of acetic acid was added, the solvent was removed under reduced pressure, and the residue was flash chromatographed (*n*-hexane/ethyl ether 8:2) to give 0.62 g (96% yield) of pure (*S*)-methyl *O*-benzyl-3,3,3-trifluorolactate (**7**): $[\alpha]^{20}_D$ +65.1° (*c* 1.00, $CHCl_3$); ^1H NMR (250 MHz) δ 3.83 (s, 3 H, CH_3O), 4.32 (q, $^3J_{H,F}$ = 7 Hz, 1 H, CHO), 4.69 and 4.82 (AB system, 2 H, CH_2Ar), 7.37 (m, 5 H, ArH). [No splitting of any proton signal was observed in the presence of $Eu(hfc)_3$.]; ^{19}F NMR (75 MHz) δ −74.8 (d, *J* = 7.0 Hz). Anal. Calcd for $C_{11}H_{11}F_3O_3$: C, 53.23; H, 4.47. Found: C, 53.41; H, 4.68.

(2*R*)-1,1,1-Trifluoro-2-phenyl-3(*R*)-[(4-methylphenyl)-sulfinyl]propan-2-ol (9) and (2*S*,R_S)-9. A solution of (*R*)-methyl 4-methylphenyl sulfoxide (**1**) (5.78 g, 37.5 mmol) in THF (60 mL) was added dropwise at −78 °C and under argon into a stirred solution of lithium diisopropylamide (41.2 mmol) in the same solvent (45 mL). After 3 min, 2,2,2-trifluoroacetophenone (**8**) (5.8 mL, 41.3 mmol) was added at the same temperature, stirring was continued for 10 min, and then a saturated aqueous solution of ammonium chloride was added. The aqueous phase was separated and extracted with ethyl acetate (3 × 100 mL), and the combined organic layers were dried with sodium sulfate and evaporated under reduced pressure to give a 75:25 mixture of (2*R*,R_S)-**9** and (2*S*,R_S)-**9** in nearly quantitative yields. Single pure diastereoisomers were isolated through flash chromatography (*n*-hexane/ethyl acetate 3:1). **(2*R*,R_S)-9**: R_f (*n*-hexane/ethyl acetate 3:1) 0.35; $[\alpha]^{20}_D$ +125.7° (*c* 1.11, $CHCl_3$); mp 85–87 °C (chloroform); ^1H NMR (90 MHz) δ 2.48 (s, 3 H, CH_3Ar), 3.49 (s, 2 H, CH_2S), 7.2–7.8 (m, 9 H, ArH). Anal. Calcd for $C_{16}H_{15}F_3O_2S$: C, 58.52; H, 4.60. Found: C, 58.80; H, 4.74.

(2*S*,R_S)-9: R_f (*n*-hexane/ethyla cetate 3:1) 0.31; $[\alpha]^{20}_D$ +171.7° (*c* 0.64, $CHCl_3$); mp 76–78 °C (chloroform); ^1H NMR (90 MHz) δ 2.41 (s, 3 H, CH_3Ar), 3.13 and 3.40 (m, 1 H each, CH_2S), 7.2–7.7 (m, 9 H, ArH). Anal. Calcd for $C_{16}H_{15}F_3O_2S$: C,58.52; H, 4.60. Found: C, 58.80; H, 4.74.

(2*R*)-1,1,1-Trifluoro-2-methoxy-2-phenyl-3-[(4-methylphenyl)sulfinyl]propane (10). A procedure similar to the one described above for the preparation of (2*R*,R_S)-**4** was employed in order to methylate the trifluoro sulfinyl alcohol (2*R*,R_S)-**9** and the pure methyl ether (2*R*,R_S)-**10** was obtained in 91% yield: $[\alpha]^{20}_D$ +66.1°; mp 65–67 °C; ^1H NMR (250 MHz) δ 2.40 (s, 3 H, CH_Ar), 3.41 and 3.69 (AB system, 2 H, CH_2S), 3.57 (q, $^5J_{H,F}$ = 1.6 Hz, CH_3O), 7.2–7.6 (m, 9 H, ArH). Anal. Calcd: C, 59.63; H, 5.01. Found: C, 59.81; H, 5.22.

(*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic Acid (12). The procedure described above for the preparation of (*S*)-*O*-benzyltrifluorolactic acid (**6**) was followed with the difference that copper(II) chloride and potassium carbonate were used to hydrolyze the intermediate geminal trifluoroacetoxy sulfenyl derivative. Starting from (2*R*,R_S)-**10**, the crystalline (−)-(*S*)-**12** was obtained in 76% yield and with physical and spectral properties identical with those of a commercially available sample (Aldrich).[14]

(14) Jeanneret-Gris, G.; Pousaz. *Tetrahedron Lett.* **1990**, *31*, 75.

The Synthesis of 1,1′-Spiroalkane or Fused Annulated 1,2,3,4-Tetrahydroisoquinolines Using a Highly Reactive Formamidine for Metalation–Alkylation

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We have, on numerous occasions, reported on the use of formamidines in the metalation of the α-carbon of amines and their subsequent alkylation to chiral and achiral amino compounds[1] (Scheme I). In a recent report from this laboratory,[2] we also described a new formamidine, which we felt was considerably more efficient in

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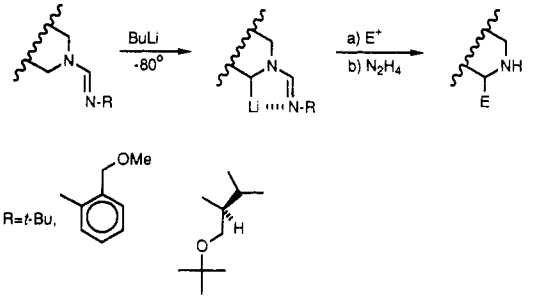
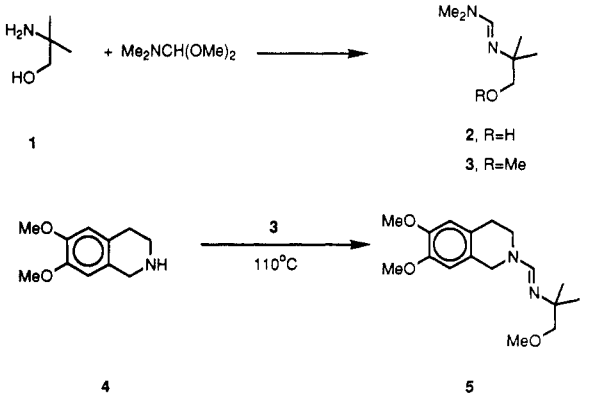
Scheme I



mediating metalation of the α-carbon (Scheme I, R = 2-(methoxymethyl)aniline). Further studies have now uncovered a considerably better formamidine **5** which is readily available and provides the quaternary substitution product in very good yields.

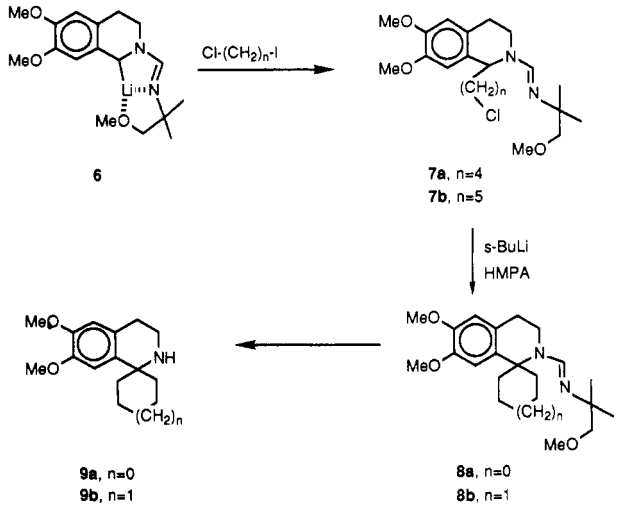
The formamidine in question is that derived from the readily available and inexpensive 2-amino-2-methylpropanol (**1**), which is transformed with dimethylformamide dimethyl acetal into the hydroxy formamidine **2**. Treatment with sodium hydride followed by methyl iodide gave the methyl ether–dimethylformamidine **3** in an overall yield of 72%. The latter may be easily exchanged for most secondary amines, and in the present case we have utilized 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**4**), which, when heated as a 2 M solution in toluene for 40–48 h, gave the isoquinoline formamidine **5** in 80–85% yield.



The present report will now describe how it was possible to prepare either spiroisoquinolines or fused annulated isoquinolines (**9** or **11**, respectively) by the appropriate choice of α,ω-dihaloalkanes. Treatment of the isoquinoline formamidine **5** with LDA in THF at −78 °C gave the red solution of the lithiated intermediate **6**, which, when treated with 4-chloro-1-iodobutane, gave the chloroalkyl derivative **7a** in 93% yield. Similarly, when 5-chloro-1-iodopentane was added to the lithio species, the analogous haloalkyl derivative **7b** was formed in 92% yield. An attempt was made to add a second equivalent of LDA to the reaction without isolation of **7**. It was our intention to generate another carbanion, followed by cyclization to the spiro derivatives **8**. However, a complex mixture of products was obtained, which quickly convinced us that this was not an appropriate route to follow. The haloalkyl derivatives were therefore isolated in the excellent yields mentioned above and were treated with various bases to ascertain the proper reaction conditions necessary for clean deprotonation. It was found that *n*-butyllithium followed by D_2O quench gave little (<5%) deuterium incorporation

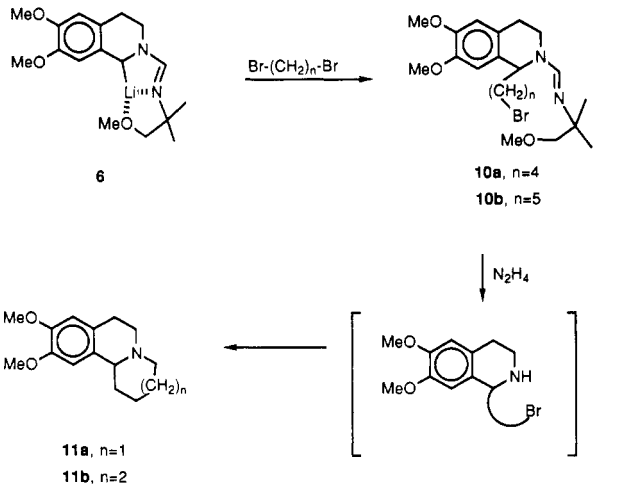
(1) Meyers, A. I.; Miller, D. B.; White, F. W. *J. Am. Chem. Soc.* **1988**, *110*, 4778 and earlier references cited.
(2) Gonzalez, M. A.; Meyers, A. I. *Tetrahedron Lett.* **1989**, *30*, 43, 47.

in 7 along with other products, which appeared to be the result of halide elimination, thus indicating that the base was inappropriate to remove a tertiary proton in this system. It is noteworthy that *n*-butyllithium was a successful base in removing the tertiary proton from a 6,7-dimethoxyisoquinoline containing the ((methoxymethyl)phenyl)formamidine (Scheme I, R = 2-$MeOCH_2C_6H_4$).[2] Furthermore, the preparation of the 1,1-dimethylisoquinoline from **6** proceeded in a sequential manner, using *n*-butyllithium and methyl iodide, in 89 and 86% yields, respectively. The spiroalkylation of **7** (**a** and **b**) was efficiently achieved by use of *sec*-butyllithium at −95 °C, which caused rapid deprotonation but did not allow intramolecular alkylation at this temperature. This was followed by addition of HMPA and warming of the solution to −50 °C and then allowing it to remain at −30 °C overnight. Under these conditions spirocyclization proceeded cleanly to produce **8a** (93%) and **8b** (87%), respectively. That the *sec*-butyllithium indeed was effective as the base at −95 °C was shown by a D_2O quench of lithiated **7a** at −95 °C, which led to the 1-*d* derivative as the only product. The spiroalkane formamidines **8a** and **8b** were not purified, and in their crude state were subjected to hydrazinolysis affording pure **9a** and **9b** in overall yields of 50% and 59% after chromatography.



Although the spiroisoquinolines **9a** and **9b** could not be reached in a one-pot procedure and required the isolation of the intermediate chloroalkyl derivatives **7a** and **7b**, we were able to form the fused systems **11a** and **11b** in a one-pot procedure. Thus, addition of 1,4-dibromobutane to lithioisoquinoline **6** gave the bromoalkyl derivative **10a**, which was treated directly with the hydrazine solution, after removal of the solvent, to give the benzo[*a*]quinolizidine **11a** in 45% overall yield. In a similar fashion the lithioisoquinoline **6** was treated with 1,5-dibromopentane and, without purification of the intermediate bromoalkyl derivative **10b**, was subjected to the hydrazine solution to produce the fused azepine system **11b**. The one-pot procedure for the generation of these fused heterocycles indicates how convenient it is to utilize the formamidine moiety in elaborating amines. Further work is underway to introduce a quaternary stereocenter in the spiro derivatives **9** by use of a chiral formamidine and to reach a number of spiroisoquinoline alkaloids.[3]

In summary, the formamidine **3** is now considered as the optimum choice of activating group leading to the alkyl-



ated tetrahydroisoquinolines. Its advantages are clearly evident over the *tert*-butylformamidines[2] and the (methoxymethyl)anilino derivatives (Scheme I) in that it allows high yields of quaternary substitution, reliable scale ups, and stability to silica gel if separations are required, and the crude alkylation products are sufficiently clean to proceed to further transformations. These favorable characteristics are not all present with the earlier formamidines employed. For example, the (methoxymethyl)-anilino system was not amenable to scale up (up to multigram scale). Purification of formamidine-containing isoquinolines have not been suitable on silica gel due to various degrees of fragmentation during the chromatography process. However, if **5** is employed, the stability to silica gel was noteworthy (see the Experimental Section for **7a**,**7b**).

Experimental Section

***N*,*N*-Dimethyl-*N'*-(1-hydroxy-2-methyl-2-propyl)formamidine (2).** A mixture of freshly distilled 2-amino-2-methylpropanol (10.3 g, 115 mmol) and dimethylformamide dimethyl acetal (Aldrich, 14.4 g, 120 mmol) was heated to 40 °C for 90 min under an argon atmosphere. The volatiles were evaporated in vacuo (water aspirator), and the residue was distilled: bp 64 °C (2.4 mm); IR (film) 3600–3100, 2960, 1650, 1370, 1100, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (s, 1 H), 3.29 (s, 2 H), 2.83 (s, 6 H), 1.12 (s, 6 H); ^{13}C NMR 151.43, 72.24, 55.75, 36.52, 25.31. This material was carried on without further characterization to the methyl ether **3**.

***N*,*N*-Dimethyl-*N'*-(1-methoxy-2-methyl-2-propyl)formamidine (3).** The hydroxyformamidine **2** (10.0 g) was dissolved in 50 mL of dry THF and added slowly, under argon, to a suspension of sodium hydride (7 g of 60% oil emulsion after washing with hexane, 175 mmol) in 50 mL of THF. The mixture was kept at room temperature for 3 h and then cooled to 0 °C. Iodomethane (11 mL, 177 mmol) was added, and the mixture was stirred at room temperature overnight. The excess sodium hydride was destroyed by addition of $Na_2SO_4 \cdot 10H_2O$, the solids were filtered through Celite and washed with ethyl acetate, and the organic solvents were removed in vacuo. The residue was distilled (Kugelrohr), 90 °C (0.5 Torr), to give 13 g (72%) of a colorless oil: ^1H NMR ($CDCl_3$) δ 7.31 (s, 1 H), 3.30 (s, 3 H), 3.14 (s, 2 H), 2.76 (s, 6 H), 1.09 (s, 6 H). Anal. Calcd for $C_8H_{18}N_2O$: C, 60.72; H, 11.47; N, 17.70. Found: C, 60.33; H, 11.60; N, 17.58.

Methoxy Formamidine of 6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline (5). A mixture of 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**4**) (7.22 g, 37.4 mmol) and the (dimethylamino)formamidine **3** (6.5 g, 41 mmol) dissolved in 35 mL of dry toluene was heated to reflux for 48 h under an argon atmosphere. The solvent was removed in vacuo, and the residue was dissolved in 100 mL of ethyl acetate. The solution was washed successively with 15 mL of saturated sodium bicarbonate and 15 mL of brine, dried (K_2CO_3), and concentrated. Kugelrohr distillation gave 9.46 g (83%) of an oil: ^1H NMR ($CDCl_3$) δ 7.52 (s,

(3) Kametani, T. The Total Synthesis of Isoquinoline Alkaloids. In *The Total Synthesis of Natural Products*; Apsimon, J., Ed.; Wiley-Interscience: New York, 1977; pp 47–49.

1 H), 6.61 (d, 2 H), 4.43 (s, 2 H), 3.83 (d, 6 H), 3.49 (t, 3 H), 3.35 (s, 3 H), 3.22 (s, 2 H), 2.77 (t, 2 H), 1.16 (s, 6 H); IR (film) 1644, 1612, 1517 cm^{-1}. Anal. Calcd for $C_{17}H_{26}N_2O_3$: C, 66.64; H, 8.55; N, 9.14. Found: C, 66.28; H, 8.50; N, 9.00.

1-(4-Chlorobutyl)isoquinoline Formamidine 7a. A solution of 92 mg (0.30 mmol) **5** in 20 mL of THF was cooled to −78 °C under argon, and then 261 μL of lithium diisopropylamide (1.15 M, 0.30 mmol) in THF was added dropwise. The mixture was stirred for 50 min, and 72.2 mg of 1-chloro-4-iodobutane (0.33 mmol) in 1 mL of THF was added. The halide had been passed through a short plug of alumina, just prior to use. After 5–10 min the reaction was quenched with 0.5 mL of saturated ammonium chloride, and the solution was concentrated in vacuo. The residue was taken up in dichloromethane, washed with bicarbonate, brine, dried (K_2CO_3), and concentrated. The residue was purified on silica gel (hexane–ethyl acetate–triethylamine, 10:1:1) and gave 111 mg (93%) of **7a**: IR (film) 1640, 1518, 1463 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (s, 1 H), 6.58 (d, 2 H), 4.69–4.66 (br s, 1 H), 3.85 (d, 7 H), 3.54 (t, 2 H), 3.33 (s, 3 H), 3.12 (s, 2 H), 2.88 (m, 2 H), 2.59 (m, 2 H), 1.91–1.70 (m, 4 H), 1.59–1.48 (m, 2 H), 1.13 (s, 6 H). This material was carried on without further characterization.

Spiro[cyclopentane-1,1′-(6′,7′-dimethoxy-1′,2′,3′,4′-tetrahydroisoquinoline)] (9a). To an anhydrous solution of 124 mg (0.31 mmol) of **7a** in 20 mL of THF, cooled to −95 °C (cooling bath), was added 351 μL of *sec*-butyllithium (0.89 M, 0.31 mmol) in a dropwise manner. After the mixture was stirred for 1 h at −95 °C, 326 μL (336 mg, 1.87 mmol) of hexamethyl phosphoramide (HMPA) was added, and the mixture was stirred at −45 °C for 3 h and then at −20 °C (freezer) overnight. The mixture was quenched with 0.5 mL of saturated ammonium chloride, and the solution was concentrated in vacuo. The residue **8a** was treated with 8 mL of 95% ethanol and 1 mL of glacial acetic acid and cooled to 0 °C before addition (exothermic) of 2 mL of hydrazine hydrate ($N_2H_4 \cdot 2H_2O$). The solution was warmed to 50 °C and allowed to stir overnight. Removal of the volatiles in vacuo gave an oil, which was chromatographed (hexane–ethyl acetate–Et_3N, 10:1:1) to give 36 mg (50%) of **9a** as a clear oil: picrate, mp 180 °C; IR (film) 3312 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.66 (s, 1 H), 6.52 (s, 1 H), 3.85, 3.84 (d, 6 H), 3.06 (t, 2 H), 1.90–1.83 (m, 8 H), 1.46 (br s, 1 H); ^{13}C NMR 147.39, 147.11, 135.7, 127.6, 111.4, 109.1, 64.4, 56.1, 55.8, 43.1, 40.1, 30.1, 25.2. Anal. Calcd for $C_{15}H_{21}O_2N$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.69; H, 8.57; N, 5.50. Picrate Anal. Calcd for $C_{21}H_{24}O_9N_4$: C, 52.94; H, 5.08; N, 11.76. Found: C, 53.05; H, 5.18; N, 11.83.

1-(5-Chloropentyl)isoquinoline Formamidine 7b. A solution of 61 mg of **6** (0.20 mmol) in 15 mL of dry THF was cooled to −78 °C and treated with 146 μL of *n*-butyllithium (0.22 mmol). The mixture was stirred 30 min, and then 51 mg of 1-chloro-5-iodopentane (0.22 mmol), in 0.5 mL of THF was added. The halide solution was first passed through a plug of silica gel prior to use. After 10 min the reaction mixture was quenched with 0.5 mL of ammonium chloride, and the solution, after being warmed to room temperature, was concentrated in vacuo. The residue was partitioned between dichloromethane and saturated bicarbonate, and the layers were separated. The aqueous layer was extracted twice with dichloromethane, and the combined organics were worked with brine, dried (K_2CO_3), and concentrated to give a yellow oil. Chromatography (hexane–ethyl acetate–Et_3N, 10:1:1) gave 75 mg (92%) of **7b**: IR (film) 1640, 1517 cm^{-1}, ^1H NMR ($CDCl_3$) δ 7.49 (s, 1 H), 6.58 (d, 2 H), 4.58 (br s, 1 H), 3.85 (d, 6 H), 3.53 (t, 2 H), 3.33 (s, 3 H), 3.17 (s, 2 H), 2.96–2.79 (m, 2 H), 2.63–2.52 (m, 2 H), 1.81–1.70 (m, 4 H), 1.57–1.41 (m, 4 H), 1.13 (s, 6 H).

Spiro[cyclohexane-1,1′-(6′,7′-dimethoxy-1′,2′,3′,4′-tetrahydroisoquinoline)] (9b). In a manner similar to the procedure described for **9a**, 56 mg of **7b** in 20 mL of THF was treated with 151 μL of *sec*-butyllithium (1.05 equiv) at −95 °C. HMPA (95 μL, 4.0 equiv) was added, and the mixture was stirred at −50 °C for 4 h and then at −30 °C (freezer) overnight. The colorless solution was quenched with 0.5 mL of ammonium chloride, and the volatiles were removed in vacuo. Hydrazinolysis at 50 °C overnight was followed by partitioning of the residue with dichloromethane and saturated bicarbonate. The bicarbonate layer was extracted (2×), combined with the organic layers, dried (K_2CO_3), and concentrated to give an oil. The oil was chromatographed (hexane–ethyl acetate–Et_3N, 10:1:1) to give 19 mg of an oil (59%): picrate, mp 178 °C (lit.[4] mp 176 °C); IR (film) 3312, 1609, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (s, 1 H), 6.54 (s, 1 H), 3.85 (d, 6 H), 3.05 (t, 2 H), 2.70 (t, 2 H), 1.76–1.55 (m, 10 H), 1.31–1.25 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 147.01, 147.0, 136.8 127.2, 111.57, 103.2, 56.1, 55.7, 54.3, 38.4, 37.9, 30.3, 25.6, 21.7. Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.51; H, 8.87; N, 5.36. Found: C, 73.49; H, 8.72; N, 5.51. Picrate Anal. Calcd for $C_{22}H_{26}O_9N_4$: C, 53.88; H, 5.34; N, 11.42. Found: C, 53.37; H, 5.51; N, 11.04.

Benzo[*a*]quinolizidine 11a. An anhydrous solution of 93 mg (0.30 mmol) of **5** in 20 mL of THF, cooled to −78 °C under argon, was treated with 246 μL of lithium diisopropylamide (1.14 M, 0.3 mmol). After 1 h, 40 mL of 1,4-dibromobutane (72 mg, 0.33 mmol) was added, and the reaction mixture was stirred for 2 h, after which 0.5 mL of saturated ammonium chloride solution was added. The solution was concentrated in vacuo, and the residue was subjected directly to the hydrazinolysis (8 mL of 95% ethanol, 1 mL of glacial acetic acid cooled to 0 °C and 2 mL of hydrazine hydrate added) at 50 °C overnight. The mixture was partitioned between dichloromethane and saturated sodium bicarbonate, and the bicarbonate layer was extracted twice with dichloromethane. The organic layers were combined, dried (K_2CO_3), and concentrated to give an oil, which was chromatographed on silica gel (hexane–ethyl acetate–Et_3N, 10:1:1); 30 mg (45%) of **11a** was obtained: picrate, mp 174 °C; hydrochloride, mp 231–233 °C (lit.[5] mp 234–235 °C); IR (film) 2993, 2932, 2852, 2751 (Bohlmann–Wenkert bands);[6] ^1H NMR ($CDCl_3$) δ 6.69 (s, 1 H), 6.56 (s, 1 H), 3.84 (s, 6 H), 3.17–2.90 (m, 4 H), 2.63–2.44 (m, 2 H), 2.35–2.22 (m, 2 H), 1.93–1.90 (m, 1 H), 1.73–1.65 (m, 2 H), 1.52–1.25 (m, 2 H); ^{13}C NMR 147.22, 147.0, 130.4, 126.7, 111.4, 108.0, 63.2, 56.9, 55.8, 55.7, 52.8, 31.4, 29.0, 25.4, 25.1. Picrate Anal. Calcd for $C_{21}H_{24}O_9N_4$: C, 52.94; H, 5.08; N, 11.76. Found: C, 52.99; H, 5.11; N, 11.53.

Homobenzo[*a*]quinolizidine 11b. In a dried flask was placed 300 mg of **5**, 20 mL of THF was added, and the atmosphere was flushed with argon. After the mixture was cooled to −78 °C, 0.6 mL of *n*-butyllithium (1.8 M, 1.08 mmol) was added dropwise over 1 h. The reaction mixture was then treated with the rapid addition of 147 μL of 1,5-dibromopentane (248 mg, 1.08 mmol). It was important to add the dihalide in one quick spurt from the syringe. After stirring for 2 h at −78 °C, 1 mL of saturated ammonium chloride was added, and the volatiles were removed in vacuo. The residue was treated with the hydrazine solution (as described for **11a**) and after chromatography (as described for **11a**) gave 112 mg (53%) of an oil, picrate, mp 120 °C (sealed tube) (from ethanol). The oil **11b** also showed Bohlmann–Wenkert bands[6] at 2851–2763 cm^{-1}; indicating a trans ring fusion: ^1H NMR ($CDCl_3$) δ 6.58 (d, 2 H), 3.84 (s, 7 H), 3.03–2.72 (m, 6 H), 2.04–1.57 (m, 8 H); ^{13}C NMR 147.1, 147.0, 132.3, 126.7, 110.9, 110.2, 62.5, 55.9, 55.7, 49.4, 36.8, 28.8, 27.4, 27.2, 26.7; mass spectrum (CI) 262 (M + 1). Picrate Anal. Calcd for $C_{22}H_{26}O_9N_4$: C, 53.88; H, 5.34; N, 11.42. Found: C, 53.62; H, 5.62; N, 11.38.

Acknowledgment. Financial support from the National Science Foundation and Bristol-Myers is gratefully acknowledged.

Registry No. 1, 124-68-5; 2, 127208-62-2; 3, 127208-63-3; 4, 1745-07-9; 5, 127208-64-4; 7a, 127208-65-5; 7a 1-*d* derivative, 127208-66-6; 7b, 127208-67-7; 8a, 127208-68-8; 8b, 127208-69-9; 9a, 127208-70-2; 9a·picrate, 127208-71-3; 9b, 122766-33-0; 9b·picrate, 122766-34-1; 11a, 4787-30-8; 11a·picrate, 99905-21-2; 11b, 121089-98-3; 11b·picrate, 127229-23-6; $Me_2NCH(OMe)_2$, 4637-24-5; 4-chloro-1-iodobutane, 10297-05-9; 5-chloro-1-iodopentane, 60274-60-4; 1,4-dibromobutane, 110-52-1; 1,5-dibromopentane, 111-24-0.

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(5) Gootjes, J.; Nauta, W. T. *Recl. Trav. Chim. Pay-Bas* **1965**, *84*, 1183. Fernandez, M.; Söllhuber, M. M. *Heterocycles* **1987**, *26*, 3059.

(6) Uskokovic, M.; Bruderer, H.; von Planta, C.; Williams, T.; Brossi, A. *J. Am. Chem. Soc.* **1964**, *86*, 3364. These authors first designated the stereochemistry of benzo[*a*]quinolizidines by use of ^1H NMR. In conjunction with the Bohlmann–Wenkert IR bands (Wenkert; et al. *J. Am. Chem. Soc.* **1956**, *78*, 6417 and Bohlmann *Angew. Chem.* **1957**, *69*, 641) assignments are usually firm with regard to the lone pair on nitrogen and the adjacent angular hydrogen.