Enzymatic Asymmetrization of 6-Amino-2-cycloheptene-1,4-diol Derivatives: Synthesis of Tropane Alkaloids (+)- and (−)-Calystegine A_3

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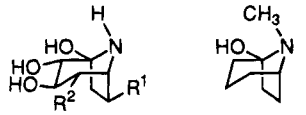
6-Azido and 6-((*tert*-butyloxycarbonyl)amino)derivatives of *meso*-2-cycloheptene-1,4-diol were prepared from cycloheptatriene and asymmetrized using *Pseudomonas cepacia* lipase. Enantiopure intermediates thus prepared were used in the syntheses of both enantiomers of the tropane alkaloid calystegine A_3.

Calystegines B_1 (**1**), B_2 (**2**), and A_3 (**3**) are new alkaloids of the tropane family, isolated from the roots of *Calystegia sepium* (morning glory).[1a-c] Recently, calystegine B_2 and A_3 have been found in the leaves and tubers of the potato (*Solanum tuberosum*); calystegine B_2 and A_3, potent inhibitors of β-glucosidases,[1d,e] have also been found in moths and butterflies, the larvae of which feed on Solanum.[1e] The calystegines and physoperuvine (**4**)[2] are



1 R^1 = OH; R^2 = H
2 R^1 = H; R^2 = OH
3 R^1 = H; R^2 = H

4

the only known members of the tropane and nortropane alkaloid families to possess an aminal functionality. The unusual structures, possible biological properties, and low natural abundance of the calystegines prompted us to examine enantiopure intermediates derived from cycloheptatriene in the synthesis of calystegine A_3. Recently, Lallemand and Boyer have reported the total enantioselective syntheis of (−)-calystegine B_2 from D-glucose.[3] The absolute configuration of calystegine B_2 was assigned based on the results of this total synthesis, and since calystegines B_1 and A_3 were isolated from the same plant, their absolute configuration was assumed to be identical to B_2. An analogue of calystegine B_2 was also synthesized from methyl α-D-glucoside by Duréault and co-workers.[4] Calystegine A_3 has been synthesized in racemic form by Lallemand and co-workers,[5] but no enantioselective synthesis has yet been reported. We report herein the enantioselective synthesis of both enantiomers of calystegine A_3, in which the seven carbon atoms present in the targets were derived from cycloheptatriene.

Results and Discussion

Cycloheptatriene (**5**) was initially oxidized to tropone (**6**) utilizing the procedure developed by Reingold.[6a] Reduction of tropone with sodium borohydride[6b] gave dienol **7**[6c] in 98% yield. This diene was subjected to the diacetoxylation conditions developed by Bäckvall[7] to produce the diacetoxy alcohol **8** in 84% yield. This yield was not reproducible on large scale reactions (>5 mmol) due to workup problems. Emulsions (possibly manganese promoted) were a serious problem during the extraction process. The manganese(IV) oxide was replaced with a stoichiometric amount of benzoquinone, but a large amount of the Diels–Alder product was also observed along with the desired 1,4-addition product. This replacement did, in fact, improve the workup procedure as no emulsions were formed during the extraction process. The alcohol **8** was converted to the mesylate **9** in quantitative yield. This mesylate was quite stable and could be stored at −20 °C for several months without decomposition. The nitrogen functionality was introduced by displacement of the mesylate **9** with sodium azide in DMF to produce the azide **10** in 82% yield (Scheme 1). The reaction was best performed at temperatures greater than 70 °C; at lower temperatures the reaction rate was too slow and decompostion of the azide was observed. Care also had to be taken to protect the reaction mixture from light as the azide also decomposes when exposed to light.

A point should be brought up here regarding the relative configuration of the azide center in compound **10**. The displacement of the mesylate **9** could be assisted by one of the acetates in the molecule; azide opening of the resulting bicyclic oxonium ion would result in a net retention of configuration. The mesylate from alcohol **11** (derived from the singlet oxygen addition to the *tert*-butyldimethylsilyl derivative of dienol **7**) would not exhibit neighboring acetate participation because of geometrical constraints. Treatment of this mesylate with azide ion gave **12** (Scheme 2) which was diastereomeric with **10** leading to the conclusion that **10** was formed in a straightforward inversion process.

[⊗] Abstract published in *Advance ACS Abstracts,* January 15, 1995.

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(2) Pinder, A. R. *J. Org. Chem.* **1982**, *47*, 3607.

(3) Lallemand, J. Y.; Boyer, F.-D. *Synlett.* **1992**, 969; Boyer, F-D.; Lallemand, J. Y. *Tetrahedron* **1994**, *50*, 10443.

(4) Duclos, O.; Duréault, A.; Depezay, J. C. *Tetrahedron Lett.* **1992**, *33*, 1059.

(5) Boyer, F.-D.; Ducrot, P.-H.; Henryon, V.; Soulié, J.; Lallemand, J. Y. *Synlett.* **1992**, 357.

(6) (a) Reingold, I. D.; DiNardo, L. J. *J. Org. Chem.* **1982**, *47*, 3544. (b) Schuster, D. I.; Palmer, J. M; Dickerman, S. C. *Ibid.* **1966**, *31*, 4281. (c) Johnson, C. R.; Golebiowski, A.; Steensma, D. H. *J. Am. Chem. Soc.* **1992**, *114*, 9414.

(7) Bäckvall, J.-E.; Bystrom, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619.

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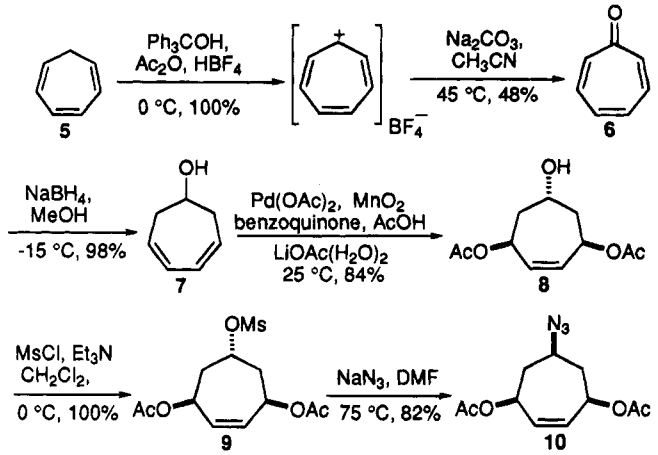
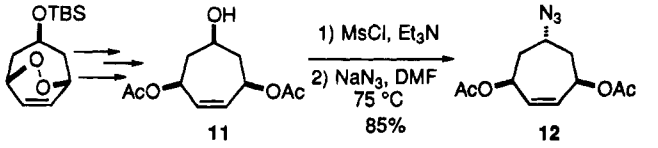
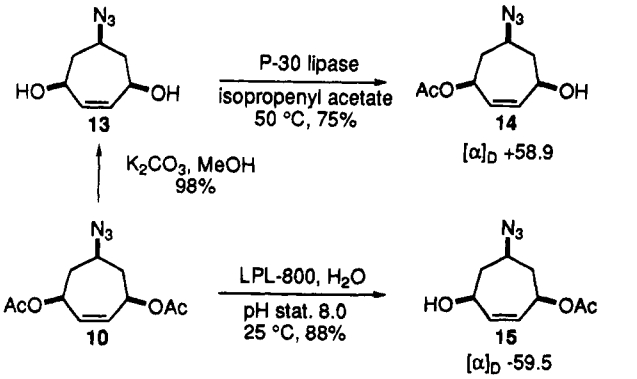
Scheme 1



Scheme 2



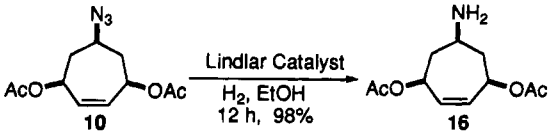
Scheme 3



Asymmetrization of *meso*-Azido Compounds. The diacetate **10** was hydrolyzed to the diol **13** and subjected to the enzyme-catalyzed transesterification by treatment with Amano P-30 lipase (from *Pseudomonas cepacia*) in isopropenyl acetate[8] at 50 °C to give the optically active monoacetate **14** in 75% yield and the *meso*-diacetate **10** in 10% yield. The diacetate **10** was treated with a purified form of the lipase from *Pseudomonas cepacia* (LPL-800) immobilized on azlactone polymer beads,[9] at room temperature, while a pH of 8.0 was maintained with an automatic titrator, to produce the monoacetate **15** in 88% yield and diol **13** in 10% yield (Scheme 3). It should be noted that monoacetates **14** and **15** are enantiomers, with the enzyme catalyzing the hydrolysis or acetylation of the same stereogenic center in each molecule.[8]

As the starting materials were hydrolyzed or acetylated during the asymmetrizations in Scheme 3, to furnish monoacetate, subsequent hydrolysis or acetylation ensued to give the *meso*-diol or diacetate, respectively, before the starting material completely disappeared. In larger scale reactions (greater than 100 mg substrate), this problem was more pronounced. Attempts to alleviate this differentiation problem by varying the reaction conditions proved unsuccessful. It was conjectured that the azide functionality was too small (a long flat functional group lacking large spatial requirements) and the enzyme could not efficiently distinguish the two flanks of the stereogenic center; thus, both enantiotopic groups could fit into the active site of the enzyme. Our laboratory has carried out enzymatic asymmetrizations on *meso*-diols similar to **13** but instead of an azide at the apex carbon, the systems had much larger silyl (*tert*-butyldimethylsilyl or triisopropylsilyl)-protected alcohols.[10]

Scheme 4



Synthesis and Asymmetrization of *meso*-Carbamates. To test this hypothesis (azide not large enough), the azide was converted into a larger group. The azide **10** was hydrogenated[11] using Lindlar catalyst to give the primary amine **16** in 98% yield (Scheme 4).

The amine **16** was protected as either the benzyl carbamate **17** or the *tert*-butyl carbamate **18**. These two protecting groups are considerably larger than the azide and should provide a "handle" for the enzyme to differentiate the enantiotopic groups. The carbamates **17** and **18** were then converted to diols **19** and **20** in 93% and 95% yield, respectively, with potassium carbonate and methanol. Diols **19** and **20** were subsequently treated with Amano P-30 lipase in isopropenyl acetate and *tert*-butyl methyl ether to yield optically active monoacetates **21** and **22** in 91% and 92% yields, respectively (Scheme 5). These reactions were conducted at 50 °C to increase the solubility of the starting material. The diols were sparingly soluble in the solvent, but as more diol was transformed into monoacetate, the remaining diol would dissolve.

Monoacetates **21** and **22** were converted to their corresponding Mosher (MTPA) esters[12] and the enantiomeric excesses determined to be >98%. Attempts to determine ee of the azido monoacetates **14** and **15** using this method proved to be unsuccessful because the racemic MTPA derivative did not show the required diastereomeric splitting in ^{1}H, ^{13}C, or ^{19}F NMR.

Determination of Absolute Stereochemistry. Alcohol **23** of known absolute configuration[13] was transformed into its mesylate; the latter was subjected to sodium azide in DMF to produce azide **24** in 74% yield for the two steps. Reduction by hydrogenolysis and protection of the incipient amine produced the carbamate **25** in 85% yield. Alcohol **22** was transformed to the same carbamate **25** in 82% yield by treatment with benzoyl chloride and pyridine (Scheme 6). The spectroscopic

(8) For a recent review of the use of enol esters in enzymatic transesterifications see: Fang, J.-M.; Wong, C.-H. *Synlett* **1994**, 393.

(9) Purified *Pseudomonas cepacis* lipase LPL-800 from Amano Enzyme Co. was immobolized on an acrylate/4,4-dimethyl-2-vinyl-2-oxazolin-5-one (vinyl dimethyl azalactone) copolymer provided by the 3M Co. Details of this immobilization technique will be reported separately.

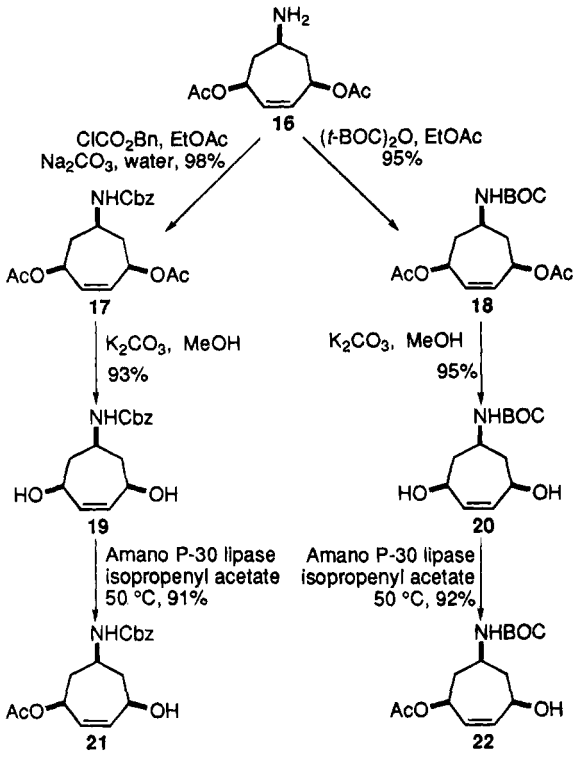
(10) Johnson, C. R.; Golebiowski, A.; McGill, T. K.; Steensma, D. H. *Tetrahedron Lett.* **1991**, *32*, 2597.

(11) Corey, E. J.; Nicolaou, K. C.; Balansons, R.; Michida, Y. *Synthesis* **1975**, 590.

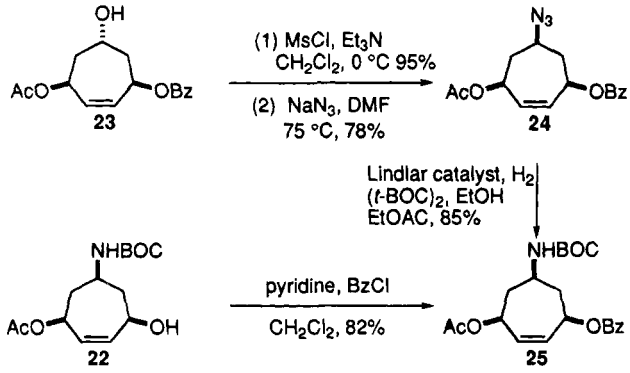
(12) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(13) Johnson, C. R.; Golebiowski, A.; Steensma, D. H.; Scialdone, M. A. *J. Org. Chem.* **1993**, *58*, 7185.

Scheme 5



Scheme 6



properties and optical rotations were identical for compound **25** from both routes, thus proving the absolute configuration of **22** as 1*R*,4*S*,6*R* (as shown).

It is reasonable to assume that alcohol **21** has the same absolute configuration as **22** because of the structural similarities. All similar cyclic compounds which we have examined in asymmetrization or resolution studies have conformed to the empirical model (Figure 1a) regarding the preferred stereogenic center (Figure 1a) for *Pseudomonas cepacia* lipase-catalyzed reactions;[10] Kazlauskas has formulated a similar and more general rule for secondary alcohols with various esterases and lipases.[14] The absolute stereochemistry of **24** was further confirmed using the benzoate sector rule (Figure 1b) as described by Nakanishi.[15] Benzoate **24** exhibited a positive Cotton effect in its CD determined in MeOH. This observation is consistent with the more polarizable C=C bond present in a positive sector and points to an absolute stereochemistry of *R* at the benzoate substituted carbon.

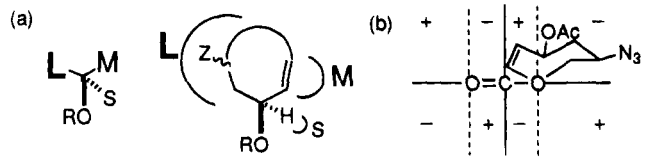
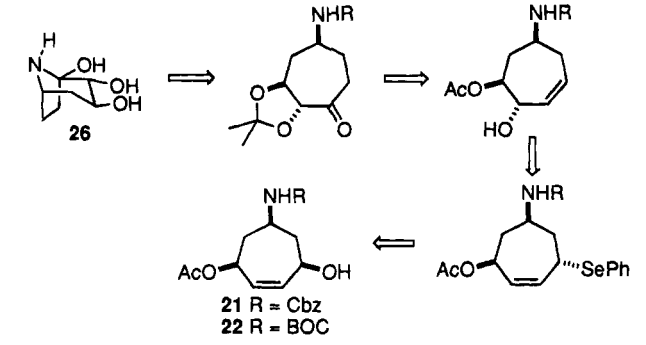
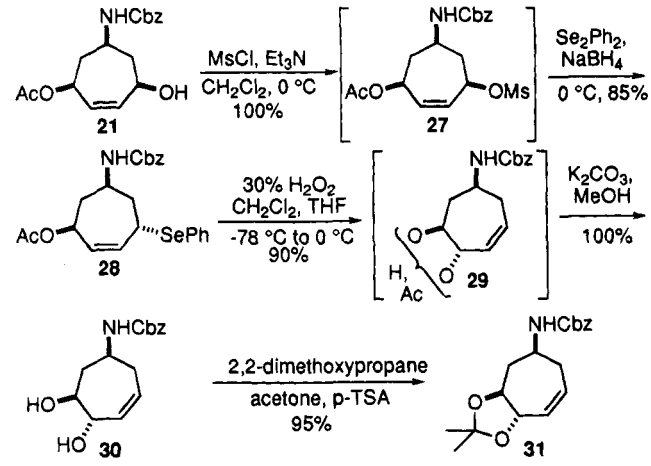


Figure 1. (a) Model of alcohol (R = H) or ester (R = Ac) in lipase active site. (b) Sector diagram for benzoate **24**.

Scheme 7



Scheme 8



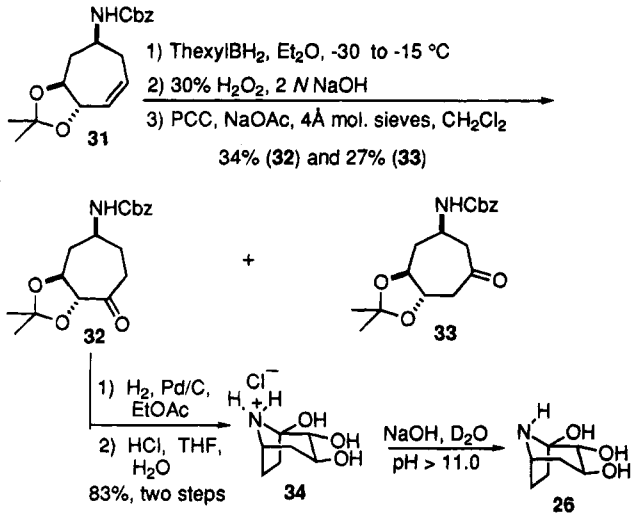
Synthesis of Calystegines A_3. By taking advantage of the pseudosymmetry of alcohols **21** and **22**, both enantiomers of calystegine A_3 should be accessible from the same starting alcohol. A retrosynthetic analysis for *ent*-calystegine A_3 (**26**) from alcohols **21** or **22** is depicted in Scheme 7.

It has been shown that oxidation of allylic selenides produces allylic alcohols *via* an sigmatropic process; at low temperatures, the selenenate is favored in the equilibrium between the selenoxide and the selenenate.[16] Alcohol **21** was converted to its mesylate **27** which was treated with the phenylselenyl anion (Ph_2Se_2, $NaBH_4$, EtOH)[17] to give selenide **28** in 85% yield for the two steps. Oxidation of selenide **28** with 30% H_2O_2 at −78 to 0 °C gave olefinic alcohol **29** in 90% yield.[18] Monoacetate **29** was isolated as an inseparable mixture of regioisomers resulting from acetyl migration. Hydrolysis (K_2CO_3, MeOH) of the acetate provided diol **30** which was protected as the acetonide **31** (Scheme 8).

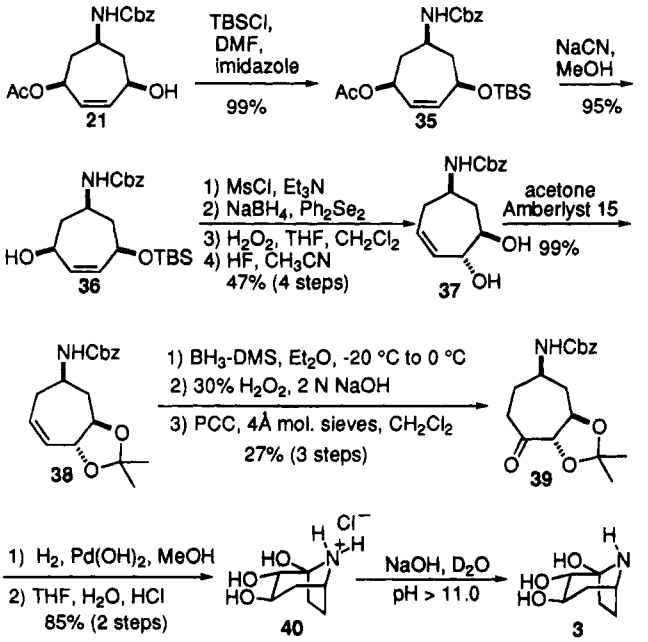
Evans has shown that α-oxygenated alkenes can be regioselectively hydroborated to produce alcohols with the

(14) Kazlauskas, R. J.; Weissfloch, A. N. E.; Rappaport, A. T.; Cuccia, L. A. *J. Org. Chem.* **1991**, *56*, 2656.
(15) Harada, N.; Ohashi, M.; Nakanishi, K. *J. Am. Chem. Soc.* **1968**, *90*, 7349.
(16) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947.
(17) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697. Sjöberg, B.; Herdevall, S. *Acta Chem. Scand.* **1958**, *12*, 1347.
(18) A byproduct which appeared to be *cis*-5-acetoxy-7-((benzyloxycarbonyl)amino)-1,4-cycloheptadiene was observed in 8% yield.

Scheme 9



Scheme 10



boron addition to the carbon nearer the oxygen.[19] However, in our case, hydroboration of olefin **31** with BH_3–DMS in diethyl ether with oxidative workup gave a complex mixture of inseparable regio- and stereoisomers. Further oxidation of this mixture gave two products; the desired ketone **32** was produced in 25% yield (three steps) and the regioisomer **33** was produced in 31% yield. The use of thexylborane gave similar results with the desired ketone **32** produced in 34% yield and the regioisomer **33** in 27% yield for the three-step process (Scheme 9).

The deprotection of the diol and amine functionality in **32** proved to be problematic. The order of removal was important as the α,β-hydroxy ketone was not stable to the acidic conditions necessary to remove the acetonide. Therefore, the benzyl carbamate was first removed by hydrogenation; the resulting amine was treated with HCl in aqueous THF to produce the hydrochloride **34** (83% from **32**) of *ent*-calystegine A_3. It is probable that the free amine acts intramolecularly to form an aminal which decreases the chance of elimination processes occuring during the acidic deprotection of the acetonide. The amine hydrochloride **34** was dissolved in D_2O after which a solution of NaOH in D_2O was added to attain a pH > 11 to produce the free base *ent*-calystegine A_3 (**26**). The ^1H and ^{13}C data of compound **26** were identical to that reported in the literature for calystegine A_3. Unfortunately, **26** could not be isolated from the basic D_2O solution without decomposition occuring.

By taking advantage of the pseudosymmetry of alcohol **21**, a similar route to calystegine A_3 (**3**) was also completed with initial protecting group manipulation necessary to enter the enantiomeric manifold adding two steps to the synthesis (Scheme 10). Alcohol **21** was first protected as a *tert*-butyldimethylsilyl ether in 99% yield. The hydrolysis of the acetate of **35** with NaCN in methanol produced alcohol **36** in 95% yield. Alcohol **36** was transformed into diol **37** in four steps in 47% yield. The diol **37** was then protected as the acetonide **38** in 99% yield with acetone and Amberlyst 15 acidic resin. Conversion of the olefin with BH_3–DMS/H_2O_2 followed by pyridinium chlorochromate provided the desired ketone **39** in 27% yield. The regioisomeric ketone was also produced but was not isolated. Deprotection of the benzyl carbamate by hydrogenation followed by acidic aqueous hydrolysis yielded the calystegine A_3 hydrocholoride (**40**) in 85% yield after recrystallization. The hydrochloride **40** was dissolved in D_2O after which a solution of NaOH in D_2O was added to attain a pH > 11. The ^1H and ^{13}C data obtained from this solutions were identical to that reported for calystegine A_3 (**3**). As in the case of its enantiomer described above, **3** could not be isolated from the basic D_2O solution without decomposition.

Conclusions

This paper describes several new asymmetrizations of *meso*-6-amino-2-cycloheptene-1,4-diol derivatives utilizing the lipase from *Pseudomonas cepacia*. Alcohol **21**, thusly prepared, was used in the synthesis of both enantiomers of calystegine A_3, all carbons of which originate from the ultimate starting material, cycloheptatriene. Alcohols **21** and **22** are new enantiopure intermediates of potential synthetic use for a variety of targets.

Experimental Section

Thin layer chromatography was performed on silica gel glass-backed plates containing a fluorescent indicator (0.25 mm, Whatman silica gel 60 Å, KSF). Flash chromatography was performed as described by Still[20] using silica gel 60 (230–400 mesh, Kieselgel, EM Reagents). Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter using spectrograde solvents or deionized water. Infrared (IR) spectra were recorded on Nicolet 20 DX Fourier transform spectrophotometer and are reported in wavenumbers (cm^{-1}). Samples were analyzed as films unless otherwise noted. Proton nuclear magnetic resonance (^1H NMR) spectra were measured at 300 MHz on a General Electric QE-300 or GN-300 Fourier transform spectrometer. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were measured at 75.48 MHz on a General Electric QE-300 or GN-300 Fourier transform spectrometer. $CDCl_3$ was used as solvent for all NMR experiments unless otherwise noted. Mass spectra were recorded on either a Kratos AEI-MS-902 or a Kratos MS50TC spectrometer at 20 or 70 eV. Isobutane was the reagent used for all chemical

(19) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917.

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2933.

ionization (CI) experiments. Microanalyses were performed by Midwest Microlabs, Indianapolis, IN.

***meso*-(1*S*,3*R*,6*S*)-3,6-Diacetoxycyclohept-4-en-1-ol (8).** Lithium acetate dihydrate (2.75 g, 22.9 mmol), mangenese-(IV) oxide (438 mg, 5.04 mmol), benzoquinone (99 mg, 0.92 mmol), and palladium(II) acetate[7] (51 mg, 0.23 mmol) were added to acetic acid (8.0 mL). Diene **7**[6b,c] (500 mg, 4.58 mmol) was added, and the viscous suspension was stirred for 64 h. Diethyl ether (60 mL) was added and stirred for 30 min. The diethyl ether was decanted and washed with saturated aqueous sodium bicarbonate (5 × 50 mL). The aqueous extracts were back-extracted with diethyl ether (50 mL). The combined organics were washed with brine (10 mL) and the diethyl ether removed under reduced pressure. The crude product was purified by column chromatography (3:1, petroleum ether:ethyl acetate) to provide **8** (865 mg, 84%) as a pale yellow oil:[10] IR (cm^{-1}) ν_{max} 3475, 3045, 2940, 2870, 1740, 1720, 1655, 1440, 1375, 1240, 1085, 1030, 990, 970, 815; ^1H NMR δ 5.75−5.68 (m, 4 H), 4.28 (m, 1 H), 2.90 (s, 1 H), 2.01 (s, 6 H), 2.00−1.86 (m, 4 H); ^{13}C NMR δ 21.1, 39.1, 65.3, 68.4, 132.7, 170.2; MS {CI} *m/z* 66 (3), 80 (9), 91 (4), 109 (54), 126 (47), 151 (12), 169 (100), 211 (7), 229 [M + H] (0.3); HRMS calcd for $C_{11}H_{16}O_5$ − OAc 169.0864, found 169.0861.

***meso*-(3*R*,5*S*,7*S*)-3,7-Diacetoxy-5-((methylsulfonyl)-oxy)cyclohept-1-ene (9).** Alcohol **8** (2.90 g, 12.7 mmol), dichloromethane (30 mL), and triethylamine (3.54 mL, 25.4 mmol) were added to a round-bottomed flask and cooled to 0 °C. Methanesulfonyl choride (1.47 mL, 19.0 mmol) was added dropwise over 10 min. After 10 min of additional stirring, water (30 mL) was added to the reaction mixture. The layers were separated, and the organic layer was washed with saturated aqueous ammonium chloride (30 mL). The aqueous washes were back-extracted with dicholormethane (30 mL). The combined dichloromethane extracts were dried over sodium sulfate and filtered. The dichloromethane was removed under reduced pressure to provide **9** (3.89 g, 100%) as an oil: IR (cm^{-1}) ν_{max} 3025, 2940, 1740, 1495, 1440, 1370, 1240, 1175, 1145, 1035, 970, 905; ^1H NMR δ 5.73 (s, 2 H), 5.61 (dm, J = 10.3 Hz, 2 H), 5,21 (m, 1 H), 3.09 (s, 3 H), 2.22 (ddd, J = 14.2, 5.6, 2.2 Hz, 2 H), 2.15−2.05 (m, 2 H), 2.02 (s, 6 H); ^{13}C NMR δ 20.9, 37.4, 38.9. 67.3, 75.5, 132.5, 169.7; MS {CI} *m/z* 66 (11), 80 (28), 91 (17), 108 (100), 126 (18), 150 (13), 168 (9), 211 (31), 247 (33), 307 [M + H] (1); HRMS calcd for $C_{12}H_{18}O_7S$ − OAc 247.0640, found 247.0636.

***meso*-(3*R*,5*R*,7*S*)-3,7-Diacetoxy-5-azidocyclohept-1-ene (10).** Mesylate **9** (4.15 g, 13.5 mmol) and sodium azide (2.86 g, 44.0 mmol) were added to a round-bottomed flask charged with dry DMF (50 mL). The solution was heated at 50 °C and stirred for 35 h. Water (350 mL) was added, and the product was extracted with petroleum ether:diethyl ether (1:1) (3 × 100 mL). The organic extracts were dried over magnesium sulfate and filtered. The crude azide was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **10** (2.81 g, 82%) as a crystalline solid: mp 77−78 °C; IR (cm^{-1}, KBr) ν_{max} 2965, 2940, 2875, 2500, 2205, 2140, 2090, 1740, 1725, 1435, 1375, 1250, 1235, 1115, 1080, 1040, 985, 945, 875; ^1H NMR δ 5.68 (s, 2 H), 5.31 (d, J = 10.5 Hz, 2 H), 3.72 (tt, J = 11.3, 3.7 Hz, 1 H), 2.16 (dm, J = 11.9 Hz, 2 H), 2.06 (s, 6 H), 1.72 (q, J = 11.5 Hz, 2 H); ^{13}C NMR δ 21.0, 37.6, 56.6, 68.9, 131.9, 169.8; MS {CI} *m/z* 80 (12), 94 (10), 106 (35), 124 (132), 151 (18), 166 (100), 194 (38), 211 [M − N_3] (3). Anal. Calcd for $C_{11}H_{15}O_4N_3$: C, 52.17; H, 5.97; N, 16.59. Found: C, 52.11; H, 6.02; N, 16.38.

***meso*-(3*R*,5*S*,7*S*)-3,7-Diacetoxy-5-azidocyclohept-1-ene (12).** Alcohol **11** (203 mg, 0.889 mmol) (derived from singlet oxygen addition to the *tert*-butyldimethylsilyl ether of diene **7**),[6c] dichloromethane (10 mL), and triethylamine (0.25 mL, 1.823 mmol) were added to a round-bottomed flask and cooled to 0 °C. Methanesulfonyl choride (153 mg, 0.10 mL, 1.334 mmol) was added dropwise over 10 min. After 10 min of additional stirring, water (10 mL) was added to the reaction mixture. The layers were separated, and the organic layer was washed with saturated aqueous ammonium chloride (5 mL). The aqueous washes were back-extracted with dicholormethane (10 mL). The combined dichloromethane extracts were dried over $NaSO_4$ and filtered. The dichloromethane was removed under reduced pressure to provide the crude mesylate as a colorless oil. The mesylate was dissolved into DMF (5 mL), and sodium azide (173 mg, 2.67 mmol) was added. The solution was heated at 85 °C while being stirred for 3 h. Water (5 mL) was added, and the product was extracted with petroleum ether:diethyl ether (1:1) (3 × 20 mL). The organic extracts were dried over magnesium sulfate and filtered. The crude azide was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **12** (191 mg, 85% two steps) as a low-melting solid: mp 48−51 °C; IR (cm^{-1}, KBr) ν_{max} 2920, 2110, 1740, 1370, 1235, 1070, 1035, 715, 695; ^1H NMR δ 5.71 (s, 2 H), 5.40 (d, 2 H), 3.75 (bt, 1), 2.17 (bd, 2H), 2.10 (s, 6H), 1.75 (dd, 2H); ^{13}C NMR δ 20.9, 36.3, 56.0, 68.0, 132.5, 169.7.

***meso*-(1*R*,4*S*,6*R*)-6-Azidocyclohept-2-ene-1,4-diol (13).** Diacetate **10** (350 mg, 1.38 mmol) was placed in a round-bottomed flask and dissolved in methanol (5.0 mL). Potassium carbonate (70 mg, 0.5 mmol) was added and the suspension stirred for 3.5 h. The suspension was filtered, and methanol was removed under reduced pressure. The crude diol was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to give **13** (229 mg, 98%) as a white crystalline solid: mp 88−89.5 °C; IR (cm^{-1}, KBr) ν_{max} 3355, 2945, 2860, 2115, 2095, 1460, 1390, 1365, 1310, 1285, 1260, 1245, 1030, 730, 700, 685; ^1H NMR δ 5.72 (s, 2H), 4.31 (d, J = 10.8 Hz, 2 H), 3.60 (dt, J = 11.5, 3.4 Hz, 1 H), 2.20−1.25 (m, 6 H); ^{13}C NMR δ 41.4, 57.4, 67.6, 134.9; MS {CI} *m/z* 70 (48), 82 (100), 96 (59), 109 (89), 124 (98), 142 (15), 170 [M + H] (8); HRMS calcd for $C_7H_{11}O_2N_3$ − N_2OH 124.0762$_3$, found 124.0758. Anal. Calcd for $C_7H_{11}O_2N_3$: C, 49.70; H, 6.55; N, 24.84. Found: C, 49.39; H, 6.62; N, 24.59.

(1*R*,4*S*,6*S*)-4-Acetoxy-6-azidocyclohept-2-en-1-ol (14). Diol **13** (80 mg, 0.47 mmol) and Amano P-30 lipase (crude *Pseudomonas cepacia* lipase) (*ca.* 80 mg) were added to a round-bottomed flask charged with isopropenyl acetate (5.0 mL). The suspension was stirred at 45 °C for 24 h after which more P-30 lipase was added (100 mg). The suspension was allowed to stir for an additional 24 h. The biocatalyst was removed by filtration and rinsed with ethyl acetate. The filtrate was removed under reduced pressure, and the crude product was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **14** (75 mg. 75%) as a colorless oil: $[\alpha]^{25}_D$ = +58.9 (*c* 1.42, $CHCl_3$); IR (cm^{-1}) ν_{max} 3425, 2935, 2885, 2085, 1740, 1725, 1450, 1370, 1245, 1040, 990; ^1H NMR δ 5.72 (d, J = 11.9 Hz, 1 H), 5.56 (d, J = 11.9 Hz, 1 H), 5.19 (d, J = 9.9 Hz, 1 H), 4.28 (d, J = 9.9 Hz, 1 H), 3.61 (tm, J = 11.3 Hz, 1 H), 3.28 (bs, 1 H), 2.10 (m, 2 H), 2.03 (s, 3 H), 1.63 (q, J = 11.5 Hz, 2 H); ^{13}C NMR δ 20.9, 37.5, 41.0, 56.9, 66.9, 69.2, 130.5, 136.0, 170.3; MS {CI} *m/z* 82 (19), 96 (16), 109 (36), 124 (100), 151 (4), 166 (13), 184 (4), 194 (20), 212 [M + H] (1). Anal. Calcd for $C_9H_{13}O_3N_3$: C, 51.18; H, 6.20; N, 19.89. Found: C, 51.23; H, 6.22; N, 19.78.

(1*S*,4*R*,6*R*)-4-Acetoxy-6-azidocyclohept-2-en-1-ol (15). Diacetate **10** (75 mg, 0.30 mmol) and LPL-800 lipase (a purified form of *Pseudomonas cepacia* lipase available from Amono Enzyme Co.) supported on azlactone polymer beads[9] (250 mg, 25 mg enzyme) were added to distilled water (20 mL). While stirring (overhead mechanical stirrer), the reaction was kept at a constant pH of 8.0 with an automatic titrater (0.1 N NaOH) for 65 h. The biocatalyst was removed by filtration and rinsed with water (50 mL). The monoacetate was isolated by extraction with ethyl acetate and purified by column chromatography (1:1 petroleum ether:ethyl acetate) to give **15** (56 mg, 88%) as a colorless oil: $[\alpha]^{25}_D$ = −59.5 (*c* 1.27, $CHCl_3$); IR (cm^{-1}) ν_{max} 3435, 2940, 2870, 2100, 1735, 1370, 1250, 1115, 1040, 710, 680; ^1H NMR δ 5.73 (d, J = 12.1 Hz, 1 H), 5.56 (d, J = 12.1 Hz, 1 H), 5.20 (dd, J = 9.9, 1.2 Hz, 1 H), 4.29 (d, J = 10.9 Hz, 1 H), 3.61 (tt, J = 11.5, 3.40 Hz, 1 H), 3.04 (bs, 1 H), 2.06−2.15 (m, 2 H), 2.03 (s, 3 H), 1.64 (q, J = 11.5 Hz, 2 H); ^{13}C NMR δ 21.0, 37.5, 41.0, 57.0, 67.0, 69.2, 130.5, 136.0, 170.3; MS {CI} *m/z* 68 (9), 82 (35), 96 (24), 109 (54), 124 (100), 151 (7), 166 (19), 184 (5), 194 (31), 212 [M + H] (2); HRMS calcd for $C_9H_{13}O_3N_3$ − AcOH 151.0745, found 151.0748. Anal. Calcd for $C_9H_{13}O_3N_3$: C, 51.18; H, 6.20. Found: C, 50.75; H, 6.13.

***meso*-(1*R*,3*R*,6*S*)-3,6-Diacetoxy-4-cycloheptenyl-**

amine (16). Azide **10** (4.90 g, 19.3 mmol) was dissolved into ethanol (45 mL). Lindlar catalyst was added (1.15 g) and the flask evacuated and flushed with hydrogen gas. The suspension was stirred in an atmosphere of hydrogen gas for 50 h while being protected from light (wrap flask with foil). The suspension was filtered through a pad of Celite to remove the Lindlar catalyst, and the ethanol was removed under reduced pressure to provide **16** (4.39 g, 100%) as a pale green oil: IR (cm^{-1}) ν_{max} 3365, 2925, 1735, 1575, 1370, 1240, 1030, 980, 915, 845; ^1H NMR δ 5.58 (s, 2 H) 5.24 (dd, J = 11.2, 1.0 Hz, 2 H), 3.18 (tt, J = 10.9, 3.0 Hz, 1 H), 2.82 (bs, 2 H), 1.98 (s, 6 H), 1.96–1.89 (m, 2 H), 1.47 (q, J = 11.4 Hz, 2 H); ^{13}C NMR δ 21.0, 41.8, 48.0, 70.0, 131.9, 169.9; MS {EI} m/z 53 (6), 60 (6), 72 (5), 80 (0.2), 91 (18), 108 (100), 125 (14), 168 (85), 228 [M + H] (3); HRMS calcd for $C_{11}H_{17}O_4N$ + H 228.1236, found 228.1233.

***meso*-(3*R*,5*R*,7*S*)-3,7-Diacetoxy-5-((benzyloxycarbonyl)amino)cyclohept-1-ene (17).** Amine **16** (8.10 g, 35.6 mmol) was dissolved in ethyl acetate (80 mL). A saturated aqueous solution of sodium bicarbonate was added (50 mL) followed by addition of benzyl chloroformate (7.90 g, 46.3 mmol). The solution was stirred at 25 °C for 3 h after which time water (10 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined ethyl acetate extracts were washed with 2 N HCl (30 mL), dried over magnesium sulfate, and filtered and the solvent removed under reduced pressure. The crude carbamate was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to provide **17** (12.70 g, 99%) as a white crystalline solid: mp 122–124 °C; IR (cm^{-1}, KBr) ν_{max} 3320, 3060, 3040, 2940, 2930, 2895, 2865, 1730, 1710, 1680, 1540, 1440, 1370, 1330, 1285, 1220, 1160, 1105, 1025, 985, 915, 850, 755, 730, 700; ^1H NMR δ 7.33 (m, 5 H), 5.68 (s, 2 H), 5.36 (d, J = 10.4 Hz, 2 H), 5.08 (s, 2 H), 5.01 (d, J = 7.3 Hz, 1 H), 4.03 (m, 1 H), 2.17 (d, J = 12.4 Hz, 2 H), 2.04 (s, 6 H), 1.70 (q, J = 11.2 Hz, 2 H); ^{13}C NMR δ 21.0, 38.8, 47.2, 66.6, 69.5, 128.0, 128.4, 132.2, 136.3, 154.9, 169.7; MS {CI} m/z 91 (70), 108 (28) 135 (7), 152 (21), 171 (7), 194 (28), 212 (42), 242 (100), 302 (77), 362 [M + H] (3); HRMS calcd for $C_{19}H_{23}O_6N$ – OAc 301.1313$_9$, found 301.1309. Anal. Calcd for $C_{19}H_{23}O_6N$: C, 63.15; H, 6.41; N, 3.86. Found: C, 62.99; H, 6.37; N, 3.86.

***meso*-(3*R*,5*R*,7*S*)-3,7-Diacetoxy-5-((*tert*-butyloxycarbonyl)amino)cyclohept-1-ene (18).** Amine **16** (2.00 g, 8.80 mmol) was dissolved in ethyl acetate (20 mL). A saturated aqueous solution of sodium bicarbonate was added (10 mL) followed by addition of di-*tert*-butyl dicarbonate (2.30 g, 10.5 mmol). The solution was stirred at 25 °C for 3 h after which time water (10 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined ethyl acetate extracts were dried over magnesium sulfate and filtered, and the solvent was removed under reduced pressure. The crude carbamate was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to provide **18** (2.80 g, 97%) as a white crystalline solid: mp 119–120 °C; IR (cm^{-1}, $CHCl_3$ solution) ν_{max} 3445, 3020, 1710, 1735, 1500, 1240, 1165, 1030, 725, 670; ^1H NMR δ 5.67 (s, 2 H), 5.34 (dm, J = 10.6 Hz, 2 H), 4.61 (m, 1 H), 2.82 (bs, 2 H), 3.93 (m, 1 H), 2.15 (dm, J = 12.7 Hz, 2 H), 2.05 (s, 6 H), 1.65 (q, J = 11.3 Hz, 2 H), 1.43 (s, 9 H); ^{13}C NMR δ 20.9, 28.2, 38.9, 46.8, 69.7, 79.4, 132.2, 154.4, 169.7; MS {EI} m/z 57 (100), 69 (11), 81 (26), 108 (44), 125 (7), 151 (16), 168 (20), 211 (24), 256 (4). Anal. Calcd for $C_{16}H_{25}O_6N$: C, 58.70; H, 7.70; N, 4.28. Found: C, 58.59; H, 7.60; N, 4.32.

***meso*-(1*R*,4*S*,6*R*)-6-((Benzyloxycarbonyl)amino)cyclohept-2-ene-1,4-diol (19).** Diacetate **17** (700 mg, 1.94 mmol) was dissolved in methanol (20 mL). Potassium carbonate (50 mg, 0.36 mmol) was added and the suspension stirred for 2 h. Silica gel was added and the solvent removed under reduced pressure. The crude diol was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to provide **19** (510 mg, 95%) as a white crystalline solid: mp 174–176 °C; IR (cm^{-1}, KBr) ν_{max} 3310, 3090, 3065, 2945, 2930, 2855, 1690, 1550, 1455, 1370, 1335, 1290, 1220, 1100, 1030, 1010, 735, 695;.^1H NMR (CD_3OD) δ 7.32 (m, 6 H), 5.64 (s, 2 H), 5.05 (s, 2 H), 4.22 (d, J = 10.7 Hz, 2 H), 3.76 (tm, J = 11.6 Hz, 1 H), 2.00 (d, J = 12.1 Hz, 2 H), 1.47 (q, J = 11.6 Hz, 2 H); ^{13}C NMR (CD_3OD) δ 43.8, 49.6, 67.3, 68.6, 128.8, 128.9, 129.4, 136.1, 138.4, 157.6; MS {CI} m/z 91 (100), 108 (21), 124 (10), 135 (3), 152 (26), 170 (28), 216 (13), 242 (3), 260 (2), 278 [M + H] (2); HRMS calcd for $C_{15}H_{19}O_4N$–OBn 170.0817$_0$, found 170.0821. Anal. Calcd for $C_{15}H_{19}O_4N$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.61; H, 6.84; N, 5.05.

***meso*-(1*R*,4*S*,6*R*)-6-((*tert*-Butyloxycarbonyl)amino)cyclohept-2-ene-1,4-diol (20).** Diacetate **18** (3.50 g, 10.7 mmol) was dissolved in methanol (50 mL). Potassium carbonate (148 mg, 1.07 mmol) was added and the suspension stirred for 4 h. Silica gel was added and the solvent removed under reduced pressure. The crude diol was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to provide **20** (2.51 g, 97%) as a white crystalline solid: mp 163–165 °C; IR (cm^{-1}, KBr) ν_{max} 3320, 2965, 2935, 1675, 1540, 1445, 1430, 1390, 1370, 1255, 1175, 1115, 1040, 995, 955, 865, 755, 695; ^1H NMR (CD_3OD) δ 6.76 (d, J = 2.4 Hz, 1 H), 5.63 (s, 2 H), 4.20 (d, J = 10.2 Hz, 2 H), 3.66 (m, 1 H), 1.96 (d, J = 11.4 Hz, 2 H), 1.42 (bs, 11 H); ^{13}C NMR (CD_3OD) δ 28.8, 43.9, 49.1, 68.7, 80.0, 136.1, 157.2. MS {CI} m/z 81 (8), 91 (26), 108 (13), 126 (33), 144 (100), 170 (44), 188 (49), 244 [M + H] (31); HRMS calcd for $C_{12}H_{21}O_4N$ – t-BuOH: 169.0739, found 169.0743. Anal. Calcd for $C_{12}H_{21}O_4N$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.10; H, 8.70; N, 5.77.

(1*R*,4*S*,6*R*)-4-Acetoxy-6-((benzyloxycarbonyl)amino)cyclohept-2-en-1-ol (21). Diol **19** (220 mg, 0.79 mmol) and Amano P-30 lipase (330 mg) were added to a round-bottomed flask charged with isopropenyl acetate (11 mL) and *tert*-butyl methyl ether (3 mL). The suspension was heated at 50 °C for 86 h while being stirred continuously. The biocatalyst was removed by filtration and rinsed with ethyl acetate. The filtrate was removed under reduced pressure, and the crude product was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to give **21** (232 mg, 91%) as a white crystalline solid: mp 144–146 °C; $[\alpha]^{25}_D$ = +21.7 (*c* 0.97, $CHCl_3$). IR (cm^{-1}, KBr) ν_{max} 3315, 3070, 3035, 2940, 2890, 2850, 1730, 1690, 1545, 1455, 1430, 1375, 1340, 1290, 1290, 1270, 1230, 1100, 1035, 915, 735, 695; ^1H NMR δ 7.33 (bs, 5 H), 5.78 (d, J = 12.0 Hz, 1 H), 5.60 (d, J = 12.1 Hz, 1 H), 5.31 (d, J = 11.0 Hz, 1 H), 5.14 (d, J = 8.1 Hz, 1 H), 5.07 (bs, 2 H), 4.38 (d, J = 9.5 Hz, 1 H), 3.97 (m, 1 H), 2.56 (bs, 1 H), 2.13 (d, J = 11.4 Hz, 2 H), 2.05 (s, 3 H), 1.64 (m, 2 H); ^{13}C NMR δ 21.1, 39.0, 42.3, 47.6, 66.7, 67.5, 69.9, 128.1, 128.5, 131.3, 135.8, 136.3, 155.2, 170.1; MS {CI} m/z 91 (100), 108 (22), 135 (6), 152 (24), 171 (8), 198 (12), 216 (22), 242 (8), 260 (34), 302 (6), 320 [M + H] (2); HRMS calcd for $C_{17}H_{21}O_5N$ – H_2O 301.1313$_9$, found 301.1310. Anal. Calcd for $C_{17}H_{21}O_5N$: C, 63.94 H, 6.63; N, 4.39. Found: C, 63.79; H, 6.57; N, 4.43.

(1*R*,4*S*,6*R*)-4-Acetoxy-6-((*tert*-butyloxycarbonyl)amino)cyclohept-2-en-1-ol (22). Diol **20** (2.51 g, 10.3 mmol) and Amano P-30 lipase (2.50 g) were added to a round-bottomed flask charged with isopropenyl acetate (140 mL) and *tert*-butyl methyl ether (40 mL). The suspension was heated at 50 °C for 42 h while being stirred continuously. The biocatalyst was removed by filtration and rinsed with ethyl acetate. The filtrate was removed under reduced pressure, and the crude product was purified by column chromatography (2:1 petroleum ether:ethyl acetate) to give **22** (2.71 g, 92%) as a white crystalline solid: mp 145–146 °C; $[\alpha]^{25}_D$ = +19.6 (*c* 1.00, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3355, 2975, 2935, 2890, 2850, 1730, 1675, 1520, 1460, 1375, 1340, 1250, 1170, 1110, 1095, 1035, 1005, 915, 860; ^1H NMR δ 5.76 (d, J = 12.0, 1 H), 5.55 (d, J = 12.0 Hz, 1 H), 5.25 (d, J = 10.0 Hz, 1 H), 4.86 (d, J = 8.1 Hz, 1 H), 4.35 (d, J = 9.8 Hz, 1 H), 3.83 (m, 1 H), 3.05 (bs, 1 H), 2.08 (d, J = 12.3 Hz, 2 H), 2.03 (s, 3 H), 1.57 (q, J = 11.4 Hz, 2 H), 1.40 (s, 9 H); ^{13}C NMR δ 21.1, 28.3, 39.1, 42.6, 47.2, 67.5, 70.1, 79.5, 131.0, 136.1, 154.7, 170.1; MS {EI} m/z 57 (100), 69 (7), 81 (30), 91 (8), 108 (29), 126 (39), 152 (13), 169 (10), 212 (6), 286 [M + H] (1); HRMS calcd for $C_{14}H_{23}O_5N$ + H 286.1654, found 286.1650. Anal. Calcd for $C_{14}H_{23}O_5N$: C, 58.93 H, 8.12; N, 4.91. Found: C, 59.01; H, 8.19; N, 4.87.

(3*S*,5*S*,7*R*)-3-Acetoxy-7-(benzoyloxy)-5-((methylsulfonyl)oxy)cyclohept-1-ene. Alcohol **23**[13] (1.10 g, 3.79 mmol), dichloromethane (20 mL), and triethylamine (1.09 mL, 7.81 mmol) were added to a round-bottomed flask and cooled to 0 °C. Methanesulfonyl choride (0.44 mL, 5.67 mmol) was

added dropwise over 10 min. After 10 min of additional stirring, water (30 mL) was added to the reaction mixture. The layers were separated, and the organic layer was washed with saturated aqueous ammonium chloride (30 mL). The aqueous washes were back-extracted with dicholormethane (30 mL). The combined dichloromethane extracts were dried over sodium sulfate and filtered. The dichloromethane was removed under reduced pressure to provide the title mesylate (1.33 g, 95%) as a colorless oil: $[\alpha]^{25}_D = +16.8$ (*c* 0.51, $CHCl_3$); IR (cm^{-1}) ν_{max} 3030, 2940, 1740, 1720, 1450, 1450, 1355, 1270, 1240, 1180, 1115, 1030, 975, 900, 720; ^1H NMR δ 8.00 (d, J = 7.7 Hz, 2 H), 7.55 (m, 1 H), 7.42 (t, J = 7.6 Hz, 2 H), 5.93–5.67 (m, 4 H), 5.31 (m, 1 H), 3.13 (s, 3 H), 2.42–2.14 (m, 4 H), 2.03 (s, 3 H); ^{13}C NMR δ 20.9, 37.6, 38.9, 67.4, 67.9, 75.5, 128.3, 129.5, 131.7, 132.4, 132.8, 165.2, 179.8; MS {CI} *m/z* 91 (15), 105 (100), 123 (4), 151 (10), 213 (6), 247 (30), 273 (22), 309 [M−OAc] (26); HRMS calcd for $C_{17}H_{20}O_7S$ − OAc 309.0797, found 309.0799.

(3*S*,5*R*,7*R*)-3-Acetoxy-5-azido-7-(benzoyloxy)cyclohept-1-ene (24). The above mesylate (1.16 g, 3.14 mmol) and sodium azide (0.61 g, 9.42 mmol) were added to a round-bottomed flask charged with dry DMF (25 mL). The solution was heated at 70 °C while being stirred for 8 h. Water (100 mL) was added, and the product was extracted with petroleum ether:diethyl ether (1:1) (3 × 75 mL). The organic extracts were dried over magnesium sulfate and filtered. The crude product was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **24** (0.78 g, 79%) as a waxy solid: mp 70–72 °C; $[\alpha]^{25}_D = +19.6$ (*c* 1.08, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3425, 3065, 3035, 2930, 2870, 2095, 1740, 1720, 1585, 1450, 1370, 1315, 1270, 1255, 1240, 1180, 1110, 1070, 1025, 990,715, 685; ^1H NMR δ 8.04 (d, J = 7.5 Hz, 2 H), 7.56 (m, 1 H), 7.43 (t, J = 7.6 Hz, 2 H), 5.84 (dm, J = 12.0 Hz, 1 H), 5.74 (dm, J = 12.1 Hz, 1 H), 5.58 (dm, J = 11.0 Hz, 1 H), 5.39 (dm, J = 11.0 Hz, 1 H), 3.81 (tt, J = 11.2, 3.6 Hz, 1 H), 2.31 (dm, J = 12.5 Hz, 1 H), 2.21 (dm, J = 12.1 Hz, 1 H), 2.07 (s, 3 H), 1.82 (m, 2 H); ^{13}C NMR δ 20.9, 37.6, 56.5, 68.9, 69.4, 128.3, 129.5, 129.6, 131.9, 133.1, 165.2, 169.7; MS {CI} *m/z* 61 (5), 80 (5), 91 (7), 105 (76), 124 (19), 228 (100), 256 (64), 273 [M − N_3] (5). Anal. Calcd for $C_{16}H_{17}O_4N_3$: C, 60.94; H, 5.43; N, 13.33. Found: C, 61.63; H, 5.46; N, 13.19.

(3*S*,5*R*,7*R*)-3-Acetoxy-7-(benzoyloxy)-5-((*tert*-butyloxycarbonyl)amino)cyclohept-1-ene (25). A. Azide **24** (610 mg, 1.93 mmol) and di-*tert*-butyl dicarbonate (545 mg, 2.50 mmol) were dissolved in a mixture of ethanol (10 mL) and ethyl acetate (2 mL). Lindlar catalyst was added (700 mg) and the flask evacuated and flushed with hydrogen gas. The suspension was stirred in an atmosphere of hydrogen gas for 5 h while being protected from light (wrap flask with foil). The suspension was filtered through a pad of Celite to remove the Lindlar catalyst, and the solvent was removed under reduced pressure. The crude carbamate was purified by column chromatography (5:1 petroleum ether:ethyl acetate) to give **25** (640 mg, 85%) as a white crystalline solid: mp 169–171 °C; $[\alpha]^{25}_D = +29.1$ (*c* 1.08, $CHCl_3$).

B. Alcohol **22** (107 mg, 0.38 mmol) and DMAP (small crystal) were dissolved into dry dichloromethane (4 mL). Pyridine (45 mg, 0.56 mmol) was added dropwise followed by addition of benzoyl chloride (54 mg, 0.38 mmol). The solution was stirred at room temperature for 12 h. A saturated aqueous solution of ammonium chloride (5 mL) and dichloromethane (20 mL) was added, and the layers were separated. The organic layer was washed with 2 N HCl (10 mL), dried over magnesium sulfate, and filtered and the crude product purified by column chromatography (5:1 petroleum ether:ethyl acetate) to give **25** (120 mg, 82%) as a white crystalline solid: mp 169–172 °C; $[\alpha]^{25}_D = +29.9$ (*c* 1.42, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3365, 3010, 2990, 2975, 2935, 2900, 1735, 1715, 1680, 1525, 1450, 1370, 1395, 1210, 1275, 1240, 1170, 1105, 1070, 1025, 985, 715; ^1H NMR δ 8.03 (d, J = 7.5 Hz, 2 H), 7.56 (m, 1 H), 7.44 (t, J = 7.6 Hz, 2 H), 5.84 (dm, J = 12.0 Hz, 1 H), 5.74 (dm , J = 12.2 Hz, 1 H), 5.61 (dm, J = 10.4 Hz, 1 H), 5.41 (dm, J = 9.1 Hz, 1 H), 4.71 (bm, 1 H), 4.02 (bm, 1 H), 2.31 (dm, J = 12.3 Hz, 1 H), 2.22 (dm, J = 12.5 Hz, 1 H), 2.07 (s, 3 H), 1.79 (m, 2 H), 1.42 (s, 9 H); ^{13}C NMR δ 21.0, 28.3, 39.0, 39.1, 46.8, 69.8, 70.3, 79.5, 128.3, 129.6, 129.7, 129.9, 132.2, 132.5, 133.0, 154.4, 165.3, 169.8; MS {EI} *m/z* 57 (83), 69 (7), 81 (30), 91 (8), 105 (100), 124 (10), 151 (17), 168 (14), 211 (18), 230 (15), 273 [M − NHBOC] (17). Anal. Calcd for $C_{21}H_{27}O_6N$: C, 64.77; H, 6.99; N, 3.60. Found: C, 64.50; H, 6.94; N, 3.58.

(3*S*,5*R*,7*S*)-3-Acetoxy-5-((benzyloxycarbonyl)amino)-7-(phenylseleno)cyclohept-1-ene (28). Alcohol **21** (508 mg, 1.59 mmol), dichloromethane (10 mL) and triethylamine (0.33 mL, 2.39 mmol) were added to a round-bottomed flask and cooled to 0 °C. Methanesulfonyl choride (0.15 mL, 1.91 mmol) was added dropwise over 15 min. After 10 min of additional stirring, water (10 mL) was added to the reaction mixture. The layers were separated, and the organic layer was washed with saturated aqueous ammonium chloride (10 mL). The aqueous washes were back-extracted with dicholormethane (15 mL). The combined dichloromethane extracts were dried over $NaSO_4$ and filtered. The dichloromethane was removed under reduced pressure to provide crude mesylate **27** as an oil: IR (cm^{-1}) ν_{max} 3340, 3080, 3055, 3030, 2935, 1730, 1525, 1455, 1355, 1335, 1240, 1175, 1025, 960, 910, 800; 700; ^1H NMR δ 7.30 (bs, 5 H), 5.81 (d, J = 12.1 Hz, 1 H), 5.72 (d, J = 11.9 Hz, 1 H), 5.38 (m, 1 H), 5.29 (d, J = 10.8 Hz, 1 H), 5.23 (d, J = 10.2 Hz, 1 H), 5.04 (s, 2 H), 4.02 (m, 1 H), 2.97 (s, 3 H), 2.29 (dm, J = 12.6 Hz, 1 H), 2.13 (dm, J = 11.8 Hz, 1 H), 2.02 (s, 3 H), 1.87 (m, 1 H), 1.69 (m, 1 H); ^{13}C NMR δ 20.7, 31.3, 38.2, 38.4, 39.3, 46.6, 66.4, 69.1, 76.6, 127.8, 127.9, 128.3, 130.0, 133.8, 136.1, 154.9, 169.6. A suspension of diphenyl diselenide (496 mg, 1.59 mmol) in absolute ethanol (10 mL) was cooled to 0 °C. Sodium borohydride was added in small portions until the solution was colorless.[17] The above mesylate **27** was dissolved into absolute ethanol (5 mL) and added *via* cannula to the selenide solution. The solution was allowed to stir for 3 h. The reaction mixture was concentrated, and the residue was dissolved into ethyl acetate (25 mL), which was washed with saturated aqueous sodium bicarbonate (2 × 10 mL). The ethyl acetate was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The crude selenide was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to provide **28** (729 mg, 85% two steps) as a crystalline solid: mp 97–99 °C; $[\alpha]^{25}_D = -146.8$ (*c* 0.98, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3445, 3070,3035, 2930, 1745, 1550, 1505, 1475, 1235, 1220, 1075, 1005, 980; ^1H NMR δ 7.66 (m, 2 H), 7.40–7.27 (m, 8 H), 5.93 (m, 1 H), 5.68 (dd, J = 11.8, 2.1 Hz, 1 H), 5.53 (dm, J = 9.5 Hz, 1 H), 5.10 (s, 2 H), 4.84 (m, 1 H), 4.43 (m, 1 H), 4.04 (m, 1 H), 2.33 (d, J = 11.9 Hz, 1 H), 2.14 (dm, J = 9.3 Hz, 1 H), 2.06 (s, 3 H), 1.93 (m, 1 H), 1.76 (m, 1 H); ^{13}C NMR δ 21.2, 38.6, 39.3, 39.7, 47.0, 66.6, 69.7, 128.1, 128.5, 129.0, 129.1, 131.2, 134.1, 135.6, 136.4, 155.1, 169.8; MS {EI} *m/z* 51 (5). 78 (13), 91 (100), 108 (11), 158 (7), 198 (9), 242 (9), 302 (8), 399 [M − AcOH] (2); HRMS calcd for $C_{23}H_{25}O_4NSe$ − AcOH 399.0737$_3$, found 399.0745. Anal. Calcd for $C_{23}H_{25}O_4NSe$: C, 60.26; H, 5.50; N, 3.06. Found: C, 59.90; H, 5.40; N, 2.93.

(1*S*,2*S*,6*S*)-6-((Benzyloxycarbonyl)amino)cyclohept-3-ene-1,2-diol (30). Selenide **28** (800 mg, 1.75 mmol) was dissolved into THF (15 mL) and dichloromethane (15 mL) and cooled to −78 °C. While the selenide solution was being stirred, 30% H_2O_2 (2.0 mL, 17.5 mmol) was added and stirring was continued for 3 h, after which time the solution was allowed to slowly warm to room temperature over 3 h. Dichloromethane (50 mL) was added, and the entire mixture was washed with saturated aqueous sodium bicarbonate (50 mL). The dichloromethane solution was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to provide monoacetate **29** (500 mg, 90%) as mixture of isomers (acetate migration): mp 143–153 °C; HRMS calcd for $C_{17}H_{21}O_5N$ 319.1419, found 319.1413.

The monoacetate mixture **29** (500 mg, 1.566 mmol) was dissolved into methanol (50 mL) after which K_2CO_3 (216 mg, 1.566 mmol) was added. The solution was stirred for 25 min. Silica gel was added to the solution and the solvent removed under reduced pressure. The crude diol was purified by column chromatography (ethyl acetate) to give **30** (434 mg, 100%) as a white crystalline solid: mp 158–159 °C; $[\alpha]^{25}_D = -49.3$ (*c* 0.99, MeOH); IR (cm^{-1}, KBr) ν_{max} 3475, 3300, 3200,

3055, 3020, 2950, 2850, 2835, 1680, 1545, 1290, 1235, 1055, 1010, 695; ^{1}H NMR (CD_3OD) δ 7.32 (m, 5 H), 5.75–5.55 (m, 2 H), 5.05 (s, 2 H), 4.00 (d, J = 8.9 Hz, 1 H), 3.35 (m, 2 H), 2.27 (dm, J = 12.9 Hz, 2 H), 2.06 (tm, J = 11.5 Hz, 1 H), 1.66 (m, 1 H); ^{13}C NMR (CD_3OD) δ 35.6, 45.1, 67.3, 72.0, 75.7, 126.8, 128.8, 129.0, 129.5, 136.7, 138.4, 157.8; MS {CI} m/z 91 (100), 108 (32), 126 (14), 152 (32), 170 (73), 198 (9), 216 (32), 234 (86), 260 (45), 278 [M + H] (73). Anal. Calcd for $C_{15}H_{19}O_4N$: C, 64.97; H, 6.91. Found: C, 64.95; H, 6.89.

(1*S*,5*S*,7*S*)-5-((Benzyloxycarbonyl)amino)-9,9-dimethyl-8,10-dioxabicyclo[5.3.0]cyclodec-2-ene (31). Diol **30** (145 mg, 0.523 mmol) was dissolved in acetone (3 mL) and 2,2-dimethoxypropane (3 mL). A small crystal of *p*-toluenesulfonic acid was added, and the solution was stirred at room temperature for 15 min. Silica gel was added to the solution and the solvent removed under reduced pressure. The residue was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **31** (157 mg, 95%) as an oil: $[\alpha]^{25}_D = -0.5$ (c 0.75, $CHCl_3$); $[\alpha]^{25}_{334} = -44.8$ (c 0.75, $CHCl_3$); IR (cm^{-1}) ν_{max} 3330, 3065, 3035, 2985, 2935, 2890, 2840, 1695, 1530, 1455, 1370, 1275, 1230, 1170, 1130, 1085, 1010, 870, 735, 700; ^{1}H NMR δ 7.33 (bs, 5 H), 5.93 (d, J = 10.8 Hz, 1 H), 5.75 (bm, 1 H), 5.08 (bs, 3 H), 4.31 (d, J = 8.4 Hz, 1 H), 3.50 (m, 2 H), 2.50 (m, 2 H), 2.10 (m, 1 H), 1.66 (m, 1 H), 1.41 (s, 6 H); ^{13}C NMR δ 26.9, 35.0, 39.8, 46.6, 66.7, 76.2, 80.0, 108.9, 126.1, 128.2, 128.5, 131.4, 136.3, 155.2; MS {EI} m/z 65 (6), 79 (8), 91 (100), 108 (10), 124 (5), 152 (2), 170 (3), 259 (4), 317 [M$^+$] (9); HRMS calcd for $C_{18}H_{23}O_4N$ 317.1627, found 317.1630.

(1*R*,5*S*,7*S*)-5-((Benzyloxycarbonyl)amino)-9,9-dimethyl-8,10-dioxabicyclo[5.3.0]cyclodecan-2-one (32). A thexylborane solution was prepared by adding 2,3-dimethyl-2-butene (499 mg, 5.813 mmol, 0.7 mL) to diethyl ether (5 mL). This solution was cooled to 0 °C, BH_3–DMS (1.938 mmol, 0.2 mL of 10M solution) was added, and the mixture was stirred for 30 min with the ice bath removed after 15 min. Olefin **31** (410 mg, 1.292 mmol) was dissolved into diethyl ether (3 mL) and added dropwise to the thexylborane solution cooled to −30 °C. The mixture was stirred for 4 h at −15 °C after which 30% H_2O_2 (0.8 mL) and 2 N NaOH (0.8 mL) was added. The reaction mixture was stirred for 2 h, and then the layers were separated. Saturated aqueous NaCl (10 mL) was added, and the mixture was extracted with diethyl ether (3 × 20 mL). The combined diethyl ether was dried over magnesium sulfate and the solvent removed under reduced pressure. The residue was purified by column chromatography (1:1 petroleum ether:ethyl acetate) to provide a mixture of stereo- and regioisomeric alcohols. These alcohols (345 mg, 1.028 mmol) were dissolved into dichloromethane (10 mL) to which 4 Å molecular sieves (300 mg, crushed) was added. PCC (333 mg, 1.543 mmol) was added and the suspension stirred for 19 h. Diethyl ether (10 mL) was added, and the slurry was filtered through a bed of silica gel. The solvent was removed under reduced pressure, and the crude regioisomeric ketones were separated by column chromatography (3:1 petroleum ether:ethyl acetate) to give the desired ketone **32** (147 mg, 34% from olefin) as a low melting solid: mp 42–46 °C; $[\alpha]^{25}_D = -17.8$ (c 0.41, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3340, 3035, 2985, 2935, 2900, 2870, 1720, 1530, 1455, 1375, 1315, 1270, 1235, 1090, 1015, 870, 780, 700; ^{1}H NMR δ 7.36 (bs, 5 H), 5.10 (bs, 2 H), 4.94 (m, 1 H), 4.56 (d J = 9.7 Hz, 1 H), 3.88 (tm, J = 9.0 Hz, 1 H), 3.67 (m, 1 H), 2.71–2.57 (m, 2 H), 2.49 (m, 1 H), 2.10 (m, 1 H), 1.93–1.60 (m, 2 H), 1.45 (s, 3 H), 1.43 (s, 3 H); ^{13}C NMR δ 26.2, 26.9, 30.0, 38.7, 39.5, 49.6, 66.8, 74.0, 85.5, 110.5, 128.0, 128.2, 128.5, 136.1, 155.1, 203.9; MS {CI} m/z 91 (100), 124 (7), 140 (7), 168 (7), 184 (7), 209 (7), 232 (70), 276 (42), 290 (14), 316 (70), 334 [M + H] (21); HRMS calcd for $C_{18}H_{23}O_5N - CH_3$ 318.1341, found 318.1337.

(1*S*,5*R*,7*S*)-5-((Benzyloxycarbonyl)amino)-9,9-dimethyl-8,10-dioxabicyclo[5.3.0]cyclodecan-3-one (33), also produced (117 mg, 27% from olefin) in the above experiment, was isolated as a solid: mp 117–118 °C; $[\alpha]^{25}_D = +24.0$ (c 0.35, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3340, 2995, 2950, 2935, 2895, 2870, 1710, 1690, 1540, 1455, 1375, 1310, 1280, 1215, 1170, 1075, 1020, 690; ^{1}H NMR δ 7.35 (bs, 5 H), 5.10 (bs, 2 H), 4.98 (d, J = 7.2 Hz, 1 H), 4.07 (m, 1 H), 3.81 (m, 1 H), 3.60 (m, 1 H), 3.04 (ddm, J = 17.6, 5.5 Hz, 1 H), 2.71 (m, 2 H), 2.50 (m, 2 H), 1.75 (m, 1 H), 1.42 (s, 3 H), 1.40 (s, 3 H); ^{13}C NMR δ 26.9, 27.0, 38.8, 45.4, 46.5, 51.2, 66.9, 75.7, 78.2, 109.0, 128.2, 128.3, 128.6, 136.1, 154.9, 204.9; MS {EI} m/z 65 (9), 91 (100), 108 (14), 141 (6), 184 (4), 275 (20), 333 [M$^+$] (4); HRMS calcd for $C_{18}H_{23}O_5N$ 333.1576$_1$, found 333.1580. Anal. Calcd for $C_{18}H_{23}O_5N$: C, 64.83; H, 6.96; N, 4.20. Found: C, 64.64; H, 7.05; N, 3.99.

***ent*-Calystegine A_3 Hydrochloride [(1*S*,2*R*,3*S*,5*S*)-8-Azabicyclo[3.2.1]cyclooctane-1,2,3-triol Hydrochoride] (34).** Carbamate **33** (165 mg, 0.495 mmol) was dissolved in ethyl acetate (5 mL), and 10% palladium on carbon (50 mg) was added after which time the flask was evacuated and filled with hydrogen gas (a balloon was placed through septum to maintain hydrogen atmosphere). The reaction mixture was stirred for 1 h. The Pd/C was removed by filtering the reaction mixture through a pad of Celite. The solvent was removed under reduced pressure. The crude amine was dissolved into THF (2 mL), and water (0.1 mL) was added. Concentrated hydrochloric acid (3–4 drops) was then added, and the solution was stirred at room temperature for 15 h. The solvent was then removed under reduced pressure to yield the crude hydrochloride salt, which was purified by recrystalization from methanol/petroleum ether to provide **34** (80 mg, 83% from carbamate) as a white crystalline solid: mp 171–173 °C dec; $[\alpha]^{25}_D = +12.4$ (c 0.33, H_2O); IR (cm^{-1}, KBr) ν_{max} 3415, 3310, 2960, 1610, 1475, 1395, 1285, 1255, 1110, 1075, 1060, 1020, 990, 975, 815, 765, 620, 560; ^{1}H NMR (D_2O) δ 4.02 (m, 1 H), 3.83 (m, 1 H), 3.73 (m, 1 H), 2.32 (m, 2 H), 2.19 (m, 1 H), 1.83 (m, 3 H); ^{13}C NMR (D_2O) δ 25.3, 26.8, 35.0, 53.0, 68.2, 76.3, 93.7.

***ent*-Calysategine A_3 [(1*S*,2*R*,3*S*,5*S*)-8-Azabicyclo[3.2.1]-cyclooctane-1,2,3-triol] (26).** The hydrochloride salt **34** (50 mg) was dissolved into D_2O (1 mL) and placed into NMR tube. The initial pH of this solution was 5.0. The solution was treated with sodium hydroxide (2 N in D_2O) to increase the pH to >11: ^{1}H NMR (D_2O) δ 3.66 (m, 1 H), 3.40 (m, 1 H), 3.34 (m, 1 H), 2.04–1.90 (m, 3 H), 1.53–1.38 (m, 3 H); ^{13}C NMR (D_2O) δ 29.0, 31.5, 42.2, 53.7, 72.3, 82.3, 93.0 [lit.[1a] for enantiomer, see data under **3** below).

(3*S*,5*R*,7*R*)-3-Acetoxy-5-((benzyloxycarbonyl)amino)-7-((*tert*-butyldimethylsilyl)oxy)cyclohept-1-ene (35). Alcohol **21** (1.30 g, 4.0 mmol) was added to a round-bottomed flask. Imidazole (0.30 g, 4.5 mmol) was dissolved into DMF (2.0 mL) and was added to the flask cooled to 0 °C. The *tert*-butyldimethylsilyl chloride (0.72 g, 4.8 mmol) was added to the flask at 0 °C and stirred for 30 min. The solution was allowed to warm to room temperature and stirred for an additional 2 h. Water (15 mL) and dichloromethane (20 mL) were added and the layers separated. The dichloromethane was dried over magnesium sulfate and then filtered. The solvent was removed under reduced pressure, and the crude product was purified using column chromatography (10:1 petroleum ether:ethyl acetate) to provide **35** (1.71 g, 99%) as a white crystalline solid: mp 68–70 °C; $[\alpha]^{25}_D = +19.2$ (c 1.21, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 2955, 2930, 2855, 1740(b), 1525, 1370, 1250, 1100, 1060, 1025; ^{1}H NMR δ 7.34 (bs, 5 H), 5.74 (dm, J = 11.7 Hz, 1 H), 5.59 (dm, J = 10.5 Hz, 1 H), 5.32 (dm, J = 9.8 Hz, 1 H), 5.09 (s, 2 H), 4.35 (m, 1 H), 4.02 (m, 1 H), 2.17–2.04 (m, 2 H), 2.05 (s, 3 H), 1.70 (m, 2 H), 0.89 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR δ −4.9, −4.8, 18.0, 21.1, 25.7, 39.4, 41.8, 47.3, 66.5, 68.5, 69.6, 128.0, 128.0, 128.5, 131.5, 136.3, 136.5, 155.1, 169.9; MS {CI} m/z 75 (5), 91 (100), 117 (30), 152 (5), 198 (22), 242 (40), 272 (18), 302 (23), 330 (5), 376 (31), 434 [M + H] (4); HRMS calcd for $C_{23}H_{35}O_5NSi$ − *tert*-butyl 376.1580, found 376.1586. Anal. Calcd for $C_{23}H_{35}O_5NSi$: C, 63.71; H, 8.14; N, 3.23. Found: C, 63.66; H, 8.17; N, 3.28.

(1*S*,4*R*,6*S*)-6-((Benzyloxycarbonyl)amino)-4-((*tert*-butyldimethylsilyl)oxy)cyclohept-2-en-1-ol (36). Acetate **35** (2.80 g, 6.4 mmol) was dissolved into methanol (30 mL) to which sodium cyanide (50 mg) was added. The solution was allowed to stir at room temperature for 18 h. Removal of the solvent under reduced pressure followed by purification by column chromatography (5:1 petroleum ether:ethyl acetate) provided **36** (2.38 g, 95%) as a waxy solid: mp 57–59 °C; $[\alpha]^{25}_D = 0$ (c 1.01, $CHCl_3$); $[\alpha]^{25}_{334} = +13.1$ (c 1.01, $CHCl_3$); IR (cm^{-1}, KBr) ν_{max} 3410, 3330, 3035, 2955, 2930, 2885, 2855, 1690, 1535, 1470, 1360, 1260, 1220, 1110, 1095, 1055, 1010, 885, 840, 780,

700; ^{1}H NMR δ 7.31 (bs, 5 H), 5.68 (bm, 2 H), 5.44 (d, J = 6.9 Hz, 1 H), 5.06 (bs, 2H), 4.30 (d, J = 9.5 Hz, 2 H), 3.90 (m, 1 H), 3.42 (s, 1 H), 2.13 (d, J = 10.8 Hz, 1 H), 2.01 (d, J = 14.2 Hz, 1 H), 1.62 (m, 2 H), 0.90 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR δ −4.9, 17.9, 25.7, 42.2, 43.0, 47.7, 66.5, 67.3, 68.6, 127.9, 128.3, 134.9, 135.3, 136.3, 155.3; MS {CI} *m/z* 75 (9), 91 (100), 108 (9), 133 (4), 152 (14), 198 (13), 242 (48), 260 (14), 284 (7), 316 (5), 334 (11), 374 (13), 392 [M + H] (11); HRMS calcd for $C_{21}H_{33}O_4NSi$ − *tert*-butyl 334.1474, found 334.1479.

(1*R*,2*R*,6*R*)-6-((Benzyloxycarbonyl)amino)cyclohept-3-ene-1,2-diol (37). Alcohol **36** (1.05 g, 2.68 mmol), dichloromethane (50 mL), and triethylamine (0.77 mL, 5.50 mmol) were added to a round-bottomed flask and cooled to 0 °C. Methanesulfonyl choride (0.31 mL, 4.02 mmol) was added dropwise over 15 min. After 10 min of additional stirring, water (20 mL) was added to the reaction mixture. The layers were separated, and the organic layer was washed with saturated aqueous ammonium chloride (50 mL). The aqueous washes were back-extracted with dicholormethane (25 mL). The combined dichloromethane extracts were dried over sodium sulfate and filtered. The dichloromethane was removed under reduced pressure to provide crude product (1.24 g) as an oil. A suspension of diphenyl diselenide (820 mg, 2.64 mmol) in absolute ethanol (50 mL) was cooled to 0 °C. Sodium borohydride was added in small portions until the solution was colorless. The above mesylate was dissolved into absolute ethanol (10 mL) and added *via* cannula to the selenide solution. The solution was allowed to stir for 3 h. The reaction mixture was concentrated, and the residue was dissolved into ethyl acetate (50 mL), which was washed with saturated aqueous sodium bicarbonate (2 × 30 mL). The ethyl acetate was dried over magnesium sulfate and the solvent removed under reduced pressure to give crude selenide (1.00 g) as a yellow solid. The selenide (1.00 g, 1.89 mmol) was dissolved into THF (20 mL) and dichloromethane (20 mL) and cooled to −78 °C. While the selenide solution was being stirred 30% H_2O_2 (2.1 mL, 18.8 mmol) was added and stirring continued for 3 h, after which time the solution was allowed to slowly warm to room temperature over 3 h. Dichloromethane (60 mL) was added, and the mixture was washed with saturated aqueous sodium bicarbonate (50 mL). The dichloromethane was dried over magnesium sulfate and the solvent removed under reduced pressure to provide the crude silyl ether (500 mg). The silyl ether (500 mg, 1.28 mmol) was dissolved into acetonitrile (1 mL) and cooled to 0 °C. A solution of HF in acetonitrile (0.83 M, 1.7 mL, 1.41 mmol) was added and the solution stirred for 2 h while the temperature increased to 25 °C. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate) to give **37** (351 mg, 47% four steps) as a white cyrstalline solid: mp 158−159 °C; $[\alpha]^{25}_D$ = +49.5 (*c* 0.99, MeOH); IR and ^{1}H and ^{13}C NMR identical to that of enantiomer **30**; HRMS calcd for $C_{15}H_{19}O_4N$ 277.1314, found 277.1309.

(1*R*,5*R*,7*R*)-5-((Benzyloxycarbonyl)amino)-9,9-dimethyl-8,10-dioxabicyclo[5.3.0]cyclodec-2-ene (38). Diol **37** (212 mg, 0.764 mmol) was dissolved in acetone (5 mL). Amberlyst 15 resin (a few granules) was added, and the mixture was stirred at room temperature for 2 h. The resin was removed by filtration, and the crude product was purified by column chromatography (3:1 petroleum ether:ethyl acetate) to give **38** (240 mg, 99%) as an oil: $[\alpha]^{25}_D$ = +0.3 (*c* 1.35, $CHCl_3$); $[\alpha]^{25}_{334}$ = +43.3 (*c* 1.35, $CHCl_3$); IR and ^{1}H and ^{13}C NMR identical to that of enantiomer **31**; HRMS calcd for $C_{18}H_{23}O_4N$: 317.1627, found 317.1630.

(1*S*,5*R*,7*R*)-5-((Benzyloxycarbonyl)amino)-9,9-dimethyl-8,10-dioxabicyclo[5.3.0]cyclodecan-2-one (39). Olefin **38** (448 mg, 1.412 mmol) was dissolved into diethyl ether (10 mL) and cooled to −30 °C. BH_3−THF (0.21 mL, 2.117 mmol) was added dropwise, and this solution was stirred for 2 h at −15 °C and 2 h at 0 °C after which time 30% H_2O_2 (1 mL) and 2 N NaOH (1 mL) were added. The reaction mixture was stirred for 3 h, and then the layers were separated. Saturated NaCl (10 mL) was added to the aqueous phase and was extracted with diethyl ether (3 × 20 mL). The combined diethyl ether was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was isolated by column chromatography (1:1 petroleum ether:ethyl acetate) to provide a mixture of stereo- and regioisomeric alcohols (308 mg). These alcohols (308 mg, 0.918 mmol) were dissolved into dichloromethane (8 mL) to which 4 Å molecular sieves (500 mg, crushed) was added. PCC (297 mg, 1.377 mmol) was added and the suspension stirred for 25 h. Diethyl ether (10 mL) was added and the slurry filtered through a bed of silica gel. The solvent was removed under reduced pressure, and the crude regioisomeric ketones were separated by column chromatography (3:1 petroleum ether:ethyl acetate) to give the desired ketone **39** (126 mg, 27% from olefin) as a low melting solid: mp 44−46 °C; $[\alpha]^{25}_D$ = +18.0 (*c* 1.10, $CHCl_3$); IR and ^{1}H and ^{13}C NMR identical to that of enantiomer **32**.

Calystegine A_3 Hydrochoride [(1*R*,2*S*,3*R*,5*R*)-8-Azabicyclo[3.2.1]octane-1,2,3-triol Hydrochloride] (40). Carbamate **39** (120 mg, 0.360 mmol) was dissolved in methanol (5 mL). Pearlman's catalyst [$Pd(OH)_2$] (small scoop) was added after which the flask was evacuated and filled with hydrogen gas (a balloon was placed through septum to maintain hydrogen atmosphere). The reaction mixture was stirred for 3 h. The palladium was removed by filtering the reaction mixture through a pad of Celite. The solvent was removed under reduced pressure. The crude amine was dissolved into THF (2 mL), and water (0.1 mL) was added. Concentrated hydrochloric acid (3−4 drops) was then added and the solution stirred at room temperature for 5 h. The solvent was then removed under reduced pressure to yield the crude hydrochloride salt, which was purified by recrystallization from methanol/petroleum ether to provide **48** (60 mg, 85% from carbamate) as a white crystalline solid: mp 172 °C dec; $[\alpha]^{25}_D$ = −12.2 (*c* 0.63, H_2O); ^{1}H and ^{13}C NMR identical to that of enantiomer **34**.

Calysategine A_3 [(1*R*,2*S*,3*R*,5*R*)-8-Azabicyclo[3.2.1]-octane-1,2,3-triol] (3). The hydrochloride salt **40** (60 mg) was dissolved into D_2O (1 mL) and placed into an NMR tube. The initial pH of this solution was 5.0. The solution was treated with sodium hydroxide (2 N in D_2O) to increase the pH to >11: ^{1}H NMR (D_2O) δ 3.64 (m, 1 H), 3.38 (m, 1 H), 3.32 (m, 1 H), 2.05−1.90 (m, 3 H), 1.49−1.42 (m, 3 H); ^{13}C NMR (D_2O) δ 29.0, 31.5, 42.2, 53.7, 72.3, 82.2, 93.0 [lit.[1a] ^{1}H NMR δ 3.6 (m, 1 H), 3.4 (m, 1 H), 3.3 (m, 1 H), 1.9−1.4 (m, 3 H); ^{13}C NMR δ 29.1, 31.0, 42.5, 54.0, 72.5, 82.5, 93.0].

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Supplementary Material Available: ^{1}H NMR spectra of compounds **8**, **9**, **12**, **16**, **23**, **30**, **31**, **32**, **34**, **36**, and **3** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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