To conclude, we report the syntheses and complete ^1H and ^{13}C NMR assignments of 17α-propynyl estradiol and its $Co_2(CO)_6$ and $(C_5H_5)_2Mo_2(CO)_4$ derivatives. The proton shifts in the C and D rings of the hormone are discussed in terms of the anisotropy in diamagnetic susceptibility associated with the free and complexed acetylenic fragments.

Experimental Section

NMR spectra were acquired at 11.74 T with a Bruker AM500 spectrometer. Proton spectra (500 MHz) and carbon spectra (125.7 MHz) were observed by using proton and proton/carbon dual probeheads, respectively. All spectra were recorded at 300 K and all chemical shifts measured relative to the chemical shift of tetramethylsilane. Homonuclear chemical shift correlation (COSY) experiments were carried out by using the following pulse sequence: delay-(π/2,^{1}H)-t_1-(π/2,^{1}H)-acquisition. Pulses were phase cycled according to reference 21. A 2-s recycle delay was used: the π/2,^{1}H pulse was 8 μs. A total of 32 transients were collected per unit time; 256 time increments of 1 ms were applied to characterize the t_1 domain and 1024 points were used to characterize t_2. A pseudo echo window function was applied in both t_1 and t_2 following zero filling once in the t_2 domain. Heteronuclear shift correlated experiments were carried out as described previously.[7]

All syntheses were carried out under an atmosphere of argon. Dry tetrahydrofuran and diglyme were distilled from sodium benzophenone ketyl. Infrared data were obtained on Perkin-Elmer 325 and 457 spectrometers.

Synthesis of 17α-Propynylestra-1,3,5(10)-triene-3,17β-diol. Magnesium turnings (2.4 g, 0.1 mol) covered with THF were placed in a three-necked flask fitted with a thermometer and a dropping funnel. Pure ethyl bromide was added dropwise until the magnesium began to react; at this point the remaining ethyl bromide (7 mL, 0.1 mol) was dissolved in 50 mL of THF, and this solution was added dropwise to the reaction mixture. When the addition was complete, a gas inlet tube was fitted to the flask and propyne (13 mL, 0.1 mol) was gradually led from a -78 °C cold trap into the reaction mixture, which was stirred a further 2 h. Estrone (5.44 g, 0.02 mmol) in THF was added to the excess propynyl magnesium complex and the reaction mixture stirred for 4 h. After hydrolysis with aqueous ammonium chloride solution, extraction with ether and recrystallization from H_2O-MeOH, the sole product was the 17α-propynylestradiol (**2**) (5.0 g, 16.1 mmol; 80%), mp 134 °C, exhibiting in the mass spectrum a parent peak at m/z 310.[22] ^1H and ^{13}C data are collected in Tables I and II.

Reaction of 2 with $Cp_2Mo_2(CO)_4$. As described by Curtis,[23] $[CpMo(CO)_3]_2$ (1.1 g, 2.25 mmol) in diglyme was heated under reflux for 2 h to form $[CpMo(CO)_2]_2$. The solution was filtered and cooled, and **2** (0.6 g, 2.25 mmol) was added, and the solution was then heated at 80 °C for 3 h. After removal of solvent, the crude product was purified by TLC on silica gel plates using CH_2Cl_2 as eluent to give **3** (0.74 g, 0.99 mmol; 45%), mp 115 °C dec. The IR in CH_2Cl_2 exhibited ν_{CO} at 1980, 1915, and 1825 cm^{-1}. Anal. Calcd for $C_{35}H_{36}O_6Mo_2$: C, 56.45; H, 4.87. Found: C, 56.82; H, 4.88.

Reaction of 2 with Dicobalt Octacarbonyl. $Co_2(CO)_8$ (0.4 g, 1.1 mmol) in THF (25 mL) was placed in a Schlenk tube, and **2** (0.31 g, 1.0 mmol) in THF (5 mL) was added dropwise and stirred at room temperature for 2 h. After filtration of the solution and evaporation of the solvent, the product was purified by TLC on silica gel plates using CH_2Cl_2/ethyl acetate (2:1) as eluent to give dark red crystals of **4** (0.24 g, 0.4 mmol; 40%), mp 125 °C. The IR in hexane exhibited ν_{CO} at 2088, 2049, 2027, 2024, and 2016 cm^{-1}. Anal. Calcd for $C_{27}H_{26}O_8Co_2$: C, 54.35; H, 4.36. Found: C, 54.41; H, 4.45.

Reaction of $Co_2(CO)_8$ with Mestranol. As with **4**, treatment of mestranol and dicobalt octacarbonyl gave dark red crystals of **5** (62%), mp 140 °C.[24] The IR in cyclohexane exhibited ν_{CO} at 2090, 2050, 2023, 2019, and 2010 cm^{-1}. An analytically pure sample was obtained by recrystallization from ether/petroleum ether. Anal. Calcd for $C_{27}H_{26}O_8Co_2$: C, 54.35; H, 4.36. Found: C, 54.51; H, 4.48.

Acknowledgment. We thank the C.N.R.S. (France) and N.S.E.R.C. (Canada) for financial support.

Registry No. **2**, 101915-79-1; **3**, 101859-58-9; **4**, 101859-59-0; **5**, 93122-00-0; propyne, 74-99-7; estrone, 53-16-7; mestranol, 72-33-3.

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Synthesis of Optically Active Isoquinuclidines Utilizing a Diastereoselectivity Control Element

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Received September 30, 1985

The development of a palladium-mediated cyclization via isomerization using a vinyl epoxide as an initiator and an amine as a terminator led to a facile cyclization to produce isoquinuclidines. The synthesis of the requisite cyclization precursor from (-)-quinic acid led to obtention of the isoquinuclidines in optically pure form. The substitution pattern of the resultant isoquinuclidine would allow further cyclization to either enantiomeric series of the iboga alkaloids. This "pseudo-meso" intermediate then can become a common intermediate to either ibogamine or catharanthine, the latter of particular importance in the synthesis of vinblastine analogues. During this study it has been observed that the olefination of an epoxy ketone proceeds with high geometrical control.

The azabicyclo[2.2.2]octane skeleton is found in many biologically active natural products, including the iboga alkaloids catharanthine (**1**) and ibogamine (**2**) as well as nonindole-containing alkaloids such as the cannivonines

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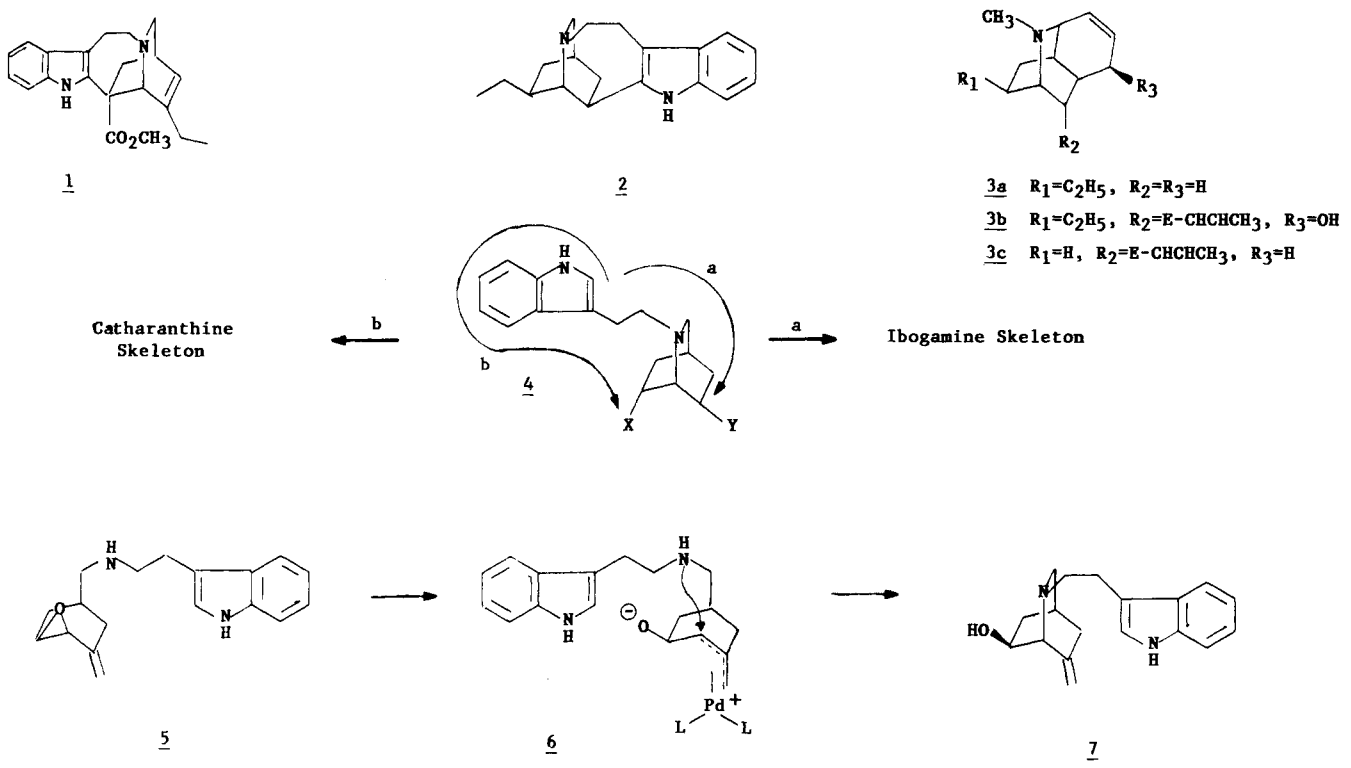

(**3a–c**).[1] These types of compounds are of interest due to their pronounced biological activity and also, in the case of catharanthine, as precursors to more structurally complex alkaloids. For example, catharanthine has been converted both biomimetically[2] and enzymatically[3] into bisindole dimers of the vinblastine class, potent clinical antileukemics. This elegant work has conceptually made available vinblastine analogues for biological testing, based upon the availability of structurally modified catharanthine analogues.

The isoquinuclidine ring system common to these alkaloids appears ideally suited to take advantage of palladium(0)-catalyzed chemistry.[4] With this in mind, we sought to develop methodology for isoquinuclidine formation which would lend itself to an optically active isoquinuclidine synthesis, preferably containing functionality favorably disposed to enter into *both* the catharanthine and ibogamine skeletons, which exist as configurational antipodes. Thus we would need to construct a pseudo-meso intermediate such as **4** which would allow cyclization at either of the two enantiotopic carbons of the isoquinuclidine nucleus.

We envisioned a palladium(0)-catalyzed cyclization of vinyl epoxide **5** as the key step. This system would give an unambiguous cyclization pathway for the π-allyl palladium intermediate, since terminal cyclization would lead to a highly strained bridgehead olefin. The presence of an alcohol group at C(6) and a methylene group at C(8) can permit cyclization at either C(6) or C(8)—thus providing our "pseudo-meso" intermediate as an entry into either optically active series. Thus, in principle, both catharanthine (**1**) and ibogamine (**2**) can be synthesized in optically active form from the same precursor. We have shown that vinyl epoxides serve as palladium(0) substrates under exceptionally mild conditions.[5] However, simple amines have not previously been used as nucleophiles with vinyl epoxides.

A racemic route was first pursued to examine the utility of this new amine cyclization reaction (see Scheme I). The palladium(0) cyclization proved to be extremely facile, requiring only 3 h at 25 °C to go to completion, in 93% isolated yield. As a further example, the (*Z*)-ethylidene vinyl epoxide (**13**), which was the only geometrical isomer obtained in the Wittig condensation of epoxy ketone **10** with ethylidenetriphenylphosphorane,[6] was found to cyclize stereospecifically with palladium(0) in refluxing THF to afford the more sterically congested (*Z*)-ethylidene substituted isoquinuclidine **14** in 91% yield.[7]

On these positive notes, we embarked upon the optically active synthesis, selecting D-(−)-quinic acid (**15**), an inexpensive plant metabolite, as our starting material.[8] This highly functionalized substrate, which has seen only limited use as an optically active synthetic precursor,[9] seemed

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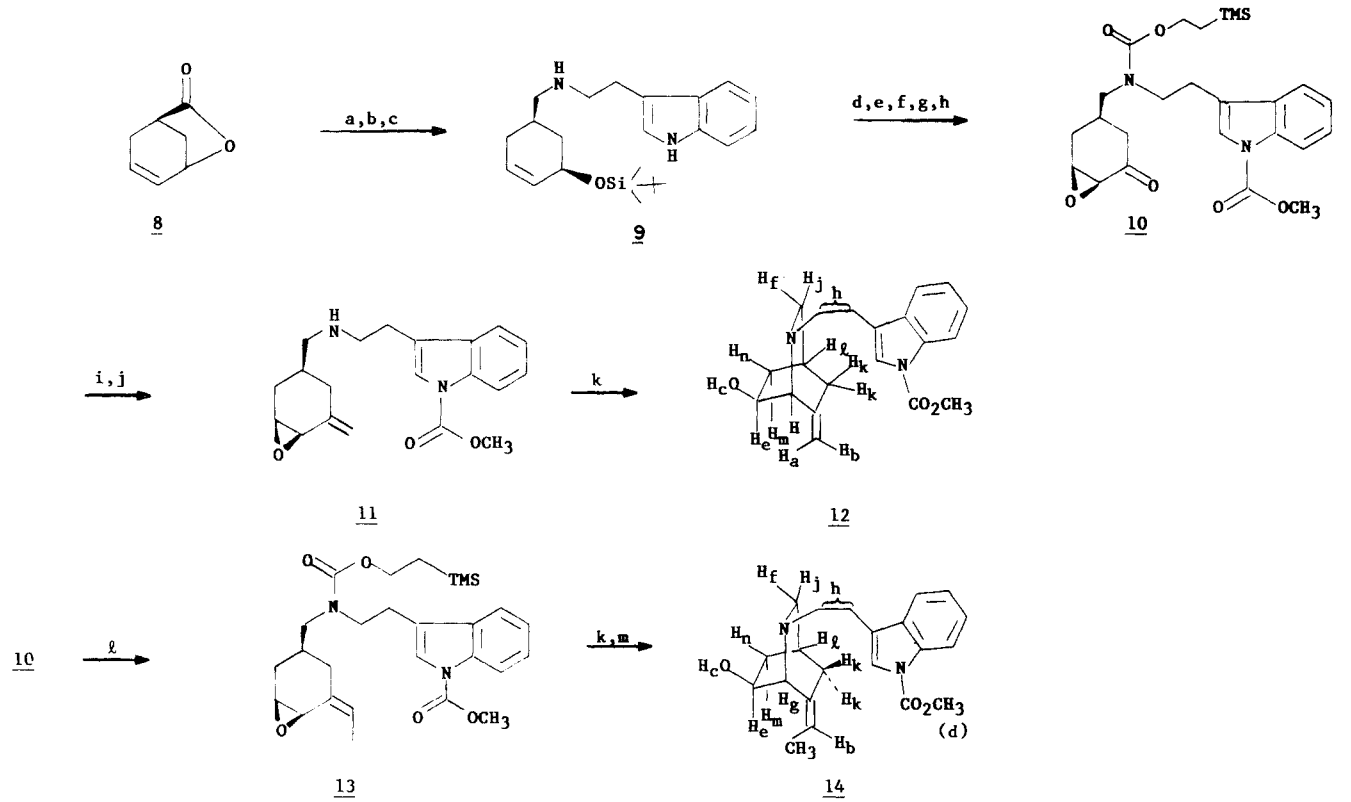
(5) (a) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969. Also see: Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22*, 2575. (b) *N*-Alkylation of indole with vinyl epoxides mediated by Pd(O) has been observed.

(6) Still has described the synthesis of (*Z*)-trisubstituted allylic ethers via the Wittig condensation of hydroxy acetone derivatives. This may be an electronic as well as a steric effect. Streekumar, C.; Darst, K. P.; Still, W. C. *J. Org. Chem.* **1980**, *45*, 4260.

(7) Evidence for this assignment comes from a comparison of the ^{1}H NMR signals from the allylic bridgehead proton in the methylidene **12** and ethylidene **14** isoquinuclidines. This proton resonaates at 3.03 ppm in isoquinuclidine **12** but is deshielded by 0.4 ppm in **14**, coming at 3.43 ppm. This is explained by the steric compression caused by the (*Z*)-allylic methyl. ($A_{1,3}$ crowding).

(8) Sigma Chemical Co., St. Louis, MO.

Scheme I. Racemic Route to Isoquinuclidines[a]



8 9 10 11 12 13 14

[a] (a) Tryptamine, PhCl, 130 °C, 18 h, 87%. (b) TBDMS-Cl, imidazole, DMF, 25 °C, 95%. (c) Redal, THF, 0–60 °C, 100%. (d) $TMSC_2H_4OCOCl$, Et_3N, CH_2Cl_2, 0 °C, 75%. (e) (i) KH, THF, 20 °C; (ii) CH_3OCOCl, 0 °C, 83%. (f) HOAc, H_2O, THF, (3:1:1), 12 h, 25 °C, 79%. (g) MCPBA, $NaHCO_3$, CH_2Cl_2, 0 °C, 90%. (h) 1.1 equiv $(COCl)_2$, 2.2 equiv Me_2SO, 5.0 equiv Et_3N, CH_2Cl_2, −78 to 25 °C, 93%. (i) Ph_3PCH_2, THF, −30 to 25 °C, 77%. (j) 2.0 equiv anhydrous $(n\text{-}C_4H_9)_4NF$, THF, 60 °C, 1 h, 79%. (k) 0.05 equiv $Pd(PPh_3)_4$, THF, 25 °C, 3 h, 93%. (l) Ph_3PCHCH_3, THF, −30 to 25 °C, 87%. (m) as in (k) above, except reflux, 91%.

ideal for the generation of our vinyl epoxide due to the juxtaposition of the secondary hydroxyl groups.

Treatment of D-(−)-quinic acid with dry hydrogen chloride in acetone gave the acetonide which lactonized spontaneously to afford **16** in high yield.[9] The lactone was reduced with LAH to triol **17**, which was converted into the cyclic ortho ester with triethyl orthoformate and a catalytic amount of benzoic acid and thermolyzed neat at 200 °C to obtain olefin **18**.[10] This reaction was remarkably clean when one considers the high concentration of functionality present in the molecule.

Olefin **18** was treated with a variety of hydroborating agents in an attempt to obtain diol **20**, the results of which are summarized in Table I. Hydroboration with borane/dimethyl sulfide complex, alkyl- or dialkylboranes, in THF, followed by basic peroxide oxidation, consistantly gave a 2:1 ratio of diastereomers **20** and **21**.[11]

Table I. Diastereoselectivity of Hydroboration of 18 and 19[d]

R	hydride source[a]	solvent	Lewis acid[b]	20/21
H	$BH_3{\cdot}S(CH_3)_2$	THF		2:1
H	B_2H_6	ether		2:1
H	$(i\text{-}C_4H_9)_2BH$	THF		2:1
H	$(C_6H_{11})_2BH$	THF		2:1
H	disiamylBH	THF		2:1
H	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	(BH_3)	5:1
H	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	Et_2AlCl	9:1
H	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	(1) BuLi (2) Et_2AlCl	dec
H	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	Et_2AlOAr[c]	5:1
H	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	DIBAL-H	3:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$		5:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	Et_2AlOAr[c]	10:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	DIBAL-H	4:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	Et_2AlCl	12:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	Et_2AlOEt	5:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	$(CH_3)_3Al$	12:1
Ac	$BH_3{\cdot}S(CH_3)_2$	$PhCH_3$	$BF_3{\cdot}OEt_2$	dec

[a] 1.0–1.1 molar equiv of hydrometalating reagent used. [b] 1.0–1.1 molar eqquiv of Lewis acid used. [c] OAr = alkoxide of butylated hydroxy toluene (BHT). [d] See ref 11.

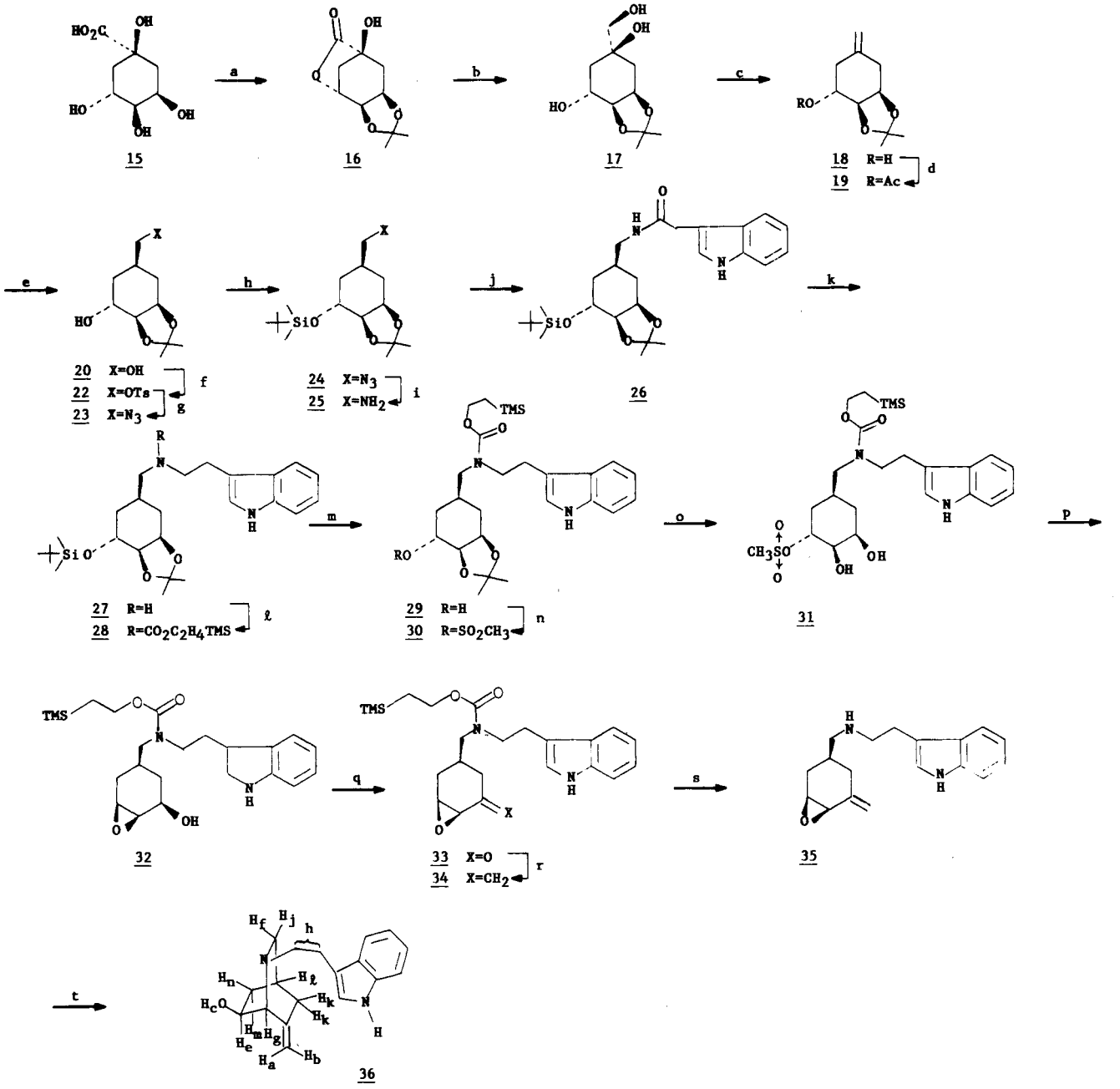
The stereochemistry of the major hydroboration product **20** can be assigned on the basis of NMR coupling constants. The appearance of Hc as a clean dd at δ 3.97 ppm (J = 5.5, 5.2 Hz) supports placing Hc in an equatorial position with two adjacent gauche protons as depicted in

(9) (a) For prostaglandin intermediates: Elliot, J. D.; Kelson, A. B.; Purcell, N.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2441. Barriere, J.-C.; Cleophax, J.; Gero, S. D.; Vuilhorgne, M. *Helv. Chem. Acta* **1983**, *66*, 296. Mercier, D.; Leboul, J.; Cleophax, J.; Gero, S. D. *Carbohydr. Res.* **1971**, *20*, 299. Elliott, J. D.; Hetmanski, M.; Stoodley, R. J.; Palfreyman, M. N. *J. Chem. Soc., Perkin Trans 1* **1981**, 1782. Barton, D. H. R.; Gero, S. D.; Maycock, C. D. *J. Chem. Soc., Chem. Commun.* **1980**, 1089. Cleophac, J.; Gero, S. D.; Leboul, J.; Akhtar, M.; Barnett, J. E. G.; Pearce, C. J. *J. Am. Chem. Soc.* **1976**, *98*, 7110. (b) For daunomycinone intermediates: Dyong, I.; Hermann, R.; Mattes, R. *Chem. Ber.* **1980**, *113*, 1931. (c) For mevalonolactone: Eberle, M.; Arigoni, D. *Helv. Chem. Acta* **1960**, *43*, 1508. Lee, L.; Park, J. W.; Park, S. C. *J. Chem. Soc., Chem. Commun.* **1983**, 268. (d) For analogues: Grewe, R.; Nolte, E. *Justus Liegigs Ann. Chem.* **1952**, *575*, 1. Fischer, H. O. L.; Dangschat, G. *Chem. Ber.* **1932**, *65*, 1009. Fischer, H. O. L. *Ibid.* **1921**, *54*, 775. (e) For chorismic acid: Lesiusse, D.; Berchtold, G. A. *J. Org. Chem.* **1985**, *50*, 888.

(10) Josan, J. S.; Eastwood, F. W. *Aust. J. Chem.* **1968**, *21*, 2013.

(11) The diastereomeric ratio was based on the integration of the isopropylidene methyl singlets in the ^1H NMR spectrum (1.50, 1.38 ppm) and peak heights of the methyls in the ^{13}C NMR spectrum (28.0, 25.7 ppm).

Scheme II. Optically Active Route to Isoquinuclidines[a]



[a] (a) Dry HCl, Me_2CO, 25 °C, 24 h, 78%. (b) LAH, THF, 87%. (c) (i) $(EtO)_3CH$, cat. $PhCO_2H$, 200 °C; (ii) H_3O^+, 80%. (d) Ac_2O, Et_3N, CH_2Cl_2, 0 °C, 92%. (e) (i) Me_3Al, BH_3-SMe_2, $PhCH_3$, -20 to 25 °C; (ii) H_2O_2, NaOH, 89%. (f) TsCl, pyr, CH_2Cl_2, 0–25 °C, 92%. (g) NaN_3, DMF, 50 °C, 91%. (h) TBDMS-Cl, imidazole, DMF, 25 °C, 77%. (i) 1 atm H_2, 10% Pd/C, THF, 97%. (j) $(PhO)_2P(O)N_3$, indole-3-acetic acid, Et_3N, DMF, 0–25 °C, 15 h, 64%. (k) DIBAL-H, THF, 0 °C, 95%. (l) $TMSC_2H_4OCOCl$, Et_3N, CH_2Cl_2, 0 °C, 90%. (m) $(n\text{-}C_4H_9)_4NF$ (5% H_2O), THF, 25 °C, 82%. (n) CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0 °C, 91%. (o) H_3O^+, 98%. (p) NaOH, CH_3OH, 0 °C, 95%. (q) Collins oxid. 86%. (r) Ph_3PCH_2, THF, -30 to -25 °C, 90%. (s) anhydrous $(n\text{-}C_4H_9)_4NF$, THF, 60 °C, 72%. (t) 0.05 equiv $Pd(PPh_3)_4$, THF, 25 °C, 95%.

Scheme III. If diastereomer **21** were the structure, one would expect a large trans-diaxial coupling. Furthermore, Ha (δ 4.34) shows a large trans-diaxial and a smaller gauche coupling (J = 11.8, 5.5 Hz), also in agreement with structure **20**. That the absorption at δ 4.08 corresponds to the secondary carbinol proton can be shown by D_2O exchange whereupon this signal simplifies considerably.

We interpreted the lack of diastereoselectivity as an indication that the steric bulk of the hydrometalating agent was not important but that our product ratio reflected the conformational bias of the cyclohexane ring system. If such an interpretation is correct, control of ring conformation should translate into diastereoselectivity. As outlined in Scheme III, the two conformers, **18** or **19**, differ only in the preference of the OR group to be axial or equatorial. By utilizing a Lewis acid to complex the acyclic oxygen, its increased steric bulk should anchor it into an equatorial position. Least hindered approach to such a fixed conformer should then lead to **20**. Realizing that borane itself is a Lewis acid, we tried 1 equiv of borane/dimethyl sulfide complex in toluene, a noncoordinating solvent, and obtained diols **20** and **21** in an improved 5:1 ratio. Adding exogenous Lewis acids gave diol ratios as high as 12:1. Employing the acetate **19** instead of the free hydroxyl group **18** gave a cleaner reaction and slightly better diol ratios. The use of the diastereoselective control element was performed on scales as large as 20 g, by using trimethylaluminum as the Lewis acid.

Selective tosylation of the primary hydroxyl group followed by azide displacement and silylation of the re-

Scheme III. Diastereoselective Control of Hydroboration

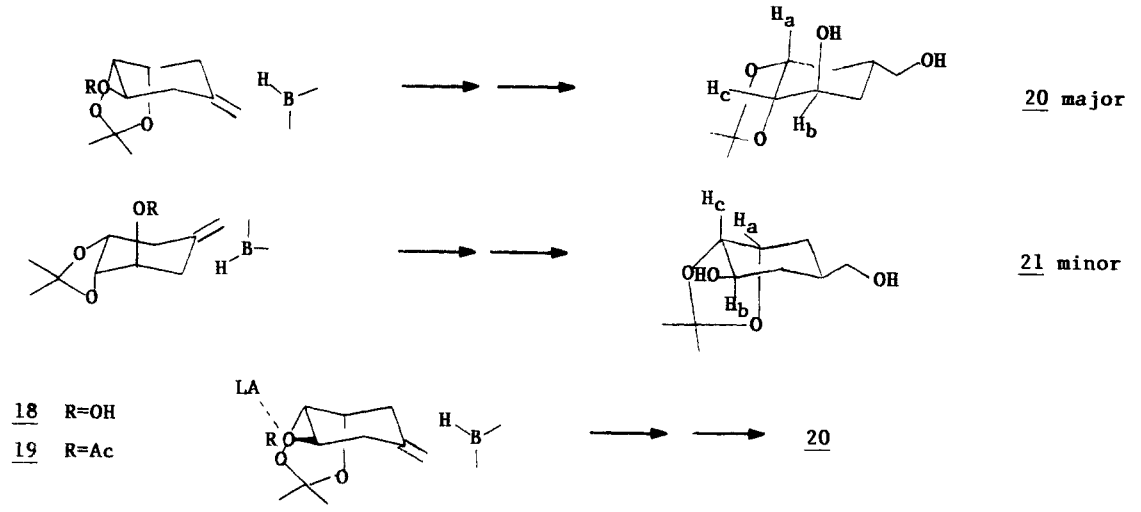


Table II. ^{1}H NMR Data for Isoquinuclidines 12, 14, and 36

proton	12	14	36
H_a	4.95 (s)		4.91 (s)
H_b	4.91 (s)	5.46 (qt, J = 6.8, 0.3 Hz)	4.86 (s)
H_c	4.50 (br s)	not seen	not seen
H_d	4.00 (s, 3 H)	4.00 (s, 3 H)	
H_e	3.84 (dt, J = 9.3, 3.3 Hz)	3.75 (d, J = 7.0 Hz)	3.83 (dm, J = 9.0 Hz)
H_f	3.30 (d, J = 9.9 Hz)	3.23 (d, J = 9.9 Hz)	3.24 (d, J = 10.7 Hz)
H_g	3.03 (d, J = 2.9 Hz)	3.43 (s)	2.91 (d, J = 4.3 Hz)
H_h	2.72–2.84 (m, 4 H)	2.52–3.00 (m, 4 H)	2.87 (t, J = 8.1 Hz, 2 H)
			2.75 (t, J = 8.1 Hz, 2 H)
H_j	2.25 (d, J = 9.9 Hz)	2.23 (dt, J = 9.9, 2.2)	2.23 (d, J = 9.6 Hz)
H_k	2.15 (br s, 2 H)	2.09 (br s, 2 H)	2.12 (br s, 2 H)
$H_l + H_m$	1.91–2.00 (m, 2 H)	1.7–2.15 (m, 2 H)	1.90–2.00 (m, 2 H)
H_n	1.50 (d, J = 14.7 Hz)	1.44 (d, J = 13.7 Hz)	1.46 (d, J = 12.5 Hz)
H_o		1.60 (dt, J = 6.8, 2.0 Hz, 3 H)	

maining hydroxyl group gave **24**. The azide was hydrogenated over 10% palladium on carbon to obtain amine **25**, which was condensed with indole-3-acetic acid in the presence of diphenylphosphoryl azide[12] to afford the amide. Excess DIBAL-H reduced the amide to the secondary amine. Amine **27** was protected with 2-trimethylsilyl chloroformate,[13] and the alcohol was desilylated with commercial tetra-*n*-butylammonium fluoride (containing 5% water). The alcohol was then methanesulfonylated, and the acetonide was hydrolyzed with aqueous acid. Epoxide formation, followed by Collins oxidation and Wittig methylenation, afforded the vinyl epoxide **34**. Deprotection of the amine with anhydrous tetra-*n*-butylammonium fluoride[14] afforded **35**, which underwent cyclization with a catalytic amount of tetrakis(triphenylphosphine)palladium(0) at 25 °C to afford the optically active isoquinuclidine **36** in 95% isolated yield.

37a

The conformation of the isoquinuclidines is rigid, and the nitrogen substituent lies predominantly to exclusively to one side as revealed by the ^{1}H NMR spectra as summarized in Table II. Most diagnostic is the large difference ($\Delta\delta \sim 1$) in chemical shift between the two protons of the CH_2N bridge of the isoquinuclidine nucleus. A similar effect has been seen with the unsaturated isoquinuclidine **37** and associated with its preference for invertomer **37a**.[4,15] On the basis of this analogy, we assign the preferred invertomers for **12**, **14**, and **36** as depicted in Schemes I and II.

Discussion

The effectiveness of the Pd(0)-initiated cyclization of the vinyl epoxides to the strained isoquinuclidines requires that cyclization be faster than Pd-catalyzed single proton transfers, a process known to be fast. No complication arises from the presence of the unprotected indole nitrogen in the cyclization of **35** even though this proton is undoubtedly much more acidic than the simple amine. It is likely that the neutral amine, and not its anion, is the actual nucleophile. π-Allylpalladium cationic intermediates normally prefer soft nucleophiles.

The stereochemistry of displacements catalyzed by Pd(0) which occurs with net retention of configuration[4,16] serves very well in these cyclizations. By virtue of its mode of synthesis, **11** requires an intramolecular displacement with retention of configuration. Similarly, **34** also requires a displacement with retention of configuration. The fact

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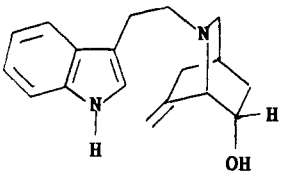
that **36** correlates with **12** provides chemical confirmation of the stereochemistry of hydroboration of **19**. If **21** had been the major product, the isoquinuclidine obtained would have been **38** which is epimeric at C(6) as well as belonging to the enantiomeric isoquinuclidine series.



38

The ability of the Lewis acid to control the diastereoselectivity of reaction is a key to the success of this enantioselective isoquinuclidine synthesis. It differs from the many examples of Lewis acids affecting diastereoselectivity where they coordinate at the reaction site in that the coordinating site and reaction center are remote from each other.

The introduction of alkyl groups, such as the ethyl group of ibogamine and catharanthine, can easily be accomplished at the epoxy ketone stage as has been specifically illustrated in the conversion of **10** to **13**. The high degree of geometrical control is surprising and is reminiscent of the α-alkoxy effect observed by Still.[6] While any comments on the source of this geometrical control can only be highly speculative, it seems that a simple steric argument would be insufficient. The question of its generality must also be answered. Stabilized ylides have not shown this high degree of geometrical control.[17]

The high success of this cyclization reaction expands the concept of Pd-mediated cyclization by isomerization[18] to amines as nucleophiles. The question of ring sizes available must yet be determined, but the success of this approach for carbon nucleophiles leads to high expectations for the nitrogen systems to be very general as well. This report establishes its utility to convert the readily available quinic acid into the very useful optically pure isoquinuclidines.

Experimental Section

General Methods. All reactions were run under a positive pressure of dry nitrogen. Reactions requiring anhydrous conditions were performed in flame-dried glassware which was cooled under nitrogen. Solvents were distilled before use: dimethyl sulfoxide (Me_2SO), dimethylformamide (DMF), methylene chloride, chlorobenzene, pyridine, toluene, and triethylamine from calcium hydride; tetrahydrofuran (THF) and ether from sodium benzophenone ketyl; acetic anhydride was fractionated; chlorotrimethylsilane from tri-*n*-butylamine. The term in vacuo refers to solvent removal via a Buchi rotoevaporator at water aspirator pressure, followed by evaporation of the flask at 0.5 mm for several hours. Preparative thin-layer chromatography was performed on glass plates coated with 1.5 mm of silica gel (Machery-Nagel, MN-Kieselgel, P/UV_{254}). Column chromatography was performed on silica gel from W. R. Grace (Grade 62, 60–200 mesh). Flash chromatography was performed on silica gel from E. Merck (Kieselgel 60, 200–400 mesh). Melting points were obtained on a Thomas-Hoover apparatus by using open capillary tubes. Melting points are uncorrected.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were determined on a Bruker WH-270 (270 MHz), Bruker WP-270 (270 MHz), or a Bruker WP-200 (200 MHz) instrument. Chemical shifts are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Infrared spectra (IR) were determined in the indicated solvent in sodium chloride cavity cells on a Beckman Acculab 7 or a Perkin-Elmer 1420. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were determined on a Jeol Fx-60 (15.04 MHz) or a Jeol FX-200 (50 MHz). Chemical shifts are reported in δ units, parts per million downfield from tetramethylsilane. Mass spectra (MS) were obtained on an AEI-902 instrument at an ionizing current of 98 mA with an ionizing voltage of 70 eV unless otherwise indicated. Microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI. Optical rotations were measured on a Perkin-Elmer 241 polarimeter by using a 10-cm cell (1 mL) in the indicated solvent and concentration (c) in grams of solute per 100 mL of solution.

***N*-(2-Indol-3′-ylethyl)-3(*R**)-hydroxycyclohex-4-ene-1-(*R**)-carboxamide.** 7-Oxabicyclo[3.2.1]oct-2-en-6-one (**8**)[19] (15.0 g, 121 mmol) was placed in a 500-mL flask with tryptamine (21.3 g, 133 mmol). Chlorobenzene (250 mL) was added, and the reaction was heated to 120 °C for 20 h (after approximately 12 h a viscous oil separated from the solution). The reaction was cooled, and the solvent was removed in vacuo. Ethyl acetate was added (300 mL), and heat was applied to dissolve the viscous residue. This solution was extracted with 2 N aqueous hydrochloric acid (3 × 200 mL), followed by water (3 × 200 mL), saturated aqueous sodium bicarbonate (200 mL), and brine (200 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford a viscous oil. This was filtered through silica gel (6 cm column, 15 cm silica gel) with ethyl acetate. Evaporation of solvent afforded a foam (30 g, 104 mmol, 87%): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.26 (br s, 1 H), 7.55 (d, 1 H, J = 8 Hz), 7.35 (d, 1 H, J = 8 Hz), 7.26–7.04 (m, 2 H), 6.97 (s, 1 H), 5.84–5.73 (m, 2 H), 4.16 (m, 1 H), 3.60 (dt, 2 H, J = 7.7 Hz), 2.95 (t, 2 H, J = 7 Hz), 2.45 (m, 1 H), 2.20 (br s, 2 H), 2.0–2.2 (m, 2 H), 1.80 (m, 2 H); ^{13}C NMR (15.04 MHz, acetone-d_6) δ 174.9, 137.5, 132.6, 126.2, 126.4, 122.9, 121.6, 118.9, 118.7, 113.0, 111.8, 66.6, 40.6, 36.6, 31.0, 28.9, 25.0; IR ($CHCl_3$) 3490, 3460, 3340, 1662, 1525 cm^{-1}. Anal. Calcd for $C_{17}H_{20}N_2O_2$: 284.1525. Found: 284.1534.

***N*-(2-Indol-3′-ylethyl)-3(*R**)-(*tert*-butyldimethylsiloxy)-cyclohex-4-ene-1(*R**)-carboxamide.** The above alcohol (0.875 g, 308 mmol) was placed in a 10-mL flask with *tert*-butyldimethylchlorosilane (0.636 g, 4.22 mmol) and imidazole (0.359 g, 5.28 mmol). DMF (10 mL) was added, and the reaction was stirred for 12 h at room temperature. Ether (50 mL) was added, and the solution was extracted with 2 N aqueous hydrochloric acid (50 mL), saturated aqueous sodium bicarbonate (50 mL), water (6 × 50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford a brown viscous liquid. This was placed on a 2-cm flash column (15 cm of silica gel) and eluted with ethyl acetate/hexane (15:85, 300 mL). Solvent removal in vacuo gave 1.17 g (2.95 mmol, 95%) of a white solid. The silyl ether was recrystallized from benzene/cyclohexane (1:1) to afford a white microcrystalline powder, mp 138–139 °C: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.14 (br s, 1 H), 7.55 (d, 1 H, J = 7 Hz), 7.33 (d, 1 H, J = 7 Hz), 7.25–7.00 (m, 2 H), 6.97 (d, 1 H, J = 0.7 Hz) 5.74 (m, 1 H), 5.65 (ddd, 1 H, J = 11.0 Hz, 3.5, 2.8), 5.54 (br d, 1 H, J = 11.0 Hz), 4.28 (m, 1 H), 3.59 (dt, 2 H, J = 7.7 Hz), 2.97 (t, 2 H, J = 7.0 Hz), 2.35 (m, 1 H), 2.09 (m, 2 H), 1.64 (m, 1 H), 0.87 (s, 9 H), 0.48 (s, 3 H), 0.43 (s, 3 H); ^{13}C NMR (15.04 MHz, $CDCl_3$) δ 174.5, 136.4, 131.7, 127.4, 126.3, 122.1, 121.9, 119.2, 118.5, 112.7, 111.4, 67.7, 40.6, 40.0, 35.3, 28.2, 25.8, 25.3, 18.1, -4.4, -4.6. IR ($CHCl_3$) 3480, 3440, 3300, 1660, 1510, 1455 cm^{-1}. Anal. Calcd for $C_{23}H_{34}N_2O_2Si$: 398.2388. Found: 398.2388.

(2-Indol-3′-ylethyl)[(3(*R)-(*tert*-butyldimethylsiloxy)-cyclohex-4-en-1(*R**)-yl)methyl]amine (9).** To a solution of the above amide (4.0 g, 10 mmol) in 50 mL of THF at 0 °C was added sodium bis(methoxyethoxy)aluminum hydride (20.3 mL of a 3.4 M solution in toluene, 70.4 mmol). After hydrogen evolution ceased, the reaction was refluxed for 3 h, then cooled

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to 0 °C, and quenched by careful addition of water (2 mL), 15% aqueous sodium hydroxide (5 mL), and water (20 mL). The solution was extracted, and the organic layer was washed with water (5 × 50 mL) and brine (50 mL), then dried over sodium sulfate. Removal of solvent in vacuo gave the title compound as a brown solid (3.9 g, 10 mmol, 100%), pure by NMR: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.22 (br s, 1 H), 7.6 (d, 1 H, J = 8.9 Hz), 7.34 (d, 1 H, J = 8.9 Hz), 7.18 (app t, 1 H, J = 8 Hz), 7.14 (app t, 1 H, J = 8 Hz), 6.97 (m, 1 H), 5.66 (ddd, 1 H, J = 2.8 Hz, 3.5, 11.0), 5.56 (br d, 1 H, J = 11.0 Hz), 4.29 (m, 1 H), 2.96 (m, 4 H), 2.57 (d, 2 H, J = 5.9 Hz), 2.10–1.56 (m, 5 H), 1.21 (q, 1 H, J = 11.9 Hz), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 136.5, 132.1, 127.5, 127.0, 121.9, 119.2, 118.7, 113.7, 111.1, 68.2, 55.3, 50.0, 37.3, 33.1, 29.9, 25.9, 25.5, 18.2, −4.5, −4.6; IR ($CHCl_3$) 3690, 1460 cm^{-1}. Anal. Calcd for $C_{23}H_{36}N_2OSi$: 384.2588. Found: 384.2597.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(3-(*R)-(*tert*-butyldimethylsiloxy)cyclohex-4-en-1(*R**)-yl)-methyl]carbamate.** Secondary amine **9** (9.01 g, 23.4 mmol) and triethylamine (3.03 g, 30 mmol) were dissolved in 60 mL of methylene chloride. The solution was cooled to 0 °C, and 2-(trimethylsilyl)ethyl chloroformate[13] (5.07 g, 280 mmol) was added slowly. After 3 h, the solution was diluted with 200 mL of ether and washed with 2 N aqueous hydrochloric acid (100 mL), water (3 × 100 mL), saturated aqueous sodium bicarbonate (100 mL), and brine (100 mL). The organic layer was dried over magnesium sulfate, and the solvent was evaporated to afford 11.3 g of crude solid. This was filtered on a silica gel column with ethyl acetate/hexane (15:85). After solvent removal, 9.04 g (17.1 mmol, 75%) of pure semisolid product was obtained: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.04 (s, 1 H), 7.63 (m, 1 H), 7.34 (d, 1 H, J = 8.9 Hz), 7.18 (app t, 1 H, J = 8 Hz), 7.14 (app t, 1 H, J = 8.0 Hz), 6.99 (br s, 1 H), 5.64 (dm, 1 H, J = 9.9 Hz), 5.55 (d, 1 H, J = 9.9 Hz), 4.0–4.4 (m, 3 H), 3.51 (m, 2 H), 3.13 (br d, 2 H, J = 6.6 Hz), 2.98 (m, 2 H), 1.91 (m, 3 H), 1.68 (m, 2 H), 1.24 (m, 2 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H), 0.02 (s, 9 H); IR ($CHCl_3$) 3500, 1687 cm^{-1}. Anal. Calcd for $C_{29}H_{48}N_2O_3Si_2$: 528.3201. Found: 528.3200.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*R)-(*tert*-butyldimethylsiloxy)cyclohex-4-en-1(*R**)-yl)methyl]carbamate.** The above carbamate (3.60 g, 6.82 mmol) dissolved in THF (20 mL) was added to a slurry of potassium hydride (287 mg, 7.17 mmol) in THF (30 mL) at 0 °C. After hydrogen evolution ceased, methyl chloroformate (773 mg, 8.18 mmol) was added. The reaction was stirred for 30 min and quenched by the addition of saturated aqueous ammonium chloride. The solution was extracted, and the organic layer was washed with water (3 × 50 mL) and brine (50 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford the title compound (3.07 g, 5.64 mmol, 83%) which was used in the next step without purification: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.13 (m, 1 H), 7.6 (m, 1 H), 7.4–6.9 (m, 3 H), 5.65 (br d, 1 H, J = 10.7 Hz), 5.55 (d, 1 H, J = 10.7 Hz), 4.26–4.12 (m, 3 H), 4.00 (s, 3 H), 3.51 (br t, 2 H, J = 6.6), 3.13 (m, 2 H), 2.92 (m, 2 H), 1.90 (m, 2 H), 1.70–0.90 (m, 5 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H), 0.02 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.4, 151.0, 135.4, 132.0, 130.2, 126.5, 124.5, 122.6, 118.7, 115.1, 68.0, 63.3, 53.4, 52.8, 48.2, 36.8, 32.6, 29.3, 25.8, 23.8, 17.9, −1.6, −4.6; IR ($CHCl_3$) 1740, 1690, 1455 cm^{-1}. Anal. ($C_{32}H_{50}N_2O_5Si_2$) C, H, MW.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[3(*R)-hydroxycyclohex-4-en-1(*R**)-yl)-methyl]carbamate.** The above silyl ether (1.63 g, 2.87 mmol) was dissolved in a solution of acetic acid/THF/water (3:1:1, 25 mL) and stirred for 20 h at 25 °C. The solvent was removed in vacuo, and the residue was dissolved in ether (25 mL) and extracted with saturated aqueous sodium bicarbonate until carbon dioxide evolution ceased. The organic layer was separated and dried over magnesium sulfate. After solvent removal in vacuo the title compound was obtained (1.15 g, 2.44 mmol, 79%) and carried on without further purification: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.15 (br d, 1 H, J = 8.1 Hz), 7.6–7.2 (m, 4 H), 5.70 (d, 1 H, J = 11.0 Hz), 5.63 (d, 1 H, J = 10.7 Hz), 4.21–4.11 (m, 3 H), 3.99 (s, 3 H), 3.50 (dd, 2 H, J = 6.3, 5.8 Hz), 3.17 (m, 2 H), 2.91 (m, 2 H), 2.00–0.99 (m, 9 H), 0.01 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.6, 151.2, 135.4, 131.4, 130.3, 127.4, 124.5, 122.7, 118.8, 118.6, 115.1, 67.2, 63.5, 53.6, 52.2, 47.7, 36.6, 32.4, 29.4, 23.9, 17.8, −1.5; IR ($CHCl_3$) 3600, 3460, 1735, 1690 cm^{-1}. Anal. Calcd for $C_{25}H_{36}N_2O_5Si$: 472.2384. Found: 472.2393.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*S),4(*R**)-epoxy-5(*R**)-hydroxycyclohex-1-(*S**)-yl)methyl]carbamate.** MCPBA (1.37 g, 6.77 mmol) was added in portions to a solution of the above allylic alcohol (2.10 g, 4.51 mmol) in 20 mL of methylene chloride at 0 °C. After epoxidation was completed (approximately 4 h by TLC), saturated aqueous sodium sulfite (20 mL) was added, and the reaction was stirred for an additional 15 min. The organic layer was extracted and washed with saturated aqueous sodium bicarbonate (10 mL), water (3 × 10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford a pure white foam (1.96 g, 4.05 mmol, 90%): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.15–7.00 (m, 5 H), 4.20–3.75 (m, 3 H), 4.00 (s, 3 H), 3.45 (m, 2 H), 3.25 (m, 2 H), 3.1–2.8 (m, 2 H), 2.0–0.9 (m, 9 H), 0.02 (s, 9 H); ^{13}C NMR (15 MHz) δ 156.5, 151.3, 135.4, 130.3, 124.7, 122.8, 122.6, 118.6, 118.5, 115.2, 68.7, 55.9, 54.2, 53.6, 48.1, 32.9, 31.6, 27.3, 24.0, 17.8, −1.5; IR ($CHCl_3$) 3600, 1740, 1685, 1445 cm^{-1}. Anal. Calcd for $C_{25}H_{32}N_2O_6Si$: 488.2333. Found: 488.2341.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[(4(*S),5(*S**)-epoxy-3-oxocyclohex-1(*R**)-yl)-methyl]carbamate (10).** Neat oxalyl chloride (6.65 g, 52.4 mmol) was added to a solution of 8.17 g (104.7 mmol) of Me_2SO in 200 mL of methylene chloride at −78 °C. After 10 min, a cooled solution of the above alcohol (23.2 g, 47.6 mmol) in 50 mL of methylene chloride was cannulated into the reaction mixture. Stirring proceeded for 30 min, at which point 24 g (238 mmol) of neat triethylamine was added by syringe. After an additional 10 min at −78 °C, the solution was allowed to warm to room temperature and proceed for 30 min. The solution was then diluted with 300 mL of ether and washed with saturated aqueous sodium bisulfate (2 × 50 mL), water (3 × 100 mL), saturated aqueous sodium bicarbonate (100 mL), and brine (100 mL). The organic layer was dried over magnesium sulfate, and the solvent was evaporated to afford a foam. The crude product was eluted on a 4 cm flash silica gel column (15 cm of silica gel) with ethyl acetate/hexane (35:65). Solvent removal in vacuo afforded 21.3 g (44.3 mmol, 93%) of the title compound as a foam: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.25–7.10 (m, 5 H), 4.1 (m, 2 H), 4.00 (s, 3 H), 3.50 (m, 2 H), 3.17 (m, 2 H), 3.09 (m, 2 H), 2.90 (br s, 2 H), 2.2–1.0 (m, 7 H), 0.05 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 206.2, 156.3, 151.0, 135.3, 130.1, 124.5, 122.5, 118.7, 118.2, 115.1, 63.5, 57.6, 54.5, 53.5, 52.4, 47.8, 39.1, 36.8, 26.9, 23.8, 17.7, −1.7; IR ($CHCl_3$) 1730, 1685, 1455 cm^{-1}. Anal. ($C_{25}H_{34}N_2O_6Si$) C, H, MW.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*S),4(*R**)-epoxy-5-methylidenecyclohex-1-(*S**)-yl)methyl]carbamate.** THF (50 mL) was added to a flask containing methyltriphenylphosphonium iodide (9.82, 24.3 mmol) and potassium *tert*-butoxide (2.51 g, 22.4 mmol). The yellow slurry was stirred for 3 h after which it was cooled to −40 °C, and a solution of ketone **10** (9.00 g, 18.7 mmol) in THF (50 mL) was added by cannulation. The solution was stirred for 20 min and then allowed to warm to 25 °C and stir for an additional 30 min. The reaction was diluted with 100 mL of ether and extracted with water (3 × 50 mL) and brine (50 mL). After drying over magnesium sulfate and solvent removal in vacuo, the crude product was eluted on a 5 cm flash silica gel column (15 cm of silica gel) with ethyl acetate/hexane (17:83) to rid it of triphenylphosphine oxide. Solvent removal in vacuo afforded 6.96 g (14.4 mmol, 77%) of the vinyl epoxide: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.12 (br d, 1 H, J = 8.1 Hz), 7.6–7.2 (m, 4 H), 5.18 (s, 1 H), 5.04 (s, 1 H), 4.14 (m, 2 H), 4.00 (s, 3 H), 3.48 (ddd, 2 H, J = 8, 8, 8 Hz), 3.37 (d, 1 H, J = 6 Hz), 3.31 (t, 1 H, J ≈ 6 Hz), 3.06 (br s, 2 H), 2.89 (br s, 2 H), 1.95 (m, 2 H), 1.60 (m, 1 H), 0.99–0.89 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.1, 150.7, 142.9, 135.1, 130.0, 124.6, 122.4, 122.2, 118.5, 118.2, 114.8, 113.9, 63.0, 55.3, 53.6, 53.1, 52.4, 47.6, 34.5, 31.9, 27.9, 23.5, 17.4, −1.8; IR ($CHCl_3$) 1738, 1690, 1455 cm^{-1}. Anal. Calcd for $C_{26}H_{36}N_2O_5Si$: 484.2392. Found: 484.2400.

[2-(1′-Carbomethoxyindol-3′-yl)ethyl][(3(*S),4(*R**)-epoxy-5-methylidenecyclohex-1(*S**)-yl)methyl]amine (11).** Anhydrous tetra-*n*-butylammonium fluoride (16.6 g, 63.6 mmol) was added to an acetonitrile solution (75 mL) of the above car-

bamate at 25 °C. The reaction was heated to 50 °C, stirred for 3 h, and then cooled, and ether (100 mL) was added followed by 200 mL of water. After extraction, the organic layer was washed with water (5 × 100 mL) and brine (100 mL) and dried over sodium sulfate. Solvent removal in vacuo afforded 6.70 g of the title compound (19.9 mmol, 79%). An analytical sample was purified by silica gel column chromatography, eluting with methanol/chloroform/diethylamine (10:89:1): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.07 (m, 1 H), 7.40 (d, 1 H, J = 7.4 Hz), 7.34 (s, 1 H), 7.20 (t, 1 H, J = 7.2 Hz), 7.10 (t, 1 H, J = 7.0 Hz), 5.11 (s, 1 H), 4.95 (s, 1 H), 3.95 (s, 3 H), 3.30 (d, 1 H, J = 3.8 Hz), 3.20 (t, 1 H, J = 4.0 Hz), 2.75 (m, 2 H) 2.33 (d, 2 H, J = 6.3 Hz), 2.03–1.39 (m, 7 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 150.1, 141.7, 134.2, 130.2, 125.2, 122.7, 122.3, 118.3, 118.0, 114.9, 113.4, 56.1, 55.6, 54.5, 53.6, 49.2, 35.9, 32.9, 28.9, 25.7; IR ($CHCl_3$) 1735, 1455, 1382 cm^{-1}. Anal. Calcd for $C_{20}H_{24}N_2O_3$: 340.1786. Found: 340.1793.

***N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-6(*S**)-hydroxy-7-methylene-(1*R**,4*S**)-2-azabicyclo[2.2.2]octane (12).** Under an inert atmosphere of nitrogen, tetrakis(triphenylphosphine)-palladium(0) (221 mg, 0.192 mmol) was added to a flask containing amine **11** (1.29 g, 3.84 mmol). THF (9 mL) was added, and the solution was stirred for 6 h at 25 °C. An aliquot was examined by ^{1}H NMR to discern when all the starting material had disappeared. The solution was evaporated, and the residue was placed on a 2 cm flash silica gel column (15 cm of silica gel) and eluted with ethyl acetate/hexane (1:1), changing to methanol/chloroform/diethylamine (10:89:1) to recover the title compound. After solvent removal in vacuo, 1.20 g (3.57 mmol, 93%) of viscous liquid was obtained: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.15 (d, 1 H, J = 7.0 Hz), 7.40 (d, 1 H, J = 8 Hz), 7.27 (s, 1 H), 7.05–7.25 (m, 2 H), 4.95 (s, 1 H), 4.91 (s, 1 H), 4.50 (br s, 1 H), 3.90 (s, 3 H), 3.85 (dt, 1 H, J = 9.2, 2.9 Hz), 3.30 (d, 1 H, J = 9.9 Hz), 2.95 (d, 1 H, 2.9), 2.8–2.7 (m, 4 H), 2.25 (d, 1 H, J = 9.9 Hz), 2.15 (s, 2 H), 1.95 (m, 2 H), 1.50 (d, 1 H, J = 14.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.1, 142.0, 135.4, 130.3, 124.4, 122.6, 122.2, 119.3, 118.7, 115.1, 111.7, 67.6, 64.5, 55.7, 55.5, 53.4, 36.3, 33.6, 27.6, 23.3; IR ($CHCl_3$) 3400, 1732 cm^{-1}. Anal. Calcd for $C_{20}H_{24}N_2O_3$: 340.1786. Found: 340.1782. Combustion analysis was obtained on the corresponding acetate. Anal. ($C_{22}H_{26}N_2O_4$) C, H, MW.

2-(Trimethylsilyl)ethyl *N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*S),4(*R**)-epoxy-5(*Z*)-ethylidenecyclohex-1(*S**)-yl)methyl]carbamate (13).** THF (100 mL) was added to a flask containing ethyltriphenylphosphonium bromide (9.60 g, 25.5 mmol) and potassium *tert*-butoxide (2.95 g, 25.5 mmol). The resulting yellow slurry was stirred for 2 h at 25 °C and then cooled to −40 °C. Epoxy ketone **10** (12.0 g, 24.7 mmol) was dissolved in 100 mL of THF and added to the reaction flask. After an additional 30 min at −40 °C, the reaction mixture was allowed to warm to room temperature, and the reaction proceeded for 30 min. The reaction was diluted with 200 mL of ether and washed with water (5 × 100 mL) and brine (100 mL). The organic layer was dried over sodium sulfate, and the solvent was evaporated. The residue was placed on a 5 cm flash silica gel column and eluted with ethyl acetate/hexane (25:75). Solvent removal in vacuo afforded 11.1 g (21.5 mmol, 87%) of the title compound as a viscous oil: ^{1}H NMR (270 MHz, $CDCl_3$) 8.18 (br s, 1 H), 7.58 (m, 1 H), 7.48–7.09 (m, 3 H), 5.60 (q, 1 H, J = 6.8 Hz), 4.10 (m, 2 H), 4.00 (s, 3 H), 3.70 (d, 1 H, J = 3.4 Hz), 3.43 (m, 2 H), 3.32 (t, 1 H, J = 4.0 Hz), 3.15 (m, 2 H), 2.98 (m, 2 H), 2.09–1.55 (m, 5 H), 1.76 (d, 3 H, J = 7.1 Hz), 1.00 (m, 2 H); IR ($CHCl_3$) 1737, 1682 cm^{-1}. Anal. Calcd for $C_{27}H_{38}N_2O_5Si$: 498.2549. Found: 498.2551.

[2-(1′-Carbomethoxyindol-3′-yl)ethyl][(3(*S),4(*R**)-epoxy-5(*Z*)-ethylidenecyclohex-1(*S**)-yl)methyl]amine.** THF (10 mL) was introduced into a flask containing tetra-*n*-butylammonium fluoride (14.03 g, 53.75 mmol) and the above carbamate (11.13 g, 21.51 mmol) at 25 °C; the solution darkened. The solution was heated to 50 °C, stirred for 3 h, and then cooled. The reaction was diluted with 150 mL of ether and washed with water (5 × 100 mL) and brine (100 mL). The organic layer was dried over sodium sulfate, and the solvent was removed in vacuo to afford the title compound as a viscous oil (6.01 g, 17.7 mmol, 79%): ^{1}H NMR (270 MHz, $CDCl_3$) 8.09 (m, 1 H), 7.50–7.10 (m, 4 H), 5.57 (q, 1 H, J = 6.8 Hz), 3.98 (s, 3 H), 3.70 (d, 1 H, J = 3.8 Hz), 3.31 (t, 1 H, J = 4.8 Hz), 3.0–2.8 (m, 4 H), 2.41 (d, 2 H, J = 6.0 Hz), 2.25–1.3 (m, 6 H), 1.70 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (15 MHz, $CDCl_3$) 151.3, 135.5, 133.3, 130.5, 125.0, 124.5, 122.6, 122.4, 119.5, 118.9, 115.1, 55.4, 54.2, 53.6, 50.8, 49.1, 35.3, 34.2, 29.1, 25.5, 12.6; IR ($CHCl_3$) 3480, 1733 cm^{-1}. Anal. Calcd for $C_{21}H_{26}N_2O_3$: 354.1943. Found: 354.1942.

***N*-[2-(1′-Carbomethoxyindol-3′-yl)ethyl]-7(*Z*)-ethylidene-6(*S**)-hydroxy-(1*R**,4*S**)-2-azabicyclo[2.2.2]octane (14).** Tetrakis(triphenylphosphine)palladium(O) (200 mg, 0.173 mmol, 1.0 mol%) was introduced into a flask containing the above vinyl epoxide (6.00 g, 17.7 mmol) under an inert atmosphere. Tetrahydrofuran (50 mL) was added, and the solution was heated to reflux and maintained for 8 h. After cooling to 25 °C, the solvent was removed by evaporation, and the residue was placed on a flash silica gel column, eluting first with ethyl acetate/hexane (1:10), then chloroform/methanol/diethylamine (89:10:1). After solvent removal in vacuo the title compound was obtained as a viscous liquid (5.70 g, 16.1 mmol, 91%). (The reaction was followed by observance of the olefinic protons, as monitored by aliquots on a NMR spectrometer): ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.15 (d, 1 H, J = 7.5 Hz), 7.75–7.10 (m, 4 H), 5.46 (q, 1 H, J = 6.8 Hz), 3.98 (s, 3 H), 3.75 (d, 1 H, J = 7.2 Hz), 3.41 (s, 1 H), 3.26 (d, 1 H, J = 9.9 Hz), 3.00–2.57 (m, 5 H), 2.23 (dt, 1 H, J = 9.9, 2.0 Hz), 2.03–1.75 (m, 4 H), 1.60 (dt, 3 H, J = 6.8, 2.0 Hz), 1.44 (d, 1 H, J = 13.7 Hz); ^{13}C NMR (15 MHz, $CDCl_3$) δ 150.9, 135.1, 132.6, 130.2, 124.2, 122.3, 121.9, 121.1, 119.4, 118.5, 114.9, 67.5, 57.6, 55.9, 55.7, 53.4, 36.7, 34.5, 27.9, 23.6, 12.8; IR ($CHCl_3$) 3420, 1730 cm^{-1}. Anal. Calcd for $C_{21}H_{26}N_2O_3$: 354.1943. Found: 354.1943.

3,4-*O*-Isopropylidene-1(*S*),3(*R*),4(*R*)-trihydroxy-6-oxabicyclo[3.2.1]octan-7-one (16). D-(−)-Quinic acid (**15**) (200 g, 1.19 mol) was dissolved in acetone (5.5 L) which contained dry hydrogen chloride (0.3–0.4% by weight) and stirred for 24 h at 25 °C. During this time, all of the organic acid went into solution. A stream of dry ammonia gas was passed through the reaction until the pH was basic to litmus paper. The precipitated ammonium chloride was filtered through a Buchner funnel, and the acetone was rotoevaporated. When approximately 300 mL of acetone remained, hexane was added to cause crystallization of the product. The white needles were recrystallized from chloroform/hexane (1:1), affording 199 g (0.932 mol, 78%) of the title compound, mp 143–144 °C (lit.[9d] mp 141–142 °C), $[\alpha]^{25}_{589}$ −34.46° (*c* 1.625/$CHCl_3$): ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.72 (dd, 1 H, J = 6.1, 2.5 Hz), 4.50 (dt, 1 H, J = 7.0, 2.8 Hz), 4.32 (dm, 1 H, J = 6.6 Hz), 3.07 (s, 1 H), 2.64 (d, 1 H, J = 11.8), 2.5–2.3 (m, 2 H), 2.17 (dd, 1 H, J = 14.6, 2.9 Hz), 1.52 (s, 3 H), 1.3 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 178.3, 109.7, 75.7, 72.2, 71.6, 38.5, 34.6, 27.1, 24.4; IR ($CHCl_3$) 3580, 1796, 1072, cm^{-1}. Anal. ($C_{10}H_{14}O_5$) C, H.

3,4-*O*-Isopropylidene-1-(hydroxymethyl)-1(*R*),3(*R*),4-(*S*),5(*R*)-tetrahydroxycyclohexane (17). Lactone **16** (100 g, 0.467 mol) dissolved in 500 mL of THF was added slowly to a slurry of lithium aluminum hydride (22.5 g, 0.59 mol) in THF (1.25 L) at 0 °C. After the addition was completed, the temperature was raised to reflux for 18 h. The reaction was then cooled to 0 °C and excess hydride was quenched by the careful, successive addition of water (22.5 mL), 15% aqueous sodium hydroxide (22.5 mL), and water (67.5 mL). Celite was added (250 g), and the slurry was stirred for 2 h. The aluminum salts were separated by vacuum filtering the slurry through a Celite pad. The salts were repeatedly washed with hot chloroform/absolute ethanol (95:5). The filtrate was stripped of solvent until approximately 300 mL remained; hexane was then added slowly to crystallize the triol. The white needles were recrystallized from chloroform to afford 88 g (0.40 mol, 87%), mp 117–117.5 °C, $[\alpha]^{25}_{589}$ −56.07° (*c* 1.437/CH_3OH): ^{1}H NMR (270 MHz, $CDCl_3$) 4.50 (ddd, 1 H, J = 6.1, 4.5, 2.7 Hz), 4.10 (ddd, 1 H, J = 10.6, 7.1, 4.9 Hz), 3.97 (t, 1 H, 5.9), 3.45 (d, 1 H, J = 12.0), 3.40 (d, 1 H, J = 12.0 Hz), 3.20 (br s, 1 H), 2.6 (br s, 1 H), 2.4 (br s, 1 H), 2.28 (dt, 1 H, J = 15.8, 2.4 Hz), 2.00 (ddd, 1 H, J = 13.6, 4.4, 2.2 Hz), 1.85 (dd, 1 H, J = 15.8, 3.7 Hz), 1.55 (s, 3 H), 1.48 (dd, 1 H, J = 12.5 Hz), 1.38 (s, 3 H); ^{13}C NMR (15 MHz, Me_2SO-d_6) δ 97.1, 70.5, 63.2, 61.3, 59.5, 57.3, 29.3, 25.2, 18.1, 15.6; IR ($CHCl_3$) 3590, 3500, 1105, 1045 cm^{-1}. Anal. ($C_{10}H_{18}O_5$) C, H.

1,2-*O*-Isopropylidene-5-methylene-1(*R*),2(*S*),3(*R*)-trihydroxycyclohexane (18). Triol **17** (10.0 g, 45.9 mmol) was placed in a round-bottomed flask with benzoic acid (30 mg, 0.5 mol %) and triethyl orthoformate (70 mL). The temperature was

raised to 130 °C, distilling off the ethanol which was generated. After all the ethanol had been removed, the temperature was raised to 155 °C, and excess triethyl orthoformate was also removed by distillation. The temperature was again raised to 200 °C and maintained until carbon dioxide and ethanol evolution ceased. The flask was cooled to 25 °C, and the reaction mixture was dissolved in 100 mL of THF/water/2 N aqueous hydrochloric acid (100:100:1) and stirred for 1 h, followed by the addition of solid sodium hydroxide (2.0 g, 50 mmol), which was allowed to stir for 12 h. Ether (100 mL) was added, and the aqueous phase was saturated with sodium chloride. The organic phase was separated, washed with brine (3 × 50 mL), and then dried over magnesium sulfate. Solvent removal in vacuo afforded 6.74 g (36.3 mmol, 80%) of the title compound, $[\alpha]^{25}_{589}$ −31.96° (*c* 5.038/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 4.92 (s, 1 H), 4.90 (s, 1 H), 4.35 (q, 1 H, *J* = 5.1 Hz), 3.97 (t, 1 H, *J* = 12.1 Hz), 3.87 (m, 1 H), 2.60–2.58 (m, 2 H), 2.15 (dd, 1 H *J* = 15, 1.8 Hz), 1.49 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 139.8, 112.2, 108.3, 79.1, 73.6, 70.4, 36.7, 34.4, 27.7, 25.4; IR ($CHCl_3$) 3600, 3440, 1665, 1210, 1050, cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_3$: 184.1098. Found: 184.1100.

1,2-*O*-Isopropylidene-3(*R*)-acetoxy-5-methylene-4(*R*),5-(*R*)-dihydroxycyclohexane (19). Alcohol **18** (21.7 g, 118 mmol), triethylamine (14.2 g, 141 mmol), and 4-(dimethylamino)pyridine (DMAP) (290 mg, 2 mol %) were dissolved in 200 mL of methylene chloride and cooled to 0 °C. Acetic anhydride (13.3 g, 130 mmol) was added slowly, and the solution was stirred for 2 h. Addition of 200 mL of water quenched excess anhydride. Ether (200 mL) was added, and the solution was extracted. The organic phase was washed successively with 2 N aqueous hydrochloric acid (100 mL), saturated aqueous sodium bicarbonate (100 mL), and brine (100 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo. The remaining liquid was distilled (82–88 °C/1.0 mmHg) to afford 24.4 g (108 mmol, 92%) of a clear liquid, $[\alpha]^{25}_{589}$ −29.92° (*c* 5.01/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 5.02–4.95 (m, 1 H), 4.95 (s, 1 H), 4.91 (s, 1 H), 4.40 (q, 1 H, *J* = 6.0 Hz), 4.1 (t, 1 H, *J* = 14.1 Hz), 2.7–2.5 (m, 2 H), 2.1–2.3 (m, 2 H), 2.05 (s, 3 H), 1.46 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 168.9, 138.6, 112.3, 108.5, 75.4, 73.3, 72.0, 34.0, 33.3, 27.2, 25.2, 20.8. IR ($CHCl_3$) 1735, 1660, 1055 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_4$: 226.1204. Found: 226.1206.

1,2-*O*-Isopropylidene-1(*R*),2(*S*),3(*R*)-trihydroxy-5(*R*)-(hydroxymethyl)cyclohexane (20). Acetate **19** (9.00 g, 39.8 mmol) was dissolved in toluene (80 mL) and cooled to −40 °C. Trimethylaluminum (2 M in toluene, 23.9 mL, 47.8 mmol) was added via syringe and stirred for 10 min. Borane–dimethyl sulfide complex (10 M in dimethylsulfide, 4.8 mL, 47.8 mmol) was added slowly, and the solution was allowed to warm very slowly to room temperature. For the highest yield of the title epimer, it is important to thermally buffer the solution against an exotherm between 0 and 25 °C (the temperature where hydroboration takes place). After having been stirred at 25 °C for 30 min, the solution was cooled to 0 °C, and THF (100 mL) was added, followed by careful addition of water (10 mL) to destroy excess hydride. After stirring for 10 min, 3 N aqueous sodium hydroxide (6 equiv, 80 mL, 240 mmol) was added followed by slow addition of 30% aqueous hydrogen peroxide (6.8 mL, 60 mmol), maintaining a reaction temperature of approximately 50 °C during addition and for 1 additional h. After cooling, sodium chloride was added to the saturation point, and the phases were separated. The aqueous layer was extracted with methylene chloride (5 × 300 mL). The organic layers were separately back-extracted with brine (3 × 75 mL), then combined, and dried over anhydrous potassium carbonate, and the solvent was removed in vacuo to afford 7.20 g (35.6 mmol, 89%) of diol. A continuous extraction apparatus was often used to advantage to insure a good recovery of diol from the aqueous washings. Proton (integration of methyls) and ^{13}C (height of methyl resonances) NMR spectra show greater than a 10:1 ratio of epimers, $[\alpha]^{25}_{589}$ −23.86° (*c* 5.26/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 4.34 (q, 1 H, *J* = 5.5 Hz), 4.07 (m-sharpens upon addition of D_2O, 2 H, *J* = 5.5 Hz), 2.66 (d-disappears upon addition of D_2O, 1 H, *J* = 3.3 Hz), 2.55 (t-disappears upon addition of D_2O, 1 H, *J* = 5.5 Hz), 2.08–1.54 (m, 5 H), 1.50 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 103.0, 78.0, 73.2, 67.6, 66.4, 31.5, 30.6, 30.0, 28.0, 25.7; IR 3610, 3450, 1050 cm^{-1}. Anal. ($C_{10}H_{18}O_4$) C, H.

1,2-*O*-Isopropylidene-5(*R*)-(((4-toluenesulfonyl)oxy)-methyl)-1(*R*),2(*S*),3(*R*)-trihydroxycyclohexane (22). Diol **20** (1.60 g, 7.92 mmol) was dissolved in pyridine/methylene chloride (12 mL, 1:1) and cooled to 0 °C. *p*-Toluenesulfonyl chloride (1.51 g, 7.92 mmol) was added, and the reaction was allowed to stir overnight at 0 °C. The reaction was diluted with ether (50 mL) and washed with water (25 mL), 10% aqueous copper(II) sulfate (3 × 50 mL), water (25 mL), and brine (25 mL). The organic layer was dried over magnesium sulfate, and the residue was placed on a 3-cm flash silica gel column (15 cm of silica gel) and eluted with ethyl acetate/hexane (1:4), changing to ethyl acetate/hexane (1:2.5) to recover the tosylate. Solvent removal in vacuo afforded 2.59 g (7.28 mmol, 92%) of the title compound: ^1H NMR (270 MHz, $CDCl_3$) δ 7.78 (d, 2 H, *J* = 8.3 Hz), 7.35 (d, 2 H, *J* = 8.2 Hz), 4.24 (q, 1 H, *J* = 6.0 Hz), 3.90 (m, 4 H), 3.32 (s, 1 H), 2.44 (s, 3 H), 1.85 (dt, 1 H, *J* = 14.0, 4.6 Hz), 1.69–1.22 (m, 4 H), 1.39 (s, 3 H), 1.30 (s, 3 H). Anal. Calcd for $C_{17}H_{24}O_6Si$: 342.1136. Found: 296.1617.

1,2-*O*-Isopropylidene-5(*R*)-(azidomethyl)-1(*R*),2(*S*),3-(*R*)-trihydroxycyclohexane (23). Tosylate **22** (20.52 g, 60 mmol) was placed in a flask with sodium azide (3.5 equiv, 13.6 g, 210 mmol), and 100 mL of DMF was added. The slurry was heated to 50 °C and stirred for 12 h. The solution was diluted with 500 mL of ether and washed with water (5 × 150 mL) and brine (100 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford 12.44 g (54.8 mmol, 91%) of azide. It is important to note that every effort should be made to remove any tosyl chloride remaining from the previous reaction—a vacuum pump cold trap once exploded, presumably from adventitious tosyl azide formed in this reaction, $[\alpha]^{25}_{589}$ +0.618° (*c* 6.307/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 4.31 (dt, 1 H, *J* = 13.2, 5.5 Hz), 4.09 (m, 1 H), 3.96 t, 1 H, *J* = 5.52 Hz), 3.29 (d, 2 H, *J* = 6.6 Hz), 2.92 (d-disappears upon addition of D_2O, 1 H, *J* = 3.3 Hz), 2.06–1.63 (m, 5 H), 1.49 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 107.8, 77.6, 72.7, 66.9, 56.1, 31.3, 30.4, 29.2, 27.8, 25.4; IR ($CHCl_3$) 3602, 3460, 2100, 1060 cm^{-1}. Anal. ($C_{10}H_{17}N_3O_3$) C, H.

1,2-*O*-Isopropylidene-5(*S*)-(azidomethyl)-1(*R*)-(*tert*-butyldimethylsiloxy)-2(*R*),3(*R*)-dihydroxycyclohexane (24). Alcohol **23** (5.00 g, 22.0 mmol) was dissolved in 50 mL of DMF. The solution was cooled to 0 °C, and imidazole (2.40 g, 35.2 mmol) and *tert*-butyldimethylchlorosilane (3.65 g, 24.2 mmol) were added. Upon dissolution, the solution was allowed to warm to 25 °C and proceed for 14 h. The solution was then diluted with 300 mL of ether and washed with water (3 × 200 mL), 2 N aqueous hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL), and brine (200 mL). The solution was dried over magnesium sulfate, and the solvent was removed in vacuo. The residue was bulb-to-bulb distilled (130 °C/0.1 mmol) (a blast shield was used as a safety precaution) to afford 5.77 g (16.9 mmol, 77%) of the title compound as a clear liquid, $[\alpha]^{25}_{589}$ +3.03° (*c* 3.10/$CHCl_3$): ^1H NMR (270 mHz, $CDCl_3$) δ 4.25 (q, 1 H, *J* = 6.0 Hz), 4.03 (m, 1 H), 3.82 (m, 1 H), 3.19 (t, 2 H, *J* = 2.1 Hz), 2.01–1.50 (m, 5 H), 1.42 (s, 3 H), 1.30 (s, 3 H), 0.80 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 107.8, 77.1, 72.9, 68.0, 57.0, 31.8, 30.7, 28.8, 28.0, 25.6, 17.8, −4.7; IR ($CHCl_3$) 2100, 1107, 1049 cm^{-1}. Anal. Calcd for $C_{16}H_{31}N_3O_3Si$: 341.2134. Found: 341.2142.

1,2-*O*-Isopropylidene-5(*S*)-(aminomethyl)-3(*R*)-(*tert*-butyldimethylsiloxy)-1(*R*),2(*R*)-dihydroxycyclohexane (25). Azide **24** (5.77 g, 16.9 mmol) dissolved in 100 mL of THF was treated with 10% palladium on carbon (250 mg) and subjected to atmospheric hydrogenation. After 5 h, the slurry was filtered through a Celite pad which was then washed with methylene chloride. The solvent was removed in vacuo to afford 5.19 g (16.5 mmol, 97%) of pure amine, $[\alpha]^{25}_{589}$ −3.80° (*c* 2.36/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 4.22 (q, 1 H, *J* = 6.0 Hz), 4.07 (m, 1 H), 3.86 (m, 1 H), 2.59 (d, 2 H, *J* = 6.5 Hz), 2.00 (br s, 2 H), 1.91–1.44 (m, 5 H), 1.43 (s, 3 H), 1.29 (s, 3 H), 0.83 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 107.9, 77.5, 73.4, 68.3, 47.7, 32.3, 31.4, 28.2, 26.0, 25.8, 18.1, −4.7, −4.8. Anal. Calcd for $C_{16}H_{23}NO_3Si$: 315.2228. Found: 315.2239.

***N*-[(3(*R*)-(*tert*-Butyldimethylsiloxy)-4(*R*),5(*R*)-dihydroxy-4,5-*O*-isopropylidenecyclohex-1(*S*)-yl)methyl]-2-(indol-3′-yl)acetamide (26).** Indole-3-acetic acid (1.64 g, 9.38 mmol) was dissolved in 10 mL of DMF with 2.07 g (20.5 mmol) of triethylamine. The solution was cooled to −20 °C, and neat

diphenylphosphoryl azide (2.26 g, 8.20 mmol) was added. After 30 min, a solution of amine **25** (1.85 g crude, 5.86 mmol) was added in 5 mL of DMF. Stirring was continued at −20 °C for 3 h, after which the solution was allowed to gradually warm to 25 °C and proceed for 12 h. The reaction was diluted with ether (25 mL) and methylene chloride (15 mL) and washed with water (3 × 100 mL), 2 N aqueous hydrochloric acid (50 mL), saturated aqueous sodium carbonate (50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo. The residue was eluted on a silica gel column with ethyl acetate/hexane (10:90), gradually changing to ethyl acetate/hexane (30:70) to recover the amide. Solvent removal in vacuo afforded 1.78 g (3.77 mmol, 64% for both steps) of pure foam, $[\alpha]^{25}_{589}$ +3.32° (*c* 0.995/$CHCl_3$): ^1H NMR (200 MHz, $CDCl_3$) δ 8.32 (br s, 1 H), 7.60 (d, 1 H, *J* = 8.1 Hz), 7.40 (d, 1 H, *J* = 8.0 Hz), 7.20–7.03 (m, 3 H), 5.85 (br t, 1 H, *J* = 7.0 Hz), 4.20 (q, 1 H, *J* = 7.2 Hz), 4.02 (m, 1 H), 3.80 (m, 1 H), 3.72 (s, 2 H), 3.10 (q, 2 H, *J* = 7.3 Hz), 1.95–1.15 (m, 5 H), 1.40 (s, 3 H), 1.28 (s, 3 H), 0.80 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 171.4, 136.5, 127.1, 123.4, 122.5, 119.9, 118.5, 111.3, 109.3, 108.7, 77.5, 73.1, 68.4, 44.9, 33.5, 31.7, 30.8, 28.5, 27.9, 25.7, 17.9, −4.9; IR ($CHCl_3$) 3490, 3430, 3345, 1655, 1055, cm^{-1}. Anal. Calcd for $C_{26}H_{40}N_2O_4Si$: 427.2755. Found: 472.2759.

(2-Indol-3′-ylethyl)[(3(*R*)-(*tert*-butyldimethylsiloxy)-4-(*R*),5(*R*)-dihydroxy-4,5-*O*-isopropylidenecyclohex-1(*S*)-yl)methyl]amine (27). Amide **26** (4.17 g, 8.83 mmol) was dissolved in 30 mL of THF and cooled to 0 °C. Diisobutylaluminum hydride (DIBAL-H, 1.5 M solution in toluene, 23.5 mL, 35.3 mmol) was added slowly, after which the solution was heated to reflux and allowed to stir for 4 h. The solution was then cooled, diluted with 100 mL of ether, and quenched by the slow addition of water. The solution was washed with 15% aqueous sodium hydroxide (3 × 50 mL), water (4 × 50 mL), and brine (50 mL). The organic layer was dried over sodium sulfate, and the solvent was removed in vacuo to afford 3.84 g (8.39 mmol, 95%) of amine, $[\alpha]^{25}_{589}$ = +7.65° (*c* 13.3/$CHCl_3$): ^1H NMR (200 MHz, $CDCl_3$) δ 8.31 (br s, 1 H), 7.59 (d, 1 H, *J* = 7.9 Hz), 7.42 (d, 1 H, *J* = 7.7 Hz), 7.20–7.03 (m, 3 H), 4.23 (m, 1 H), 4.06 (m, 1 H), 3.88 (m, 1 H), 2.95 (m, 4 H), 2.57 (d, 2 H, *J* = 7.0 Hz), 2.20 (br s, 1 H), 2.00–1.17 (m, 5 H), 1.50 (s, 3 H), 1.32 (s, 3 H), 0.90 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 136.3, 127.2, 121.8, 121.2, 119.1, 118.6, 113.0, 111.0, 108.0, 77.5, 73.3, 68.3, 54.9, 49.5, 32.6, 31.6, 28.1, 27.9, 25.8, 24.9, 18.1, −4.7, −4.8; IR ($CHCl_3$) 3480, 1045 cm^{-1}. Anal. Calcd for $C_{26}H_{42}N_2O_3Si$: 458.2963. Found: 458.2959.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(3-(*R*)-(*tert*-butyldimethylsiloxy)-4,5-*O*-isopropylidene-4-(*R*),5(*R*)-dihydroxycyclohex-1(*S*)-yl)methyl]carbamate (28). Amine **27** (7.50 g, 16.4 mmol) and triethylamine (1.98 g, 19.6 mmol) were dissolved in 50 mL of methylene chloride and cooled to 0 °C. Neat 2-(trimethylsilyl)ethyl chloroformate[19] (3.25 g, 18.0 mmol) was added, and stirring proceeded for 3 h. The solution was diluted with 100 mL of ether and washed with 2 N aqueous hydrochloric acid (50 mL), water (3 × 50 mL), saturated aqueous sodium bicarbonate (50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford 8.87 g (14.7 mmol, 90%) of a viscous liquid, $[\alpha]^{25}_{589}$ +8.87° (*c* 3.23/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 8.40 (br s, 1 H), 7.59 (m, 1 H), 7.0–7.4 (m, 3 H), 6.91 (s, 1 H), 4.21–4.09 (m, 6 H), 3.85 (m, 1 H), 3.46 (m, 2 H), 2.96 (m, 2 H), 2.25–1.20 (m, 5 H), 1.47 (s, 3 H), 1.39 (s, 3 H), 1.00–0.90 (m, 2 H), 0.08 (s, 9 H), 0.03 (m, 15 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.5, 136.2, 127.3, 121.7, 121.6, 119.1, 118.5, 113.0, 110.9, 108.1, 77.6, 73.5, 68.2, 63.3, 52.7, 48.7, 32.7, 32.0, 28.3, 27.9, 26.2, 25.8, 24.1, 18.1, −1.3, −4.7; IR ($CHCl_3$) 3480, 1730 cm^{-1}. Anal. Calcd for $C_{32}H_{54}N_2O_5Si_2$: 602.3568. Found: 602.3574.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(3,4-*O*-isopropylidene-3(*R*),4(*S*),5(*R*)-trihydroxycyclohex-1(*R*)-yl)methyl]carbamate (29). Silyl ether **28** (1.63 g, 2.84 mmol) was dissolved in 5 mL of THF and cooled to 0 °C. A 1.0 M solution of tetra-*n*-butylammonium fluoride in THF (5% water) (5.68 mL, 5.68 mmol) was added, and the dark solution was stirred for 2.5 h. The reaction was diluted with 30 mL of ether and washed with water (5 × 35 mL) and brine (35 mL). The organic layer was dried over sodium sulfate, and the solvent was removed in vacuo to afford 987 mg (2.33 mmol, 82%) of pure alcohol. Care must be taken in this reaction since the 2-trimethylsilylethyl carbamate can also cleave if conditions are forced, $[\alpha]^{25}_{589}$ −5.41° (*c* 1.48/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 8.21 (br s, 1 H), 7.62 (m, 1 H), 7.41 (d, 1 H, *J* = 7.7 Hz), 7.23–7.00 (m, 3 H), 4.29–4.03 (m, 6 H), 3.93 (t, 1 H, *J* = 7.1 Hz), 3.69–3.25 (m, 2 H), 3.10–2.87 (m, 2 H), 2.03 (m, 1 H), 1.93–1.30 (m, 5 H), 1.45 (s, 3 H), 1.30 (s, 3 H), 1.00 (m, 2 H), 0.02 (m, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.9, 136.5, 127.6, 121.9, 121.6, 119.2, 118.7, 113.2, 111.1, 108.4, 78.8, 73.6, 68.1, 63.4, 52.5, 48.7, 32.0, 31.3, 28.7, 28.2, 25.9, 24.3, 17.9, −1.5; IR ($CHCl_3$) 3602, 3483, 1680, 1050 cm^{-1}. Anal. ($C_{26}H_{40}N_2O_5Si$) C, H.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(4,5-*O*-isopropylidene-4(*R*),5(*R*)-dihydroxy-3(*R*)-((methanesulfonyl)oxy)cyclohex-1(*S*)-yl)methyl]carbamate (30). Alcohol **29** (660 mg, 1.56 mmol) and triethylamine (189 mg, 1.87 mmol) were dissolved in 5 mL of methylene chloride and cooled to 0 °C. Neat methanesulfonyl chloride (196 mg, 1.71 mmol) was slowly added, and the solution was stirred for 3 h at 0 °C. The reaction was diluted with 20 mL of ether and washed with 2 N aqueous hydrochloric acid (10 mL), water (2 × 10 mL), saturated aqueous sodium bicarbonate (10 mL), and brine (10 mL). The organic layer was dried over magnesium sulfate, and the solvent was evaporated. The residue was placed on a flash silica gel column and eluted with ethyl acetate/hexane (25:75). Solvent evaporation afforded 880 mg (1.56 mmol, 91%) of the title compound as a viscous oil, $[\alpha]^{25}_{589}$ −25.5° (*c* 1.145/$CHCl_3$): ^1H NMR (200 MHz, $CDCl_3$) δ 8.09 (br s, 1 H), 7.61 (m, 1 H), 7.27 (d, 1 H, *J* = 7.7 Hz), 7.23–6.95 (m, 3 H), 4.88 (m, 1 H), 4.26–4.05 (m, 3 H), 4.03 (t, 1 H, *J* = 6.0 Hz), 3.50 (m, 4 H), 3.1–2.8 (m, 2 H), 3.00 (s, 3 H), 2.0–1.5 (m, 5 H), 1.48 (s, 3 H), 1.32 (s, 3 H), 0.92 (m, 2 H), 0.04 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.8, 136.5, 127.5, 122.0, 119.5, 118.3, 113.4, 111.3, 108.6, 79.6, 76.1, 73.5, 63.3, 52.1, 47.8, 38.2, 30.2, 29.3, 27.8, 25.7, 23.8, 17.8, −1.5; IR ($CHCl_3$) 3483, 1682, 1457, 1250, 1172, 1056 cm^{-1}. Anal. Calcd for $C_{27}H_{42}N_2O_7SSi$: 566.2480. Found: 566.2483.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(4-(*R*),5(*R*)-dihydroxy-3(*R*)-((methanesulfonyl)oxy)cyclohex-1(*S*)-yl)methyl]carbamate (31). Dioxolane **30** (600 mg, 1.06 mmol) was dissolved in THF/water (65 mL, 1:1) which was 0.24 N in hydrochloric acid. This solution was stirred for 16 h at 25 °C, then diluted with 20 mL of ether and washed with brine (50 mL), water (2 × 50 mL), saturated aqueous sodium bicarbonate (50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford 546 mg (1.04 mmol, 98%) of pure diol, $[\alpha]^{25}_{589}$ −9.69° (*c* 1.47/$CHCl_3$): ^1H NMR (270 MHz, $CDCl_3$) δ 8.07 (s, 1 H), 7.59 (br d, 1 H, *J* = 7.5 Hz), 7.35 (d, 1 H, *J* = 8.0 Hz), 7.21–6.98 (m, 3 H), 4.89 (m, 1 H), 4.40–2.80 (m, 13 H), 2.03–1.50 (m, 7 H), 1.00–0.95 (m, 2 H), 0.03 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 157.0, 136.1, 127.2, 121.9, 121.7, 119.0, 118.4, 112.7, 111.1, 79.9, 70.4, 68.3, 63.8, 53.8, 52.2, 42.8, 38.4, 31.1, 30.5, 24.0, 17.9, −1.3; IR ($CHCl_3$) 3489, 3400, 1676, 1420, 1355, 1214, 1171 cm^{-1}.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(3-(*S*),4(*R*)-epoxy-5(*R*)-hydroxycyclohex-1(*S*)-yl)methyl]carbamate (32). Potassium hydroxide (86.7 mg, 1.55 mmol) dissolved in 10 mL of methanol was added quickly to a solution of mesylate **31** (740 mg, 1.41 mmol) in 10 mL of ether at 0 °C. After 5 min of stirring, the reaction was diluted with 30 mL of ether and filtered through silica gel (8 g), eluting with ether. The solvent was removed in vacuo, and the residue was placed on a 0.5 cm flash silica gel column (12 cm of silica gel) and eluted with ethyl acetate/hexane (75:25). The solvent was removed in vacuo to afford 704 mg (1.34 mmol, 95%) of pure epoxide, $[\alpha]^{25}_{589}$ −11.0° (*c* 2.55/$CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 8.06 (s, 1 H), 7.56 (m, 1 H), 7.29 (d, 1 H, *J* = 10.1), 7.17–7.02 (m, 2 H), 6.91 (br s, 1 H), 4.07 (m, 2 H), 3.84 (m, 1 H), 3.46 (t, 2 H, *J* = 6.8 Hz), 3.25 (m, 2 H), 2.97 (m, 4 H), 2.00–1.50 (m, 5 H), 1.38 (m, 1 H), 0.95 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.6, 136.1, 127.2, 121.8, 121.2, 119.2, 118.4, 112.8, 111.1, 68.8, 63.5, 56.1, 54.3, 52.7, 49.1, 33.0, 31.8, 27.4, 24.4, 18.0, −1.3; IR ($CHCl_3$) 3590, 3490, 3400, 1681, 1422, 1252, 1211 cm^{-1}. Anal. Calcd for $C_{23}H_{34}N_2O_4Si$: 430.2286. Found: 430.2291.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(1-(*S*),5(*S*)-epoxy-3-oxocyclohex-1(*R*)-yl)methyl]carbamate (33). Chromium trioxide (1.26 g, 12.6 mmol) was added in portions to a methylene chloride solution (15 mL) of pyridine (1.99 g, 225.2

mmol), containing 2.5 g of Celite at 0 °C. The solution was warmed to 25 °C and allowed to stir for 2 h. After the solution cooled to 0 °C, alcohol **32** (542 mg, 1.26 mmol) dissolved in 5 mL of methylene chloride was added. The blackened solution was stirred for 1 h and then filtered through a plug of silica gel (30 g) with ethyl acetate/hexane (4:6). The solvent was partially evaporated, and the residue was washed with 10% aqueous sodium bisulfate (20 mL), water (2 × 25 mL), saturated aqueous sodium bicarbonate (25 mL), and brine (25 mL). The organic layer was dried over magnesium sulfate, and the solvent was removed in vacuo to afford 462 mg (1.08 mmol, 86%) of pure ketone, $[\alpha]^{25}_{589}$ −9.46° (*c* 1.21/$CHCl_3$): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.03 (br s, 1 H), 7.59 (m, 1 H), 7.30 (d, 1 H, *J* = 9.1 Hz), 7.20 (t, 1 H, *J* = 8.1 Hz), 7.11 (t, 1 H, *J* = 8.3 Hz), 6.97 (m, 1 H), 4.10 (m, 2 H), 3.46 (m, 2 H), 3.25–2.81 (m, 6 H), 2.50–1.25 (m, 5 H), 0.93 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 206.2, 156.3, 135.9, 127.0, 121.7, 121.6, 119.1, 118.3, 112.6, 110.9, 63.4, 57.8, 54.7, 52.6, 48.4, 39.3, 37.1, 27.0, 24.0, 17.9, −1.4; IR ($CHCl_3$) 1716, 1684, 1420, 1250 cm^{-1}. Anal. Calcd for $C_{23}H_{32}N_2O_4Si$: 428.2130. Found: 428.2130.

2-(Trimethylsilyl)ethyl *N*-(2-Indol-3′-ylethyl)-*N*-[(3-(*S*),4(*R*)-epoxy-5-methylenecyclohex-1(*S*)-yl)methyl]carbamate (34). Methylenetriphenylphosphorane (2.17 mmol), generated from the phosphonium iodide and potassium *tert*-butoxide, in THF (7 mL) was cooled to −30 °C, and a solution of ketone **33** (620 mg, 1.45 mmol) in 3 mL of THF was added. Stirring was allowed to proceed for 30 min at −30 °C, then warmed to 25 °C, and continued for 20 min. The solution was diluted with 30 mL of ether and washed with water (4 × 20 mL) and brine (25 mL). The organic layer was dried over sodium sulfate, and the solvent was evaporated. The residue was placed on a 2-cm flash silica gel column (15 cm of silica gel) and eluted with ethyl acetate/hexane (25:75). After solvent removal in vacuo, 556 mg (1.30 mmol, 90%) of the title compound, $[\alpha]^{25}_{589}$ +0.17° (*c* 2.31/$CHCl_3$), was obtained: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.09 (br s, 1 H), 7.61 (m, 1 H), 7.28 (d, 1 H, *J* = 7.9 Hz), 7.25–7.02 (m, 2 H), 6.93 (m, 1 H), 5.19 (s, 1 H), 5.05 (s, 1 H), 4.14 (m, 2 H), 3.51–3.44 (m, 4 H), 3.00 (m, 4 H), 2.08–1.28 (m, 5 H), 0.93 (m, 2 H), 0.03 (s, 9 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 156.4, 142.8, 136.1, 127.1, 119.9, 118.3, 114.2, 112.6, 111.0, 63.7, 55.8, 54.1, 52.7, 48.8, 34.8, 32.3, 28.3, 23.9, 17.9, −1.4; IR ($CHCl_3$) 3482, 1732, 1420, 1250, 1065 cm^{-1}. Anal. Calcd for $C_{24}H_{34}N_2O_3Si$: 426.2337. Found: 426.2333.

(2-Indol-3′-ylethyl)[(3(*S*),4(*R*)-epoxy-5-methylenecyclohex-1(*S*)-yl)methyl]amine (35). Tetra-*n*-butylammonium fluoride (1.00 g, 3.66 mmol) and carbamate **34** (624 mg, 1.46 mmol) were dissolved in 5 mL of acetonitrile and heated to 50 °C. The darkened solution was allowed to stir for 2.5 h, then cooled, and diluted with 25 mL of ether. The solution was washed with water (5 × 15 mL) and brine 20 mL). The organic layer was dried over sodium sulfate, and the solvent was removed in vacuo to afford 297 mg (1.05 mmol, 72%) of the title compound, $[\alpha]^{25}_{589}$ −3.17° (*c* 2.69/$CHCl_3$): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.30 (br s, 1 H), 7.59 (d, 1 H, *J* = 7.9 Hz), 7.29 (d, 1 H, *J* = 8.0 Hz), 7.21 (t, 1 H, *J* = 7.7 Hz), 7.10 (t, 1 H, *J* = 7.3 Hz), 6.97 (s, 1 H), 5.20 (s, 1 H), 5.03 (s, 1 H), 3.39 (d, 1 H, *J* = 4.2 Hz), 3.31 (t, 1 H, *J* = 4.3 Hz), 2.94 (m, 4 H), 2.47 (d, 2 H, *J* = 6.2 Hz), 2.09–1.25 (m, 5 H); ^{13}C NMR (15 MHz, $CDCl_3$) δ 143.2, 136.1, 127.0, 121.6, 121.1, 118.9, 118.5, 113.7, 113.5, 110.9, 55.9, 55.4, 49.9, 35.7, 32.7, 28.8, 25.7. Anal. Calcd for $C_{18}H_{22}N_2O$: 282.1732. Found: 282.1729.

***N*-(2-Indol-3′-ylethyl)-6(*S*)-hydroxy-7-methylene-1(*R*),4-(*S*)-2-azabicyclo[2.2.2]octane (36).** Vinyl epoxide **35** (720 mg, 2.55 mmol) and tetrakis(triphenylphosphine)palladium(0) (118 mg, 0.102 mmol) were placed in a flask under an inert atmosphere. THF (5 mL) was added, and the solution was stirred for 3 h at 25 °C. The solution was poured onto a 1-cm flash silica gel column (12 cm of silica gel) and eluted with ethyl acetate/hexane (1:1), changing to methanol/chloroform/diethylamine (10:89:1 v/v/v) to recover the product. Solvent removal in vacuo afforded 683 mg (2.42 mmol, 95%) of pure isoquinuclidine, $[\alpha]^{25}_{589}$ +43.5° (*c* = 0.715/$CHCl_3$): ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.37 (br s, 1 H), 7.58 (d, 1 H, *J* = 7.4 Hz), 7.27 (d, 1 H, *J* = 7.6 Hz), 7.18–7.07 (m, 2 H), 6.92 (s, 1 H), 4.91 (s, 1 H), 4.86 (s, 1 H), 3.83 (dm, 1 H, *J* = 9.6 Hz), 3.24 (d, 1 H, *J* = 10.7 Hz), 2.91 (d, 1 H, *J* = 4.3 Hz), 2.87 (m, 2 H), 2.75 (m, 2 H), 2.23 (dm, 1 H, *J* = 9.6 Hz), 2.12 (br s, 2 H), 1.90–2.79 (m, 2 H), 1.46 (dm, 1 H, *J* = 12.9); ^{13}C NMR (15 MHz, $CDCl_3$) δ 142.6, 135.8, 127.9, 127.6, 125.9, 121.6, 118.9, 118.5, 114.0, 111.0, 67.9, 64.5, 55.7, 36.9, 34.2; IR ($CHCl_3$) 3480, 3359, 1455, 1439, 1119, 1017 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2O$: 282.1732. Found: 282.1738.

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Registry No. (±)-**8**, 68217-48-1; (±)-**9**, 101917-40-2; (±)-**10**, 101917-41-3; (±)-**11**, 101917-42-4; (±)-**12**, 101917-43-5; (±)-**13**, 101917-44-6; (±)-**14**, 101917-45-7; **16**, 32384-42-2; **17**, 101917-46-8; **18**, 101917-47-9; **19**, 101917-48-0; **20**, 101917-49-1; **22**, 101917-50-4; **23**, 101917-51-5; **24**, 101917-52-6; **25**, 101917-53-7; **26**, 101917-54-8; **27**, 101917-55-9; **28**, 101917-56-0; **29**, 101917-57-1; **30**, 101917-58-2; **31**, 101917-59-3; **32**, 101917-60-6; **33**, 101917-61-7; **34**, 101917-62-8; **35**, 101917-63-9; **36**, 101917-64-0; D-(−)-quinic acid, 77-95-2; tryptamine, 61-54-1; 2-(trimethylsilyl)ethyl chloroformate, 20160-60-5; methyltriphenylphosphonium iodide, 2065-66-9; 3-indoleacetic acid, 87-51-4; *N*-(2-indol-3′-ylethyl)-3(*R**)-hydroxycyclohex-4-ene-1(*R**)-carboxamide, 101917-34-4; *N*-(2-indol-3′-ylethyl)-3(*R**)-(*tert*-butyldimethylsiloxy)cyclohex-4-ene-1(*R**)-carboxamide, 101917-35-5; 2-(trimethylsilyl)ethyl *N*-(2-indol-3′-ylethyl)-*N*-[(3(*R**)-(*tert*-butyldimethylsiloxy)cyclohex-4-en-1-(*R**)-yl)methyl]carbonate, 101917-36-6; 2-(trimethylsilyl)ethyl *N*-[2-(1′-carbomethoxyindol-3′-yl)ethyl)-*N*-[(3(*R**)-((*tert*-butyldimethylsilyl)oxy)cyclohex-4-en-1(*R**)-yl)methyl]carbamate, 101917-37-7; 2-(trimethylsilyl)ethyl *N*-[2-(1′-carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*R**)-hydroxycyclohex-4-en-1(*R**)-yl)-methyl]carbonate, 101917-38-8; 2-(trimethylsilyl)ethyl *N*-[2-(1′-carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*S*),4(*R**)-epoxy-5(*R**)-hydroxycyclohex-1(*S**)-yl)methyl]carbamate, 101932-70-1; 2-(trimethylsilyl)ethyl *N*-[2-(1′-carbomethoxyindol-3′-yl)ethyl]-*N*-[(3(*S**),4(*R**)-epoxy-5-methylenecyclohex-1(*S**)-yl)methyl]-carbamate, 101917-39-9; ethyltriphenylphosphonium bromide, 1530-32-1; methylenetriphenylphosphorane, 3487-44-3; 2-1′-carbomethoxyindol-3′-ethyl [(3(*S**),4(*R**)-epoxy-5(*Z*)-ethylidenecyclohex-1(*S**)-ylmethyl]amine, 101917-65-1.