Total Syntheses of Strychnan- and Aspidospermatan-Type Alkaloids. 2. Generation of 15-(3-Furanyl) ABCE Tetracyclic Intermediates

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Received July 22, 1993[•]

The synthesis of N^b-benzyl-2-(dimethyl 2-malonyl)- and 2-(methyl 2-acetyl)tryptamines (**21**, **25**) provides access to methyl 4-(3-furanyl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (**12**) and methyl 3-benzyl-5-(3-furanyl)-2,3,3a,4,5,7-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (**9**), potential intermediates for the syntheses of strychnos alkaloids. A new condensation—sigmatropic rearrangement reaction gives the tetracyclic product **9** directly from the tryptamine **25**.

The synthesis of D-nor-ψ-vincadifformine compounds (**1**) with substitution at position 14 had provided versatile intermediates for elaboration of a variety of ψ-tabersonine (**2**)- and coronaridine (**3**)-type alkaloids (Scheme I).[1] Furthermore, such intermediates were utilized for generation of 20-*epi*-dihydroakuammicine (**4**) and tubotaiwine (**5**).[2] The key steps in these syntheses were based on generation and intramolecular reactions of transient enamine indoloacrylates **6** and **7**.

As an alternative approach to the latter syntheses of strychnan and aspidospermatan-type alkaloids, we started on a path, which would assemble all but the acetate-derived, ring F, two-carbon fragment of the strychnine (**8**) skeleton at an early stage. The tetracyclic D-nor-intermediate **9** (Scheme II), bearing a 3-furyl substituent at the methylene adjacent to the previously substituted position (i.e. formally at C17, structure **1**, corresponding to C15 of the strychnos alkaloids),[3] offered the prospect of oxidative opening of the furan ring to a compound (i.e. **10**) which might be converted to akuammicine (**11**) and/or strychnine (**8**).

The 3-furanyl-substituted indoloazepine **12** suggested itself as a possible precursor for the desired tetracyclic D-nor-intermediate **9**, since we had great success in transformations of the parent unsubstituted indoloazepine **13** into analogous tetracyclic compounds (**1**, Scheme I).[1] Our most adaptable synthesis of the indoloazepine **13** proceeds by chlorination of *N*-benzyltetrahydro-β-carboline (**14**, R = H) and reaction of the resulting chloro imine **15** with thallium dimethyl malonate (Scheme III).[4,5] The 2-indoline alkene diester **16**, which is formed intially, quantitatively rearranges to the indoloazepine diester **17** on heating in tetrahydrofuran. Monodecarbomethoxylation and debenzylation had then provided the indoloazepine **13**.

Unfortunately, the tetrahydrocarboline chlorination step could not be extended to the analogue with a 3-furanyl substituent (**14**, R = 3-furanyl) and consequently an alternative route to the spiroindoline alkene **16**, with a 3-furanyl substituent, was required. This was found in the chlorination of N^b,N^b-dibenzyltryptamine (**18**) and reaction of the resulting chloro imine **19** with thallium dimethyl malonate, followed by monodebenzylation of the product **20** and condensation of the secondary amine **21** with 3-furancarboxaldehyde (Scheme IV). The spiroindoline 2-alkene **22** was formed readily and, analogously, condensations with 2-furfural provided the isomer **23**.

Remarkably, these furanyl-substituted spiropyrrolidines **22** and **23**, as well as the 3-hydroxypropyl-substituted spiropyrrolidine **24**,[6] resisted the facile thermal rearrangement of the unsubstituted parent **16**.[5] Rearrangement of the 3-furanyl derivative **22** could only be achieved in modest yield (30%) with simultaneous monodecarbomethoxylation, using lithium chloride in refluxing *N*,*N*-dimethylacetamide.

This result led directly to a condensation of 3-furfural with the N^b-benzyltryptamine monoester derivative **25**, which was readily obtained by monodecarbomethoxylation and hydrogenolysis of the N^b,N^b-dibenzyltryptamine malonate derivative **20**. The spiropyrrolidine–indoline alkene **26** product (44%) rearranged to the indoloazepine **27** in refluxing *N*,*N*-dimethylacetamide (59%). On hydrogenolysis the secondary amine **12** was obtained.

Condensation of the furan-substituted indoloazepine **12** with acetaldehyde readily provided two bridged indoloazepines **28** and **29** (57 and 28% respectively, Scheme V). In contrast to our experience with analogous compounds lacking the furan substituent,[7] these products did not, however, react with benzyl bromide in refluxing tetrahydrofuran, and in toluene, at reflux, only the more reactive[7] α-methyl compound **29** was consumed. But, the expected quaternary salt[7] and its rearrangement product **9** were not obtained. The bridged indoloazepine **29** was converted only to lower molecular weight degradation products.

We had previously seen that the sequence of condensation of the parent indoloazepine **13** with an aldehyde, followed by benzylation, could be reversed and that the tetracyclic products **1** (Scheme I) could thus be obtained in good yields in refluxing toluene.[8] However, in contrast to those results, it was now found that the furan substituent in the *N*-benzylindoloazepine **27** also prevented conversion of this compound with acetaldehyde to the tetracyclic

[•] Abstract published in *Advance ACS Abstracts*, November 15, 1993.

(1) Bornmann, W. G.; Kuehne, M. E. *J. Org. Chem.* **1992**, *57*, 1752.

(2) Kuehne, M. E.; Frasier, D. A.; Spitzer, T. D. *J. Org. Chem.* **1991**, *56*, 2696.

(3) For a biogenetic numbering system see Le Men, J.; Taylor, W. I. *Experientia* **1965**, *21*, 508.

(4) Kuehne, M. E.; Roland, D. M.; Hafter, R. *J. Org. Chem.* **1978**, *43*, 3705.

(5) Kuehne, M. E.; Matsko, T. H.; Bohnert, J. C.; Kirkemo, C. L. *J. Org. Chem.* **1979**, *44*, 1063.

(6) Berk, J. D. Ph.D. Thesis, University of Vermont, 1987.

(7) Kuehne, M. E.; Matsko, T. H.; Bohnert, J. C.; Motyka, L.; Oliver-Smith, D. *J. Org. Chem.* **1981**, *46*, 2002.

(8) Kuehne, M. E.; Kuehne, S. E. *J. Org. Chem.* **1993**, *58*, 4147.

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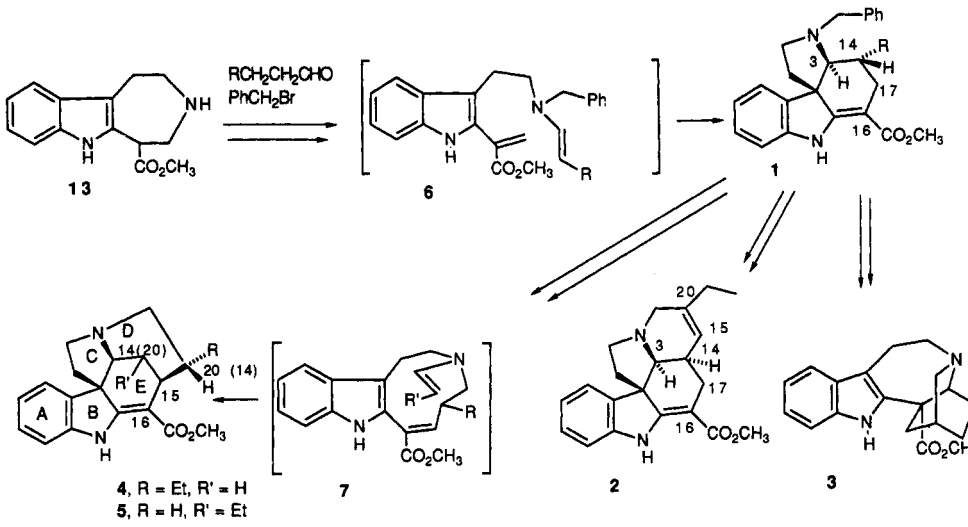
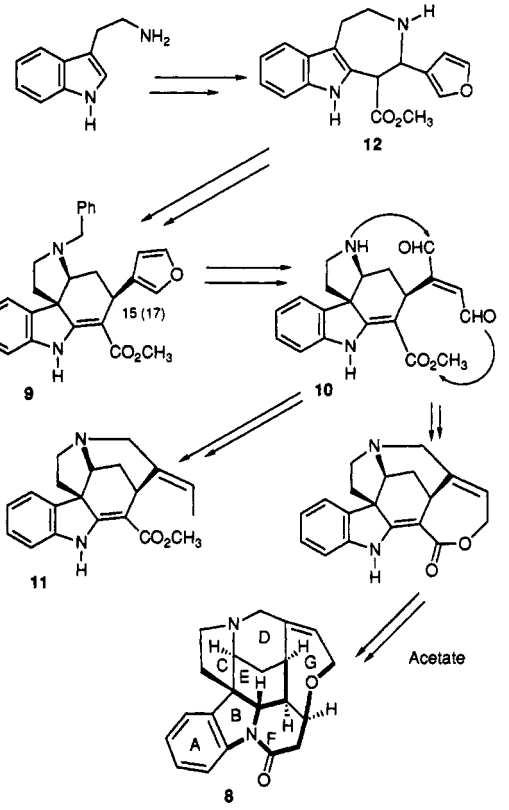
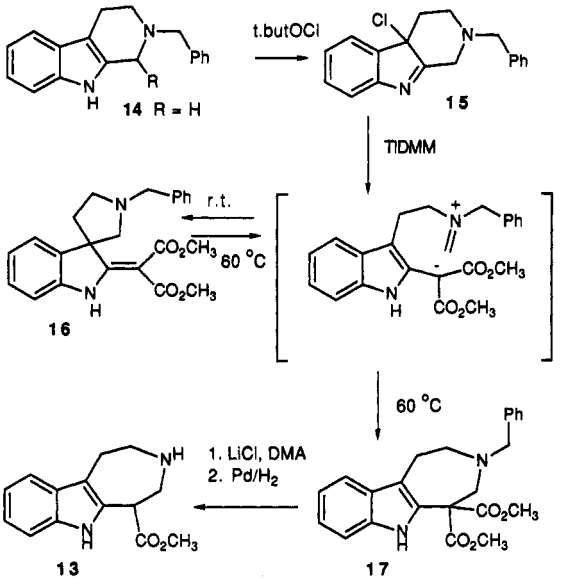
Scheme I



Scheme II



Scheme III



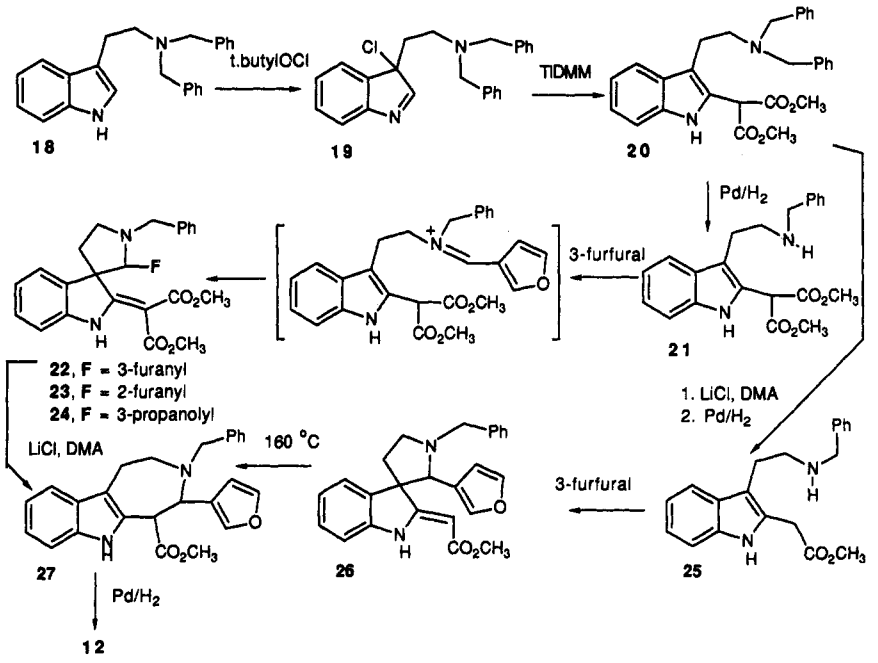
product **9**. Consequently, an alternative access to the tetracyclic intermediate **9** was required.

Availability of the 2-malonyl and 2-acetyl N^b-benyltryptamines **21** and **25** from the preceding work suggested their condensation with an aldehyde that already incorporates the complete carbon complement of the strychnos alkaloids. Thus, in a synthesis of the key 5-(3-furanyl)-substituted tetracyclic intermediate **9**, rather than depending on a biomimetic secodine-like intramolecular cyclization of indolo acrylate and enamine functions for introduction of the two-carbon C3a–C4 (C3–C14, Scheme I) fragment, this segment might be introduced as part of a Mannich-type condensation of the tryptamines **21** or **25** with a vinylogous 3-furfural (Scheme VI). Indeed, condensation of the malonyl tryptamine **21** with 3-(3-furanyl)-acrolein (**30**) in refluxing toluene and BF_3–etherate provided the diester imines **31a** and **31b** as a 1:1 mixture of two C15 epimers. The epimeric nature of these compounds was substantiated by their reductive transformation with sodium borohydride in acetic acid, at 94 °C, into a single cleavamine product **32**.

Condensation of the N^b-benzyltryptamine monoester **25** with 3-(3-furanyl)acrolein (**30**), under the same conditions, gave the indolo acrylate **9** as a single diastereomer. According to molecular modeling calculations (Macromodel), its two possible C5 epimers have respective energies of 191.8 kJ/mol for the C3a,5-H cis diastereomer and 196.6 kJ/mol for the C3a,5-H trans diastereomer. ORTEP structures show a boat conformation for the unsaturated ring Figure 1).

Consistent with this picture and a C3a,5-cis H assignment is the NMR spectrum, which gives the C5 hydrogen at δ 4.19 as a doublet (J = 5 Hz) due to coupling with C4α, with additional very fine splitting due to coupling with C4β and the C3a hydrogen at δ 3.35 as a doublet (J = 5 Hz) due to coupling to C4α, as expected for equatorial type C3a,5 hydrogens flanked by the C4α H (δ 1.60) and C4β H (δ 2.29). Chemical shifts were established by a 2D COESY spectrum. Final confirmation of the assigned stereochemical structure was obtained from a single crystal X-ray analysis (Figure 2). It provided a good match to the optimized structure obtained by molecular modeling.

Scheme IV



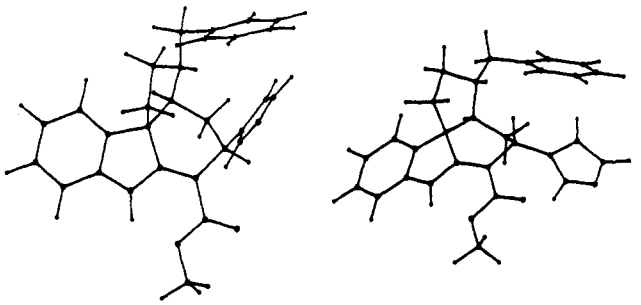


Figure 1. Ortep structures of the 15-furanyl tetracyclic intermediate **9** and of its C-15 epimer.

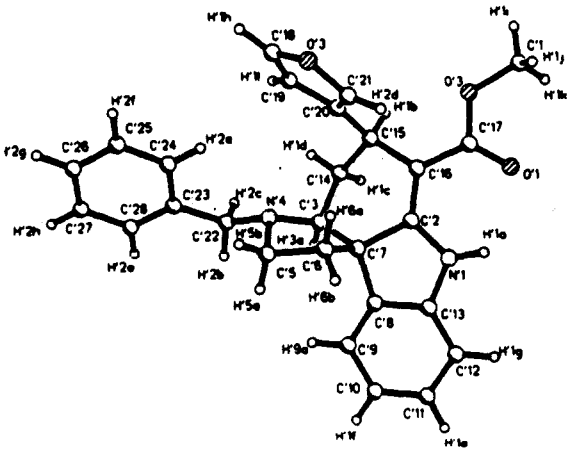
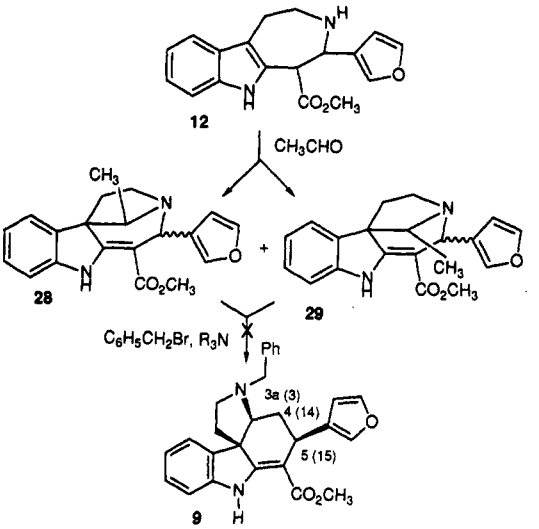


Figure 2. X-ray structure of the 15-furanyl tetracyclic intermediate **9**.

When the 1:1 mixture of diesters **31a,b** was heated in *N,N*-dimethylacetamide with lithium chloride, only the monodecarbomethoxylation product **9** was formed (45%), suggesting epimerization through reversible formation of an imonium cleavamine (or selective destruction of one epimer).

As shown in Scheme VI, the condensation of 3-(3-furanyl)acrolein (**30**) with the N^b-benzyltryptamines **21** and **25** may be understood in terms of a sigmatropic

Scheme V



rearrangement of the initial Mannich condensation products **33a,b**, followed by acid-catalyzed cyclization of the resulting enamine **34**; though alternative reactions of an initial unsaturated imonium salt **35** can be considered. For instance, formation of the tetracyclic ring structure from an unsaturated imonium precursor has precedence in the mechanistic interpretation of the epimerization of **20**-*epi*-dihydroakuammicine (**4**) to dihydroakuammicine.[2,9] Unfortunately, it was not possible to find any intermediates in the overall transformation to products **31a,b** or **9** since, under less vigorous conditions, no reaction of the tryptamines **21** and **25** with 3-(3-furanyl)acrolein (**30**) took place.

The 3-(3-furanyl)acrolein (**30**) required for these condensations had previously been prepared in low yield.[10] In an alternative sequence (Scheme VII), 3-furaldehyde was subjected to Wittig reactions with [(methoxy- or ethoxycarbonyl)methylene]triphenylphosphorane ylides; and

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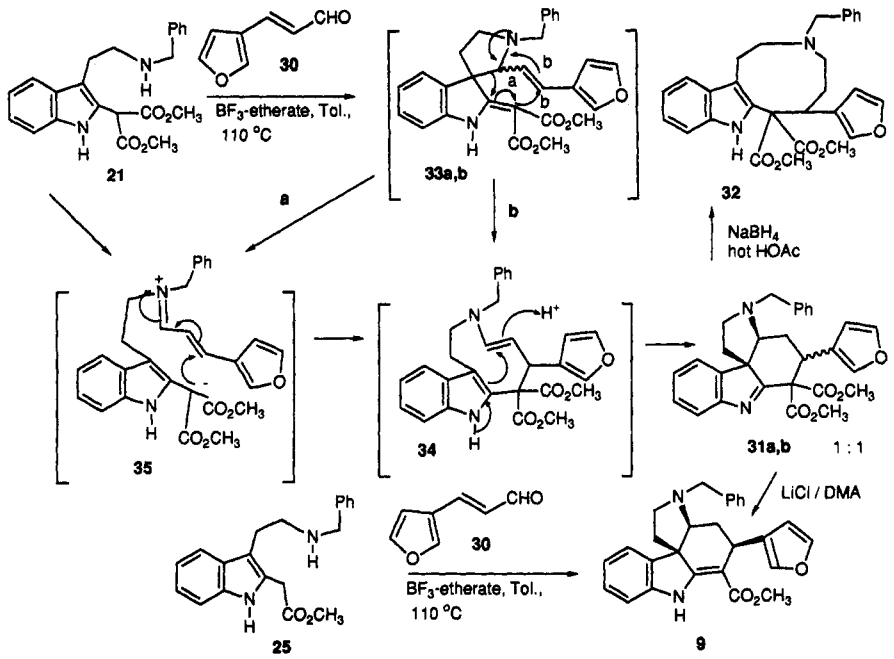
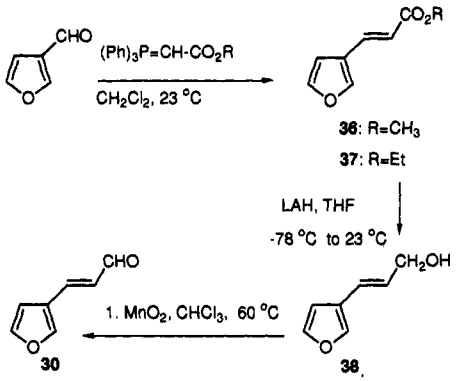
(10) Ingham, C. F.; Massy-Westropp, R. A. *Aust. J. Chem.* **1974**, *27*, 1491.

Scheme VI



Scheme VII



the resulting acrylates **36** and **37** were reduced with lithium aluminum hydride. Oxidation of the allylic alcohol **38** with MnO_2 gave the aldehyde **30** in 71% overall yield.

Syntheses of subsequent strychnos alkaloid precursors, in which the furan ring of the tetracyclic product **9** is oxidized, will be presented in following papers.

Experimental Section

General Methods. All reactions were run under an argon atmosphere, unless otherwise stated. Melting points were obtained on a Kofler micro hotstage with thermometers calibrated against a National Bureau of Standards certified set. NMR spectra were obtained with a Bruker 250-MHz or 270-MHz instrument, and chemical shifts are expressed as parts per million (δ) downfield from tetramethylsilane. Mass spectra were obtained with a Finnigan 4610 quadrupole instrument at 70 eV, calibrated with perfluorotributylamine and hexafluorortriphenyl-*s*-triazine for higher molecular weight compounds. Chemical ionization spectra employed methane as the reagent gas. IR spectra were obtained with a Nicolet 6000 FT grating instrument and are reported as strong (s), medium(m), or weak (w) absorptions in cm^{-1}. Perkin-Elmer 402 or Hewlett-Packard 8452A instruments were used for recoring UV spectra. TLC data were obtained with E. Merck 60 PF 254 precoated silica gel on aluminum sheets. Indole derivatives were characterized with a 10% solution of ceric ammonium sulfate (CAS) in phosphoric acid as a spray reagent and other compounds were visualized by either UV, 10% phosphomolybdic acid in ethanol, or iodine vapor. For gravity column chromatography, 60-200 mesh Baker R3405 silica was used. Flash chromatography employed Baker 7024-R 40-μm diameter silica gel. Radial enhanced thin-layer chromatography was performed on a Harrison chromatatron with plates made from EM 7749-3 silica gel 60 (PF254) containing gypsum. Microanalyses were provided by Robertson Laboratories, Florham Park, NJ. High-resolution mass spectra were performed by Dr. P. Keller at Norwich Eaton Pharmaceuticals, Norwich, NY.

3-[2-[N^b,N^b-Bis(phenylmethyl)amino]ethyl]indole (18). Into 1 L of distilled methanol was placed 30.0 g (0.188 mol) of tryptamine, 68.4 g (0.4 mol) of benzyl bromide, and 70.0 g of potassium carbonate. The reaction mixture was mechanically stirred and heated at reflux for 70 h. The mixture was cooled, filtered, and concentrated. The brown oily residue was taken up in dichloromethane, adsorbed onto silica, and chromatographed (dry gravity column; eluting solvent: ether/hexane 1:1) to yield 57 g of product **18** as a golden oil (89%): TLC R_f = 0.6 (SiO_2, ether/hexane 2:1; CAS yellow/brown); UV (ethanol) λ_{max} 290, 282, 270, 220, 210 nm; IR (NaCl) ν_{max} 3422 (s), 3079 (m), 3052 (s), 3025 (s), 2916 (s), 2795 (s), 1598 (w), 1494 (s), 1451 (s), 1413 (m), 13 58 (m), 1325 (m), 1222 (w), 1124 (m), 1091 (m), 1069 (m), 1015 (m), 1010 (m), 966 (w), 912 (w), 797 (w) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.85 (bs, 1 H), 7.6–6.85 (m, 14 H), 3.81 (s, 1 H), 3.68 (s, 4 H), 2.93 (bt, 2 H), 2.79 (bt, 2 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 139.9, 128.8, 128.1, 126.8, 121.8, 121.4, 119.0, 118.8, 114.5, 110.9, 58.3, 53.9, 23.1; EIMS *m/z* (rel int) 341 (M^{+1}, 1), 340 (M^+, 4), 210 (83), 130 (27), 91 (100).

Dimethyl 2-[3-[2-[N^b,N^b-Bis(phenylmethyl)amino]ethyl]-indolyl]propanedioate (20). To a solution of 30.0 g (0.0882 mol) of *N*,*N*-dibenzyltryptamine (**18**) in dry tetrahydrofuran (300 mL) and triethylamine (9 mL) at −78 °C (dry ice/acetone) was added, dropwise, 12.4 g of *tert*-butyl hypochlorite (1.3 equiv) dissolved in tetrahydrofuran (50 mL) over a 30-min period. The chloroindolenine formation was monitored by TLC: starting material R_f = 0.5 (CAS Yellow); chloro indolenine R_f = 0.9 (CAS brown) (SiO_2 ether/hexane 1:1). When no starting material remained (2 h), the reaction mixture was concentrated under vacuum without heating, the residue dissolved into 75 mL of dry tetrahydrofuran and the triethylamine hydrochloride salts filtered from the mixture. The brown solution was then cannulated into a mechanically stirred suspension of 31.08 g (0.093 mol) of thallium dimethyl malonate in 500 mL of dry tetrahydrofuran at −78 °C. The mixture was mechanically stirred at −78 °C for 1 h, warmed to 23 °C, and stirred for 12 h. Then the mixture was filtered through a plug of Celite to remove the thallium salts, concentrated, and triturated with ether/pentane 1:1. Crystallization from ether/pentane yielded 41.5 g of diester **20** (83%): mp 104 °C; TLC R_f = 0.48 (SiO_2, ether/hexane 3:2; CAS green/maroon); UV (ethanol)

λ_{max} 292, 284, 276, 216, 202 nm; IR (NaCl) ν_{max} 3408 (m), 3063 (w), 3020 (w), 2948 (m), 2796 (w), 1731 (s), 1489 (w), 1453 (m), 1428 (m), 1313 (m), 1277 (w), 1241 (m), 1192 (m), 1144 (m), 1023 (m), 738 (s), 696 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 8.79 (bs, 1 H), 7.39-6.97 (m, 14 H), 4.81 (s, 1 H), 3.72 (s, 4 H), 3.64 (s, 6 H), 2.89 (dd, 2 H), 2.70 (dd, 2 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) 167.59, 139.81, 135.90, 128.72, 128.19, 127.45, 126.81, 124.44, 122.38, 119.26, 118.85, 113.40, 111.06, 79.74, 79.21, 58.62, 53.81, 53.01, 48.68, 22.12; EIMS *m/z* (rel inten) 471 (1), 470 (M^+, 5), 210 (77), 91 (100). Anal. Calcd for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 6.14. Found: C, 74.09; H, 6.28; N, 5.92.

Dimethyl 2-[3-[2-[*N*^{b}-(phenylmethyl)amino]ethyl]indolyl]-propanedioate (21). To a flask containing an argon-flushed solution of 2.0 g (4.30 mmol) of **20** in 75 mL of wet acetic acid was added 0.5 g of 10% palladium on charcoal. The vessel was degassed and saturated with hydrogen, and the mixture was hydrogenated with a positive pressure of hydrogen (via balloon). The reaction mixture was monitored by TLC to show consumption of the starting material and formation of the product. When no more dibenzyl compound **20** remained, the mixture was filtered through Celite and the catalyst washed with three 15-mL portions of acetic acid. The solution was poured onto crushed ice and made strongly basic with saturated ammonium hydroxide. The organic material was extracted with dichloromethane 5 × 50 mL, washed with 100 mL of distilled water, and dried over magnesium sulfate. Concentration and chromatography (dry gravity column; eluting solvent: ether/methanol 9:1) afforded 1.37 g of secondary amine **21** as a golden oil (84%). An analytical sample was prepared by crystallization of the acetic acid salt from ether: mp 122–123 °C; TLC R_f = 0.4 (SiO_2, ether/methanol 4:1; CAS pastel green); UV (ethanol) λ_{max} 292, 284, 276, 266, 220, 202 nm; IR (NaCl) ν_{max} 3399 (w), 2955 (w), 2835 (w), 1731 (s), 1454 (m), 1430 (m), 1304 (m), 1328 (m), 1196 (m), 1142 (m), 1022 (w), 740 (s), 686 (w) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 9.14 (s, 1 H), 7.70–6.90 (m, 12 H), 5.15 (bs, 1 H), 3.76 (s, 2 H), 3.64 (s, 6 H), 2.95 (dd, 4 H), 2.06 (bs, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 167.6, 140.3, 136.1, 128.0, 127.9, 127.4, 126.5, 125.2, 122.4, 119.3, 118.7, 113.1, 111.1, 77.5, 53.7, 52.7, 49.4, 49.0, 24.8; EIMS *m/z* (rel inten) 380 (M^+, 13), 262 (12), 261 (73), 260 (25), 202 (31), 170 (16), 169 (23), 120 (31), 91 (69), 60 (100). Anal. Calcd for $C_{22}H_{24}N_2O_4 - C_2H_4O_2$: C, 65.44; H, 6.41; N, 6.35. Found: C, 65.29; H, 6.58; N, 6.31.

Methyl 3-[2-[*N*^{a},*N*^{b}-Bis(phenylmethyl)amino]ethyl]indole-2-ethanoate. To a flask containing 3.27 g (6.94 mmol) of diester **21** in 30 mL of *N,N*-dimethylacetamide was added 0.324 g (7.64 mmol) of lithium chloride and 0.239 g (1.74 mmol) triethylamine hydrochloride. The mixture was heated in an oil bath at 130 °C for 2.5 h and then cooled to 23 °C. To the reaction mixture were added 30 mL of brine and 30 mL of saturated ammonium hydroxide and the dark two-phase solution was extracted with 10 × 50 mL of ether. The ether extracts were washed with water (5 × 15 mL), dried with magnesium sulfate and concentrated. Adsorption of the dark oil onto silica and chromatography (dry gravity column; eluting solvent: ether/hexane 1:1.5) yielded 2.41 g (84%) of a gummy tan solid. Crystallization from ether/hexane 1:1 afforded a sample for elemental analysis; mp 81–83 °C; TLC R_f = 0.36 (SiO_2, ether/hexane 1:1; CAS green); UV (ethanol) λ_{max} 292, 284, 268, 222, 216, 206 nm; IR (NaCl) ν_{max} 3393 (m), 3021 (w), 2949 (w), 2913 (w), 2781 (w), 1731 (s), 1485 (m), 1449 (m), 1304 (w), 1226 (m), 1202 (m), 1154 (m), 1118 (m), 1022 (w), 728 (s), 698 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 8.33 (bs, 1 H), 7.37–6.90 (m, 14 H), 3.64 (s, 4 H), 3.52 (s, 3 H), 3.46 (s, 2 H), 2.81 (t, 2 H), 2.60 (t, 2 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 170.9, 167.6, 139.8, 135.6, 128.7, 128.1, 128.0, 126.7, 122.3, 121.5, 119.2, 119.1, 118.8, 118.4, 110.6, 58.5, 53.8, 52.9, 52.1, 31.4; EIMS *m/z* (rel int) 413 (5), 412 (M^+, 13), 211 (19), 210 (100), 91 (70). Anal. Calcd for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79. Found: C, 78.59; H, 6.79; N, 6.66.

Methyl 3-[2-[*N*^{b}-(Phenylmethyl)amino]ethyl]indole-2-ethanoate (25). To a flask containing an argon-flushed solution of 2.4 g (5.85 mmol) of methyl 3-[2-[*N*^{a},*N*^{b}-bis(phenylmethyl)-amino]ethyl]indole-2-ethanoate in 75 mL of wet acetic acid was added 0.75 g of 10% palladium on charcoal. The vessel was degassed and saturated with hydrogen, and the mixture was hydrogenated with a positive pressure of hydrogen (via balloon). The reaction progress was monitored by TLC to show consumption of the starting material and formation of the product. When no more dibenzylamine remained, the mixture was filtered through Celite and the catalyst washed with three 15-mL portions of acetic acid. The solution was poured onto crushed ice and made strongly basic with saturated ammonium hydroxide. The organic material was extracted with ether (10 × 30 mL), washed with 100 mL of distilled water, and dried over magnesium sulfate. Concentration and chromatography (dry gravity column; eluting solvent: ether/methanol 9:1) afforded 1.64 g of product **25** as an oil (87%). Crystallization from toluene afforded a sample for elemental analysis: colorized at 170 °C and decomposed at 210 °C; TLC R_f = 0.57 (SiO_2, ether/methanol 4:1; CAS green/brown); UV (ethanol) λ_{max} 292, 282, 268, 222, 210, 204 nm; IR (NaCl) ν_{max} 3398 (w), 3057 (w), 3024 (w), 2948 (w), 2916 (w), 2853 (w), 1732 (s), 1488 (w), 1456 (m), 1342 (w), 1304 (w), 1229 (m), 1158 (m), 1115 (w), 1007 (w), 732 (s) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 8.54 (bs, 1 H), 7.70–6.95 (m, 9 H), 3.89 (s, 2 H), 3.85 (s, 2 H), 3.66 (s, 3 H), 3.09–2.85 (dt, 4 H), 1.80 (bs, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 170.8, 140.2, 135.9, 128.1, 127.9, 127.2, 126.7, 121.7, 120.7, 119.2, 118.4, 111.3, 110.7, 53.6, 51.8, 49.4, 31.7, 24.7; EIMS *m/z* (rel inten) 322 (M^+, 15), 204 (15), 203 (94), 202 (13), 149 (13), 144 (20), 143 (15), 142 (17), 120 (49), 91 (100); high resolution MS; FAB ionization, calcd for $C_{20}H_{23}N_2O_2$ 323.1760, found 323.1772.

Dimethyl 2-[2′-[3″-Furanyl]-1′-(*N*^{b}-phenylmethyl)spiro-[3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-ylidene]propanedioate (22). To a flask containing 75 mL of dry benzene was added 1.39 g (3.65 mmol) of diester **21**, 0.347 mL (4.01 mmol) of 3-furaldehyde, and 1.25 g of molecular sieve powder. The mixture was evacuated and flushed with argon three times, 0.055 mL (0.728 mmol) of boron trifluoride etherate was added, and the mixture was heated at reflux with a Dean–Stark condenser for 24 h. After completion, the reaction mixture was cooled, filtered, concentrated, and chromatographed (flash column; eluting solvent: ether/hexane 1:1) to afford 0.868 g of product **22** as a white foam (52%): TLC R_f = 0.60 (SiO_2, ether/hexane 3:1; CAS blue/green); UV (ethanol) λ_{max} 330, 321, 220, 210, 204 nm; IR (NaCl) ν_{max} 3419 (w), 3305 (m), 3029 (w), 2949 (m), 2921 (w), 2827 (w), 1718 (s), 1669 (s), 1617 (s), 1578 (s), 1496 (s) , 1480 (s), 1436 (s), 1296 (s), 1225 (s), 1172 (s), 1108 (s), 1072 (s), 1022 (s), 873 (m), 736 (m), 676 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 10.7 (bs, 1 H), 7.70 (d, 1 H; J = 7 Hz), 7.50–6.90 (m, 9 H), 6.67 (d, 1 H; J = 8 Hz), 5.90 (s, 1 H), 4.20 (s, 1 H), 3.89 (d, 1 H; J = 12 Hz), 3.75 (s, 6 H), 3.32 (dt, 1 H), 3.12 (d, 1 H; J = 14 Hz), 2.8 (m, 1 H), 2.50 (m, 1 H), 2.10 (m, 1 H); EIMS *m/z* (rel inten) 459 (6), 458 (M^+, 26), 221 (14), 108 (21), 91 (100); high resolution MS, FAB ionization, calcd for $C_{27}H_{27}N_2O_5$ 459.1920, found 459.1929.

Dimethyl 2-[2′-Furanyl]-1′-(*N*^{b}-phenylmethyl)spiro]3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-ylidene]propanedioate (23). To a solution of 1.0 g of the amino ester **21** hydrochloride (0.0024 mol) in dry benzene (50 mL) and triethylamine (3 mL) was added 2-furaldehyde (0.003 mol, 0.25 mL). The mixture was heated at 80 °C under a nitrogen atmosphere for 2 h. Monitoring by thin-layer chromatography showed consumption of the starting alkaloid, with concomitant formation of a bluish grey spraying compound (CAS). The reaction mixture was cooled and washed with saturated ammonium hydroxide (50 mL) and with brine (50 mL), dried, concentrated, and chromatographed to yield 700 mg of product **23** (64%), which crystallized from ether/methanol/pentane: mp 142–143 °C; TLC R_f 0.6 (SiO_2, ether/hexane 3:1; CAS blue/grey); ^1H 270-MHz NMR ($CDCl_3$) δ 10.72 (bs, 1 H), 7.63 (d, 1 H), 7.45–7.2 (m, 5 H), 7.15–7.05 (m, 2 H), 6.99 (t, 1 H), 6.68 (d, 1 H), 6. 01 (t, 1 H), 5.81 (d, 1 H), 4.51 (s, 1 H), 4.02 (d, 1 H, J = 14 Hz), 3.74 (s, 3 H), 3.72 (s, 3 H), 3.27 (dt, 1 H), 3.21 (d, 1 H, J = 14 Hz), 2.74 (dt, 1 H), 2.59 (q, 1 H), 2.21 (m, 1 H); MS (EI) *m/z* (rel inten) 458 (18), 427 (2), 367 (8), 335 (9), 242 (5), 199 (31), 108 (28). Anal. Calcd for $C_{27}H_{26}N_2O_5$: C, 70.73; H, 5.72; N, 6.11. Found: C, 70.51; H, 5.82; N, 5.97.

Methyl 2-[2′-[3′-Furanyl]-1′-(*N*$_b$-phenylmethyl)-spiro[3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-ylidene]acetate (26). To a flask containing 75 mL of dry toluene was added 0.728 g (2.26 mmol) of amino ester **25**, 0.215 mL (2.48 mmol) of 3-furaldehyde, and 1.0 g molecular sieve powder. The mixture was evacuated and flushed with argon three times, and after addition of 0.017 mL (0.023 mmol) of boron trifluoride etherate the reaction mixture was heated at reflux with a Dean–Stark condenser for 18 h. After

completion the reaction mixture was cooled, filtered, concentrated, and chromatographed (flash column; eluting solvent: ether/hexane 1:1) to afford 0.398 g of an inseparable 2:1 mixture of epimers of product **26** as a white foam (44%): TLC R_f = 0.23 (SiO_2, ether/hexane 3:2; CAS blue/aqua green); UV (ethanol) λ_{max} 326, 296, 212 nm; IR (NaCl) ν_{max} 3424 (w), 3310 (w), 2952 (w), 1718 (s), 1450 (w), 1416 (w), 1268 (m), 124 0 (m), 1188 (m), 1143 (w), 1079 (s), 1017 (w), 734 (m), 590 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 9.60 (bs, 1 H), 9.50 (bs, 0.5 H), 7.60 (d, 1.5 H), 7.50-6.90 (m, 16 H), 6.67 (dd, 1.5 H), 6.13 (s, 0.5 H), 5.90 (s, 1 H), 5.59 (s, 0.5 H), 5.00 (s, 1 H), 4.20–4.00 (m, 1.5 H), 3.80 (d, 2 H), 3.75 (d, 4.5 H), 3.70 (d, 1.5 H), 3.32 (m, 1.5 H), 3.12 (dd, 1.5 H), 2.40 (m, 2.5 H), 2.10 (m, 3.5 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 170.5, 170.4, 169.0, 168.0, 144.0, 143.0, 142.4, 142.3, 140.9, 140.6, 139.3, 139.0, 134.6, 133.1, 129.3, 128.4, 128.0, 127.0, 125.4, 122.4, 121.1, 121.0, 120.9, 110.0, 109.9, 108.7, 108.6, 84.0, 80.5, 73.8, 72.4, 60.8, 60.7, 59.2, 57.8, 57.7, 52.0, 51.7, 50.6, 50.5, 37.8, 37.4; EIMS m/z (rel inten) 401 (M^{+1}, 24), 400 (M^+, 63), 200 (11), 199 (60), 166 (10) 156 (11), 149 (26), 18 (100), 91 (43), high resolution MS, FAB ionization, calcd for $C_{25}H_{25}N_2O_3$ 401.1865, found 401.1881.

2-(N^b-Phenylmethyl)-1-(3′-furanyl)-1,2,3,4-tetrahydrocarbazole (14, R = 3-furanyl). To a solution of 128 mg (0.510 mmol) of N^b-monobenzyltryptamine in dry benzene was added 60.6 μL (0.70 mmol) of 3-furfuraldehyde and 0.25 g of molecular sieve powder. The mixture was flushed with argon and after addition of 1.0 μL (0.15 mmol) of boron trifluoride etherate was heated at reflux with a Dean–Stark condenser for 3 h. The reaction mixture was then cooled, filtered, concentrated, and chromatographed (flash column; eluting solvent: ether/hexane 2:1) to yield 0.102 g of product **14** as a white crystalline film (62.5%). Crystallization from methanol afforded a sample for elemental analysis: mp 194–195 °C; TLC R_f = 0.85 (SiO_2, ether/hexane 3:2; CAS green/orange); UV (ethanol) λ_{max} 290, 282, 264, 224, 208 nm; IR (NaCl) ν_{max} 3395 (s), 3057 (w), 2954 (w), 2910 (m), 2845 (w), 2807 (w), 1592 (w), 1494 (m), 1445 (s), 1380 (m), 1358 (m), 1298 (s), 1255 (m), 1157 (s), 1010 (s), 868 (s), 814 (m), 803 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) 9.87 (s, 1 H), 7.99 (s, 1 H), 7.66–7.00 (m, 10 H), 6.77 (s, 1 H), 6.45 (s, 1 H), 4.64 (s, 1 H), 3.92 (d, 1 H), 3.43 (d, 1 H), 3.21 (d, 1 H), 2.71 (d, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) 143.7, 141.4, 139.5, 136.3, 133.9, 128.7, 128.2, 127.5, 127.0, 125.7, 121.6, 119.4, 118.3, 110.8, 110.4, 109.0, 58.0, 54.8, 47.7, 20.8; EIMS m/z (rel inten) 328 (M^+, 20), 279 (16), 262 (12), 209 (100), 180 (76), 167 (52), 149 (92), 143 (87), 91 (96). Anal. Calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.19; H, 6.28; N, 8.60.

Methyl 3-(Phenylmethyl)-4-(3′-furanyl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (27a). Into 30 mL of *N,N*-dimethylacetamide were placed 1.62 g (3.53 mmol) of spiro diester **22**, 0.194 g (4.59 mmol) of lithium chloride, and 0.485 g (3.53 mmol) of triethylamine hydrochloride. The mixture was heated in an oil bath at 130 °C for 3.5 h. The mixture was cooled, 15 mL brine and 15 mL saturated ammonium hydroxide were added to the resulting dark solution, and then it was extracted with ether (10 × 50 mL). The ether extracts were washed with water (5 × 15 mL), dried with magnesium sulfate, and concentrated. Adsorption of the dark oil onto silica and chromatography (flash column; eluting solvent: ether/hexane 1:1.5) yielded 0.486 g of a white foam (34%). Crystallization from methanol afforded a sample for elemental analysis: mp 162–163 °C; TLC R_f = 0.36 (SiO_2, ether/hexane 1:1; CAS pale green/black); UV (ethanol) λ_{max} 290, 283, 222, 202, 192 nm; IR (NaCl) ν_{max} 3398 (s), 3384 (s), 3027 (m), 2948 (s), 2926 (m), 2842 (m), 1742 (s), 1728 (s), 1494 (s), 1462 (m), 1452 (m), 1434 (s), 1337 (m), 1280 (s), 1266 (s), 1241 (s), 1204 (s), 1156 (m), 1122 (m), 1027 (s), 1022 (m), 1012 (m), 873 (m), 795 (s), 743 (m), 700 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.90 (bs, 1 H), 7.66 (d, 1 H, J = 7 Hz), 7.50–7.00 (m, 9 H), 6.90 (s, 1 H), 5.94 (s, 1 H), 4.80 (d, 1 H, J = 3 Hz), 3.99 (d, 1 H, J = 4 Hz), 3.85 (d, 1 H, J = 14 Hz), 3.75 (s, 3 H), 3.55 (d, 1 H, J = 11 Hz), 2.90 (m, 2 H), 2.74 (m, 2 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 171.4, 142.1, 140.9, 139.8, 135.2, 130.3, 128.7, 128.6, 128.2, 126.9, 121.5, 121.1, 119.3, 118.3, 114.7, 111.6, 110.7, 61.2, 59.3, 52.1, 51.6, 47.5, 30.7, 28.2, 24.7; EIMS m/z (rel inten) 401 (8), 400 (M^+, 30), 199 (26), 108 (79), 91 (100). Anal. Calcd for $C_{25}H_{24}N_2O_3$: C, 74.89; H, 6.08; N, 7.00. Found: C, 74.77; H, 5.81; N, 7.03.

27b: Into 3 mL of *N,N*-dimethylacetamide was placed 16.4 mg (40.9 μmol) of spiro ester **26**, and the solution was heated in an oil bath at 160 °C for 0.75 h. The resulting dark mixture was cooled, and the solvent was removed under high vacuum. Chromatography of the dark residue (flash column; eluting solvent: ether/hexane 1:1) yielded 9.80 mg of a white crystalline film (59%): TLC R_f = 0.36 (SiO_2, ether/hexane 1:1; CAS pale green/black); UV (ethanol) λ_{max} 290, 283, 222, 202, 192 nm; IR (NaCl) ν_{max} 3398 (s), 3384 (s), 3027 (m), 2948 (s), 2926 (m), 2842 (m), 1742 (s), 1728 (s), 1494 (s), 1462 (m), 1452 (m), 1434 (s), 1337 (m), 1280 (s), 1266 (s), 1241 (s), 1204 (s), 1156 (m), 1122 (m), 1027 (s), 1022 (m), 1012 (m), 873 (m), 795 (s), 743 (m), 700 (m) cm^{-1}.

Methyl 4-(3′-Furanyl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (12). To a flask containing an argon-flushed solution of 94.9 mg (0.24 mmol) of the N^b-benzylindoloazepine **27** in 10 mL of wet acetic acid was added 0.050 g of 10% palladium on charcoal. The vessel was degassed and saturated with hydrogen and the mixture hydrogenated with a positive pressure of hydrogen (via balloon). The reaction progress was monitored by TLC to show consumption of the starting material and formation of the product. When no more starting compound **27** remained, the mixture was filtered through Celite and the catalyst washed with three 5-mL portions of acetic acid. The solution was poured onto crushed ice and made strongly basic with saturated ammonium hydroxide. The organic material was extracted with ether (10 × 15 mL), washed with 15 mL of distilled water, and dried over magnesium sulfate. Concentration and chromatography (flash column; eluting solvent: ethyl acetate/triethylamine 10:0.4) afforded 37.7 mg of product **12** as a white crystalline film (52%): TLC R_f = 0.46 (SiO_2, ethyl acetate/triethylamine 10:0.4; CAS pale green/black); UV (ethanol) λ_{max} 292, 284. 276, 222, 206 nm; IR (NaCl) ν_{max} 3389 (m), 3134 (w), 3045 (w), 2921 (m), 1719 (s), 1459 (m), 1429 (w), 1334 (w), 1263 (m), 1198 (m), 1151 (m), 1020 (m), 1003 (w), 902 (w), 866 (m), 790 (w), 730 (s) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 8.17 (bs, 1 H), 7.48 (d, 1 H, J = 8 Hz), 7.30–7.10 (m, 5 H), 6.36 (s, 1 H), 4.57 (d, 1 H, J = 6 Hz), 4.11 (d, 1 H, J = 6 Hz), 3.64 (s, 3 H), 3.11–2.91 (m, 4 H), 2.27 (bs, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 172.0, 142.8, 140.0, 135.3, 130.2, 128.8, 125.8, 121.8, 119.5, 118.2, 114.5, 110.7, 110.0, 54.6, 53.6, 52.1, 45.4, 26.9; EIMS m/z (rel inten) 311 (3), 310 (M^+, 21), 203 (11), 202 (75), 170 (10), 154 (8), 142 (25), 129 (10), 115 (11), 108 (16), 71 (100).

Bridged Indoloazepines 28 and 29 from Furanylazepine 12. To a sealed tube vessel containing an argon-flushed solution of 37.7 mg (0.121 mmol) of amine **12** in 10 mL of THF was added 7.5 μL (0.133 mmol) of acetaldehyde. The solution was stirred at room temperature for 24 h and then concentrated. Column chromatography (flash column; eluting solvent: ethyl acetate/triethylamine 10:0.4) afforded 27.7 mg of less-polar product isomer **28** as a white crystalline film (57%) and 14.0 mg of the more-polar isomer **29** as a white crystalline film (29%). Less-polar isomer **28**: TLC R_f = 0.56 (SiO_2, ethyl acetate/triethylamine 10:0.4; CAS blue/aqua green then fade to yellow/green); UV (ethanol) λ_{max} 324, 298, 222, 206 nm; IR (NaCl) ν_{max} 3366 (m), 3049 (w), 2977 (w), 2942 (m), 1730 (m), 1665 (s), 1605 (s), 1480 (m), 1462 (s), 1432 (s), 1372 (m), 1282 (s), 1241 (s), 1181 (s), 1151 (w), 1122 (m), 1098 (m), 1026 (s), 907 (m), 871 (m), 829 (w), 782 (m), 734 (s) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 9.28 (bs, 1 H), 7.36 (d, 2 H, J = 14 Hz), 7.10 (m, 2 H), 6.93 (t, 1 H), 6.87 (d, 1 H, J = 7 Hz), 6.48 (s, 1 H), 5.22 (s, 1 H), 3.73 (m, 1 H), 3.60 (s, 3 H), 2.93 (m, 2 H), 2.25 (m, 2 H), 1.46 (d, 3 H, J = 14 Hz); EIMS m/z (rel inten) 337 (12), 336 (M^+, 49), 293 (16), 280 (35), 266 (12), 248 (100), 220 (77), 191 (33), 165 (17), 154 (9), 128 (17). More-polar isomer **29**: TLC R_f = 0.39 (SiO_2, ethyl acetate/triethylamine 10:0.4; CAS blue then fade to yellow); UV (ethanol λ_{max} 322, 298, 204 nm; IR (NaCl) ν_{max} 3365 (m), 2924 (m), 2876 (w), 1730 (w), 1671 (s), 1605 (s), 1480 (m), 1462 (s), 1432 (m), 1378 (m), 1283 (s), 1229 (s), 1181 (s), 1151 (w), 1098 (m), 1020 (m), 871 (m), 728 (s) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 9.16 (bs, 1 H), 7.39 (d, 2 H, J = 14 Hz), 7.20 (m, 2 H), 6.94 (t, 1 H), 6.86 (d, 1 H, J = 7 Hz), 6.48 (s, 1 H), 5.16 (s, 1 H), 3.71 (m, 1 H), 3.61 (s, 3 H), 3.07 (m, 1 H), 2.93 (m, 1 H), 2.15 (m, 2 H), 1.19 (d, 3 H, J = 7 Hz); EIMS m/z (rel inten) 337 (13), 336 (M^+, 54), 293 (15), 280 (36), 266 (13), 248 (100), 221 (17), 220 (78), 191 (33), 165 (17), 154 (8), 128 (17).

Attempted Quaternization and Rearrangement of the Bridged Azepines 28 and 29. To a flask containing an argon-flushed solution of 41.7 mg (0.12 mmol) of bridged azepines **28**

and **29** in 10 mL of dry THF was added 0.015 mL (0.122 mmol) of benzyl bromide. The pale yellow solution was stirred at 23 °C for 24 h, but no quaternary salt was observed by TLC or by precipitation in the reaction flask. The reaction mixture was then concentrated and dissolved in 25 mL of toluene. The golden solution was heated at reflux for 24 h. Again no quaternary product was observed. To the toluene solution was added 0.042 mL (0.24 mmol) of diisopropylethylamine and heating continued at reflux. Mass spectral analysis of the reaction mixture provided peaks for the starting material and complex decomposition fragments.

Attempted Condensation and Rearrangement of the Furanylazepine 27. To a sealed tube vessel containing an argon-flushed solution of 0.543 g (1.35 mmol) of **27** in 50 mL of dry toluene was added 4.23 mL (13.5 mmol) of acetaldehyde. The solution was heated in an oil bath at 120 °C for 6 h and then cooled and concentrated. The resulting red solution did not contain any of the desired tetracyclic product **9** when examined by TLC or mass spectral analysis.

Methyl 3-(3′-Furanyl)prop-2-en-1-oate (36). To a flask containing 150 mL of dry dichloromethane were added 25 g (0.075 mol) of (carbomethoxymethylene)triphenylphosphorane and 6.21 mL (0.075 mol) of 3-furaldehyde. The red solution was stirred for 2 h and then adsorbed on silica and chromatographed (dry gravity column; eluting solvent: ether/hexane 1:2.5) to yield 12.0 g of ester **36** as a semicrystalline oily white solid (95%). A sample for elemental analysis was prepared by high-vacuum sublimation: 90–95 °C; mp >23 °C; TLC R_f = 0.65 (SiO_2, ether/hexane 1:1; CAS black/green fade golden); UV (ethanol) λ_{max} 274, 249, 235, 221, 215 nm; IR (NaCl) ν_{max} 3140 (w), 3120 (w), 2947 (m), 1709 (s), 1640 (s), 1502 (w), 1426 (m), 1315 (s), 1267 (s), 1212 (s), 1177 (s), 1149 (s), 1073 (m), 1011 (m), 962 (m), 866 (s), 783 (m), 665 (m), 582 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.65 (s, 1 H), 7.60 (d, 1 H; J = 16 Hz), 7.43 (s, 1 H), 6.59 (s, 1 H), 6.18 (d, 1 H; J = 15 Hz), 3.78 (s, 3 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 167.2, 144.4, 144.3, 134.7, 122.7, 117.8, 107.5, 51.4; EIMS m/z (rel inten) 152 (M^+ 80), 124 (31), 121 (94), 111 (3), 109 (10), 95 (11), 93 (50), 88 (10), 86 (66), 84 (100), 81 (12); high resolution MS, EI ionization, calcd for $C_8H_8O_3$ 152.0473; found 152.0468. Anal. Calcd for $C_8H_8O_3$: C, 63.15; H, 5.30. Found: C, 61.85; H, 3.96.

Ethyl *trans*-3-(3′-Furanyl)prop-2-en-1-oate (37). To a flask containing 150 mL of dry dichloromethane were added 25 g (0.072 mol) of (carbomethoxymethylene)triphenylphosphorane and 6.21 mL (0.072 mol) of 3-furaldehyde. The red solution was stirred for 2 h and then adsorbed on silica and chromatographed (dry gravity column; eluting solvent: ether/hexane 1:2.5) to yield 11.4 g of ester **37** as a crystalline oily white solid (96%). A sample for elemental analysis was prepared by high vacuum sublimation; 90–95 °C; mp 40 °C; TLC R_f = 0.70 (SiO_2, ether/hexane 1:1; CAS black/green fade to gold); UV (ethanol) λ_{max} 272, 252, 228, 216 nm; IR (NaCl) ν_{max} 3132 (m), 3116 (m), 2976 (s), 2900 (m), 1715 (m), 1694 (s), 1655 (m), 1640 (s), 1564 (w), 1510 (w), 1483 (w), 1364 (m), 1315 (s), 1272 (m), 1218 (s), 1185 (s), 1148 (s), 1034 (m), 1007 (w), 980 (w), 861 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.65 (s, 1 H), 7.60 (d, 1 H, J = 16 Hz), 7.40 (s, 1 H), 6.60 (s, 1 H), 6.15 (d, 1 H, J = 15 Hz), 4.22 (q, 2 H), 1.30 (t, 3 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 166.6, 144.3, 144.1, 134.3, 122.8, 118.4, 107.6, 60.1, 14.2; EIMS m/z (rel inten) 166 (M^+ 64), 138 (22), 121 (100), 110 (31), 96 (12), 94 (12), 93 (40), 82 (32); high resolution MS, EI ionization; calcd for $C_9H_{10}O_3$ 166.0630, found 166.0623. Anal. Calcd for $C_9H_{10}O_3$: C, 65.09; H, 6.07. Found: C, 64.94; H, 6.03.

***trans*-3-(3′-Furanyl)prop-2-en-1-ol (38).** An amount of 13.66 g (0.082 mol) of ester **37** was dissolved in dry tetrahydrofuran and cooled to −78 °C with a dry ice/acetone bath. To this solution was cannulated 172.6 mL (0.173 mol) of a 1 M DIBAL-H solution in dichloromethane. The reaction mixture was stirred at −78 °C for 2 h and then warmed to 23 °C and stirred for 3 h. The remaining hydride was quenched with 10% HCl solution and the mixture extracted with ether (10 × 50 mL). The ether extracts were washed with saturated bicarbonate (2 × 150 mL), dried with magnesium sulfate and concentrated to yield 9.39 g of a light yellow oil (92%). The resulting oil could be high-vacuum flash distilled with significant polymerization to yield a clear oil: bp 56–57 °C (0.05 mmHg); lit.[10] 55–56 °C (0.05 mmHg); TLC R_f = 0.31 (SiO_2, ether/hexane 2:1; CAS purple fade to black); UV (ethanol) λ_{max} 240, 230, 212 nm; IR (NaCl) ν_{max} 3327 (s), 2919 (w), 2864 (m), 1661 (w), 1502 (m), 1364 (w), 1156 (s), 1080 (w), 1066 (m), 1011 (s), 949 (s), 866 (s), 769 (s), 720 (w), 590 (s), 478 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.38 (s, 1 H), 7.34 (s, 1 H), 6.50 (s, 1 H), 6.40 (d, 1 H, J = 18 Hz), 6.07–6.01 (m, 1 H), 4.20 (d, 2 H, J = 5 Hz), 3.15 (s, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 143.5, 140.4, 128.5, 123.8, 121.1, 107.8, 63.4; EIMS m/z (rel inten) 124 (M^+ 84), 107 (10), 96 (31), 95 (100), 82 (54), 81 (93), 77 (40).

***trans*-3-(3′-Furanyl)prop-2-en-1-al (30).** To a solution of 3.70 g (0.029 mol) of alcohol **38** in 200 mL of dry chloroform was added 10.23 g (0.118 mol) of manganese dioxide (activated by azeotrope distillation with benzene and oven drying at 250 °C for 5 days).[11] The mixture was heated at reflux for 20 h and then filtered through Celite and chromatographed (gravity column; eluting solvent: ether/hexane 2:1) to afford 3.04 g of aldehyde **30** as a yellow oil (85%). The oil could be high-vacuum distilled at 61 °C (0.50 mmHg); (lit. 0.1 mmHg, 58 °C)[10] to yield a clear oil (81%): TLC R_f = 0.51 (SiO_2, ether/hexane 2:1; CAS light green faded to golden); UV (ethanol) λ_{max} 289, 253, 222, 217 nm; IR (NaCl) ν_{max} 3120 (w), 2816 (w), 2729 (w), 1673 (s), 1623 (s), 1605 (w), 1505 (m), 1139 (s), 1114 (s), 1071 (m), 1015 (m), 965 (m), 860 (s), 785 (m), 735 (m), 592 (s) cm^{-1}; 270-MHz ^1H NMR (CDC l_3) δ 9.75 (d, 1 H, J = 4 Hz), 7.80 (s, 1 H), 7.50 (d, 1 H, J = 8 Hz), 7.35 (d, 1 H, J = 6 Hz), 6.70 (s, 1 H), 6.45 (dd, 1 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 192.8, 145.0, 144.7, 141.8, 128.8, 122.8, 107.5; EIMS m/z (rel inten) 123 (12), 122 (M^+ 100), 94 (44), 93 (25), 68 (23), 66 (75), 65 (75), 63 (20).

Dimethyl 5-(3′-Furanyl)-3-(phenylmethyl)-2,3,3a,4,5,6-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazole-6,6-dicarboxylate (31a,b). To 0.9443 g (0.214 mmol) of the hydrochloride of diester **21** suspended in 70 mL of dry benzene was added 0.341 g (0.279 mmol) of aldehyde **30** and 1.0 g of molecular sieve powder. This mixture was flushed with argon, and after addition of 0.026 mL of boron trifluoride etherate, the reaction mixture was heated at reflux for 5 days. The dark solution was then filtered and the filtrate washed with methanol and concentrated. The resultant brown residue was dissolved in dichloromethane and neutralized with saturated ammonium hydroxide, and the aqueous phase was extracted with 5 × 20 mL of dichloromethane. Drying with magnesium sulfate and chromatography (Chromatatron: 4-mm plate; eluting solvent: ether/hexane 1:1) afforded 1.04 g (64%) of a mixture of furan epimers of **31a,b** as a white foam. A pure sample of the less-polar epimer **31a**, which could be isolated for spectroscopic characterization and a crystallization from methanol, afforded a sample which contained 0.5 mol of methanol for elemental analysis: mp 127 °C; TLC **31a** R_f = 0.25 (SiO_2, ether/hexane 3:2; CAS very light yellow fade golden), TLC **31b** R_f = 0.22 (SiO_2, ether/hexane 3:2, CAS very light yellow fade golden); UV (ethanol) λ_{max} 268, 222, 206 nm; IR (NaCl) ν_{max} 2946 (w), 2792 (w), 1733 (s), 1566 (w), 1447 (m), 1430 (m), 1334 (w), 1239 (s), 1204 (m), 1168 (w), 1061 (m), 1091 (m), 870 (w), 746 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 7.70 (t, 2 H), 7.50–7.10 (m, 9 H), 6.50 (m, 1 H), 4.66 (d, 0.5 H, J = 13 Hz), 4.28 (dd, 0.5 H), 4.04 (d, 1 H), 3.88 (s, 0.5 H), 3.78 (s, 3 H), 3.75 (s, 0.5 H), 3.62 (s, 3 H), 3.60–3.50 (m, 0.5 H), 3.40–3.15 (m, 1.5 H), 3.10–2.80 (m, 1 H), 2.50–2.00 (m, 1.5 H), 1.98–1.65 (m, 1.5 H), 1.24 (t, 0.5 H), 1.04 (t, 0.5 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 180.3, 169.4, 168.2, 153.7, 146.6, 141.8, 141.5, 138.8, 128.7, 128.3, 128.2, 127.9, 127.1, 126.3, 124.5, 121.5, 121.2, 111.2, 66.8, 65.5, 62.0, 58.1, 53.2, 52.2, 34.5, 33.2, 31.9, 29.6; EIMS m/z (rel inten) 485 (2), 484 (M^+ 8), 425 (7), 390 (11), 274 (8), 267 (13), 259 (3), 167 (6), 155 (3), 134 (5), 105 (3), 92 (6), 91 (100), 75 (25). Anal. Calcd for $C_{29}H_{28}N_2O_5$: C, 70.78; H, 6.04; N, 5.59. Found: C, 70.69; H, 5.98; N, 5.24.

Methyl 5-(3′-Furanyl)-3-(phenylmethyl)-2,3,3a,4,5,7-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (9). (a) To 0.466 g (1.45 mmol) of amino ester **25**, dissolved in 50 mL of dry toluene, was added 0.341 g (2.79 mmol) of 3-(3′-furanyl)-prop-2-enal (**30**) and 0.5 g of molecular sieve powder. This mixture was flushed with argon and after addition of 0.018 mL (3% mol equiv) of boron trifluoride etherate, the reaction mixture was heated at reflux for 5 days. The dark solution was then filtered the filtrate washed with methanol and concentrated. The resultant brown residue was dissolved in dichloromethane and neutralized with saturated ammonium hydroxide and the aqueous

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phase extracted with 5 × 20 mL of dichloromethane. Drying with magnesium sulfate and chromatography (Chromatotron: 4-mm plate; eluting solvent: ether/hexane 1:7) afforded 0.321 g of product **9** as a white foam (52%). Trituration with methanol and recrystallization from methanol provided a sample for elemental analysis and a crystal suitable for single crystal X-ray analysis: mp 81–83 °C; TLC for **9** R_f = 0.76 (SiO_2, ether/hexane 1:1; CAS blue faded to yellow); UV (ethanol) λ_{max} 324, 298, 224, 208 nm; IR (NaCl) ν_{max} 3367 (w), 2942 (w), 2906 (w), 2792 (w), 1667 (s), 1601 (s), 1458 (m), 1428 (m), 1374 (w), 1338 (w), 1272 (m), 1231 (s), 1201 (s), 1117 (m), 1081 (w), 1051 (w), 866 (w), 740 (m), 692 (m), 590 (m) cm^{-1}; 270-MHz ^1H NMR ($CDCl_3$) δ 9.35 (s, 1 H), 7.46–7.20 (m, 7 H), 7.15 (t, 1 H, J = 9 Hz), 7.06 (d, 1 H, J = 8 Hz), 6.84 (dt, 2 H), 6.46 (s, 1 H), 4.19 (d, 1 H; J = 5 Hz), 4.12 (d, 1 H; J = 12 Hz), 3.75 (s, 3 H), 3.64 (d, 1 H, J = 12 Hz), 3.37 (d, 1 H, J = 5 Hz), 2.71 (m, 1 H), 2.55 (m, 1 H), 2.29 (d, 1 H), 2.10 (m, 1 H), 1.70–1.46 (m, 2 H); 67.9-MHz ^{13}C NMR ($CDCl_3$) δ 168.8, 166.6, 142.8, 141.9, 139.9, 139.1, 138.1, 129.6, 128.8, 128.2, 127.7, 126.9, 122.0, 120.5, 111.5, 109.2, 96.3, 66.4, 58.6, 55.7, 50.9, 50.7, 50.5, 43.0, 32.5, 30.1; EIMS m/z (rel inten) 426 (M^+ 17), 400 (10), 374 (23), 342 (6), 293 (15), 241 (26), 210 (10), 172 (20), 149 (13), 146 (60), 131 (16), 91 (100). Anal. Calcd for $C_{27}H_{26}N_2O_3$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.43; H, 6.45; N, 6.08.

(b) Into 3 mL of *N,N*-dimethylacetamide were placed 37.8 mg (78.2 μmol) of diesters **31a,b**, 4.30 mg (0.10 mmol) of lithium chloride, and 3.20 mg (23.4 μmol) of triethylamine hydrochloride. The mixture was heated in an oil bath at 130 °C for 0.75 h. The mixture was cooled, 5 mL brine and 5 mL saturated ammonium hydroxide were added and then the dark solution was extracted with ether (10 × 5 mL). The ether extracts were washed with water (5 mL), dried with magnesium sulfate, and concentrated. Chromatography of the dark oil (flash column; eluting solvent: ethyl acetate/hexane 1:5) yielded 15.9 mg of a white crystalline film (48%): TLC for **9** R_f = 0.76 (SiO_2, ether/hexane 1:1; CAS blue fade yellow); UV (ethanol) λ_{max} 324, 298, 224, 208 nm; IR (NaCl) ν_{max} 3367 (w), 2942 (w), 2906 (w), 2792 (w), 1667 (s), 1601 (s), 1458 (m), 1428 (m), 1374 (w), 1338 (w), 1272 (m), 1231 (s), 1201 (s), 1117 (m), 1081 (w), 1051 (w), 8 66 (w), 740 (m), 692 (m), 590 (m) cm^{-1}.

Acknowledgment. This work was supported by the National Cancer Institute through research grant R01 12010. We are indebted to Mr. Richard Grazul for mass spectra and Dr. P. Keller of Norwich Eaton Pharmaceuticals for high-resolution mass spectra. We thank Prof. K. Ahmed for an X-ray structure determination.

Supplementary Material Available: Copies of ^1H NMR spectra for all intermediates (33 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.