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Syntheses of Strychnan- and Aspidospermatan-Type Alkaloids. 9.[1] The Enantioselective Generation of Tetracyclic ABCE Intermediates by a Tandem Condensation, [3,3]-Sigmatropic Rearrangement, and Cyclization Sequence

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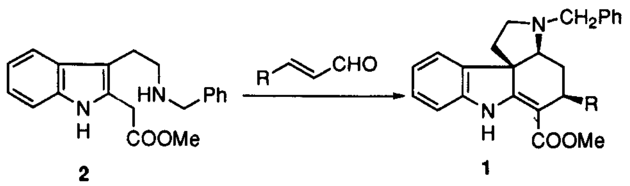
Reactions of substituted acroleins with the tryptophan-derived benzyl 2-(benzylamino)-3-[3-[2-[(methoxycarbonyl)methyl]indolyl]]propionate gave tetracyclic hexahydro-1*H*-pyrrolo[2,3-*d*] intermediates with stereoselective placement of substituents for cyclization to pentacyclic *Strychnos* alkaloids. The benzyl ester moiety was readily removed by formation of a corresponding nitrile and reduction, thus providing enantioselective syntheses of the tetracyclic compounds.

In 1992, Rodney Parsons found in our laboratories a remarkable new condensation, [3,3]-sigmatropic rearrangement, and cyclization reaction sequence (Scheme 1).[2] It provides, in one operation and with complete diastereoselectivity, tetracyclic intermediates **1** for syntheses of *Strychnos* alkaloids[3] by the acid-catalyzed reaction of an N^b-alkyl-2-[(methoxycarbonyl)methyl-]tryptamine derivative **2** with α,β-unsaturated aldehydes.[4,5] In this paper, we report a more detailed study of the scope of this reaction and its extension to the enantioselective generation of tetracyclic ABCE *Strychnos* alkaloid precursors.

For optimization of this transformation crotonaldehyde was chosen as a model aldehyde, with variations of the acid catalyst. In addition to the desired product **1a**, four other products were generated in these reactions (Scheme 2). Best yields of the tetracyclic product **1a** were obtained at 70 °C in benzene, with benzoic acid and magnesium sulfate. At elevated temperatures, some cyclization of the amino ester **2** to the lactam **3** was always found (Table 1). In addition, the Diels−Alder reaction product of a crotonaldehyde and amine **2** derived enamine, with crotonaldehyde, furnished the aldehyde **4**. While the other two products **5** and **6** are formally derived, respectively, from cyclization of the aldehyde **4** and from its condensation with a third equivalent of crotonaldehyde, the actual formation of these products is more likely to arise by alternative condensations. Thus, *N*,*N*-dibenzyl-2-[(methoxycarbonyl)methyl]tryptamine[2] failed to react with crotonaldehyde under the same reaction conditions, and prolonged heating of the aldehyde **4** in toluene led only to a retro-Diels−Alder reaction and cyclization to the lactam **3**. For the formation of products **5** and **6**, condensation α to the ester function may be obtained by an intramolecular alkyl transfer from an initial *N*-benzyliminium salt. A subsequent second enamine formation and intramolecular Diels−Alder reaction would provide the tetracycle **5**, while an intermolecular Diels−Alder reaction of that enamine with a third equivalent of crotonaldehyde would lead to the formation of product **6**.

Scheme 1



Structure assignment to the aminocyclohexene **4** was derived from an H−H COSY spectrum, which clearly showed respective C−C connections. The stereochemistry of substitution of the cyclohexene ring is based on coupling constants $J_{H-H} = 10.8$ Hz for the three adjacent methine hydrogens.

The stereochemistry of the indoloazonine **5** was elucidated by its NOESY spectrum. NOE links between the acrylate hydrogen and the methyl and adjacent methine hydrogens indicate an *E* geometry for the acrylate double bond. NOE signals for interaction of the methyl group with the two methine hydrogens adjacent to N^b and the acrylate substituent and the NOE of the acrylate hydrogen with the methyl group and with its adjacent methine hydrogen establish the relative stereochemistry of substitution and the conformation of the cyclohexene ring.

In the triene **6** the *Z*,*E* diene ester moiety was revealed by $J = 11.3$ and 13.6 Hz coupling constants. Interestingly, the cyclohexenyl olefinic hydrogens appeared as a two-hydrogen singlet at δ 5.77. An H−C COSY spectrum showed coupling of the δ_H 5.77 peak to the δ_C 129.04 and 125.54 ppm olefinic carbon peaks.

Variations of substituents on the acrolein reactant (Table 2) revealed that formation of the tetracyclic products **1** was only incompatible with simultaneous α- and β-substitution of the unsaturated aldehyde (last entry).[6,7] In these examples diastereoselectivity for formation of cis N^b- and R-substituents in the tetracyclic

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[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1997.

(1) Part 8: Kuehne, M. E.; Wang, T.; Seraphin, D. *J. Org. Chem.* **1996**, *61*, 7873.

(2) Parsons, R. L.; Berk, J. D.; Kuehne, M. E. *J. Org. Chem.* **1993**, *58*, 7482.

(3) For a review of *Strychnos* alkaloid syntheses see: Bosch, J.; Bonjoch, J.; Amat, M. Cordell, G. A., Ed. *Alkaloids (Academic Press)* **1996**, *48*, 75.

(4) Kuehne, M. E.; Xu, F. *J. Org. Chem.* **1993**, *58*, 7490.

(5) Kuehne, M. E.; Xu, F.; Brook, C. S. *J. Org. Chem.* **1994**, *59*, 7803.

(6) Compound **1j** was previously synthesized by two alternative methods. Spectroscopic comparisons with the product of the present method showed their identity. (a) Kuehne, M. E.; Matsko, T. H.; Bohnert, J. C.; Motyka, L.; Oliver-Smith, D. *J. Org. Chem.* **1981**, *46*, 2002. (b) Kuehne, M. E.; Kuehne, S. E. *J. Org. Chem.* **1993**, *58*, 4147.

(7) Only an insignificant amount of the disubstituted tetracyle **1k** was formed. Such compounds would be of interest for the synthesis of tubotaiwine-type alkaloids. Kuehne, M. E.; Frasier, D. A.; Spitzer, T. D. *J. Org. Chem.* **1991**, *56*, 2696.

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Scheme 2

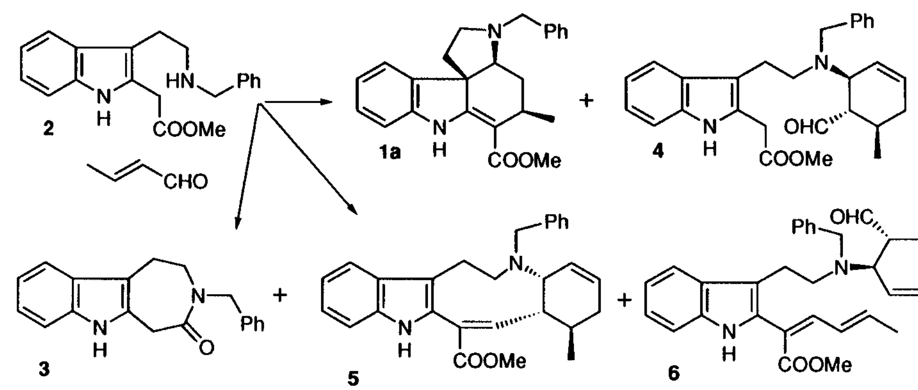


Table 1

	acids	*T* (°C)	solvents		yields (%) 1a	6	4[a]	5	3
1	$BF_3 \cdot Et_2O$	70	C_6H_6	4 Å M.S.[g]	30			23	10
2	CF_3CO_2H	35	CH_2Cl_2		8	7	32		
3	$B(OH)_3$	70	C_6H_6	4 Å M.S.	35		6	15	8
4	$B(OH)_3$	RT[b]	C_6H_6	4 Å M.S.	20[c]				
5	$PhCO_2H$	70	C_6H_6	$MgSO_4$	54[d]	T[e]	T	9	8
6	$PhCO_2H$	35	CH_2Cl_2	$MgSO_4$	40	8	12	7	6
7	$Et_3N \cdot HCl$	70	C_6H_6	$MgSO_4$	48	4	18	8	10
8	$(CHCO_2H)_2$[f]	70	C_6H_6	$MgSO_4$	35	6	14	T	14
9	PPTS	70	C_6H_6	$MgSO_4$	19		30		17
10	NaH_2PO_4	70	C_6H_6	$MgSO_4$	34		16	19	14
11	$PhCO_2H$	60	THF	$MgSO_4$	36		10	5	12
12	$PhCO_2H$	70	dioxane	$MgSO_4$	40	6	9	5	10

[a] **4** could be converted into **3** under conditions of reaction 1. [b] 2 days. [c] Recover 50% of **2**. [d] Add **2** slowly or fast. [e] T = trace. [f] Fumaric acid. [g] M.S. = molecular sieves.

Scheme 3

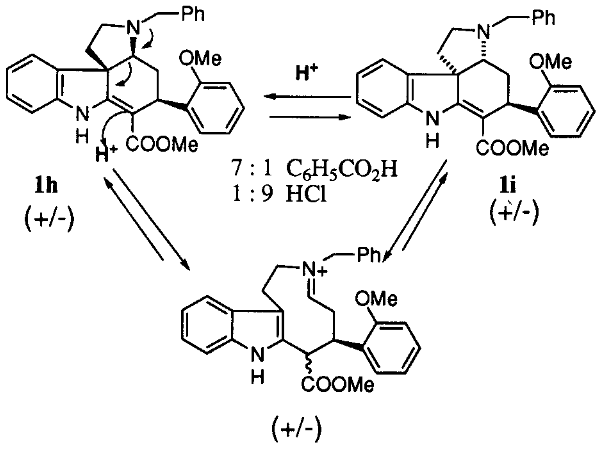
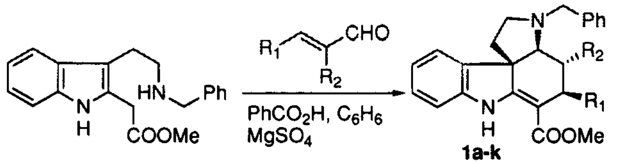
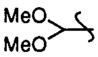
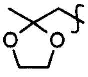
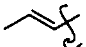
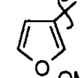
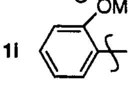


Table 2



Product	R_1	R_2	Yield (%)
1. **1a**	CH_3	H	54
2. **1b**[4]		H	66 (51% with BF_3)[4]
3. **1c, 1d**	COOEt	H	74 + 9 (C-15 epimer)
4. **1e**[5]		H	55 (30% with BF_3)[5]
5. **1f**		H	54
6. **1g**[2]		H	60 (52% with BF_3)[2]
7. **1h, 1i**		H	58 + 7.5 (C-15 epimer)
8. **1j**[6]	H	Et	57 + 40 (lactam **3**)
9. **1k**[7]	Me	Me	< 5 + 80 (lactam **3**)

products was >97–98%. It was somewhat diminished with ester and alkoxyaryl substituents (Table 2, entries 3 and 7) due to partial epimerization of the products. Thus, the major 2-methoxyphenyl-substituted product **1h**, or the minor epimer **1i**, could be equilibrated to a 7:1 mixture of N and methoxyaryl cis (**1h**) and trans (**1i**) compounds with benzoic acid in benzene, but an equilibration with aqueous HCl reversed the equilibrium to >9:1 of **1i**/**1h** (Scheme 3). The epimerization in these examples may be due to repulsion of a positive protonated N^b-amonium group and the positive ester or bulky aryl substituent, in accord with a ring E boatlike conformation, which had been established by molecular modeling calculations and by an X-ray structure determination for product **1g**.[2] Solvation of the amonium group would magnify this effect, as seen in the dramatic increase of **1i**/**1h** in aqueous acid.

Having demonstrated the generality of diastereoselective formation of the tetracyclic products **1**, it became of interest to explore their enantioselective formation. Initially, we examined the effect of some chiral N^b-substituents in the tryptamine esters **7**–**9** on the reaction. However, the diastereomeric ratio (N^b-substituent vs chiral centers of the tetracyclic products **10**–**13**) was quite low (Scheme 4, Table 3), prompting us to examine reactions of a tryptophan derived diester **14** with α,β-unsaturated aldehydes.

The key N^b-benzyl diester **14** was readily prepared from L-tryptophan benzyl ester (Scheme 5). Reductive benzylation of the tryptophan benzyl ester with benzaldehyde and N^b-acylation of the secondary amine **15** with BOC-anhydride (**16**) allowed installation of an indolic 2-malonyl substituent (**17**) by chlorination and reaction of the resulting chloroindoline imine with lithium dimethyl malonate and zinc chloride.[8] A final decar-

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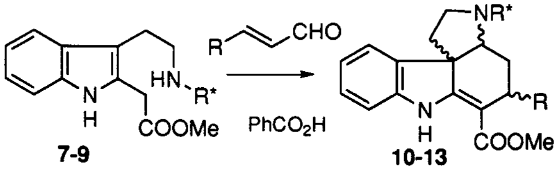
[8] This methodology was developed by J. Champoux and S. Cowen in our laboratories. It avoids the use of the potentially toxic thallium malonate. A full report of its scope will be published later.

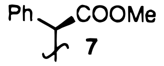
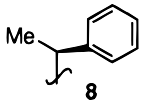
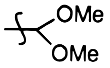
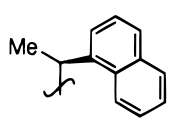
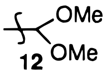
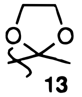
[9] Modified methodology of Krapcho et al.: Krapcho, A. P.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, E. G. E. Jr.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *43*, 138.

Scheme 4

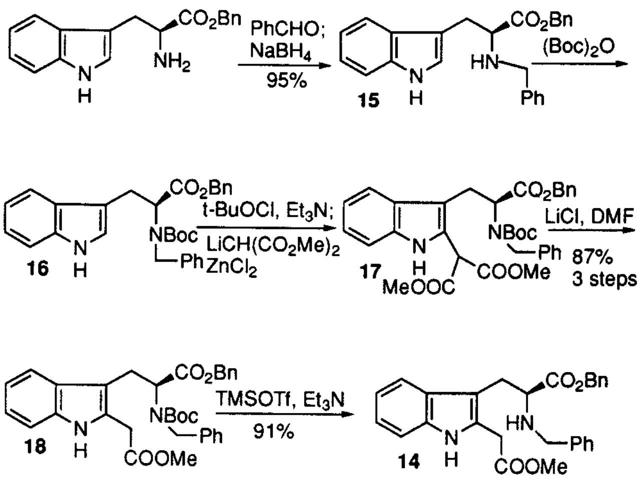


7-9 → 10-13

Table 3

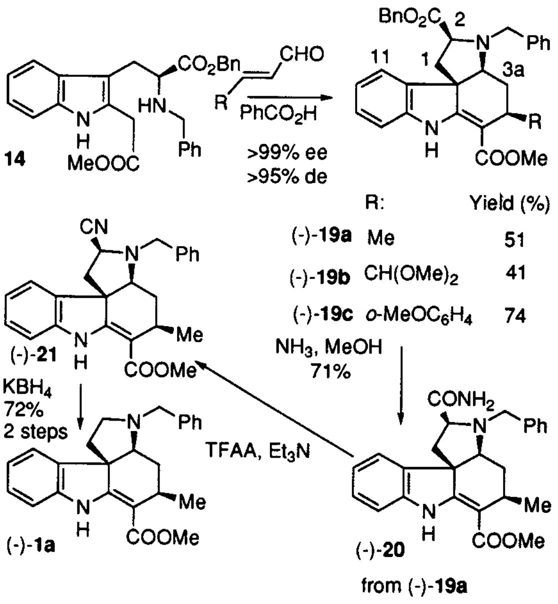
R*	R	ratio of isomers	yield (%)
 7	Me 10	5 : 1 : 1 : 0.9	35
 8	 11	3 : 2	40
 9	 12	5 : 4	30
	 13	3 : 2	26

Scheme 5



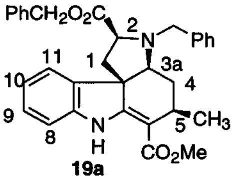
15, 16, 17, 18, 14

Scheme 6



14, (-)-21, (-)-1a, (-)-20

Table 4. NMR Correlations



19a

^{1}H no.	δ	H−H COSY	NOESY
1α	1.98	1β, 2	
1β	2.42	1α, 2	5-Me
2	3.74	1α, 1β	3a, 11, NCH$_2$Ph
3a	3.57	4α	2, 11, 4α, 4β, NCH$_2$Ph
4α	1.29	4β, 3a	5
4β	1.75	4α	5-Me, NCH$_2$Ph, 3a, 5
5	3.05	5-Me	4α, 4β
5-Me	1.47	5	4β, 1β
8	7.37−7.25	9	
9	7.11	10, 8	
10	6.77	11, 9	
11	6.67	10	3a, 2
CO$_2$Me	3.75		
NH	8.98		
PhCH$_2$O	4.90, 4.87	PhCH$_2$O	
PhCH$_2$N	3.98		4β, 3a, 2

bomethoxylation (**18**)[9] and urethane cleavage provided the diester **14** in 75% overall yield. No racemization could be detected by NMR using a chiral Eu shift reagent and comparison with the independently prepared racemic compound (±)-**14**.

On condensation of the tryptophan-derived diester **14** with crotonaldehyde, a single diastereomer of the tetracyclic product (−)-**19a** was generated (Scheme 6). Analogously, a condensation with 4,4-dimethoxycrotonaldehyde led selectively to the synthetically valuable tetracyclic acetal (−)-**19b**. The stereochemistry of these products was established by 2D-NOESY spectra (Tables 4, 5), which showed pertinent NOE's for H-3a/H-11, H-3a/H-2, H-2/H-11, and H-1b/C-5 CH$_3$ but no NOE for H-3a/C-5 CH$_3$ in product (−)-**19a** and H-3a/H-11, H-3a/H-2, H-2/H-11, but no NOE for the acetal hydrogen/H-2 or H-3a in product (−)-**19b**. The *o*-methoxyphenyl congener (−)-**19c** was obtained in relatively highest yield (74%) as the only isolated product.

The utility of this process depends, of course, on a facile removal of the tryptophan-derived benzyl ester substituent. This was readily achieved by conversion to an amide, (−)-**20**, its dehydration to a nitrile, (−)-**21**, and final reduction of the α-aminonitrile with potassium borohydride. Thus, the tetracyclic compound (−)-**1a**, $[\alpha]^{22}_D = -387$, was obtained with complete enantioselection, as demonstrated, again by comparison with the racemic compound, in an NMR-chiral europium shift reagent study. Exclusive formation of the tetracyclic ABCE enantiomer (−)-**1a** from L-tryptophan may be contrasted with the formation of an analogous tetracyclic ABCE *Strychnos* alkaloid precursor from L-tryptophan, using the *seco*-secamine type intramolecular Diels−Alder cyclization methodology, where primarily the *enantiomerically opposite* (unnatural) stereochemistry was obtained (70% ee).[10,11] On the other hand, enantioselective syntheses of tetracyclic ABCE intermediates, using chiral N^b-substituents and *seco*-secodine cyclizations, have provided the desired enantiomeric series of products with

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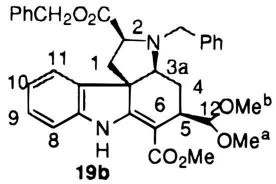
(10) Henin, J.; Massiot, G.; Vercauteren, J. *Tetrahedron Lett.* **1987**, *28*, 1271.

(11) An inventive photochemical cyclization, also starting from L-tryptophan as precursor, provided another noteworthy approach to such tetracyclic ABCE alkaloid intermediates. Winkler, J. D.; Scott, R. D.; Williard, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 8971.

Table 5. NMR Correlations



19b

	δ			
^{1}H no.	CDCl$_3$	C$_6$D$_6$	H−H COSY	NOESY
1α	1.99	1.83	1β, 2	
1β	2.22	2.37	1α, 2	12, OMe^a
2	3.77	3.79	1α, 1β	3a, 11, NCH$_2$Ph
3a	3.52	3.38	4α	4β, 11, NCH$_2$Ph
4α	1.20	1.03	4β, 3a, 5	
4β	2.22	2.26	4α	3a, 5, 12, OMe^b, NCH$_2$Ph
5	3.28	3.70	4α, 12	4β, OMe^a
8	6.75	6.18	9	
9	7.09	6.87	8, 10	
10	6.70	6.45	9, 11	
11	6.38	6.62	10	2, 3a
12	5.23	5.57	5	4β, 1β, OMe^a, OMe^b
CO$_2$Me	3.76	3.61		
NH	9.13	9.41		
OMe^a	3.29	3.37		1β, 12, OMe^b
OMe^b	3.53	3.59		4β. 12, OMe^a, NCH$_2$Ph
PhCH$_2$O	4.99	4.80, 4.77	PhCH$_2$O	
PhCH$_2$N	3.96, 4.03	3.93, 3.83	PhCH$_2$N	4β, 3a, 2, OMe^b

excellent to good selectivity (in contrast to the results shown in Table 3).[12−15]

An explanation of the remarkable diastereoselectivity found on formation of the racemic tetracycles **1** and the additional stereoselectivity introduced with the tryptophan-derived ester functionality leading to (−)-**19** can be derived from the proposed tandem condensation and [3,3]-sigmatropic rearrangement sequence, followed by a final indole−iminium cyclization step (Scheme 7). In support of this three-step pathway, one finds that the sequence is stopped after the first step if the diester **14** is condensed with an aryl aldehyde (rather than an olefinic aldehyde) and that four diastereomeric spiroindolenines **22**−**25** are then formed (Scheme 8). These diastereomers were readily recognized in an NMR spectrum of the total reaction product by comparison with the two diastereomeric products **26** and **27**, formed in a 2:1 ratio, from condensation of the tryptamine derived monoester **2** with benzaldehyde (Scheme 8).

On the other hand, with 4,4-dimethoxycrotonaldehyde only three analogous spiroindolenines **28**−**30** could be isolated, in a ratio of 11:17:10 (69% yield), accompanied by the tetracyclic product (−)-**19b** (22%). A fourth stereoisomer **31** (Scheme 7), with optimum geometry for a [3,3]-sigmatropic rearrangement, eludes capture and proceeds to formation of an indolic nine-membered ring enamine **32** (Scheme 7). In two of the alternative spiroindolenines (**29**, **30**) the olefinic functions are trans substituents on a five-memberd ring and thus unsuitable for the sigmatropic rearrangement. In the third spiroindolenine **28** (enantiomeric with **31** at all but the predetermined α-amino ester carbon), steric congestion of the benzyl, saturated ester and indolic moieties (**33**) hinders formation of the conformation required for the sigmatropic rearrangement. Formation of epimeric substitution (N^b, R trans) of the tetracyclic product (−)-**19** would require a boat rather than the chair conformation **34** for this rearrangement.

For the final cyclization step, which requires protonation of the nine-membered ring enamine **32**, a conformation of the indolic iminium intermediate **35**, analogous to that for the preceding sigmatropic rearrangement step, is clearly advantageous over the enantiofacial alternative **36**, where one encounters not only the congestion of ester, benzyl, and aryl substituents but also now the new enantiomerically fixed vicinal methyl ester and R [CH(OCH$_3$)$_2$] substituents would have to be axial on the incipient six-membered ring.

Under typical reaction conditions for the preparation of the tetracyclic products **1** (benzene, benzoic acid, MgSO$_4$, 70 °C), the initially generated three spiroindolenines that do not undergo a [3,3]-sigmatropic rearrangement (**28**−**30**) were not separated, but they could be identified by NMR. With prolonged heating (48 h) they reverted to starting materials and thus led to eventual generation of the tetracyclic product (−)-**19** through formation of the one uniquely reactive spiroindolenine diastereomer **31**.

The application of this new synthetic methodology to the enantioselective generation of (−)-*ent*-lochneridine, (−)-20-*epi*-lochneridine, and the Wieland−Gumlich aldehyde (and thus strychnine) will be presented in subsequent papers.

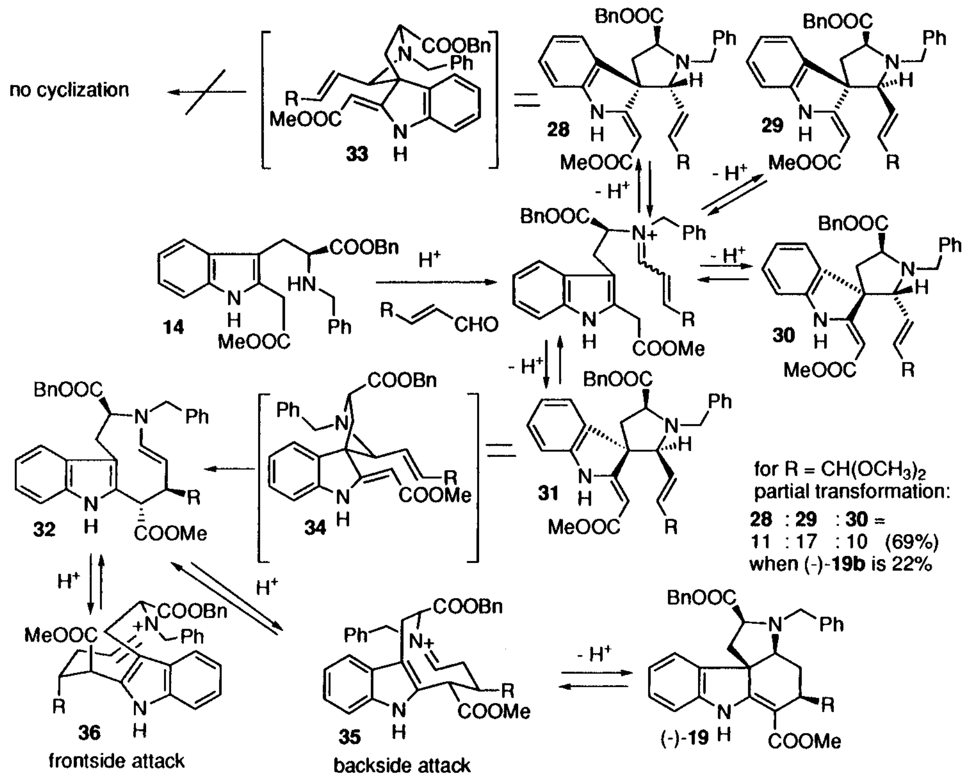
Experimental Section

General Procedure for the Preparation of the Tetracyclic Compounds 1a−k. A mixture of N^b-benzyl-2-[(methoxycarbonyl)methyl]tryptamine (**2**, 1 mmol),[2] a catalytic amount of acid from Table 1, but preferably benzoic acid (0.1 mmol), an unsaturated aldehyde from Table 2 (1.2−1.4 mmol), and 600 mg of freshly activated MgSO$_4$ in 8 mL of anhydrous solvent, under an atmosphere of Ar, was heated at 70−75 °C for 6−10 h. Filtration and concentration gave the crude product, which was dissolved in dichloromethane and washed with 2% Na$_2$CO$_3$. Chromatography on a silica gel column afforded the desired product. Products **1b**,**e**,**g**,**j** matched authentic samples in TLC, NMR, and IR spectra that are given in refs 2, 5, and 6. Respective yields are listed in Table 2.

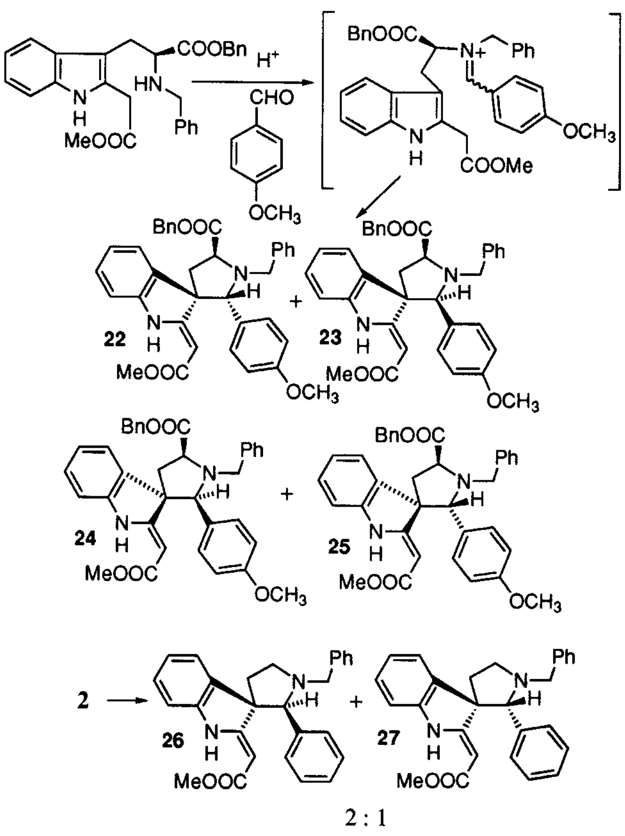
(±)-Methyl (3a*S,5*S**,11b*R**)-3-Benzyl-2,3,3a,4,5,7-hexahydro-5-methyl-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (1a).** Using the general procedure with crotonaldehyde, and with benzoic acid as catalyst, this product was obtained in 54% yield after eluting the crude reaction mixture from a silica gel column with CH$_2$Cl$_2$/hexane/Et$_2$O (3:6:1): TLC R_f = 0.22 (hexane/EtOAc 92:8; CAS blue); mp 209 °C (HCl salt); UV (EtOH) $\lambda_{\max}$ 324, 300, 228, 204 nm; IR (KBr) $\nu_{\max}$ 3369, 3057, 3029, 2949, 2920, 2868, 2788, 1674, 1610, 1465, 1435, 1292, 1277, 1236, 1215, 1190, 1149, 1230, 1103, 1049, 791, 742, 769 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.48 (s, 1 H), 7.41 (d, J = 7.4 Hz, 2 H), 7.34 (t, J = 7.4 Hz, 2 H), 7.26 (t, J = 7.4 Hz, 1 H), 7.16 (d, J = 7.3 Hz, 1 H), 7.15 (t, J = 7.7 Hz, 1 H), 6.86 (t, J = 7.4 Hz, 1 H), 6.82 (d, J = 7.6 Hz, 1 H), 4.20 (d, J = 13.3 Hz, 1 H), 3.78 (s, 3 H), 3.54 (d, J = 13.3 Hz, 1 H), 3.33 (d, J = 5.2 Hz, 1 H), 3.11 (m, 1 H), 2.92 (dd, J = 6.4, 9.2 Hz, 1 H), 2.56 (ddd, J = 5.0, 9.2, 12.2 Hz, 1 H), 2.20 (ddd, J = 6.4, 12.2, 12.2 Hz, 1 H), 1.89 (d, J = 14.0 Hz, 1 H), 1.72 (dd, J = 5.0, 12.2 Hz, 1 H), 1.47 (d, J = 7.3 Hz, 3 H), 1.41 (ddd, J = 5.2, 5.2, 14.0 Hz, 1 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.99, 166.28, 143.03, 139.79, 138.32, 127.69, 126.88, 121.57, 120.15, 109.18, 99.97, 66.89, 58.66, 55.41, 50.93, 50.89, 45.95, 33.34, 29.13, 21.77; MS m/z (relative intensity) 375 (4), 374 (M$^+$, 11), 283 (2), 241 (31), 226 (7), 209 (3), 180 (7), 167 (11), 154 (5), 146 (60), 134 (7), 117 (5), 107 (4), 91 (100). Anal. Calcd for C$_{24}$H$_{26}$N$_2$O$_2$·HCl·0.83H$_2$O: C, 67.66; H, 6.86; N, 6.58; Cl, 8.32. Found: C, 67.73; H, 6.70; N, 6.35, Cl, 8.13.

(±)-2-[(Methoxycarbonyl)methyl]-3-[2-[*N*-benzyl-*N*-(3*S,4*S**,5*R**)-3-(4-formyl-5-methylcyclohexenyl)amino]-**

Scheme 7



Scheme 8



ethyl]indole (4). Obtained in 32% yield with trifluoroacetic acid as catalyst: TLC R_f = 0.11 (hexane/EtOAc, 4:1; CAS green); UV (EtOH) $\lambda_{\max}$ 288, 224, 204 nm; IR (KBr) $\nu_{\max}$ 3403, 3059, 3027, 2952, 2923, 2873, 2852, 2830, 2707, 1725, 1459, 1436, 1440, 1435, 1342, 1310, 1265, 1233, 1165, 1123, 1027, 1014, 741 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.41 (d, J = 5.2 Hz, 1 H), 8.44 (s, 1 H), 7.32 (m, 5 H), 7.26 (m, 2 H), 7.12 (t, J = 7.3 Hz, 1 H), 7.04 (t, J = 7.3, 1 H), 5.83 (m, 2 H), 3.87 (d, J = 13.8 Hz, 1 H), 3.80 (d, J = 10.8 Hz, 1 H), 3.71 (s, 3 H), 3.67 (s, 2 H), 3.60 (d, J = 13.8 Hz, 1 H), 2.81 (m, 1 H), 2.72 (m, 1 H), 2.66 (m, 2 H), 2.24 (ddd, J = 5.2, 10.8, 10.8 Hz, 1 H), 2.14 (app d, J = 17.3 Hz, 1 H), 1.96 (m, 1 H), 1.71 (m, 1 H), 0.90 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 205.39, 171.05, 140.02, 135.68, 129.26, 128.91, 128.28, 128.00, 127.04, 126.69, 125.39, 121.75, 119.29, 118.46, 111.63, 110.73, 58.08, 57.93, 55.77, 52.26, 51.27, 33.94, 31.51, 29.47, 24.59, 19.62; MS *m/z* (relative intensity) 445 (2), 444 (M$^+$, 3), 242 (71), 202 (5), 172 (6), 156 (4), 142 (14), 123 (12), 120 (69), 91 (100); HRMS calcd for $C_{28}H_{32}N_2O_3$ 444.2413, found 444.2412.

Indoloazonine 5. This product was obtained in 23% yield using the general procedure and BF$_3$ etherate as catalyst, followed by chromatography on a silica gel column, eluting with CH$_2$Cl$_2$/hexane/Et$_2$O (3:6:1): TLC R_f = 0.27 (hexane/EtOAc, 4:1; CAS violet); UV (EtOH) $\lambda_{\max}$ 290, 226, 204 nm; IR (KBr) $\nu_{\max}$ 3387, 3060, 3025, 2948, 2922, 2840, 1714, 1604, 1493, 1460, 1436, 1435, 1239, 1153, 1141, 1047, 1028, 909, 738 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.93 (s, 1 H), 7.54 (d, J = 9.1 Hz, 1 H), 7.52 (d, J = 8.1 Hz, 1 H), 7.35 (t, J = 8.1 Hz, 1 H), 7.31 (m, 4 H), 7.21 (m, 1 H), 7.19 (dt, J = 1.0, 8.1 Hz, 1 H), 7.11 (dt, J = 0.8, 7.9 Hz, 1 H), 5.76 (m, 1 H), 5.71 (m, 1 H), 3.95 (d, J = 15.2 Hz, 1H), 3.88 (d, J = 15.2 Hz, 1 H), 3.79 (s, 3 H), 3.64 (m, 1 H), 3.17 (m, 1 H), 2.80 (m, 2 H), 2.72 (m, 1 H), 2.40 (ddd, J = 6.9, 6.9, 9.1 Hz, 1 H), 2.34 (app d, J = 18.7 Hz, 1 H), 1.80 (m, 1 H), 1.62 (app d, J = 18.7 Hz, 1 H), 0.92 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 166.85, 154.32, 141.21, 135.92, 128.92, 128.28, 128.16, 128.06, 127.46, 126.88, 126.48, 122.00, 119.18, 118.52, 115.78, 110.78, 59.78, 54.20, 52.17, 51.69, 47.90, 30.00, 23.33, 20.14; MS *m/z* (relative intensity) 426 (M$^+$, 2), 335 (2), 332 (3), 274 (7), 267 (3), 241 (4), 225 (4), 217 (2), 204 (2), 194 (7), 180 (6), 172 (56), 167 (6), 154 (6), 146 (10), 135 (3), 129 (3), 117 (4), 105 (6), 91 (100); HRMS calcd for $C_{28}H_{30}N_2O_2$ 426.2307, found 426.2300.

(±)-Methyl 2-[3-[2-[*N*-Benzyl-*N*-(3*S,4*S**,5*R**)-3-(4-formyl-5-methylcyclohexenyl)amino]ethyl]indol-2-yl]-2,4-hexadienoate (6).** This product was obtained in 8% yield using the general procedure and benzoic acid as catalyst: TLC R_f = 0.13 (hexane/EtOAc, 4:1; CAS green); UV (EtOH) $\lambda_{\max}$ 320, 268, 224, 204 nm; IR (KBr) $\nu_{\max}$ 3387, 3058, 3027, 2955, 2924, 2850, 2709, 1717, 1639, 1454, 1437, 1336, 1282, 1239, 1174, 1130, 1048, 1025, 980, 741 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.41 (d, J = 5.0 Hz, 1 H), 8.00 (s, 1 H), 7.50 (d, J = 11.3 Hz, 1 H), 7.37 (d, $J = 8.0$ Hz, 1 H), 7.28 (m, 6 H), 7.25 (t, $J = 7.5$ Hz, 1 H), 7.16 (t, $J = 7.3$ Hz, 1 H), 6.26 (qd, $J = 6.8, 13.6$ Hz, 1 H), 6.05 (dd, $J = 11.3, 13.6$ Hz, 1 H), 5.77 (s, 2 H), 3.79 (d, $J = 13.9$, 1 H), 3.74 (m, 1 H), 3.73 (s, 3 H), 3.52 (d, $J = 13.9$ Hz, 1 H), 2.75 (m, 2 H), 2.60 (m, 2 H), 2.20 (ddd, $J = 5.0, 10.9, 10.9$ Hz, 1 H), 2.12 (m, 1 H), 1.94 (m, 1 H), 1.78 (d, $J = 6.8$ Hz, 3 H), 1.69 (m, 1 H), 0.99 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.26, 167.58, 144.44, 141.53, 140.09, 136.05, 129.04, 128.80, 128.61, 128.20, 128.13, 127.92, 126.90, 125.54, 122.18, 120.89, 119.26, 119.10, 114.08, 110.83, 57.93, 57.69, 55.33, 52.11, 50.76, 33.92, 29.42, 25.15, 19.61, 18.92; MS m/z (relative intensity) 497 (1), 496 (M^+, 2), 374 (1), 274 (2), 268 (2), 255 (7), 242 (94), 222 (2), 208 (3), 194 (11), 181 (2), 179 (8), 167 (5), 154 (2), 146 (3), 142 (2), 123 (12), 120 (58), 105 (6), 91 (100); HRMS calcd for $C_{32}H_{36}N_2O_3$ 496.2726, found 496.2701.

(±)-Methyl (3aS*,5R* and 5S*,11bR*)-3-Benzyl-2,3,3a,4,5,7-hexahydro-5-(ethoxycarbonyl)-1H-pyrrolo[2,3-d]carbazole-6-carboxylate (1c and 1d). Using the general procedure, 3-formyl ethyl acrylate, and benzoic acid as catalyst, a 74% yield of the N^b-ethoxycarbonyl cis product **1c** was obtained, together with 9% of its C-5 epimer **1d**. For **1c**: TLC $R_f = 0.28$ (hexane/EtOAc/CH_2Cl_2, 6:1:3, CAS blue fades to gray); UV (EtOH) λ_{max} 322, 296, 226, 204 nm; IR (KBr) ν_{max} 3374, 3060, 3028, 2980, 2950, 2927, 2788, 1724, 1682, 1609, 1477, 1463, 1438, 1379, 1341, 1279, 1256, 1231, 1210, 1185, 1151, 1123, 1041, 747, 735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (s, 1 H), 7.34 (m, 4 H), 7.26 (m, 1 H), 7.14 (t, $J = 7.7$ Hz, 1 H), 7.04 (d, $J = 7.3$ Hz, 1 H), 6.86 (t, $J = 7.5$ Hz, 1 H), 6.83 (d, $J = 8.0$ Hz, 1 H), 4.23 (m, 1 H), 4.14 (d, $J = 13.1$ Hz, 1 H), 4.08 (m, 1 H), 3.84 (dd, $J = 2.4, 6.9$, 1 H), 3.76 (s, 3 H), 3.51 (d, $J = 13.1$ Hz, 1 H), 3.27 (d, $J = 4.2$ Hz, 1 H), 2.77 (dd, $J = 5.6, 8.0$ Hz, 1 H), 2.63 (d, $J = 13.9$ Hz, 1 H), 2.46 (m, 2 H), 1.58 (dd, $J = 4.1, 10.1$ Hz, 1 H), 1.51 (ddd, $J = 5.6, 5.6, 13.9$ Hz, 1 H), 1.21 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.59, 168.28, 167.25, 142.83, 138.48, 137.68, 129.17, 128.10, 127.80, 127.02, 121.42, 120.63, 109.39, 93.17, 65.02, 60.49, 58.04, 55.92, 51.08, 50.60, 43.81, 38.86, 30.79, 14.13; MS m/z (relative intensity) 433 (7), 432 (M^+, 7), 373 (2), 359 (2), 341 (2), 327 (2), 300 (15), 267 (2), 226 (4), 207 (3), 194 (6), 180 (8), 167 (10), 146 (52), 91 (100). Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.52; N, 6.48. Found: C, 71.92; H, 6.28; N, 6.48.

For the C-5 (S*)-epimer **1d**: TLC $R_f = 0.17$ (hexane/EtOAc/CH_2Cl_2, 6:1:3, CAS blue fades to gray); UV (EtOH) λ_{max} 324, 294, 224, 206 nm; IR (KBr) ν_{max} 3375, 3058, 3030, 2979, 2949, 2924, 2850, 2793, 1734, 1683, 1609, 1468, 1437, 1279, 1251, 1235, 1195, 1154, 1120, 1042, 746 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1 H), 7.39 (d, $J = 7.2$ Hz, 2 H), 7.34 (t, $J = 7.3$ Hz, 2 H), 7.27 (t, $J = 7.2$ Hz, 1 H), 7.16 (t, $J = 7.5$ Hz, 1 H), 7.05 (d, $J = 7.3$ Hz, 1 H), 6.87 (t, $J = 7.5$ Hz, 1 H), 6.83 (d, $J = 7.7$ Hz, 1 H), 4.19 (m, 1 H), 4.15 (m, 1 H), 4.08 (d, $J = 13.4$ Hz, 1 H), 3.73 (d, $J = 13.4$ Hz, 1 H), 3.72 (s, 3 H), 3.59 (dd, $J = 3.1, 10.7$, 1 H), 3.33 (d, $J = 3.1$, 1 H), 2.86 (dd, $J = 6.8, 7.8$ Hz, 1 H), 2.64 (ddd, $J = 4.9, 7.8, 11.8$ Hz, 1 H), 2.04 (ddd, $J = 2.2, 2.2, 13.4$, 1 H), 1.99 (ddd, $J = 6.8, 11.8, 11.8$ Hz, 1 H), 1.72 (dd, $J = 4.9, 11.8$ Hz, 1 H), 1.57 (ddd, $J = 4.1, 10.8, 13.4$ Hz, 1 H), 1.27 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.98, 167.55, 166.48, 142.90, 138.72, 136.92, 128.75, 128.24, 127.88, 127.02, 121.80, 120.71, 109.35, 94.02, 67.71, 60.40, 57.59, 55.86, 50.78, 49.84, 44.17, 37.92, 33.93, 14.17; MS m/z (relative intensity) 433 (4), 432 (M^+, 9), 299 (13), 226 (9), 194 (10), 180 (11), 166 (13), 154 (6), 146 (57), 134 (10), 117 (4), 107 (4), 91 (100).

(±)-Methyl (3aS*,5R*,11bR*)-3-Benzyl-2,3,3a,4,5,7-hexahydro-5-allyl-1H-pyrrolo[2,3-d]carbazole-6-carboxylate (1f). Using the general condensation procedure with 2,4-hexadienal and with benzoic acid as catalyst, a 54% yield of the tetracyclic product **1f** was obtained: TLC $R_f = 0.38$ (hexane/EtOAc, 9:1; CAS blue fade to violet); mp 140 °C (dec, HCl salt); UV (EtOH) λ_{max} 324, 298, 226, 208 nm; IR (KBr) ν_{max} 370, 3062, 3025, 2945, 2918, 2855, 2787, 1675, 1609, 1479, 1466, 1436, 1474, 1277, 1234, 1213, 1188, 1147, 1118, 1053, 744 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (s, 1 H), 7.42 (d, $J = 7.5$ Hz, 2 H), 7.33 (t, $J = 7.4$ Hz, 2 H), 7.25 (m, 1 H), 7.16 (m, 2 H), 6.87 (t, $J = 7.5$ Hz, 1 H), 6.82 (d, $J = 8.1$ Hz, 1 H), 6.00 (dd, $J = 4.8, 14.8$ Hz, 1 H), 5.45 (qd, $J = 6.3, 14.8$ Hz, 1 H), 4.19 (d, $J = 13.4$ Hz, 1 H), 3.76 (s, 3 H), 3.67 (s, br, 1 H), 3.53 (d, $J = 13.4$ Hz, 1 H), 3.32 (d, $J = 5.5$ Hz, 1 H), 2.89 (dd, $J = 6.4, 8.8$ Hz, 1 H), 2.55 (ddd, $J = 4.8, 8.8, 11.9$ Hz, 1 H), 2.26 (ddd, $J = 6.4, 11.9, 11.9$ Hz, 1 H), 2.03 (d, $J = 13.8$ Hz, 1 H), 1.73 (d, $J = 6.3$ Hz, 3 H), 1.62 (dd, $J = 4.8, 11.9$ Hz, 1 H), 1.42 (ddd, $J = 5.5, 5.5, 12.8$ Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.88, 166.23, 142.88, 139.88, 138.19, 136.34, 128.38, 128.14, 127.63, 126.73, 122.57, 121.55, 120.22, 109.14, 97.48, 66.22, 58.16, 55.56, 50.91, 50.77, 44.38, 36.80, 33.80, 17.73; MS m/z (relative intensity) 401 (5), 400 (M^+, 14), 332 (2), 309 (2), 267 (15), 254 (3), 222 (4), 208 (7), 199 (4), 194 (10), 180 (5), 175 (7), 167 (6), 154 (3), 146 (71), 134 (3), 117 (5), 91 (100). Anal. Calcd for $C_{26}H_{28}N_2O_2 \cdot 0.5CH_2Cl_2$: C, 71.85; H, 6.60; N, 6.32. Found: C, 72.06; H, 6.54; N, 6.37.

(±)-Methyl (3aS*,5-(S* and R*),11bR*)-3-Benzyl-2,3,3a,4,5,7-hexahydro-5-(2-methoxyphenyl)-1H-pyrrolo[2,3-d]carbazole-6-carboxylate (1h and 1i). The N^b/aryl cis product **1h** was obtained in 58% yield, using the general procedure with *o*-methoxycinamaldehyde and benzoic acid as catalyst, together with 7.5% of its C-5 (R*)-epimer **1i**.

For **1h**: TLC $R_f = 0.28$ (hexane/CH_2Cl_2/Et_2O, 7:2:1, CAS blue); mp 212−3 °C (HCl salt); UV (EtOH) λ_{max} 326, 298, 230, 206 nm; IR (KBr) ν_{max} 3364, 3058, 3026, 2950, 2916, 2837, 2789, 1672, 1608, 1487, 1476, 1464, 1435, 1276, 1293, 1215, 1188, 1125, 1028, 750, 733 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (s, 1 H), 7.30 (d, $J = 7.3$ Hz, 1 H), 7.23 (m, 2 H), 7.15 (m, 4 H), 6.89 (m, 4 H), 6.82 (m, 2 H), 4.47 (dd, $J = 3.7, 6.2$ Hz, 1 H), 3.97 (d, $J = 13.5$ Hz, 1 H), 3.82 (s, 3 H), 3.62 (s, 3 H), 3.37 (d, $J = 13.5$ Hz, 1 H), 3.30 (dd, $J = 3.7, 4.7$ Hz, 1 H), 2.66 (ddd, $J = 3.7, 3.7, 14.3$ Hz, 1 H), 2.49 (m, 1 H), 2.39 (m, 2 H), 1.76 (ddd. $J = 4.7, 6.2, 14.3$ Hz, 1 H), 1.61 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.09, 167.25, 157.63, 143.24, 139.90, 138.34, 134.27, 128.73, 128.01, 127.91, 127.64, 126.43, 126.32, 121.88, 120.48, 120.04, 110.42, 109.18, 96.46, 65.90, 57.20, 55.20, 55.12, 50.99, 50.19, 42.36, 34.99, 29.94; MS m/z (relative intensity): 467 (2), 466 (M^+, 6), 345 (2), 333 (15), 320 (3), 300 (8), 288 (5), 274 (8), 265 (6), 260 (6), 241 (3), 230 (3), 225 (6), 217 (3), 180 (3), 167 (3), 154 (3), 146 (44), 135 (9), 130 (2), 212 (3), 117 (4), 107 (4), 91 (100). Anal. Calcd for $C_{30}H_{30}N_2O_3 \cdot HCl \cdot 0.5H_2O$: C, 70.37; H, 6.30; N, 5.47; Cl, 6.93. Found: C, 70.29; H, 6.24; N, 5.41, Cl, 7.22.

For **1i**: TLC $R_f = 0.17$ (hexane/CH_2Cl_2/Et_2O, 7:2:1; CAS blue); mp 215−216 °C (HCl salt); UV (EtOH) λ_{max} 326, 296, 226, 204 nm; IR (KBr) ν_{max} 3374, 3057, 3024, 2939, 2839, 1676, 1607, 1493, 1476, 1464, 1437, 1288, 1278, 1232, 1200, 1119, 1027, 751, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (s, 1 H), 7.40 (d, $J = 7.4$ Hz, 2 H), 7.31 (t, $J = 7.4$ Hz, 2 H), 7.27 (d, $J = 7.3$ Hz, 1 H), 7.23 (m, 1 H), 7.16 (dt, $J = 1.1, 7.6$ Hz, 1 H), 7.12 (dt, $J = 1.6, 7.6$ Hz, 1 H), 6.96 (d, $J = 7.2$ Hz, 1 H), 6.85 (m, 4 H), 4.46 (s, br, 1 H), 3.95 (d, $J = 13.4$ Hz, 1 H), 3.85 (s, 3 H), 3.71 (d, $J = 13.4$ Hz, 1 H), 3.37 (s, 3 H), 3.30 (dd, $J = 4.4, 4.4$ Hz, 1 H), 2.83 (dd, $J = 8.1, 8.1$ Hz, 1 H), 2.72 (ddd, $J = 5.4, 8.1, 11.7$ Hz, 1 H), 2.26 (ddd, $J = 8.1, 11.7, 11.7$ Hz, 1 H), 2.02 (ddd, $J = 4.4, 4.4, 13.5$ Hz, 1 H), 1.80 (dd, $J = 5.4, 11.7$ Hz, 1 H), 1.71 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.00, 166.12, 156.73, 143.68, 139.76, 137.62, 135.07, 128.59, 128.17, 127.94, 127.68, 126.82, 126.42, 122.18, 120.40, 120.35, 110.51, 109.18, 98.02, 62.55, 56.95, 55.56, 55.47, 50.28, 49.41, 44.12, 35.11; MS m/z (relative intensity) 467 (3), 466 (M^+, 9), 345 (2), 333 (13), 320 (2), 300 (12), 288 (5), 274 (7), 265 (5), 260 (6), 240 (3), 230 (3), 225 (5), 217 (3), 209 (2), 180 (3), 167 (2), 154 (3), 146 (38), 135 (10), 130 (2), 121 (3), 117 (4), 107 (7), 91 (100). Anal. Calcd for $C_{30}H_{30}N_2O_3 \cdot HCl \cdot 0.5H_2O$: C, 70.37; H, 6.30; N, 5.47; Cl, 6.93. Found: C, 70.48; H, 6.03; N, 5.40; Cl, 7.19.

Equilibration of C-5 Aryl Products 1h and 1i with Benzoic Acid or HCl. a. A solution of 20 mg of the minor epimer **1i** and 2 mg of PhCOOH in 2 mL of dry benzene was heated at reflux for 6 h. The solution was diluted with ethyl acetate and washed with 5% Na_2CO_3 solution. The residue, obtained upon drying and concentration, was subjected to ^{1}H NMR analysis, showing a 7:1 ratio of **1h**/**1i**. Purification on a silica gel column gave 15 mg of the epimer **1h** (75% yield).

b. A solution of 20 mg of the 5S* epimer **1h** and three drops of 2 *N* HCl in 2 mL of THF−H_2O (4:1) was kept at rt for 5 h.

The solution was then basified with 10% Na_2CO_3 solution and extracted with ethyl acetate. Using the above workup procedure and NMR analysis of the product (**1h**/**1i** = 1:9), 17 mg of the C-5 (*R**)-epimer **1i** was obtained (85% yield).

***N*^{b}-(Benzyloxycarbonyl)-*N*^{b}-((*R*)-1-phenethyl)tryptamine.** To a solution of *N*^{b}-((*R*)-α-phenethyl)tryptamine, prepared by alkylation[12,17] of the corresponding amine with tryptophyl bromide, (4.0 g, 15 mmol) and Na_2CO_3 (2.4 g, 22.5 mmol) in 60 mL of THF and 20 mL of H_2O at 0 °C, was added CbzCl (2.9 mL, 19.5 mmol) dropwise. The solution was stirred at 0 °C for an additional 30 min and then at room temperature for 30 min. Water was added to the reaction mixture, and the aqueous phase was extracted with EtOAc. The residue, obtained upon drying and concentration, was purified on a silica gel column, eluting with Et_2O/hexane (1:1) to afford 5.8 g of the desired product (97% yield): TLC $R_f = 0.22$ (hexane/Et_2O 3:2; CAS brown); $[\alpha]^{30}_D = 60$ ($c = 0.3$, MeOH); IR (KBr) ν_{max} 3423, 3331, 3062, 3036, 2977, 2931, 2855, 1686, 1457, 1418, 1341, 1295, 1202, 1173, 1093, 1028, 987, 911, 769, 742, 699 cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1 H), 7.45−7.16 (m, 12 H), 7.07 (m, 2 H), 6.90 (s, br, 1 H), 6.65 (s, br, 1 H), 5.56 (s, br, 1 H), 5.23 (d, J = 12.4 Hz, 1 H), 5.19 (d, J = 12.4 Hz, 1 H), 3.20 (s, br, 2 H), 2.82 (s, br, 1 H), 2.55 (s, br, 1 H), 1.51 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.23, 136.79, 136.13, 128.51, 128.40, 128.01, 127.36, 121.83, 121.66, 119.17, 118.81, 113.44, 110.97, 67.39, 53.96, 29.65; MS *m/z* (relative intensity) 399 (M^+ + 1, 25), 264 (2), 203 (2), 196 (2), 159 (2), 143 (22), 130 (39), 120 (33), 105 (46), 91 (100). Anal. Calcd for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.19; H, 6.56; N, 6.77.

2-[(Methoxycarbonyl)methyl]-3-[2-(benzyloxycarbonyl)-(*R*)-1-(phenethylamino)ethyl]indole. To a solution of 6.5 g (16.3 mmol) of *N*^{b}-(benzyloxycarbonyl)-*N*^{b}-((*R*)-1-phenethyl)-tryptamine and 2.5 mL (17.93 mmol) of Et_3N in 150 mL of THF, at −78 °C, was added 2.1 mL (17.93 mmol) of *t*-BuOCl dropwise. The solution was stirred for another 40 min, 3.26 mL of a 1.0 M solution of $ZnCl_2$ in Et_2O (3.26 mmol) was introduced, and the reaction mixture was stirred for 5 min. A solution of 2.7 g (19.56 mmol) of lithium dimethyl malonate in 10 mL of THF was added dropwise, and the resulting solution was stirred for another 40 min at −78 °C and for 1 h at room temperature. The reaction was quenched by adding water, and the aqueous layer was extracted with EtOAc. The combined organic phase was twice washed with brine. The residue, obtained upon concentration, was pure enough for the next reaction.

The above diester product was taken into 100 mL of DMF, and 760 mg (17.93 mmol) of LiCl and 561 mg (4.08 mmol) of $Et_3N{\cdot}HCl$ were added. The solution was heated in a 130 °C oil bath for 4 h and cooled to room temperature. Water was added. The aqueous layer was extracted with ether several times. The combined organic phase was washed with water and brine several times. The residue, obtained upon concentration, was purified on a silica gel column (EtOAc/Hex, 1:4) to give 7.2 g of the monoester (85% yield).

For the diester: TLC $R_f = 0.5$ (hexane/EtOAc 3:2; CAS greenish); $[\alpha]^{31}_D = 50$ ($c = 0.4$, MeOH); IR (KBr) ν_{max} 3404, 3060, 3031, 2953, 1750, 1737, 1697, 1686, 1457, 1418, 1375, 1299, 1243, 1201, 1172, 1152, 1026, 908, 744, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, br, 1 H), 7.52−7.25 (m, 5 H), 7.14 (s, br, 2 H), 6.97 (s, br, 1 H), 6.88 (s, br, 1 H), 5.72 (s, br, 1 H), 5.33 (s, 2 H), 4.54 (s, br, 1 H), 3.77 (s, 3 H), 3.70 (s, 3 H), 3.22 (s, br, 1 H), 3.09 (s, br, 1 H), 2.86 (s, br, 1 H), 2.42 (s, br, 1 H), 1.58 (s, br, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 peaks due to rotomers) δ 167.49, 140.97, 136.51, 135.73, 128.49, 128.35, 128.10, 127.66, 127.42, 127.13, 126.81, 124.78, 122.38, 119.34, 118.67, 112.23, 110.92, 67.66, 65.16, 53.60, 52.95, 52.92, 43.42, 24.41, 16.59; MS *m/z* (relative intensity) 529 (M^+ + 1, 4), 393 (8), 274 (7), 261 (44), 258 (5), 228 (15), 200 (7), 172 (4), 169 (22), 154 (3), 140 (3), 120 (22), 105 (49), 91 (100). Anal. Calcd for $C_{31}H_{32}N_2O_6{\cdot}0.5H_2O$: C, 69.25; H, 6.18; N, 5.21. Found: C, 68.92; H, 5.84; N, 4.98.

For the mono ester: TLC $R_f = 0.37$ (hexane/EtOAc 7:3; CAS green); $[\alpha]^{27}_D = 45$ ($c = 0.5$, MeOH); IR (KBr) ν_{max} 3392, 3335, 3060, 3033, 2981, 2953, 1737, 1692, 1496, 1462, 1451, 1416, 1368, 1332, 1298, 1278, 1245, 1202, 1168, 1121, 1025, 743, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (s, br, 1 H), 7.49−7.14 (m, 11 H), 7.08 (s, br, 1 H), 6.95 (s, br, 1 H), 6.87 (s, br, 1 H), 5.68 (s, br, 0.7 H), 5.34 (s, br, 0.3 H), 5.29 (s, 2 H), 3.69 (s, 3 H), 3.34 (s, br, 1 H), 3.17 (s, br, 1 H), 3.05 (s, br, 1 H), 2.80 (s, br, 1 H), 2.39 (s, br, 1 H), 1.58 and 1.56 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.12, 135.53, 128.61, 128.48, 127.52, 121.78, 119.33, 118.39, 110.59, 53.78, 52.21, 31.13; MS *m/z* (relative intensity) 471 (M^+ + 1, 6), 366 (2), 335 (2), 279 (1), 216 (12), 202 (33), 195 (2), 183 (1), 170 (4), 156 (4), 142 (30), 134 (3), 120 (24), 115 (6), 105 (51), 91 (100).

2-[(Methoxycarbonyl)methyl]-3-[2-[(*R*)-1-phenethylamino]ethyl]indole (8). A mixture of 1.0 g (2.125 mmol) of 2-[(methoxycarbonyl)methyl]-3-[2-(benzyloxycarbonyl)-(*R*)-1-(phenethylamino)ethyl]indole and 226 mg (0.213 mmol) of 10% Pd−C in 20 mL of MeOH was vigorously stirred for 1 h at room temperature under 1 atm of H_2. Filtration and concentration gave the crude product, which was purified on a silica gel column, eluting with CH_2Cl_2/MeOH (96:4), to give 660 mg of the title product (92% yield): TLC $R_f = 0.24$ (CH_2Cl_2/MeOH, 96:4; CAS green); $[\alpha]^{29}_D = 49$ ($c = 0.23$, $CHCl_3$); IR (KBr) ν_{max} 3400, 3062, 3028, 2953, 2926, 2852, 1736, 1494, 1461, 1437, 1340, 1305, 1267, 1239, 1213, 1167, 1123, 1011, 764, 741, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1 H), 7.48 (d, J = 7.9 Hz, 1 H), 7.34−7.22 (m, 5 H), 7.20 (m, 1 H), 7.17 (t, J = 8.0 Hz, 1 H), 7.05 (t, J = 7.6 Hz, 1 H), 3.74 (s, 2 H), 3.72 (m, 1 H), 3.68 (s, 3 H), 2.90 (m, 2 H), 2.76 (m, 1 H), 2.67 (m, 1 H), 1.78 (s, br, 1 H, NH), 1.28 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.14, 145.61, 135.79, 128.37, 128.07, 127.16, 126.80, 126.56, 121.87, 119.34, 118.58, 111.47, 110.74, 58.20, 52.27, 47.84, 31.67, 24.88, 24.31; MS *m/z* (relative intensity) 337 (M^+ + 1, 13), 217 (2), 204 (69), 170 (2), 156 (4), 142 (17), 134 (30), 105 (100), 91 (3).

Methyl (3a*S,5*S**,11b*R**) and (3a*R**,5*R**,11b*S**)-3-((*R*)-1-Phenethyl)-2,3,3a,4,5,7-hexahydro-5-(dimethoxymethyl)-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (11).** Using the general procedure for preparation of the *N*-benzyl compound **1b**, the title compound was obtained as a 3:2 ratio of diastereomers and purified on a silica gel column, which was eluted with hexane/EtOAc (9:1) (40% yield): TLC $R_f = 0.25$ (hexane/EtOAc/CH_2Cl_2, 7:2:1; CAS blue); UV (EtOH) λ_{max}: 328, 294, 224, 208 nm; IR (KBr) ν_{max} 3371, 3058, 3028, 2972, 2948, 2831, 1677, 1608, 1466, 1436, 1373, 1277, 1237, 1212, 1189, 1152, 1123, 1090, 910, 745, 731, 702 cm^{-1}; MS *m/z* (rel intens) 449 (2), 448 (M^+, 0.4), 434 (7), 418 (7), 374 (19), 342 (4), 282 (2), 270 (9), 238 (3), 228 (10), 215 (3), 210 (6), 194 (8), 182 (5), 180 (6), 167 (7), 160 (10), 154 (3), 148 (6), 130 (2), 119 (35), 105 (100), 91 (3).

Selected distinguishing data for obtaining the product ratio: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.14 (t, J = 7.6 Hz, 1 H), 6.90 (t, J = 7.3 Hz, 1 H), 6.80 (d, J = 7.9 Hz, 1 H), 4.79 (d, J = 5.7 Hz, 1 H), 3.79 (s, 3 H), 3.42 (s, 3 H), 3.41 (s, 3 H), 1.49 (d, J = 6.6 Hz, 3 H). Compared with: δ 9.80 (s, 1H), 7.08 (t, J = 7.6 Hz, 1 H), 6.75 (d, J = 7.8 Hz, 1 H), 4.90 (d, J = 7.1 Hz, 1 H), 3.78 (s, 3 H), 3.51 (s, 3 H), 3.40 (s, 3 H), 1.54 (d, J = 6.7 Hz, 3 H).

***N*^{b}-(*tert*-Butoxycarbonyl)-*N*^{b}-[1(*R*)-(1-naphthylethyl)]tryptamine.** To a solution of *N*^{b}-[1(*R*)-(1-naphthylethyl)]tryptamine, prepared by alkylation[12,17,18] of the corresponding amine with tryptophyl bromide (4.30 g, 13.68 mmol) and K_2CO_3 (3.80 g, 27.35 mmol) in 30 mL of THF and 30 mL of H_2O, was added (*t*-BuOCO)$_2$O (3.3 g, 15.04 mmol) in several portions at room temperature. After the addition, the solution was stirred for another 1 h. The aqueous phase was extracted

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with EtOAc. The residue, obtained upon drying and concentration, was purified on a silica gel column, eluting with EtOAc/Hex (1:4) to afford 5.3 g of the title product (96% yield): TLC $R_f = 0.35$ (hexane/EtOAc 4:1; CAS yellow); mp 79−81 °C; $[\alpha]^{29}_{D} = 98$ ($c = 0.3$, MeOH); UV (EtOH) λ_{max} 222, 274, 282, 292 nm; IR (KBr) ν_{max} 3423, 3329, 3051, 2977, 2931, 2874, 1664, 1511, 1458, 1408, 1367, 1337, 1303, 1253, 1170, 1160, 1106, 1034, 911, 868, 803, 780, 738 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 (s, br, 1 H), 7.84 (m, 2 H), 7.80 (s, 1 H), 7.54 (m, 2 H), 7.50 (m, 2 H), 7.20 (m, 1 H), 7.08 (m, 1 H), 6.97 (m, 2 H), 6.50 (s, br, 1 H), 6.22 (s, br, 1 H), 3.21 (s, br, 1 H), 2.98 (s, br, 1 H), 2.03 (s, br, 2 H), 1.60 (m, 12 H); MS *m/z* (relative intensity) 415 (8), 414 (M$^+$, 30), 358 (6), 228 (11), 184 (9), 155 (100), 143 (18), 130 (55), 128 (4), 103 (4). Anal. Calcd for $C_{27}H_{30}N_2O_2\cdot0.5H_2O$: C, 76.57; H, 7.38; N, 6.62. Found: C, 76.48; H, 7.35; N, 6.47.

2-[(Methoxycarbonyl)methyl]-3-[2-[*N*-(tert-butoxycarbonyl)-*N*-[1(*R*)-(1-naphthylethyl]amino]ethyl]indole. Using the preceding procedures for preparation of the corresponding α-phenethyl analogue, the title product was obtained in 85% yield (two steps) after purification by silica gel column chromatography, eluting with Et$_2$O/hexane (1:1): TLC $R_f = 0.28$ (hexane/EtOAc, 4:1, CAS, gray); mp 76−8 °C; IR (KBr) ν_{max} 3397, 3055, 2974, 1740, 1735, 1685, 1680, 1664, 1459, 1407, 1366, 1337, 1306, 1244, 1159, 1119, 1027, 910, 870, 806, 782, 741 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.35 (s, br, 1 H), 8.24 (s, br, 1 H), 7.89 (d, $J = 8.1$ Hz, 2 H), 7.52 (m, 4 H), 7.20 (m, 1 H), 7.07 (t, $J = 6.7$ Hz, 1 H), 6.97 (m, 2 H), 6.27 (s, br, 1 H), 3.77 (s, 0.6 H), 3.71 (s, 3 H), 3.70 (s, 0.4 H), 3.26 (s, br, 2 H), 2.83 (s, br, 1 H), 2.64 (s, br, 1 H), 1.68 (s, 9 H), 1.62 (m, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) (29 peaks due to the rotomers) δ 136.76, 135.72, 135.43, 133.74, 132.58, 128.68, 127.68, 126.61, 125.88, 125.02, 124.60, 124.30, 122.43, 121.64, 119.13, 118.99, 118.44, 110.53, 79.95, 52.98, 55.15, 49.76, 48.42, 43.14, 30.92, 28.77, 23.93, 16.98; MS *m/z* (relative intensity) 487 (5), 486 (M$^+$, 16), 275 (9), 260 (5), 231 (4), 226 (6), 215 (8), 202 (42), 184 (9), 169 (4), 155 (100), 142 (22), 130 (4), 115 (6). Anal. Calcd for $C_{30}H_{34}N_2O_4\cdot H_2O$: C, 71.41; H, 7.19; N, 5.55. Found: C, 71.08; H, 6.88; N, 5.39.

2-[(Methoxycarbonyl)methyl]-3-[2-[1(*R*)-(1-naphthylethyl)amino]ethyl)indole (9). The title compound was prepared using the preceding procedures for preparation of the corresponding α-phenethyl compound **8**. After purification by silica gel column chromatography, eluting with EtOAc, an 88% yield was obtained: TLC $R_f = 0.21$ (EtOAc, CAS green); $[\alpha]^{30}_{D} = 67$ ($c = 0.5$, MeOH); IR (KBr) ν_{max} 3406, 3057, 2953, 2928, 2846, 1734, 1457, 1436, 1306, 1259, 1208, 1168, 1122, 1010, 847, 802, 780, 742 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.49 (s, 1 H), 8.10 (d, $J = 7.6$ Hz, 1 H), 7.85 (d, $J = 7.2$ Hz, 1 H), 7.71 (d, $J = 8.0$ Hz, 1 H), 7.53−7.38 (m, 5 H), 7.32 (d, $J = 8.0$ Hz, 1 H), 7.17 (t, $J = 7.8$ Hz, 1 H), 7.07 (m, 1 H), 4.60 (q, $J = 6.4$ Hz, 1 H), 3.79 (s, 2 H), 3.66 (s, 3 H), 2.97−2.82 (m, 4 H), 1.69 (s, br, 1 H), 1.45 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.07, 141.23, 135.01, 133.94, 131.31, 128.85, 128.05, 127.22, 127.00, 125.62, 125.19, 122.90, 122.65, 121.88, 119.34, 118.59, 111.47, 110.73, 53.64, 52.20, 47.97, 31.65, 24.97, 23.50; MS *m/z* (relative intensity) 387 (M$^+$ + 1, 7), 276 (7), 262 (3), 204 (50), 185 (9), 170 (3), 156 (100), 142 (21), 129 (6), 115 (9).

Methyl (3a*S,5*S**,11b*R**)- and (3a*R**,5*R**,11b*S**)-3-[(*R*)-1-(1-Naphthylethyl)]-2,3,3a,4,5,7-hexahydro-5-(dimethoxymethyl)-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (12).** Using the general procedure for preparation of the *N*-benzyl compound **1b**, the title compounds were obtained as a 5:4 ratio of diastereomers and purified on a silica gel column, which was eluted with hexane/EtOAc (4:1) (30% yield): TLC $R_f = 0.39$ (hexane/EtOAc, 4:1; CAS blue); UV (EtOH) λ_{max} 328, 296, 224, 206 nm; IR (KBr) ν_{max} 3369, 3049, 2968, 2949, 2932, 2830, 1675, 1608, 1466, 1437, 1376, 1278, 1236, 1212, 1191, 1128, 1081, 970, 802, 793, 781, 744 cm^{-1}; MS *m/z* (rel intens) 499 (2), 498 (M$^+$, 0.5), 484 (7), 467 (7), 424 (13), 312 (2), 270 (6), 243 (2), 227 (5), 210 (2), 194 (5), 180 (4), 167 (6), 155 (97), 145 (11), 127 (6), 119 (4), 115 (5), 101 (6), 97 (5).

Selected distinguishing data for determination of diastereomeric ratio follows. Major product: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.47 (s, 1H), 6.97 (t, $J = 7.3$ Hz, 1 H), 6.83 (d, $J = 7.5$ Hz, 1 H), 4.80 (d, $J = 6.3$ Hz, 1 H), 3.81 (s, 3 H), 3.48 (s, 3 H), 3.38 (s, 3 H). Minor product: ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.30 (s, 1H), 7.12 (t, $J = 7.4$ Hz, 1 H), 6.78 (d, $J = 7.7$ Hz, 1 H), 4.92 (d, $J = 6.0$ Hz, 1 H), 3.76 (s, 3 H), 3.54 (s, 3 H), 3.40 (s, 3 H).

Methyl (3a*S,5*S**,11b*R**)- and (3a*R**,5*R**,11b*S**)-3-[(*R*)-1-(1-Naphthylethyl)]-2,3,3a,4,5,7-hexahydro-5-[1-(2-ethylenedioxy)propyl]-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (13).** Using the general procedure for preparation of the *N*-benzyl compound **1b**, the title compounds were obtained as a 3:2 ratio of diastereomers and purified on a silica gel column, which was eluted with hexane/EtOAc (4:1) (26% yield): TLC $R_f = 0.33$ (hexane/EtOAc, 7:3; CAS violet); UV (EtOH) λ_{max}: 326, 294, 226, 206 nm; IR (KBr) ν_{max}: 3375, 3049, 2979, 2948, 2927, 2878, 1677, 1609, 1466, 1435, 1380, 1275, 1236, 1215, 1190, 1149, 1097, 1048, 801, 781, 746 cm^{-1}; MS *m/z* (rel intens) 525 (M$^+$ + 1, 5), 510 (2), 397 (3), 384 (6), 370 (5), 328 (3), 268 (1), 243 (2), 226 (2), 211 (8), 194 (3), 180 (3), 167 (4), 155 (100), 141 (2), 129 (4), 115 (3), 87 (78).

Selected distinguishing data for the major diastereomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.26 (s, 1H), 7.16 (s, 1 H), 3.78 (s, 3 H), 1.48 (s, 3 H). Selected data for the minor diastereomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.12 (s, 1H), 7.11 (s, 1 H), 3.80 (s, 3 H), 1.55 (s, 3 H).

2-[(Methoxycarbonyl)methyl]-3-[2-[(*S*)-[[(methoxycarbonyl)phenylmethyl]amino]ethyl]indole (7). The title compound was prepared starting from tryptophyl bromide and (*S*)-phenylglycine, using the preceding procedures for preparation of the tryptamine ester compounds **8**−**10** and obtained in 61% overall yield (four steps) after final purification on a silica gel column, eluting with CH$_2$Cl$_2$/EtOAc (7:3): TLC $R_f = 0.18$ (CH$_2$Cl$_2$/EtOAc, 7:3; CAS green); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.62 (s, 1 H), 7.49 (d, $J = 7.8$ Hz, 1 H), 7.33 (m, 6 H), 7.15 (t, $J = 7.8$ Hz, 1 H), 7.07 (t, $J = 7.7$ Hz, 1 H), 4.41 (s, 1 H), 3.80 (s, 2 H), 3.68 (s, 3 H), 3.61 (s, 3 H), 2.95 (m, 2 H), 2.85 (m, 1 H), 2.78 (m, 1 H), 2.10 (s, 1 H, NH); ^{13}C NMR (125 MHz, CDCl$_3$) δ 173.37, 138.18, 135.82, 128.65, 128.03, 128.01, 127.46, 127.27, 121.87, 119.35, 118.50, 111.08, 110.83, 65.61, 52.26, 52.10, 49.97, 31.68, 24.99.

Methyl (3a*S,5*R** and *S**,11b*R**)- and (3a*R**,5*S** and *R**,11b*S**)-3-[(*S*)-(Methoxycarbonyl)phenylmethyl]-2,3,3a,4,5,7-hexahydro-5-methyl-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (10).** Using the general procedure for preparation of the *N*-benzyl compound **1a**, the title compounds were obtained as a 5:1:1:0.9 ratio of diastereomers and purified on a silica gel column, which was eluted with hexane/EtOAc (9:1) (35% yield): TLC $R_f = 0.24$ (hexane/EtOAc, 9:1; CAS blue); UV (EtOH) λ_{max} 326, 294, 226, 208 nm; IR (KBr) ν_{max} 3372, 3060, 3032, 2951, 2927, 2854, 1739, 1680, 1609, 1479, 1467, 1453, 1434, 1352, 1291, 1279, 1252, 1236, 1215, 1191, 1167, 1132, 1104, 1048, 1024, 788, 749, 702 cm^{-1}; MS *m/z* (rel intens) 433 (8), 432 (M$^+$, 22), 401 (3), 389 (8), 373 (57), 341 (10), 283 (34), 267 (13), 241 (81), 226 (23), 208 (20), 204 (83), 193 (23), 182 (27), 170 (40), 149 (100), 121 (60).

Selected data for the major diastereomer: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.08 (s, 1H), 7.67 (d, $J = 7.5$ Hz, 1 H), 7.44−7.24 (m, 5 H), 7.15 (t, $J = 7.5$ Hz, 1 H), 6.93 (t, $J = 7.5$ Hz, 1 H), 6.81 (d, $J = 7.7$ Hz, 1 H), 4.69 (s, 1 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 3.59 (m, 1 H), 3.11 (m, 1 H), 2.70 (dd, $J = 7.1$, 7.1 Hz, 1 H), 2.06 (m, 1 H), 1.91 (d, $J = 14.1$ Hz, 1 H), 1.70 (dd, $J = 5.1$, 11.7 Hz, 1 H), 1.39 (d, $J = 7.3$ Hz, 3 H).

L-[N^b-Benzyl-N^b-(*tert*-butoxycarbonyl)]tryptophan Benzyl Ester (16). A mixture of 2.20 g (7.48 mmol) of tryptophan benzyl ester,[16] 794 mg (7.48 mmol) of benzaldehyde, and 2.0 g of magnesium sulfate in 25 mL of dichloromethane was stirred for 8 h. Filtration and concentration gave an imine, which was dissolved in 25 mL of methanol. At 0 °C, 314 mg (8.23 mmol) of sodium borohydride was added. After 1 h at 0 °C, the solvent was evaporated and the residue partitioned between ethyl acetate and a saturated sodium bicarbonate solution. Concentration and chromatography on silica gel, eluted with ethyl acetate/hexane, gave 2.73 g (95% yield) of the N^b-benzylated product **15**: TLC R_f 0.10 (EtOAc/hexane, 3:7, CAS brown).

To a solution of 12.0 g (31.3 mmol) of L-benzyl-N^b-benzyltryptophan benzyl ester (**15**) in 200 mL of THF and H$_2$O (1:1) was added 8.64 g (62.5 mmol) of potassium carbonate, followed by 7.5 g (34 mmol) of (t-BOC)$_2$O, added in several portions at room temperature. The solution was stirred for another 1 h. The residue, obtained upon concentration, was dissolved in ethyl acetate and washed with water and brine. The crude product was pure enough for the next reaction, but it could be further purified on a silica gel column (EtOAc/hexane, 3:7) to afford 14.6 g of the desired product (96% yield): TLC $R_f = 0.24$ (hexane/EtOAc 7:3; CAS brown); $[\alpha]^{27}{}_D = -74$ ($c = 0.5$, MeOH); IR (KBr) ν_{max} 3351, 3060, 3035, 2979, 2933, 1740, 1735, 1701, 1696, 1685, 1676, 1496, 1456, 1366, 1340, 1274, 1252, 1215, 1161, 743, 697 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.01 (s, 1 H), 7.46−6.89 (m, 15 H), 5.05 (s, br, 1.6 H), 4.95 (app s, br, 0.4 H), 4.57 (d, br, J = 12.9 Hz, 0.6 H), 4.37 (app s, 0.8 H), 4.18 (s, br, 0.6 H), 3.79 (d, br, J = 12.9 Hz, 0.4 H), 3.64 (d, br, J = 13.9 Hz, 0.6 H), 3.52 (m, 1 H), 3.40 (s, br, 0.4 H), 3.26 (s, br, 0.6 H), 1.55 (s, 5.4 H), 1.52 (s, 3.6 H); MS m/z (relative intensity) 485 (2), 484 (M$^+$, 6), 385 (5), 277 (13), 220 (5), 186 (2), 157 (3), 143 (8), 130 (100), 117 (4), 103 (5), 91 (69). Anal. Calcd for $C_{30}H_{32}N_2O_4 \cdot H_2O$: C, 71.69; H, 6.82; N, 5.57. Found: C, 72.11; H, 6.91; N, 5.02.

2-[Bis(methoxycarbonyl)methyl]-3-[2(*S*)-(benzyloxycarbonyl)-2-[N^b-*tert*-(butoxycarbonyl)-N^b-benzylamino]ethyl]indole (17) and 2-[(Methoxycarbonyl)methyl]-3-[2-(*S*)-(benzyloxycarbonyl)-2-[N^b-(*tert*-butoxycarbonyl)-N^b-benzylamino]ethyl]indole (18). To a solution of 11.0 g (22.7 mmol) of the urethane ester **16** and 3.47 mL (25.0 mmol) of Et$_3$N in 250 mL of THF, at −78 °C, was added 3.0 mL (25 mmol) of *tert*-butyl hypochlorite dropwise. The solution was stirred for a further 20 min, and 4.54 mL of a 1.0 M solution of ZnCl$_2$ in Et$_2$O (4.54 mmol) was introduced. The reaction mixture was stirred for 5 min. A solution of 3.79 g (27.2 mmol) of lithium dimethyl malonate in 20 mL of THF was added dropwise, and the resulting solution was stirred for 1 h at −78 °C and for 1 h at room temperature. The reaction was quenched by adding water, and the aqueous layer was extracted with dichloromethane. The product **17**, obtained upon concentration, was pure enough for the next reaction, but it could be purified by chromatography on silica gel (EtOAc/hexane, 1:4).

The above product was taken into 120 mL of DMF, and 1.9 g (45.4 mmol) of LiCl was added. The solution was heated in at 130 °C in an oil bath for 3 h and cooled to room temperature. Water was added. The aqueous layer was extracted with ether several times. The combined organic phase was washed with water and brine several times. The residue, obtained upon concentration, was purified on a silica gel column (EtOAc/hexane, 25:75) to give 11.0 g of product **18** (87% yield for two steps).

For triester **17**: TLC $R_f = 0.2$ (hexane/EtOAc 4:1; CAS light green); IR (KBr) ν_{max} 3397, 3059, 3031, 2974, 2955, 2930, 1740, 1735, 1718, 1700, 1686, 1457, 1436, 1368, 1317, 1277, 1247, 1211, 1160, 743, 699 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.89 (s, 1 H), 7.36−6.94 (m, 14 H), 5.12−5.05 (m, 2 H), 4.94 (m, 1 H), 4.45 (d, br, J = 13.2 Hz, 0.6 H), 4.28 (d, br, J = 13.2 H, 0.4 H), 4.11 (m, 1 H), 3.76 (s, 6 H), 3.74−3.52 (m, 2.6 H), 3.25 (m, br, 0.4 H), 1.49−1.40 (3 s, 9 H).

For diester **18**: TLC $R_f = 0.16$ (hexane/EtOAc 4:1; CAS green/gray); mp 92−4 °C; $[\alpha]^{24}{}_D = -100$ ($c = 0.23$, CHCl$_3$); UV (EtOH) λ_{max} 286, 224, 210 nm; IR (KBr) ν_{max} 3382, 3063, 3030, 3007, 2980, 2957, 2930, 1739, 1693, 1497, 1457, 1435, 1367, 1313, 1275, 1245, 1217, 1165, 998, 744, 898 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.62 (s, 1 H), 7.38−6.92 (m, 14 H), 5.08−4.92 (m, 2 H), 4.51 (d, br, J = 14.7 Hz, 0.53 H), 4.29 (d, br, J = 14.9 Hz, 0.47 H), 4.09 (t, J = 7.6 Hz, 1 H), 3.76 (s, 2 H), 3.72 (s, 3 H), 3.58 (m, 1 H), 3.47 (app s, br, 1.47 H), 3.22 (m, 0.53 H), 1.49 (s, 5 H), 1.40 (s, 4 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.89, 155.00, 137.02, 135.69, 128.69, 128.36, 128.22, 128.02, 127.13, 121.95, 119.54, 118.31, 118.06, 110.94, 66.87, 60.66, 59.65, 52.80, 52.24, 51.99, 31.24, 28.36, 25.22, 24.25; MS m/z (relative intensity) 557 (0.5), 556 (M$^+$, 2), 500 (2), 457 (2), 349 (3), 292 (3), 260 (5), 254 (2), 218 (4), 202 (100), 188 (2), 169 (5), 154 (2), 142 (22), 130 (2), 115 (4). Anal. Calcd for $C_{33}H_{36}N_2O_6$: C, 71.20; H, 6.52; N, 5.03. Found: C, 71.06; H, 6.46; N, 5.02.

2-[(Methoxycarbonyl)methyl]-3-[2(*S*)-(benzyloxycarbonyl)-2-(N^b-benzylamino)ethyl]indole (14). To a solution of 4.0 g (7.2 mmol) of the urethane **18** and 2.0 mL (14 mmol) of triethylamine in 60 mL of dichloromethane, at 0 °C, was added 2.8 mL (14 mmol) of TMSOTf, dropwise. The solution was stirred at room temperature for 2 h, and then saturated sodium bicarbonate was added and the aqueous layer was extracted with dichloromethane. The residue, obtained upon concentration, was chromatographed on a silica gel column, eluting with CH$_2$Cl$_2$/EtOAc (9:1), to provide 3.0 g of the amine **14** (91% yield): TLC $R_f = 0.22$ (CH$_2$Cl$_2$/EtOAc 9:1; CAS green); $[\alpha]^{24}{}_D = 0.9$ ($c = 1.1$, CHCl$_3$); UV (EtOH) λ_{max} 282, 222, 210 nm; IR (KBr) ν_{max} 3402, 3090, 3063, 3034, 2953, 2928, 2850, 1733, 1497, 1460, 1437, 1340, 1309, 1172, 1127, 1008, 740, 298 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.55 (s, 1 H), 7.49 (d, J = 7.8 Hz, 1 H), 7.32−7.13 (m, 12 H), 7.07 (m, 3 H), 4.97 (s, 2 H), 3.78 (d, J = 16.8 Hz, 1 H), 3.76 (d, J = 13.1 Hz, 1 H), 3.70 (d, J = 16.8 Hz, 1H), 3.66 (t, J = 6.8 Hz, 1 H), 3.64 (s, 3 H), 3.61 (d, J = 13.1 Hz, 1 H), 3.11 (d, J = 6.8 Hz, 2 H), 1.75 (s, br, 1 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 175.00, 171.08, 139.73, 135.67, 128.43, 128.27, 128.12, 128.08, 126.93, 121.94, 119.54, 118.57, 110.75, 108.80, 66.47, 61.43, 52.23, 52.20, 31.49, 28.69; MS m/z (relative intensity) 458 (10), 457 (M$^+$, 46), 321 (2), 292 (2), 254 (3), 230 (3), 202 (92), 188 (2), 169 (5), 142 (26), 130 (3), 115 (7), 91 (100).

(−)-Methyl (2*S*,3a*S*,5*R*,11b*R*)-2-(Benzyloxycarbonyl)-3-benzyl-2,3,3a,4,5,7-hexahydro-5-methyl-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate ((−)-19a). A mixture of the amine **14** (290 mg, 0.636 mmol), benzoic acid (78 mg, 0.64 mmol), crotonaldehyde (63 uL, 0.76 mmol), and 600 mg of freshly activated MgSO$_4$, in 8 mL of anhydrous benzene under an atmosphere of Ar, was heated at 65−70 °C for 2 days. The residue, obtained upon filtration and concentration, was dissolved in CH$_2$Cl$_2$ and washed with 5% Na$_2$CO$_3$. Purification of the crude product on a silica gel column (hexane/EtOAc, 9:1) afforded 165 mg of the product **19a** (51% yield): TLC $R_f = 0.22$ (hexane/EtOAc 9:1; CAS blue); mp 86−7 °C (HCl salt); $[\alpha]^{23}{}_D = -236$ ($c = 1.0$, CHCl$_3$); UV (EtOH) λ_{max} 326, 300, 232, 204 nm; IR (KBr) ν_{max} 3379, 3059, 3033, 2982, 2954, 2933, 2794, 1723, 1684, 1614, 1478, 1466, 1437, 1377, 1343, 1278, 1257, 1229, 1213, 1183, 1153, 1119, 1085, 1056, 1043, 749, 732, 701 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.98 (s, 1 H), 7.37−7.25 (m, 11 H), 7.11 (dd, J = 7.6 Hz, 1 H), 6.77 (dd, J = 7.6 H, 1 H), 6.67 (d, J = 7.5 Hz, 1 H), 4.90 (d, J = 12.4 Hz, 1 H), 4.87 (d, J = 12.4 Hz, 1 H), 3.98 (s, 2 H), 3.75 (s, 3 H), 3.74 (dd, J = 5.3, 11.8 Hz, 1 H), 3.57 (d, J = 5.4 Hz, 1 H), 3.05 (m, 1 H), 2.42 (dd, J = 11.8, 11.8 Hz, 1 H), 1.98 (dd, J = 5.3, 11.8 Hz, 1 H), 1.75 (d, J = 14.1 Hz, 1 H), 1.47 (d, J = 7.1 H, 3 H), 1.29 (m, 1 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 172.30, 168.86, 164.75, 142.87, 137.20, 137.05, 135.63, 129.97, 128.47, 128.18, 128.02, 127.34, 121.47, 120.32, 109.29, 100.40, 66.71, 66.53, 64.34, 57.34, 54.05, 50.94, 49.59, 33.95, 28.95, 20.92; MS m/z (relative intensity) 509 (1), 508 (M$^+$, 2), 280 (2), 242 (5), 228 (27), 208 (4), 196 (5), 180 (6), 167 (10), 154 (2), 134 (1), 107 (4), 91 (100).

(−)-Methyl (2*S*,3a*S*,5*S*,11b*R*)-2-(Benzyloxycarbonyl)-3-benzyl-2,3,3a,4,5,7-hexahydro-5-(dimethoxymethyl)-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate ((−)-19b). A solution of the amine **14** (400 mg, 0.877 mmol), benzoic acid (107 mg, 0.877 mmol), and 4,4-dimethoxycrotonaldehyde (137 mg, 1.05 mmol) in 10 mL of benzene, under an atmosphere of Ar, was heated at reflux with a Dean−Stark water trap for 3 days. A workup as for **19a**, above, and chromatography on a silica gel column (EtOAc/Hex, 25:75) gave 205 mg of the product **19b** (41% yield): TLC $R_f = 0.26$ (hexane/EtOAc 75:25; CAS blue); mp 65−67 °C; $[\alpha]^{23}{}_D = -182$ ($c = 1.2$, CHCl$_3$); UV (EtOH) λ_{max} 324, 296, 230, 206 nm; IR (KBr) ν_{max} 3371, 3059, 3031, 2948, 2845, 1743, 1675, 1610, 1468, 1493, 1284, 1238, 1192, 1160, 1126, 1095, 1078, 1002, 72, 749, 699 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.13 (s, 1 H), 7.38−7.26 (m, 10 H), 7.09 (dd, J = 7.7, 7.7 Hz, 1 H), 6.75 (d, J = 7.7 Hz, 1 H), 6.70 (dd, J = 7.5, 7.5 1H), 6.38 (d, J = 7.3 Hz, 1 H), 5.23 (d, J = 9.0 Hz, 1 H), 4.99 (s, 2 H), 4.03 (d, J = 13.8 Hz, 1 H), 3.96 (d, J = 13.8 Hz, 1 H), 3.77 (dd, J = 5.2, 12.0 Hz, 1 H), 3.76 (s, 3 H), 3.53 (s, 3 H), 3.52 (d, J = 5.5 Hz, 1 H), 3.29 (s, 3 H), 3.28 (m, 1 H), 2.22 (m, 2 H), 1.99 (dd, J = 5.2, 12.0 Hz, 1 H), 1.20 (ddd, J = 5.5, 5.5, 14.2 Hz, 1 H); ^{1}H NMR (500 MHz, C$_6$D$_6$) δ 9.41 (s, 1 H), 7.29

(d, $J = 7.0$ Hz, 2 H), 7.18−7.10 (m, 6 H), 7.04 (m, 2 H), 6.87 (ddd, $J = 1.0, 7.7, 7.7$ Hz, 1 H), 6.62 (dd, $J = 7.3, 7.3$ Hz, 1 H), 6.45 (d, $J = 7.4$ Hz, 1 H), 6.18 (d, $J = 7.7$ Hz, 1 H), 5.57 (d, $J = 8.9$ Hz, 1 H), 4.80 (d, $J = 12.2$ Hz, 1H), 4.77 (d, $J = 12.2$ Hz, 1 H), 3.93 (d, $J = 13.8$ Hz, 1 H), 3.83 (d, $J = 13.8$ Hz, 1 H), 3.79 (dd, $J = 5.3, 11.9$, 1 H), 3.70 (dd, $J = 6.1, 8.9$ Hz, 1 H), 3.61 (s, 3 H), 3.59 (s, 3 H), 3.38 (d, $J = 5.6$ Hz, 1 H), 3.37 (s, 3 H), 2.37 (dd, $J = 11.9, 11.9$ Hz, 1 H), 2.26 (d, $J = 14.3$ Hz, 1 H), 1.83 (dd, $J = 5.3, 11.9$ Hz, 1 H), 1.03 (ddd, $J = 5.6, 5.6, 14.3$ Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.24, 169.22, 164.77, 142.72, 136.96, 135.50, 135.05, 130.56, 128.59, 128.53, 128.47, 128.07, 127.61, 121.34, 120.44, 109.30, 106.83, 96.61, 66.71, 63.51, 62.61, 55.68, 55.57, 55.06, 53.53, 51.15, 48.77, 38.49, 28.88; MS *m/z* (relative intensity) 568 (M^+, 1), 494 (1), 433 (1), 387 (1), 359 (7), 276 (3), 268 (3), 229 (5), 226 (5), 218 (3), 202 (4), 194 (3), 182 (2), 177 (4), 155 (8), 150 (2), 139 (1), 107 (5), 91 (100).

(−)-Methyl (2*S*,3a*S*,5*S*,11b*R*)-2-(Benzyloxycarbonyl)-3-benzyl-2,3,3a,4,5,7-hexahydro-5-(2-methoxyphenyl)-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate ((−)-19c). A solution of the amine **14** (300 mg, 0.658 mmol), benzoic acid (80 mg, 0.658 mmol), and 3-(2-methoxyphenyl)propenal (133 mg, 0.79 mmol) in 8 mL of benzene, under an atmosphere of Ar, was heated in a 100 °C oil bath with a Dean−Stark water trap for 36 h. Workup as above for (−)-**19a** and chromatography on a silica gel column (EtOAc/Hex, 1:9) afforded 290 mg of the product (−)-**19c**, (74% yield): TLC $R_f = 0.25$ (hexane/Et_2O, 4:1; CAS blue); mp 99−100 °C (HCl salt); $[\alpha]^{23}_D = -234$ ($c = 0.5$, $CHCl_3$); UV (EtOH) λ_{max} 326, 298, 230, 208 nm; IR (KBr) ν_{max} 3369, 3061, 3031, 2948, 2834, 1742, 1674, 1607, 1487, 1466, 1436, 1285, 1234, 1210, 1157, 1128, 1089, 1031, 908, 752, 734, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1 H), 7.25 (m, 3 H), 7.21 (m, 3 H), 7.15 (d, $J = 7.8$ Hz, 2 H), 7.10 (m, 3 H), 7.04 (m, 2 H), 6.86 (d, $J = 7.7$ Hz, 1 H), 6.79 (m, 3 H), 6.72 (t, $J = 7.3$ Hz, 1 H), 4.69 (d, $J = 12.3$ Hz, 1 H), 4.53 (d, $J = 12.3$ Hz, 1 H), 4.42 (dd, $J = 3.7, 6.1$ Hz, 1 H), 3.92 (d, $J = 14.0$ Hz, 1 H), 3.82 (d, $J = 14.0$ Hz, 1 H), 3.80 (s, 3 H), 3.60 (dd, $J = 5.5, 11.5$ Hz, 1 H), 3.57 (s, 3 H), 3.47 (dd, $J = 2.9, 5.4$ Hz, 1 H), 2.73 (ddd, $J = 3.2, 3.2, 14.5$ Hz, 1 H), 2.62 (dd, $J = 11.5, 11.5$ Hz, 1 H), 1.84 (dd, $J = 5.5, 11.5$ Hz, 1 H), 1.70 (ddd, $J = 6.1, 6.1, 14.5$ Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.46, 168.79, 165.20, 157.58, 143.11, 137.52, 137.08, 135.88, 133.11, 129.24, 128.85, 128.28, 128.24, 127.99, 127.91, 127.87, 126.83, 126.44, 121.66, 120.44, 119.96, 110.01, 109.24, 97.21, 65.85, 65.56, 63.67, 56.10, 55.03, 53.68, 50.90, 45.56, 35.02, 32.03; MS *m/z* (relative intensity) 601 ($M^+ + 1$, 5), 510 (10), 466 (70), 334 (5), 321 (36), 301 (7), 289 (25), 274 (5), 265 (7), 260 (26), 241 (5), 230 (5), 212 (5), 180 (7), 167 (5), 154 (2), 121 (2), 107 (3), 91 (100). Anal. Calcd for $C_{30}H_{30}N_2O_3$: C, 74.98; H, 6.04; N, 4.66; Found: C, 75.01; H, 5.93; N, 4.60.

Spiro[pyrrolidinoindolenines] 28−30. A solution of the amine **14** (200 mg, 0.438 mmol), benzoic acid (54 mg, 0.438 mmol), and 4,4-dimethoxycrotonaldehyde (51 mg, 0.395 mmol) in 6 mL of benzene, under an atmosphere of Ar, was heated at reflux with a Dean−Stark water trap for 3 h. Workup as for (−)-**19a**, above, and chromatography on a silica gel column (Et_2O/Hex, 1:1) gave 125 mg of the spiro compounds **28**−**30** (69% yield) and 50 mg of tetracyclic product (−)-**19a** (22% yield). For the spiro compounds: TLC $R_f = 0.12$ (Et_2O/Hex, 1:1; CAS blue); UV (EtOH) λ_{max} 328, 296, 232, 206 nm; IR (KBr) ν_{max} 3355, 3087, 3063, 3033, 2993, 2948, 2833, 1731, 1672, 1609, 1482, 1472, 1455, 1443, 1285, 1229, 1164, 1106, 1073, 1051, 980, 792, 748, 697 cm^{-1}; MS *m/z* (relative intensity) 569 (3), 568 (M^+, 9), 553 (2), 536 (3), 493 (2), 433 (7), 352 (3), 292 (2), 276 (17), 268 (9), 248 (2), 232 (3), 220 (3), 214 (2), 202 (5), 194 (2), 188 (3), 169 (4), 154 (34), 140 (2), 122 (2), 114 (3), 101 (4), 91 (100).

Determination of the ratio of the spiro compounds (ratio **28**:**29**:**30** = 11:17:10) by NMR follows. For **28**: ^1H NMR (500 MHz, $CDCl_3$) δ 9.72 (s, 1 H), 7.87 (d, $J = 7.4$ Hz, 1 H), 7.46 -- 7.23 (m, 10 H), 7.10 (t, $J = 6.8$ Hz, 1 H), 6.89 (t, $J = 6.4$ Hz, 1 H), 6.73 (d, $J = 7.7$ Hz, 1 H), 5.62 (dd, $J = 9.1, 15.6$ Hz, 1 H), 5.30 (s, 1 H), 5.25 (m, 1 H), 5.10 (m, 2 H), 4.57 (d, $J = 9.1$ Hz, 1 H), 3.95 (m, 2 H), 3.76 (s, 3 H), 3.61 (m, 1 H), 3.09 (s, 3 H), 3.03 (s, 3 H), 2.55 (m, 1 H), 2.42 (m, 1 H).

For **29**: ^1H NMR (500 MHz, $CDCl_3$) δ 9.72 (s, 1 H), 7.87 (d, $J = 7.4$ Hz, 1 H), 7.46−7.23 (m, 10 H), 7.10 (t, $J = 6.8$ Hz, 1 H), 6.89 (t, $J = 6.4$ Hz, 1 H), 6.73 (d, $J = 7.7$ Hz, 1 H), 5.50 (dd, $J = 4.6, 15.9$ Hz, 1 H), 5.21 (m, 1 H), 4.92 (d, $J = 12.1$ Hz, 1 H), 4.88 (d, $J = 12.1$ Hz, 1 H), 4.84 (s, 1 H), 4.41 (d, $J = 4.6$ Hz, 1 H), 3.99 (m, 1 H), 3.71 (s, 3 H), 3.63 (d, $J = 12.4$ Hz, 1 H), 3.58 (m, 1 H), 3.25 (d, $J = 8.5$ Hz, 1 H), 3.06 (s, 3 H), 2.94 (s, 3 H), 2.42 (m, 2 H).

For **30**: ^1H NMR (500 MHz, $CDCl_3$) δ 9.70 (s, 1 H), 7.50 (d, $J = 6.8$ Hz, 1 H), 7.46−7.23 (m, 10 H), 7.17 (t, $J = 7.9$ Hz, 1 H), 6.98 (t, $J = 7.4$ Hz, 1 H), 6.76 (d, $J = 7.8$ Hz, 1 H), 5.56 (dd, $J = 4.6, 15.8$ Hz, 1 H), 5.17 (s, 1 H), 5.16 (m, 1 H), 5.10 (m, 2 H), 4.47 (d, $J = 4.6$ Hz, 1 H), 4.08 (d, $J = 8.8$ Hz, 1 H), 3.99 (m, 2 H), 3.74 (s, 3 H), 3.67 (m, 1 H), 3.07 (s, 3 H), 2.97 (s, 3 H), 2.55 (m, 1 H), 2.25 (dd, $J = 4.4, 13.9$ Hz, 1 H).

(−)-Methyl (2*S*,3a*S*,5*R*,11b*R*)-2-(Aminocarbonyl)-3-benzyl-2,3,3a,4,5,7-hexahydro-5-methyl-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate ((−)-20). Method a. A solution of the tetracyclic diester (−)-**19a** (220 mg, 0.509 mmol) in 8 mL of absolute MeOH was cooled to 0 °C and saturated with dry NH_3 (g). The solution was stirred at room temperature for 5 days. Concentration and chromatography on a silica gel column, eluting with EtOAc/Hex (7:3), gave 150 mg of amide **20** (71% yield).

Method b. The above reaction solution, in a sealed tube, was heated at 100−110 °C for 18 h. Workup as above gave 95 mg of amide (45% yield): TLC $R_f = 0.5$ (hexane/EtOAc 3:7; CAS blue); $[\alpha]^{23}_D = -306$ ($c = 1.0$, $CHCl_3$); mp 125 °C (from CH_2Cl_2/hexane); UV (EtOH) λ_{max} 328, 298, 228, 208 nm; IR (KBr) ν_{max} 3448, 3379, 3064, 3034, 2985, 2953, 2925, 2868, 1682, 1609, 1478, 1466, 1455, 1436, 1386, 1355, 1285, 1237, 1216, 1197, 1164, 1131, 1103, 1080, 1027, 988, 910, 790, 735, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.98 (s, 1 H), 7.39 (m, 3 H), 7.32 (m, 2 H), 7.31 (t, $J = 7.6$ Hz, 1 H), 6.86 (s, br, 1 H), 6.77 (d, $J = 7.7$ Hz, 1 H), 6.71 (t, $J = 7.6$ Hz, 1 H), 6.42 (d, $J = 7.4$ Hz, 1 H), 5.52 (s, br, 1 H), 4.08 (d, $J = 13.4$ Hz, 1 H), 3.90 (d, $J = 13.4$ Hz, 1 H), 3.75 (s, 3 H), 3.68 (m, 2 H), 3.06 (m, 1 H), 2.25 (dd, $J = 12.1, 12.1$ Hz, 1 H), 2.10 (dd, $J = 5.6, 12.1$ Hz, 1 H), 1.62 (d, $J = 13.8$ Hz, 1 H), 1.39 (d, $J = 7.5$ Hz, 3 H), 1.35 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.11, 168.57, 164.55, 142.58, 136.79, 135.53, 130.35, 128.65, 128.08, 127.86, 121.46, 120.45, 109.90, 99.48, 65.88, 65.78, 57.09, 54.29, 50.91, 50.11, 34.65, 28.69, 21.77; MS *m/z* (relative intensity) 418 (8), 417 (M^+, 7), 405 (2), 389 (11), 373 (49), 341 (6), 326 (13), 267 (2), 259 (2), 241 (7), 228 (57), 208 (11), 196 (9), 189 (6), 180 (11), 178 (4), 168 (16), 154 (4), 134 (5), 91 (100). Anal. Calcd for $C_{25}H_{27}N_3O_3 \cdot CH_2Cl_2$: C, 62.15; H, 5.82; N, 8.36. Found: C, 62.36; H, 5.54; N, 8.26.

(−)-Methyl (3a*S*,5*S*,11b*R*)-3-Benzyl-2,3,3a,4,5,7-hexahydro-5-methyl-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate ((−)-1a). To a solution of the amide (−)-**20** (80 mg, 0.192 mmol) and Et_3N (187 uL, 1.344 mmol) in 3 mL of dichloromethane, at 0 °C, was added $(CF_3CO)_2O$ (81 μL, 0.576 mmol), dropwise. The solution was allowed to warm to room temperature and stirred for an additional 2 h, and the reaction was quenched by adding 10% Na_2CO_3 solution. The aqueous phase was extracted with dichloromethane. The residual nitrile (−)-**21**, obtained upon drying ($MgSO_4$) and concentration, was dissolved in 3 mL of dry EtOH. KBH_4 (52 mg, 0.96 mmol) was added in several portions at room temperature. Then, the reaction mixture was heated in a 75−80 °C oil bath for 4 h. The solvent was removed in vacuum. Water was added, and the aqueous solution was basified with concentrated NH_4OH to pH 10. The aqueous phase was extracted with dichloromethane. The residue, obtained upon drying and concentration, was chromatographed on a silica gel column, eluting with EtOAc/Hex (1:9) to afford 52 mg of the product (72% yield): $[\alpha]^{22}_D = -387.5$ ($c = 0.24$, $CHCl_3$).

Spiro[pyrrolidinoindolenines] 26 and 27. A mixture of N^b-benzyl-2-[(methoxycarbonyl)methyl]tryptamine (**2**, 322 mg, 1 mmol), benzaldehyde (122 uL, 1.2 mmol), $BF_3 \cdot Et_2O$ (4 μL, 0.03 mmol), and 4 Å molecular sieve powder in 8 mL of dry toluene was heated at reflux for 5.5 h. Using the workup of the general procedure and purification on a silica gel column (EtOAc/hexane, 1:9) afforded 240 mg of a 2:1 mixture (by NMR) of the products **26** and **27** as a white foam (58% yield):

TLC $R_f = 0.17$ (hexane/EtOAc, 9:1; CAS blue); UV (EtOH) $\lambda_{\max}$ 328, 298, 232, 216 nm; IR (KBr) $\nu_{\max}$ 3356, 3086, 3060, 3028, 2948, 2796, 1668, 1609, 1482, 1471, 1451, 1440, 1284, 1227, 1150, 1104, 790, 745, 700 cm^{-1}; MS *m*/*z* (relative intensity) 411 (6), 410 (M$^+$, 21), 319 (3), 230 (1), 216 (6), 208 (26), 196 (3), 183 (4), 169 (6), 156 (14), 140 (2), 128 (4), 118 (95), 105 (5), 91 (100).

For the major product **26**: ^{1}H NMR (500 MHz, CDCl$_3$) d 9.53 (s, 1 H), 7.51 (d, $J = 7.4$ Hz, 1 H), 7.43−7.01 (m, 11 H), 6.86 (dt, $J = 0.7$, 7.4 Hz, 1 H), 6.50 (d, $J = 7.7$ Hz, 1 H), 5.13 (s, 1 H), 4.04 (d, $J = 13.4$ Hz, 1 H), 3.79 (s, 1 H), 3.77 (s, 3 H), 3.43 (ddd, $J = 4.7$, 9.4, 9.4 Hz, 1 H), 3.11 (d, $J = 13.4$ Hz, 1 H), 2.63 (ddd, $J = 7.6$, 9.8, 9.8 Hz, 1 H), 2.29 (m, 2 H).

For the minor product **27**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.22 (s, 1 H), 7.43−7.01 (m, 13 H), 6.60 (d, $J = 7.7$ Hz, 1 H), 5.33 (s, 1 H), 4.06 (d, $J = 13.3$ Hz, 1 H), 3.86 (s, 1 H), 3.70 (s, 1 H), 3.39 (ddd, $J = 5.7$, 9.3, 9.3 Hz, 1 H), 3.06 (d, $J = 13.3$ Hz, 1 H), 2.59 (m, 1 H), 2.44 (ddd, $J = 3.5$, 10.0, 13.5 Hz, 1 H), 2.29 (m, 1 H).

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for compounds **1a**,**c**,**d**,**f**,**h**,**i**, **4**−**6**, **8**, **9**, **14**, **15**, **18**−**20**, **22**−**25**, and **28**−**30**, and ^{1}H NMR spectra for compounds **1e**, **7**, **16**, **17**, **26**, and **27**. Spectra for compound **1g** are found in ref 2 (75 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.

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