c* = 1.0, $CHCl_3$).

*(−)-11-Hydroxyvattitine [(−)-**3**]*. *Step i:* A magnetically stirred solution of compound ***ent*-54** (85 mg, 0.27 mmol) in 1,2-dichloroethane (10 mL) was treated with paraformaldehyde (42 mg) and trifluoroacetic acid (420 μL, 5.49 mmol) then heated at 60 °C for 18 h before being cooled then concentrated under reduced pressure. The resulting yellow oil was subjected, directly, to step i. *Step ii:* A solution of yellow oil from step i in methanol (5 mL) was treated with potassium carbonate (71 mg, 0.54 mmol) and the mixture so-formed stirred at 22 °C for 1 h before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.6), target (−)-**3** (50 mg, 65%) as a white foam. ^{1}H NMR (400 MHz, CD_3OD) δ 6.94 (s, 1H), 6.56 (s, 1H), 6.43 (d, *J* = 10.1 Hz, 1H), 6.17 (dd, *J* = 10.1 and 5.1 Hz, 1H), 5.89 (s, 2H), 4.32 (d, *J* = 16.6 Hz, 1H), 4.29 (m, 1H), 3.96 (m, 1H), 3.77 (d, *J* = 16.6 Hz, 1H), 3.44-3.40 (complex m, 2H), 3.14 (dd, *J* = 13.9 and 3.3 Hz, 1H), 2.26 (m, 1H), 1.82 (m, 1H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, CD_3OD) δ 148.2, 147.7, 137.2, 132.9, 128.0, 127.0, 107.8, 104.3, 102.2, 81.0, 64.7, 63.8, 63.7, 61.8, 51.4, 33.1; IR (KBr): ν_{max} 3271, 2896, 1619, 1500, 1482, 1324, 1237, 1093, 1033 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 90%), 269 (55),

243 (85), 227 (100), 181 (67); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158, Found: 287.1155; $[\alpha]_D^{20} = -10.4$ (c = 0.88, MeOH).

*(3*S*,3a*R*,6*S*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indole-3,6-diyl Diacetate (**ent**-55).* A magnetically stirred solution of alcohol ***ent*-53** (270 mg, 0.57 mmol) in THF (15 mL) was treated with acetic acid (49 mg, 0.86 mmol), triphenyl phosphine (230 mg, 0.86 mmol) and di-*tert*-butyl azodicarboxylate (200 mg, 0.86 mmol). The resulting mixture was stirred at 22 °C for 1 h then concentrated under reduced pressure. The residue so-formed was subjected to flash chromatography (1:3 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4) and recrystallization (methanol/chloroform) of the ensuing solid, diacetate ***ent*-55** (240 mg, 83%) as a white solid, m.p. = 159−161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 6.50 (d, J = 8.1 Hz, 1H), 6.33 (m, 2H), 6.00 (dd, J = 10.3 and 3.0 Hz, 1H), 5.90 (s, 2H), 5.72 (dd, J = 10.3 and 1.7 Hz, 1H), 5.40 (m, 1H), 5.26 (t, J = 5.0 Hz, 1H), 3.90 (m, 1H), 3.74 (m, 1H), 3.47 (m, 1H), 2.42 (s, 3H), 2.38 (m, 1H), 2.25 (m, 1H), 2.09 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.0, 148.0, 146.7, 143.7, 134.0(4), 134.0(0), 129.9, 129.6, 129.1, 127.2, 119.6, 108.0, 106.9, 101.2, 75.3, 66.1, 62.9, 53.2, 51.4, 31.7, 21.5, 21.2, 20.9; IR (KBr): ν_{max} 2893, 1735, 1598, 1506, 1489, 1436, 1372, 1347, 1240, 1162, 1036 cm^{-1}; MS (EI, 70 eV): *m/z* 513 ($M^{+\bullet}$, 20%), 453 (27), 238 (70), 198 (100); HRMS $M^{+\bullet}$ Calcd for $C_{26}H_{27}NO_8S$: 513.1457, Found: 513.1457; $[\alpha]_D^{20} = -323.7$ (c = 0.82, $CHCl_3$).

*(−)-Bulbispermine [(−)-**4**].* *Step i:* A magnetically stirred solution of diacetate ***ent*-55** (240 mg, 0.47 mmol) in THF (10 mL) maintained at −100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[22] until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (1 mL of a saturated aqueous solution), $NaHCO_3$ (500 mg) and Na_2SO_4 (500 mg) were then added to the reaction mixture that was allowed to warm to 22 °C and stirred at this temperature for 12 h before being filtered. The solids thus retained were rinsed with dichloromethane (3 × 20 mL) and the combined filtrates concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions, a light-yellow oil that was used directly in step ii. *Step ii:* A magnetically stirred mixture of the crude product from step i in 1,2-dichloroethane (10 mL) was treated with paraformaldehyde (75 mg) and trifluoroacetic acid (750 μL, 9.8 mmol) and the resulting solution heated at 60 °C for 18 h then cooled before being concentrated under reduced pressure. The yellow oil thus obtained was subjected, directly, to step iii. *Step iii:* A solution of the yellow oil from step ii in methanol (5 mL) was treated with potassium carbonate (120 mg, 0.94 mmol) and the

mixture so-formed stirred at 22 °C for 1 h then concentrated under reduced pressure. The ensuing solid mass was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.6) and recrystallization (methanol/chloroform) of the ensuing solid, compound (−)-**4** (56 mg, 43% over 3 steps) as white, crystalline masses, m.p. = 131−133 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 6.86 (s, 1H), 6.53 (s, 1H), 6.22 (dd, *J* = 10.3 and 2.3 Hz, 1H), 6.03 (d, *J* = 10.3 Hz, 1H), 5.88 (s, 2H), 4.32 (m, 1H), 4.26 (d, *J* = 16.8 Hz, 1H), 3.96 (m, 1H), 3.72 (d, *J* = 16.8 Hz, 1H), 3.44 (m, 1H), 3.22 (m, 2H), 2.10 (m, 1H), 1.96 (m, 1H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, CD_3OD) δ 148.1, 147.7, 137.4, 137.1, 126.7, 124.8, 107.8, 104.2, 102.2, 81.0, 68.4, 67.5, 63.7, 61.5, 51.4, 34.4; IR (KBr): ν_{max} 3368, 2905, 1645, 1501, 1482, 1311, 1240, 1093, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 1%), 286 (4), 269 [$(M-H_2O)^{+\bullet}$, 100]; HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158, Found: 287.1160; $[\alpha]_D^{20}$ = −110.5 (*c* = 1.02, MeOH).

*(3*R*,3a*S*,6*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**56**).* A magnetically stirred solution of alcohol **53** (570 mg, 1.21 mmol) in dry THF (5 mL) was treated with iodomethane (6.00 mL, 96.3 mmol) and silver oxide (5.00 g, 21.6 mmol). The flask was wrapped in aluminium foil to exclude light and the reaction mixture stirred at 22 °C for 24 h then filtered through a pad of Celite™ and the filtrate concentrated under reduced pressure to give a light-yellow oil that was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.3) then gave ether **56** (330 mg, 56%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 2H), 6.56 (d, *J* = 8.2 Hz, 1H), 6.43 (dd, *J* = 8.2 and 2.6 Hz, 1H), 6.30 (d, *J* = 2.6 Hz, 1H), 6.20 (d, *J* = 10.4 Hz, 1H), 5.89 (s, 2H), 5.68 (d, *J* = 10.4 Hz, 1H), 4.94 (t, *J* = 7.0 Hz, 1H), 4.10 (broad s, 1H), 3.92 (m, 1H), 3.72 (m, 1H), 3.41 (s, 3H), 3.22 (m, 1H), 2.50 (m, 1H), 2.45 (s, 3H), 1.95 (s, 3H), 1.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 147.9, 146.7, 144.0, 133.5, 133.5, 132.0, 129.8, 127.5, 127.4, 120.3, 107.9, 107.0, 101.1, 74.2, 71.8, 63.7, 56.3, 52.2, 50.7, 29.4, 21.5, 20.6; IR (KBr): ν_{max} 2896, 1745, 1597, 1506, 1489, 1438, 1347, 1239, 1163, 1095, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 485 ($M^{+\bullet}$, 20%), 401 (40), 330 (100), 270 (63), 198 (47); HRMS $M^{+\bullet}$ Calcd for $C_{25}H_{27}NO_7S$: 485.1508, Found: 485.1512; $[\alpha]_D^{20}$ = +141.7 (*c* = 1.7, $CHCl_3$).

*(3R,3a*S*,6*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate*. A magnetically stirred solution of ether **56** (330 mg, 0.68 mmol) in THF (10 mL) maintained at −100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[22] until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (2 mL of a saturated

aqueous solution), $NaHCO_3$ (1.0 g) and Na_2SO_4 (1.0 g) were then added to the reaction mixture that was allowed to warm to 22 °C, stirred at this temperature for 12 h before being filtered and the solids thus retained rinsed with dichloromethane (3 × 30 mL). The combined filtrates were concentrated under reduced pressure and the resulting yellow oil subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.7), (3*R*,3a*S*,6*S*,7a*S*)-3a-(benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl acetate (190 mg, 86%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 1.8 Hz, 1H), 6.81 (dd, *J* = 8.2 and 1.8 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 6.11 (d, *J* = 10.4 Hz, 1H), 5.90 (s, 2H), 5.75 (d, *J* = 10.4 Hz, 1H), 5.55 (t, *J* = 6.1 Hz, 1H), 4.02 (m, 1H), 3.46 (broad s, 2H), 3.38 (s, 3H), 2.87 (m, 1H), 2.22 (broad s, 1H), 2.07 (m, 1H), 1.99 (s, 3H), 1.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.8, 146.2, 136.7, 130.0, 129.0, 119.9, 107.9, 107.4, 101.0, 79.9, 72.1, 62.4, 56.0, 52.6, 50.6, 29.4, 20.9; IR (KBr): ν_{max} 3351, 2929, 2821, 1735, 1505, 1488, 1436, 1374, 1244, 1096, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 30%), 271 (60), 233 (90), 56 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420, Found: 331.1418; $[\alpha]_D^{20}$ = +62.1 (*c* = 1.08, $CHCl_3$).

*(3*R*,3a*S*,6*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-formyl-6-methoxy-2,3,3a,6,7,7a-hexa-hydro-1*H*-indol-3-yl Acetate (**57**).* A magnetically stirred solution of (3*R*,3a*S*,6*S*,7a*S*)-3a-(benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl acetate (190 mg, 0.57 mmol) in ethyl formate (5.0 mL) was heated under reflux for 6 h before being cooled then concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (ethyl acetate elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), formamide **57** (140 mg, 68%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of rotamers) 8.29 (s, 0.55H), 8.23 (s, 0.45H), 6.88 (dd, *J* = 4.8 and 1.7 Hz, 1H), 6.80 (m, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.19 (m, 1H), 5.94 (s, 2H), 5.86 (d, *J* = 10.4 Hz, 1H), 5.66 (t, *J* = 6.2 Hz, 0.6H), 5.49 (t, *J* = 6.2 Hz, 0.4H), 4.23 (m, 1H), 4.09-4.02 (m, 1H), 3.84 (m, 1H), 3.39 (s, 1.7H), 3.37 (s, 1.3H), 3.28 (m, 1H), 2.71 (m, 0.45H), 2.26 (m, 0.55H), 2.01 (s, 3H), 1.95 (m, 0.55H), 1.66 (m, 0.45H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of rotamers) 170.2, 169.9, 161.6, 160.6, 148.2, 148.1, 147.0, 146.9, 133.8, 133.5, 132.3, 129.5, 129.2, 127.7, 120.2, 120.0, 108.3, 108.2, 107.4, 107.3, 101.3, 101.2, 74.9, 74.8, 71.5, 71.0, 59.5, 59.3, 56.4, 56.3, 52.7, 51.5, 48.5, 47.3, 30.8, 26.1, 20.9, 20.7; IR (KBr): ν_{max} 2890, 1743, 1671, 1505, 1489, 1437, 1380, 1240, 1084, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 359 ($M^{+\bullet}$, 50%), 275 (40), 230 (60), 198 (100); HRMS $M^{+\bullet}$ Calcd for $C_{19}H_{21}NO_6$: 359.1369, Found: 359.1367; $[\alpha]_D^{20}$ = +92.7 (*c* = 1, $CHCl_3$).

*(−)-Haemanthidine [(−)-**5**]*. *Step i*: A magnetically stirred mixture of formamide **57** (140 mg, 0.39 mmol) in phosphorus oxychloride (3.0 mL) was heated at 90 °C for 4 h before being cooled then concentrated under reduced pressure. The residue thus obtained was subjected, directly, to step ii. *Step ii*: The residue from step i was dissolved in THF/water (6 mL of a 1:1 v/v mixture) and the resulting solution stirred magnetically at 22 °C for 12 h then concentrated under reduced pressure. The residue so-formed was dissolved in dichloromethane (40 mL) and the solution so-obtained was washed with NaOH (20 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phases then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing residue pale-yellow oil was immediately subjected to step iii. *Step iii*: A solution of yellow oil from step ii was dissolved in methanol (5 mL) and the resulting solution treated with potassium carbonate (150 mg, 1.1 mmol) then stirred at 22 °C for 1 h before being concentrated under reduced pressure. The while residue so obtained was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.7), compound (−)-**5** (58 mg, 47% over 3 steps) as an opaque film. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of epimers) 6.96 (s, 0.45H), 6.81 (s, 0.55H), 6.78 (s, 0.55H), 6.75 (s, 0.45H), 6.36 (m, 2H), 5.90 (m, 2H), 5.63 (s, 0.45H), 5.01 (s, 0.55H), 4.18 (m, 0.55H), 3.89 (m, 2.45H), 3.56 (m, 0.45H), 3.36 (s, 1.3H), 3.33 (s, 1.7H), 3.30 (m, 0.55H), 3.20 (m, 0.55H), 2.88 (m, 0.45H), 2.30 (m, 0.45H), 2.17 (m, 0.55H), 2.03 (m, 1H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of epimers) 147.7, 147.4, 146.5, 146.3, 135.7, 134.6, 132.6, 132.1, 129.1, 127.7, 126.7, 126.4, 109.5, 108.2, 102.8, 102.7, 101.0, 88.3, 85.7, 79.1, 78.2, 72.4, 72.1, 61.6, 57.8, 56.8, 56.4, 56.2, 52.0, 50.6, 50.2, 27.8, 27.6; IR (KBr): ν_{max} 3401, 2889, 1503, 1482, 1298, 1246, 1108, 1059, 1036 cm^{-1}; MS (EI, 70 eV): *m/z* 317.1 ($M^{+\bullet}$, 40%), 284 (70), 227 (100); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}NO_5$: 317.1263. Found: 317.1270; $[\alpha]_D^{20}$ = −21.9 (*c* = 0.45, $CHCl_3$) {lit[31] $[\alpha]_D^{25}$ = −24.4 (*c* = 0.41, $CHCl_3$)}.

*(+)-Pretazettine [(+)-**6**]*. A magnetically stirred mixture of compound (−)-**5** (40 mg, 0.13 mmol) in methanol (10 mL) was treated with iodomethane (2.0 mL, 32 mmol) and the ensuing stirred at 22 °C for 14 h then concentrated under reduced pressure. The residue so-obtained was treated with HCl (10 mL of a 0.01 M aqueous solution) for 3 min and the pH of the mixture then adjusted to 8 with $NaHCO_3$ (saturated aqueous solution) then extracted with dichloromethane (3 × 40 mL). The combined organic phases were dried (Na_2SO_4), filtered then concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after

concentration of the appropriate fractions (R_f = 0.6), compound (+)-**6** (35 mg, 84% over 2 steps) as white film. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.76 (s, 1H), 6.10 (s, 1H), 5.92 (s, 2H), 5.86 (d, *J* = 10.4 Hz, 1H), 5.51 (d, *J* = 10.4 Hz, 1H), 4.33 (m, 1H), 4.16 (m, 1H), 3.43 (s, 3H), 3.00−2.95 (complex m, 2H), 2.65 (m, 1H), 2.52 (m, 1H), 2.49 (s, 3H), 1.76 (broad t, *J* = 11.0 Hz, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.4, 135.3, 129.1, 128.8, 127.5, 108.1, 104.8, 101.2, 93.8, 73.8, 73.1, 64.1, 56.0, 54.0, 46.1, 43.3, 30.1; IR (KBr): ν_{max} 3368, 2924, 1504, 1483, 1255, 1090, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 30%), 316 (31), 257 (45), 247 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420. Found: 331.1429; $[\alpha]_D^{20}$ = +182.1 (*c* = 0.9, $CHCl_3$) {lit[32] $[\alpha]_D^{24}$ = +180 (*c* = 0.2, $CHCl_3$)}.

*(+)-Tazettine [(+)-**7**]*. A magnetically stirred mixture of compound (+)-**6** (35 mg, 0.11 mmol) in methanol (3 mL) was treated with NaOH (2 mL 0.1 M aqueous solution) then stirred at 22 °C for 0.5 h before being concentrated under reduced pressure. The residue thus formed was extracted with dichloromethane (3 × 40 mL) and the combined organic phases dried (Na_2SO_4), filtered then concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.6), compound (+)-**7** (32 mg, 91%) as white film. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 1H), 6.48 (s, 1H), 6.12 (d, *J* = 10.4 Hz, 1H), 5.88 (s, 2H), 5.61 (d, *J* = 10.4 Hz, 1H), 4.93 (d, *J* = 14.7 Hz, 1H), 4.61 (d, *J* = 14.7 Hz, 1H), 4.13 (m, 1H), 3.45 (s, 3H), 3.29 (d, *J* = 10.6 Hz, 1H), 2.86 (broad s, 1H), 2.66 (d, *J* = 10.6 Hz, 1H), 2.39 (s, 3H), 2.21 (m, 1H), 11.61 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 146.5, 130.7, 128.4, 127.4, 125.5, 109.3, 104.0, 101.7, 100.9, 72.5, 70.4, 65.0, 62.0, 56.1, 49.8, 42.3, 26.3; IR (KBr): ν_{max} 3306, 2938, 2863, 1502, 1484, 1246, 1182, 1084, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 40%), 247 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420, Found: 331.1420; $[\alpha]_D^{20}$ = +141.0 (*c* = 0.75, $CHCl_3$) {lit[33] $[\alpha]_D^{16}$ = +150 ($CHCl_3$)}.

Total syntheses of (+)-haemanthidine [(+)-5], (–)-pretazettine [(–)-6] and (–)-tazettine [(–)-7]

*(3*S*,3a*R*,6*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-1-tosyl-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate (**ent**-56).* A magnetically stirred mixture of alcohol *ent*-53 (670 mg, 1.42 mmol) in dry THF (5 mL) was treated with iodomethane (6.0 mL, 96.3 mmol) and silver oxide (5.0 g, 21.6 mmol). The flask was wrapped in aluminium foil to exclude light and the reaction mixture stirred at 22 °C for 24 h then filtered through a pad of Celite™ (to remove

the silver salts) and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.3), ether ***ent*-56** (390 mg, 56%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.7 Hz, 2H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 6.32 (s, 1H), 6.20 (d, *J* = 10.4 Hz, 1H), 5.90 (s, 2H), 5.69 (d, *J* = 10.4 Hz, 1H), 4.95 (t, *J* = 7.0 Hz, 1H), 4.10 (m, 1H), 3.92 (m, 1H), 3.71 (m, 1H), 3.43 (s, 3H), 3.23 (dd, *J* = 11.4 and 6.8 Hz, 1H), 2.51 (m, 1H), 2.45 (s, 3H), 1.93 (s, 3H), 1.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 148.0, 146.8, 144.1, 133.6, 133.5, 132.0, 129.9, 127.4(2), 127.3(7), 120.3, 107.9, 107.1, 101.2, 74.2, 71.9, 63.8, 56.4, 52.2, 50.7, 29.5, 21.5, 20.7; IR (KBr): ν_{max} 2896, 1745, 1597, 1505, 1489, 1438, 1347, 1228, 1163, 1063, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 485 ($M^{+\bullet}$, 20%), 401 (38), 330 (90), 270 (57), 238 (80), 198 (100), 91 (51); HRMS $M^{+\bullet}$ Calcd for $C_{25}H_{27}NO_7S$: 485.1508, Found: 485.1512; $[\alpha]_D^{20} = -136.2$ (*c* = 1.1, $CHCl_3$).

*(3*S*,3a*R*,6*R*,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-2,3,3a,6,7,7a-hexahydro-1*H*-indol-3-yl Acetate*. A magnetically stirred mixture of ether ***ent*-56** (360 mg, 0.74 mmol) in THF (10 mL) maintained at –100 °C (diethyl ether/dry ice bath) was treated with sodium naphthalenide[6] until a dark-green colour persisted (*ca*. 5 min). NH_4Cl (2 mL of a saturated aqueous solution), $NaHCO_3$ (1.0 g) and Na_2SO_4 (1.0 g) were then added to the reaction mixture that was allowed to warm to 22 °C, stirred at this temperature for 12 h before being filtered and the solids thus retained rinsed with dichloromethane (3 × 30 mL). The combined filtrates were concentrated under reduced pressure and the resulting yellow oil subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.7), (3*S*,3a*R*,6*R*,7a*R*)-3a-(benzo[*d*][1,3]dioxol-5-yl)-6-methoxy-2,3,3a,6,7,7a-hexahydro-1H-indol-3-yl acetate (200 mg, 82%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 1.8 Hz, 1H), 6.81 (dd, *J* = 8.2 and 1.8 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.12 (dd, *J* = 10.4 and 1.6 Hz, 1H), 5.91 (s, 2H), 5.77 (d, *J* = 10.4 Hz, 1H), 5.56 (t, *J* = 6.1 Hz, 1H), 4.03 (m, 1H), 3.48 (broad s, 2H), 3.39 (s, 3H), 2.87 (m, 1H), 2.17 (broad s, 1H), 2.06 (m, 1H), 2.00 (s, 3H), 1.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.9, 146.3, 136.7, 130.0, 129.0, 119.9(8), 108.0, 107.4, 101.0, 79.9, 72.1, 62.5, 56.0, 52.6, 50.7, 29.5, 21.0; IR (KBr): ν_{max} 3350, 2926, 1733, 1505, 1488, 1435, 1374, 1240, 1095, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 30%), 271 (60), 247 (50), 233 (90), 56 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420, Found: 331.1419; $[\alpha]_D^{20} = -59.3$ (*c* = 1.2, $CHCl_3$).

*(3*S*,3a*R*,6R,7a*R*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-1-formyl-6-methoxy-2,3,3a,6,7,7a-hexa-hydro-1*H*-indol-3-yl Acetate (**ent**-57).* A magnetically stirred mixture of hydroindole ***ent*-58** (80 mg, 0.24 mmol) in ethyl formate (5 mL) was heated under reflux for 6 h before being cooled then concentrated under reduced pressure. The ensuing residue was subjected to flash chromatography (ethyl acetate elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), formamide ***ent*-57** (60 mg, 69%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (mixture of rotamers) 8.28 (s, 0.55H), 8.22 (s, 0.45H), 6.88 (m, 1H), 6.83 (m, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.19 (m, 1H), 5.92 (s, 2H), 5.86 (d, *J* = 10.4 Hz, 1H), 5.65 (t, *J* = 6.2 Hz, 0.55H), 5.49 (t, *J* = 6.2 Hz, 0.45H), 4.23 (m, 1H), 4.08 (dd, *J* = 10.4 and 6.4 Hz, 0.65H), 4.03 (dd, *J* = 10.4 and 6.4 Hz, 0.35H), 3.84 (m, 1H), 3.38 (s, 1.7H), 3.37 (s, 1.3H), 3.28 (m, 1H), 2.71 (m, 0.45H), 2.26 (m, 0.55H), 2.01 (s, 3H), 1.95 (m, 0.55H), 1.66 (m, 0.45H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (mixture of rotamers) 170.2, 169.9, 161.6, 160.6, 148.2, 148.1, 146.9(2), 146.8(9), 133.8, 133.5, 132.2, 129.5, 129.2, 127.7, 120.2, 120.0, 108.3, 108.2, 107.4, 107.3, 101.2(4), 101.2(1), 74.9, 74.8, 71.5, 71.0, 59.5, 59.3, 56.4, 56.3, 52.7, 51.4, 48.4, 47.2, 30.8, 26.1, 20.8, 20.7; IR (KBr): ν_{max} 2890, 1742, 1671, 1505, 1489, 1436, 1378, 1239, 1084, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 359 ($M^{+\bullet}$, 80%), 275 (56), 230 (90), 198 (100); HRMS $M^{+\bullet}$ Calcd for $C_{19}H_{21}NO_6$: 359.1369, Found: 359.1369; $[\alpha]_D^{20}$ = −92.3 (*c* = 0.8, $CHCl_3$).

*(+)-Haemanthidine [(+)-**5**]*. *Step i*: A magnetically stirred mixture of formamide ***ent*-57** (150 mg, 0.42 mmol) in phosphorus oxychloride (3 mL) was heated at 90 °C for 4 h before being cooled then concentrated under reduced pressure. The yellow oil so-formed was subjected to step ii. *Step ii*: The residue from step i was dissolved in THF/H_2O (6 mL of a 1:1 v/v mixture) and the resulting solution allowed to stir at 22 °C for 12 h then concentrated under reduced pressure. The residue thus obtained was dissolved in dichloromethane (40 mL) and the resulting solution washed with NaOH (20 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with dichloromethane (3 × 10 mL) and the combined organic phases dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue do formed was subjected to step iii. *Step iii*: A solution of the residue obtained from step ii was dissolved in methanol (5 mL), the resulting solution treated with potassium carbonate (150 mg, 1.1 mmol) and the ensuing mixture stirred at 22 °C for 1 h before being concentrated under reduced pressure. The white solid thus obtained was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.7), compound (+)-**5** (65 mg, 49% over 3 steps) as an opaque film. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 0.45H), 6.81 (s, 0.55H), 6.78 (s, 0.55H), 6.75 (s,

0.45H), 6.37−6.34 (complex m, 2H), 5.90 (m, 2H), 5.64 (s, 0.45H), 5.02 (s, 0.55H), 4.18 (m, 0.55H), 3.91−3.87 (complex m, 2.45H), 3.56 (m, 0.45H), 3.36 (s, 1.3H), 3.33 (s, 1.7H), 3.30 (m, 0.55H), 3.21 (m, 0.55H), 2.91 (dd, J = 14.2 and 2.1 Hz, 0.45H), 2.30 (m, 0.45H), 2.17 (m, 0.55H), 2.07 (m, 0.45H), 2.06 (m, 0.55H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 147.4, 146.5, 146.4, 135.8, 134.6, 132.7, 132.2, 129.1, 127.7, 126.7, 126.3, 109.5, 108.2, 102.9, 102.7, 101.0, 88.3, 85.8, 79.1, 78.2, 72.4, 72.0, 61.6, 57.8, 56.8, 56.4, 56.2, 52.0, 50.6, 50.2, 27.8, 27.6; IR (KBr): ν_{max} 3401, 2891, 1502, 1483, 1299, 1246, 1109, 1060, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* 317 ($M^{+\bullet}$, 40%), 284 (70), 227 (100); HRMS $M^{+\bullet}$ Calcd for $C_{17}H_{19}NO_5$: 317.1263, Found: 317.1270; $[\alpha]_D^{20}$ = +23.2 (c = 0.62, $CHCl_3$).

*(−)-Pretazettine [(−)-**6**]*. A magnetically stirred solution of compound (+)-**5** (65 mg, 0.21 mmol) in methanol (10 mL) was treated with iodomethane (2.0 mL, 32 mmol) then stirred at 22 °C for 14 h before being concentrated under reduced pressure. The residue so-formed was treated with HCl (10 mL of a 0.01 M aqueous solution) for 3 min then the pH of the reaction mixture was adjusted to pH 8 with using $NaHCO_3$ (saturated aqueous solution) before being extracted with dichloromethane (3 × 40 mL). The combined organic phases were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The light-yellow oil so produced was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.6), compound (−)-**6** (59 mg, 87% over 2 steps) as white film. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.76 (s, 1H), 6.10 (s, 1H), 5.92 (s, 2H), 5.86 (d, J = 10.4 Hz, 1H), 5.51 (d, J = 10.4 Hz, 1H), 4.33 (m, 1H), 4.16 (m, 1H), 3.43 (s, 3H), 3.00−2.95 (complex m, 2H), 2.65 (dd, J = 10.0 and 7.8 Hz, 1H), 2.52 (m, 1H), 2.49 (s, 3H), 1.76 (broad t, J = 11.0 Hz, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.4, 135.3, 129.1, 128.8, 127.5, 108.1, 104.8, 101.2, 93.8, 73.8, 73.1, 64.1, 56.0, 54.0, 46.2, 43.3, 30.1; IR (KBr): ν_{max} 3306, 2934, 1503, 1484, 1254, 1089, 1038 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 30%), 247 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420, Found: 331.1414; $[\alpha]_D^{20}$ = −177.1 (c = 1.4, $CHCl_3$).

*(−)-Tazettine [(−)-**7**]*. A magnetically stirred solution of compound (−)-**6** (30 mg, 0.09 mmol) in methanol (3 mL) was treated with NaOH (2 mL of a 0.1 M aqueous solution) then stirred at 22 °C for 0.5 h before being concentrated under reduced pressure. The residue was extracted with dichloromethane (3 × 40 mL) and the combined organic phases dried (Na_2SO_4), filtered then concentrated under reduced pressure. The yellow oil thus obtained was subjected to flash chromatography (1:9 v/v ammonia-saturated methanol/chloroform) and so affording,

after concentration of the appropriate fractions (R_f = 0.6), compound (−)-**7** (27 mg, 90%) as white film. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 1H), 6.48 (s, 1H), 6.12 (d, *J* = 10.4 Hz, 1H), 5.88 (s, 2H), 5.61 (d, *J* = 10.4 Hz, 1H), 4.93 (d, *J* = 14.7 Hz, 1H), 4.61 (d, *J* = 14.7 Hz, 1H), 4.13 (m, 1H), 3.45 (s, 3H), 3.29 (d, *J* = 10.6 Hz, 1H), 2.86 (broad s, 1H), 2.66 (d, *J* = 10.6 Hz, 1H), 2.39 (s, 3H), 2.20 (m, 1H), 1.61 (m, 1H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 146.3, 130.5, 128.7, 128.0, 125.5, 109.3, 103.9, 102.0, 100.9, 72.9, 70.0, 65.5, 62.0, 56.0, 49.9, 42.0, 26.6; IR (KBr): ν_{max} 3338, 2938, 2861, 1502, 1484, 1246, 1189, 1083, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 331 ($M^{+\bullet}$, 40%), 247 (100); HRMS $M^{+\bullet}$ Calcd for $C_{18}H_{21}NO_5$: 331.1420, Found: 331.1419; $[\alpha]_D^{20}$ = −147.5 (*c* = 0.94, $CHCl_3$).

Total syntheses of (±)-hamayne [(±)-8], (±)-apohaemanthamine [(±)-9] and (±)-11-hydroxyvattitine [(±)-3]

*Electrocyclic ring-opening of cyclopropane (**42**) in the presence of amine **28**.* A magnetically stirred mixture of cyclopropane **42** (10.00 g, 26.7 mmol) and (*S*)-(−)-4-methoxy-*α*-methylbenzylamine (**28**) (8.10 g, 53.4 mmol) was heated at 120 °C under an atmosphere of nitrogen for 1 h. The cooled reaction mixture was diluted with ethyl acetate (100 mL) and the resulting mixture treated with NH_4Cl (100 mL of a saturated aqueous solution). The separated aqueous phase was extracted with ethyl acetate (2 × 50 mL) and the combined organic phases were washed with brine (1 × 200 mL) before being dried (Na_2SO_4), filtered then concentrated under reduced pressure. The residue so obtained was subjected to flash chromatography (1:20 v/v ethyl acetate/hexane) to afford, after concentration of the appropriate fractions (R_f = 0.6), a mixture of the four expected diastereoisomers (8.90 g, 75%) as a yellow oil. The two *trans* diastereoisomers **58** and **59** were the major products and the corresponding *cis* forms, **60** and **61**, tentatively identified as the the minor ones. The spectroscopic data for compounds **58** and **59** are reported above (page S48) but, because of the small amounts of material formed, analogous data could not be acquired on compounds **60** and **61**. This product mixture was subjected directly to the next step of the reaction sequence as detailed below.

N-*(2-Bromo-5-((*tert-*butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-2,2,2-trifluoro*-N-*((*S*)-1-(4-methoxyphenyl)ethyl)acetamide.* A magnetically stirred mixture of the ring-opening products **58**−**61** (8.90 g, 20.2 mmol) in dry pyridine (40 mL) was treated with trifluoroacetic anhydride (5.60 mL, 40.4 mmol) and the resulting mixture stirred at 22 °C for 1 h then quenched with HCl (20 mL of a 10% w/v aqueous solution) before being diluted with ethyl acetate (50 mL). The separated aqueous layer was extracted with ethyl acetate (3 × 20 mL) and the combined organic phases washed with brine (1 × 40 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue so obtained was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), *N*-(2-bromo-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-2,2,2-trifluoro-*N*-((*S*)-1-(4-methoxyphenyl)ethy-l)acetamide (9.70 g, 90%) as a yellow oil and a mixture of diastereoisomers. This material were subjected directly to the next step of the reaction sequence.

Small amounts of pure forms of each of the two major diastereoisomers could be obtained by collecting early or late fractions, as appropriate, during the course of the flash chromatographic purification process. This allowed for the acquisition of the following data on each of these pure diastereoisomers.

More mobile diastereoisomer (R_f = 0.7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.88 (m, 1H), 5.35 (m, 1H), 4.32 (m, 1H), 4.26 (m, 1H), 3.80 (s, 3H), 2.61 (t, *J* = 12.0 Hz, 1H), 2.35 (ddd, *J* = 17.9, 6.5 and 2.9 Hz, 1H), 2.00−1.92 (complex m, 2H), 1.63 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 155.3 (q, *J* = 35 Hz), 130.5, 128.2, 127.1, 120.3, 116.5 (q, *J* = 287 Hz), 113.5, 65.6, 55.8, 55.2(3), 55.2(1), 35.7, 35.4, 25.8, 19.1, 18.0, −4.8(2), −4.8(3); IR (KBr): ν_{max} 2953, 2931, 1692, 1612, 1515, 1462, 1287, 1254, 1204, 1141 cm^{-1}; MS (EI, 70 eV): *m/z* 537 and 535 ($M^{+\bullet}$, 30 and 28%), 456 (100); HRMS $M^{+\bullet}$ Calcd for $C_{23}H_{33}{}^{79}Br^{19}F_3NO_3Si$: 535.1365, Found: 535.1364; Calcd for $C_{23}H_{33}{}^{81}Br^{19}F_3NO_3Si$: 537.1345, Found: 537.1328; $[\alpha]_D^{25}$ = +30.0 (*c* = 1, $CHCl_3$).

Less mobile diastereoisomer (R_f = 0.65): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.24 (m, 1H), 5.45 (m, 1H), 4.22 (m, 1H), 4.07 (m, 1H), 3.99 (s, 3H), 2.46 (m, 1H), 2.26 (m, 1H), 2.10 (m, 1H), 2.02 (m, 1H), 1.96 (d, *J* = 7.0 Hz, 3H), 0.98 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 155.3 (q, *J* = 35 Hz), 129.6, 129.2, 128.7, 120.3, 116.5 (q, *J* = 287 Hz), 114.5, 65.2, 55.2, 54.8, 54.0, 35.7, 33.9, 25.8, 18.0, 17.4, −5.0, −5.3; IR (KBr): ν_{max} 2953, 2930, 1691, 1612, 1514, 1461, 1255, 1214, 1200, 1140, 1001, 836, 777 cm^{-1}; MS (EI, 70 eV): *m/z* 537 and 535 ($M^{+\bullet}$, 100 and 98%); HRMS $M^{+\bullet}$ $C_{23}H_{33}{}^{79}Br^{19}F_3NO_3Si$: 535.1365, Found: 535.1365; Calcd for $C_{23}H_{33}{}^{81}Br^{19}F_3NO_3Si$: 537.1345, Found: 537.1344; $[\alpha]_D^{25}$ = +54.0 (*c* = 1, $CHCl_3$).

4-Bromo-5-(2,2,2-trifluoroacetamido)cyclohex-3-en-1-yl 2,2,2-Trifluoroacetate. A magnetically stirred mixture of N-(2-bromo-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-2,2,2-trifluoro-N-((S)-1-(4-methoxyphenyl)ethyl)acetamide (9.70 g, 18.1 mmol) in dry dichloromethane (50 mL) was treated with anisole (3.9 mL, 36.2 mmol), trifluoroacetic acid (2.8 mL, 36.2 mmol) and trifluoromethanesulfonic acid (3.2 mL, 36.2 mmol). The ensuing solution, which developed a dark-red coloration within few minutes, was stirred at 22 °C for 2 h then quenched with $NaHCO_3$ (50 mL of a saturated aqueous solution). The separated aqueous layer was extracted with dichloromethane (3 × 30 mL) and the combined organic layers washed with brine (1 × 50 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:10 v/v ethyl acetate/hexane) to afford, after concentration of the appropriate fractions (R_f = 0.4), 4-bromo-5-(2,2,2-trifluoroacetamido)cyclohex-3-en-1-yl 2,2,2-trifluoroacetate (4.60 g, 67%) as a pale-yellow oil and a ca. 1:6 mixture of *cis*- and *trans*-diastereoisomers. ^1H NMR (400 MHz, $CDCl_3$) δ (major diastereoisomer) 6.55 (broad d, *J* = 7.2 Hz, 1H), 6.26 (t, *J* = 3.8 Hz, 1H), 5.30 (m, 1H), 4.85 (m, 1H), 2.67 (m, 1H), 2.43−2.32 (complex m, 2H), 2.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diastereoisomer) 130.2, 119.2, 70.2, 50.4, 33.8, 32.0 (four signals obscured or overlapping); ^{19}F NMR (376 MHz, $CDCl_3$) δ (major diastereoisomer) −75.0, −75.8; IR (KBr): ν_{max} 3297, 3090, 2936, 1785, 1707, 1551, 1357, 1218, 1159 cm^{-1}; MS (EI, 70 eV): *m/z* 385 and 383 ($M^{+\bullet}$, both 30%), 381 (50), 379 (100), 377 (65); HRMS $[M-H\bullet]^+$ Calcd for $C_{10}H_7{}^{79}BrF_6NO_3$: 381.9513, Found: 381.9521; Calcd for $C_{10}H_7{}^{81}BrF_6NO_3$: 383.9493, Found: 383.9492.

N-*(2-Bromo-5-((*tert-*butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide.*

Step i: A magnetically stirred solution of 4-bromo-5-(2,2,2-trifluoroacetamido)cyclohex-3-en-1-yl 2,2,2-trifluoroacetate (4.60 g, 12.0 mmol) and triethylbenzylammonium chloride (273 mg, 1.2 mmol) in dichloromethane (50 mL) was treated with KOH (50 mL of a 20% w/w aqueous solution). The ensuing mixture was stirred at 22 °C for 14 h then the separated aqueous layer extracted with dichloromethane (50 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing yellow oil was subjected directly to step ii. *Step ii*: A magnetically stirred solution of the yellow oil from step i in dichloromethane (30 mL) was treated with triethylamine (1.70 mL, 12.0 mmol), 2-nitrobenzenesulfonyl chloride (2.66 g, 12.0 mmol) and DMAP (150 mg, 1.2 mmol). The ensuing solution was stirred at 22 °C for 2 h before being concentrated under reduced pressure. The ensuing brown foam was subjected to step iii. *Step iii*: A solution of the brown foam from step ii in DMF (10 mL) was treated with imidazole (1.60 g, 24.0 mmol) and TBS-Cl (2.70 g, 18.0 mmol). The resulting solution was stirred at 22 °C for 6 h before being poured into water (30 mL) and extracted with ethyl acetate (3 × 40 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), *N*-(2-bromo-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide (3.50 g, 60%) as a pale-yellow oil and a ca. 1:6 mixture of *cis*- and *trans*-diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major diastereoisomer) 8.14 (m, 1H), 7.89 (m, 1H), 7.74 (m, 2H), 6.06 (m, 1H), 5.66 (m, 1H), 4.17 (m, 1H), 4.03 (m, 1H), 2.36 (m, 1H), 2.11 (m, 1H), 1.97 (m, 2H), 0.85 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diastereoisomer) 147.6, 134.0, 133.6, 132.9(4), 132.8(9), 130.7, 125.5, 118.8, 62.8, 57.1, 41.0, 36.9, 25.7, 17.9, −4.9 (one signal obscured or overlapping); IR (KBr): ν_{max} 3350, 3097, 2953, 2928, 2894, 2856, 1541, 1412, 1359, 1257, 1172, 1109 cm^{-1}; MS (ESI, +ve): *m/z* 493 and 491 [(M+H)$^{+}$, both 100%]; HRMS [M+Na]$^{+}$ Calcd for $C_{18}H_{27}{}^{79}BrN_2O_5SSiNa$: 513.0491, Found: 513.0487; Calcd for $C_{18}H_{27}{}^{81}BrN_2O_5SSiNa$: 515.0471, Found: 515.0479.

N-*(2-(Benzo[*d*][1,3]dioxol-5-yl)-5-((*tert-*butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide.* A magnetically stirred solution of *N*-(2-bromo-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide (3.50 g, 7.1 mmol), benzo[*d*][1,3]dioxol-5-yl-boronic acid (**47**) (1.77 g, 10.7 mmol), $PdCl_2dppf\bullet CH_2Cl_2$ (420 mg, 0.5 mmol) and triethylamine (5.0 mL) in THF/water (30 mL of a 9:1 v/v mixture) was purged with nitrogen for 0.25 h then heated under reflux for 2 h before being cooled, poured into water (50 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (1 × 30 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.35), *N*-(2-(benzo[*d*][1,3]dioxol-5-yl)-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide as a yellow foam and a ca. 6:1 a mixture of diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major diastereoisomer) 8.10 (d, *J* = 7.7 Hz, 1H), 7.73−7.65 (complex m, 3H), 6.43 (dd, *J* = 8.2 and 1.6 Hz, 1H), 6.37 (d, *J* = 8.2 Hz, 1H), 5.83 (s, 2H), 5.79 (m, 1H), 5.37 (d, *J* = 6.1 Hz, 1H), 4.46 (m, 1H), 4.10 (1H), 2.48 (dt, *J* = 18.2 and 5.2 Hz, 1H), 2.28 (m, 1H), 2.11 (m, 1H), 1.85 (m, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diastereoisomer)147.1, 147.0, 146.7, 135.5, 134.1, 133.0, 132.9, 130.8, 128.3, 125.6, 120.3, 107.8, 106.9, 100.9, 63.6, 53.1, 40.1, 35.6, 25.8, 18.0, −4.7 (two signals obscured or overlapping); IR (KBr): ν_{max} 3346, 2952, 2927, 2854, 1540, 1489, 1440, 1361, 1343, 1246, 1170, 1105, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 532 (M$^{+\bullet}$, 10%), 346 (50), 273 (56), 259 (72), 243 (58), 214 (60), 188 (61), 75 (100); HRMS M$^{+\bullet}$ Calcd for $C_{25}H_{32}N_2O_7SSi$: 532.1700, Found: 532.1701.

N-*(2-(Benzo[*d*][1,3]dioxol-5-yl)-5-((*tert-*butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)*-N-*(but-2-yn-1-yl)-4-nitrobenzenesulfonamide*. A magnetically stirred mixture of *N*-(2-(benzo-[*d*][1,3]dioxol-5-yl)-5-((*tert*-butyldimethylsilyl)oxy)cyclohex-2-en-1-yl)-4-nitrobenz-enesulf-onamide (3.20 g, 6.0 mmol) in dry DMF (20 mL) was treated with NaH (490 mg, 12.0 mmol) then the reaction mixture was stirred at 0 °C for 0.5 h before being treated with 1-bromo-2-butyne (1.00 mL, 12.0 mmol). The resulting solution was stirred at 22 °C for 3.5 h at which point the solution was poured into water (100 mL) (CAUTION HYDROGEN EVOLUTION POSSIBLE) and extracted with ethyl acetate (3 × 40 mL). The combined organic phases were washed with brine (1 × 50 mL) then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:3 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4), *N*-(2-(benzo[*d*][1,3]dioxol-5-yl)-5-((*ter*t-butyldimethyl-silyl)oxy)cyclohex-2-en-1-yl)-*N*-(but-2-yn-1-yl)-4-nitrobenzenesulfonamide (3.10 g, 88%) as a white foam and a ca. 6:1 a mixture of diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major diasteroisomer) 8.00 (d, *J* = 8.0 Hz, 1H), 7.65 (m, 1H), 7.57 (m, 2H), 6.52 (complex m, 2H), 6.43 (s, 1H), 5.88 (m, 1H), 5.84 (m, 2H), 5.11 (m, 1H), 4.29 (m, 1H), 4.05 (m, 1H), 3.67 (m, 1H), 2.47 (m, 1H), 2.32 (m, 1H), 2.14 (m, 2H), 1.70 (t, *J* = 2.4 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diasteroisomer) 148.0, 147.0, 146.6, 136.0, 133.9, 133.5, 133.2, 132.8, 131.1, 130.9, 130.0, 123.9, 120.2, 107.8, 107.3, 100.8, 80.3, 75.5, 64.8, 55.4, 37.5, 34.8, 25.7, 17.9, 3.6, −4.6, −4.8; IR (KBr): ν_{max} 2927, 2855, 1544, 1504, 1489, 1437, 1371, 1247, 1161, 1039 cm^{-1}; MS (EI, 70 eV): *m/z* 584 ($M^{+\bullet}$, 10%), 527 (60), 273 (73), 243 (90), 75 (100); HRMS $M^{+\bullet}$ Calcd for $C_{29}H_{36}N_2O_7SSi$: 584.2013, Found: 584.2011.

*(*r-*3a*R,*6*R,*7a*S,Z*)-3a-(Benzo[d][1,3]dioxol-5-yl)-6-((*tert-*butyldimethylsilyl)oxy)-3-ethylidene -1-((4-nitrophenyl)sulfonyl)-2,3,3a,6,7,7a-hexahydro-1*H-*indole [(±)-**62**] and (*r-*3a*R,*6*S,*7a*S, Z*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert-*butyldimethylsilyl)oxy)-3-ethylidene-1-((4-nitroph-enyl)sulfonyl)-2,3,3a,6,7,7a-hexahydro-1*H-*indole [(±)-**63**]*. A solution of *N*-(2-(benzo[*d*][1,3]dioxol-5-yl)-5-((*ter*t-butyldimethyl-silyl)oxy)cyclohex-2-en-1-yl)-*N*-(but-2-yn-1-yl)-4-nitrobenzenesulfonamide (500 mg, 0.85 mmol) in benzene (2.5 mL) containing $Pd(OAc)_2$ (38 mg, 0.17 mmol) and BBEDA (40 mg, 0.11 mmol) was purged with nitrogen for 0.25 h then subjected to microwave irradiation (100 W, 120 °C, 200 psi) for 4 h in a CEM Discover microwave reactor. The cooled reaction mixture was combined with those obtained from repeating the same reaction, as detailed above, five more times. The combined reaction mixtures thus obtained were concentrated under reduced pressure then subjected to flash chromatography (1:5 v/v ethyl acetate/hexane elution) to afford two fractions, A and B.

Concentration of fraction A (R_f = 0.4) gave the compound (±)-**63** (1.67 g, 56%) as white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.52 (m, 1H), 7.40−7.34 (complex m, 2H), 6.64−6.60 (complex m, 2H), 6.43 (d, *J* = 7.9 Hz, 1H), 5.85 (dd, *J* = 6.0 and 1.4 Hz, 2H), 5.81 (m, 1H), 5.59 (d, *J* = 9.8 Hz, 1H), 5.39 (m, 1H), 4.44 (m, 2H), 4.33−4.30 (complex m, 2H), 2.07 (m, 1H), 1.82 (m, 1H), 1.72 (d, *J* = 7.0 Hz, 3H), 0.97 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 147.2, 146.1, 139.3, 138.0, 132.6, 132.0, 131.8, 130.9, 130.2, 127.8, 123.5, 121.6, 120.8, 108.2, 107.5, 100.9, 64.9, 63.9, 55.3, 49.4, 35.5, 25.8, 18.0, 14.6, −4.5, −4.8; IR (KBr): ν_{max} 2953, 2928, 2885, 2856, 1545, 1505, 1484, 1436, 1371, 1359, 1249, 1238, 1166, 1068 cm^{-1}; MS (EI, 70 eV): *m/z* 584 ($M^{+\bullet}$, 1%), 527 (100); HRMS $M^{+\bullet}$ Calcd for $C_{29}H_{36}N_2O_7SSi$: 584.2013, Found: 584.2024.

Concentration of fraction B (R_f = 0.35) gave the compound (±)-**62** (280 mg, 9%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.38 (dd, *J* = 7.9 and 1.2 Hz, 1H), 7.31 (m, 1H), 6.53−6.48 (complex m, 2H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.85 (m, 2H), 5.70 (d, *J* = 10.1 Hz, 1H), 5.57 (dd, *J* = 10.1 and 2.0 Hz, 1H), 5.47 (m, 1H), 4.53 (m, 1H), 4.32 (m, 2H), 4.30 (dd, *J* = 12.7 and 4.2 Hz, 1H), 2.29 (m, 1H), 1.76 (d, *J* = 6.9 Hz, 3H), 1.69 (m, 1H), 0.91 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 147.3, 146.2, 139.2, 138.7, 132.5, 132.2, 131.6, 130.9, 129.7, 129.6, 123.3, 122.6, 120.4, 107.8, 107.7, 101.0, 67.3, 66.8, 55.0, 49.0, 38.2, 25.9, 18.2, 14.7, −4.5, −4.7; IR (KBr): ν_{max} 2953, 2928, 2856, 1544, 1505, 1484, 1437, 1372, 1359, 1248, 1166, 1085, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 584 ($M^{+\bullet}$, <1%), 527 (100); HRMS $M^{+\bullet}$ Calcd for $C_{29}H_{36}N_2O_7SSi$: 584.2013, Found: 584.2006.

*(*r*-3a*S*,6*R*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert*-butyldimethylsilyl)oxy)-1-((4-nitrophenyl)sulfonyl)-1,2,3a,6,7,7a-hexahydro-3*H*-indol-3-one [(±)-**64**].* *Step i:* A magnetically stirred mixture of compound (±)-**62** (280 mg, 0.48 mmol) in acetonitrile/water (10 mL of a 4:1 v/v mixture) was treated with citric acid (280 mg, 1.44 mmol), *N*-methylmorpholine-*N*-oxide (110 mg, 0.96 mmol) and potassium osmate dihydrate (18 mg, 0.048 mmol). The ensuing mixture was stirred at 22 °C for 72 h before being diluted with ethyl acetate (50 mL) and HCl (20 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with ethyl acetate (2 × 30 mL) and the combined organic phases were washed with brine (1 × 30 mL) then dried (Na_2SO_4), filtered through a short plug of TLC-grade silica gel and the filtrate concentrated under reduced pressure. The ensuing brown oil was immediately subjected to step i. *Step ii:* A solution of the the brown oil from step i in dichloromethane (20 mL) was treated with iodobenzene diacetate (310 mg, 0.96 mmol). The ensuing solution was stirred at 22 °C for 2 h before being concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after

concentration of the appropriate fractions (R_f = 0.2), ketone (±)-**64** (130 mg, 47%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.9 and 1.3 Hz, 1H), 7.62 (m, 1H), 7.52−7.47 (complex m, 2H), 6.50−6.45 (complex m, 3H), 5.91−5.85 (complex m, 3H), 5.66 (dd, *J* = 10.1 and 2.1 Hz, 1H), 4.65 (m, 1H), 4.45 (m, 1H), 4.41 (d, *J* = 18.7 Hz, 1H), 4.02 (d, *J* = 18.7 Hz, 1H), 2.45 (m, 1H), 1.65 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2, 148.0, 147.7, 147.1, 134.8, 133.4, 133.0, 132.6, 131.5, 130.0, 126.1, 123.9, 119.7, 108.2, 107.0, 101.3, 65.9, 64.0, 59.4, 52.1, 37.8, 25.7, 18.1, –4.6, –4.7; IR (KBr): ν_{max} 2954, 2929, 2857, 1761, 1545, 1506, 1485, 1438, 1371, 1249, 1164, 1085, 1065, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 572 ($M^{+\bullet}$, <1%), 385 (12), 328 (100); HRMS $[M+Na]^+$ Calcd for $C_{27}H_{32}N_2O_8SSiNa$: 595.1546, Found: 595.1554.

*(*r*-3a*S*,6*R*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert*-butyldimethylsilyl)oxy)-3a,6,7,7a-tetra-hydro-3*H*-indol-3-one [(±)-**65**]*. A magnetically stirred mixture of ketone (±)-**64** (130 mg, 0.23 mmol) in THF/methanol (4 mL of a 1:1 v/v mixture) maintained at 0 °C was treated with potassium carbonate (63 mg, 0.46 mmol). The resulting mixture was stirred at 0 °C for 1 h before being treated with TLC-grade silica gel (300 mg) then concentrated under reduced pressure. The resulting free-flowing solid was subjected to flash chromatography (1:5 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), imine (±)-**65** (78 mg, 89%) as a pale-green glass. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.5 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.55−6.52 (complex m, 2H), 6.09 (m, 1H), 5.93 (s, 2H), 5.74 (d, *J* = 10.0 Hz, 1H), 4.68 (m, 1H), 4.35 (m, 1H), 2.32 (m, 1H), 2.04 (m, 1H), 0.87 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 160.5, 148.2, 146.8, 134.6, 134.5, 126.5, 120.0, 108.6, 107.3, 101.2, 76.6, 63.9, 54.9, 35.7, 25.7, 18.0, −4.6(7), −4.7(4); IR (KBr): ν_{max} 2953, 2928, 2856, 1737, 1504, 1489, 1245, 1098, 1072, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 385 ($M^{+\bullet}$, <1%), 328 (100); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{27}NO_4Si$: 385.1709, Found: 385.1712.

*(±)-Hamayne [(±)-**8**] and Apohaemanthamine [(±)-**9**]*. *Step i:* A magnetically stirred mixture of imine (±)-**65** (100 mg, 0.26 mmol) in THF/methanol (8 mL of a 1:1 v/v mixture) maintained at −40 °C was treated with $NaBH_4$ (30 mg, 0.78 mmol). The reaction mixture was warmed to 22 °C over 6 h before being treated with NH_4Cl (*ca*. 3 drops of a saturated aqueous solution) then concentrated under reduced pressure. The residue so-formed was subjected to flash chromatography (5:1 v/v ammonia-saturated methanol/chloroform) to afford, after concentration of the appropriate fractions (R_f = 0.6), a *ca.* 3:1 a mixture of diastereoisomers **66** and **67**. *Step ii:* A magnetically stirred mixture of the diastereoisomers obtained from step i in formic acid (5.0 mL) was treated with paraformaldehyde (30 mg). The

resulting solution was heated under reflux for 14 h before being cooled then concentrated under reduced pressure. The resulting light-yellow oil was subjected to step ii. *Step ii:* A magnetically stirred mixture of the oil obtained from step i in ammonia-saturated methanol (10 mL) was stirred at 22 °C for 1 h before being concentrated under reduced pressure. The resulting yellow oil was subjected to flash chromatography (1:9 → 1:5 v/v chloroform/ammonia-saturated methanol gradient elution) to afford two fractions, A and B.

Concentration of fraction A (R_f = 0.7 in 9:1 *v/v* chloroform/ammonia-saturated methanol) and recrystallization of the resulting solid (methanol/chloroform) gave (±)-apohaemanthamine [(±)-**9**] (30 mg, 40%) as white, crystalline masses, m.p. = 141−143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 1H), 6.77 (dd, *J* = 8.4 and 5.4 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.49 (s, 1H), 5.92 (s, 2H), 4.42 (m, 1H), 4.32 (d, *J* = 16.8 Hz, 1H), 3.73 (d, *J* = 16.8 Hz, 1H), 3.72 (m, 1H), 3.30 (d, *J* = 13.6 Hz, 1H), 3.14−3.07 (complex m, 2H), 1.90 (m, 1H), 1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 146.3, 137.9, 135.5, 126.1, 123.2, 106.9, 103.2, 100.9, 79.9, 67.4, 66.3, 63.4, 60.9, 50.0, 33.9; IR (KBr): ν_{max} 2933, 1503, 1482, 1252, 1231, 1035, 933 cm^{-1}; MS (EI, 70 eV): *m/z* 269 ($M^{+\bullet}$, 100%); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{15}NO_3$: 269.1052, Found: 269.1052.

Concentration of fraction B (R_f = 0.6 in 5:1 *v/v* chloroform/ammonia-saturated methanol) and recrystallization of the resulting solid (methanol/chloroform) gave (±)-hamayne[34] [(±)-**8**] (12 mg, 13%) as a white solid, m.p.= 87−89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (s, 1H), 6.46 (s, 1H), 6.19 (m, 2H), 5.89 (d, *J* = 2.8 Hz, 2H), 4.37 (m, 1H), 4.30 (d, *J* = 17.0 Hz, 1H), 3.97 (m, 1H), 3.68 (d, *J* = 17.0 Hz, 1H), 3.39 (m, 1H), 3.31 (m, 1H), 3.22 (m, 1H), 2.13−2.03 (complex m, 2H) (resonances due to two protons obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 146.3, 137.9, 135.5, 126.1, 123.2, 106.9, 103.2, 100.9, 79.9, 67.4, 66.3, 63.4, 60.9, 50.0, 33.9; IR (KBr): ν_{max} 3333, 2916, 1501, 1482, 1239, 1038, 934 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 5%), 269 [$(M-H_2O)^{+\bullet}$, 100]; HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158, Found: 287.1162.

*(*r*-3a*S*,6*S*,7a*S*)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert*-butyldimethylsilyl)oxy)-1-((4-nitrophe -nyl)sulfonyl)-1,2,3a,6,7,7a-hexahydro-3*H*-indol-3-one [(±)-**68**]*. *Step i:* A magnetically stirred mixture of compound (±)-**63** (1.67 g, 2.85 mmol) in acetonitrile/water (10 mL of a 4:1 v/v mixture) was treated with citric acid (1.60 g, 8.55 mmol), *N*-methylmorpholine-*N*-oxide (670 mg, 5.7 mmol) then potassium osmate dihydrate (100 mg, 0.29 mmol). The ensuing mixture was stirred at 22 °C for 72 h before being diluted with ethyl acetate (50 mL) and HCl (20 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with ethyl acetate (2 × 30 mL) and the combined organic phases were washed with brine (1 × 30 mL)

then dried (Na_2SO_4), filtered through a short plug of TLC-grade silica gel and the filtrate concentrated under reduced pressure. The ensuing brown oil was subjected to directly to step i. *Step ii:* A solution of the brown oil from step i in dichloromethane (20 mL) was treated with iodobenzene diacetate (1.80 g, 5.7 mmol) and the ensuing solution stirred at 22 °C for 2 h before being concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.2), ketone (±)-**64** (830 mg, 51%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 1H), 7.63 (m, 1H), 7.51 (m, 2H), 6.56 (m, 1H), 6.52 (m, 2H), 6.02 (dd, *J* = 9.8 and 4.8 Hz, 1H), 5.86 (m, 2H), 5.63 (d, *J* = 9.8 Hz, 1H), 4.70 (m, 1H), 4.41−4.38 (complex m, 2H), 4.00 (d, *J* = 18.9 Hz, 1H), 2.14 (m, 1H), 1.93 (m, 1H), 0.96 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 147.9, 147.7, 147.0, 133.5, 132.9, 131.8, 131.6, 131.4, 130.8, 127.7, 124.1, 120.4, 108.0, 107.7, 101.2, 63.1, 62.9, 60.2, 53.3, 34.7, 25.8, 18.0, −4.6, −4.9; IR (KBr): ν_{max} 2929, 2856, 1761, 1545, 1506, 1485, 1437, 1371, 1248, 1164, 1085, 1065, 1040 cm^{-1}; MS (EI, 70 eV): *m/z* 515 {[M–$(H_3C)_3C$•]$^+$, 90%}, 328 (100); HRMS {[M–$(H_3C)_3C$•]$^+$ Calcd for $C_{23}H_{23}N_2O_8SSi$: 595.1546, Found: 595.1554.

*(*r*-3aS,6S,7aS)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert*-butyldimethylsilyl)oxy)-3a,6,7,7a-tetrahydro-3*H*-indol-3-one [(±)-69].* A magnetically stirred mixture of ketone (±)-**68** (290 mg, 0.51 mmol) in THF/methanol (8 mL of a 1:1 v/v mixture) maintained at 0 °C was treated with potassium carbonate (140 mg, 1.02 mmol). The ensuing mixture was stirred at 0 °C for 1 h then treated with TLC-grade silica gel (700 mg) before being concentrated under reduced pressure. The resulting free-flowing solid was subjected to flash chromatography (1:5 v/v ethyl acetate/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.7), imine (±)-**69** (160 mg, 82%) as a pale-green glass. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.9 Hz, 1H), 6.76 (dd, *J* = 8.5 and 0.4 Hz, 1H), 6.61 (m, 2H), 6.00 (broad d, *J* = 10.0 Hz, 1H), 5.94 (s, 2H), 5.39 (broad d, *J* = 10.0 Hz, 1H), 4.51 (m, 1H), 4.01 (m, 1H), 2.60 (m, 1H), 1.94 (m, 1H), 0.91 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 164.5, 148.1, 147.0, 137.9, 133.0, 124.7, 120.9, 108.5, 107.9, 101.2, 76.4, 63.5, 55.7, 33.3, 25.8, 18.1, −4.6, −4.8; IR (KBr): ν_{max} 2930, 2857, 1737, 1510, 1506, 1494, 1255, 1091 cm^{-1}; MS (EI, 70 eV): *m/z* 385 ($M^{+\bullet}$, 20%), 328 (100); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{27}NO_4Si$: 385.1709, Found: 385.1708.

*(*r*-3R,3aS,6S,7aS)-3a-(Benzo[*d*][1,3]dioxol-5-yl)-6-((*tert*-butyldimethylsilyl)oxy)-2,3,3a,6,7,-7a-hexahydro-1*H*-indol-3-ol [(±)-70].* A magnetically stirred solution of imine (±)-**69** (160 mg, 0.41 mmol) in THF/methanol (8 mL of a 1:1 v/v mixture) maintained at −40 °C was

treated with $NaBH_4$ (47 mg, 1.2 mmol) and the ensuing mixture warmed to 22 °C then stirred at this temperature for 6 h before being treated with NH_4Cl (*ca*. 7 drops of a saturated aqueous solution) then concentrated under reduced pressure. The resulting mixture was subjected to flash chromatography (1:5 v/v chloroform/ammonia-saturated methanol) to afford, after concentration of the appropriate fractions (R_f = 0.7), hydroindole (±)-**70** (130 mg, 81%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (broad s, 1H), 6.83 (m, 1H), 6.74 (broad d, *J* = 8.2 Hz, 1H), 6.04 (d, *J* = 10.4 Hz, 1H), 5.92 (s, 2H), 5.75 (d, *J* = 10.4 Hz, 1H), 4.45 (t, *J* = 6.1 Hz, 1H), 4.47 (m, 1H), 3.44 (m, 1H), 3.23 (m, 1H), 2.90 (m, 1H), 2.60 (broad s, 1H), 1.99 (m, 1H) 1.59 (m, 1H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H) (resonance due to one proton obscured or overlapping); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 146.1, 137.8, 135.0, 131.1, 127.1, 120.1, 108.0, 107.5, 101.1, 79.0, 64.1, 63.2, 52.9, 33.7, 25.9, 18.2, −4.5, −4.6; IR (KBr): ν_{max} 3338, 2953, 2929, 2885, 2856, 1505, 1487, 1243, 1084 cm^{-1}; MS (EI, 70 eV): *m/z* 389 ($M^{+\bullet}$, 20%), 333 (85), 205 (100); HRMS $M^{+\bullet}$ Calcd for $C_{21}H_{31}NO_4Si$: 389.2022, Found: 389.2025.

*Apohaemanthamine [(±)-**9**]*. A magnetically stirred solution of hydroindole (±)-**70** (70 mg, 0.18 mmol) in formic acid (5 mL) was treated with paraformaldehyde (30 mg). The resulting solution was heated under reflux for 14 h before being cooled then concentrated under reduced pressure. The light-yellow oil so obtained was subjected to flash chromatography (1:9 v/v chloroform/ammonia-saturated methanol) to afford, after concentration of the appropriate fractions (R_f = 0.7), apoheamanthamine [(±)-**9**] (33 mg, 68%) as a white solid. The spectroscopic data recorded on this compound were identical, in all respects, with those derived from the material obtained earlier.

*(±)-11-Hydroxyvattitine [(±)-**3**]*. A magnetically stirred solution of hydroindole (±)-**70** (120 mg, 0.31 mmol) in 1,2-dichloroethane (10 mL) was treated with paraformaldehyde (30 mg) and trifluoroacetic acid (480 μL, 6.2 mmol) then heated at 60 °C for 18 h before being cooled and concentrated under reduced pressure. The yellow oil thus obtained was subjected to flash chromatography (1:9 v/v chloroform/ammonia-saturated methanol) to afford, after concentration of the appropriate fractions (R_f = 0.6), (±)-11-hydroxyvattitine [(±)-**3**] (44 mg, 50%) as a white foam. ^{1}H NMR (400 MHz, CD_3OD) δ 6.93 (s, 1H), 6.55 (s, 1H), 6.42 (d, *J* = 10.1 Hz, 1H), 6.18 (m, 1H), 5.89 (s, 2H), 4.31 (d, *J* = 16.6 Hz, 1H), 4.28 (m, 1H), 3.95 (m, 1H), 3.78 (d, *J* = 16.6 Hz, 1H), 3.44−3.29 (complex m, 2H), 3.16 (dd, *J* = 13.8 and 3.2 Hz, 1H), 2.27 (m, 1H), 1.83 (dd, *J* = 13.3 and 4.2 Hz, 1H) (resonances due to two protons not observed); ^{13}C NMR (100 MHz, CD_3OD) δ 148.1, 147.7, 137.1, 132.9, 128.0, 126.9, 107.8, 104.3, 102.2, 80.9, 64.7, 63.8, 63.7, 61.7, 51.3, 33.0; IR (KBr): ν_{max} 3392, 2914, 1641, 1502,

1483, 1324, 1239, 1094, 1035 cm^{-1}; MS (EI, 70 eV): *m/z* 287 ($M^{+\bullet}$, 90%), 269 (75), 243 (73), 227 (100), 181 (75); HRMS $M^{+\bullet}$ Calcd for $C_{16}H_{17}NO_4$: 287.1158, Found: 287.1158.

X-ray crystallographic data for compounds (±)-3, (±)-7, (±)-9, 36, 41, ent-41, 45, 53, 55, and (±)-56

Crystal data

Compound (–)-3: $C_{16}H_{18}NO_4^+C_6H_2N_3O_7^-\bullet CH_3OH$, *M* = 548.46, *T* = 200(1) K, orthorhombic, space group $P2_12_12_1$, *Z* = 4, *a* = 6.9388(1), *b* = 13.9009(2), *c* = 23.9512(4) Å; *V* = 2310.23(6) Å^3, D_x = 1.577 g.cm^{-3}, 3004 unique data ($2\theta_{max}$ = 55°), 2713 with *I* > 2.0σ(*I*); *R* = 0.032, *Rw* = 0.078, *S* = 1.00.

Compound (±)-3: $C_{16}H_{18}NO_4^+C_6H_2N_3O_7^-$, *M* = 516.42, *T* = 200(1) K, monoclinic, space group *P*21/*a*, *Z* = 4, *a* = 8.6279(1), *b* = 26.7808(5), *c* = 9.8839(2) Å, β = 110.4722(10)°, *V* = 2139.55(7) Å^3, D_x = 1.603 g.cm^{-3}, 4899 unique data ($2\theta_{max}$ = 55°), 3417 with *I* > 2.0σ(*I*); *R* = 0.044, *Rw* = 0.105, *S* = 0.95.

Compound (±)-7: $C_{18}H_{22}NO_5^+C_6H_2N_3O_7^-$, *M* = 560.47, *T* = 200(1) K, monoclinic, space group $P2_1/c$, *Z* = 4, *a* = 14.1046(2), *b* = 7.5282(1), *c* = 23.5058(3) Å, β = 98.4742(9)°, *V* = 2468.65(6) Å^3, D_x = 1.508 g.cm^{-3}, 5652 unique data ($2\theta_{max}$ = 55°), 4198 with *I* > 2.0σ(*I*); *R* = 0.043, *Rw* = 0.110, *S* = 0.95.

Compound (±)-9: $C_{16}H_{15}NO_3$, *M* = 269.30, *T* = 200(1) K, triclinic, space group P$\bar{1}$, *Z* = 2, *a* = 7.0347(2), *b* = 9.4014(2), *c* = 10.0921(3) Å, α = 88.6579(19)°, β = 77.6969(14)°, γ = 69.8404(18)°, *V* = 611.26(3) Å^3, D_x = 1.463 g.cm^{-3}, 2793 unique data ($2\theta_{max}$ = 55°), 2355 with *I* > 2.0σ(*I*); *R* = 0.038, *Rw* = 0.103, *S* = 0.98.

Compound 36: $C_{15}H_{18}BrN$, *M* = 292.22, *T* = 200(1) K, orthorhombic, space group $P2_12_12_1$, *Z* = 4, *a* = 8.2756(2), *b* = 11.1236(4), *c* = 14.6580(5) Å, *V* = 1352.15(7) Å^3, D_x = 1.435 g.cm^{-3}, 3078 unique data ($2\theta_{max}$ = 55°), 2694 with *I* > 2.0σ(*I*); *R* = 0.029, *Rw* = 0.064, *S* = 1.01.

Compound 41: $C_8H_9BrF_3NO$, *M* = 272.06, *T* = 200(1) K, triclinic, space group *P*1, *Z* = 2, *a* = 5.0292(8), *b* = 7.7369(11), *c* = 13.795(2) Å, α = 101.537(6)°, β = 91.971(9)°, γ = 107.637(8), *V* = 498.61(13) Å^3, D_x = 1.812 g.cm^{-3}, 3022 unique data ($2\theta_{max}$ = 50.6°), 2354 with *I* > 2.0σ(*I*); *R* = 0.095, *Rw* = 0.257, *S* = 0.99.

Compound* ent-*41: $C_8H_9BrF_3NO$, *M* = 272.06, *T* = 200(1) K, triclinic, space group *P*1, *Z* = 2, *a* = 5.0260(3), *b* = 7.7300(4), *c* = 13.7908(8) Å, α = 101.669(3)°, β = 91.920(4)°, γ = 107.523(4), *V* = 497.80(5) Å^3, D_x = 1.815 g.cm^{-3}, 4224 unique data ($2\theta_{max}$ = 55.2°), 3590 with *I* > 2.0σ(*I*); *R* = 0.054, *Rw* = 0.151, *S* = 0.99.

Compound 45: $C_{21}H_{32}BrNOSi$, *M* = 422.48, *T* = 200(1) K, monoclinic, space group $P2_1$, *Z* = 4, *a* = 10.8031(2), *b* = 7.9845(1), *c* = 25.7942(4) Å, β = 90.4980(7)°, *V* = 2224.86(6) Å^3, D_x = 1.261 g.cm^{-3}, 10191 unique data ($2\theta_{max}$ = 55°), 7942 with *I* > 2.0σ(*I*); *R* = 0.037, *Rw* = 0.068, *S* = 0.97.

Compound 53: $C_{24}H_{25}NO_7S$, *M* = 471.53, *T* = 200 K, monoclinic, space group $P2_1$, *Z* = 2, *a* = 9.9367(3), *b* = 9.0913(2), *c* = 13.3553(5) Å, β = 109.6417(15)°, *V* = 1136.28(6) Å^3, D_x = 1.378 g.cm^{-3}, 5212 unique data ($2\theta_{max}$ = 55.2°), 4660 with *I* > 2.0σ(*I*); *R* = 0.044, *Rw* = 0.116, *S* = 0.99.

Compound* ent-*53: $C_{24}H_{25}NO_7S$, *M* = 471.53, *T* = 200 K, monoclinic, space group $P2_1$, *Z* = 2, *a* = 9.9369(2), *b* = 9.0908(2), *c* = 13.3586(3) Å, β = 109.6363(12)°, *V* = 1136.56(4) Å^3, D_x = 1.378 g.cm^{-3}, 4938 unique data ($2\theta_{max}$ = 55°), 4572 with *I* > 2.0σ(*I*); *R* = 0.033, *Rw* = 0.084, *S* = 1.00.

Compound 55: $C_{26}H_{27}NO_8S$, *M* = 513.57, *T* = 200(1) K, orthorhombic, space group $P2_12_12_1$, *Z* = 8, *a* = 10.4700(1), *b* = 20.6793(3), *c* = 22.5086(4) Å, *V* = 4873.39(12) Å^3, D_x = 1.400 g.cm^{-3}, 11158 unique data ($2\theta_{max}$ = 55°), 8674 with *I* > 2.0σ(*I*); *R* = 0.042, *Rw* = 0.091, *S* = 0.98.

Compound (±)-56: $C_{25}H_{27}NO_7S$, *M* = 485.56, *T* = 200 K, triclinic, space group *P*1, *Z* = 2, *a* = 9.5083(4), *b* = 10.2316(3), *c* = 13.3051(6) Å, α = 110.082(2)°, β = 97.268(2)°, γ = 100.494(2), *V* = 1170.04(8) Å^3, D_x = 1.378 g.cm^{-3}, 5375 unique data ($2\theta_{max}$ = 55.2°), 4303 with *I* > 2.0σ(*I*); *R* = 0.052, *Rw* = 0.146, *S* = 0.99.

Structure Determinations

Images were measured on a Nonius Kappa CCD diffractometer (MoKα, graphite monochromator, λ = 0.71073 Å) and data extracted using the DENZO package.[35] Structure solution was by direct methods (SIR92).[36] The structures of compounds (–)-**3**, (±)-**3**, (±)-**7**, (±)-**9**, **36**, **41**, *ent*-**41**, **45**, **53**, *ent*-**53**, **55**, and (±)-**56** were refined using the CRYSTALS program package.[37] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC Deposition numbers 1876936 to 1876947). These data can be obtained free-of-charge *via* www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free-of-charge on the ACS Publications website at DOI: 10.1021/acs.jacs.XXXXXX.

Experimental procedures and characterization data for all new compounds (PDF)

X-ray crystallographic data for the picrate salt of compound (–)-**3** (CIF)

X-ray crystallographic data for the picrate salt of compound (±)-**3** (CIF)

X-ray crystallographic data for the picrate salt of compound (±)-**7** (CIF)

X-ray crystallographic data for compound (±)-**9** (CIF)

X-ray crystallographic data for compound **36** (CIF)

X-ray crystallographic data for compound **41** (CIF)

X-ray crystallographic data for compound *ent*-**41** (CIF)

X-ray crystallographic data for compound **45** (CIF)

X-ray crystallographic data for compound **53** (CIF)

X-ray crystallographic data for compound *ent*-**53** (CIF)

X-ray crystallographic data for compound **55** (CIF)

X-ray crystallographic data for compound (±)-**56** (CIF)

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

We are grateful to the Chinese National Natural Science Foundation (Grant 21801094), the Pearl River Scholar Program of Guangdong Province, The Institute of Advanced Studies, The Australian Research Council and the Famous Foreign Supervisor Program (grant 2018-HWMS001) of the Ministry of Education, People's Republic of China, for financial support. BASF (Ludwigshafen) is thanked for the generous provision of samples of amines **20**-**23**, *ent*-**23**, **23**-**28**, *ent*-**28**, **28**-**35** and *ent*-**35**.

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