Research Laboratories, who recorded the cyclic voltammograms.

**Registry No.** 2, 23897-15-6; 3, 75558-19-9; 4, 75558-20-2; 5, 20676-64-6; 6, 53888-89-4; 7, 75558-21-3; 8, 75558-22-4; 9, 75558-23-5; 10, 75558-24-6; 11, 75558-25-7; 12, 75558-26-8; 13, 75558-27-9; 14, 75558-28-0; 15, 75558-29-1; 17 (isomer 1), 75558-30-4; 17 (isomer 2), 75558-31-5; 18, 75558-32-6; $Ph_3N$, 603-34-9; $Ph_3P$, 603-35-0; $Ph_3As$, 603-32-7; $Ph_3Sb$, 603-36-1; $Ph_3Bi$, 603-33-8; acetone, 67-64-1; isobutyraldehyde, 78-84-2.

# Vinylogous *N*-Acyliminium Ion Cyclizations: Application to the Synthesis of Depentylperhydrogephyrotoxin

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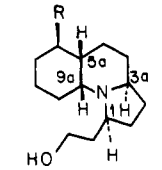
The use of vinylogous *N*-acyliminium ions as olefin cyclization initiators is discussed within the context of a total synthesis of depentylperhydrogephyrotoxin (**2**). It was found that certain *N*-acyliminium and vinylogous *N*-acyliminium ion cyclizations follow a similar stereochemical course.

The structure of gephyrotoxin (**1**), an alkaloid isolated from skin extracts of the neotropical frog *Dendrobates histrionicus*, was recently reported.[1] The inavailability of **1** in more than milligram quantities from the natural source and the interesting pharmacological properties[2] of gephyrotoxin render this structure an attractive target for total synthesis. During the course of studies directed toward the synthesis of **1**, we have examined the stereochemical course of several *N*-acyliminium and vinylogous *N*-acyliminium ion cyclizations.[3,4] This report describes the details of these studies within the context of a synthesis of depentylperhydrogephyrotoxin (**2**).[5]

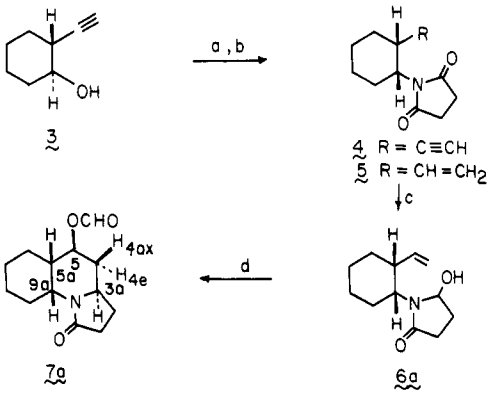


**1** R = $CH_2CH_2CH{=}CHC{\equiv}CH$

**2** R = H

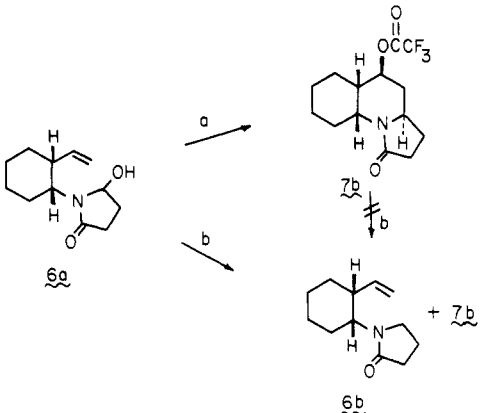
Our initial approach to **2** focused on the preparation of tricyclic lactam **7** via an *N*-acyliminium ion cyclization. The required carbinolamide **6a** was prepared as outlined in Scheme I. Treatment of *trans*-2-ethynylcyclohexanol (**3**) with succinimide under the conditions of Mitsunobu[6] afforded imide **4** in a 59% yield in addition to a 20% yield of *cis*-2-ethynylcyclohexanol.[7] Catalytic hydrogenation of alkyne **4** followed by reduction of the resulting imide **5** with diisobutylaluminum hydride[8] gave **6a** in 63% overall

Scheme I[a]



[a] a, $Ph_3P$, $EtO_2CN{=}NCO_2Et$, succinimide, THF; b, $H_2$, $Pd/BaSO_4$, pyr; c, $i\text{-}Bu_2AlH$, toluene; d, 97% HCOOH.

Scheme II[a]



[a] a, $CF_3COOH$; b, $CF_3COOH$, $Et_3SiH$, $CH_2Cl_2$.

yield. Treatment of **6a** with formic acid gave an 85% yield of a single tricyclic lactam which was assigned structure **7a** on the basis of spectral data.[9,10] In a similar fashion (Scheme II) treatment of **6a** with trifluoroacetic acid gave lactam **7b** in a 62% yield. In the case of the trifluoroacetic

(1) Daly, J. W.; Witkop, B.; Tokuyama, T.; Nishikawa, T.; Karle, I. L. *Helv. Chim. Acta* **1977**, *60*, 1128.

(2) Daly, J. W.; Brown, G. B.; Mensah-Dwumah, M.; Myers, C. W. *Toxicon* **1978**, *16*, 163. Daly, J. W.; Mensah-Dwumah, M. *Toxicon* **1978**, *16*, 189.

(3) For an overview of research in the area of acyliminium ion initiated olefin cyclizations, see: Speckamp, W. N. "Stereoselective Synthesis of Natural Products-Workshop Conferences Hoechst"; Bartmann and Winterfeldt, Eds.; Excerpta Medica (Elsevier): Amsterdam, 1979; Vol. 7, p 50. For reference to what is probably vinylogous *N*-acyliminium ion initiated arylation, see: Winterfeldt, E. *Synthesis* **1975**, 617, ref 129.

(4) For stereochemical studies which complement those presented here and elsewhere,[10] see: Maryanoff, B. E.; McComsey, D. F. *Tetrahedron Lett.* **1979**, 3797; Speckamp, W. N.; Nossin, P. M. M. *Ibid.* **1980**, 1991.

(5) For a total synthesis of perhydrogephyrotoxin, see: Overman, L. E.; Fukaya, C. *J. Am. Chem. Soc.* **1980**, *102*, 1454.

(6) Mitsunobu, D.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679.

(7) The *cis*-2-ethynylcyclohexanol presumably reflects the amount of O-alkylation which occurs during the Mitsunobu reaction.[6]

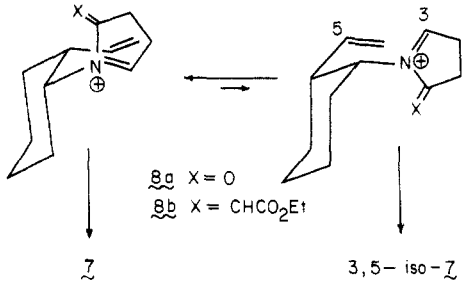
(8) Winterfeldt, E. *Synthesis* **1975**, 617.

(9) The following critical coupling constants for **7** were determined by $^1H$-$^1H$ decoupling experiments at 360 MHz: $J_{3a,4e} = 4$, $J_{3a,4ax} = 11$, $J_{5,4e} = 4$, $J_{5,4ax} = 11$, $J_{5,5a} = 4$, $J_{5a,9a} = 9$ Hz.

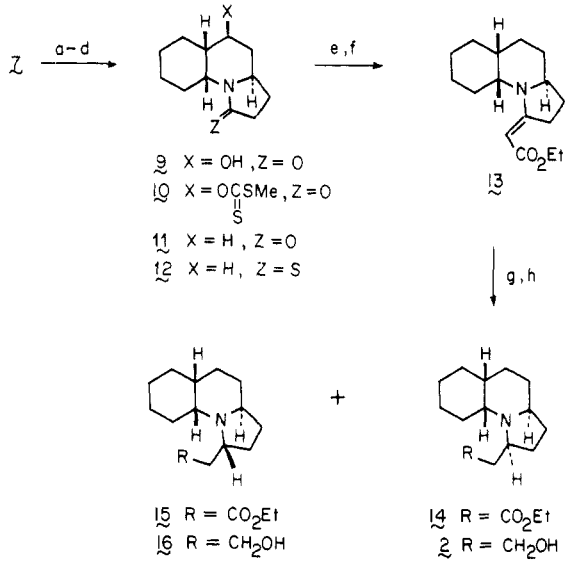
(10) Hart, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 397.

0022-3263/81/1946-0367$01.00/0 

Scheme III

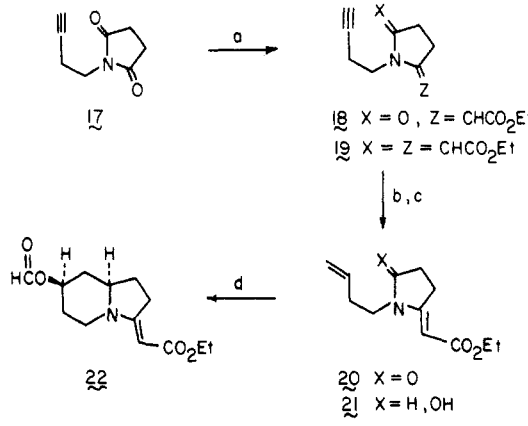



Scheme IV[a]



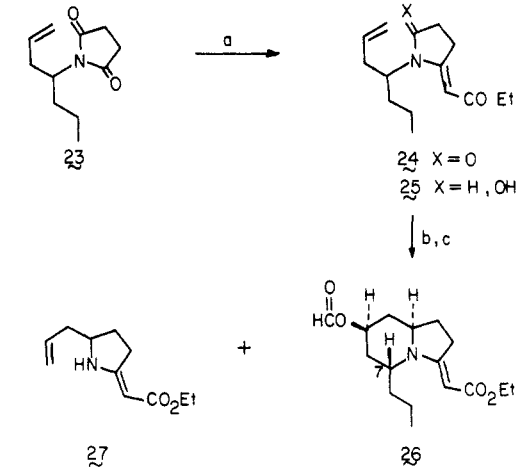

[a] a, NaOH, $H_2O$-MeOH; b, NaH, THF, $CS_2$, $CH_3I$; c, *n*-$Bu_3SnH$, toluene; d, $P_2S_5$, toluene; e, $BrCH_2CO_2Et$, $Et_2O$; f, $Ph_3P$, $CHCl_3$, $Et_3N$; g, MeOH, $NaBH_3CN$, HCl; h, $LiAlH_4$, THF.

Scheme V[a]




[a] a, $PhP{=}CHCO_2Et$, 175 °C; b, $H_2$, $Pd/BaSO_4$, pyridine; c, *i*-$Bu_2AlH$, *toluene*; d, $HCOOH$-$CH_2Cl_2$.

Scheme VI[a]




[a] a, $Ph_3P{=}CHCO_2Et$, 175 °C; b, *i*-$Bu_2AlH$, toluene; c, $HCOOH$-$CH_2Cl_2$.

acid cyclization, the question of whether the product was formed under conditions of kinetic or thermodynamic control was addressed by performing the experiments outlined in Scheme II. Thus when **6a** was treated with trifluoroacetic acid in the presence of triethylsilane, reduction of the presumed acyliminium ion intermediate was competitive with cyclization and a 5:1 mixture of lactams **7b** and **6b**, respectively, was obtained in a 60% yield.[11] When lactam **7b** was subjected to these reductive conditions, no **6b** was formed. Although this result does not rule out undetected rapid and reversible formation of isomers of **7b**, it does demonstrate that formation of **7b** is irreversible and suggests that **7b** is the product of kinetic control. The stereoselectivity observed in the cyclization of **6a** can be attributed to a pronounced conformational preference of the intermediate iminium ion **8a** (Scheme III).

The synthesis of **2** was completed as outlined in Scheme IV. The formyloxy group was removed by using the excellent procedure developed by Barton.[12] Thus, formate **7a** was saponified and the resulting alcohol **9** was converted to xanthate **10**. Treatment of **10** with tri-*n*-butyltin hydride gave lactam **11** in a 75% overall yield from **7a**. The two-carbon C-1 side chain was introduced in 43% yield via thioamide **12**, using the sulfide-contraction procedure.[13,14]

Reduction of **13** with sodium cyanoborohydride[15] gave a separable 4:1 mixture of esters **14** (55%) and **15** (14%), respectively.[16] These esters were reduced to their corresponding alcohols **2** (96%) and **16** (91%) with lithium aluminum hydride. The stereochemical assignments of **2** and **16** obtained from this sequence were based on a comparison of their $^1H$ and $^{13}C$ NMR spectra with those reported for gephyrotoxin (**1**) and perhydrogephyrotoxin.[1,5]

In an effort to render the above route to **2** more efficient, an alternate scheme was examined. Based on our experience with **8a**, it was anticipated that conformational factors would encourage an iminium ion such as **8b** to give the desired stereochemistry at C-3 relative to C-5a and C-9a upon cyclization. Before generation of a precursor to **8b** was attempted, the use of vinylogous *N*-acyliminium ions as olefin-cyclization initiators was explored in two simpler systems (Schemes V and VI).[17] Treatment of

(11) Reduction of carbinolamides with TFA-$Et_3SiH$ has been previously noted: Auerbach, J.; Zamose, M.; Weinreb, S. M. *J. Org. Chem.* **1976**, *41*, 725.

(12) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

(13) Roth, M.; Dubs, P.; Götschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710.

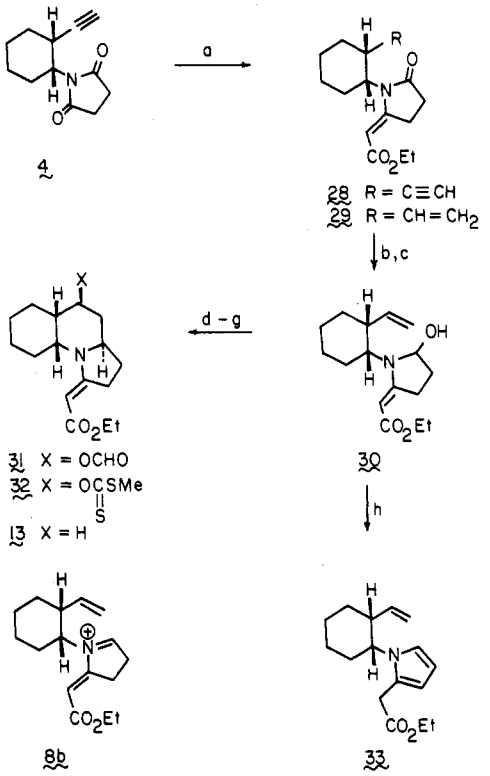
(14) For the first application of the "sulfide-contraction" procedure to *N,N*-dialkylamides, see: Yamaguchi, H. *Chem. Abstr.* **1972**, *78*, P29617.

(15) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897.

(16) Amino esters **14** and **15** did not interconvert under the reaction conditions. Thus the mixture represents a kinetically controlled mixture of isomers.

(17) To our knowledge this report documents the first use of this initiator in unactivated olefin cyclizations.

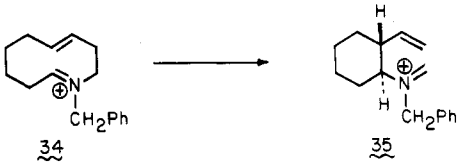
Scheme VII



[a] a, $Ph_3P{=}CHCO_2Et$, 175 °C; b, $H_2$, $Pd/BaSO_4$, pyr; c, *i*-$Bu_2AlH$, toluene; d, HCOOH; e, NaOH, MeOH-$H_2O$; f, NaH-THF, $CS_2$, $CH_3I$; g, *n*-$Bu_3SnH$, toluene; h, activity II alumina.

imide **17** with (carbethoxymethylidene)triphenylphosphorane afforded vinylogous urethane **18** (53%) and bis Wittig product **19** (5%) along with 17% recovered **17**.[18] Catalytic hydrogenation of **18** followed by selective reduction of the resulting imide **20** with diisobutylaluminum hydride gave carbinol **21** in an overall yield of 60%. Treatment of the sensitive carbinol with formic acid afforded formate **22** in 23% yield along with several other unidentified products.[19,21] In a similar fashion, crystalline carbinol **25** was prepared from imide **23**. Treatment of **25** with formic acid gave a 20% yield of formate **26** as a single stereoisomer[20] along with a 54% yield of vinylogous urethane **27**.[21] In accord with earlier results,[10] the stereochemistry of **26** can be rationalized by assuming that **25** cyclizes via the chair conformation of an iminium ion in which the incipient C-7 substituent occupies an axial site to avoid developing $A^{(1,3)}$ interactions. It is presumed that **27** is formed by sequential 3,3-sigmatropic rearrangement and hydrolysis of the resulting iminium ion.[22]

We next turned our attention to the generation of iminium ion **8b** (Scheme VII). Treatment of imide **4** with the appropriate ylid gave vinylogous urethane **28** in a 30% yield along with 40% of recovered starting material.[23] Catalytic hydrogenation of **28** (91%) followed by reduction of the resulting olefin **29** wiith diisobutylaluminum hydride gave carbinol **30** after rapid chromatography over silica gel. Carbinol **30** was a sensitive substance which was easily converted to pyrrole **33** upon filtration through alumina. Nonetheless, immediate treatment of **30** with formic acid gave vinylogous urethane **31** in a 67% overall yield from **29**. The stereochemistry of **31** was established by converting it to urethane **13** via xanthate **32** in a 90% overall yield. Thus the cyclizations of *N*-acyliminium ion **8a** and vinylogous *N*-acyliminium ion **8b** follow the same stereochemical course. The dramatic improvement in yield of cyclized product going from **21** and **25** to **30** may be related to the known propensity for iminium ion **34** to rearrange to the thermodynamically more stable ion **35**.[25] Therefore



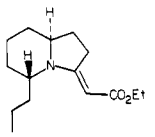
the rate of 3,3-sigmatropic rearrangement of **8b** may be slow enough that cyclization competes favorably with sequential rearrangement and hydrolysis (e.g., **25** → **27**).

The studies outlined herein establish a protocol for constructing the tricyclic nucleus of gephyrotoxin (**1**) with four of the five asymmetric centers intact. In addition, it has been demonstrated that vinylogous *N*-acyliminium ions will initiate olefin cyclizations. The pharmacological properties of depentylperhydrogephyrotoxin (**2**) will be investigated and reported in the future.

## Experimental Section

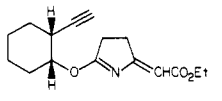
All melting points were taken with a Thomas-Hoover capilliary melting-point apparatus and are uncorrected as are boiling points. $^1H$ magnetic resonance spectra were recorded on a Varian Associates EM-390 or EM-360 spectrometer and are reported in parts per million from internal tetramethylsilane on the $\delta$ scale. Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration, interpretation]. $^{13}C$ magnetic resonance spectra were recorded on a Bruker WP-80 spectrometer and are reported in parts per million from internal tetramethylsilane. Infrared spectra were taken with a Perkin-Elmer 457 instrument. Mass spectra were recorded on an AEI-MS9. Samples on which exact masses were measured exhibited no significant peaks at $m/e$ greater than that of the parent. Combustion analyses were performed by MicroAnalysis, Inc., Wilmington, DE.

(18) For a review of imide olefination, see: Flitsch, W.; Schindler, S. R. *Synthesis* **1975**, 685.
(19) Vinylogous urethane **27** was not detected.
(20) $^{13}C$ NMR indicated that only one stereoisomer was produced. The stereochemistry of **26** was proven by chemical correlation with i, whose stereochemistry was determined by 360-MHz $^1H$ NMR studies performed on a precursor. The details will be presented at a later date.



i

(21) Only small amounts of substances believed to be substituted pyrroles were obtained.
(22) [3,3]-Sigmatropic rearrangements of simple iminium ions have been noted: Geissman, T. A.; Horowitz, R. M. *J. Am. Chem. Soc.* **1950**, *72*, 1518. We did not attempt to isolate the butyraldehyde presumably formed in this reaction.
(23) Treatment of *trans*-2-ethynylcyclohexanol with 5-(carbethoxymethylidene)-2-pyrrolidinone[24] under the Mitsunobu conditions[6] gave the imino ether ii in 40% yield; $^1H$ NMR ($CCl_4$) $\delta$ 1.00–2.20 (m with t, $J$ = 7, at $\delta$ 1.41 and d, $J$ = 2, at $\delta$ 1.96, 12 H), 2.67 (m, 2 H), 3.08 (m, 3 H), 4.07 (q, $J$ = 7, 2 H), 4.85 (d of t, $J$ = 8, 4, 1 H), 5.58 (t, $J$ = 2, 1 H). Hydrolysis of ii gave *cis*-2-ethynylcyclohexanol and the starting pyrrolidinone.



ii

(24) Flitsch, W.; Peters, H. *Chem. Ber.* **1970**, *103*, 805.
(25) Marshall, J. A.; Babler, J. H. *J. Org. Chem.* **1969**, *34*, 4186.

Solvents and reagents were dried and purified prior to use when deemed necessary: tetrahydrofuran (distilled from Na metal); toluene (distilled from calcium hydride); methanol (distilled from magnesium methoxide); dichloromethane (passed through activity I alumina). All reaction temperatures refer to those of the reaction mixture. Reactions requiring an inert atmosphere were run under a blanket of nitrogen or argon. Formic acid (97%) was used in all cyclizations. Analytical thin-layer chromatography was performed by using EM Laboratories 0.25-mm precoated silica gel 60 F-254 plates. Column chromatography was performed over EM Laboratories silica gel (70–230 mesh) and Woelm neutral alumina.

***N*-(*cis*-2-Ethynylcyclohexyl)succinimide (4).** To 13.3 g (0.107 mol) of *trans*-2-ethynylcyclohexanol (**3**),[26] 12.0 g (0.12 mol) of succinimide, and 27.9 g (0.107 mol) of triphenylphosphine in 175 mL of tetrahydrofuran was added a solution of 18.6 g (0.107 mol) of diethyl azodicarboxylate in 25 mL of tetrahydrofuran over a 60-min period with cooling in an ice bath. The mixture was stirred at room temperature for an additional 36 h and the solvent was removed in vacuo. The residual oil was dissolved in 200 mL of hexane–ethyl acetate (1:1). The resulting crystals were collected and rinsed with 100 mL of hexane–ethyl acetate (1:1). The filtrate was concentrated in vacuo and the residue was chromatographed over 450 of silica gel (eluted with ethyl acetate–hexane, 1:2) to give 2.7 g (20%) of *cis*-2-ethynylcyclohexanol and 12.0 g (59%) of imide **4** as a white, crystalline solid: mp 94–97 °C; IR ($CCl_4$) 3320, 1710 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.23–2.23 (m, 8 H, $CH_2$), 2.01 (d, $J$ = 3, 1 H, ≡CH), 2.66 (s, 4 H, succinimidoyl $CH_2$), 2.80–3.20 (m, 1 H, CH), 3.91 (d of t, $J$ = 13, 4, 1 H, NCH); $^{13}C$ NMR ($CDCl_3$) 20.92 (t), 24.66 (t), 26.22 (t), 28.11 (t), 30.97 (t), 32.14 (d), 55.68 (d), 71.46 (d), 83.65 (s), 177.49 (s); mass spectrum (70 eV), $m/e$ 205 (parent).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.23; H, 7.29.

***N*-(*cis*-2-Vinylcyclohexyl)succinimide (5).** A solution of 5.12 g (25.0 mmol) of alkyne **4** in 40 mL of pyridine was hydrogenated at 1 atm over 0.5 g of 5% palladium on barium sulfate until 1 equiv of hydrogen had been absorbed. The mixture was diluted with 200 mL of dichloromethane, washed with three 200-mL portions of 3 N aqueous hydrochloride acid, dried ($Na_2SO_4$), filtered through Celite, and concentrated in vacuo. The residue was crystallized from petroleum ether (15 mL) to give 4.7 g (90%) of alkene **5** as pale yellow needles suitable for use in subsequent reactions: mp 63–66 °C; IR ($CCl_4$) 1710 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.17–2.18 (m, 8 H, ring $CH_2$), 2.60 (s with underlying m, 5 H, succinimidoyl $CH_2$ and CH), 4.13 (d of t, $J$ = 13, 4, 1 H, NCH), 4.72–5.15 (five-line multiplet, 2 H, =$CH_2$), 5.95–6.62 (twelve-line m, 1 H, =CH); $^{13}C$ NMR ($CDCl_3$) 20.68 (t), 24.51 (t), 26.51 (t), 28.11 (t), 31.80 (t), 43.94 (d), 55.88 (d), 116.03 (t), 137.88 (d), 177.74 (s); exact mass calcd for $C_{12}H_{17}NO_2$ 207.1259, found 207.1263.

**1-(*cis*-2-Vinylcyclohexyl)-5-hydroxy-2-pyrrolidinone (6a).** To a solution of 3.6 g (17.3 mmol) of imide **5** in 50 mL of toluene was added 20 mL of diisobutylaluminum hydride (25 wt %) in toluene with cooling such that the temperature did not exceed –65 °C. The progress of the reaction was followed by TLC analysis of aliquots taken directly from the reaction mixture (silica gel, ethyl acetate). The cold mixture was poured into 200 mL of dichloromethane, washed with 90 mL of 10% aqueous sulfuric acid, dried ($Na_2SO_4$), and concentrated in vacuo. The residual oil was chromatographed over 50 g of silica gel to give 2.47 g (69%) of carbinolamide **6a** as a white crystalline solid: mp 93–108 °C; IR ($CHCl_3$) 3360, 1680 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.70–3.10 (m, 13 H, methylenes and allylic methine), 3.47 (d, $J$ = 7, 1 H, OH), 4.03 (m, 1 H, NCH), 4.80–5.67 (m, 2 H, =$CH_2$), 5.87–6.66 (m, 1 H, =CH); mass spectrum (70 eV), $m/e$ 191 (parent – $H_2O$).

***rel*-(3a*R*,5*S*,5a*S*,9a*R*)-5-(Trifluoroacetoxy)-1-oxododecahydropyrrolo[1,2-*a*]quinoline (7b).** To 2.0 mL of trifluoroacetic acid was added 103 mg (0.49 mmol) of solid carbinolamide **6a** in a single portion. The solution was stirred at room temperature for 15 min, diluted with 20 mL of dichloromethane, and washed with two 15-mL portions of water. The organic phase was dried ($Na_2SO_4$) and concentrated in vacuo. The residual oil was chromatographed over 15 g of silica gel (eluted with ethyl acetate) to give 95 mg (62%) of trifluoroacetate **7b** as a colorless oil: IR (neat) 1780, 1690 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.0–2.7 (m, 15 H), 3.77 (m, 1 H, CHN), 4.13 (m, 1 H, CHN), 5.37 (t of d, $J$ = 12, 4, 1 H, CH–O); exact mass calcd for $C_{14}H_{18}NO_3F_3$ 305.1238, found 305.1247.

***N*-(*cis*-2-Vinylcyclohexyl)-2-pyrrolidinone (6b).** To a solution of 3.0 mL of triethylsilane–trifluoroacetic acid–dichloromethane (1:1:1) at room temperature was added 113 mg (0.54 mmol) of carbinolamide **6a** in a single portion. The solution was stirred for 15 min, diluted with 15 mL of dichloromethane, and washed with 15 mL of water. The organic phase was dried ($Na_2SO_4$) and concentrated in vacuo. The residual yellow oil was chromatographed at medium pressure (Lobar size A column; eluted with ethyl acetate–hexane, 4:1) to afford 80 mg (50%) of trifluoroacetate **7b** and 11 mg (10%) of lactam **6b** as a colorless oil. Lactam **6b** obtained in this manner was identical with a sample of **6b** obtained by reduction of **6a** with sodium cyanoborohydride: IR (neat) 1680 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.1–2.35 (m, 12 H), 2.67 (m, 1 H, CHCH=), 3.33 (m, 2 H, $NCH_2$), 3.86 (m, 1 H, CHN), 5.00 (m, 2 H, =$CH_2$), 6.10 (m, 1 H, =CH); exact mass calcd for $C_{12}H_{19}NO$ 193.1466, found 193.1471.

***rel*-(3a*R*,5*S*,5a*S*,9a*R*)-5-(Formyloxy)-1-oxododecahydropyrrolo[1,2-a]quinoline (7a).** To 35 mL of 97% formic acid was added 2.47 g (11.8 mmol) of solid carbinolamide **6a**. The mixture was stirred at room temperature for 30 min followed by removal of the formic acid in vacuo. The yellow residue was dissolved in 30 mL of dichloromethane, stirred vigorously with 50 mL of saturated aqueous sodium bicarbonate for 20 min, dried ($Na_2SO_4$), and concentrated in vacuo. The residual oil was dissolved in 14 mL of ethyl acetate–hexane (3:11) to give 1.7 g of formate **7a** as a white solid, mp 100–102 °C. The mother liquor was chromatographed at medium pressure (LoBar size B column; eluted with ethyl acetate) to afford an additional 0.5 g (79% total) of **7a**: IR ($CCl_4$) 1730, 1695 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.06–2.67 (m, 15 H, methylene and methine manifold), 3.77 (m, 1 H, $H_{3a}$), 4.27 (m, 1 H, $H_{9a}$), 5.38 (t of d, $J$ = 11, 4, 1 H, $H_5$), 8.12 (s, 1 H, CHO); $^{13}C$ NMR ($CDCl_3$) 19.86 (t), 24.81 (t), 24.95 (t), 25.24 (t), 25.68 (t), 30.48 (t), 39.18 (d), 39.37 (t), 49.76 (d), 51.95 (d), 67.87 (d), 160.50 (d), 172.98 (s); mass spectrum (70 eV), $m/e$ 237 (parent).

Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07. Found: C, 66.44; H, 7.97.

***rel*-(3a*R*,5*S*,5a*S*,9a*R*)-1-Oxododecahydropyrrolo[1,2-*a*]quinol-5-yl *S*-Methyl Dithiocarbonate (10).** To a solution (7.17 mmol) of formate **7** in 20 mL of methanol was added 0.5 g of sodium hydroxide in 3 mL of water. The mixture was stirred at room temperature for 10 min and partitioned between 75 mL of dichloromethane and 50 mL of water. The aqueous phase was extracted with two 25-mL portions of dichloromethane. The combined organic phases were dried ($Na_2SO_4$) and concentrated in vacuo to give 1.30 g (87%) of hydroxy lactam **9** as a white solid, mp 106–109 °C. This material was homogeneous by thin-layer chromatography (silica gel, eluted with ethyl acetate) and was used directly in the preparation of xanthate **10**.

To 240 mg (10.0 mmol) of sodium hydride in 20 mL of tetrahydrofuran was added 1.26 g (6.0 mmol) of alcohol **9** in 15 mL of tetrahydrofuran followed by 20 mg of imidazole. The solution was warmed under reflux for 3 h followed by the addition of 2.0 mL of carbon disulfide in one portion. The solution was warmed under reflux for 30 min followed by the addition of 2.0 mL of iodomethane in one portion. The mixture was warmed under reflux for 30 min, cooled to room temperature, and partitioned between 100 mL of dichloromethane and 50 mL of water. The organic phase was dried ($Na_2SO_4$) and concentrated in vacuo. The solid residue was chromatographed over 40 g of silica gel (eluted with ethyl acetate) to give 1.65 g (92%) of xanthate **10** as a pale yellow solid: mp 138–141 °C; IR ($CCl_4$) 1690 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.07–2.53 (m, 15 H, methine and methylene manifold), 2.53 (s, 3 H, $SCH_3$), 3.70 (m, 1 H, $H_{3a}$), 4.10 (m, 1 H, $H_{9a}$), 6.00 (t of d, $J$ = 11, 4, 1 H, $H_5$); mass spectrum (70 eV), $m/e$ 299 (parent).

Anal. Calcd for $C_{14}H_{21}NO_2S_2$: C, 56.50; H, 7.07. Found: C, 56.37; H, 7.05.

***rel*-(3a*S*,5a*R*,9a*R*)-1-Oxododecahydropyrrolo[1,2-*a*]quinoline (11).** To 2.18 g (7.5 mmol) of tri-*n*-butyltin hydride in 45 mL of toluene under reflux was added a solution of 1.49 g (5.0 mmol) of xanthate **10** in 40 mL of toluene over a 40-min

(26) Hanack, M.; Kunzmann, E.; Schumacher, W. *Synthesis* **1978**, 26.

period. The mixture was warmed under reflux for 4 h, cooled to room temperature, and concentrated in vacuo. The residual oil was chromatographed over 100 g of silica gel to give 0.91 g (93%) of lactam **11** as a colorless oil (eluted with ethyl acetate): IR (film) 1680 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.7–2.43 (m, 17 H, methylene and methine manifold), 3.40 (m, 1 H, $H_{3a}$), 3.91 (m, 1 H, $H_{9a}$); $^{13}C$ NMR ($CDCl_3$) 20.34 (t), 24.18 (t), 24.18 (t), 25.29 (t), 25.49 (t), 30.88 (t), 30.88 (t), 34.13 (t), 34.52 (d), 50.15 (d), 53.16 (d), 173.37 (s); exact mass calcd for $C_{12}H_{19}NO$ 193.1466, found 193.1471.

***rel*-(3a*S*,5a*R*,9a*R*)-1-Thioxododecahydropyrrolo[1,2-*a*]quinoline (12).** A mixture of 768 mg (4.0 mmol) of lactam **11** and 448 mg (2.0 mmol) of phosphorus pentasulfide in 18 mL of toluene was warmed under reflux for 20 min. The solution was cooled and the toluene solution was decanted from the sticky residue. The residue was rinsed with 10 mL of toluene and the combined organic solutions were concentrated in vacuo. The residual yellow liquid was chromatographed over 25 g of silica gel (eluted with ethyl acetate–hexane, 1:5) to give 0.57 g (68%) of thiolactam **12** as a white crystalline solid: mp 90–94 °C; IR ($CCl_4$) 1475, 1463 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.7–2.53 (m, 15 H, methylene and methine manifold), 2.78 (m, 2 H, C-2 methylene), 3.75 (m, 1 H, $H_{3a}$), 4.66 (m, 1 H, $C_{9a}$); exact mass calcd for $C_{12}H_{19}NS$ 209.1238, found 209.1243.

***rel*-(3a*S*,5a*R*,9a*R*)-1(*E*)-(Carbethoxymethylidene)-dodecahydropyrrolo[1,2-*a*]quinoline (13).** A solution of 209 mg (1.0 mmol) of thiolactam **12** and 200 mg (1.2 mmol) of ethyl bromoacetate in 5.0 mL of ether was stirred at room temperature for 72 h. The ether phase was withdrawn from the resulting oil via pipet. The oil was dissolved in 5.0 mL of dry chloroform followed by sequential addition of 262 mg (1.0 mmol) of triphenylphosphine and 200 mg (2.0 mmol) of triethylamine in single portions. The mixture was stirred at room temperature for 10 min and concentrated in vacuo. The residual semicrystalline material was chromatographed over 40 g of silica gel (eluted with ethyl acetate–hexane, 1:5) to give vinylogous urethane **13** contaminated with some triphenylphosphine sulfide. Trituration with hexane–ethyl acetate (9:1) gave 170 mg (64%) of **13** as a homogeneous ($R_f$ 0.25, silica gel, ethyl acetate–hexane, 1:5) oil which crystallized on standing: mp 56–61 °C; IR ($CCl_4$) 1690, 1595 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.67–2.97 (m with t, $J$ = 7, at $\delta$ 1.15, 17 H, methylenes, C-5a methine and $CH_3$), 3.33 (m, 2 H, $H_{3a}$ and $H_{9a}$), 3.90 (q, $J$ = 7, 2 H, $OCH_2$), 4.32 (s, 1 H, vinyl-H); $^{13}C$ NMR ($CDCl_3$) 14.80 (q), 20.49 (t), 21.36 (t), 24.08 (t), 25.44 (t), 28.50 (t), 31.07 (t), 31.70 (t), 33.11 (t), 34.66 (d), 53.60 (d), 57.24 (d), 58.11 (t), 77.34 (d), 164.10 (s), 169.73 (s); mass spectrum (70 eV), *m/e* 263 (parent); exact mass calcd for $C_{16}H_{25}NO_2$ 263.1885, found 263.1889.

**Ethyl $\alpha$-*rel*-(1*S*,3a*S*,5a*R*,9a*R*)-Dodecahydropyrrolo[1,2-*a*]quinol-1-ylacetate (14) and Ethyl $\alpha$-*rel*-(1*R*,3a*S*,5a*R*,9a*R*)-Dodecahydropyrrolo[1,2-*a*]quinol-1-ylacetate (15).** To a solution of 0.8 g (3.04 mmol) of vinylogous urethane **13** in 10 mL of methanol was added a pinch of bromocresol green followed by 192 mg (3.04 mmol) of solid sodium cyanoborohydride. A solution of 1.14 M methanolic hydrogen chloride was added dropwise over a 10-min period until the mixture maintained a yellow color. The mixture was stirred at room temperature for 60 min, poured into 30 mL of 0.1 N aqueous sodium hydroxide, and extracted with two 50-mL portions of dichloromethane. The combined extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residual liquid was chromatographed over 90 g of activity III alumina to give 0.67 g (83%) of a mixture of **14** and **15** (eluted with ethyl acetate–hexane, 1:9). The mixture of amino esters was then chromatographed over 150 g of silica gel (eluted with chloroform–methanol, 19:1) to give 440 mg (55%) of the less polar ester **14** [mp (HCl salt) 176–180 °C; IR ($CCl_4$) 1735 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.83–2.00 (m with t, $J$ = 7, at $\delta$ 1.23, 20 H, methylene manifold and $CH_3$), 2.13 (d of d, $J$ = 15, 9, 1 H, CHC(O)), 2.50 (m, 1 H, CHN), 4.07 (q, $J$ = 7, 2 H, O–$CH_2$); NMR ($C_6D_6$) $\delta$ 0.83–2.03 (m with t, $J$ = 7, at $\delta$ 1.00, 20 H), 2.18 (d of d, $J$ = 15, 9, 1 H), 2.37 (m, 1 H), 2.61 (d of d, $J$ = 15, 4.5, 1 H), 2.90 (d of t, $J$ = 10.5, 4, 1 H), 3.14 (m, 1 H), 3.97 (q, $J$ = 7, 2 H); exact mass calcd for $C_{16}H_{27}NO_2$ 265.2041, found 265.2033], 42 mg (5%) of a mixture of **14** and **15**, and 110 mg (14%) of ester **15**: mp (HCl salt) 183–186 °C; IR ($CCl_4$) 1735 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.00–2.13 (m with *t*, $J$ = 7, at $\delta$ 1.27, 20 H, alkyl and $CH_3$), 2.17 (d of d, $J$ = 15, 8, 1 H, CHC(O)), 2.53 (d of d, $J$ = 15, 4, 1 H, CHC(O)), 2.63 (m, 1 H, CHN), 3.30 (m, 2 H, CHN), 4.08 (q, $J$ = 7, 2 H, O–$CH_2$); NMR ($C_6D_6$) $\delta$ 0.83–2.10 (m with t, $J$ = 7, at $\delta$ 1.02, 20 H), 2.23 (d of d, $J$ = 15, 8, 1 H), 2.52 (d of d, $J$ = 15, 4, 1 H), 2.60 (m, 1 H), 3.10 (br four-line m, 1 H), 3.43 (septuplet, 1 H), 3.98 (q, $J$ = 7, 2 H); exact mass calcd for $C_{16}H_{27}NO_2$ 265.2041, found 265.2048.

**2-[*rel*-(1*S*,3a*S*,5a*R*,9a*R*)-Dodecahydropyrrolo[1,2-*a*]-quinolin-1-yl]ethanol (2).** To 120 mg (0.45 mmol) of amino ester **14** in 3 mL of tetrahydrofuran was added 20 mg of solid lithium aluminum hydride. The mixture was stirred at room temperature for 10 min, diluted with 5 mL of tetrahydrofuran, and quenched by sequential addition of 1 drop of water, 1 drop of 3 N aqueous sodium hydroxide, and 2 drops of water. The mixture was dried ($MgSO_4$), filtered, and concentrated in vacuo to give 96 mg (96%) of amino alcohol **2** as a colorless oil which was homogeneous by TLC (alumina, ethyl acetate–hexane, 1:9): IR ($CCl_4$) 3250 (br) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.80–2.27 (m, 19 H, alkyl), 2.47 (twelve-line signal appearing as t ($J$ = 10) of q ($J$ = 4.5, 3), 1 H, CHN), 3.17 (m, 2 H, CHN), 3.57 (d of t, $J$ = 11, 4.5 1 H, CH–O), 3.97 (t of d, $J$ = 11, 3, 1 H, CH–O), 5.56 (br s, 1 H, OH); NMR ($C_6D_6$) $\delta$ 0.83–2.10 (m, 19 H, alkyl), 2.30 (m, 1 H), 3.06 (m, 2 H), 3.67 (d of t, $J$ = 11, 4.5, 1 H), 3.97 (t of d, $J$ = 11, 4.5, 1 H), 4.90 (br s, 1 H); $^{13}C$ NMR ($C_6D_6$) 16.6 (t), 21.55 (t), 24.71 (t), 25.92 (t), 26.55 (t), 31.17 (t), 31.31 (t), 31.80 (t), 32.77 (t), 36.56 (d), 54.67 (d), 55.78 (d), 56.02 (d), 59.67 (t); exact mass calcd for $C_{14}H_{25}NO$ 223.1936, found 223.1943.

**2-[*rel*-(1*R*,3a*S*,5a*R*,9a*R*)-Dodecahydropyrrolo[1,2-*a*]-quinolin-1-yl]ethanol (16).** To 28 mg (0.11 mmol) of amino ester **15** in 2.0 mL of tetrahydrofuran was added 10 mg of solid lithium aluminum hydride. The mixture was stirred at room temperature for 10 min followed by sequential addition of 1 drop of water, 1 drop of 3 N aqueous sodium hydroxide, 2 drops of water, a spatula-tip full of $MgSO_4$, and 5 mL of tetrahydrofuran. The solution was filtered and concentrated in vacuo to give 22 mg (90%) of amino alcohol **16** as a colorless oil, homogeneous by TLC (alumina, ethyl acetate–hexane, 1:9): IR ($CCl_4$) 3250 (br) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.80–2.27 (m, 19 H, alkyl), 2.82 (m, 1, CHN), 3.00–3.73 (m with d of t ($J$ = 10.5, 4.5) at $\delta$ 3.57, 3 H, CHN and CH–O), 3.94 (t of d, $J$ = 10.5, 2, 1 H, CH–O), 5.73 (br s, 1 H, OH); NMR ($C_6D_6$) $\delta$ 0.7–2.16 (m, 19 H), 2.63–3.33 (m, 3), 3.73 (d of t, $J$ = 10.5, 1 H), 4.04 (d of t, $J$ = 10.5, 2, 1 H), 5.13 (br s, 1 H); $^{13}C$ NMR ($C_6D_6$) 21.26, 24.22, 26.07, 26.51, 27.14, 27.77, 28.84, 30.29, 31.51, 32.91, 54.81, 54.81, 57.38, 59.90; exact mass calcd for $C_{14}H_{25}NO$ 223.1936, found 223.1943.

***N*-(But-1-yn-4-yl)-2(*E*)-(carbethoxymethylidene)-5-oxopyrrolidine (18).** A mixture of 3.02 g (20.0 mmol) of imide **17** and 14.0 g (40.0 mmol) of (carbethoxymethylidene)triphenylphosphorane was warmed with stirring at 170 °C for 20 h. The mixture was cooled slightly and 30 mL of ethyl acetate–hexane (1:1) was carefully added. The mixture was allowed to stand at room temperature for 1–2 h and the resulting solid was collected. The filtrate was concentrated in vacuo and the residue was chromatographed over 200 g of silica gel (eluted with ethyl acetate–hexane, 1:2). Appropriate fractions were concentrated and bulb-to-bulb distilled to give 0.5 g (17%) of recovered imide **17**, 0.3 g (5%) of the bis Wittig product (**19**) [bp 110–115 °C (0.1 mm); IR ($CCl_4$) 1730, 1615 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7, 6 H, $CH_3$), 2.00 (t, $J$ = 3, 1 H, ≡CH), 2.50 (t of d, $J$ = 8, 3, 2 H, ≡$CCH_2$), 3.60 (s, 4 H,$CH_2CH_2$), 4.13 (q with underlying signals, $J$ = 7, 6 H, $OCH_2$ and $CH_2N$), 5.97 (s, 2 H, =CH); exact mass calcd for $C_{16}H_{21}NO_4$ 291.1470, found 291.1476], and 2.35 g (53%) of vinylogous urethane **18** [bp 105–110 °C (0.1 mm)] as a white solid: mp 55–58 °C: IR ($CCl_4$) 3320, 1745, 1710, 1625 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.30 (t, $J$ = 7, 3 H, $CH_3$), 2.00 (t, $J$ = 3, 1 H, ≡CH), 2.50 (m, 4 H, $CH_2$), 3.23 (m, 2 H, =C(N)$CH_2$), 3.70 (t, $J$ = 7, 2 H, $CH_2N$), 4.15 (q, $J$ = 7, 2, $OCH_2$), 5.23 (S, 1 H, =CH); exact mass calcd for $C_{12}H_{15}NO_3$ 221.1051, found 221.1058.

***N*-(But-4-*en*-1-yl)-2(*E*)-(carbethoxymethylidene)-5-oxopyrrolidine (20).** A solution of 884 mg (4.0 mmol) of alkyne **18** in 10 mL of pyridine was stirred over 70 mg of 5% palladium on charcoal under 1 atm of hydrogen. After 90 mL of hydrogen had been absorbed, the mixture was diluted with 70 mL of dichloromethane, filtered, washed with two 50-mL portions of 1.5 M aqueous hydrochloric acid, dried ($Na_2SO_4$), and concentrated in vacuo. The residue was chromatographed over 40 g of silica gel (eluted with ethyl acetate–hexane, 1:2) to give 627 mg (70%)

of alkene **20** as a colorless liquid: IR ($CCl_4$) 1745, 1710, 1620 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.27 (t, $J$ = 7, 3 H, $CH_3$), 2.40 (m, 4 H, $CH_2C(O)$ and $=CCH_2$), 3.17 (m, 2 H, $=C(N)CH_2$), 3.53 (t, $J$ = 8, 2 H, $CH_2N$), 4.05 (q, $J$ = 7, 2 H, $OCH_2$), 5.03 (m, 3 H, $=CH_2$ and $=CHC(O)$), 5.67 (m, 1 H, CH=); exact mass calcd for $C_{12}H_{17}NO_3$ 223.1208, found 223.1213.

***N*-(But-4-en-1-yl)-2(*E*)-(carbethoxymethylidene)-5-hydroxypyrrolidine (21).** To a stirred solution of 600 mg (2.87 mmol) of lactam **20** in 10 mL of toluene was added 2.8 mL of diisobutylaluminum hydride (25 wt %) in toluene over a 10-min period. The temperature of the reaction mixture was kept below −65 °C throughout the addition. The mixture was stirred for 30 min at −70 °C followed by addition of 20 mL of tetrahydrofuran and 1.0 mL of 3 N aqueous sodium hydroxide. The mixture was allowed to warm toward room temperature for 5 min and was filtered with the aid of air pressure through a 25-g plug of silica gel. Appropriate fractions were rechromatographed over 25 g of silica gel (eluted with ethyl acetate–hexane, 1:1) to give 520 g (85%) of carbinol **21** as a colorless oil which crystallized on standing (mp 44–52 °C). Carbinol **21** decomposed upon standing at room temperature and was generally used immediately in subsequent reactions: IR ($CCl_4$) 3380, 1740 (weak), 1690, 1660, 1595 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.20 (t, $J$ = 7, 3 H, $CH_3$), 1.58–2.57 (m, 4 H, $=C(C)CH_2$ and $CH_2C(OH)$), 2.80–3.40 (m, 4 H, $=C(N)CH_2$ and $CH_2N$), 3.93 (q with underlying signals, 3 H, $OCH_2$ and OH), 4.40 (br s, 1 H, $=CHC(O)O$), 5.00 (m, 3 H, $=CH_2$ and NCHOH), 5.77 (m, 1 H, =CH); mass spectrum (70 eV), $m/e$ 207 (parent − $H_2O$).

***rel*-(1*R*,3*R*)-7(*E*)-(Carbethoxymethylidene)-3-(formyloxy)-6-azabicyclo[4.3.0]nonane (22).** To 5.0 mL of 97% formic acid was added a solution of 200 mg (0.89 mmol) of carbinolamine **21** in 1.0 mL of dichloromethane over a 2-min period. The solution was stirred at room temperature for 5–10 min and the formic acid was removed in vacuo. The residual orange oil was chromatographed over 30 g of silica gel (eluted with ethyl acetate–hexane, 1:2) to give 51 mg (23%) of formate **22** as a pale yellow oil: IR ($CCl_4$) 1732, 1692, 1605 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.10–2.47 (m with t, $J$ = 7, at $\delta$ 1.22, 9 H, $CH_3$ and $CH_2$), 2.47–3.80 (m, 5 H, $=C(N)CH_2$ and $CH_2NCH$), 4.03 (q, $J$ = 7, 2 H, $OCH_2$), 4.55 (s, 1 H, $=CHC(O)$), 4.93 (t of t, $J$ = 10, 4, 1 H, O–CH), 7.90 (s, 1 H, CHO); exact mass calcd for $C_{13}H_{19}NO_4$ 253.1313, found 253.1320.

***N*-(Hept-1-en-4-yl)succinimide (23).** To a solution of 34.2 g (0.3 mol) of hept-1-en-4-ol, 78.6 (0.3 mol) of triphenylphosphine, and 36.0 g (0.36 mol) of succinimide in 450 mL of tetrahydrofuran was added 52.2 g (0.3 mol) of diethyl azodicarboxylate over a 45-min period with cooling in an ice–water bath. The mixture was stirred at room temperature for 16 h. The tetrahydrofuran was removed in vacuo and 600 mL of ethyl acetate–hexane (1:3) was added to the residue. The resulting precipitate was collected and the filtrate was concentrated in vacuo. The residual oil was chromatographed over 200 g of silica gel (eluted with ethyl acetate–hexane, 1:2). Fractions containing imide **23** were concentrated and distilled to give 39.5 g (67%) of imide **23**: bp 85–90 °C (0.15 mm); IR ($CCl_4$) 1710 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.70–2.93 (m with s at $\delta$ 2.50, 13 H, $(O)CCH_2CH_2C(O)$ and alkyl), 4.05 (m, 1 H, CHN), 4.90 (m, 2 H, $=CH_2$), 5.57 (m, 1 H, =CH); exact mass calcd for $C_{11}H_{17}NO_2$ 195.1259, found 195.1263.

***N*-(Hept-1-en-4-yl)-2(*E*)-(carbethoxymethylidene)-5-oxopyrrolidine (24).** A mixture of 7.8 g (40.0 mmol) of imide **23** and 28.0 g (80.0 mmol) of (carbethoxymethylidene)triphenylphosphorane was warmed with stirring at 175 °C for 36 h. The mixture was cooled slightly and 50 mL of ethyl acetate–hexane (1:1) was added to the black mixture. The mixture was cooled to room temperature and the resulting crystals were collected and rinsed with 50 mL of ethyl acetate–hexane (1:1). The filtrate was concentrated in vacuo and the residual oil was chromatographed over 200 g of silica gel (eluted with ethyl acetate–hexane, 1:2). Appropriate fractions were pooled, concentrated, and bulb-to-bulb distilled to give 2.88 g (36%) of recovered imide **23** (oven temperature of 110 °C at 0.1 mm) and 3.37 g (32%) of vinylogous urethane **24** (oven at 120 °C at 0.1 mm): IR ($CCl_4$) 1740 (weak), 1710, 1620 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.70–2.87 (m with t, $J$ = 7, at $\delta$ 1.25, 14 H, $OCH_2CH_3$ and alkyl), 3.13 (m, 2 H, $=C(N)CH_2$), 4.03 (q with underlying m, $J$ = 7, 3 H, $OCH_2$ and CHN), 4.73–5.20 (m, 3, =CHC(O) and $=CH_2$), 5.27–5.93 (m, 1 H, CH); exact mass calcd for $C_{15}H_{23}NO_3$ 265.1677, found 265.1684.

***N*-(Hept-1-en-4-yl)-2(*E*)-(carbethoxymethylidene)-5-hydroxypyrrolidine (25).** To a solution of 3.3 g (12.4 mmol) of vinylogous urethane **24** in 40 mL of toluene was added 13.0 mL of diisobutylaluminum hydride (25 wt %) in toluene with cooling such that the temperature did not exceed −65 °C. The reaction was monitored by thin-layer chromatography of aliquots withdrawn directly from the reaction mixture (silica gel, ethyl acetate–hexane, 1:1). When no starting material remained the mixture was poured into 100 mL of tetrahydrofuran and 3.0 mL of 3 N aqueous sodium hydroxide was added. The mixture was stirred for 15 min and passed through a 100-g column of silica gel with the aid of air pressure. Appropriate fractions were concentrated and the residue was crystallized from 30 mL of hexane to give 1.88 g of carbinolamine **25** as a creamy white solid (mp 77–79 °C). A second crop of 0.3 g (67% total) was obtained from the mother liquor: IR ($CCl_4$) 3380, 1745 (weak), 1665, 1590 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.7–3.67 (m with t, $J$ = 7, at $\delta$ 1.27, 18 H), 4.03 (q, $J$ = 7, 2 H, $OCH_2$), 4.67 (s, 1 H, $=CHCO_2$), 5.07 (m, 3 H, $=CH_2$ and OCHN), 5.67 (m, 1 H, =CH); mass spectrum (70 eV), $m/e$ 249 (parent − $H_2O$).

Anal. Calcd for $C_{15}H_{25}NO_5$: C, 67.38; H, 9.42. Found: C, 67.99; H, 9.38.

**2-(Carbethoxymethylidene)-5-(prop-1-en-3-yl)pyrrolidine (27) and *rel*-(1*R*,3*R*,5*R*)-7(*E*)-(carbethoxymethylidene)-3-(formyloxy)-5-propyl-6-azabicyclo[4.3.0]nonane (26).** To 20 mL of 97% formic acid was added a solution of 534 mg (2.0 mmol) of carbinolamine **25** in 5 mL of dichloromethane over a 15-min period at room temperature. Upon completion of the addition, the dichloromethane and formic acid were removed in vacuo over a 30-min period. The dark residue was chromatographed over 35 g of silica gel (eluted with ethyl acetate–hexane, 1:2) to give, after distillation, 210 mg (54%) of vinylogous urethane **27** as a colorless liquid [bp 100 °C (0.1 mm); IR ($CCl_4$) 3360, 1665, 1600 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.00–2.70 (m with t, $J$ = 7, at $\delta$ 1.18, 9 H, $CH_3$ and $CH_2$), 3.80 (m, 1 H, CHN), 3.97 (q, $J$ = 7, 2 H, $OCH_2$), 4.30 (s, 1 H, $=CHC(O)$), 5.08 (m, 2 H, $=CH_2$), 5.70 (m, 1 H, =CH), 7.97 (br s, 1 H, NH); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.73 (q), 27.82 (t), 31.82 (t), 40.56 (t), 58.40 (t), 58.96 (d), 76.85 (d), 117.97 (t), 134.24 (d), 165.58 (s), 170.67 (s); mass spectrum (70 eV), $m/e$ 195 (parent)] and 123 mg (21%) of formate **26** as an orange oil: IR ($CCl_4$) 1730, 1690, 1600 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.70–2.67 (m with t, $J$ = 7, at $\delta$ 1.17, 16 H, $CH_3$ and alkyl), 2.67–4.20 (m, with q ($J$ = 7) at 3.93, 6 H, $=C(N)CH_2$, CHN, and $OCH_2$), 4.37 (s, 1 H, $=CHC(O)$), 5.05 (m, 1 H, O–CH), 7.90 (s, 1 H, CHO); $^{13}C$ NMR ($CDCl_3$) 13.90 (q), 14.81 (q), 19.96 (t), 27.91 (t), 31.43 (t), 31.62 (t), 32.22 (t), 38.23 (t), 50.73 (d), 55.89 (d), 58.38 (t), 67.54 (d), 79.19 (d), 160.33 (d), 163.73 (s), 169.56 (s); exact mass calcd for $C_{16}H_{25}NO_4$ 295.1783, found 295.1790.

***N*-(*cis*-2-Ethynylcyclohexyl)-2-(carbethoxymethylidene)-5-oxopyrrolidine (28).** A mixture of 12.3 g (0.06 mol) of imide **4** and 70.0 g (0.2 mol) of (carbethoxymethylidene)triphenylphosphorane was warmed in a molten salt bath at 175 °C for 24 h. The solution was cooled slightly and 150 mL of ethyl acetate–hexane (1:2) was added carefully. The dark solution was stored in a refrigerator for 15 h and the resulting precipitate (32 g) was collected and rinsed with 75 mL of ethyl acetate–hexane (1:2). The filtrate was concentrated in vacuo and the residual oil was chromatographed over 500 g of silica gel (eluted with ethyl acetate–hexane, 1:2). Appropriate fractions were pooled, concentrated, and bulb-to-bulb distilled to afford 4.8 g (40%) of imide **4** [bp 110 °C (0.1 mm); mp 87–95 °C] and 4.73 g (30%) of vinylogous urethane **28** [bp 145 °C (0.1 mm); mp 113–118 °C] as a white crystalline solid: IR ($CCl_4$) 3320, 1750, 1710, 1620 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.0–2.18 (m with t, $J$ = 7, at $\delta$ 1.38 and d, $J$ = 2, at $\delta$ 2.02, 12 H, $CH_3$, ≡CH, and alkyl), 2.45 (m, 2 H, $CH_2C(O)N$), 3.05 (m, 3 H, CH and $=C(N)CH_2$), 3.70 (d of t, $J$ = 12, 3, 1 H, CHN), 4.03 (q, $J$ = 7, 2 H, $OCH_2$), 5.28 (t, $J$ = 1.5, 1 H, $=CHC(O)$); exact mass calcd for $C_{16}H_{21}NO_3$ 275.1521, found 275.1526.

***N*-(*cis*-2-Vinylcyclohexyl)-2-(carbethoxymethylidene)-5-oxopyrrolidine (29).** A solution of 4.5 g (16.3 mmol) of alkyne **28** in 60 mL of pyridine was hydrogenated at 1 atm over 1.0 g of 5% palladium on barium sulfate until 390 mL of hydrogen had been absorbed. The solution was filtered, diluted with 150 mL of dichloromethane, washed with two 300-mL portions of 3 N aqueous hydrochloric acid, dried ($Na_2SO_4$), and concentrated in

vacuo. The residual solid was chromatographed over 120 g of silica gel (eluted with ethyl acetate–hexane, 1:2) to give 4.10 g (91%) of olefin **29** as a white crystalline solid: mp 105–109 °C; IR ($CCl_4$) 1740, 1710, 1615 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.11–3.35 (m with t, $J$ = 7, at $\delta$ 1.28, 16 H, alkyl and $CH_3$), 3.61 (d of t, $J$ = 12, 3, 1 H, CHN), 4.08 (q, $J$ = 7, 2 H, $OCH_2$), 4.91 (five-line m, 2 H, $=CH_2$), 6.21 (eight-line m, 1 H, =CH); exact mass calcd for $C_{16}H_{23}NO_3$ 277.1677, found 277.1685.

Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.27. Found: C, 69.26; H, 8.25.

***rel*-(3a*R*,5*S*,5a*S*,9a*R*)-1(*E*)-(Carbethoxymethylidene)-5-(formyloxy)dodecahydropyrrolo[1,2-*a*]quinoline (31).** To a solution of 2.77 g (10.0 mmol) of lactam **29** in 35 mL of toluene was added 11.0 mL of diisobutylaluminum hydride (25 wt %) in toluene with cooling such that the temperature did not exceed –65 °C. The reaction was monitored by thin-layer chromatography of aliquots withdrawn directly from the reaction mixture (silica gel, ethyl acetate–hexane, 1:2). To the cold mixture was added 50 mL of tetrahydrofuran followed by 5.0 mL of 3 N aqueous sodium hydroxide. The mixture was allowed to warm to 0 °C and was chromatographed directly over 100 g of silica gel (eluted with ethyl acetate–hexane, 1:1) to give 2.90 g (100%) of carbinolamine **30** suitable for use in the next reaction; NMR ($CCl_4$) $\delta$ 0.7–2.37 (m with t at $\delta$ 1.20, 13 H), 2.37–4.47 (m with q at $\delta$ 3.91, 8 H), 4.97 (m, 3 H, $=CH_2$ and NCHO), 5.93 (m, 1 H, =CH).

To 40 mL of 97% formic acid, cooled in an ice–water bath, was added a solution of carbinolamine **30** (2.9 g, 10.0 mmol) in 12 mL of dichloromethane via pipet over a 5-min period. The mixture was stirred for an additional 15 min and the formic acid was removed at room temperature in vacuo over a period of 15–20 min. The deep brown residual oil was dissolved in 50 mL of dichloromethane, washed with water (2 × 40 mL), dried ($Na_2SO_4$), and concentrated in vacuo. The residual material was recrystallized from 40 mL of ethyl acetate–hexane (1:3) to give 1.56 g of **31** as white needles. An additional two crops (0.51 g) were obtained to afford a 67% yield of **31**: mp 140–141 °C; IR ($CCl_4$) 1730, 1690, 1600 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.10–3.87 (m with t, $J$ = 7, at $\delta$ 1.25, 20 H, alkyl), 4.08 (q, $J$ = 7, 2 H, $OCH_2$), 4.57 (br s, 1 H, =CHC(O)), 5.35 (t of d, $J$ = 12, 4, 1 H, O–CH), 8.08 (s, 1 H, CHO); $^{13}C$ NMR ($CDCl_3$) 14.76 (q), 20.05 (t), 22.82 (t), 25.10 (t), 25.58 (t), 28.25 (t), 31.60 (t), 38.40 (t), 39.18 (d), 53.21 (d), 56.12 (d), 58.35 (t), 67.92 (d), 78.84 (d), 160.50 (d), 163.17 (s), 169.43 (s); exact mass calcd for $C_{17}H_{25}NO_4$ 307.1783, found 307.1788.

Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20. Found: C, 66.42; H, 8.10.

When crude carbinol **30** was chromatographed over activity II alumina, a 75% yield of pyrrole **33** was obtained: bp (bulb-to-bulb) 100 °C (0.05 mm); IR (neat) 1735 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.22 (t, $J$ = 7, 3 H, $CH_3$), 1.3–2.4 (m, 8 H, $CH_2$), 2.61 (m, 1 H, CHC=), 3.43 (s, 2 H, $CH_2CO_2$), 4.05 (q with underlying m, 3 H, $OCH_2$ and CHN), 4.88 (m, 2 H, $=CH_2$), 4.78 (m, 3 H, CH= and aromatic), 6.46 (t, $J$ = 3, 1 H, aromatic); exact mass calcd for $C_{16}H_{23}NO_2$ 261.1728, found 261.1734.

***O*-*rel*-(3a*R*,5*S*,5a*S*,9a*R*)-1(*E*)-(Carbethoxymethylidene)dodecahydropyrrolo[1,2-*a*]quinol-5-yl *S*-Methyl Dithiocarbonate (32).** To 1.23 g (4.0 mmol) of formate **3** suspended in 30 mL of methanol was added 2.0 mL of 3 N aqueous sodium hydroxide. The yellow solution was stirred at room temperature for 30 min, diluted with 100 mL of dichloromethane, and washed with two 50-mL portions of water. The aqueous phase was extracted with 100 mL of dichloromethane and the combined organic phases were dried ($Na_2SO_4$) and concentrated in vacuo to give 1.10 g (100%) of crude alcohol as a yellow foam, homogeneous by thin-layer chromatography (silica gel, ethyl acetate–hexane 1:1).

To the crude alcohol in 25 mL of tetrahydrofuran was added 216 mg (9.0 mmol) of sodium hydride and 15 mg of imidazole. The mixture was warmed on an oil bath at 60 °C for 60 min followed by the addition of 1.8 mL of carbon disulfide. The mixture was warmed for an additional 10 min followed by the addition of 1.8 mL of iodomethane. The mixture was warmed for 10 min, cooled to room temperature, and partitioned between 150 mL of dichloromethane and 75 mL of water. The organic phase was dried ($Na_2SO_4$) and concentrated in vacuo. The residual yellow oil was chromatographed over 45 g of silica gel (eluted with ethyl acetate–hexane, 1:4) to afford 1.4 g (91%) of xanthate **32** as a pale yellow solid: mp 129–130.5 °C; IR ($CCl_4$) 1690, 1600 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.0–3.87 (m with t, $J$ = 7, at $\delta$ 1.25 and s at $\delta$ 2.57, 23 H, alkyl, $CH_3$, and $SCH_3$), 4.10 (q, $J$ = 7, 2 H, $OCH_2$), 4.57 (br s, 1 H, =CHC(O)), 6.05 (t of d, $J$ = 11, 4, 1 H, O–CH); mass spectrum (70 eV), $m/e$ 369 (parent).

Anal. Calcd for $C_{18}H_{27}NO_3S_2$: C, 58.50; H, 7.37. Found: C, 58.99; H, 7.28.

***rel*-(3a*S*,5a*R*,9a*R*)-1(*E*)-(Carbethoxymethylidene)-dodecahydropyrrolo[1,2-*a*]quinoline (13).** To 1.57 g (5.4 mmol) of tri-*n*-butyltin hydride in 30 mL of toluene warmed under reflux was added 1.4 g (3.6 mmol) of xanthate **32** in 30 mL of toluene over a 45-min period. The solution was warmed under reflux for an additional 6 h, cooled, and concentrated in vacuo. The residue was chromatographed over 30 g of silica gel (eluted with ethyl acetate–hexane, 1:4) to give 0.94 mg (98%) of vinylogous urethane **13** as a pale yellow solid, mp 55–63 °C. This material was identical ($^1H$ NMR, $^{13}C$ NMR, IR, TLC) with a sample of **13** prepared from lactam **7** as outlined above.

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