(d of t, H(6exo), 1 H), 3.40 (d, H(1) and H(4), 2 H), 3.92 (d, H(5), 1 H), 6.80–7.40 (m, arom H, 8 H, $J_{1,5} = J_{1,6endo} = 0$, $J_{1,6exo} = 2.5$ Hz, $J_{6exo,6endo} = 6.3$ Hz, $J_{5endo,6endo} = 7.5$ Hz); UV (methanol) λ_{max} (log ϵ) 273 (3.24), 265 (3.24), 259 (3.17), 252 (3.10, sh), 220 (4.10); mass spectrum 220 (M^+, 4), 205 (2), 204 (2), 203 (2), 202 (1), 128 (6), 121 (2), 115 (5), 105 (100).

Registry No. *cis*-**4**, 59154-50-6; *exo*-**5**, 58719-66-7; **12**, 27685-27-4; **15**, 80663-29-2; **18**, 80663-30-5; *cis*-**20**, 80663-31-6; *trans*-**20**, 80663-32-7; *cis*-**21**, 80663-33-8; *trans*-**21**, 80663-34-9; **22**, 80663-35-0; **23**, 80663-36-1; **24**, 80663-37-2; **25**, 80663-38-3; **26**, 80663-39-4; *cis*-**27**, 80663-40-7; *trans*-**27**, 80663-41-8; *endo*-**28**, 80663-42-9; *exo*-**28**, 80734-35-6; **29**, 80663-43-0; **30**, 80663-44-1; **31**, 80663-45-2; **32**, 80734-36-7; **33**, 80679-17-0; **34**, 1942-39-8; **35**, 80679-18-1; **36**, 60300-71-2; *trans*-**38**, 80663-46-3; benzyltriphenylphosphonium bromide, 1449-46-3; 2-methyl-α,α,α-trifluoroacetophenone, 341-39-9; *trans*-α-(trifluoromethyl)-2-methylstilbene, 80663-47-4; *cis*-α-(trifluoromethyl)-2-methylstilbene, 80679-19-2; (*E*)-α-(trifluoromethyl)-2-(bromomethyl)stilbene, 80663-48-5; (*Z*)-α-(trifluoromethyl)-2-(bromomethyl)stilbene, 80663-49-6; 4-methylbenzaldehyde, 104-87-0; 2-methylbenzonitrile, 529-19-1; 2-cyanostilbene, 80663-50-9; 4′-methyl-2-stilbenyl benzyl ketone, 80663-51-0; *p*-methylbenzyl bromide, 104-81-4; 1-chloro-2-(*p*-tolyl)-3-phenylnaphthalene, 80663-52-1; β-cyano-2-methylstilbene, 80663-53-2; *p*-xylyltriphenylphosphonium bromide, 2378-86-1; 2-vinylbenzaldehyde, 28272-96-0; 2-stilbenecarbaldehyde, 63104-89-2; *cis*-2-(4-methylstyryl)tolane, 80663-54-3; *trans*-2-(4-methylstyryl)tolane, 80663-55-4; *exo*-5-(*p*-tolyl)benzobicyclo[2.1.1]hex-2-ene, 80663-56-5; *trans*-stilbene, 103-30-0.

New Approach to Lythraceae Alkaloids: Total Synthesis of (±)-Vertaline

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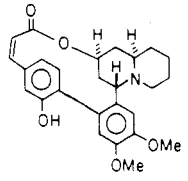
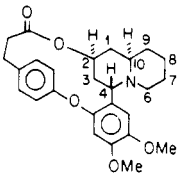
A new approach to Lythraceae alkaloids is described within the context of a total synthesis of (±)-vertaline (**2**). The use of *N*-silyl imines in the preparation of benzylic amines as well as a stereoselective bicycloannelation approach to the synthesis of quinolizidinones is discussed.

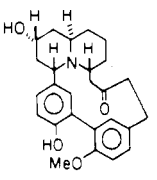
Macrocyclic quinolizidine alkaloids isolated from members of the Lythraceae plant family can be classified according to three structural types. These are represented below by the biphenyl lactone cryogenine (**1**), the diphenyl



1



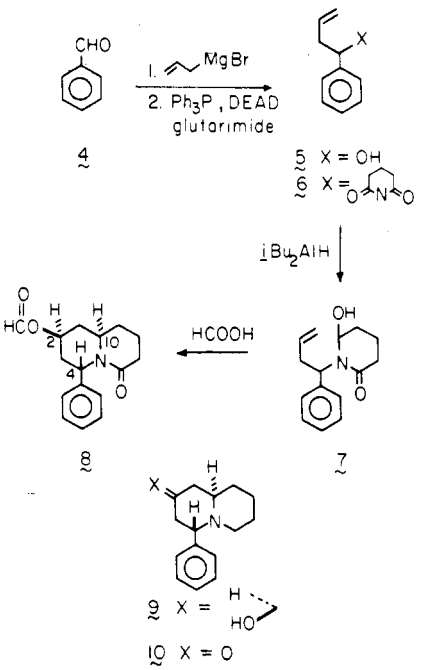
2



3

ether lactone vertaline (**2**), and the carbocyclic biphenyl lythrumine (**3**).[1] Several total syntheses of lactonic Lythraceae alkaloids have been reported, all of which use Mannich reactions of pelletierine with substituted benzaldehydes, biaryls, or diaryl ethers to assemble the quinolizidine moiety.[2-5] We recently reported a highly stereoselective quinolizidinone synthesis which suggested an efficient alternative to the pelletierine route to Lythraceae alkaloids.[6] This report outlines the development of this method within the context of a total synthesis of (±)-vertaline (**2**).

Scheme I



Our approach to vertaline was based on the model studies[6] shown in Scheme I. Treatment of benzaldehyde (**4**) with allylmagnesium bromide gave carbinol **5** (91%) which was converted to glutarimide **6** (55%) by using the conditions of Mitsunobu.[7] Imide **6** was reduced with diisobutylaluminum hydride[8] to afford carbinol amide **7**

(1) For a review see: Fujita, E.; Fuji, K. "International Review of Science, Organic Chemistry Series Two"; Wiesner, K., Ed.; Butterworths: London, 1976, 119.

(2) For syntheses of diphenyl ether lactones see the following. Vertaline: Hanaoka, M.; Ogawa, N.; Arata, Y. *Chem. Pharm. Bull.* **1974**, *22*, 973. Hanaoka, M.; Ogawa, N.; Arata, Y. *Ibid.* **1976**, *24*, 1045. Lagerine: Hanaoka, M.; Kamei, M.; Arata, Y. *Ibid.* **1975**, *23*, 2191. Decaline: Hanaoka, M.; Ogawa, N.; Arata, Y. *Ibid.* **1975**, *23*, 2140. Hanoaka, M.; Ogawa, N.; Arata, Y. *Tetrahedron Lett.* **1973**, 2355. Wróbel, J. T.; Golebiewski, W. M. *Ibid.* **1973**, 4293.

(3) For syntheses of biphenyl lactones see the following: Decinine: Lantos, I.; Loev, B. *Tetrahedron Lett.* **1975**, 2011. Decamine: Lantos, I.; Razgaitis, C.; VanHoeven, H.; Loev, B. *J. Org. Chem.* **1977**, *42*, 228.

(4) No syntheses of the macrocarbocyclic quinolizidines (e.g., **3**) have been reported.

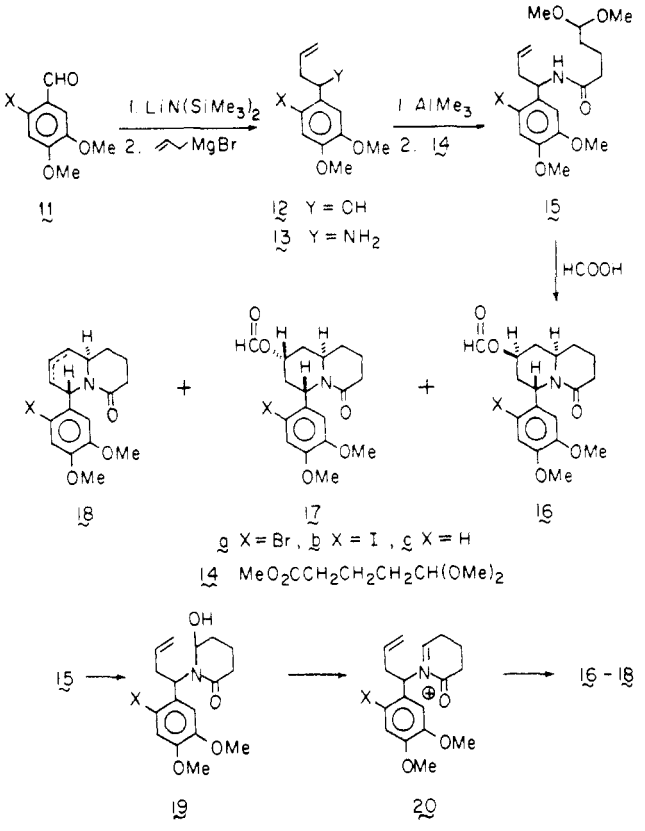
(5) For other relevant reports see: Fuji, K.; Ichikawa, K.; Fujita, E. *Tetrahedron Lett.* **1979**, 361. Horhammer, R. B.; Schwarting, A. E.; Edwards, J. M. *J. Org. Chem.* **1975**, *40*, 656.

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

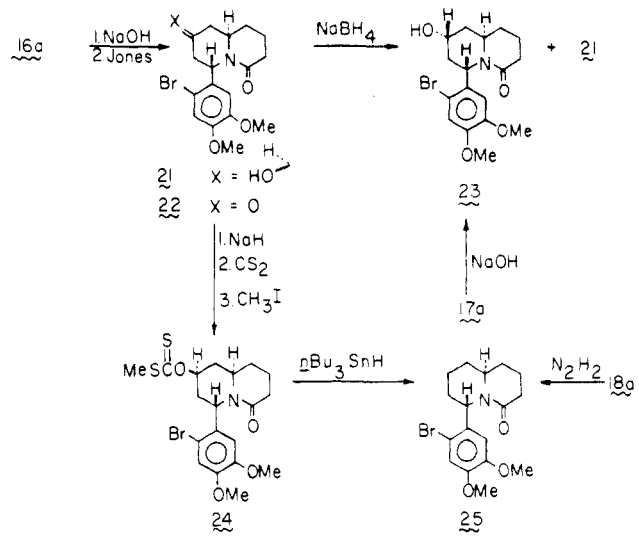
(7) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679.

0022-3263/82/1947-1555$01.25/0

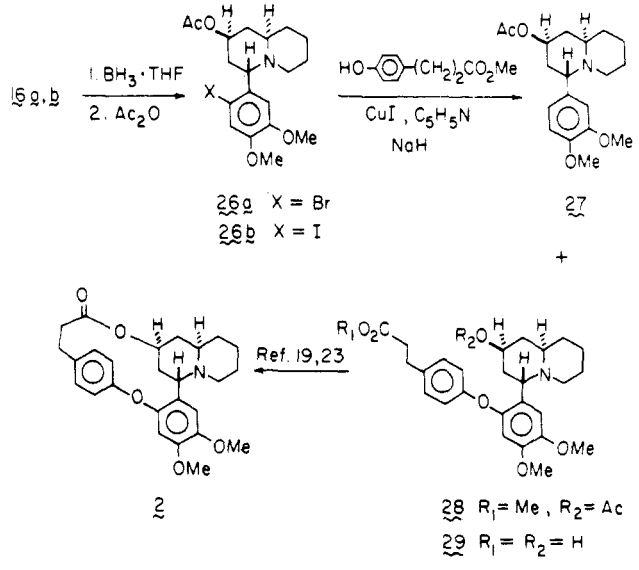
Scheme II



Scheme III



Scheme IV



(67%) which was converted to lactam **8** (63%) upon treatment with formic acid. The stereochemistry of **8** was established by conversion to the known quinolizidines **9** ($LiAlH_4$, 72%)[9] and **10** (Jones, 60%).[10] Quinolizidinone **8** has the basic structural elements present in vertaline with the proper stereochemistry at carbons 2, 4, and 10.

With this background, we felt that by merely starting with an appropriately substituted benzaldehyde, it would be a simple task to prepare the seco acid **29**, which had already been lactonized to vertaline. Treatment of 6-bromoveratraldehyde (**11a**)[11] with allylmagnesium bromide gave alcohol **12a** in a 95% yield. Unfortunately, treatment of **12a** with glutarimide under the Mitsunobu conditions[7] did not afford any of the desired N-alkylation product. Only products derived from initial dehydration of **12a** were obtained. The electronic effects of the *p*-methoxy group are presumably responsible for this facile elimination. Several other routes to carbinol amides related to **7** were examined, and eventually the convenient route outlined in Scheme II was developed. Treatment of bromo aldehyde **11a** with 1.2 equiv of lithium bis(trimethylsilyl)amide in tetrahydrofuran followed by addition of 1.25 equiv of ethereal allylmagnesium bromide gave a 97% yield of amine **13a** after an aqueous workup and purification. Similar treatment of 6-iodoveratraldehyde (**11b**)[12] gave a 77% yield of amine **13b** along with 8% of reduction product **13c**. This reaction sequence presumably proceeds via initial *N*-silyl imine formation followed by addition of the organometallic reagent.[13] Amine **13a** was converted to amide **15** by using the excellent method of Weinreb.[14] Thus, sequential treatment of **13a** with trimethylaluminum and ester **14**[15] gave amide **15a** in a 88% yield. Treatment of **15a** with formic acid in dichloromethane (4 h, 25 °C) gave a mixture of four products. The major product was the desired quinolizidinone **16a** (60%). In addition, isomeric formate **17a** (9%) and an equal mixture of olefins **18a** (21%) were obtained. The stereochemical relationships between **16a**, **17a**, and **18a** were established by the sequence of reactions outlined in Scheme III without comment. When the forementioned reaction sequence was applied to iodo amine **13b**, the chemistry proceeded without incident to afford a similar mixture of **16b**, **17b**, and **18b**.

Several points about Scheme II are notable. The conversion of **15** to **16–18** presumably proceeds via initial C–N

(8) Winterfeldt, E. *Synthesis* **1975**, 617.
(9) Matsunaga, T.; Kawasaki, I.; Kaneko, T. *Tetrahedron Lett.* **1967** 2471.
(10) Quick, J.; Oterson, R. *Tetrahedron Lett.* **1977**, 603. Quick, J.; Meltz, C. *J. Org. Chem.* **1979**, *44*, 573.
(11) Pschorr, R. *Justus Liebigs Ann. Chem.* **1912**, *391*, 23.
(12) Piatak, D. M.; Flynn, G.; Yim, K.; Roosenberg, J. *J. Org. Chem.* **1977**, *42*, 1068.

(13) The conditions used to prepare the intermediate *N*-silyl imine represent a mild variant of a previously reported method: Krüger, C.; Rochow, E. G.; Wannagat, U. *Chem. Ber.* **1963**, *96*, 2132. To our knowledge this is the first report of an organometallic adding to an *N*-silyl imine. The scope, limitations, and mechanistic details of these addition reactions have been studied and will be reported in due course (Thomas, D., unpublished results).
(14) Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, 4171.
(15) Stevens, R. V.; Lee, A. W. M. *J. Am. Chem. Soc.* **1979**, *101*, 7032.

bond formation to give a carbinol amide such as **19** or a derivative thereof. At the onset of this work we had worried that C–O bond formation, due to the ambident nucleophilic nature of the amide moiety, might compete favorably with the desired process. The results obtained however, suggest that any C–O bond formation that takes place does so via a reversible path as no products anticipated from O-alkylation (e.g., amine **13**) were detected.[16] It is also noted that the subsequent iminium ion cyclization[17] (**20** → **16–18**) proceeds with very clean stereochemistry at carbons 4 and 10. All of the quinolizidinone products have the stereorelationship predicted by the transition-state model proposed earlier for such iminium ion cyclizations.[6]

The final stages of the synthesis were completed in a straightforward manner as shown in Scheme IV. Treatment of lactam **16a** with BH_3·THF complex[18] followed by acetylation of the resulting amino alcohol gave aminoacetate **26a** (90%), a late intermediate in a previously reported synthesis of (±)-vertaline.[19] Lactam **16b** was converted to aminoacetate **26b** in a similar manner (85%). The structures of **26a** and **26b** were confirmed by conversion to (±)-**2** by following a procedure similar to that described by Hanaoka.[19] Thus bromide **26a** was treated with the preformed copper salt of methyl *p*-hydroxydihydrocinnamate[20] in pyridine (3 h, reflux) to give diaryl ether **28** (32%) and reduction product **27** (8%) along with 38% of recovered **26a**.[21] Unfortunately, the use of iodide **26b** did not offer any improvement in the yield of **28**.[22] Hydrolysis of **28** followed by lactonization of the resulting seco acid **29** under previously reported conditions[23] gave (±)-vertaline (53%) which was identical (TLC, IR, 300-MHz ^{1}H NMR) with an authentic sample of (−)-**2**, kindly provided by Professor Ferris.[24]

This synthesis of (±)-vertaline represents a new and efficient entry to Lythraceous alkaloids bearing a 4β,10α-hydrogen relationship. The remarkable control that allylic strain exerts on the stereochemical course of *N*-acyl iminium ion cyclizations is presumably responsible for the success of this route.[6] Furthermore, this approach passes through C-6-functionalized intermediates and thus should be adaptable to the synthesis of carbocyclic Lythraceous alkaloids such as lythrumine (**3**).[25] Efforts directed toward this end are underway.

Experimental Section

All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. ^{1}H magnetic resonance spectra were recorded on a Varian Associates EM-390 spectrometer (90 MHz) and are reported in parts per million from internal tetramethylsilane on the δ scale. Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, qu = quintet, m = multiplet), integration, coupling constants (in hertz), interpretation]. Infrared spectra were taken with a Perkin-Elmer 457 instrument. Mass spectra were recorded on an AEI MS9 spectrometer. Samples on which exact masses were measured exhibited no significant peaks at *m/e* values greater than that of the parent. Combustion analyses were performed by Micro-Analysis, Inc., Wilmington, DE.

Solvents and reagents were dried and purified prior to use when deemed necessary: acetic anhydride (distilled from P_2O_5); tetrahydrofuran and ether (distilled from sodium metal); dichloromethane (passed through activity I alumina); xylene, pyridine, and toluene (distilled from CaH_2). All reaction temperatures refer to that of the reaction mixture. Reactions requiring an inert atmosphere were run under a blanket of argon. Formic acid (98%) was used in all cyclizations. Analytical thin-layer chromatography was performed by using EM Laboratories glass-backed 0.25-mm precoated silica gel 60 F-254 plates and EM Laboratories glass-backed 0.25-mm precoated aluminum oxide 60 F-254 plates. Column chromatography was performed over EM Laboratories silica gel 60 (70–230 mesh) and Woelm neutral alumina. Medium-pressure liquid chromatography was performed over EM Laboratories Lobar columns.

1-Phenylbut-3-en-1-ol (5). To a stirred solution of 5.3 g (50 mmol) of benzaldehyde in 50 mL of diethyl ether was added 175 mL (77 mmol) of 0.44 M ethereal allylmagnesium bromide[26a] over a 30-min period. The mixture was stirred for 2 h and poured into 230 mL of aqueous hydrochloric acid. The layers were separated, and the aqueous phase was extracted with 100 mL of dichloromethane. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residual oil was bulb to bulb distilled to give 6.77 g (91%) of alcohol **5** as a colorless liquid: bp 65 °C (0.25 mm) [lit.[26b] bp 71 °C (0.75 mm)]; ^{1}H NMR and IR spectra agreed with those reported elsewhere.[26b]

***N*-(1-Phenylbut-3-en-1-yl)glutarimide (6).** To a stirred solution of 4.44 g (30 mmol) of alcohol **5**,[26] 7.86 g (30 mmol) of triphenylphosphine, and 4.52 g (40 mmol) of glutarimide in 35 mL of tetrahydrofuran at 2–4 °C was added 5.22 g (30 mmol) of diethyl azodicarboxylate[27] over a 15-min period. The mixture was allowed to warm to room temperature, stirred for 17 h, and concentrated in vacuo. The residual yellow oil was dissolved in 120 mL of hexane–ethyl acetate (3:1), and the resulting solid (10.3 g) was collected and discarded. The filtrate was concentrated and chromatographed over 140 g of silica gel (ethyl acetate–hexane, 1:4; 75-mL fractions). Fractions 13–20 were concentrated to afford 4.0 g (55%) of imide **6** as a colorless oil: IR ($CHCl_3$) 1625 cm^{-1}; NMR (CCl_4) δ 1.6–2.1 (m, 2 H, CH_2), 2.2–3.6 (m, 6 H, =CCH_2 and C(O)CH_2), 4.8–5.2 (m, 2 H, =CH_2), 5.3–6.1 (m, 2 H, CHN and =CH), 7.05–7.5 (m, 5 H, Ar H); exact mass calcd for $C_{15}H_{17}NO_2$ *m/e* 243.1259, found *m/e* 243.1265.

6-Hydroxy-1-(1-phenylbut-3-en-1-yl)-2-piperidinone (7). To a solution of 2.43 g (10 mmol) of imide **6** in 30 mL of toluene was added 10 mL of 25 wt % diisobutylaluminum hydride[27] in toluene over a 15-min period at −70 °C. The solution was stirred for 30 min and poured into a mixture of 150 mL of chloroform and 100 mL of 5% aqueous sulfuric acid. The organic phase was concentrated, the residual oil was chromatographed over 100 g of silica gel (ethyl acetate–hexane, 3:1; 50-mL fractions). Fractions 8–13 were concentrated to give 1.65 g (67%) of carbinol amide **7** as a pale yellow oil: IR ($CHCl_3$) 1630, 3350 cm^{-1}; NMR (CCl_4) δ 1.0–3.1 (m, 9 H, CH_2 and OH), 4.5–5.35 (m, 3 H, =CH_2 and NCHO), 5.40–6.20 (m, 2 H, =CH and ArCHN), 7.0–7.6 (m, 5 H, Ar H); mass spectrum, *m/e* 245 (parent), 227, 186 (base).

***rel*-(2*R*,4*S*,10*R*)-2-(Formyloxy)-4-phenyloctahydro-4*H*-quinolizin-6-one (8).** To 600 mg (2.4 mmol) of carbinol amide **7** was added 6.0 mL of formic acid. The resulting solution was stirred at room temperature for 15 min, poured into 150 mL of cold saturated aqueous sodium bicarbonate, and extracted with 75 mL of dichloromethane. The extract was dried (Na_2SO_4) and concentrated in vacuo. The resulting pale yellow oil was dissolved in 4.0 mL of ethyl acetate–hexane (1:1) and cooled to give 400 mg of formate **8** as a crystalline solid, mp 135–137 °C. The mother

(16) For several other bicycloannelations involving iminium ions see: Overman, L. E.; Fukaya, C. *J. Am. Chem. Soc.* **1980**, *102*, 1454. Gribble, G. W.; Soll, R. M. *J. Org. Chem.* **1981**, *46*, 2433.
(17) Schoemaker, H. E.; Dijkink, J.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 163.
(18) Brown, H. C.; Heim, P. *J. Am. Chem. Soc.* **1964**, *86*, 3566.
(19) Hanaoka, M.; Ogawa, N.; Arata, Y. *Chem. Pharm. Bull.* **1976**, *24*, 1045.
(20) Marvell, E. N.; Sturmer, D.; Rowell, C. *Tetrahedron* **1966**, *22*, 861.
(21) This method is a modification of a procedure developed by: Whitesides, G. M.; Sadowski, J. S.; Lilburn, J. *J. Am. Chem. Soc.* **1974**, *96*, 2829.
(22) For a review on the Ullmann diaryl ether synthesis see: Moroz, A. A.; Shvartsberg, M. S. *Russ. Chem. Rev. (Engl. Transl.)* **1974**, *43*, 679.
(23) Corey, E. J.; Nicolaou, K. C.; Melvin, L. S. *J. Am. Chem. Soc.* **1975**, *97*, 654.
(24) Ferris, J. P. *J. Org. Chem.* **1962**, *27*, 2985. Hamilton, J. A.; Steinrauf, L. K. *J. Am. Chem. Soc.* **1971**, *93*, 2939.
(25) Wright, H.; Clardy, J.; Ferris, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 6467.
(26) (a) Grummitt, D.; Budewitz, E. P.; Chudd, C. C. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 748. (b) Smith, G. G.; Voorhees, K. J. *J. Org. Chem.* **1970**, *35*, 2182.
(27) Purchased from Aldrich Chemical Co.

liquor was chromatographed over silica gel (ethyl acetate–hexane, 1:1; Lobar size A column) to give an additional 62 mg (63% total) of **8**: IR ($CHCl_3$) 1722, 1626 cm^{-1}; NMR ($CDCl_3$) δ 1.3–3.1 (m, 10 H, CH_2), 3.1–3.6 (m, 1 H, CHN), 5.18 (tt, 1 H, J = 10, 4, OCH), 6.32 (dd, 1 H, J = 6, 1.5, ArCHN), 7.25 (br s, 5 H, Ar H), 8.00 (s, 1 H, CHO); exact mass calcd for $C_{16}H_{19}NO_3$ m/e 273.1364, found m/e 273.1371.

***rel*-(2*R*,4*S*,10*R*)-2-Hydroxy-4-phenyloctahydro-4*H*-quinolizine (9).** To a suspension of 74 mg (2.0 mmol) of lithium aluminum hydride[28] in 5 mL of tetrahydrofuran was added 273 mg (1.0 mmol) of solid formate **8** in a single portion. The solution was warmed under gentle reflux for 60 min followed by the addition of 15 mL of ether, 5 drops of water, 5 drops of 15% aqueous sodium hydroxide, and 15 drops of water. The solution was filtered and concentrated in vacuo. The residual yellow oil was chromatographed over 40 g of alumina (activity III; ethyl acetate) to give 166 mg (72%) of amino alcohol **9** as a white solid: mp 95–97 °C (lit.[9] mp 100–102 °C); IR ($CHCl_3$) 3580, 3380 cm^{-1}; NMR ($CDCl_3$) δ 1.0–3.3 (m, 14 H, CH_2 and NCH and OH), 4.2 (m, 2 H, ArCHN and OCH), 7.35 (br s, 5 H, Ar H); exact mass calcd for $C_{15}H_{21}NO$ m/e 231.1623, found m/e 231.1629.

***rel*-(4*S*,10*R*)-4-Phenyloctahydro-4*H*-quinolizin-2-one (10).** To 50 mg (0.21 mmol) of amino alcohol **9** in 4.0 mL of acetone cooled in an ice bath was added 0.10 mL (0.26 mmol) of Jones reagent. The resulting mixture was stirred for 60 min followed by the addition of 0.1 mL of 15% aqueous sodium hydroxide, 6.0 mL of water, and 15 mL of dichloromethane. The organic phase was washed with 10 mL of saturated aqueous sodium bicarbonate, dried (Na_2SO_4), and concentrated in vacuo to give 30 mg (60%) of amino ketone **10** as a colorless oil, homogeneous by TLC (silica gel; benzene–ether, 5:1): mp (picrate) 193–195 °C (lit.[10] mp 188–189 °C); NMR ($CDCl_3$) δ 1.1–3.2 (m, 13 H, CH_2 and NCH), 4.26 (dd, 1 H, J = 6, 4, ArCHN), 7.2 (m, 5 H, Ar H).

4-Amino-4-(6-bromo-3,4-dimethoxyphenyl)-1-butene (13a). To a solution of 5.6 mL (26.5 mmol) of hexamethyldisilazane[27] in 20 mL of tetrahydrofuran was added 15.8 mL (24.5 mmol) of 1.55 M n-butyllithium[27] in hexane with cooling in an ice bath. The solution was stirred for 10 min and added via syringe to a suspension of 5.0 g (20.4 mmol) of aldehyde **11a**[11] in 20 mL of tetrahydrofuran with cooling in an ice bath. The mixture was stirred at room temperature for 1 h followed by the addition of 86.4 mL (26.5 mmol) of 0.59 M ethereal allylmagnesium bromide with cooling in an ice bath. The resulting mixture was stirred for 20 min at room temperature, poured into saturated aqueous ammonium chloride, and extracted with dichloromethane. The combined organic phases were washed with saturated aqueous sodium chloride, dried ($MgSO_4$), and concentrated in vacuo. The residual pale yellow oil was chromatographed over 200 g of silica gel (chloroform–10% ammonium hydroxide in methanol; 20:1) to give 5.7 g (97%) of amine **13a** as a pale yellow oil: IR ($CHCl_3$) 3380, 1639 cm^{-1}; NMR ($CDCl_3$) δ 1.50 (br s, 2 H, NH_2), 1.97–2.67 (m, 2 H, CH_2C=), 3.87 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.34 (dd, 1 H, J = 9, 4.5, CHN), 5.03–5.23 (m, 2 H, =CH_2), 5.60–6.06 (m, 1 H, =CH), 6.99 (s, 1 H, Ar H), 7.10 (s, 1 H, Ar H); exact mass calcd for $C_{12}H_{16}{}^{79}BrNO_2$ m/e 285.0365, found m/e 285.0372.

4-Amino-4-(3,4-dimethoxy-6-iodophenyl)-1-butene (13b) and 4-Amino-4-(3,4-dimethoxyphenyl)-1-butene (13c). Iodo amine **13b** (3.57 g) was prepared in a 77% yield from aldehyde **11b**[12] (4.07 g) as described for the preparation of **13a**: IR ($CHCl_3$) 3360, 1638 cm^{-1}; NMR ($CDCl_3$) δ 1.56 (br s, 2 H, NH_2), 1.92–2.62 (m, 2 H, CH_2C=), 3.86 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.17 (dd, 1 H, J = 9, 4.5, CHN), 5.02–5.22 (m, 2 H, =CH_2), 5.61–6.06 (m, 1 H, =CH), 7.09 (s, 1 H, ArH), 7.20 (s, 1 H, Ar H); exact mass calcd for $C_{12}H_{16}INO_2$ m/e 333.0228, found m/e 333.0234. Amine **13c** (0.23 g, 8%) was also isolated from this reaction after product separation by chromatography over 200 g of silica gel (chloroform–10% ammonium hydroxide in methanol, 40:1): mp 56–57 °C (colorless feathers, ether–hexane); IR (CCl_4) 3390, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.56 (s, 2 H, NH_2), 2.37 (m, 2 H, CH_2C=), 3.88 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 3.80–4.01 (m, 1 H, CHN), 5.01–5.20 (m, 2 H, =CH_2), 5.53–6.00 (m, 1 H, =CH), 6.73–6.93 (m, 3 H, Ar H); exact mass calcd for $C_{12}H_{17}NO_2$ m/e 207.1259, found m/e 207.1264.

***N*-[1-(6-Bromo-3,4-dimethoxyphenyl)but-3-en-1-yl]-5,5-dimethoxypentanamide (15a).** To a solution of 4.55 g (15.9 mmol) of amine **13a** in 50 mL of dichloromethane at room temperature was added 12.8 mL (19.1 mmol) of 1.49 M trimethylaluminum[29] in heptane. The solution was stirred for 30 min followed by addition of 2.8 g (15.9 mmol) of methyl 5,5-dimethoxypentanoate (**14**)[15] in 5 mL of dichloromethane. The resulting solution was warmed under reflux for 20 h, cooled to room temperature, poured into 0.1 N aqueous sodium hydroxide, and extracted with dichloromethane. The organic extracts were washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residual pale yellow solid was chromatographed over 150 g of silica gel (ethyl acetate–ether, 2:3) to give 6.04 g (88%) of amide **15a** as colorless feathers: mp 99–99.5 °C (ether); IR ($CHCl_3$) 3440, 1672, 1605 cm^{-1}; NMR ($CDCl_3$) δ 1.67 (m, 4 H, CH_2), 2.22 (m, 2 H, CH_2CON), 2.58 (br t, 2 H, J = 7.5, CH_2C=), 3.33 (s, 6 H, acetal CH_3), 3.88 (s, 6 H, $ArOCH_3$), 4.33 (m, 1 H, CH(OCH_3)), 5.03–5.34 (m, 3 H, =CH_2 and ArCHN), 5.51–6.11 (m, 2 H, =CH and NH), 6.77 (s, 1 H, Ar H), 7.03 (s, 1 H, Ar H).

Anal. Calcd for $C_{19}H_{28}BrNO_5$: C, 53.03; H, 6.56. Found: C, 53.31; H, 6.67.

***N*-[1-(3,4-Dimethoxy-6-iodophenyl)but-3-en-1-yl]-5,5-dimethoxypentanamide (15b).** Iodo amide **15b** (4.02 g) was prepared in an 84% yield from iodo amine **13b** (3.35 g) as described for the preparation of **15a**: mp 125.5–126 °C (colorless feathers, ethyl acetate–ether); IR ($CHCl_3$) 3425, 1665, 1593 cm^{-1}; NMR ($CDCl_3$) δ 1.67 (m, 4 H, CH_2), 2.23 (m, 2 H, CH_2CON), 2.52 (br t, 2 H, J = 7.5, CH_2C=), 3.31 (s, 6 H, acetal OCH_3), 3.86 (s, 6 H, $ArOCH_3$), 4.31 (m, 1 H, CH(OCH_3)), 4.94–5.30 (m, 3 H, =CH_2 and ArCHN), 5.51–6.00 (m, 2 H, =CH and NH), 6.70 (s, 1 H, Ar H), 7.23 (s, 1 H, Ar H).

Anal. Calcd for $C_{19}H_{28}INO_5$: C, 47.80; H, 5.91. Found: C, 47.93; H, 6.16.

***rel*-(2*R*,4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-2-(formyloxy)octahydro-4*H*-quinolizin-6-one (16a), *rel*-(2*S*,4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-2-(formyloxy)octahydro-4*H*-quinolizin-6-one (17a), and *rel*-(4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-1,6,7,8,9,10-hexahydro-4*H*-quinolizin-6-one (18a).** To a solution of 6.26 g (14.6 mmol) of amide **15a** in 50 mL of dichloromethane at room temperature was added 149 mL of formic acid. The solution was stirred at room temperature for 4 h, and the formic acid was removed in vacuo. The residual pale brown oil was dissolved in dichloromethane, washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo. The residual solid was recrystallized from ethyl acetate–ether to give 3.13 g (52%) of formate **16a**: mp 128–128.5 °C; IR ($CHCl_3$) 1718, 1631, 1603 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.57–2.14 (m, 8 H, CH_2) 2.44–2.52 (m, 2 H, CH_2CON), 3.69 (m, 1 H, NCH), 3.85 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 5.31 (tt, 1 H, J = 10.5, OCH), 6.02 (dd, 1 H, J = 6.2, 4.0, ArCHN), 6.91 (s, 1 H, Ar H), 7.04 (s, 1 H, Ar H), 8.04 (s, 1 H, CHO).

Anal. Calcd for $C_{18}H_{22}BrNO_5$: C, 52.44; H, 5.38. Found: C, 52.31; H, 5.65.

The mother liquor was chromatographed over a Lobar size B column (ethyl acetate–ether, 1:4) to afford an additional 0.46 g (8%) of formate **16a**, 0.52 g (9%) of isomeric formate **17a** [mp 166–167 °C (ethyl acetate–ether); IR ($CHCl_3$) 1721, 1632 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.6–2.5 (m, 10 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 4.23 (m, 1 H, NCH), 5.19 (qu, 1 H, J = 5, OCH), 5.62 (t, 1 H, J = 7, ArCHN), 6.71 (s, 1 H, Ar H), 6.99 (s, 1 H, Ar H), 7.83 (s, 1 H, CHO). Anal. Calcd for $C_{18}H_{22}BrNO_5$: C, 52.44; H, 5.38. Found: C, 52.16; H, 5.55], and 1.10 g (21%) of a solid mixture of isomeric olefins **18a**. Recrystallization of the mixture from ethyl acetate-ether gave a pure sample of the $\Delta^{2,3}$ isomer as colorless leaflets: mp 165–166 °C; IR ($CHCl_3$) 1630, 1600 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.65–2.46 (m, 8 H, CH_2), 3.82 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.85 (m, 1 H, NCH), 5.91 (m, 2 H, CH=CH), 6.16 (br s, 1 H, ArCHN), 6.74 (s, 1 H, Ar H), 7.04 (s, 1 H, Ar H); exact mass calcd for $C_{17}H_{20}{}^{79}BrNO_3$ m/e 365.0627, found m/e 365.0620. The aryl hydrogens of the $\Delta^{1,2}$ isomer appeared at δ 6.97 and 7.00 in the ^1H NMR spectrum of the mixture.

(28) Purchased from Alfa-Ventron.

(29) From Texas Alkyls Inc.

***rel*-(2*R*,4*S*,10*R*)-4-(3,4-Dimethoxy-6-iodophenyl)-2-(formyloxy)octahydro-4*H*-quinolizin-6-one (16b), *rel*-(2*S*,4*S*,10*R*)-4-(3,4-Dimethoxy-6-iodophenyl)-2-(formyloxy)octahydro-4*H*-quinolizin-6-one (17b), and *rel*-(4*S*,10*R*)-4-(3,4-Dimethoxy-6-iodophenyl)-1,6,7,8,9,10-hexahydro-4*H*-quinolizin-6-one (18b).** Treatment of 3.0 g of **15b** as described above for **15a** gave 1.95 g (67%) of **16b**, 0.21 g (7%) of **17b**, and 0.59 g (23%) of **18b**. Spectral data are recorded below.

Formate **16b**: mp 146–146.5 °C (ethyl acetate–ether); IR ($CHCl_3$) 1720, 1632, 1592 cm^{-1}; NMR ($CDCl_3$) δ 1.50–2.54 (m, 10 H, CH_2), 3.60–4.00 (m, 1 H, NCH), 3.87 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.33 (m, 1 H, OCH), 5.80 (t, 1 H, J = 6, ArCHN), 6.89 (s, 1 H, Ar H), 7.30 (s, 1 H, Ar H), 8.06 (s, 1 H, CHO).

Anal. Calcd for $C_{18}H_{22}INO_5$: C, 47.07; H, 4.83. Found: C, 46.84; H, 5.00.

Formate **17b**: mp 134–135 °C (ethyl acetate–ether); IR ($CHCl_3$) 1722, 1632, 1595 cm^{-1}; NMR ($CDCl_3$) δ 1.54–2.51 (m, 10 H, CH_2), 3.84 (s, 6 H, OCH_3), 4.22 (m, 1 H, NCH) 5.17 (m, 1 H, OCH), 5.40 (t, 1 H, J = 9, ArCHN), 6.71 s, 1 H, Ar H), 7.22 (s, 1 H, Ar H), 7.88 (s, 1 H, CHO).

Anal. Calcd for $C_{18}H_{22}INO_5$: C, 47.07; H, 4.83. Found: C, 47.27; H, 4.96.

Olefins **18b**: colorless solid; NMR ($CDCl_3$) δ 1.36–2.86 (m, 8 H, CH_2), 3.84, 3.86 and 3.87 (3 s, 6 H total, OCH_3), 3.89 (m, 1 H, NCH), 5.52–6.02 (m, 3 H, =CH and ArCHN), 6.73, 7.00, and 7.34 (3 s, 2 H total, Ar H). Recrystallization from ether gave a pure sample of the $\Delta^{2,3}$ isomer, mp 149–150 °C.

Anal. Calcd for $C_{17}H_{20}INO_3$: C, 49.41; H, 4.88. Found: C, 49.44; H, 4.99.

***rel*-(2*R*,4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-2-hydroxyoctahydro-4*H*-quinolizin-6-one (21).** To a solution of 200 mg (0.48 mmol) of formate **16a** in 2 mL of methanol at room temperature was added 0.48 mL of 3 N aqueous sodium hydroxide. The mixture was stirred at room temperature for 75 min, poured into saturated aqueous sodium bicarbonate, and extracted with dichloromethane. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give 182 mg (98%) of alcohol **21** as colorless, microcrystalline needles: mp 148.5–149 °C (ether); IR ($CHCl_3$) 3380, 1629 cm^{-1}; NMR ($CDCl_3$) δ 1.27–2.53 (m, 10 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.83 (m, 2 H, CHOH and NCH), 3.84 (s, 3 H, OCH_3), 5.98 (dd, 1 H, J = 7, 3, ArCHN), 6.70 (s, 1 H, Ar H), 7.03 (s, 1 H, Ar H); exact mass calcd for $C_{17}H_{22}BrNO_4$ – Br m/e 304.1549, found m/e 304.1556.

Anal. Calcd for $C_{17}H_{22}BrNO_4$: C, 53.13; H, 5.77. Found: C, 53.39; H, 5.86.

***rel*-(4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)octahydro-4*H*-quinolizine-2,6-dione (22).** To a solution of 182 mg (0.47 mmol) of alcohol **21** in 3 mL of acetone, cooled in a dry ice–carbon tetrachlorode bath, was added 0.27 mL (0.71 mmol) of Jones reagent (2.66 M). The mixture was stirred at −15 °C for 1 h, and excess oxidant was destroyed by the addition of 2-propanol. The mixture was diluted with ether and filtered through a magnesium sulfate pad which was rinsed with ethyl acetate. The filtrate was concentrated in vacuo, and the residue was chromatographed over 7 g of silica gel (ethyl acetate) to give 146 mg (79%) of ketone **22** as colroless crystals: mp 178–178.5 °C; IR ($CHCl_3$) 1712, 1639 cm^{-1}; NMR ($CDCl_3$) δ 1.52–2.56 (m, 8 H, CH_2), 2.86 (d, 2 H, J = 6, CH_2CO), 3.70 (m, 1 H, NCH), 3.81 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3) 6.18 (t, 1 H, J = 6, ArCHN), 6.73 (s, 1 H, Ar H), 7.03 (s, 1 H, Ar H); exact mass calcd for $C_{17}H_{20}BrNO_4$ – Br m/e 302.1392, found m/e 302.1401.

Similar oxidation of alcohol **23** gave a sample of **22** identical in all respects with the material described above.

***rel*-(2*S*,4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-2-hydroxyoctahydro-4*H*-quinolizin-6-one (23) and Alcohol 21.** To a solution of 58 mg (0.15 mmol) of ketone **22** in 2 mL of *N*,*N*-dimethylformamide, cooled in a dry ice–carbon tetrachloride bath, was added 11.5 mg (0.30 mmol) of sodium borohydride.[28] The mixture was stirred at −15 °C for 1 h, poured into saturated brine, and extracted with dichloromethane. The combined organic phases were washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography over alumina (ethyl acetate–ether, 1:2) to afford 9 mg of recovered **22**, 8 mg (14%) of alcohol **21** (mp 148.5–149 °C), and 35 mg (60%) of alcohol **23** as colorless crystals: mp 175–176 °,c (ether); IR ($CHCl_3$) 3390, 1630 cm^{-1}; NMR ($CDCl_3$) δ 1.53–2.47 (m, 10 H, CH_2), 3.83 (s, 6 H, OCH_3), 4.16 (m, 2 H, CHOH and NCH) 5.53 (t, 1 H, J = 7.5, ArCHN), 6.78 (s, 1 H, Ar H), 6.98 (s, 1 H, Ar H); exact mass calcd for $C_{17}H_{22}BrNO_4$–Br m/e 304.1549, found m/e 304.1556.

Hydrolysis of formate **17a** as described above for **16a** gave a sample of alcohol **23** identical in all respects with the material described above.

***rel*-(2*R*,4*S*,10*R*)-4-(6-Bromo-3,4-dimethoxyphenyl)-6-oxooctahydro-4*H*-quinolizin-2-yl *S*-Methyl Dithiocarbonate (24).** To a solution of 100 mg (0.26 mmol) of alcohol **21** in 2 mL of tetrahydrofuran at room temperature was added 51 mg (1.30 mmol) of sodium hydride[28] (61.14% mineral oil dispersion) and a pinch of imidazole. The mixture was warmed at 60 °C for 30 min followed by the addition of 0.094 mL (1.56 mmol) of carbon disulfide. The mixture was warmed at 60 °C for 30 min followed by the addition of 0.097 mL (1.56 mmol) of iodomethane. The mixture was warmed at 60 °C for 30 min, poured into saturated brine, and extracted with dichloromethane. The organic extracts were washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 7 g of silica gel (ethyl acetate–ether, 1:1) to give 114 mg (93%) of xanthate **24** as colorless crystals: mp 181–182 °C (ethyl acetate–ether); IR ($CHCl_3$) 1633, 1056 cm^{-1}; NMR ($CDCl_3$) δ 1.53–2.77 (m, 10 H, CH_2), 2.57 (s, 3 H, SCH_3), 3.63 (m, 1 H, NCH), 3.84 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 6.02 (m, 2 H, ArCHN and OCH), 6.96 (s, 1 H, Ar H), 7.01 (s, 1 H, Ar H); exact mass calcd for $C_{19}H_{24}BrNO_4S_2$ – Br m/e 394.1147, found m/e 394.1156.

***rel*-(4*S*,10*S*)-4-(6-Bromo-3,4-dimethoxyphenyl)octahydro-4*H*-quinolizin-6-one (25).** To a solution of 80 mg (0.22 mmol) of olefins **18a** (1:1 mixture of isomers by ^1H NMR) and 487 mg (2.62 mmol) of *p*-toluenesulfonylhydrazide in 2 mL of ethanol warmed under reflux was added a solution of 358 mg (4.36 mmol) of sodium acetate in 2 mL of water over a 5-h period.[30] The mixture was cooled, poured into saturated aqueous ammonium chloride, and extracted with dichloromethane. The organic extracts were washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography over SiO_2 (ethyl acetate–ether, 1:3) to give 8 mg of recovered **18a** and 63 mg (79%) of lactam **25** as colorless needles: mp 122–123 °C (ether); IR ($CHCl_3$) 1627 cm^{-1}; NMR ($CDCl_3$) δ 1.39–2.59 (m, 12 H, CH_2), 3.84 (m, 1 H, NCH), 3.84 (s, 6 H, OCH_3), 5.73 (t, 1 H, J = 6, ArCHN), 6.74 (s, 1 H, Ar H), 7.03 (s, 1 H, Ar H).

Anal. Calcd for $C_{17}H_{22}BrNO_3$: C, 55.44; H, 6.02. Found: C, 55.64; H, 6.18.

Preparation of Lactam 25 from Xanthate 24.[31] A solution of 74 mg (0.156 mmol) of xanthate **24**, 0.103 mL (0.39 mmol) of tri-*n*-butyltin hydride,[32] and a pinch of 2,2′-azobis(2-methylpropionitrile)[27] in 3 mL of toluene was warmed at 80 °C for 2 h followed by removal of the solvent in vacuo. The residue was subjected to thin-layer chromatography over silica gel (ethyl acetate–ether, 1:2) to give 27 mg (47%) of lactam **25**, identical with the material prepared by reduction of olefins **18a**.

***rel*-(2*R*,4*S*,10*R*)-2-Acetoxy-4-(6-bromo-3,4-dimethoxyphenyl)octahydro-4*H*-quinolizine (26a).** To a solution of 303 mg (0.74 mmol) of formate **16a** in 3.0 mL of tetrahydrofuran, cooled in an ice–water bath, was added 2.2 mL (2.21 mmol) of 1.0 M borane in tetrahydrofuran. The solution was stirred at room temperature for 2 h, quenched with saturated aqueous ammonium chloride while being cooled in an ice bath, and stirred at room temperature for 17 h. The mixture was poured into saturated aqueous sodium bicarbonate and extracted with dichloromethane. The organic phase was washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo.

The residual colorless foam was dissolved in 1.5 mL of pyridine and 1.5 mL of acetic anhydride and stirred at room temperature for 20 h. The solvent was removed at room temperature in vacuo, and the resulting colorless oil was partitioned between saturated

(30) Sunagawa, M.; Katsube, J. "Abstracts of Papers", 7th Symposium on Progress in Organic Reactions and Syntheses"; Gifu, Japan, 1980, p 52.

(31) This is a slight modification of a procedure developed by: Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

(32) Prepared by the method described by: Kuivila, H. G. *Synthesis* **1970**, 499.

aqueous sodium bicarbonate and dichloromethane. The organic phase was washed with saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 25 g of silica gel (chloroform–10% ammonium hydroxide in methanol, 40:1) to give 274 mg (90%) of aminoacetate **26a** as a colorless foam: IR ($CHCl_3$) 1726 cm^{-1}; NMR ($CHCl_3$) δ 1.11–2.91 (m, 12 H, CH_2), 2.08 (s, 3 H, CH_3COO), 3.14 (m, 1 H, NCH), 3.84 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3) 4.66 (dd, 1 H, J = 9, 4.5, ArCHN), 5.10 (qu, 1 H, J = 4.5, OCH), 6.97 (s, 1 H, Ar H), 7.01 (s, 1 H, Ar H); exact mass calcd for $C_{19}H_{26}BrNO_4$ m/e 411.1046, found m/e 411.1055.

***rel*-(2*R*,4*S*,10*R*)-2-Acetoxy-4-(3,4-dimethoxy-6-iodophenyl)octahydro-4*H*-quinolizine (26b).** Treatment of 0.5 g of **16b** as described above for **16a** gave 0.4 g (85%) of aminoacetate **26b** as a colorless foam: IR ($CHCl_3$) 1726 cm^{-1}; NMR ($CDCl_3$) δ 1.06–2.92 (m, 12 H, CH_2), 2.11 (s, 3 H, CH_3COO), 3.16 (m, 1 H, CHN), 3.86 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.43 (dd, 1 H, J = 9, 4.5, ArCHN), 5.10 (qu, 1 H, J = 4.5, OCH), 6.99 (s, 1 H, Ar H), 7.19 (s, 1 H, Ar H); exact mass calcd for $C_{19}H_{26}INO_4$ m/e 459.0908, found m/e 4259.0920.

Methyl 3-[4-[2-[*rel*-(2*R*,4*S*,10*R*)-2-Acetoxyoctahydro-4*H*-quinolizin-4-yl]-4,5-dimethoxyphenoxy]phenyl]propionate (28). To a solution of 348 mg (1.93 mmol) of methyl 3-(4-hydroxyphenyl)propionate[20] in 2 mL of pyridine, cooled in an ice bath, was added 72 mg (1.84 mmol) of sodium hydride (61.14% dispersion in mineral oil). The mixture was stirred for 15 min, 191 mg (1.93 mmol) of cuprous chloride was added at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. To the resulting brown solution was added 531 mg (1.29 mmol) of bromide **26a** in 3 mL of pyridine at room temperature. The mixture was warmed under reflux for 3 h followed by removal of the pyridine at room temperature in vacuo. The brown residue was partitioned between saturated aqueous ammonium chloride and dichloromethane. The organic phase was washed with 1.0 N aqueous sodium hydroxide and saturated brine, dried ($MgSO_4$), and concentrated in vacuo. The residual brown oil was chromatographed over alumina (ether–hexane, 1:1) to give a mixture of 33 mg (8%, based on NMR integration) of reduction product **27** and 201 mg (38%, based on NMR integration) of starting bromide **26a** in addition to 209 mg (32%) of pure diaryl ether **28**[19] as a colorless foam: IR ($CHCl_3$) 1727 cm^{-1}; NMR ($CDCl_3$) δ 1.10–3.23 (m, 17 H, CH_2 and NCH), 1.90 (s, 3 H, CH_3COO), 3.68 (s, 3 H, CO_2CH_3), 3.79 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.51 (t, 1 H, J = 6, ArCHN), 5.11 (qu, 1 H, J = 5, OCH), 6.49 (s, 1 H, Ar H), 6.73 (d, 2 H, J = 9, Ar H), 7.02 (s, 1 H, Ar H), 7.07 (d, 2 H, J = 9, Ar H); exact mass calcd for $C_{29}H_{37}NO_7$ m/e 511.2570, found m/e 511.2586.

Similar treatment of iodo amine **26b** gave **27**, recovered **26b**, and ether **28** in 12%, 18%, and 30% yields, respectively.

(±)-Vertaline (2). A solution of 126 mg (0.25 mmol) of diester **28** in 3.0 mL of 5% aqueous sodium hydroxide and 6.1 mL of methanol was warmed under reflux for 30 min. The solution was partially concentrated in vacuo, and the residual liquid was adjusted to pH 6 with 3 N aqueous hydrochloric acid by using bromthymol blue as an indicator. The solvent was removed in vacuo, and the residual solids were suspended in dichloromethane. The dichloromethane-soluble material was concentrated to afford 123 mg of crude hydroxy acid **29** as a pale green foam. This material gave spectral data (IR, ^1H NMR) in accord with those reported elsewhere[19] and was used directly in the next reaction.

A solution of 123 mg (0.25 mmol) of hydroxy acid **29**, 87 mg (0.394 mmol) of 2,2′-dipyridyl disulfide,[27] and 103 mg (0.394 mmol) of triphenylphosphine in 2.0 mL of dichloromethane was stirred at room temperature for 50 min followed by removal of the solvent in vacuo. The residual pale green oil was dissolved in 500 mL of xylenes and heated under reflux for 20 h. The solvent was removed at 60 °C in vacuo over a 2-h period, and the residual pale brown oil was chromatographed over alumina (ether–hexane, 2:3) to give 57 mg (53%) of **2** as colorless prisms after recrystallization from methanol. This material was identical (TLC, IR, 300-MHz ^1H NMR) with an authentic sample of (−)-vertaline: mp 220–220.5 °C (lit[19] mp 224–225 °C); IR ($CHCl_3$) 1723 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.03–1.98 (m, 10 H), 2.22–2.32 (m, 1 H), 2.39 (br t, 1 H), 2.53–2.60 (m, 2 H), 2.84 (td, 1 H, J = 13, 5), 2.99–3.06 (m, 2 H), 3.41 (br d, 1 H, J = 10, ArCHN), 3.86 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.89 (br s, 1 H, OCH), 6.48 (dd, 1 H, J = 9, 3, Ar H), 6.76 (s, 1 H, Ar H), 6.85 (br s, 1 H, Ar H), 6.93 (dd, 1 H, J = 9, 3, Ar H), 7.22 (dd, 1 H, J = 8.5, 3, Ar H), 7.28 (dd, 1 H, J = 8.5, 3, Ar H).

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Registry No. (±)-**2**, 53494-86-3; (±)-**5**, 80735-94-0; (±)-**6**, 80696-76-0; **7**, 73157-68-3; (±)-**8**, 80696-77-1; (±)-**9**, 80696-78-2; (±)-**10**, 80696-79-3; (±)-**10** picrate, 80696-80-6; **11a**, 5392-10-9; **11b**, 61203-53-0; (±)-**12a**, 80696-81-7; (±)-**13a**, 80696-82-8; (±)-**13b**, 80696-83-9; (±)-**13c**, 80696-84-0; **14**, 23068-91-9; (±)-**15a**, 80718-98-5; (±)-**15b**, 80696-85-1; (±)-**16a**, 80696-86-2; (±)-**16b**, 80696-87-3; (±)-**17a**, 80696-88-4; (±)-**17b**, 80696-89-5; (±)-**18a** (isomer I), 80696-90-8; (±)-**18a** (isomer II), 80696-91-9; (±)-**18b** (isomer I), 80696-92-0; (±)-**18b** (isomer II), 80696-93-1; (±)-**21**, 80696-94-2; (±)-**22**, 80696-95-3; (±)-**23**, 80696-96-4; (±)-**24**, 80696-97-5; (±)-**25**, 80696-98-6; (±)-**26a**, 53425-27-7; (±)-**26b**, 80696-99-7; (±)-**27**, 60352-71-8; (±)-**28**, 53510-38-6; (±)-**29**, 53425-29-9; glutarimide, 1121-89-7; hexamethyldisilazane, 999-97-3; allyl bromide, 106-95-6; methyl 3-(4-hydroxyphenyl)propionate, 5597-50-2.

β-Substituted Organolithium Compounds. Reaction with Alkyl Halides, Dimethyl Disulfide, and Imines

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The reaction of β-substituted organolithium derivatives with several electrophiles leads to mono- as well as bifunctionalized organic compounds. Thus, by treatment of these dianions with alkyl halides a direct attack on the carbanionic carbon atom is performed, giving as a result substituted amines. When dimethyl disulfide is used, β-amino and β-hydroxy thioethers are obtained. Finally, on reaction with imines, 1-amino-3-hydroxy compounds and 1,3-diamines are obtained. Since these dianions are easily prepared by mercury–lithium transmetalation from β-substituted organomercurials resulting from the addition of mercury(II) salts to olefins, this whole process gives an appropriate way of functionalizing olefins.

The preparation of β-substituted organometallic compounds containing main-group metals has been a point of interest for two particular reasons: (a) a theoretical concern reflecting the difficulty of preparation and the instability of such compounds and (b) a practical concern since their reaction with electrophiles leads to bifunc-

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