= 3.9 Hz, H13), 2.81 (1 H, dd, J = 3.9, 0.62 Hz, H 13'), 2.61 (1 H, dd, J_{gem} = 15.6, $J_{3,4}$ = 7.6 Hz, H3 exo), 2.02–1.97 (2 H, m, allylic CH₂), 1.93 (1 H, dd, br, H7), 1.9 (1 H, ddd, J_{gem} = 15.7, $J_{3,2}$ = 5.5, $J_{3,4}$ = 3.2 Hz, H3 endo), 1.7 (3 H, q, J = 0.6 Hz), 1.52 (1 H, m, OH, exch D₂O), 1.47–1.40 (1 H, m, 7H exo or endo), 0.88 (3 H, s, Me), 0.8 (3 H, s, Me). High-resolution mass spectrum calcd for C₁₅H₂₂O₃ 250.1569, found 250.1560. Spectral data for (±)-trichodermol have not been previously reported.

Acknowledgment. We are very grateful to the U.S. Public Health Service, National Institutes of Health, for

Supplementary Material Available: ¹H NMR spectra of compounds 1, 6, 7, 23, 28, 37–39, 54–58, and 61–70 and ¹³C NMR spectra of 68 (31 pages). Ordering information is given on any current masthead page.

Asymmetric Synthesis of the (4aS,8aR,8S)-Hydrolilolidone System. A Formal Total Synthesis of Unnatural (+)-Aspidospermine

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An approach to the aspidosperma alkaloid precursor 15 using chiral, nonracemic bicyclic lactam 3 as starting material is described in 10 steps (8.2% overall).

There have been a number of outstanding efforts over the past 25 years to totally synthesize the *aspidosperma* alkaloids, and the pioneering studies by Stork and Dolfini,[1] along with Ban and co-workers,[2] are particularly noteworthy. These groups were the first to obtain aspidospermine 1 in *racemic* form, whereas Saxton and co-workers[3] completed the racemic total synthesis of a number of C-18-functionalized derivatives. In all of the reported syntheses of the *aspidosperma* alkaloids, the tricyclic hydrolilolidone system (2 and 15) has served as a key precursor for the critical Fischer indole synthesis.[4]

2 (X = H₂)
1
15 (X = O)
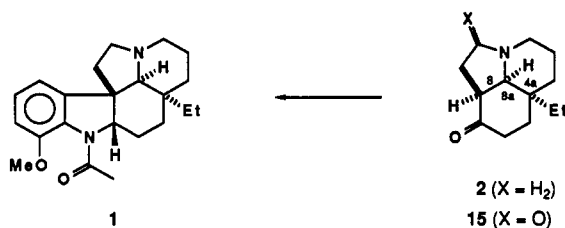
Based upon our recent studies with chiral bicyclic lactams of which (+)-3 is a typical example,[5] we envisioned that under the proper stereochemical control we should be in a position to produce the tricyclic amino ketone 2 or its immediate precursor 15 in nonracemic form. Although this would lead to the unnatural enantiomer of aspidospermine 1, we felt it would adequately demonstrate our methodology. Our route required that we alkylate (+)-3 in a sequential manner with ethyl iodide followed by allyl bromide via the enolate.[6] In this manner, we were

able to obtain (+)-4 in 48–50% yield. The ratio of diastereomers was at least 25:1 with the *endo*-allyl isomer as the major component. Transformation to the chiral cyclohexenone 5 was accomplished in 77% yield by Red-Al (Aldrich) treatment followed by mild acidic hydrolysis, as described in earlier reports from this laboratory.[5,7]

The synthetic scheme (see Scheme I) required that the terminal olefin be hydrated to the alcohol, and this was done by treatment of 5 with 9-BBN. The resulting diol 6 was obtained as a 1:1 mixture of diastereomers and was directly oxidized by the Jones reagent to the keto acid 7, which was isolated in 77% yield for the two steps. A small sample of 7 was transformed into the methyl ester 8 for characterization purposes while the major portion of the material was transformed into the acid chloride 9 using oxalyl chloride. Addition of ammonia gave the amide 10 in 73% yield from the acid.[8]
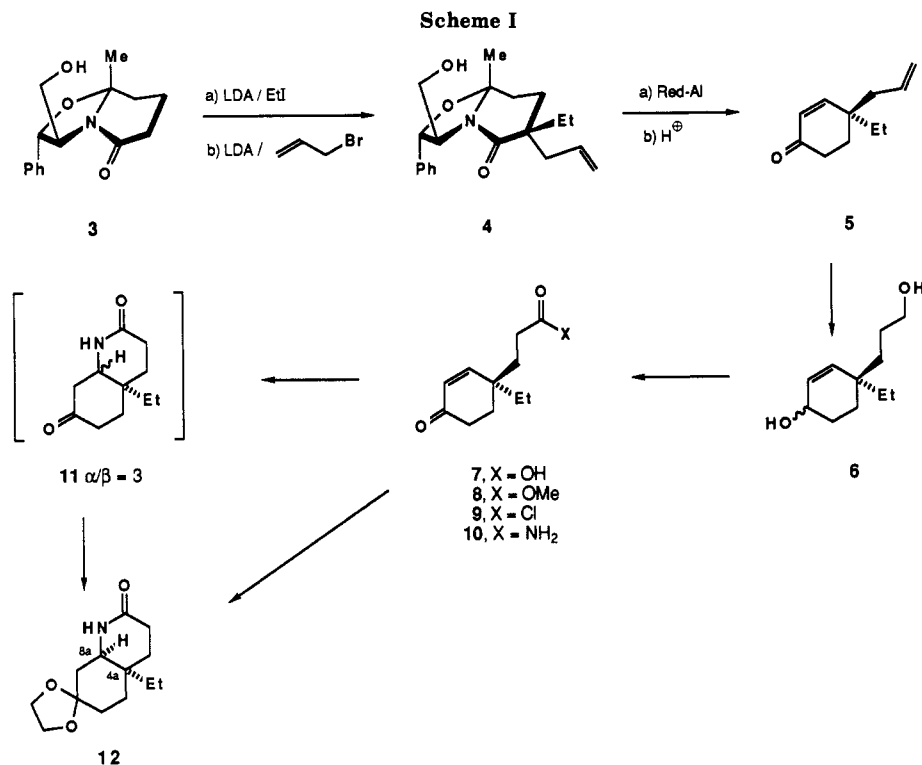
In order to form the hydroquinolinone system 11, reported earlier,[2,3] the amide 10 was heated in benzene containing a catalytic amount of *p*-toluenesulfonic acid which produced 11 as a 3:1 mixture of cis–trans isomers. Although these were partially separable, the lackluster ratios demanded another approach before proceeding forward. It was subsequently found that adding ethylene glycol to the mixture of 11 and heating at reflux with the acid catalyst converted the 3:1 mixture to the dioxolane

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(1) Stork, G.; Dolfini, J. E. *J. Am. Chem. Soc.* **1963**, *85*, 2872.

(2) Ban, Y.; Sato, Y.; Inoue, I.; Nagai, M.; Oishi, T.; Terashima, M.; Yonematsu, O.; Kanaoka, Y. *Tetrahedron Lett.* **1965**, 2261.

(3) Lawton, G.; Saxton, J. E.; Smith, A. J. *Tetrahedron* **1977**, *33*, 1641.

(4) (a) Stevens, R. V.; Fitzpatrick, J. M.; Kaplan, M.; Zimmerman, R. L. *J. Chem. Soc., Chem. Commun.* **1971**, 857. (b) Wu, P.-L.; Chu, M.; Fowler, F. W. *J. Org. Chem.* **1988**, *53*, 963. (c) Martin, S. F.; Desai, S. R.; Phillips, G. W.; Miller, A. C. *J. Am. Chem. Soc.* **1980**, *102*, 3294. (d) Kuehne, M. E.; Bayha, C. *Tetrahedron Lett.* **1966**, 1311.

(5) Meyers, A. I.; Lefker, B. A. *Tetrahedron* **1987**, *43*, 5663.

(6) The alkylation of (+)-3 using first allyl bromide and then ethyl iodide also proceeded with equal efficiency (~10:1 crude diastereomeric ratio) to afford the epimer of 4. Although carrying this through to the enantiomer of 5 would have ultimately given the natural hydrolilolidone system and a formal total synthesis of natural aspidospermine, we elected to proceed with the unnatural series for two reasons: (a) Chromatography would have been necessary to obtain the pure epimer of 4, rather than simple recrystallization (see the Experimental Section), and we wished to demonstrate that this entire synthetic sequence to 15 could be performed without chromatography. (b) Our belief that a major, but sometimes overlooked, value of asymmetric syntheses is the ability to prepare unnatural materials so their biological properties may be evaluated.

(7) The preparation of 5 has been submitted to *Organic Syntheses* and has been successfully checked. It will appear in a future issue.

(8) Amide 10 was reported by Stork (ref 1) in racemic form.

Scheme I

Scheme II

12 as a single diastereomer.[9] The material was formed cleanly in 85% yield and was undoubtedly the result of acid-catalyzed equilibration via a retro-Michael process. It may be assumed that the cis isomer of 11 forms faster and is the more stable ketal under acidic conditions. This allows for the trans isomer to undergo the retro-Michael reaction and reform the original cis–trans mixture. It was also found that heating the keto amide 10 in benzene and adding the ethylene glycol after several hours also gave the single ketal lactam 12 in comparable yields. Thus, the requisite unnatural aspidospermine precursor was reached in good yield in a single step. The cis ring fusion was confirmed by NOE measurements, which showed strong enhancement between the CH_2 of the angular ethyl group and the C-8a proton. The enantiomeric purity of 12 was expected to be at least 92% (96:4) based on the enantiomeric purity found earlier for the bicyclic lactam 4. Nevertheless, it was felt that an independent check would be desirable at this stage. Employing the chiral Pirkle solvent, (R)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol,[10] an NMR experiment showed different shifts for each enantiomer of 12 with integration of 97:3, in very good agreement with the diastereomeric ratio (96:4) observed for bicyclic lactam 4. The lactam was treated with lithium aluminum hydride and furnished the amino ketone 13 after hydrolytic removal of the ketal group (Scheme II). Stork, Ban, and Stevens[11] all reported the racemic version of this material in their synthesis of aspidospermine[1,2] and described it as a low-melting solid (mp 47–50 °C, 51–52 °C, respectively). The material in our hands, which was 92% ee, was an oil for which we were unable to induce crystallization. The acylation to the chloroacetyl amide 14 was performed according to Stork's procedure and gave the product in 61% yield as a crystalline solid, mp 112–114
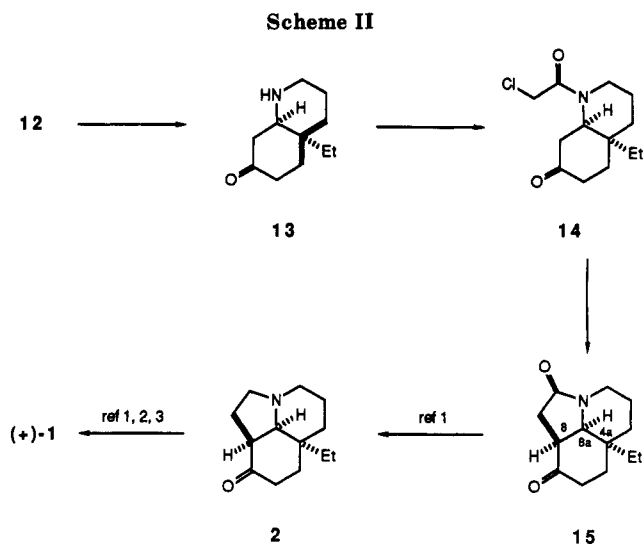
°C. It is interesting that the melting points of the racemic material varied rather widely (122 °C from Ban's study[2] and 75–79 °C from Stork's[1] and Fowler's[4b] work). The discrepancies in the melting points between Ban and Stork's racemic material are due to the different stereochemistry at C-8a, but this was also reported to be of no consequence in forming aspidospermine. The ring closure of the chloro amide 14 was carried out in benzene using potassium *tert*-butoxide, as described previously,[1] affording the hydrolilolidone system 15 in 72% yield. This chiral material was crystalline, mp 152–154 °C, and as expected, differed significantly from the racemic material reported by Stork (mp 116–118 °C), Fowler (mp 118–119 °C), and Ban (mp 165–166 °C). However, all spectral properties were in complete agreement with those reported by Fowler in his very nice 1-aza-Cope rearrangement which gave the material with almost certain cis alignment of C-4a ethyl, C-8H, and C-8aH. Additionally, the elegant (4 + 2) cycloadditions described by Martin[4c] also support the all cis ring fusion in 15. NOE studies at 500 MHz showed en-

(9) The racemic ketal has been reported to have mp 64–66 °C (ref 1) whereas the enantiomeric material reported here has mp 135–137 °C.

(10) Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *J. Org. Chem.* 1977, 42, 384.

(11) Stevens, R. V.; Mehra, R. K.; Zimmerman, R. L. *J. Chem. Soc., Chem. Comm.* 1969, 877.

hancement when either C-8H, C-8aH, or the α-proton of the ethyl group was irradiated, thus adding further support to the all-cis configuration of **15**. It now appears that both Stork and Fowler had prepared the *cis*-hydroquinolines (e.g. **13**) and the tricyclic ketone **15** and **2** while Ban's group had made the trans isomers (epimeric at C-8a of **15** and **2**). This could, therefore, explain the melting point discrepancies arising out of their studies. Kuehne[4d] has reported the synthesis of both isomers of **2**, but gave no specific physical data, other than mass spectral comparisons with Stork's and Ban's material.

In summary, we have demonstrated that the bicyclic lactam **3** is a viable chiral, nonracemic precursor to the key tricyclic systems **15**, required to reach either enantiomer of the *Aspidosperma* alkaloids in optically active form. In addition, the entire synthetic scheme to the unnatural system **15** was performed without any chromatography for separation of diastereomers (or other undesired materials).

Experimental Section[12]

(2S,3S,6R,8aR)-6-Allyl-6-ethyl-3-(hydroxymethyl)-8a-methyl-2-phenyl-5-oxo-2,3,6,7,8,8a-hexahydro-5H-oxazolo-[3,2-a]pyridine (4). In an oven-dried 500-mL round-bottomed flask containing a magnetic stirring bar was placed 14.4 g (55.2 mmol) of dry bicyclic lactam **3**.[5] The flask was flushed with argon and filled with 150 mL of anhydrous tetrahydrofuran and then sealed with a rubber septum. The air in the flask was replaced by argon. After dissolution of the bicyclic lactam, the flask was cooled in dry ice/acetone, and the solution was stirred while lithium diisopropylamide (LDA) was prepared.

In a oven-dried 200-mL conical flask containing 50 mL of dry tetrahydrofuran and sealed with a rubber septum, 13.9 g (19.3 mL, 137.4 mmol) of diisopropylamine was added with a syringe. The flask was placed into an ice–water bath. After 15 min, 84 mL (134.4 mmol) of 1.6 M n-butyllithium in hexane was slowly added with a syringe and with gentle swirling of the flask. The solution was kept 5 min at this temperature.

The lithium diisopropylamide solution prepared above was transferred dropwise via a cannula into the bicyclic lactam solution. The dry ice/acetone bath was replaced by an ice–water bath, where the reaction mixture was kept for 40 min to complete the formation of the lithium enolate. The reaction mixture was cooled again (30 min) with a dry ice/acetone bath. Freshly distilled ethyl iodide (25.8 g, 13.4 mL, 165.4 mmol) was added slowly via syringe to the mixture, and stirring was continued for 55 min. The cooling bath was replaced by an ice–water bath, and the mixture was stirred for exactly 40 min and poured immediately into a separatory funnel containing 400 mL of 1.0 N HCl. The resulting emulsion was extracted once with 400 mL of ether, and the organic layer washed with 200 mL of a 1:1 mixture of brine and saturated solution of sodium bicarbonate. The ether extract was dried over MgSO₄ and evaporated to dryness. The residue was dissolved in 60 mL of dry benzene and evaporated again using a water bath (60 °C for 45 min) to remove all traces of water and benzene. The product (14.6 g, 92%) was used in the next step without further purification.

The 500-mL flask containing the crude dry product (14.6 g, 50.4 mmol) was filled with dry tetrahydrofuran (150 mL), a magnetic stirring bar was added, the flask was then sealed with a rubber septum, and argon was introduced. The flask was gently swirled until the viscous oil was totally dissolved, then the flask was immersed into a dry ice/acetone bath.

Another portion of LDA was prepared, as described above, using 12.6 g of diisopropylamine (17.6 mL, 124.6 mmol) in THF (50 mL) and 78.0 mL (124.8 mmol) of 1.6 M n-BuLi/hexane. The LDA solution was added through a cannula to the ethylated bicyclic lactam solution, and the mixture was allowed to warm up to 0 °C and kept at this temperature for 3.0 h. The solution was cooled to −75 to −80 °C in a dry ice/acetone bath. A solution of 9.4 g of freshly distilled allyl bromide (6.8 mL, 77.6 mmol) in dry THF (50 mL) was prepared in a 100-mL oven-dried conical flask flushed

with argon and sealed with a rubber septum. This solution was cooled in a dry ice/acetone bath and was slowly added to the reaction mixture through a cannula under argon pressure. After the addition of the allyl bromide, the mixture was kept in dry ice/acetone for 2.5 h, and the bath was replaced by acetone at −50 °C which was allowed to warm up to −30 °C within a period of 45 min. The reaction mixture was poured into 1 N HCl, extracted with ether, washed with NaHCO₃–brine, dried over MgSO₄, and evaporated. The viscous or solid residue was dissolved in methylene chloride (10 mL), and hexane (140 mL) was added. The product was allowed to crystallize at room temperature for 1 h and then at −15 °C overnight, giving 12.4 g (75%, mp 92–95 °C) of crude **4**. This material was recrystallized 3 times with the same mixture of solvents, and the product was collected after 1 h at 0 °C to give 8.2 g (50%): mp 102–104 °C as a 25:1 mixture of diastereoisomers; $[\alpha]^{21}_D$ +38.89° (c 1.77, EtOH); IR (KBr, cm⁻¹) 3250, 2940, 1600, 1450, 1370, 1330, 1070, 890, 750; ¹H NMR (270 MHz, CDCl₃) δ 7.37 (s, 5 H), 5.73–5.88 (m, 1 H), 5.11–5.16 (m, 2 H), 4.78 (d, J = 8.5 Hz, 1 H), 4.13 (dt, J = 8.8, 2.5 Hz, 1 H), 3.90 (dd, J = 11.2, 2.5 Hz, 1 H), 3.75 (dd, J = 11.3, 8.8 Hz, 1 H), 3.65 (br, 1 H, OH), 2.42 (ddd, J = 63.6, 13.4, 7.4 Hz, 2 H), 1.57 (s, 3 H), 0.91 (t, J = 7.3 Hz, 3 H), and unresolved signals. Anal. Calcd for C₂₀H₂₇NO₃: C, 72.91; H, 8.26; N, 4.25. Found: C, 72.77; H, 8.25; N, 4.24.

(R)-4-Allyl-4-ethyl-2-cyclohexen-1-one (5). In an oven-dried 500-mL round-bottomed flask containing dry toluene (300 mL) and a magnetic stir bar was placed the dialkylated **4** (7.8 g, 23.7 mmol). The solution was cooled in a dry ice/acetone bath, and a 1 M solution of Red-Al in toluene (52 mL, 52.0 mmol) was slowly added.[12] The reaction mixture was allowed to warm to room temperature and stirred for 3 days. The mixture was cooled to 0 °C, and methanol (10 mL) was cautiously added with stirring to destroy the excess of Red-Al. The solution was poured over 7% aqueous KOH solution (400 mL) in a 2-L separatory funnel and thoroughly shaken with ether (200 mL) until both layers had become almost clear. The aqueous layer was extracted twice with ether (100 mL), and after combining them, the ethereal solution was dried over MgSO₄ and evaporated to dryness.

The residue was dissolved in ethanol (250 mL), a 1 M aqueous solution of tetrabutylammonium dihydrogen phosphate (80 mL, Aldrich) was added, and the mixture was stirred at reflux for 24 h. After cooling, the solution was partly evaporated on a rotatory evaporator with a bath temperature not exceeding 40 °C to remove most of the ethanol. Water was added (500 mL), and the solution was extracted twice with chloroform (200 mL). The chloroform extracts were washed with a 1:1 mixture of brine and 1 N HCl and then with brine and saturated sodium bicarbonate. Both aqueous phases were extracted twice with chloroform; the extracts were combined, dried over MgSO₄, and evaporated to dryness, giving 2.9–3.1 g of the crude 4,4-disubstituted cyclohexenone **5**. The product was distilled rapidly in a Kugelrohr apparatus at 0.5 mmHg and 150 °C, giving 2.4–2.9 g (62–75%) of pure cyclohexenone: $[\alpha]^{20}_D$ 23.17° (c 1.67, EtOH); IR (film, cm⁻¹) 2960, 1680, 1450, 1380, 1210; ¹H NMR (270 MHz, CDCl₃) δ 6.71 (d, J = 10.3 Hz, 1 H), 5.94 (d, J = 10.3 Hz, 1 H), 5.65–5.82 (m, 1 H), 5.07–5.14 (m, 1 H), 2.45 (t, J = 6.8 Hz, 2 H), 2.23 (d, J = 6.6 Hz, 2 H), 1.87 (t, J = 6.8 Hz, 2 H), 1.49–1.57 (m, 2 H), 0.95 (t, s, J = 7.6 Hz, 3 H). Anal. Calcd for C₁₁H₁₆O: C, 80.45; H, 9.82. Found: C, 80.20; H, 10.08. The GC–MS spectrum indicated 3–5% 4,4-diethylcyclohexenone as an impurity; however, this was not discernible in the ¹H or ¹³C NMR spectrum.[13]

(1RS,4R)-4-Ethyl-4-(3-hydroxypropyl)-2-cyclohexen-1-ol (6). 4-Ethyl-4-propenylcyclohexenone (**5**) (1 g, 6.1 mmol) was dissolved in dry THF (75 mL) and cooled to 0 °C, and 9-BBN (0.5 M, 25.2 mL, 12.6 mmol) was added dropwise with stirring under argon atmosphere. The reaction mixture was kept in the refrigerator (0 °C) for 24 h and then placed in ice/water. Sodium hydroxide (3 N, 5 mL, 15.0 mmol) was slowly added, followed by

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(12) Microanalyses were performed by Desert Analytics, Tucson, AZ.

(13) 1 M Red-Al was prepared by diluting to 100 mL with toluene (29.5 mL of commercially available 3.4 M Red-Al solution in toluene, Aldrich). Before use, this solution should be warmed to room temperature since it tends to separate into two layers at low temperatures. The first milliliter of Red-Al produced a vigorous gas evolution; therefore, the flask should be kept open until the Red-Al addition is complete. Then the reaction vessel was sealed as described.

hydrogen peroxide (30%, 50 mL) (exothermic and gas evolution). The mixture was kept for 30 min at room temperature and then poured into water (800 mL); the flask was rinsed with $CHCl_3$ and water until no further viscous material was present. The mixture was extracted with chloroform (4×), and the extracts were washed twice with a 1:1 mixture of brine and saturated sodium thiosulfate, dried ($MgSO_4$), and evaporated to give 1.1 g of crude product (very viscous oil) containing a 1:1 mixture of both diastereoisomer, plus some 9-BBN byproducts. This product was directly used in the next step without purification.

(4R)-4-Ethyl-4-(2-carboxyethyl)-2-cyclohexen-1-one (7). Crude 4-ethyl-4-(hydroxypropyl)cyclohexenol (6) (1.1 g, 6.1 mmol) was dissolved in acetone (100 mL), and Jones reagent[14] (about 6-8 mL) was added dropwise with stirring until a persistent yellow color remained. The reaction mixture was stirred for an additional 20 min at 25 °C, and the excess Jones reagent was destroyed by the addition of isopropyl alcohol. The mixture was filtered through Celite and concentrated. The residue was dissolved in ether and extracted with 10% sodium bicarbonate, which was washed twice with ether. The aqueous extract was acidified with 1 N HCl and extracted (3×) with $CHCl_3$, dried ($MgSO_4$), and concentrated to give 840 mg (70% over two steps) of almost pure acid. The acid was characterized by transforming it to ester 8, as follows.

The above acid (75 mg, 0.4 mmol) was dissolved in dry CH_2Cl_2 (20 mL), and oxalyl chloride (50.8 mg, 0.4 mmol) was added. The mixture was stirred for 1 h and then evaporated to dryness. Methanol (20 mL) was added to the residue, and the reaction mixture was stirred at room temperature for 8 h. The solvent was evaporated, and the residue was dissolved in ether which was washed with 1 N $NaHCO_3$, dried ($MgSO_4$), and evaporated. The residue was distilled (Kugelrohr), giving 40 mg (40%) of pure 8: $[\alpha]^{21}_D$ -40.4° (c 1.73, EtOH); ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.65 (d, J = 10.3 Hz, 1 H), 5.94 (d, J = 10.3 Hz, 1 H), 3.67 (s, 3 H), 2.45 (t, J = 6.8 Hz, 2 H), 1.80-1.86 (m, 4 H), 1.49-1.54 (m, 2 H), 0.91 (t, J = 7.4 Hz, 3 H); IR (neat, cm^{-1}) 2940 (s), 1735 (s), 1670 (s), 1430 (m), 1190 (m), 1160 (m). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.21; H, 8.62.

(4R)-4-Ethyl-4-(2-carbamoylethyl)-2-cyclohexen-1-one (10). The crude carboxylic acid 7 (79 mg, 0.4 mmol) was dissolved in dichloromethane (20 mL), and oxalyl chloride (55.9 mg, 0.42 mmol) was added. The reacting mixture was stirred for 2 h at room temperature and evaporated to dryness, and the crude acid chloride 9 was dissolved in THF (20 mL). Ammonia was slowly bubbled through the solution, and then the reaction mixture was evaporated to dryness. The residue was dissolved in chloroform, washed with a 1:1 mixture of brine and saturated sodium bicarbonate and then with a 1:1 solution of brine and 0.5 N HCl. Both aqueous solutions were back-extracted twice with chloroform (the amide was quite soluble in water). The chloroform extracts were combined, dried over $MgSO_4$, and evaporated to dryness, giving 57 mg (72.5%) of rather pure amide. A small amount was purified by chromatography on a TLC silica plate: $[\alpha]^{20}_D$ +55.4° (c 1.75, EtOH); ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.70 (d, J = 10.3 Hz, 1 H), 6.12 (br, 2 H), 5.96 (d, J = 10.3 Hz, 1 H), 2.46 (t, J = 6.4 Hz, 2 H), 2.25-2.19 (m, 2 H), 1.90-1.81 (m, 4 H), 1.60-1.49 (m, 2 H), 0.93 (t, J = 7.5 Hz, 3 H); IR (neat, cm^{-1}) 3400, 2950, 1670 (s), 1610 (m), 1450, 1400, 1380, 1230, 1110.

(4aR,8aR)-4a-Ethyl-7,7-(ethylenedioxy)decahydroquinolin-2-one (12). The amide 10 (255 mg, 1.31 mmol) was dissolved in dry benzene (50 mL), and p-TsOH (25 mg) was added. The reaction mixture was heated to reflux for 24 h. Ethylene glycol (146 mg, 2.3 mmol) was added to the mixture, and heating was resumed for 6 h. After cooling, the solution was evaporated almost to dryness and dissolved in chloroform, washed with 10% sodium bicarbonate, dried ($MgSO_4$), and evaporated to dryness. The residue was recrystallized from dichloromethane/ether to give 267 mg (85%) of ketal: mp 135-137 °C; $[\alpha]^{21}_D$ +47.9° (c 1.56, EtOH); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.87 (br s, 1 H), 3.84 (sharp m, 4 H), 3.18 (q, J = 4.4 Hz, 1 H), 2.27 (dd, J = 5.4, 8.5 Hz, 2 H), 1.2-2.05 (m, 10 H), 0.80 (t, j = 7.7 Hz, 3 H). Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.20; H, 8.80; N, 5.90. Found: C, 65.20; H, 9.00; N, 5.90.

(4aS,8aR)-4a-Ethyldecahydroquinolin-7-one (13). The ketal 12 (267 mg, 1.12 mmol) was dissolved in dry THF (60 mL), and lithium aluminium hydride (200 mg, 5.27 mmol) was added. The mixture was heated at reflux for 2 h and then cooled to 0 °C. A solution (1.5 mL) of 3 N NaOH was added very slowly while the reaction mixture was stirred vigorously. The mixture was filtered, and the THF was evaporated to dryness. The residue was dissolved in 1 N HCl (30 mL), and THF (3 mL) was added. The acidified solution was heated to reflux for 30 min to hydrolyze the ethylene ketal. The mixture was made alkaline with 1 N NaOH, brine was added, and the mixture was extracted (5×) with small portions of chloroform. The organics were combined, dried ($MgSO_4$), and evaporated to dryness to give 177 mg (87.2%) of crude amino ketone. A small amount was purified (TLC) for characterization: $[\alpha]^{21}_D$ +28.4° (c 1.45, EtOH); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.04 (dd, J = 11.9, 2.1 Hz, 1 H), 2.84 (br signal, 1 H), 2.76 (dd, J = 15.0, 3.6 Hz, 1 H), 2.56 (dt, J = 11.9, 2.4 Hz, 1 H), 2.02 (dd, J = 1.9, 14.9 Hz, 1 H), 0.94 (t, J = 7.6 Hz, 3 H), and some unresolved signals.

(4aS,8aR)-1-(Chloroacetyl)-4a-ethyldecahydroquinolin-7-one (14). Crude decahydroquinolinone 13 (51.6 mg, 2 mmol) was dissolved in dry benzene, and triethylamine (223 mg, 2.2 mmol) was added. A solution of chloroacetyl chloride (237 mg, 2.1 mmol) in benzene (2 mL) was added dropwise, and the solution was stirred for 20 min and then poured over 1 N HCl. The organic layer was dried and evaporated to dryness, giving a residue which was recrystallized from dichloromethane-ether giving 45 mg (61%) of the desired chloroacetylated product: mp 112-114 °C (lit.[4b] mp 78-79 °C; lit.[1] mp 75-77 °C; lit.[2] mp 122-122.5 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.66 (dd, 1 H, J = 5.1 Hz), 4.01 and 4.09 (d, 2 H, J = 12 Hz), 3.6-3.8 (m, 2 H), 1.1-2.8 (m, 12 H), 0.82 (t, 3 H, J = 7.5 Hz).

(4aS,8S,8aR)-4a-Ethyl-7,10-dioxo-4a,8a,5,6,7,8-hexahydrolilolidine (15). (Chloroacetyl)quinolinone 14 (25.8 mg, 0.1 mmol) was dissolved in benzene (5 mL), potassium tert-butoxide (22.4 mg, 0.2 mmol) was added, and the reaction mixture was stirred at room temperature for 1 h. The mixture was poured into 1 N HCl, and the benzene solution was dried over $MgSO_4$ and evaporated to dryness. The residue was recrystallized from dichloromethane-ether, giving 16 mg (72%) of pure product: mp 152-154 °C (lit.[4b] mp 118-119 °C; lit.[1] mp 116-118 °C; lit.[2] mp 165-166 °C for racemic materials); $[\alpha]^{21}_D$ +47.0° (c 0.84, EtOH); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.02 (br d, 1 H), 3.39 (dd, 1 H, J = 2.6 Hz), 1.2-3.0 (m, 14 H), 0.94 (t, 3 H, J = 7.5 Hz).

(14) The preparation of 5, as stated above, has been checked for *Organic Syntheses*. We thank the checkers (Dr. David Coffen of Hoffmann-LaRoche) for performing the reaction on a larger scale (2×) and providing us with the GC-MS data.

(15) Prepared as described in Fieser, L. F.; Fieser, M. *Reagents in Organic Syntheses*; John Wiley & Sons: New York, 1967; Vol. 1, p 142.

(16) For information concerning the nomenclature, see: Rapoport, H.; Tretter, J. R. *J. Org. Chem.* 1958, 23, 248. Astill, B. D.; Boekelheide, V. *Ibid.* 1958, 23, 316.