Stereocontrolled Formation of Octahydro-1*H*-pyrrolo[2,3-*d*]carbazoles by Reductive Cyclization: Total Synthesis of (±)-*N*-Benzylaspidospermidine

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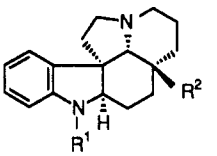
The synthesis of a series of 20-substituted octahydro-1*H*-pyrrolo[2,3-*d*]carbazoles **7**, intermediates in the synthesis of *Aspidosperma* alkaloids, is described. Nonoxidative photocyclization of aryl enaminone **12** led to hexahydrocarbazol-4-ones **15a,b**. Alkylation of the anions derived from **15a,b** with KH and iodoacetonitrile gave rise to an undesirable intramolecular cyclization while reaction with LDA and nitroethylene as Michael acceptor afforded the trisubstituted hexahydrocarbazolones **21a,b**. Reductive cyclization (H_2, PtO_2) of cyano model compounds **16a,b** and **17** provided octahydro-1*H*-pyrrolo[2,3-*d*]carbazoles **25** and **27** whose stereochemistry depended on hindrance of the α and β face of the molecule. In contrast, reduction ($HCOONH_4$, Pd/C, and then Na/EtOH) of nitro model compounds **18a,b** and **19** *via* nitrones **22a,b** and **23** and imine **24** led essentially to the more stable isomers **25B, 25C,** and **27B** with the natural stereochemistry at C-21. Reduction ($HCOONH_4$, Pd/C) of nitro compounds **21a,b**, which possess the elements for the future construction of the D and E rings, induced a tandem cyclization and afforded the pentacyclic iminium **30** which was converted by catalytic hydrogenation into (±)-*N*-benzylaspidospermidine (**4**). This compound was thus synthesized in seven steps from *N*-benzylaniline and cyclohexane-1,3-dione.

Introduction

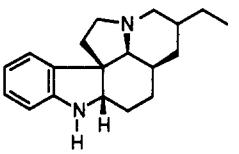
The *Aspidosperma* alkaloids constitute a large family of natural products. The presence of this structure in biologically active compounds (*e.g.*, antitumor dimeric alkaloids[1]) accounts for the continuing interest in their total synthesis.[2]

In continuation of our program[2a,3] aimed at syntheses in this series, we wish to report herein a general strategy involving 20-substituted octahydro-1*H*-pyrrolo[2,3-*d*]carbazoles **7** as direct precursors of the pentacyclic framework. Our methodology, in which the nature of the substituents at C-20[4] may be changed easily, offers access to a large variety of alkaloids such as aspidospermidine (**1**), deoxylimapodine (**2**), 12-demethoxy-*N*-acetylcylindrocarine (**3**), pseudoaspidospermidine (**5**), and aspidofractinine (**6**).

Several methods have been developed for preparing hydropyrrolocarbazoles.[5] Our approach is based on formation of the C-20 center at the start of the synthesis, followed by construction of the ABC ring system by a photocyclization reaction and then creation of the second quaternary center α to the keto group by alkylation and finally elaboration of the E ring by a reductive cyclization (Scheme I). Stereochemical control of this last reaction is a critical step of the synthesis since the stereochemistry at C-21 is established definitively at this stage. In order to evaluate possible difficulties due to the C-20 hindrance, preliminary studies were performed on model compounds **7** (R^2 = Et, R^3 = H; R^2= R^3 = Me). We then made the first application of our scheme in the total synthesis of (±)-*N*-benzylaspidospermidine (**4**)[6] from the trisubstituted hexahydrocarbazol-4-one **8**, which possesses the future D and E ring chains (R^2 = Et, R^3 = $(CH_2)_3Cl$).[7]



1: R^1 = H ; R^2 = CH_2-CH_3
2: R^1 = $COCH_3$; R^2 = CH_2-CH_2OH
3: R^1 = $COCH_3$; R^2 = CH_2-CO_2Me
4: R^1 = CH_2Ph ; R^2 = CH_2-CH_3



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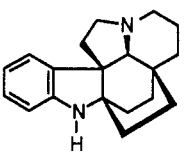

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• Abstract published in *Advance ACS Abstracts,* October 1, 1993.

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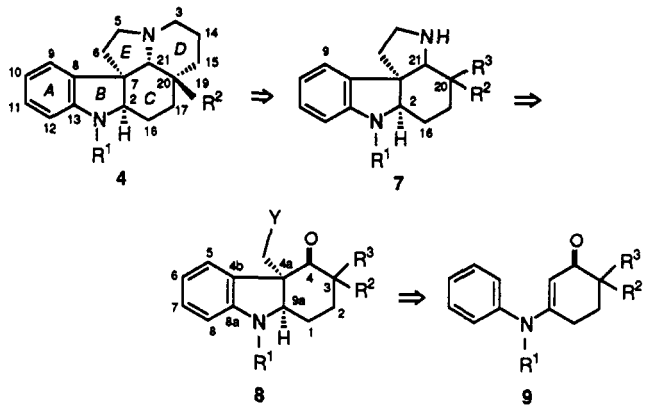
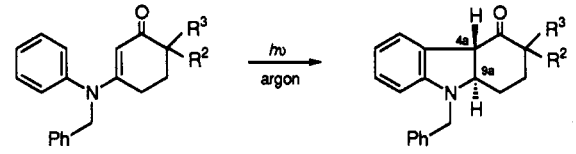
(5) Overman, L. E.; Angle, S. R. *J. Org. Chem.* **1985**, *50*, 4021 and references cited therein.

0022-3263/93/1958-6457$04.00/0

Scheme I



Scheme II



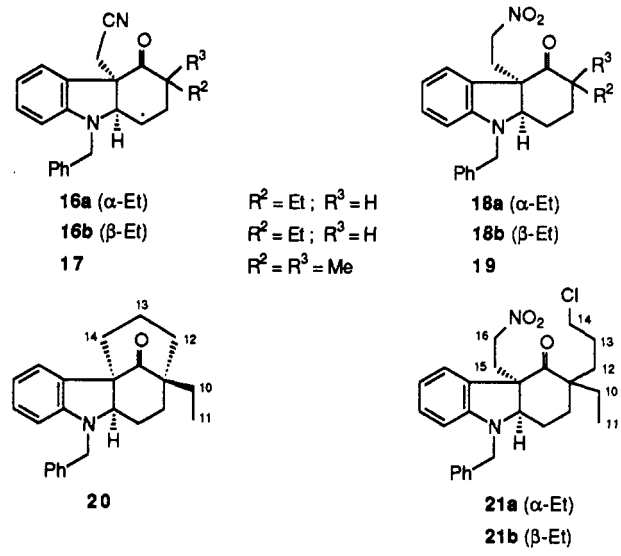
10 : R^2 = Et ; R^3 = H — **13a** (α-Et) + **13b** (β-Et)
11 : R^2 = R^3 = Me — **14**
12 : R^2 = Et ; R^3 = $(CH_2)_3$ Cl — **15a** (α-Et) + **15b** (β-Et)

Results and Discussion

I. Synthesis of Trisubstituted Hexahydrocarbazolones of Type 8. Enaminones **10**,[8] **11**,[9] and **12**[8] were obtained in two or three steps from *N*-benzylaniline and cyclohexane-1,3-dione. Then, according to the original method of our laboratory,[10] nonoxidative photocyclization of **10**, **11**, and **12** gave *trans*-hexahydrocarbazolones **13**,[11] **14**, and **15**, respectively, in 77–84% yield. Two of these compounds were obtained as diastereoisomeric mixtures: **13a,b** (30:70)[11] and **15a,b** (50:50) (Scheme II). Carbonyl absorption at 1715–1720 cm^{-1} in the IR spectrum, a *trans* diaxial coupling constant $^3J_{9a\text{-}4a}$ of 15 Hz in the ^1H NMR spectrum, and a CO signal at δ 206–209.5 in the ^{13}C NMR spectrum are in agreement with the proposed structures.

Formation of the quaternary carbon at C-4a was envisioned by alkylation with iodoacetonitrile or nitroethylene,[12,13] reagents which provide both the 2C and 1N unit of the future E ring. Reactions of *trans*-hexahydrocarbazolones with KH and activated electrophiles are known to give exclusively the more stable B/C *cis* alkylated compounds.[10b,11] Identical results were observed in Michael reactions with LDA and nitroethylene. The *cis* stereochemistry, as well as the α or β position of the 3-ethyl chain in the ethyl series, are supported by spectroscopic data in agreement with previous papers.[10b,11] *Cis* compounds in particular show carbonyl absorption at 1690–1700 cm^{-1} in the IR spectrum, an AB pattern for the NCH_2Ph methylene in the ^1H NMR spectrum, and a signal at δ 208.5–214 for CO in the ^{13}C NMR spectrum. Moreover, in *cis*-3-ethyl derivatives, C-8a (δ 149–152), C-3 (δ 47-51), and CH_3-11 (δ 11–12) are observed at higher field in α-ethyl than in β-ethyl isomers.

Scheme III



In the ethyl and dimethyl series, both iodoacetonitrile and nitroethylene afforded 4a-substituted hexahydrocarbazolones **16a,b** (70:30), **17**, **18a,b** (40:60), and **19** in 66–81% yield (Scheme III). Isomers **16a,b** and **18a,b** were easily separated.

In the 3-ethyl-3-chloropropyl series, the reaction of **15a,b** with KH and iodoacetonitrile did not provide the expected cyanohexahydrocarbazolone of type **8** (Y = CN). Compound **15b** led to a tetracyclic compound **20** generated by intramolecular cyclization of the carbanion on the α-chlorinated side chain (yield 40%) while isomer **15a** rapidly oxidizes to tetrahydrocarbazolone (see refs 10b and 11 for analogous reaction).

In contrast, reaction of **15a,b** with LDA and nitroethylene afforded the expected *cis* nitrohexahydrocarbazolone **21** as an inseparable mixture of isomers **21a,b** in approximately equal amounts (yield 62%) (Scheme III).

II. Synthesis of Octahydro-1*H*-pyrrolo[2,3-*d*]carbazoles. 1. Reduction of Nitrohexahydrocarbazolones 18 and 19. Reductive cyclization of γ or δ nitrocarbonyl compounds gives amines,[14] imines,[13a,15] hydroxylamines,[16] or nitrones,[17,18] depending on the reagent and the starting material.

(6) For (±)-aspidospermidine see: (a) Le Ménez, P.; Kunesch, N.; Liu, S.; Wenkert, E. *J. Org. Chem.* **1991**, *56*, 2915. Reference 2b and references cited therein. For (−)-aspidospermidine see ref 2b. For (+)-*N*-acetylaspidospermidine see: (b) Seki, K.; Ohnuma, T.; Oishi, T.; Ban, Y. *Tetrahedron Lett.* **1975**, 723. Ban, Y.; Yoshida, K.; Goto, J.; Oishi, T.; Takeda, E. *Tetrahedron* **1983**, *39*, 3657. For (−)-noraspidospermidine see: (c) Desmaele, D.; d'Angelo, J. *Tetrahedron Lett.* **1990**, *31*, 883.

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(11) Dugat, D.; Gramain, J.-C.; Dauphin, G. *J. Chem. Soc., Perkin Trans 2* **1990**, 605.

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(15) (a) Kloetzel, M. C.; Pinkus, J. L.; Washburn, R. M. *J. Am. Chem. Soc.* **1957**, *79*, 4222. (b) Weinreb, S. M.; Basha, F. Z.; Hibino, S.; Khatri, N. A.; Kim, D.; Pye, W.E.; Wu, T.-T. *J. Am. Chem. Soc.* **1982**, *104*, 536.

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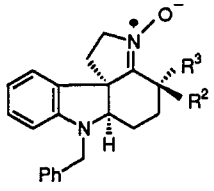
Table I. Diastereoselective Synthesis of Tetracyclic Amines 25A–C and 27A,B from Hexahydrocarbazolones 16a,b, 17, 18a,b, and 19 *via* Nitrones 22a,b and 23 and Imine 24

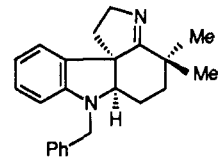
hexahydrocarbazolones	isolated nitrones and imines	tetracyclic amines: 21-epi series	tetracyclic amines: 21-natural series	ratio 21-epi:21-nat
16a (α-Et)[a]		**25A** (α-Et)	**25C** (α-Et)	85:15
16b (β-Et)[a]		**25A** (α-Et)	**25B** (β-Et) + **25C** (α-Et)	20:80
16a,b (70:30)[a]		**25A** (α-Et)	**25B** (β-Et) + **25C** (α-Et)	65:35
17[a]			**27B**	0:100
18a (α-Et)[b]	**22a** (α-Et)	**25A** (α-Et)	**25C** (α-Et)	45:55
18b (β-Et)[b]	**22b** (β-Et)		**25B** (β-Et)	0:100
18a,b (40:60)[b]	**22a,b** (40:60)	**25A** (α-Et)	**25B** (β-Et) + **25C** (α-Et)	20:80
	23		**27B**	0:100
19[b]	**24**	**27A**	**27B**	35:65
	23 + **24** (60:40)	**27A**	**27B**	15:85

[a] Reducing agents: H_2, PtO_2, EtOH. [b] Reducing agents: $HCOONH_4$, Pd/C, MeOH, and Na/EtOH.

Scheme IV



22a : $R^2 = H$; $R^3 = Et$
22b : $R^2 = Et$; $R^3 = H$
23 : $R^2 = R^3 = Me$



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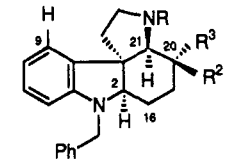
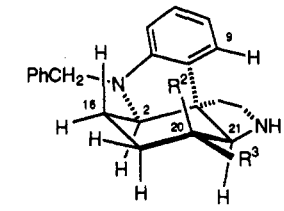
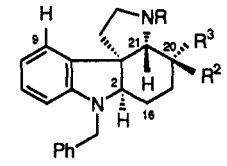
Scheme V



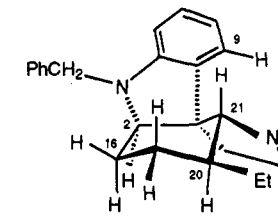
25A : R = H ; $R^2 = H$; $R^3 = Et$
26A : R = Ac ; $R^2 = H$; $R^3 = Et$
27A : R = H ; $R^2 = R^3 = Me$
28A : R = Ac ; $R^2 = R^3 = Me$



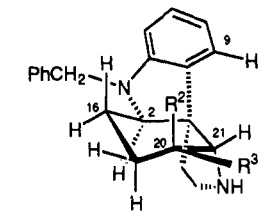
25A : $R^2 = H$; $R^3 = Et$
27A : $R^2 = R^3 = Me$



25B : R = H ; $R^2 = Et$; $R^3 = H$
26B : R = Ac ; $R^2 = Et$; $R^3 = H$
25C : R = H ; $R^2 = H$; $R^3 = Et$
26C : R = Ac ; $R^2 = H$; $R^3 = Et$
27B : R = H ; $R^2 = R^3 = Me$
28B : R = Ac ; $R^2 = R^3 = Me$



25B



25C : $R^2 = H$; $R^3 = Et$
27B : $R^2 = R^3 = Me$

a. Tetracyclic Imines and Nitrones. Various conditions were assessed for nitro compounds **18a** and **18b**: H_2, Pd/C + Pt/C, EtOH;[14] H_2, Ni-Raney, EtOH;[13a,15a] cyclohexene, Pd/C;[16] $HCOONH_4$, Pd/C, MeOH.[18,19] The first three reaction conditions provided complex mixtures. In contrast, use of ammonium formate as hydrogen transfer agent and palladium on carbon as catalyst led to a single compound in 80% yield. Nitrone **22a** was thus obtained from **18a** and nitrone **22b** from **18b**. An identical reaction, carried out on **19**, afforded a mixture of nitrone **23** and imine **24** in a 60:40 ratio and 70% yield (Scheme IV) (Table I). In the IR spectrum, imine **24** shows a characteristic strong C=N band at 1630 cm^{-1} whereas nitrones **22a,b** and **23** exhibit four weak C=N^+ absorptions between 1940 and 1700 cm^{-1}. In the ^{13}C NMR spectra, carbon C-21 (natural product numbering) gives an expected signal at δ 184.5 in imine **24** while it is strongly shielded in nitrones **22a,b** and **23** (δ 149–151).[20] COSY ^1H–^1H NMR chemical shift correlations performed on compounds **22a** and **22b** allow identification of all hydrogens. A MS/MS study of **22b** confirmed the nitrone structure.

b. Tetracyclic Amines. The unsaturated compounds **22-24** had to be reduced to amines. The reaction could give four isomers in the ethyl series and two isomers in the dimethyl series. Preponderant formation of the compound with the natural stereochemistry at C-21 required stereochemical control of the reaction. This was accomplished with sodium in ethanol.[21] The reaction afforded directly the expected tetracyclic amines which were transformed into acetamides for easier isolation and purification.

i. Ethyl series. Reduction of the β-Et nitrone **22b** led exclusively to amine **25B** whereas reduction of α-Et nitrone **22a** gave two other isomers **25A** + **25C** in a 45:55 ratio (yield 95%; conversion 50%) (Scheme V) (Table I). Acetylation of **25A**, **25B**, and **25C** provided amides **26A**, **26B**, and **26C**[22] in 90% yield. The structure, stereochemistry and conformation of each of these compounds were inferred from spectral data, in particular ^1H NMR, ^{13}C NMR, 2D NMR experiments (COSY ^1H–^1H), and inspection of molecular models. Thus, compounds **25A–C** were identified as three of the four possible isomers. In the ^{13}C NMR spectra, the C-21 signal of **22** at δ 149–151 had disappeared, while a new one was observed at δ 63–69. In the ^1H NMR spectra, comparison of the H-9 chemical shift and of the coupling constants $^3J_{20,21}$ in the three isomers allowed determination of their relative stereochemistry. Deshielding of H-9 in **25A** (δ 7.68) compared to its chemical shift in **25B** (δ 7.06) or **25C** (δ 7.08) is due to the proximity of the N_b lone pair in a C/D *trans* ring junction.[2a,3] On the other hand, the coupling constant

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(22) Letters A, B, C refer to the increasing polarity order of acetamides **26**.

$^3J_{20,21}$ = 9–11.5 Hz in amines **25A** and **25B** or amides **26A** and **26B** indicates a *trans* relationship for H-20 and H-21 while a value of 7 Hz in **25C** or **26C** suggests a *cis* H-20, H-21 relationship. These considerations enabled us to assign a natural stereochemistry to amine **25B**, a 20-epi geometry to isomer **25C**, and a 20-epi 21-epi structure to isomer **25A**.

Moreover, the coupling constants of H-2 with its two vicinal hydrogens give some information about the conformation. The observed values are consistent with an axial position of H-2 in **25A** ($J_{2,16ax}$ = 8 Hz, $J_{2,16eq}$ = 5 Hz in CD_3OD) and a pseudoequatorial position in **25B** ($J_{2,16ax}$ = $J_{2,16eq}$ = 4 Hz). The C ring adopts a rigid chair form in **25A** and a flexible flattened chair form in **25B** and **25C**. The conformations of **25B** and **25C** correspond to the two chair forms of any bi- or tricyclic system with a *cis* ring junction.[11]

Finally, shielding of H-21 in **25B** (δ 2.65) compared to its chemical shift in **25A** (δ 3.02) or **25C** (δ 4.00) may be explained by its position in the anisotropy cone of the A aromatic ring as shown by examination of molecular models.

ii. Dimethyl Series. Dimethyl compounds **23** and **24** were reduced under identical conditions (Na/EtOH). Nitrone **23** afforded the single amine **27B** (yield 95%, conversion 55%) while imine **24** gave two isomers **27A** + **27B** in a 35:65 ratio (yield 60%, conversion 50%). Acetylation of **27A** and **27B** led to the corresponding acetamides **28A** and **28B** in 90% yield (Scheme V).

Amines **27A** and **27B** show C-21 at δ 65.5 and 66.4, respectively, in the ^{13}C NMR spectra. Comparison of H-9 proton NMR chemical shifts allows assignment of a 21-epi stereochemistry to **27A** (δ 7.54) and a 21-natural stereochemistry to **27B** (δ 7.06) as seen above. Moreover, H-21 resonates at δ 3.13 in **27A** and at δ 3.69 in **27B**, *i.e.*, at chemical shifts close to those observed in **25A** and **25C**, respectively. Likewise, the coupling constants of H-2 ($J_{2,16ax}$ = 8.0 Hz; $J_{2,16eq}$ = 3.5 Hz) in **27B** are consistent with a pseudoaxial position of H-2 in analogy with **25C**. Consequently, amines **27A** and **27B** adopt conformations similar to those of **25A** and **25C**, respectively.

iii. In summary, tetracyclic amines **25** and **27** can be obtained from nitrohexahydrocarbazolones **18** and **19** *via* nitrones and imines. Reduction of those unsaturated intermediates by Na/EtOH is stereoselective and leads essentially to the more stable compounds **25B**, **25C**, and **27B** with a 21-natural stereochemistry.

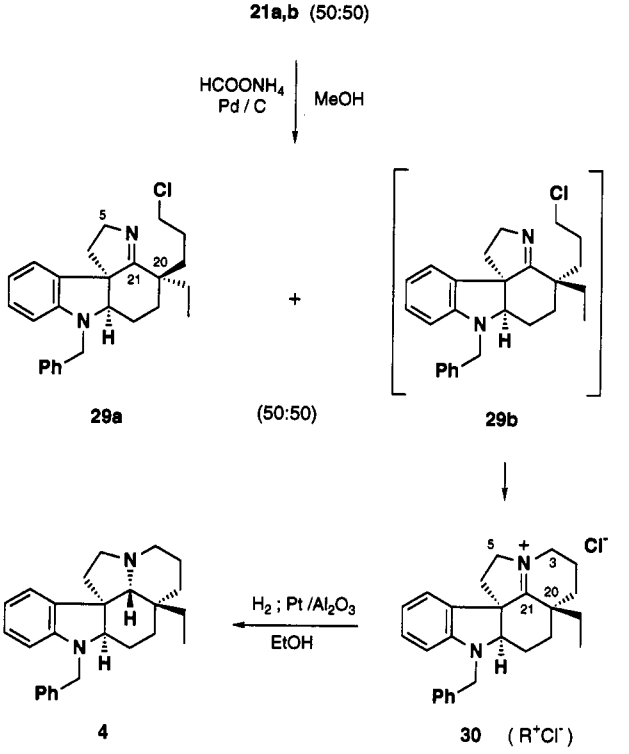
2. Reduction of Cyanohexahydrocarbazolones 16 and 17. Reductive cyclization of γ or δ cyanocarbonyl compounds involves reduction of the nitrile group to a primary amine followed by condensation on the keto group. In fact, the reaction performed by catalytic hydrogenation with platinum oxide[23] led directly to the expected tetracyclic amines as already observed in the unsubstituted series.[24]

In the ethyl series, reduction of **16a** gave the previously described amines **25A** + **25C** in a 85:15 ratio while reduction of **16b** afforded the three isomers **25A** + **25B** + **25C** in a 20:50:30 ratio (yield 66–68%) (Table I). In this last reaction, formation of α-ethyl **25A** and **25C** results from the partial epimerization of **16b** into its more stable isomer **16a** (as shown by equilibration experiments **16a**:**16b** = 70:30) prior to reduction.

In the dimethyl series, reduction of **17** gave exclusively amine **27B** with a 21-natural stereochemistry.

These results showed that reductive cyclization of monosubstituted cyanohexahydrocarbazolones leads to tetracyclic amines whose 21-stereochemistry depends on the α or β face hindrance of the molecule. In contrast, a 21-natural stereochemistry could be expected from 20-disubstituted compounds.

Scheme VI



III. Synthesis of *N*-Benzylaspidospermidine. The previous results prompted us to investigate the reductive cyclization of nitrohexahydrocarbazolone **21**, which possesses at C-3 an ethyl group and a chloropropyl chain, as a key step in the synthesis of the target alkaloid.

Reduction with ammonium formate was carried out on the diastereoisomeric mixture **21a,b** (50:50), giving imine **29a** and iminium chloride **30** in approximately equal quantities (yield 67%) (Scheme VI). The reduction of the nitro group to primary amine led to spontaneous cyclization into the tetracyclic imines **29a,b**. Imine **29b** which possesses the natural stereochemistry at C-20 cyclized spontaneously into the pentacyclic iminium **30** whereas the unnatural stereochemistry of **29a** prevented any further cyclization. The two compounds were easily separated at this stage. The EI mass spectrum of each compound shows a molecular peak at 406 amu (R^+Cl^- for **30**), and the FAB spectra of **30** are characterized by a peak at 371 (R^+) in the positive technique and a peak at 441 [$(R^+Cl^-)Cl^-$] in the negative technique. In the IR spectra, imine **29a** exhibits a C=N absorption at 1625 cm^{-1} while the $C{=}N^+$ band of iminium **30** appears at 1675 cm^{-1}. In the ^{13}C NMR spectra, the presence of a C-21 signal at δ 182.0 in imine **29a** and at δ 195.6 in iminium **30** proved that cyclization had occurred. In ^1H NMR spectroscopy, a COSY ^1H–^1H correlation performed on imine **29a** allowed identification of all hydrogens. High chemical shift values of H-5eq (δ 3.99 in **29a**; δ 4.88 in **30**) and of H-3eq in **30**

(23) (a) Hudlicky, M. In *Reductions in Organic Chemistry*, J. Wiley: New York, 1984; p 135. (b) Hancock, E. M.; Cope, A. C. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 501.

(24) Troin Y. *Thèse d'Etat*, Université de Clermont-Ferrand, no. d' ordre 334, 29 May 1984, p 56.

(δ 4.76) prove once more the formation of the unsaturated D ring in **29a** and of the D + E rings in **30**.

The synthesis was completed by reduction of the iminium salt **30**. Catalytic hydrogenation (H_2, Pt/Al_2O_3) occurred stereospecifically on the β face of the molecule and afforded *N*-benzylaspidospermidine (**4**) in 70% yield. The compound obtained was identified by TLC correlation and by comparison of its spectroscopic data with those of an authentic sample prepared from vincadifformine.[25,26,27]

Conclusion

The above synthesis, which involves the reactivity of hexahydrocarbazolones in a Michael reaction with nitroethylene and a double reductive cyclization of nitroketones, as new and original reactions, constitutes one of the shortest syntheses (seven steps) of *Aspidosperma* alkaloids. Our approach is general and can be applied to the synthesis of other indole alkaloids.

Experimental Section

General Methods. Experimental techniques and analytical measurements were applied as previously described.[2a,11] NMR spectra were recorded at 300 MHz in $CDCl_3$. *J* values are given in Hz. Organic layers were dried over $MgSO_4$ (Aldrich).

***trans*-Hexahydrocarbazol-4-ones 13a,b, 14, 15a,b. (General Procedure).** Degassed solutions of **10**,[8] **11**,[9] or **12**[8] (2.62 mmol) in benzene (150 mL) were irradiated under an atmosphere of argon. Evaporation of the solvent gave crude material which was purified by flash chromatography on silica gel. Specific details are given for each compound.

Compounds 13a,b have already been described[11] (ratio 30:70, yield 84%).

Compound 14: starting material, **11** (800 mg, 2.62 mmol); irradiation time 20 min; chromatography eluent, hexane–AcOEt (80:20); isolated compound, 546 mg, yield 80%, conversion 85%. An analytical sample was obtained by crystallization from AcOEt: mp 165–167 °C; IR (CCl_4) 1715 cm^{-1}; ^1H NMR δ 7.48 (d, 1H, H-5, *J* = 7.5), 7.35–7.20 (m, 5H, ArH), 7.00 (t, 1H, H-7, *J* = 7.5), 6.76 (t, 1H, H-6, *J* = 7.5), 6.45 (d, 1H, H-8, *J* = 7.5), 4.16 (s, 2H, NCH_2Ph), 3.86 (d, 1H, H-4a, *J* = 15.0), 3.00 (ddd, 1H, H-9a, *J* = 15.0, 10.0, 5.0), 1.99–1.86 (m, 2H, 2H-1), 1.80 (ddd, 1H, H-2eq, *J* = 14.0, 3.5, 3.5), 1.51 (ddd, 1H, H-2ax, *J* = 14.0, 11.0, 7.0), 1.23 (s, 3H, Me-10), 1.06 (s, 3H, Me-11); ^{13}C NMR δ 209.5, 153.1, 138.8, 128.6 (2C), 127.9, 127.6 (2C), 127.2, 125.8, 125.0, 119.5, 108.9, 73.5, 53.5, 52.7, 45.7, 38.8, 26.9, 26.6, 24.9; MS (EI) *m/z* 305 (60, M^+), 247 (12), 220 (31), 207 (12), 144 (8), 130 (31), 91 (100), 83 (22), 65 (14), 41 (25), 29 (13); HRMS calcd for $C_{21}H_{23}NO$ 305.1779, found 305.1780. Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59; O, 5.24. Found: C, 82.38; H, 7.62; N, 4.40; O, 5.27.

Compounds 15a,b: starting material, **12** (1 g, 2.62 mmol); irradiation time, 45 min; chromatography eluent, hexane–AcOEt (90:10). The two isomers **15a,b** (50:50) (424 mg, yield 77%, conversion 55%) showed identical R_f values and were not separated. An analytical sample of one isomer was, however, isolated as a white solid by three fractional crystallizations from AcOEt while evaporation of the mother liquor afforded mainly the second isomer as an amorphous compound.

15a: amorphous solid; IR (CCl_4) 1720 cm^{-1}; ^1H NMR δ 7.54 (d, 1H, H-5, *J* = 7.5), 7.43–7.25 (m, 5H, ArH), 7.08 (t, 1H, H-7, *J* = 7.5), 6.84 (t, 1H, H-6, *J* = 7.5), 6.53 (d, 1H, H-8, *J* = 7.5), 4.25 (s, 2H, NCH_2Ph), 3.85 (d, 1H, H-4a, *J* = 15.0), 3.52 (m, 2H, CH_2Cl), 3.06 (ddd, 1H, H-9a, *J* = 15.0, 8.5, 6.5), 2.10–1.50 (m, 9H), 0.9 (dddd, 1H, H-2ax, *J* = 14.0, 7.0, 7.0, 2.0), 0.84 (t, 3H, Me-11, *J* = 7.5); ^{13}C NMR δ 208.8, 153.1, 138.8, 128.6 (2C), 128.0, 127.6 (2C), 125.5, 127.3, 125.0, 119.6, 109.0, 73.0, 54.4, 52.9, 51.9, 45.2, 34.3, 33.8, 26.9, 26.6, 26.2, 8.0; MS (EI) *m/z* 383 [4, M^+ (^{37}Cl)], 381 [12, M^+ (^{35}Cl)], 242 (10), 241 (28), 149 (16), 144 (10), 91 (100); HRMS calcd for $C_{24}H_{28}NOCl$ 381.1860, found 381.1864.

15b: white crystals; mp 149–151 °C; IR (CCl_4) 1720 cm^{-1}; ^1H NMR δ 7.54 (d, 1H, H-5, *J* = 7.5), 7.43–7.25 (m, 5H, ArH), 7.08 (t, 1H, H-7, *J* = 7.5), 6.84 (t, 1H, H-6, *J* = 7.5), 6.53 (d, 1H, H-8, *J* = 7.5), 4.25 (s, 2H, NCH_2Ph), 3.83 (d, 1H, H-4a, *J* = 15.0), 3.56 (m, 2H, CH_2Cl), 3.04 (ddd, 1H, H-9a, *J* = 15.0, 8.5, 5.5), 2.10–1.50 (m, 10H), 0.84 (t, 3H, Me-11, *J* = 7.5); ^{13}C NMR δ 208.7, 153.1, 138.8, 128.6 (2C), 128.0, 127.6 (2C), 127.3, 125.5, 125.0, 119.6, 109.0, 73.0, 54.2, 52.9, 52.3, 45.7, 34.3, 30.9, 30.0, 27.5, 26.6, 8.1; MS (EI) *m/z* 383 [4, M^+ (^{37}Cl)], 381 [12, M^+ (^{35}Cl)], 242 (10), 241 (28), 149 (16), 91 (100); HRMS calcd for $C_{24}H_{28}NOCl$ 381.1860, found 381.1864. Anal. Calcd for $C_{24}H_{28}NOCl$: C, 75.47; H, 7.39; N, 3.66; O, 4.19; Cl, 9.28. Found: C, 75.03; H, 7.29; N, 3.62; O, 4.49; Cl, 9.19.

***cis*-3-Ethyl-4a-(cyanomethyl)-9-benzylhexahydrocarbazol-4-ones (16a,b).** A solution of **13a,b** (30:70) (610 mg, 2.0 mmol) in THF (12 mL) was added dropwise to a suspension of KH (33% in oil, 312 mg, 2.6 mmol) in THF (6 mL) and stirred at rt for 15 min under an atmosphere of argon. The resulting mixture was then added to a solution of iodoacetonitrile (400 mg, 2.4 mmol) in THF (15 mL). After the mixture had been stirred for an additional 30 min, water was added. The bulk of the THF was distilled, and the aqueous phase was extracted three times with AcOEt. The combined organic layers were washed with water, dried, and concentrated. The residue was purified by flash chromatography on silica gel [hexane–AcOEt (90:10)] to give **16a** (390 mg, 57%) and **16b** (167 mg, 24%).

16a: green crystals; mp 107–108 °C (AcOEt); IR (CCl_4) 2240, 1700 cm^{-1}; ^1H NMR δ 7.38 (m, 5H, ArH), 7.17 (t, 1H, H-7, *J* = 7.5), 6.90 (d, 1H, H-5, *J* = 7.5), 6.72 (t, 1H, H-6, *J* = 7.5), 6.54 (d, 1H, H-8, *J* = 7.5), 4.41 (AB, 2H, NCH_2Ph, *J* = 15.0, Δν = 74.5), 3.94 (dd, 1H, H-9a, *J* = 8.5, 5.0), 2.80 (AB, 2H, CH_2CN, *J* = 17.5, Δν = 96.5), 2.27 (dddd, 1H, H-3, *J* = 12.0, 6.0, 6.0, 6.0), 2.07–1.96 (m, 2H, H-1eq, H-2eq), 1.86 (ddq, 1H, H-10A, *J* = 14.0, 7.0, 6.0), 1.68 (m, 1H, H-1ax), 1.36 (ddq, 1H, H-10B, *J* = 14.0, 7.0, 6.0), 1.32 (m, 1H, H-2ax), 0.89 (t, 3H, Me-11, *J* = 7.0); ^{13}C NMR δ 208.5, 149.6, 137.4, 130.2, 128.8 (3C), 127.5 (3C), 123.3, 118.6, 117.8, 108.2, 71.0, 59.0, 49.4, 47.7, 25.3, 25.0, 23.8, 21.9, 11.3; MS (EI) *m/z* 344 (26, M^+), 276 (10), 220 (10), 91 (100); HRMS calcd for $C_{23}H_{24}N_2O$ 344.1889, found 344.1887. Anal. Calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13; O, 4.64. Found: C, 80.22; H, 6.69; N, 8.11; O, 4.96.

16b: amorphous solid; IR (CCl_4) 2240, 1700 cm^{-1}; ^1H NMR δ 7.35 (m, 5H, ArH), 7.14 (t, 1H, H-7, *J* = 7.5), 6.91 (d, 1H, H-5, *J* = 7.5), 6.65 (t, 1H, H-6, *J* = 7.5), 6.49 (d, 1H, H-8, *J* = 7.5), 4.45 (AB, 2H, NCH_2Ph, *J* = 16.0, Δν = 54.0), 4.00 (dd, 1H, H-9a, *J* = 4.0, 3.0), 2.79 (AB, 2H, CH_2CN, *J* = 16.0, Δν = 118.0), 2.30 (dddd, 1H, H-3, *J* = 9.0, 7.5, 7.5, 6.0), 1.97 (m, 1H, H-1eq), 1.82 (m, 1H, H-1ax), 1.70–1.50 (m, 2H, 2H-2), 1.63 (ddq, 1H, H-10A, *J* = 14.0, 7.3, 6.0), 1.16 (ddq, 1H, H-10B, *J* = 14.0, 8.0, 7.3), 0.83 (t, 3H, Me-11, *J* = 7.3); ^{13}C NMR δ 209.7, 151.4, 137.9, 130.5, 128.8 (2C), 127.6, 127.3 (2C), 126.0, 124.2, 117.9, 117.5, 107.2, 69.0, 58.2, 50.7, 50.0, 27.0, 26.7, 25.5, 22.7, 11.8; MS (EI) *m/z* 344 (30, M^+), 276 (11), 220 (15), 91 (100), 83 (24), 65 (14), 41 (14); HRMS calcd for $C_{23}H_{24}N_2O$ 344.1889, found 344.1889.

***cis*-3,3-Dimethyl-4a-(cyanomethyl)-9-benzylhexahydrocarbazol-4-one (17).** This compound was prepared from **14** (610 mg, 2 mmol) following the procedure described for **16a,b**. Flash chromatography on silica gel, with 80:20 hexane–AcOEt, afforded **17** (550 mg, 80%): white crystals; mp 115–117 °C (cyclohexane); IR ($CHCl_3$) 2240, 1690 cm^{-1}; ^1H NMR δ 7.36 (m, 5H, ArH), 7.14 (td, 1H, H-7, *J* = 7.5, 1.0), 6.89 (dd, 1H, H-5, *J* = 7.5, 1.0), 6.65 (t, 1H, H-6, *J* = 7.5), 6.48 (d, 1H, H-8, *J* = 7.5), 4.47 (AB, 2H, NCH_2Ph, *J* = 15.0, Δν = 64.0), 3.97 (dd, 1H, H-9a, *J* = 6.0, 5.0), 2.77 (AB, 2H, CH_2CN, *J* = 16.0, Δν = 148.0), 1.87–1.70 (m, 3H, H-2eq, 2H-1), 1.55 (m, 1H, H-2ax), 1.20 (s, 3H, Me-10), 0.97 (s, 3H, Me-11); ^{13}C NMR δ 212.4, 150.1, 137.7, 130.3, 128.9 (2C), 127.7, 127.5 (2C), 127.0, 124.0, 118.1, 117.8, 107.4, 69.2, 58.4, 49.5, 44.2, 32.4, 28.4, 26.4, 26.3, 23.1; MS (EI) *m/z* 344 (15, M^+), 220 (20), 183 (25), 104 (10), 91 (100), 65 (11); HRMS calcd for $C_{23}H_{24}N_2O$ 344.1889, found 344.1887. Anal. Calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13; O, 4.64. Found: C, 80.26; H, 6.94; N, 8.19; O, 4.98.

(25) Vincadifformine was transformed into aspidospermidine by acidic treatment[26] and reduction with $LiAlH_4$.[27] Then, benzylation with $PhCH_2Br$ (DMF, K_2CO_3) afforded *N*-benzylaspidospermidine.

(26) Hoizey, M.-J.; Olivier, L.; Lévy, J.; Le Men, J. *Tetrahedron Lett.* **1971**, 1011.

(27) Wenkert, E.; Hudlicky, T. *J. Org. Chem.* **1988**, *53*, 1953.

***cis*-3-Ethyl-4a-(nitroethyl)-9-benzylhexahydrocarbazol-4-ones (18a,b).** To a solution of LDA (2.4 mmol) at −78 °C, prepared from diisopropylamine (242 mg, 335 μL), THF (4 mL), and *n*-butyllithium (1.5 M in hexane, 1.6 mL), was slowly added, under argon, a solution of **13a,b** (30:70) (610 mg, 2 mmol) in THF (10 mL) and then HMPA (537 mg, 521 μL). The mixture was stirred for 1 h, and a solution of nitroethylene (219 mg, 3 mmol) in THF (3 mL) was added dropwise. The mixture was stirred again for 1 h at −78 °C and allowed to warm to rt. The solvent was removed, and the residue was dissolved in AcOEt. The solution was washed with brine, dried, and concentrated. Flash chromatography on silica gel, using 95:5 hexane–AcOEt, afforded **18a** (242 mg, 32%) and **18b** (363 mg, 48%).

18a: amorphous solid; IR (CCl_4) 1700, 1450, 1380 cm^{-1}; ^1H NMR δ 7.38 (m, 5H, ArH), 7.16 (t, 1H, H-7, J = 7.5), 6.85 (d, 1H, H-5, J = 7.5), 6.72 (t, 1H, H-6, J = 7.5), 6.55 (d, 1H, H-8, J = 7.5), 4.37 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 98.0), 4.36 (ABX_2, 2H, CH_2NO_2), 3.67 (dd, 1H, H-9a, J = 8.5, 5.5), 2.52 (m, 2H, 2H-15), 2.24 (dddd, 1H, H-3, J = 12.0, 7.0, 6.0, 6.0), 2.05–1.85 (m, 2H, H-1eq, H-2eq), 1.82 (ddq, 1H, H-10A, J = 14.0, 7.5, 6.0), 1.67 (m, 1H, H-1ax), 1.29 (ddq, 1H, H-10B, J = 14.0, 7.5, 7.0), 1.24 (m, 1H, H-2ax), 0.87 (t, 3H, Me-11, J = 7.5); ^{13}C NMR δ 210.9, 150.0, 137.5, 130.9, 129.8, 128.9 (2C), 127.8 (3C), 123.7, 118.5, 108.1, 72.6, 70.8, 59.4, 49.3, 47.9, 32.2, 25.7, 25.2, 22.2, 11.4; MS (EI) m/z 378 (3, $M^{+\cdot}$), 275 (6), 234 (8), 196 (9), 149 (20), 105 (20), 91 (82), 43 (100); HRMS calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1941.

18b: white crystals; mp 64–66 °C (cyclohexane); IR (CCl_4) 1695, 1450, 1380 cm^{-1}; ^1H NMR δ 7.34 (m, 5H, ArH), 7.12 (t, 1H, H-7, J = 7.5), 6.94 (d, 1H, H-5, J = 7.5), 6.68 (t, 1H, H-6, J = 7.5), 6.49 (d, 1H, H-8, J = 7.5), 4.39 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 85.5), 4.24 (t, 2H, CH_2NO_2, J = 7.6), 3.75 (dd, 1H, H-9a, J = 4.0, 3.0), 2.51 (m, 2H, 2H-15), 2.23 (dddd, 1H, H-3, J = 9.0, 7.5, 7.5, 6.0), 2.00 (m, 1H, H-1eq), 1.82 (m, 1H, H-1ax), 1.74–1.55 (m, 3H, 2H-2, H-10A), 1.15 (ddq, 1H, H-10B, J = 14.0, 7.5, 7.5), 0.83 (t, 3H, Me-11, J = 7.5); ^{13}C NMR δ 211.5, 151.5, 137.8, 129.8, 128.9 (2C), 127.6, 127.5 (2C), 126.6, 124.9, 117.8, 107.0, 72.0, 68.2, 58.8, 50.7, 49.7, 34.3, 26.6, 25.2, 23.3, 11.8; MS (EI) m/z 378 (6), 303 (4), 274 (6), 91 (100); HRMS calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1945. Anal. Calcd for $C_{23}H_{26}N_2O_3$: C, 72.99; H, 6.93; N, 7.40; O, 12.68. Found: C, 72.82; H, 6.94; N, 7.21; O, 12.65.

***cis*-3,3-Dimethyl-4a-(nitroethyl)-9-benzylhexahydrocarbazol-4-one (19).** This compound was prepared from **14** (610 mg, 2 mmol) according to the method described for **18a,b**. Flash chromatography on silica gel, with 95:5 hexane–AcOEt, afforded **19** (498 mg, 66%): white crystals; mp 67–69 °C (hexane); IR (CCl_4) 1690, 1450, 1380 cm^{-1}; ^1H NMR δ 7.37 (m, 5H, ArH), 7.14 (td, 1H, H-7, J = 7.5, 1.0 Hz), 6.89 (dd, 1H, H-5, J = 7.5, 1.0), 6.66 (t, 1H, H-6, J = 7.5), 6.51 (d, 1H, H-8, J = 7.5), 4.43 (AB, 2H, NCH_2Ph, J = 15.5, $\Delta\nu$ = 91.0), 4.26 (m, 2H, CH_2NO_2), 3.72 (t, 1H, H-9a, J = 5.0), 2.49 (m, 2H, 2H-15), 1.89–1.68 (m, 3H, 2H-1, H-2eq), 1.47 (m, 1H, H-2ax), 1.15 (s, 3H, Me-10), 0.95 (s, 3H, Me-11); ^{13}C NMR δ 214.3, 150.4, 137.7, 129.8, 128.8 (2C), 127.6 (3C), 127.5, 124.4, 117.8, 106.8, 72.3, 68.3, 58.3, 48.9, 44.2, 34.8, 32.4, 28.8, 26.6, 23.0; MS (EI) m/z 378 (24, $M^{+\cdot}$), 304 (7), 259 (6), 247 (8), 233 (7), 220 (12), 198 (5), 91 (100); HRMS calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1941. Anal. Calcd for $C_{23}H_{26}N_2O_3$: C, 72.99; H, 6.93; N, 7.40; O, 12.68. Found: C, 72.93; H, 6.95; N, 7.47; O, 12.57.

***cis*-3-Ethyl-3,4a-propano-9-benzylhexahydrocarbazol-4-one (20).** This compound was prepared from **15a,b** (762 mg, 2 mmol) following the procedure described for **16a,b**. Flash chromatography on silica gel, using 95:5 hexane–AcOEt, afforded **20** (276 mg, 40%) and a fraction of 3-ethyl-3-chloropropyltetrahydrocarbazolone (190 mg, 25%).

20: white crystals, mp 135–137 °C (cyclohexane); IR (CCl_4) 1720 cm^{-1}; ^1H NMR δ 7.28 (m, 5H, ArH), 7.15 (d, 1H, H-5, J = 7.5), 7.05 (t, 1H, H-7, J = 7.5), 6.72 (t, 1H, H-6, J = 7.5), 6.35 (d, 1H, H-8, J = 7.5), 4.40 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 27.7), 4.00 (dd, 1H, H-9a, J = 11.0 , 5.0), 2.15–1.10 (m, 12H), 0.86 (t, 3H, Me-11, J = 7.3); ^{13}C NMR δ 215.6, 150.6, 139.1, 128.6 (4C), 127.1 (3C), 126.3, 117.1, 106.0, 71.6, 60.3, 51.0, 48.9, 43.2, 41.9, 30.2, 29.4, 28.3, 17.8, 7.9; MS (EI) m/z (relative intensity) 345 (19, $M^{+\cdot}$), 279 (13), 245 (12), 167 (14), 149 (49), 119 (31), 91 (100); HRMS calcd for $C_{24}H_{27}NO$ 345.2092, found 345.2087. Anal. Calcd for $C_{24}H_{27}NO$: C, 83.44; H, 7.88; N, 4.05; O, 4.63. Found: C, 82.53; H, 7.82; N, 4.20; O, 4.75.

***cis*-3-Ethyl-3-(chloropropyl)-4a-(nitroethyl)-9-benzylhexahydrocarbazol-4-ones (21a,b).** These compounds were prepared from **15a,b** (762 mg, 2 mmol) following the procedure described for **18a,b** and purified by flash chromatography on silica gel with 95:5 hexane–AcOEt. The two isomers **21a** and **21b** (563 mg, ratio 50:50, yield 62%) showed identical R_f values after five elutions and could not be separated. Their spectroscopic data were assigned from the mixture.

21a: ^1H NMR δ 7.35 (m, 5H, ArH), 7.14 (td, 1H, H-7, J = 7.5, 1.0), 6.92 (dd, 1H, H-5, J = 7.5, 1.0), 6.66 (t, 1H, H-6, J = 7.5), 6.52 (d, 1H, H-8, J = 7.5), 4.40 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 92.0), 4.23 (m, 2H, CH_2NO_2), 3.69 (m, 1H, H-9a), 3.25 (ABX_2, 2H, CH_2Cl), 2.50 (m, 2H, 2H-15), 1.85–1.13 (m, 10H), 0.82 (t, 3H, Me-11, J = 7.5); ^{13}C NMR δ 212.8, 150.3, 137.5, 129.9, 128.9 (2C), 127.7 (3C), 127.3, 124.0, 118.0, 107.3, 72.2, 68.0, 58.1, 50.0, 49.2, 45.2, 35.2, 34.8, 28.3, 27.3, 26.8, 22.3, 8.2.

21b: ^1H NMR δ 7.35 (m, 5H, ArH), 7.14 (td, 1H, H-7, J = 7.5, 1.0), 6.92 (dd, 1H, H-5, J = 7.5, 1.0), 6.66 (t, 1H, H-6, J = 7.5), 6.52 (d, 1H, H-8, J = 7.5), 4.40 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 92.0), 4.23 (m, 2H, CH_2NO_2), 3.66 (m, 1H, H-9a), 3.55 (m, 2H, CH_2Cl), 2.50 (m, 2H, 2H-15), 1.85–1.13 (m, 10H), 0.67 (t, 3H, Me-11, J = 7.5); ^{13}C NMR δ 212.8, 149.9, 137.5, 129.7, 128.9 (2C), 127.7 (3C), 127.3, 124.0, 118.0, 107.3, 72.3, 68.3, 57.9, 50.2, 49.1, 45.4, 34.9, 32.8, 30.7, 27.4, 27.2, 22.0, 7.8.

21a,b: IR (CCl_4) 1690, 1450, 1380 cm^{-1}; MS (EI) m/z 456 [4, $M^{+\cdot}$ (^{37}Cl)], 454 [11, $M^{+\cdot}$ (^{35}Cl)], 380 (5), 344 (5), 303 (8), 247 (8), 233 (6), 220 (12), 91 (100); HRMS calcd for $C_{26}H_{31}N_2O_3Cl$ 454.2023, found 454.2020. Anal. Calcd for $C_{26}H_{31}N_2O_3Cl$: C, 68.64; H, 6.86; N, 6.16; O, 10.55; Cl, 7.79. Found: C, 68.78; H, 6.67; N, 5.77; O, 11.21; Cl, 7.72.

20-Ethyl Nitrones 22a and 22b. A mixture of nitrohexahydrocarbazolone **18a** (or **18b**) (378 mg, 1 mmol), 10% Pd/C (53 mg, 0.05 equiv with respect to Pd), and ammonium formate (315 mg, 5 mmol) in dry MeOH (5 mL) was stirred at room temperature, under N_2, for 20 h. The catalyst was removed by filtration through Celite. The filtrate was concentrated and the residue dissolved in AcOEt. The solution was washed with brine and then water, dried, and concentrated. Flash chromatography on silica gel with AcOEt gave pure nitrone **22a** (or **22b**) (277 mg, 80%).

22a: amorphous solid; IR (CCl_4) 1940, 1925,1875, 1700 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.32 (m, 5H, ArH), 7.08 (td, 1H, H-11, J = 7.5, 1.0), 6.97 (dd, 1H, H-9, J = 7.5, 1.0), 6.63 (t, 1H, H-10, J = 7.5), 6.41 (d, 1H, H-12, J = 7.5), 4.36 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 77.4), 4.28 (dddd, 1H, H-5ax, J = 14.0, 10.5, 7.5, 3.0), 3.91 (dddd, 1H, H-5eq, J = 14.0, 10.0, 2.0, 2.0), 3.53 (t, 1H, H-2, J = 5.5), 2.69 (ddq, 1H, H-19A, J = 13.5, 7.3, 4.5), 2.38 (m, 1H, H-20, ΣJ = 22), 2.27 (ddd, 1H, H-6eq, J = 13.0, 7.5, 2.0), 2.17 (dddd, 1H, H-6ax, J = 13.0, 10.5, 10.0, 2.0), 1.75–1.44 (m, 4H, 2H-16, H-17eq, H-19B), 1.38 (m, 1H, H-17ax), 0.96 (t, 3H, Me-18, J = 7.3); ^{13}C NMR δ 149.4, 148.2, 138.0, 131.8, 129.1, 128.6 (2C), 127.2 (3C), 122.3, 117.6, 106.9, 70.3, 61.8, 57.3, 48.8, 37.7, 35.7, 24.5, 23.7, 20.5, 12.2; MS (EI) m/z 346 (88), 329 (59), 256 (78), 234 (24), 220 (81), 91 (100); HRMS calcd for $C_{23}H_{26}N_2O$ 346.2045, found 346.2046.

22b: white crystals; mp 107–109 °C (AcOEt); IR (CCl_4) 1940, 1925, 1875, 1700 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.30 (m, 5H, ArH), 7.09 (td, 1H, H-11, J = 7.5, 1.0), 7.00 (dd, 1H, H-9, J = 7.5, 1.0), 6.63 (t, 1H, H-10, J = 7.5), 6.43 (d, 1H, H-12, J = 7.5), 4.39 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 72.2), 4.35 (dddd, 1H, H-5ax, J = 13.0, 10.0, 8.0, 1.0), 3.94 (ddd, 1H, H-5eq, J = 13.0, 10.0, 2.0), 3.55 (dd, 1H, H-2, J = 6.5, 4.0), 3.05 (m, 1H, H-20, ΣJ = 24), 2.37 (ddd, 1H, H-6eq, J = 12.0, 8.0, 2.0), 2.20 (ddd, 1H, H-6ax, J = 12.0, 10.0, 10.0), 1.70 (ddq, 1H, H-19A, J = 14.0, 7.3, 6.0), 1.66–1.43 (m, 4H, 2H-16, 2H-17), 1.03 (ddq, 1H, H-19B, J = 14.0, 7.3, 6.0), 0.9 (t, 3H, Me-18, J = 7.3); ^{13}C NMR δ 150.4, 149.7, 138.2, 131.8, 129.3, 128.7 (2C), 127.4 (3C), 123.1, 117.7, 107.0, 71.5, 60.7, 55.9, 49.3, 37.6, 35.8, 24.7, 23.7, 22.9, 12.0; MS (EI) m/z 346 (24, $M^{+\cdot}$), 329 (20), 302 (47), 220 (75), 91 (100); MS (CI) m/z 347 [39, $(M + H)^+$], 331 (24), 330 (26), 329 (16), 302 (4), 234 (19), 220 (6), 185 (9), 132 (9), 92 (100), 91 (74), 75 (17), 57 (13); MS/MS m/z 347 (93), 330 (14), 234 (44), 92 (100), 91 (44), and 346 (3), 329 (100); HRMS calcd for $C_{23}H_{26}N_2O$ 346.2045, found 346.2043. Anal. Calcd for $C_{23}H_{26}N_2O$: C, 79.73; H, 7.56; N, 8.09; O, 4.62. Found: C, 79.83; H, 7.26; N, 8.04; O, 4.76.

20,20-Dimethyl Nitrone 23 and 20,20-Dimethyl Imine 24. Reduction of the nitrohexahydrocarbazolone **19** (378 mg, 1 mmol) under the conditions described for the preparation of **22a** (or **22b**) afforded nitrone **23** (145mg, 42%) and imine **24** (92 mg, 28%).

Nitrone 23: amorphous solid; IR (CCl_4) 1940, 1920, 1870, 1700 cm^{-1}; ^1H NMR δ 7.30 (m, 5H, ArH), 7.08 (td, 1H, H-11, J = 7.5, 1.0), 6.98 (dd, 1H, H-9, J = 7.5, 1.0), 6.60 (t, 1H, H-10, J = 7.5), 6.40 (d, 1H, H-12, J = 7.5), 4.46 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 66.0), 4.36 (ddd, 1H, H-5ax, J = 13.0, 11.0, 7.5), 3.92 (ddd, 1H, H-5eq, J = 13.0, 10.0, 1.0), 3.65 (br s, 1H, H-2, $\Delta\nu$ = 9.0), 2.36 (dd, 1H, H-6eq, J = 12.0, 7.5, 1.0), 2.10 (ddd, 1H, H-6ax, J = 12.0, 11.0, 10.0), 1.73 (m, 1H, H-16eq), 1.52 (s, 3H, Me-18), 1.45 (m, 1H, H-17eq), 1.33–1.21 (m, 2H, H-16ax, H-17ax), 1.15 (s, 3H, Me-19); ^{13}C NMR δ 151.6, 150.0, 138.2, 131.5, 129.3, 128.6 (2C), 127.2, 127.0 (2C), 122.8, 116.6, 105.9, 69.5, 61.3, 56.8, 48.7, 37.8, 35.3, 33.8, 24.6, 24.4, 22.0; MS (EI) m/z 346 (6), 330 (28), 240 (15), 234 (28), 220 (1), 179 (19), 149 (12), 144 (36), 135 (32), 105 (33), 91 (69), 84 (54), 77 (30), 57 (39), 49 (100), 44 (64), 36 (17), 29 (36); HRMS calcd for $C_{23}H_{26}N_2O$ 346.2045, found 346.2045.

Imine 24: white crystals; mp 130–132 °C (acetone); IR (CCl_4) 1630 cm^{-1}; ^1H NMR δ 7.37 (m, 5H, ArH), 7.07 (td, 1H, H-11, J = 7.5, 1.0), 6.79 (dd, 1H, H-9, J = 7.5, 1.0), 6.62 (t, 1H, H-10, J = 7.5), 6.43 (d, 1H, H-12, J = 7.5), 4.39 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 81.0), 3.94 (dd, 1H, H-5eq, J = 15.0, 8.5), 3.74 (ddd, 1H, H-5ax, J = 15.0, 10.5, 6.5), 3.49 (dd, 1H, H-2, J = 8.5, 5.0), 2.18 (ddd, 1H, H-6eq, J = 12.0, 6.5), 1.98 (ddd, 1H, H-6ax, J = 12.0, 10.5, 8.5), 1.73 (dddd, 1H, H-16eq, J = 14.0, 5.0, 3.0, 3.0), 1.64–1.49 (m, 2H, H-16ax, H-17eq), 1.29 (ddd, 1H, H-17ax, J = 12.0, 12.0, 3.0), 1.26 (s, 3H, Me-18), 0.97 (s, 3H, Me-19); ^{13}C NMR δ 184.5, 149.1, 138.4, 132.5, 128.6 (2C), 128.4, 127.4 (2C), 127.2, 123.0, 117.3, 107.1, 72.1, 61.1, 56.4, 48.9, 43.0, 37.1, 35.1, 28.4, 27.3, 22.9; MS (EI) m/z 330 (74), 234 (64), 220 (7), 91 (100), 57 (15), 41 (13); HRMS calcd for $C_{23}H_{26}N_2$ 330.2096, found 330.2097. Anal. Calcd for $C_{23}H_{26}N_2$: C, 83.59; H, 7.93; N, 8.48. Found: C, 83.43; H, 7.81; N, 8.29.

20-Ethyl Amines 25A,B,C. Method 1. A solution of nitrone **22b** (277 mg, 0.8 mmol) in EtOH (4 mL) and toluene (2 mL) was treated with Na (184 mg, 8 mmol). After complete dissolution of the metal, the mixture was stirred for 2 h. The solvent was removed and the residue dissolved in AcOEt. The solution was washed with water, dried, and concentrated. Chromatography on alumina, using 30:70 hexane–AcOEt, gave amine **25B** (126 mg; yield 95%, conversion 50%). Reduction of nitrone **28a** (277 mg, 0.8 mmol) under identical conditions afforded amines **25A** and **25C** as a mixture (127 mg; ratio 45:55; yield 95%; conversion 50%).

Method 2. A solution of cyanohexahydrocarbazolone **16a** (344 mg, 1 mmol) in EtOH (30 mL) was hydrogenated at rt for 4 days under 3 atm of pressure (Parr apparatus) in the presence of PtO_2 (35 mg). The catalyst was removed by filtration through Celite, and the filtrate was concentrated. Chromatography on alumina, with 30:70 hexane–AcOEt, afforded amines **25A** and **25C** as a mixture (220 mg; ratio 85:15; 66% yield). Reduction of cyanohexahydrocarbazolone **16b** (172 mg, 0.5 mmol) under identical conditions gave the three isomers **25A**, **25B**, **25C** (113 mg; ratio 20:50:30; yield 68%). Spectroscopic data of **25A** and **25C** were assigned from the mixtures.

25A: ^1H NMR ($CDCl_3$) δ 7.68 (d, 1H, H-9, J = 7.5), 7.36 (m, 5H, ArH), 7.10 (t, 1H, H-11, J = 7.5), 6.80 (t, 1H, H-10, J = 7.5), 6.43 (d, 1H, H-12, J = 7.5), 4.27 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 87.7), 3.62–3.36 (m, 3H, H-2, 2H-5), 3.02 (d, 1H, H-21, J = 11.0), 2.20–1.15 (m, 10H), 0.96 (t, 3H, Me-18, J = 7.3); ^1H NMR COSY ^1H–^1H (CD_3OD) δ 7.46 (m, 5H, ArH), 7.28 (d, 1H, H-9, J = 7.5), 7.20 (t, 1H, H-11, J = 7.5), 6.80 (t, 1H, H-10, J = 7.5), 6.59 (d, 1H, H-12, J = 7.5), 4.40 (AB, 2H, NCH_2Ph, J = 15.5, $\Delta\nu$ = 79.0), 3.71 (dd, 1H, H-2, J = 8.0, 5.0), 3.62 (m, 1H, H-5eq), 3.58 (m, 1H, H-5ax), 3.33 (d, 1H, H-21, J = 11.5), 2.28 (m, 1H, H-6eq), 2.15 (m, 1H, H-6ax), 1.98 (m, 1H, H-17eq), 1.96 (m, 1H, H-16eq), 1.80 (m, 1H, H-17ax), 1.78 (m, 1H, H-19A), 1.76 (m, 1H, H-20), 1.37 (m, 1H, H-19B), 1.35 (m, 1H, H-16ax), 1.06 (t, 3H, Me-18, J = 7.3); ^{13}C NMR ($CDCl_3$) δ 150.2, 138.0, 129.8, 128.8 (2C), 128.5, 127.6, 127.4 (2C), 124.5, 118.6, 108.3, 68.2, 66.1, 54.8, 49.2, 42.3, 37.9, 36.7, 27.4, 25.8, 24.6, 10.7; ^{13}C NMR (CD_3OD) δ 151.9, 139.4, 131.4, 129.9, 129.8 (2C), 128.7 (2C), 128.3, 123.9, 118.8, 109.8, 69.2, 67.3, 55.9, 48.1, 44.3, 38.3, 37.9, 28.0, 26.5, 25.4, 10.8.

25B: amorphous solid; IR (CCl_4) 3360 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.37 (m, 5H, ArH), 7.06 (m, 2H, H-9, H-11), 6.75 (t, 1H, H-10, J = 7.5), 6.44 (d, 1H, H-12, J = 7.5), 4.29 (AB, 2H, NCH_2-Ph, J = 16.0, $\Delta\nu$ = 86.0), 3.60 (t, 1H, H-2, J = 4.0), 3.30 (ABX_2, 2H, 2H-5), 2.65 (d, 1H, H-21, J = 9.0), 2.10 (m, 2H, 2H-6), 1.94 (dddd, 1H, H-16eq, J = 14.0, 4.0, 4.0, 4.0), 1.77 (ddq, 1H, H-19A, J = 14.0, 7.3, 4.0), 1.69 (m, 2H, H-17eq, NH), 1.60 (dddd, 1H, H-16ax, J = 14.0, 12.0, 4.0, 4.0), 1.33 (dddd, 1H, H-17ax, J = 12.0, 12.0, 12.0, 4.0), 1.23 (m, 1H, H-20), 1.03 (ddq, 1H, H-19B, J = 14.0, 8.0, 7.3), 0.91 (t, 3H, Me-18, J = 7.3); ^{13}C NMR δ 151.2, 139.1, 131.3, 128.6 (2C), 127.8, 127.3 (2C), 127.0, 121.4, 118.4, 108.1, 68.1, 67.9, 53.8, 51.3, 43.6, 38.8, 35.0, 26.0, 23.2, 22.8, 11.4; MS (EI) m/z 332 (43), 233 (8), 221 (46), 144 (8), 91 (100), 84 (15), 44 (46), 29 (15); HRMS calcd for $C_{23}H_{28}N_2$ 332.2252, found 332.2251.

25C: ^1H NMR δ 7.34 (m, 5H, ArH), 7.10 (t, 1H, H-11, J = 7.5), 7.08 (d, 1H, H-9, J = 7.5), 6.75 (t, 1H, H-10, J = 7.5), 6.39 (d, 1H, H-12, J = 7.5), 4.27 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 64.3), 4.00 (br s, 1H, H-21, $\Delta\nu$ = 7.0), 3.62–3.36 (m, 3H, H-2, 2H-5), 2.55 (ddd, 1H, H-6eq, J = 13.0, 6.0, 1.0), 2.20–1.15 (m, 9H), 1.03 (t, 3H, Me-18, J = 7.3); ^{13}C NMR δ 150.4, 138.2, 130.8, 128.9, 128.8 (2C), 127.4 (2C), 127.6, 121.5, 118.3, 107.9, 66.3, 62.8, 53.7, 48.9, 43.0, 37.2, 37.1, 26.2, 24.9, 21.7, 12.0.

25A,C (ratio 85:15): IR (KBr) 3370 cm^{-1}; MS (EI) m/z 332 (15), 306 (7), 289 (22), 242 (10), 221 (17), 158 (12), 144 (17), 130 (24), 91 (79), 85 (63), 83 (100), 44 (64), 27 (17); HRMS calcd for $C_{23}H_{28}N_2$ 332.2252, found 332.2251.

20-Ethyl Acetamides 26A–C. To a solution of amine **25B** (67 mg, 0.20 mmol), NEt_3 (22 mg, 30 μL, 0.22 mmol), and DMAP (catalytic amount) in dry CH_2Cl_2 (2 mL) at 0 °C was added dropwise, under N_2, a solution of acetyl chloride (17 mg, 0.22 mmol) in CH_2Cl_2 (1 mL). After the addition was complete, the solution was stirred for 3 h and then washed with brine. The organic layer was dried and concentrated. Flash chromatography on silica gel, with 60:40 hexane–AcOEt, gave amide **26B** (67 mg, 90%). An identical reaction was performed on the mixture of amines **25A,C** (85:15) (166 mg, 0.5 mmol) [or **25A,C** (45:65) (100 mg, 0.3 mmol)]. Flash chromatography on silica gel, using 60:40 hexane–AcOEt, afforded amides **26A** (142 mg, 76%) and **26C** (26 mg, 13%) [or **26A** (45 mg, 40%) and **26C** (56 mg, 50%)].

26A: amorphous solid; IR ($CHCl_3$) 1640 cm^{-1}; ^1H NMR, COSY ^1H–^1H δ 7.33 (m, 5H, ArH), 7.02 (t, 1H, H-11, J = 7.5), 6.89 (d, 1H, H-9, J = 7.5), 6.55 (t, 1H, H-10, J = 7.5), 6.30 (d, 1H, H-12, J = 7.5), 4.39 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 64.0), 3.69 (ddd, 1H, H-5ax, J = 10.0, 10.0, 7.5), 3.63 (m, 1H, H-2), 3.56 (t, 1H, H-5eq, J = 10.0), 3.32 (d, 1H, H-21, J = 10.0), 2.22 (m, 1H, H-19A), 2.17 (s, 3H, COMe), 2.12 (m, 1H, H-6eq), 2.08 (m, 1H, H-20), 1.86 (ddd, 1H, H-6ax, J = 10.5, 10.5, 10.5), 1.60–1.40 (m, 3H, 2H-16, H-17eq), 1.21 (m, 1H, H-17ax), 1.15 (m, 1H, H-19B), 0.90 (t, 3H, Me-18); ^{13}C NMR δ 170.1, 151.1, 138.7, 132.9, 128.6 (2C), 128.2, 127.3 (2C), 127.2, 123.1, 116.6, 105.4, 67.3, 66.8, 53.6, 48.3, 46.9, 37.8, 36.1, 29.2, 24.7, 23.6, 22.3, 12.1; MS (EI) m/z 374 (50), 330 (19), 284 (15), 240 (25), 233 (33), 220 (17), 198 (19), 144 (36), 130 (33), 115 (14), 91 (100), 84 (14), 77 (19), 43 (25), 29 (17); HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2355.

26B: mp 127–129 °C (hexane); two rotamers [maj/min (3:1)]; IR ($CHCl_3$) 1645 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.37 (maj and min) (m, 5H, ArH), 7.06 (maj) and 7.00 (min) (td, 1H, H-11, J = 7.5, 1.0), 7.05 (min) and 6.78 (maj) (dd, 1H, H-9, J = 7.5, 1.0), 6.70 (maj) and 6.66 (min) (t , 1H, H-10, J = 7.5), 6.51 (maj) and 6.39 (min) (d, 1H, H-12, J = 7.5), 4.31 (maj) (ddd, 1H, H-5ax, J = 13.5, 10.0, 8.0), 4.29 (maj) and 4.25 (min) (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 78.0), 3.89 (min) (ddd, 1H, H-5ax, J = 11.0, 8.5, 8.5), 3.84 (min) and 3.07 (maj) (d, 1H, H-21, J = 10.5), 3.70 (min) (ddd, 1H, H-5eq, J = 13.5, 11.0, 7.0), 3.49 (maj and min) (m, 1H, H-2), 3.37 (maj) (ddd, 1H, H-5eq, J = 13.5, 10.0, 4.0), 2.28 (min) and 2.18 (maj) (m, 2H, 2H-6), 2.17 (min) and 1.82 (maj) (s, 3H, COMe), 2.11 (maj and min) (m, 1H, H-17eq), 2.07 (maj and min) (m, 1H, H-16eq), 1.63 (maj) and 1.59 (min) (m, 1H, H-19A), 1.60 (maj and min) (m, 1H, H-16ax), 1.37 (min) (m, 1H, H-17ax), 1.33 (maj) (dddd, 1H, H-17ax, J = 12.0, 12.0, 12.0, 3.0), 1.20 (min) (m, 1H, H-19B), 1.18 (maj) and 1.13 (min) (m, 1H, H-20), 1.01 (maj) (ddq, 1H, H-19B, J = 14.0, 7.0, 6.0), 0.93 (maj) and 0.88 (min) (t, 3H, Me-18, J = 7.0); ^{13}C NMR maj rotamer δ 170.6, 151.2, 138.9, 136.9, 128.6 (2C), 128.1, 127.4 (2C), 127.1, 121.6, 119.2, 108.6, 69.8, 67.6, 52.7, 52.0, 42.1, 40.6, 30.9, 25.4, 23.3, 23.2, 22.5,

11.6; ^{13}C NMR min rotamer δ 170.6, 151.2, 138.9, 136.9, 128.6 (2C), 128.1, 127.4 (2C), 127.0, 120.9, 118.9, 108.5, 68.0, 65.4, 52.7, 51.8, 45.1, 41.3, 32.4, 25.6, 23.6, 23.2, 22.5, 11.4; MS (EI) *m/z* 374 (10), 168 (30), 153 (21), 117 (100), 105 (19), 82 (46), 43 (72), 36 (68), 29 (12), 18 (28); HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2359. Anal. Calcd for $C_{25}H_{30}N_2O$: C, 80.17; H, 8.07; N, 7.48; O, 4.27. Found: C, 79.78; H, 7.94; N, 7.40; O, 4.73.

26C: amorphous solid; two rotamers [maj/min (2:1)]; IR ($CHCl_3$) 1640 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.37 (maj and min) (m, 5H, ArH), 7.06 (maj) and 7.01 (min) (t, 1H, H-11, J = 7.5), 6.89 (maj) and 6.87 (min) (d, 1H, H-9, J = 7.5), 6.71 (maj) and 6.67 (min) (t, 1H, H-10, J = 7.5), 6.48 (maj) and 6.40 (min) (d, 1H, H-12, J = 7.5), 4.30 (maj) and 4.28 (min) (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 69.0), 4.08 (maj) (ddd, 1H, H-5ax, J = 13.0, 10.0, 10.0), 4.05 (min) and 3.60 (maj) (d, 1H, H-21, J = 7.0), 3.93 (min) (ddd, 1H, H-5ax, J = 10.0, 10.0, 10.0), 3.66 (min) (ddd, 1H, H-5eq, J = 10.0, 10.0, 2.0), 3.55 (maj) (m, 1H, H-5eq), 3.51 (maj and min) (br s, 1H, H-2, $\Delta\nu$ = 8.0), 2.25 (min) and 2.20 (maj) (m, 1H, H-6eq), 2.18 (min) and 2.05 (maj) (m, 1H, H-6ax), 2.17 (min) and 1.97 (maj) (s, 3H, COMe), 2.00 (min) and 1.96 (maj) (m, 1H, H-20), 1.78 (maj and min) (m, 2H, 2H-17), 1.68 (maj and min) (m, 2H, 2H-16), 1.52–1.24 (maj and min) (m, 2H, 2H-19), 0.92 (maj) and 0.89 (min) (t, 3H, Me-18, J = 7.5); ^{13}C NMR maj rotamer δ 169.9, 150.9, 138.9, 138.0, 128.7 (2C), 128.2, 127.2 (2C), 127.1, 121.7, 119.3, 108.4, 67.4, 67.3, 52.0, 50.3, 45.3, 38.0, 33.9, 22.0, 19.5, 19.0, 16.8, 12.7; ^{13}C NMR min rotamer δ 169.3, 150.9, 138.9, 138.0, 128.7 (2C), 128.1, 127.1 (2C), 127.0, 121.2, 118.8, 108.2, 67.6, 65.0, 51.6, 50.3, 47.1, 35.2, 35.0, 22.5, 19.6, 19.0, 17.2, 12.5; MS (EI) *m/z* 374 (67), 358 (17), 288 (14), 233 (23), 143 (17), 91 (100), 86 (20), 77 (11), 55 (14), 43 (74), 40 (43), 36 (17), 29 (34); HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2355.

20,20-Dimethyl Amines 27A,B. Method 1. The reductions of nitrone **23** (138 mg, 0.4 mmol) and of imine **24** (82 mg, 0.25 mmol) were performed in the conditions described for the preparation of **25**. Chromatography on alumina, with 30:70 hexane–AcOEt, gave amine **27B** (70 mg) from nitrone **23** (yield 95%, conversion 55%) and a mixture of amines **27A** and **27B** (25 mg; ratio 35:65) from imine **24** (yield 60%, conversion 50%).

Method 2. The reduction of the dimethyl cyanohexahydrocarbazolone **17** (344 mg, 1 mmol) under the conditions described for the preparation of **25** afforded dimethyl amine **27B** (173 mg, yield 95%, conversion 55%).

Spectroscopic data of **27A** were assigned from the mixture **27A,B** (35:65).

27A: ^1H NMR δ 7.54 (d, 1H, H-9, J = 7.5), 7.36 (m, 5H, ArH), 7.07 (t, 1H, H-11, J = 7.5), 6.70 (t, 1H, H-10, J = 7.5), 6.42 (d, 1H, H-12, J = 7.5), 4.33 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 87.0), 3.55–3.20 (m, 4H, H-2, 2H-5, NH), 3.13 (s, 1H, H-21), 2.20 (m, 1H, H-6eq), 1.77 (ddd, 1H, H-6ax, J = 13.5, 10.5, 10.5), 1.5–0.9 (m, 4H, 2H-16, 2H-17), 1.13 (s, 3H, Me-18), 0.96 (s, 3H, Me-19); ^{13}C NMR δ 149.6, 138.3, 132.5, 128.7 (2C), 128.3, 127.5 (2C), 127.3, 125.3, 117.6, 107.7, 68.3, 65.5, 53.0, 48.9, 41.9, 37.0, 33.3, 32.4, 30.2, 23.6, 22.8.

27B: IR ($CHCl_3$) 3320 cm^{-1}; ^1H NMR δ 7.36 (m, 5H, ArH), 7.09 (t, 1H, H-11, J = 7.5), 7.06 (d, 1H, H-9, J = 7.5), 6.73 (t, 1H, H-10, J = 7.5), 6.39 (d, 1H, H-12, J = 7.5), 4.30 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 77.0), 3.69 (s, 1H, H-21), 3.51 (dd, 1H, H-2, J = 8.0, 3.5), 3.55–3.20 (m, 3H, 2H-5, NH), 2.51 (ddd, 1H, H-6eq, J = 10.5, 7.5, 3.0), 1.85 (ddd, 1H, H-6ax, J = 12.0, 10.5, 10.5), 1.50–0.90 (m, 4H, 2H-16, 2H-17), 1.16 (s, 3H, Me-18), 0.88 (s, 3H, Me-19); ^{13}C NMR δ 149.5, 138.3, 131.8, 128.7 (2C), 128.3, 127.5 (2C), 127.3, 122.2, 118.2, 107.7, 68.5, 66.4, 53.5, 48.9, 42.0, 39.7, 38.5, 29.6, 28.6, 26.8, 21.6.

27A,B: IR ($CHCl_3$) 3320 cm^{-1}; MS (EI) *m/z* 332 (64), 234 (21), 221 (21), 144(8), 130 (8), 91 (100), 84 (20), 65 (8), 41 (13), 29 (13); HRMS calcd for $C_{23}H_{28}N_2$ 332.2252, found 332.2251.

20,20-Dimethyl Acetamides 28A,B. Compound **28B** was prepared from dimethyl amine **27B** (67 mg, 0.20 mmol) following the procedure described for **26B** and purified by flash chromatography using 80:20 hexane–AcOEt (yield 90%). An identical reaction, performed on the mixture of amines **27A,B** (35:65) (23 mg, 0.07 mmol), afforded amides **28A** (8 mg, 31%) and **28B** (15 mg, 57%).

28A: amorphous solid; two rotamers [maj/min (3:2)]; IR (CCl_4) 1635 cm^{-1}; ^1H NMR δ 7.31 (maj and min) (m, 5H, ArH), 7.07 (min) and 7.02 (maj) (t, 1H, H-11, J = 7.5), 6.76 (min) and 6.55 (maj) (t, 1H, H-10, J = 7.5), 6.71 (maj) and 6.69 (min) (d, 1H, H-9, J = 7.5), 6.45 (min) and 6.30 (maj) (d, 1H, H-12, J = 7.5), 4.41 (maj) and 4.39 (min) (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 68.0), 3.85 (maj) (ddd, 1H, H-5ax, J = 12.0, 11.0, 7.0), 3.80 (maj) (ddd, 1H, H-5eq, J = 12.0, 5.0, 2.0), 3.61 (maj) and 3.58 (min) (m, 1H, H-2), 3.59 (min) (m, 2H, 2H-5), 3.47 (min) and 3.45 (maj) (s, 1H, H-21), 2.20 (min) and 2.19 (maj) (s, 3H, COMe), 2.24–1.10 (maj and min) (m, 6H), 1.46 (min) and 1.45 (maj) (s, 3H, Me-18), 0.96 (maj) and 0.92 (min) (s, 3H, Me-19); ^{13}C NMR maj rotamer δ 166.5, 150.0, 138.8, 135.7, 129.1, 128.7(2C), 128.2, 127.2 (2C), 125.5, 115.8, 105.1, 69.4, 63.2, 52.1, 48.1, 38.4, 37.1, 34.6, 31.8, 29.4, 24.9, 23.8, 23.2; ^{13}C NMR min rotamer δ 166.5, 150.0, 138.8, 135.7, 129.8, 128.7 (2C), 128.2, 127.2 (2C), 125.1, 115.8, 105.1, 72.0, 67.3, 53.8, 47.9, 38.8, 37.2, 34.0, 31.7, 29.4, 24.9, 23.7, 23.3; MS (EI) *m/z* 374 (9), 284 (100), 215 (54), 198 (16), 172 (35), 156 (59), 144 (50), 130 (44), 91 (35), 84 (20), 77 (12), 55 (13), 43 (85), 36 (16), 27 (15); HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2359.

28B: amorphous solid; two rotamers [maj/min (2:1)]; IR (CCl_4) 1635 cm^{-1}; ^1H NMR δ 7.36 (maj and min) (m, 5H, ArH), 7.05 (min) and 6.69 (maj) (d, 1H, H-9, J = 7.5), 7.04 (maj) and 6.99 (min) (t, 1H, H-11, J = 7.5), 6.70 (maj) and 6.65 (min) (t, 1H, H-10, J = 7.5), 6.48 (maj) and 6.37 (min) (d, 1H, H-12, J = 7.5), 4.33 (maj) (ddd, 1H, H-5ax, J = 13.5, 10.0, 10.0), 4.29 (maj) and 4.26 (min) (AB, 2H, NCH_2Ph, J = 16.5, $\Delta\nu$ = 84.0), 3.93 (min) (ddd, 1H, H-5ax, J = 10.5, 9.0, 9.0), 3.87 (min) (s, 1H, H-21), 3.70 (min) (ddd, 1H, H-5eq, J = 10.5, 10.5, 3.5), 3.53 (maj) and 3.50 (min) (m, 1H, H-2), 3.46 (maj) (ddd, 1H, H-5eq, J = 13.5, 11.0, 3.5), 3.20 (maj) (s, 1H, H-21), 2.32–2.05 (maj and min) (m, 2H, 2H-6), 2.21 (min) and 1.91 (maj) (s, 3H, COMe), 1.90–1.69 (maj and min) (m, 2H, 1H-16, 1H-17), 1.33–1.08 (maj and min) (m, 2H, 1H-16, 1H-17), 1.05 (min) and 1.02 (maj) (s, 3H, Me-18), 1.00 (maj) and 0.97 (min) (s, 3H, Me-19); ^{13}C NMR maj rotamer δ 171.5, 150.8, 138.8, 138.2, 128.7 (2C), 128.1, 127.3 (2C), 127.1, 121.3, 119.3, 108.5, 72.6, 67.3, 52.3, 51.9, 45.2, 35.6, 33.5, 32.8, 32.6, 22.5, 21.2, 19.2; ^{13}C NMR min rotamer δ 170.0, 150.9, 138.9, 138.1, 128.7 (2C), 128.1, 127.3 (2C), 127.0, 120.7, 119.1, 108.5, 68.7, 67.5, 51.8, 51.3, 47.2, 39.2, 35.8, 34.6, 33.2, 23.1, 21.7, 19.5; MS (EI) *m/z* 374 (7), 330 (33), 234 (38), 225 (19), 212 (3), 168 (15), 156 (7), 149 (7), 106 (19), 91 (100), 85 (7), 77 (16), 71 (9), 65 (10), 57 (37), 43 (83), 29 (30); HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2359.

20-Ethyl 20-Chloropropyl Imine 29a and Pentacyclic Iminium Chloride 30. The reduction of the nitrohexahydrocarbazolones **21a,b** (363 mg, 0.8 mmol) was carried out at 65 °C under the conditions described for the preparation of **22a** (or **22b**). Purification of the crude material by flash chromatography afforded first imine **29a** (75 mg) (elution with 80:20 hexane–AcOEt) and then pentacyclic iminium **30** (76 mg) (elution with 90:10 AcOEt-MeOH) (ratio **29a/30** 50:50, total yield 67%, conversion 70%).

29A: amorphous solid; IR (CCl_4) 1625 cm^{-1}; ^1H NMR COSY ^1H–^1H δ 7.34 (m, 5H, ArH), 7.09 (t, 1H, H-11, J = 7.5), 6.78 (d, 1H, H-9, J = 7.5), 6.60 (t, 1H, H-10, J = 7.5), 6.45 (d, 1H, H-12, J = 7.5), 4.39 (AB, 2H, NCH_2Ph, J = 16.0, $\Delta\nu$ = 72.0), 3.99 (dd, 1H, H-5eq, J = 16.0, 9.0), 3.82 (ddd, 1H, H-5ax, J = 16.0, 10.0, 6.0), 3.53 (dd, 1H, H-2, J = 6.0, 5.0), 3.26 (ABX_2, 2H, CH_2Cl), 2.26 (dd, 1H, H-6eq, J = 12.0, 6.0), 1.97 (ddd, 1H, H-6ax, J = 12.0, 10.0, 9.0), 1.87 (dq, 1H, H-19A, J = 15.0, 7.5), 1.79–1.53 (m, 5H, 2H-14, H-19B, 2H-16), 1.44–1.13 (m, 3H, H-17eq, 2H-15), 0.91 (m, 1H, H-17ax), 0.83 (t, 3H, Me-18, J = 7.5); ^{13}C NMR δ 182.0, 149.4, 138.4, 132.5, 128.7 (3C), 127.5 (2C), 127.3, 122.1, 117.3, 107.2, 71.8, 61.3, 56.8, 49.2, 45.5, 43.4, 42.4, 33.5, 30.5, 28.5, 27.2, 22.7, 7.7; MS (EI) *m/z* 408 [4, M^{+} (^{37}Cl)], 406 [11, M^{+} (^{35}Cl)], 379 (2), 372 (2), 344 (3), 329 (2), 315 (5), 303 (5), 287 (5), 260 (2), 234 (8), 220 (7), 167 (3), 156 (3), 149 (5), 144 (10), 130 (5), 115 (4), 105 (4), 91 (100), 83 (4); HRMS calcd for $C_{26}H_{31}N_2Cl$ 406.2176, found 406.2177.

30: amorphous solid; IR ($CHCl_3$) 1675 cm^{-1}; ^1H NMR δ 7.31 (m, 5H, ArH), 7.14 (td, 1H, H-11, J = 7.5, 1.0), 6.77 (dd, 1H, H-9, J = 7.5, 1.0), 6.65 (t, 1H, H-10, J = 7.5), 6.48 (d, 1H, H-12, J = 7.5), 4.88 (dd, 1H, H-5eq, J = 13.0, 9.0), 4.76 (ddd, 1H, H-3eq, J = 16.0, 9.0, 2.0), 4.37 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 84.0), 4.27 (m, 1H, H-3ax), 4.21 (m, 1H, H-5ax), 3.96 (dd, 1H, H-2, J = 7.0, 1.0), 2.78 (ddd, 1H, H-6ax, J = 12.0, 10.5, 9.0), 2.37 (dd, 1H, H-6eq, J = 12.0, 6.0), 2.35–1.62 and 1.30–1.12 (2m, 10H), 0.86 (t, 3H, Me-18, J = 7.3); ^{13}C NMR δ 195.6, 149.2, 136.8, 130.8,

129.0 (2C), 128.3, 127.9, 127.6 (2C), 121.3, 118.2, 108.4, 63.3, 60.9, 58.1, 47.4, 48.5, 39.6, 36.0, 27.0, 26.5, 23.5, 22.0, 17.1, 6.4; MS (EI) *m/z* 408 [18, $M^{\cdot+}$ (^{37}Cl)], 406 [51, $M^{\cdot+}$ (^{35}Cl)]) 386 (14), 370 (64), 358 (14), 343 (22), 330 (14), 279 (67), 256 (19), 246 (42), 234 (36), 220 (17), 149 (44), 122 (55), 105 (61), 91 (68), 83 (100), 77 (42), 69 (30), 57 (53), 47 (28), 43 (69), 36 (86), 29 (39); (+) FABMS *m/z* 371 (100, $R^+ = C_{26}H_{31}N_2^+$), 341 (10), 313 (6), 281 (7), 251 (15), 237 (10), 223 (10), 133 (30); (–) FABMS *m/z* 441 [30, $(R^+Cl^-)Cl^-$], 325 (7), 265 (14), 241 (9), 219 (15), 194 (7), 183 (19), 171 (100), 151 (8), 127 (90), 113 (8); HRMS calcd for $C_{26}H_{31}N_2Cl$ 406.2176, found 406.2165.

***N*-Benzylaspidospermidine (4).** A solution of iminium **30** (61 mg, 0.15 mmol) in EtOH (15 mL) was hydrogenated at rt for 2 d under 3 atm of pressure (Parr apparatus) in the presence of 5% Pt/Al_2O_3 (5 mg). The catalyst was removed by filtration through Celite, and the filtrate was concentrated. The residue was purified by flash chromatography on silica gel [hexane–AcOEt (80:20)] to give *N*-benzylaspidospermidine (**4**, 39 mg, 70%): white crystals; mp 127–129 °C (AcOEt); IR (CCl_4) 2860, 2790, 2740 cm^{-1}; ^1H NMR δ 7.38 (m, 5H, ArH), 7.08 (d, 1H, H-9, J = 7.5), 7.04 (t, 1H, H-11, J = 7.5), 6.68 (t, 1H, H-10, J = 7.5), 6.39 (d, 1H, H-12, J = 7.5), 4.27 (AB, 2H, NCH_2Ph, J = 15.0, $\Delta\nu$ = 109.0), 3.41 (dd, 1H, H-2, J = 10.5, 5.0), 3.12 (m, 1H, H-5eq), 3.05 (m, 1H, H-3eq), 2.37 (ddd, 1H, H-5ax, J = 13.0, 8.5, 8.5), 2.27 (m, 1H, H-6ax), 2.25 (s, 1H, H-21), 1.97 (ddd, 1H, H-3ax, J = 11.0, 11.0, 4.0), 1.85–1.07 (m, 10H), 0.91 (dq, 1H, H-19B, J = 14.0, 7.5), 0.66 (t, 3H, Me-18, J = 7.5); ^{13}C NMR δ 149.9, 138.7, 136.7, 128.5 (2C), 127.8 (2C), 127.2, 127.1, 122.4, 117.4, 106.7, 71.2, 69.1, 53.8, 53.0, 52.6, 48.4, 39.1, 35.6, 34.5, 30.2, 23.0, 22.4, 21.8, 6.9; MS (EI) *m/z* 372 (10), 344 (3), 281 (2), 234 (1), 220 (2), 190 (1), 152 (5), 124 (100), 91 (32), 69 (6), 55 (9), 41 (10), 28 (21); HRMS calcd for $C_{26}H_{32}N_2$ 372.2558, found 372.2562. Anal. Calcd for $C_{26}H_{32}N_2$: C, 83.82; H, 8.66; N, 7.52. Found: C, 84.23; H, 8.68; N, 7.17.

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Supplementary Material Available: Selected ^1H and ^{13}C NMR spectra (40 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.