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A SYNTHETIC ROAD TO THE FOREST OF *STRYCHNOS, ASPIDOSPERMA, SCHIZOZYGANE* AND *EBURNAMINE* ALKALOIDS BY WAY OF THE NOVEL PHOTOISOMERIZATION

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Abstract—The novel photoisomerization of 1-acylindoles accompanied by a conversion of indole to indolenine afforded 3-acylindolenines, a so far unknown reactive species, as a major product. This reaction was thoroughly investigated and applied with success to the total synthesis of *Strychnos*, *Aspidosperma*, *Schizozygane* and *Eburnamine* alkaloids through a versatile intermediate 9-membered ring system, synthesized in a one pot reaction by photolysis and the simultaneous ring enlargement.

Although *Strychnos* (**2**), *Aspidosperma* (**3**), *Schizozygane* (**4**) and *Eburnamine* (**5**) alkaloids are biologically important and close relatives in their biosyntheses in plants[2] and intense synthetic work still continues,[3,4] there has not been recorded any total synthesis of the entitled alkaloids from a single common intermediate. The 9-membered portion depicted by bold lines in formula **1** constitutes the common part of the skeletons of the entitled alkaloids as shown in Chart 1. We describe in this paper the details of the total synthesis of *dl*-tubifoline (**6**), *dl*-tubifolidine (**6a**) and *dl*-condyfoline (**7**) in the *Strychnos* series,[5] and *dl*-1,2-dehydroaspidospermidine (**8**),[6] *dl*-1-acetylaspidospermidine (**9**)[7] and *dl*-quebrachamine (**10**)[8] of *Aspidosperma* species, and the formal synthesis of *dl*-strempeliopine (**13**) of *Schizozygane* species[4c] via **12**, from a versatile synthetic precursor (**16a**), a realized compound corresponding to formula (**1**), which was prepared by the novel photoisomerization developed in this laboratory (Chart 2). Furthermore, as Lévy had succeeded in the conversion of **1**–**8** into *d*-eburnamine (**11**),[4d] the present work constitutes a formal synthesis of *dl*-**11**.

The photochemistry of the enamide system and its useful application have been well investigated, where simple enamides generally undergo a [1,3]-acyl radical shift to afford vinylogous amides [RN(COR^1)–CH=CHR^2→RNH–CH=C (COR^1)R^2].[9]

Also, photoisomerizations of 1-acylindoles, a special type of enamide system, have been described to effectively provide 3-, 4- and 6-acylindoles according to the usual photo-Fries type of rearrangement.[10] Prior to the present work, it was discovered by us that the photoisomerization of **14** irradiated by a 300-W high pressure mercury lamp proceeded through [1,3]-acyl radical shift accompanied by double bond migration [RN(COR^1)–CH=CR^{2}R^3→RN=CH–C (COR^1)R^{2}R^3] to give **15** as a major product. In addition to this previously unknown reactive species, there was obtained **16**, **17** and **18**, the products of the usual isomerization, in addition to the starting material **14** and **19**.[11] The structure of **15** (unstable pale yellow crystals, m.p. 66–68°, IR(Nujol)ν 1715, 1645 cm^{-1} and *m/e* 213 (M$^+$) supporting the assignment together with the other spectral data) was further confirmed by its conversion into **22**, in which **15** was reduced to the amino-alcohol **20** (37% yield) and the epimer **20a** (12% yield) with LAH. Compound **20** was tosylated to **21**, followed by reductive elimination of the tosyl groups with LAH to give **22**.

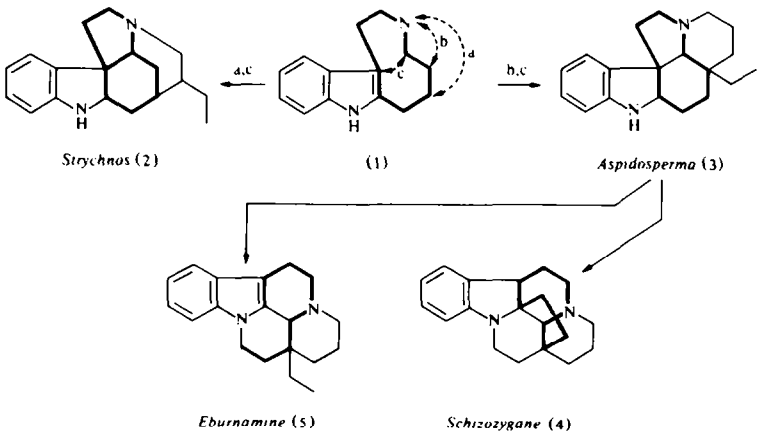
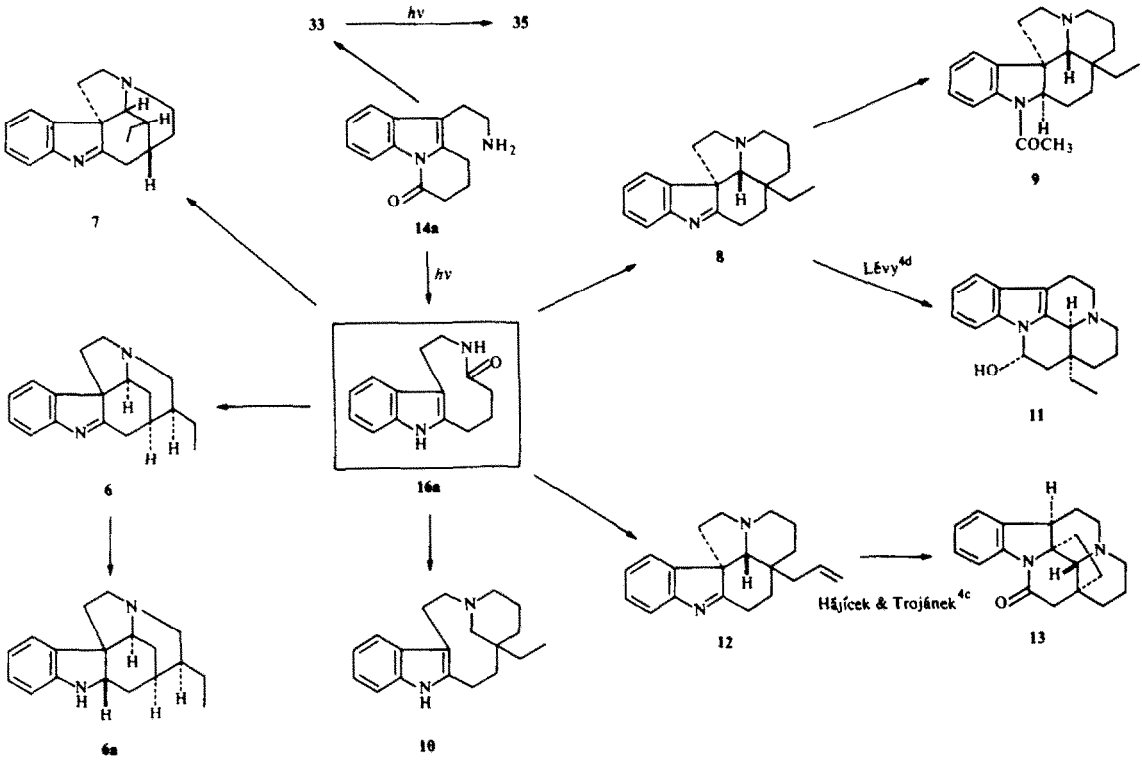
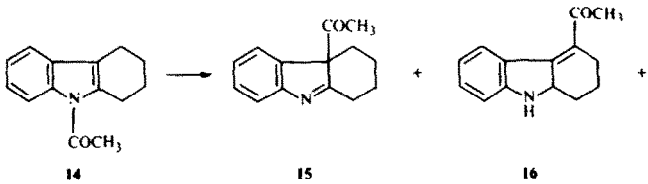
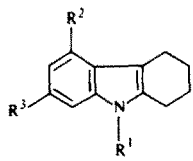


Chart 1.







17: $R^1 = R^3 = H$, $R^2 = COCH_3$
18: $R^1 = R^2 = H$, $R^3 = COCH_3$
19: $R^1 = R^2 = R^3 = H$

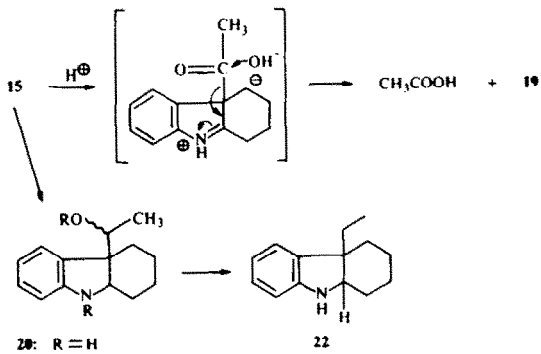


Chart 2.

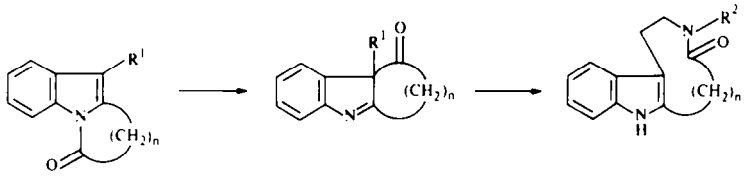
The compound **22** was identified by comparison with an authentic specimen of known structure.[12]

Due to these findings, **14a**,[13] synthesized by the Fischer indolization of methyl 5-oxoheptanoate ($C_2H_5COCH_2CH_2COOCH_3$),[14] where the acyl group is bound to the C-2 position of the indole nucleus and thus cannot rearrange to the aromatic ring, was similarly irradiated to afford the carbazolenine **15a** as a sole product, but only in 20% yield. The compound **15a**, pale yellow solid, which recrystallized with difficulty, was also very unstable. It readily hydrolyzed to the carboxylic acid **25** through **24** during silica gel chromatography, which seemed to be the reason why the yield of **15a** was actually meager. The structure of **15a** was further confirmed by conversion of **15a** to **28** of known stereochemistry[15] through **26** and **27**, as are shown in the Experimental.

To overcome the disadvantages arising from the instability of **15a**, it was attempted to transform the assumed photoproduct **15b**, which might be generated by irradiation of the substrate **14b** carrying a nucleophilic functional group ($R=CH_2CH_2NH_2$) in the molecule, immediately into the stable product **16a**. This transformation through **23a**, obtained by an intramolecular condensation leading to ring enlargement, was subsequently realized.

A solution of the amine **14b** in methanol or in ether was irradiated for 18–21 hr to furnish the 9-membered lactam **16a**, (colorless amorphous solid, m.p. 120–121°) as a sole product in an excellent yield of 90%. The intermediate **15b** was not detected, but the reaction might be assumed to have proceeded through **15b** and **23a** to **16a**.

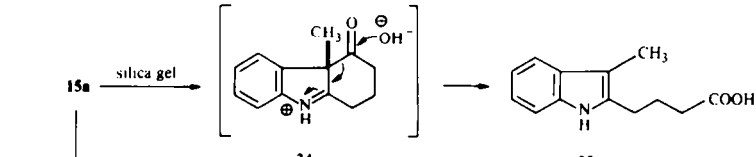
In order to confirm the structure of **16a**, reduction of **16a** to **29a** with LAH, followed by acetylation, gave the amide **29b** (m.p. 190–193°), which was identified by comparison with an authentic sample (m.p. 189–190°).[16] For clarification of the reaction processes and with expectation of gaining access to the C-nor compound **30**, the aminomethyl analog **14c**, a promising precursor for the synthesis of apparicine (**31a**) and vallesamine (**31b**),[17] was irradiated in a similar manner to provide only **32** in 44% yield. This product must have been generated from the



14a: $R^1=CH_3$, $n=3$
14b: $R^1=CH_2CH_2NH_2$, $n=3$
14c: $R^1=CH_2NH_2$, $n=3$
14d: $R^1=CH_2CH_2NH_2$, $n=2$
14e: $R^1=CH_2CH_2NHCH_2Ph$, $n=3$

15a: $R^1=CH_3$, $n=3$
15b: $R^1=CH_2CH_2NH_2$, $n=3$
15c: $R^1=CH_2NH_2$, $n=3$
15d: $R^1=CH_2CH_2NH_2$, $n=2$
15e: $R^1=CH_2CH_2NHCH_2Ph$, $n=3$

16a: $R^2=H$, $n=3$
16b: $R^2=H$, $n=2$
16c: $R^2=CH_2Ph$, $n=3$



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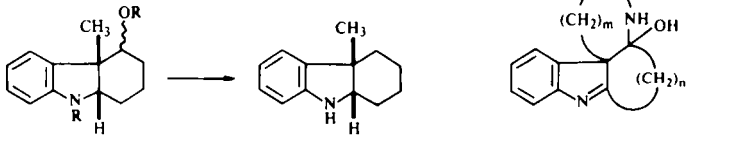


26: R = H
27: R = Ts

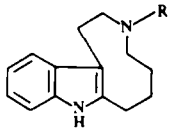
28

23a: $m=2$, $n=3$
23b: $m=1$, $n=3$
23c: $m=2$, $n=2$

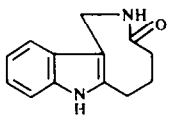
14f: $R^1=CH_2CH_2COOH$
14g: $R^1=CH_2CH_2COCl$
14h: $R^1=CH_2CH_2CON_3$
14i: $R^1=CH_2CH_2NHCOOCH_2Ph$

14j: $R^1=CH_2COOH$
14k: $R^1=CH_2COCl$
14m: $R^1=CH_2CON_3$

14n: $R^1=CH_2COOH$
14o: $R^1=CH_2COCl$
14p: $R^1=CH_2CONH_2$
14q: $R^1=CH_2CN$



29a: R = H
29b: R = $COCH_3$



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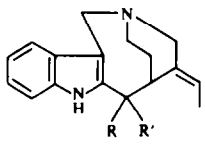
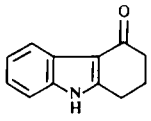


31a: R, R' = CH_2
31b: R = CH_2OH; R' = $COOCH_3$



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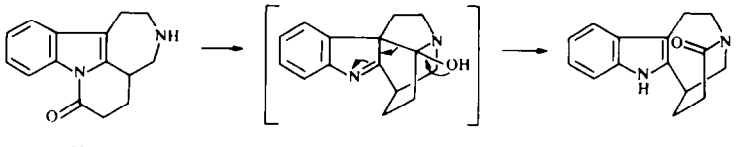
temporary photoproduct **15c** through elimination of the aminomethyl group. The objective compound **30** was not detected at all. This result suggests a reaction pathway where, in the former case, the product **16a** should have been constructed through the 5-membered intermediate **23a**, but in the latter, the corresponding intermediate should be the 4-membered ring system **23b**. As such an intermediate seems not to be readily formed, the retro-Mannich reaction of **15c** must have predominantly occurred to give 4-oxotetrahydrocarbazole (**32**).

In conformity with this assumption, the other C-nor compound **14d**, which could be expected to pass through a 5-membered intermediate **23c** via **15d** on photoirradiation, followed by ring enlargement, should give the objective product, an 8-membered lactam **16b**. Indeed, the irradiation of **14d** gave **16b** in 36% yield. Thus, at least an aminoethyl group at the C-3 position of the indole nucleus is necessary for this photosynthesis. These interesting findings urged us to survey the further applicability of this reaction.

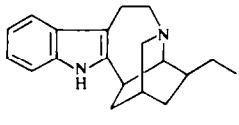
It was established that this reaction is also feasible with the secondary amine **14e** to provide **16c** via **15e**, though in a low yield of 34%. Based upon this preliminary work, the secondary amine **33** was prepared from **14b** through **37**, as the substrate for the above photoisomerization since the expected photoproduct **35** from **33** constitutes a part of the fundamental skeleton of *Iboga* alkaloid, ibogamine (**36**).[18] Thus, condensation of **14b** with formalin in formic acid at reflux for 0.5 hr provided the double Mannich reaction product **37**, m.p. 149–150°, IR(Nujol)ν 1670 cm^{-1}, UV(EtOH)λ_{max} 255, 279 nm, in 69% yield. The compound **37** was submitted to the retro-Mannich reaction by refluxing a solution of **37** in 10% oxalic acid in ethanol for 26 hr, which provided the objective **33**, IR(film)ν 3330, 1690 cm^{-1}, *m/e* 240 (M^+), in 78% yield. A solution of **33** in methanol was irradiated to afford the target **35**, m.p. 258–259°, possibly via **34**, suggesting an availability of this photoreaction in the field of alkaloid syntheses.

The synthesis of *Strychnos* alkaloids such as *dl*-tubifoline (**6**), *dl*-tubifolidine (**6a**) and *dl*-condyfoline (**7**)[5] could now be simply realized by conversion of **16a** to **38b**, since these alkaloids had been already synthesized by Harley-Mason from **38b**.[19] Thus, the lactam **16a** was reduced to **29a**, as is already described, and then acylated with α-chlorobutyryl chloride to **38a**, m.p. 203–204°, in 92% yield. Oxidation of **38a** with iodine pentoxide (I_2O_5) in 80% (v/v) aqueous tetrahydrofuran afforded **38b**, m.p. 200–201°, in 65% yield. In this reaction, other known oxidizing reagents such as sodium periodate,[20a] periodic acid,[20b] manganese dioxide,[20c] aerial oxidation[20d] and selenium dioxide,[16] were not effective. However, the reagent (I_2O_5) proved to be regioselectively effective for the oxidation of the α-methylene C of the 2-alkyl substituent of 2,3-dialkylindoles, without any unfavored side reaction.

Cyclization of **38b** with sodium t-amylate in tetrahydrofuran provided a diastereomeric mixture of the tetracyclic ketolactams, **39a** and **40a**, in 88% yield.



33 **34** **35**



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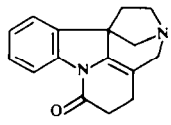

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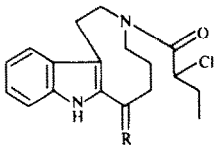
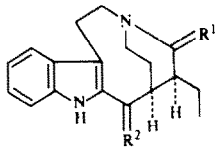


38a: R = H_2

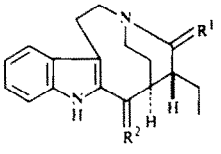
38b: R = O



39a: $R^1 = R^2 = O$

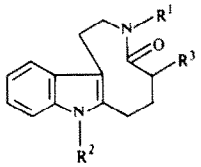
39b: $R^1 = O$, $R^2 = H_2$

39c: $R^1 = R^2 = H_2$



40a: $R^1 = R^2 = O$

40b: $R^1 = O$, $R^2 = H_2$

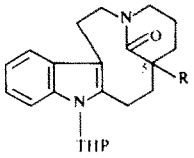


41a: R^1 = PhCO, $R^2 = R^3 = H$

41b: R^1 = PhCO, R^2 = THP, $R^3 = H$

41c: R^1 = PhCO, R^2 = THP, $R^3 = -(CH_2)_3-Cl$

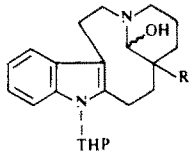
41d: $R^1 = H$, R^2 = THP, $R^3 = -(CH_2)_3-Cl$



42a: R = H

42b: R = C_2H_5

42c: R = $-CH_2CH=CH_2$



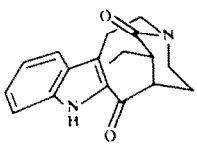
43a: R = C_2H_5

43b: R = $-CH_2CH=CH_2$

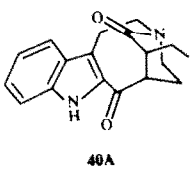
The ratio of the diastereomers immediately after the reaction was estimated to be **39a**:**40a** = 2:3 by the integrated values of two Me proton signals at δ 1.04 and 1.21 as triplets, corresponding to **39a** and **40a**, respectively. Fortunately, the diastereomeric mixture was gradually changed to the desired more stable isomer **39a** on standing in chloroform for several days or on repeated recrystallizations from ether–dichloromethane. The isomer **39a**, m.p. 187–189° (dec), was identified by comparison with an authentic sample through direct comparison of TLC behaviors, IR and ^{1}H NMR spectra.[19]

As for stereochemistry of these isomers, **39a** and **40a**, examinations on molecular models suggest the preferred conformations to be **39A** and **40A** in Fig. 1, respectively, since the Et substituent of the former is equatorial, which reasonably explains the fact that **39a** is much more stable than **40a**.

For confirmation of the later stages in the synthesis of these alkaloids by Harley–Mason required by his brief experimental description,[19] the following modified procedure was developed. The above diastereomeric mixture of **39a** and **40a** was submitted to the Wolff–Kishner–Huang–Minlon reduction, affording the isomer **39b** of a higher R_f value and the other one **40b** of the lower R_f value in 38% and 19%, respectively. The stereochemistry of these isomers, **39b** and **40b** was finally established by conversion of **39b** to *dl*-tubifoline (**6**) and *dl*-condyfoline (**7**) of known stereochemistry. The former lactam **39b** was reduced with diborane instead of LAH[19] in tetrahydrofuran to give the amine **39c** in 64% yield. This was dehydrogenated with platinum oxide to furnish *dl*-**6** and *dl*-**7** in 70% and 13% yields, respectively. *dl*-Tubifoline (**6**) was reduced with LAH to give *dl*-tubifolidine (**6a**). The spectral data of these synthetic products were identified with those of the natural alkaloids.[5]



39A



40A

Fig. 1.

With regard to the stereo- and regio-selective syntheses of *Aspidosperma* alkaloids, *dl*-1,2-dehydroaspidospermidine (**8**),[6] *dl*-1-acetylaspidospermidine (**9**),[7] *dl*-quebrachamine (**10**),[8] attention was focussed on the solution of the following problems: (1) selective protection and deprotection at N(a)H and N(b)H; (2) twofold alkylations at the α-C of the lactam CO; (3) the C3-bridge construction between the N(b) and the α-C of the CO; (4) the stereo- and regio-selective transannular cyclization. These problems were solved in the following way.

The lactam **16a** was treated with an equimolar amount of benzoyl chloride and triethylamine in tetrahydrofuran to afford the imide **41a** in 77% yield.

Even when the acylation was carried out with excess benzoyl chloride, no dibenzoyl derivative was produced at all. Furthermore, on benzoylation to generate the imide **41a**, an attempt was made to remove the unreacted benzoyl chloride with an excess of n-propylamine, and it was incidentally discovered that the generated imide was sensitive to n-propylamine, which selectively cleaved only the N–COPh bond, giving the substrate **16a**. This finding provided useful information for deprotective removal of the benzoyl group from the imide **41c** at a later stage. The imide **41a** was reacted with an excess of dihydropyran in the presence of camphor sulfonic acid[21] to provide **41b** in 89% yield. The compound **41b** was treated with lithium diisopropyl amide (LDA) at $-78°$, and then alkylated with 1-chloro-3-iodopropane to give **41c** in 71% yield as a diastereomeric mixture. Alkylations carried out at $-50°$ or at higher temperature led to generation of a significant amount of decomposed products.

With reference to the above findings about debenzoylation, selective deprotection was accomplished with n-propylamine, to furnish **41d** in 94% yield. Only the benzoyl group was eliminated by aminolysis. Cyclization of **41d** with an excess of sodium hydride and potassium iodide in the presence of a catalytic amount of 18-crown-6 gave the tetracyclic lactam **42a** in 92% yield. This constitutes the mother skeleton of quebrachamine (**10**) and therefore is an important intermediate for the synthesis of *Aspidosperma* alkaloids by further introduction of the two-C substituent into C-5 position of **42a**. The compound **42a** was lithiated with LDA in THF-HMPA at $-78°$, and then alkylated with ethyl iodide to furnish the desired product **42b** in 84% yield. It is noteworthy that the C-5 position, the α-C of the lactam CO in this ring system, was readily lithiated with LDA, and much more reactive toward electrophiles than in the first alkylation. This is presumably due to the stereochemical shape of the molecule, which should project the carbanion lobe for easy substitution. (See the molecular shape of **42b**, and put the carbanion lobe in place of Et group at C-5, in Fig. 2). Thus, problems 1–3 were solved to give **42b** in six steps and in a high yield of 35% from **16a**.

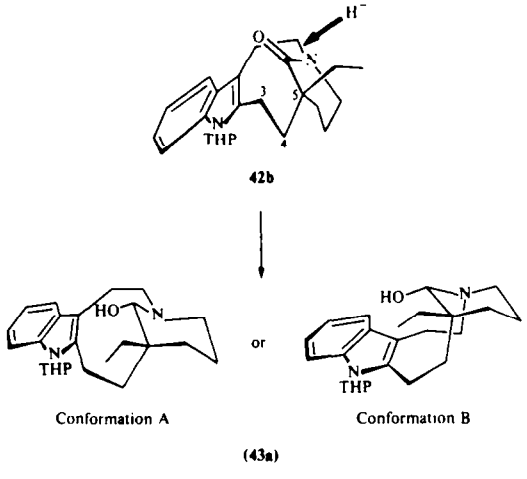


Fig. 2.

To our surprise, the compound **42b**, when reduced with LAH in tetrahydrofuran for an hr, and then treated with 10% HCl to remove the tetrahydropyranyl group gave *dl*-1,2-dehydroaspidospermidine (**8**),[6] in 48% yield from **42b**. This alkaloid had not been readily isolated, but chemically correlated with the natural quebrachamine (**10**) in a low yielding, mild oxidation.[22] Its synthesis was also effected by Pakrashi *et al.*[6d] For establishment of the structure of the synthetic **8**, it was reduced with LAH and then acylated to afford *dl*-1-acetylaspidospermidine **9** in 64% yield. This was identified by comparison with an authentic specimen synthesized through another route.[7] The mechanism of this unexpected cyclization could be explained by presuming that the OH group of the amino–alcohol **43a** in either conformation of A[23] or B[24] depicted in Fig. 2, should be generated by reduction of the lactam **42b**, and might be blocked by the 9-membered ring linked with the indole nucleus. Thereby, **43a** would be resistant to further reduction under mild conditions and would, by treatment with acid, provide the iminium salt, which may be readily cyclized to **8**. Therefore, **42b** was reduced with LAH under forcing conditions at reflux for 4 hr, and then treated with acid to furnish *dl*-quebrachamine (**10**)[6a,8,5] in 45% yield. Thus, by controlling the reduction condition at the final stages, a variety of *Aspidosperma* alkaloids could be produced through the regioselective formation of the iminium salt, thus answering problem 4.

After these syntheses were completed, there was reported the elegant work achieved by Hájícek and Trojánek,[4c] who succeeded in the steroespecific total synthesis of *dl*- and *l*-strempeliopine (**13**), the parent base of the *Schizozygane* group, via the penultimate product **12**, establishing the absolute configuration of this alkaloid as represented by formula **13**. Obviously, **12** should be readily synthesized by the present method. Thus, lactam **42a** was again treated with LDA in tetrahydrofuran at $-78°$ and then alkylated with allyl bromide to furnish the desired **42c**, which was reduced with LAH and treated with acid to provide 21-methylene-1,2-dehydroaspidospermidine (**12**) in 60% overall yield. The NMR and other spectral data of this **12** were identical to those of the authentic sample on direct comparison.[4c,26]

Thus, the present total syntheses of *dl*-**8** and *dl*-**12** provide a general entry not only to *Aspidosperma*, but also to *Schizozygane* and *Eburnamine* alkaloids in consideration of Hájícek and Trojánek's work[4c] and Lévy's success[4d] in conversion of *l*-**8** to *d*-**11**.

In conclusion, a new synthetic road leading to a forest of *Strychnos*, *Aspidosperma*, *Schizozygane and Eburnamine* alkaloids has been opened, and displayed in Chart 2, starting from a novel photoisomerization. Further studies for the syntheses of other members of these alkaloids are in progress.

EXPERIMENTAL

M.ps were taken on a Yamato MP-1 m.p. apparatus. All m.ps are uncorrected. IR spectra were recorded on JASCO IRA-2 diffraction grating IR spectrophotometer. UV spectra were measured on a Hitachi EPS-3T, or a Hitachi model 200-10 spectrophotometer. Mass spectra were taken on a Hitachi RMU-6E, or a JEOL JMS-D300 spectrometer. Microanalyses were determined with a Yanagimoto CHN recorder MT-2. NMR spectra were determined on a Hitachi

R-20B, JEOL JNM PS-100, JEOL FX-100, or a JEOL FX-200 spectrometer, and reported in ppm from internal TMS on δ scale. Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad)]. Coupling constants (J) are recorded in Herz. Column chromatography was carried out on Merck silica gel (70–325 mesh ASTM), or Merck aluminum oxide 90 (70–230 mesh ASTM). Preparative TLC was carried out on Merck silica gel GF_{254} (Type 60), or Merck aluminum oxide GF_{254} (Type 60/E). THF and dioxane were distilled over LAH before use. HMPA was distilled over calcium hydride and dried over 4 Å molecular sieves. Diisopropylamine and triethylamine were distilled over KOH and dried over KOH pellets. The following abbreviations are used: THF = tetrahydrofuran, DME = 1,2-dimethoxyethane, HMPA = hexamethylphosphoric triamide, tosyl = *p*-toluenesulfonyl, LDA = lithium diisopropylamide, 18-crown-6 = 1,4,10,16-hexaoxacyclooctadedcane.

Photoisomerization of 9-*acetyl*-1,2,3,4-*tetrahydrocarbazole* (**14**). A soln of **14** (3.50 g, 16.4 mmol) in 50 ml absolute ether was irradiated with a 300 W high pressure mercury lamp for 26 hr under N_2. The crude mixture was separated by silica gel column chromatography, eluting with CH_2Cl_2:benzene:EtOAc:hexane = 1:1:1:4 to afford **15**, (700 mg, 20.0%) as unstable pale yellow crystals, m.p. 66–68°; IR(Nujol) ν 1715, 1645, 1610 cm^{-1}; UV (EtOH) λ_{max}260 nm; ^{1}H NMR (acetone-d_6) δ 1.63 (s, 3H), 7.1–7.8 (m, 4H); mass spectrum *m/e* 213 (M^+), 170 (M^+–$COCH_3$): Compound **16** (210 mg, 6.0%), m.p. 156–158°; IR (Nujol) ν 3180, 1610 cm^{-1}; UV (EtOH) λ_{max} 245, 267, 307 nm; ^{1}H NMR ($CDCl_3$) δ 1.5–2.92 (m, 5H), 2.69 (s, 3H, 3.27 (t, J = 7 Hz, 1H), 4.8–5.3 (m, 3H), 6.9–7.5 (m, 3H), 7.8–8.2 (m, 1H), 9.1 (br, 1H); *m/e* 213 (M^+); too unstable for elemental analysis. Compound **17** (95 mg, 2.7%) m.p. 156–158°; IR (Nujol) ν 3270, 1650 cm^{-1}; UV (EtOH) λ_{max} 245, 360 nm; ^{1}H NMR (CD_3NO_2) δ 2.60 (s, 3H), 1.55–2.27 (m, 4H), 2.5–2.94 (m, 4H), 7.04 (d–d, J = 8 and 8 Hz, 1H), 7.42 (d-d, J = 8 and 1.5 Hz, 1H), 7.48 (d-d, J = 8 and 1.5 Hz, 1H); (Found: C, 78.51; H, 7.00; N, 6.55. *m/e* 213(M^+). Calc for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57%). Compound **17** was identical with a sample which was synthesized from (*m*-carboxyphenyl)hydrazine, consecutively by the Fischer indolization, separation and the Corey's ketone synthesis. Compound **18** (385 mg, 11%); m.p. 210–211° (lit.[6] 206–208°); IR (Nujol) ν 3280, 1650 cm^{-1}; UV (EtOH) λ_{max} 236, 261, 312, 352 nm; ^{1}H NMR ($CDCl_3$) δ 1.57–2.10 (m, 4H), 2.60 (s, 3H), 2.56–2.94 (m, 4H) 7.38 (d, J = 1.5 Hz, 1H), 7.68 (d–d, J = 9 and 1.5 Hz, 1H), 7.93 (d, J = 1.5 Hz, 1H) 8.12 (br, 1H); mass spectrum *m/e* 213 (M^+); (Found: C, 78.77; H, 7.11; N, 6.62. Calc for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57%). Compound **18** was also identical with a sample which was prepared from (*m*-carboxyphenyl) hydrazine in a similar manner to synthesis of **17**.

cis-4a-(1-*Hydroxyethyl*)-1,2,3,4,4a,9a-*hexahydrocarbazole* (**20**). To a stirred suspension of 0.38 g (10.0 mmol) of LAH in 30 ml dry ether was added dropwise a soln of **15** (1.07 g, 5.00 mmol) in 20 ml ether under ice cooling. The mixture was stirred in an ice bath for 2 hr. After the usual work up, the residue was purified by column chromatography on silica gel, eluting with EtOAc:hexane:CH_2Cl_2 = 2:2:1 to give 188 mg (22%) of **19**, and 408 mg (37%) of **20**, m.p. 113–116°; IR (Nujol) ν 3360, 3250, 1600, 1090, 890, 770, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.06 (d, J = 7 Hz, 3H), 0.9–2.40 (m, 8H), 3.10 (s, 2H, NH and OH), 3.4–3.8 (br, 1H), 3.82 (q, J = 7 Hz, 1H), 6.55–7.8 (m, 4H), and 130 mg (12%) of epimeric **20a**: m.p. 102–105°; IR (Nujol) ν 3330, 3240, 1600, 1080, 750, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08 (d, J = 7 Hz, 3H), 1.0–2.2 (m, 8H), 2.83 (s, 2H, NH and OH), 3.78 (q, J = 7 Hz, 1H), 3.6–4.0 (m, 1H), 6.50–7.35 (m, 4H). (Found: C, 77.26; H, 8.86; N, 6.52. Calc for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45%).

cis-4a-(1-*Tosyloxyethyl*)-9-*tosyl*-1,2,3,4,4a,9a-*hexahydrocarbazole* (**21**). To an ice-cold soln of **20** (900 mg, 4.15 mmol) in 50 ml absolute pyridine, was added 3.81 g (20.0 mmol) tosyl chloride. The mixture was allowed to stand in a refrigerator for 3 days. The solvent was concentrated *in vacuo*, and the residue was acidified with 10% H_2SO_4, and extracted with $CHCl_3$. The organic phase was washed, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel, eluting with EtOAc:hexane = 1:4, and recrystallized from ether to give 1.52 g (70%) of **21**, m.p. 102–105°; mass spectrum *m/e* 353 (M^+–TsOH); ^{1}H NMR ($CDCl_3$) δ 0.67 (d, J = 7 Hz, 3H), 0.8–2.1 (m, 8H), 2.36 (s, 3H), 2.41 (s, 3H), 4.01 (q, J = 7 Hz, 1H), 4.0–4.3 (br, 1H), 6.73–7.9 (m, 12H); (Found: C, 63.17; H, 6.19; N, 2.51. Calc for $C_{28}H_{31}NO_5S_2 \cdot 1/2H_2O$: C, 62.90; H, 6.03; N, 2.62%).

cis-4a-*Ethyl*-1,2,3,4,4a,9a-*hexahydrocarbazole* (**22**). To a soln of **21** (733 mg, 1.39 mmol) in 30 ml absolute dioxane was added LAH (380 mg, 10.0 mmol). The mixture was heated at reflux overnight. After the standard work up, chromatographic purification of the residue on silica gel eluting with EtOAc:hexane = 1:6 gave 126 mg (45%) of **22** as a pale yellowish oil: IR (film) ν 3450, 1600, 1435, 1430 cm^{-1}; mass spectrum *m/e* 201 (M^-); ^{1}H NMR ($CDCl_3$) δ 0.82 (t, J = 7 Hz, 3H), 1.15–2.1 (m, 9H), 3.48 (br, 1H), 6.25–7.35 (m, 4H). The IR, NMR, and mass spectra were identical with those of the authentic specimen.[12] The free base was converted to the hydrochloride, m.p. 190–192°, which was identical with the authentic sample, m.p. 193–195°.[12]

6-*Oxo*-10-*methyl*-6, 7, 8, 9-*tetrahydropyrido*[1, 2-a]*indole* (**14a**). A mixture of methyl 5-oxoheptanoate ($C_2H_5COCH_2CH_2CH_2COOCH_3$)[14] (13.2 g 83.0 mmol) and phenylhydrazine (8.96 g 83.0 mmol) was heated at 70° for 1 hr under N_2. The crude hydrazone obtained was suspended in 200 ml 10% H_2SO_4, and the mixture was heated at 90° for 2 hr under N_2. After cooling, the aqueous soln was extracted with $CHCl_3$, and the combined extracts were successively washed with water, sat $NaHCO_3$ aq, and water, dried over Na_2SO_4. Concentration of the solvent left 8.20 g (50%) of **14a** in an almost pure state. Recrystallization of the crude product from ether gave **14a** as colorless pillars: m.p. 79–81° (lit.[13] 81°); IR (Nujol) ν 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H), 1.8–2.2 (m, 2H), 2.5–3.0 (m, 4H), 7.1–7.6 (m, 3H), 8.3–8.6 (m, 1H); UV (EtOH) λ_{max} 244, 300 nm; mass spectrum *m/e* 199 (M^+); (Found: C, 78.13; H, 6.60; N, 7.01. Calc for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03%).

Photoisomerization of **14a**

Procedure A. A soln of **14a** (1.00 g, 5.03 mmol) in 300 ml absolute THF was irradiated with a 300 W high pressure mercury lamp under a N_2 stream for 24 hr. Evaporation of the solvent left a brown residue, which was purified on silica gel column chromatography, eluting with EtOAc:hexane = 5:2 to give 400 mg (40%) of **14a**, and 200 mg (20%) of **15a** as a pale yellowish unstable solid: IR (Nujol) ν 1720, 1590 cm^{-1}; mass spectrum 199 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 3H), 1.2–3.5 (m, 6H), 6.5–7.7 (m, 4H).

Procedure B. A soln of **14a** (1.20 g, 6.03 mmol) in 300 ml absolute benzene was irradiated in the manner described for Procedure A. The crude mixture was dissolved in 20 ml dry ether, and reduced with 0.40 g LAH at 0° for 2 hr. After the usual work up, the crude residue was purified on silica gel chromatography, eluting with EtOAc:CH_2Cl_2:hexane = 1:1:1 and recrystallized from ether to give 300 mg (25%) of **26**, m.p. 111–112°; IR (Nujol) ν 3550, 3340, 3280 cm^{-1}; UV (EtOH) λ_{max} 245, 293, nm; mass spectrum *m/e* 203 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.4–2.0 (m, 6H), 2.50 (br, 2H, NH and OH), 3.3–3.75 (m, 2H), 6.6–7.3 (m, 4H); (Found: C, 76.81; H, 8.47; N, 6.89. Calc for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89%).

cis-4-*Tosyloxy*-4a-*methyl*-9-*tosyl*-1,2,3,4,4a,9a-*hexahydrocarbazole* (**27**). Compound **26** (812 mg, 4.08 mmol) was tosylated as before from **20** to **21** to give 1.05 g (50%) of **27**. Recrystallization from EtOAc hexane gave **27** as colorless needles, m.p. 146–148°; UV (EtOH) λ_{max} 260 nm; mass

spectrum *m/e* 339 (M^+–TsOH); ^1H NMR ($CDCl_3$) δ 0.76 (s, 3H), 0.9–2.8 (m, 6H), 2.35 (s, 3H), 2.44 (s, 3H), 3.78 (t, J = 6 Hz, 1H), 4.84 (br, 1H), 6.8–7.87 (m, 12H).

cis-4a-*Methyl*-1,2,3,4,5a,9a-*hexahydrocarbazole* (**28**). To a soln of **27** (256 mg, 0.5 mmol) in 10 ml dry benzene was added 1.2 ml of a 70% toluene soln of sodium bis-(2-methoxyethoxy)aluminum hydride, and the whole mixture was refluxed for 6 hr. After cooling, the excess hydride was carefully decomposed by water. The insoluble inorganic salts were filtered off, and the filtrate was washed with water and dried over Na_2SO_4. Evaporation of the solvent left an oily residue, which was chromatographed on silica gel eluting with EtOAc:hexane = 1:3 to provide 25 mg (27%) of **28** as a colorless oil, IR (Film) ν 3350, 1610 cm^{-1}; UV (EtOH) λ_{max} 246, 293 nm; mass spectrum *m/e* 187 (M^+); ^1H NMR (CCl_4) δ 1.26 (s, 3H), 1.2–1.9 (m, 9H), 3.37 (br, 1H). The IR, UV, NMR, and mass spectrum of this sample were identical with those of the authentic sample.[15]

The synthesis of 6-*oxo*-(2-*aminoethyl*)-6,7,8,9-*tetrahydro-pyrido* [1,2-a]*indole* (**14b**)

5-*Oxoazelaic acid*[$HOOC(CH_2)_3CO(CH_2)_3COOH$]. To a cold soln of 4-carbomethoxy butyryl chloride (32.9 g; 0.200 mol), in 200 ml of dry benzene was added Et_3N (20.2 g; 0.200 mol) with vigorous stirring, keeping the temp below 25°. The mixture was heated on a water bath at 33–35° for 15 min and allowed to stand at room temp for 30 min. The ppt was removed by filtration, and the filtrate was concentrated *in vacuo*. To give a dark oily residue. The residue was heated with 200 ml of 2N KOH for 5 hr. The cold homogeneous soln was washed with ether, and slightly acidified with conc HCl, and concentrated to dryness under reduced pressure. The solid residue was successively extracted with hot actone. Evaporation of the solvent left 12.1 g (60%) of 5-oxoazelaic acid. Recrystallization from ether gave colorless prisms, m.p. 105–106° (lit.[27] 101–102°); IR (Nujol) ν 1700 cm^{-1}; (Found: C, 53.36; H, 6.92. Calc for $C_9H_{14}O_5$: C, 53.46; H, 6.98%).

6-*Oxo*-6,7,8,9-*tetrahydro-pyrido*[1,2-a]*indole*-10-*propionic acid* (**14f**). A soln of 1.08 g (10 mmol) phenylhydrazine, and 2.02 g (10 mmol) 5-oxoazelaic acid in 20 ml EtOH was stirred at room temp for 15 min. Evaporation of the solvent left an orange solid, which was collected by filtration, and washed with water to furnish 3.00 g (quant.) of the almost pure hydrazone, m.p. 152–153°. The phenylhydrazone was heated at reflux with 70 ml 10% H_2SO_4 for 1 hr. The mixture was cooled to room temp, and the ppt was collected by filtration to give 2.00 g (70%) of **14f**. Recrystallization from EtOH gave colorless prisms, m.p. 165–166°; IR (Nujol) ν 2400–2800, 1690–1700 cm^{-1}; UV (EtOH) λ_{max} 243, 255, 270 nm; mass spectrum *m/e* 257; ^1H NMR δ 1.8–2.4 (quin., 2H), 2.5–3.2 (m, 8H), 7.1–7.8 (m, 4H), 8.25–8.7 (m, 1H). (Found: C, 69.97; H, 5.87; N, 5.56. Calc for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44%).

Acid chloride **14g**. To a suspension of **14f** (7.00 g, 27.2 mmol) in 10 ml dry benzene was added dropwise 7.80 g (61.5 mmol) oxalyl chloride. The mixture was heated at 60° for 20 min, and evaporated to dryness on a flash evaporator to give crystalline acid chloride (quant.): IR (Nujol) 1790, 1680 cm^{-1}.

Acyl azide **14h**. To an ice cooled soln of 0.78 g (12 mmol) sodium azide in 2 ml water was added dropwise a soln of 2.68 g (10.2 mmol) of **14g** in 25 ml dry acetone. The soln was stirred under ice cooling for 10 min, and at room temp for 15 min. The mixture was diluted with 50 ml water, and the ppt was collected by filtration to give 2.68 g (95%) of **14h**, amorphous solid, IR(Nujol) ν (2120, 1700, 1680 cm^{-1}.

6 - *Oxo* - 10 - (2 - *aminoethyl* - 6,7,8,9 - *tetrahydro* - *pyrido*[1,2 - a]*indole* (**14b**). A soln of **14h** (31.0 g, 0.11) in 100 ml dry benzene was refluxed for 1.5 hr. On cooling, 14.2 g (0.13 mol) benzyl alcohol was added, and the whole soln was refluxed for 2.5 hr. The solvent was removed *in vacuo* to leave 36.0 g (90.5%) of **14i** as a white powder, which was recrystallized from EtOAc to furnish pure **14i**, colorless prisms, m.p. 133–134°, UV(EtOH) λ_{max} 244, λ_{min} 223.5 nm; IR(NUjol) ν 3350, 1710, 1670, 1620 cm^{-1}; NMR ($CDCl_3$) δ 5.10 (s, 2H), 7.18–7.56 (m, 8H), 8.36–8.54 (m, 1H). Mass spectrum *m/e* 362 (M^+), 271 (M^+–CH_2Ph). (Found: C, 72.93; H, 6.10; N, 7.74. Calc for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73%).

A mixture of the above **14i** (3.0 g, 8.28 mmol) in MeOH (40 ml), AcOH (10 ml) and water (5 ml) was subjected to hydrogenolysis with Pd–C (400 mg) under an atmospheric pressure of H_2 for 2.5 hr. The resulting mixture was filtered, made alkaline with K_2CO_3 under ice cooling, extracted with CH_2Cl_2, washed with water, and dried over K_2CO_3. The solvent was removed to leave the solid, which was converted to the hydrochloride. Recrystallization from aqueous EtOH gave the pure hydrochloride of **14b,** colorless prisms, m.p. 284–287° (dec), IR(Nujol) ν 2400–2800, 1690 cm^{-1}; mass spectrum *m/e* 228 (M^+–HCl). (Found: C, 63.64; H, 6.45; N, 10.63; Cl, 13.41. Calc for $C_{14}N_{17}N_2OCl$: C, 63.52; H, 6.43; N, 10.59; Cl, 13.43%).

Usually, the crude free amine obtained by the above procedure was directly submitted to photoisomerization, affordeing **16a** in 89.3% yield. Also, the direct rearrangement of **14h–14b** was done, but the benzyl carbamate procedure is preferable with respect to the quality of the free amine **14b.**

6 - *Oxo* - 6,7,8,9 - *tetrahydro* - *pyrido*(1,2 - *a*) - 10 - *acetic acid* (**14j**) 4-Oxosuberic acid [$HOOC(CH_2)_2CO(CH_2)_3COOH$][28] (188 mg, 1.00 mmol) and phenylhydrazine (120 mg, 1.10 mmol) was dissolved in 10 ml EtOH, and the mixture was stirred at room temp for 30 min. Concentration *in vacuo* afforded the organge hydrazone. The crude hydrazone was suspended in 7 ml 10% H_2SO_4, and the mixture was refluxed for 1.5 hr. The mixture was cooled to room temp, and the ppt (126 mg) was collected by filtration. Chromatographic separation on silica gel eluting with EtOAc:benzene = 1:1 gave 34 mg (14%) of **14j**, m.p. 177–179°; IR (Nujol) ν 1700 cm^{-1}; UV (EtOH) λ_{max} 242, 266, 300 nm; mass spectrum *m/e* 243 (M^+); ^1H NMR ($CDCl_3$) δ 1.8–2.3 (m, 2H), 2.4–3.0 (m, 4H), 3.10 (s, 2H), 7.1–7.8 (m, 2H), 7.8–8.2 (m, 1H), 8.3–8.7 (m, 1H), 9.0–9.7 (br, 1H), and 72 mg (28%) of indole-2,3-dipropionic acid, m.p. 135–136°; IR (Nujol) ν3400, 1740, 1690 cm^{-1}; UV (EtOH) λ_{max} 227, 284, 293 nm; mass spectrum *m/e* 261 (M^+); ^1H NMR ($CDCl_3$) δ 2.5–2.8 (m, 4H), 6.95–7.80 (m, 4H), 9.06 (s, 2H).

Acid chloride **14k**. The acid **14j** (243 mg, 1.00 mmol) was treated with oxalyl chloride in a similar manner to afford **14k** quantitatively, IR (Nujol) ν 1780, 1700 cm^{-1}.

Acyl azide **14m**. The above crude **14k** was reacted with sodium azide under the conditions described for **14h** to give 221 mg (82% overall) of **14m**, IR (Nujol) ν 2150, 1700 cm^{-1}.

6 - *Oxo* - 10 - (2 - *aminomethyl* - 6,7,8,9 - *tetrahydro* - *pyrido*(1,2-a)*indole* (**14c**). The azide (221 mg, 0.825 mmol) was converted in a similar manner to 204 mg (99%) of **14c**·HCl, m.p. 265–268° (dec), IR(Nujol) ν 1710 cm^{-1} UV (EtOH) λ_{max} 242, 302 nm; mass spectrum *m/e* 214 (M^+–HCl).

6 - *Oxo* - 10 - (*N* - *benzyl* - 2 - *aminoethyl*) - 6,7,8,9 - *tetrahydro-pyrido*(1,2-a)*indole* (**14e**). The free amine **14b** (1.74 g, 7.60 mmol) and benzaldehyde (967 mg, 9.10 mmol) were dissolved in 35 ml EtOAc. To this soln was added 1.5 g $MgSO_4$, and the mixture was stirred at room temp for 1.5 hr. Filtration of the catalyst followed by concentration gave the pale yellowish oily residue which was dissolved in 30 ml EtOH and hydrogenated over PtO_2 (40 mg) for 6.5 hr. The product was purified by column chromatography on alumina, eluting with EtOAc:hexane = 1:3 to give 1.89 g (77%) of **14e** as a colorless oil; IR (Film) ν 3300, 1700 cm^{-1}; mass spectrum *m/e* 318 (M^+), 199, 120, 91; ^1H NMR ($CDCl_3$) δ 1.50–2.2 (m, 2H), 2.2–3.1 (m, 8H), 3.64 (s, 1H, NH), 4.49 (s, 2H), 6.9–7.5 (m, 8H), 8.25–8.60 (m, 1H).

3 - *Oxo* - 1,2 - *dihydro* - 3H - *pyrrolo*[1,2a]*indole* - 9 - *acetic acid* (**14n**) A soln of diethyl 4 - oxopimelate (13.9 g, 60.5 mmol)[29] and phenylhydrazine (7.91 g, 72.6 mmol) in

0.5 ml AcOH was stirred at room temp for 0.5 hr. To this mixture was added 120 ml conc HCl, and the soln was refluxed for 5 hr. After cooling, the crystals were collected by filtration. Recrystallization from acetone gave 8.00 g (58%) of **14n**, colorless needles, m.p. 188–191°, IR (Nujol) ν 1740, 1710 cm^{-1}; UV(EtOH) λ_{max} 240, 165 (sh), 295 nm; mass spectrum *m/e* 229 (M^+), 184; ^1H NMR ($CDCl_3$) δ 3.14 (s, 4H), 3.71 (s, 2H), 7.20–7.60 (m, 3H), 8.00–8.2 (m, 1H), (Found: C, 68.31; H, 4.86; N, 6.23. Calc for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11%).

3 - *Oxo* - 9 - *carbamoylmethyl* - 1,2 - *dihydro* - 3H - *pyrrolo*[1,2-a]*indole* (**14p**). To a suspension of 11.5 g (50.0 mmol) of **14n** in 70 ml dry benzene was added 13.0 g (0.10 mmol) oxalyl chloride. The mixture was kept at 55° for 33 hr. Evaporation of the solvent left nearly colorless solid **14o**. To a suspension of **14o** in 50 ml $CHCl_3$ was added 20 ml of a $CHCl_3$ soln saturated with ammonia under ice cooling. After 0.5 hr, the ppt was collected by filtration. Recrystallization from 80% EtOH gave 10.7 g (93%) of **14p** as colorless bright needles, m.p. 209–210°; IR (Nujol) ν 3425, 3175, 1720, 1680 cm^{-1}; mass spectrum *m/e* 228 (M^+), 184 (M^+–$CONH_2$); ^1H NMR (DMSO-d_6) δ 3.09 (s, 4H), 3.45 (s, 2HO, 6.7–7.7 (m, 5H), 7.7–7.95 (m, 1H). (Found: C, 68.39; H, 5.21; N, 11.88. Calc for $C_{13}H_{12}N_2O_2$: C, 68.41, H, 5.30; N, 12.27%).

3 - *Oxo* - 9 - *cyanomethyl* - 1,2 - *dihydro* - 3H - *pyrrolo*[1,2-a]*indole* (**14q**). To a cold soln of **14p** (4.90 g, 21.5 mmol) and pyridine (4.08 g, 51.6 mmol) in 40 ml dry THF was added dropwise a soln of 5.92 g (25.8 mmol) trifluoroacetic anhydride in 6 ml THF, and the mixture was stirred at room temp for 40 min. The ppt was taken by filtration, and recrystallized from EtOAc to give 3.35 g(74%)of **14g**, colorless needles, m.p. 148–150°; IR (Nujol) ν 2280, 1760 cm^{-1}; mass spectrum *m/e* 210 (M^+); ^1H NMR ($CDCl_3$) δ 2.8–3.4 (m, 4H), 3.66 (s, 2H), 7.15–7.60 (m, 3H), 7.90–8.12 (m, 1H). (Found: C, 74.41; H, 4.60; N, 13.57. Calc for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79; N, 13.32%).

3 - *Oxo* - 9 - (2 - *aminoethyl*) - 1,2 - *dihydro* - 3H - *pyrrolo*[1,2-a]*indole* (**14d**). A soln of **14q** (514 mg, 2.44 mmol) in 25 ml AcOH was hydrogenated over Pt catalyst at 3.5–4.0 kg/cm^2 for 6 hr. The catalyst was removed by filtration. The filtrate was concentrated under diminished pressure to leave a dark residue, which was dissolved in 50 ml CH_2Cl_2, and successively washed with 10% K_2CO_3, water, and dried over K_2CO_3. Careful evaporation under N_2 left 424 mg (81%) of **14d** as a pale yellow oil, IR (Film) ν 3400, 3200, 1735 cm^{-1}, which easily formed the carbonate salt.

Photoisomerization of **14b**. A soln of 1.84 g (8.07 mmol) of **14b** in 500 ml ether was irradiated with a 300 W high pressure mercury lamp under N_2 for 21 hr. The solvent was removed *in vacuo*. The residue was chromatographed on silica gel eluting with EtOAc:acetone = 3:2 within an hr to give 1.71 g (89.3%) of **16a** as a colorless amorphous solid, m.p. 120–121°; IR (Nujol) ν 3350, 1630 cm^{-1}; mass spectrum *m/e* 228 (M^+), which should be used immediately for the subsequent reaction.

3 - *Acetyl* - 1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4-b]*indole* (**29b**), Compound **16a** (700 mg, 3.07 mmol) was reduced with LAH (380 mg, 10.0 mmol) in 100 ml THF at reflux for 4 hr to afford 603 mg crude amine **29a** as a colorless oil. The crude product was acetylated with 236 mg (3.00 mmol) acetyl chloride in the presence of K_2CO_3 0.5 g of in 20 ml of benzene. On purification by silica gel column chromatography, eluting with EtOAC:acetone = 3:2, there was obtained 380 mg (54%) of **29b** after recrystallization from ether–hexane, colorless prisms, m.p. 190–193° (lit.[16] 189–190°); IR (Nujol) ν 3200, 1610 cm^{-1}; mass spectrum *m/e* 256 (M^+); ^1H NMR ($CDCl_3$) δ 0.85–1.5 (m, 2H), 1.50–2.1 (m, 2H), 2.07, 2.23 (s, each, 3H), 2.55–3.70 (m, 8H), 6.93–7.70 (m, 4H), 8.23 (br, 1H, NH). (Found: C, 74.60; H, 7.94; N, 10.70. Calc for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93%).

Photoisomerization of **14c**. A soln of **14c** (87 mg, 4.06 mmol) in 50 ml absolute MeOH was irradiated under argon with a 300 W high pressure mercury lamp for 16 hr. The crude residue was chromatographed on silica gel, eluting with EtOAc:hexane = 2:1, and afforded 32 mg (44%) of colorless crystals. Recrystallization from hexane–EtOAc gave a pure **32**, m.p. 217–219°; IR (Nujol) 1610, 1580 cm^{-1}; UV (EtOH) λ_{max} 243, 266, 296 nm. The product was identical with the authentic **32** on comparison of IR and UV spectral data.

Photoisomerization of **14d**. A sample of **14d** 50 mg was dissolved in 160 ml absolute MeOH, and irradiated with a 40 W low pressure mercury lamp for 2 hr. Evaporation of the solvent gave a yellowish gum, which was purified on alumina preparative TLC (ethyl acetate:hexane = 2:1) to afford 18 mg (36%) of **16b**: m.p. 158–160°; IR (Nujol) ν 3400, 3200, 1660 cm^{-1}; UV (EtOH) λ_{max} 225, 283, λ_{min} 249, sh 290 nm; mass spectrum *m/e* 214 (M^+).

Photoisomerization of **14e**. A soln of 706 mg (2.22 mmol) of **14e** in 200 ml absolute MeOH was irradiated under an argon stream with a 300 W high pressure mercury lamp for 80 min. Concentration of the solvent left a yellowish gum, which, when chromatographed on alumina by eluting with EtOAc:hexane = 1:1, afforded colorless crystals. Recrystallization from EtOAc gave 239 mg (34%) of **16c**, colorless prisms, m.p. 195–197°; IR (Nujol) ν 3225, 1610 cm^{-1}; UV (EtOH) λ_{max} 227, 286, 293 nm; mass spectrum *m/e* 318 (M^+), 170, 143, 91; ^1H NMR ($CDCl_3$) δ 1.9–2.5 (m, 4H), 2.5–3.0 (m, 4H), 3.4–3.65 (m, 2H), 4.70 (br, 1H, NH), 6.95–7.6 (m, 8H), 7.85 (m, 1H); (Found: C, 78.88; H, 6.92; N, 8.54. Calc for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.80%).

Double Mannich product **37**. To a mixture of formic acid (17 ml) and formaline (4 ml) was added the hydrochloride of **14b** (1.00 g, 3.77 mmol). The mixture was refluxed for 30 min. On cooling, the mixture was concentrated to dryness, and the residue was extracted with CH_2Cl_2, and successively washed with sat. $NaHCO_3$ aq and water. Evaporation of the solvent left a slightly green solid. Recrystallization from acetone afforded 686 mg (69%) of **37**, colorless prisms, m.p. 149–150°; IR (Nujol) ν 1670 cm^{-1}; UV (EtOH) λ_{max} 255, 279, λ_{min} 239, 264 nm; mass spectrum *m/e* 252 (M^+), 210, 182; ^1H NMR ($CDCl_3$) δ 1.7–4.1 (m, 12H), 6.9–7.5 (m, 3H), 8.0–8.25 (m, 1H); (Found: C, 76.44; H, 6.47; N, 11.29. Calc for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10%).

Retro-Mannich reaction of **37**. A soln of the double Mannich product **37** (500 mg, 2.00 mmol) in 50 ml 10% alcoholic oxalic acid was refluxed for 25 hr. The solvent was concentrated under diminished pressure, and the residue was extracted with CH_2Cl_2. The extract was successively washed with 10% Na_2CO_3 aq, and brine. Concentration of the solvent followed by chromatography on alumina, eluting with CH_2Cl_2:EtOH = 15:1, gave 378 mg (78%) of the desired **33** IR (Film) ν 3330, 1690 cm^{-1}; UV (EtOH) λ_{max} 246, 270, 296 nm; mass spectrum *m/e* 240 (M^+), 198. This amine was acylated with carbobenzoxy chloride in the usual manner to provide the urethane **33a**, which was recrystallized from EtOAc to give the analytically pure material, m.p. 147–148°; IR (Nujol) ν 1700, 1680 cm^{-1}; **33** was spectrum *m/e* 374 (M^+), 283, 239, 210; 1H NMR ($CDCl_3$) δ 1.5–2.3 (m, 2H), 2.3–3.6 (m, 9H) 4.1–4.6 (m, 2H) 5.19 (s, 2H) 7.0–7.5 (m, 8H) 8.3–8.6 (m, 1H); (Found: C, 73.62; H, 6.03 N, 7.49. Calc for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48%).

Photoisomerization of **33**. The amine **33** (263 mg, 1.10 mmol) was dissolved in 200 ml absolute MeOH, and irradiated with a 300 W high pressure mercury lamp for 18 hr. Evaporation of the solvent gave a yellowish gum, which was passed through a short column packed with silica gel, eluting with CH_2Cl_2. The crude residue was recrystallized from EtOH to furnish 58 mg (22%) of **35** as colorless prisms, m.p. 258–259° (dec); IR (Nujol) ν 3170, 1640 cm^{-1}; UV (EtOH) λ_{max} 228, 285, 293 nm; mass spectrum *m/e* 240 (M^+), 211; ^1H NMR ($CDCl_3$) δ 1.75–2.17 (m,

1H), 2.2–2.65 (m, 3H), 2.7–4.05 (m, 6H), 4.59 (d–d, J = 13 and 6 Hz, 1H), 6.9–7.6 (m, 4H), 8.84 (br, 1H, NH); (Found: C, 74.73; H, 6.83; N, 11.61. Calc for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66%).

3 - (2 - *Chlorbutyryl*) - 1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4 - b]*indole* (**38a**). To a stirring mixture of 1.99 g (9.26 mmol) of the free amine **29a** in 20 ml CH_2Cl_2 and $NaHCO_3$ (3.00 g) in 20 ml water was added dropwise 1.96 g (13.9 mmol) 2-chlorobutyryl chloride over 1 hr. The organic layer was washed, dried, and concentrated to afford a solid residue. Recrystallization from EtOAc gave 2.72 g (92%) of **38a**, colorless micro needles, m.p. 203–204°; IR (Nujol) ν 3340, 1640 cm^{-1}; NMR ($CDCl_3$) δ 0.72 (t, J = 7 Hz, 3H), 0.88–2.30 (m, 6H), 2.70–4.08 (m, 8H), 4.48 (t, J = 7 Hz 1H), 6.9–7.7 (m, 4H), 7.87 (br, 1H, NH). (Found: C, 67.82; H, 7.18; N, 8.52. Calc for $C_{18}H_{23}N_2OCl$: C, 67.81; H, 7.27; N, 8.79%).

3 - (2 - *Chlorobutyryl*) - 7 - *oxo* - 1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4-b]*indole* (**38b**). To a soln of **38a** (4.91 g 15.4 mmol) in 850 ml 80% (v/v) aqueous THF was added 7.66 g (22.9 mmol) iodine pentoxide (I_2O_5), and the mixture was stirred at room temp for 18 hr. After removal of the solvent, the dark residue was extracted with CH_2Cl_2. The extract was successively washed with 5% sodium thiosulfate soln, $NaHCO_3$ aq, brine, and dried over Na_2SO_4. Removal of the solvent left of crystalline residue, which was recrystallized from EtOAc to furnish 3.30 g (65%) of **38b**, colorless prisms, m.p. 200–201° IR (Nujol) ν 3320, 1648, 1620 cm^{-1}; NMR ($CDCl_3$) δ 0.29 (t, J = 7 Hz, 3H), 0.7–1.1 (m, 1H), 1.1–1.9 (m, 2H), 1.9–2.3 (m, 1H), 2.3–3.2 (m, 4H), 3.2–3.7 (m, 4H), 3.7–4.3 (m, 1H), 7.0–7.9 (m, 4H), 9.32 (br, 1H, NH). (Found: C, 64.70; H, 6.24; N, 8.30. Calc for $C_{18}H_{21}N_2O_2Cl$: C, 64.96; H, 6.36; N, 8.42%).

Tetracyclic ketolactams, **39a** and **40a**. To a soln of sodium t-amyloxide (6.00 mmol) in 30 ml benzene was added a soln of **38b** (1.00 g, 3.00 mmol) in 10 ml THF, and the mixture was refluxed for 1 hr. After removal of the solvent, the residue was extracted with CH_2Cl_2, and washed, dried, and concentrated to give a yellowish foam (880 mg). The residue was purified through a column packed with silica gel, with EtOAc as eluent, to afford 780 mg (88%) of an amorphous solid of a mixture of **39a** and **40a**, m.p. 126–128°; IR ($CHCl_3$) ν 3420, 1640, 1610 cm^{-1}; UV (EtOH) λ_{max} 240, 320 nm; mass spectrum *m/e* 296 (M^+); NMR ($CDCl_3$) δ 1.04 and 1.21 (t, each, J = 7 Hz, 3H), 1.26–2.04 (m, 2H), 2.08–3.8 (m, 9H), 4.1–4.9 (m, 1H), 6.8–7.9 (m, 4H), 9.20 (br, 1H, NH). The ratio of **14a** and **15a** was determined to be **2:3** by NMR spectrum. Several recrystallizations from ether and ether-CH_2Cl_2 afforded pure **39a** as colorless pillars, m.p. 187–189° dec; NMR ($CDCl_3$) δ 1.04 (t, J = 7 Hz, 3H), 1.28 (m, 1H), 1.81 (m, 1H), 2.1–4.2 (m, 9H), 4.2–4.77 (m, 1H), 7.05–7.96 (m, 4H), 9,49 (br, 1H, NH). On the other hand, the isomer **40a** was completely epimerized to **39a** if kept in $CDCl_3$ for several days. The IR, NMR spectra and TLC behaviors of **39a** were in good agreement with those of the authentic sample provided by Prof. J. Harley-Mason.[19]

Tetracyclic lactams **39b** and **40b**. To a soln of 148 mg (0.50 mmol) of the mixture of **39a** and **39b** in 5 ml ethylene glycol was added 0.2 g KOH and 1 ml hydrazine hydrate, and the mixture was heated at 150° for 2 hr, and refluxed for 1 hr. The mixture was diluted with water, and extracted with CH_2Cl_2. The extract was washed, dried, and concentrated to afford a yellowish gum, which was separated by preparative TLC on alumina eluted with EtOAc-hexane (1:2) to provide 54 mg (38%) of **39b** and 27 mg (19%) of **40b**, respectively. **39b**: IR ($CHCl_3$) ν 3470, 1640 cm^{-1}; UV (EyOH) λ_{max} 285, 292 nm; mass spectrum *m/e* 282 (M^+); NMR ($CDCl_3$) δ 1.08 (t, J = 7 Hz, 3H), 4.38 (d–d, J = 12, 4 Hz, 1H), 6.6–7.7 (m, 4H), 8.69 (s, 1H, NH). **40b**: m.p. 226–228°C dec; IR ($CHCl_3$) ν 3470, 1640 cm^{-1}; UV (EtOH) λ_{max} 285, 292 nm; NMR ($CDCl_3$) δ 1.04 (t, J = 7 Hz, 3H), 4.1–4.5 (m, 2H), 6.8–7.7 (m, 4H). (Found: C, 76.77; H, 7.71; N, 9.86. Calc for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92%)

Tetracyclic amine **39c**. To a soln of 144 mg (0.51 mmol) of **39b** in 2 ml THF was added 20 ml 0.6 M diborane soln in THF, and the whole soln was refluxed for 1 hr. Evaporation of the solvent provided a colorless foam, which was treated with 10% HCl, and then basified with 10% NaOH aq. The separated oil was extracted with CH_2Cl_2, and washed, dried, and concentrated to afford an oily residue, which was purified by alumina preparative TLC (EtOAc: hexane = 1:2) to give 87 mg (64%) of **39c**: IR ($CHCl_3$) ν 3350, 1600 cm^{-1}; UV (EtOH) λ_{max} 284, 292 nm; mass spectrum *m/e* 268 (M^+); NMR ($CDCl_3$) δ0.96 (t, J = 7 Hz, 3H), 4.27 (m, 1H), 6.8–7.45 (m, 4H), 8.00 (s, 1H, NH).

dl-*Tubifoline* (**6**) *and* dl-*condyfoline* (**7**). Platinum oxide (500 mg) was suspended in 40 ml EtOAc, and hydrogenated under a H_2 atmosphere. A sample of **39c** 40 mg (0.15 mmol) in 4 ml EtOAc was added in the flask, and the mixture was stirred under an O_2 atmosphere for 15 min. The catalyst was removed by filtration, and the filtrate was concentrated to dryness. The residue was purified by preparative TLC on alumina (EtOAc:hexane = 1:8) to give *dl*-**6** 28 mg (70%), and *dl*-**7** 5 mg (13%) respectively. Compound **6**: IR (CCl_4) ν 1565 cm^{-1}; UV (Et_2O) λ_{max} 250 nm; mass spectrum *m/e* 266 (M^+), 223, 208, 182, 180, 163, 167, 158 135, 123, 115, 107. Compound **7**: IR (CCl_4) ν 1567 cm^{-1}; UV (Et_2O) λ_{max} 219, 250 nm; mass spectrum *m/e* 266 (M^+), 223, 208, 182, 180, 167, 158, 135, 123, 122, 121, 115, 107. The IR and UV spectra were identical with the reported values. Mass spectra of these alkaloids were in agreement with the natural products.

dl-*Tubifolidine* (**6a**). To a soln of *dl*-**6** (15 mg) in 10 ml dry ether was added LAH (59 mg), and the mixture was stirred for 2 hr. The excess hydride was decomposed with aqueous THF and 10% NaOH aq. The ppt was removed by filtration. The filtrate was dried, and concentrated to give an oily residue, which was purified by alumina preparative TLC (EtOAc:hexane = 1:3) and afforded 9 mg (60%) of *dl*-**6a** as a colorless foam: IR ($CHCl_3$) ν 1600 cm^{-1}; UV (EtOH) λ_{max} 248, 301 nm; mass spectrum *m/e* 268 (M^+), 240, 199, 144, 138, 130, 124, 110. A mass spectrum of this sample was identical with that of the natural product. The IR and UV spectra of the synthetic specimen were identical with those of the natural product.

3 - *Benzoyl* - 4 - *oxo* - 1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4-b]*indole* (**41a**). To a mixture of 2.60 g (11.4 mmol) of **16a** and 1.52 g (13.0 mmol) Et_3N in 50 ml THF was added 1.83 g (13.0 mmol) benzoyl chloride in 5 ml THF. After being stirred at room temp for 0.5 hr, the mixture was refluxed for 0.5 hr. After cooling, the ppt was removed by filtration, and washed with CH_2Cl_2. The filtrate and washings were concentrated, and the residue was chromatographed on silica gel. Elution with EtOAc–hexane (1:1) gave 2.90 g (77%) of **41a**. Recrystallization from EtOAc–hexane afforded colorless prisms: m.p. 162–163°; IR (Nujol) ν 3280, 1675 cm^{-1}; NMR ($CDCl_3$) δ 1.8–2.2 (m, 2H), 2.2–2.45 (m, 2H), 2.7–2.9 (m, 2H), 4.0–4.3 (m, 2H), 6.8–7.6 (m, 9H), 7.75 (br, 1H, NH). (Found: C, 75.87; H, 6.04; N, 8.66. Calc for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.07; N, 8.43%).

3 - *Benzoyl* - 4 - *oxo* - 8 - (2 - *tetrahydropyranyl*) - 1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4-b]*indole* (**41b**). To a soln of **41a** (2.75 g 8.28 mmol) in 20 ml CH_2Cl_2 was added 2 ml dihydropyran and 0.1 g camphor sulfonic acid, and the mixture was stirred at room temp for 8 hr.[21] Evaporation of the solvent gave a dark oil, which was purified by silica gel column chromatography, eluted with EtOAc–hexane (1:1), to afford 3.06 g (89%) of **41b**. Recrystallization from EtOAc–hexane (2:1) gave colorless pillars, m.p. 151–153°, IR (Nujol) ν 1725, 1665 cm^{-1}; mass spectrum *m/e* 416 (M^+), 332, 211, NMR ($CDCl_3$) δ 1.4–1.9 (m, 6H), 1.9–2.2 (m, 2H), 2.2–2.6 (m, 2H), 2.6–3.0 (m, 2H), 3.0–3.2 (m, 2H), 3.9–4.4 (m, 4H), 5.32 (d–d, J = 11, 2 Hz, 1H), 6.75–7.7 (m, 9H). (Found: C, 75.24; H, 6.94; N, 6.60. Calc. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73%).

3 - *Benzoyl* - 4 - *oxo* - 5 - (3 -*chloropropyl*) - 8 - (2 - *tetrahydropyranyl*) - 1,2,3,4,5,6,7,8 - *octahydroazonino*

[5,4-b]*indole* (**41c**). To a soln of diisopropylamine (3.0 ml) and HMPA (9 ml) in 30 ml DME at −78° was added dropwise 12.6 ml (190 mmol) of a 15% soln of n-BuLi in hexane. After 30 min at −78°, a soln of 3.00 g (7.20 mmol) of **41b** in 20 ml DME was added dropwise and the mixture was stirred at −78° for 1 hr under an atmospheric pressure of argon. To this soln was added 3.00 g (14.7 mmol) 1 - chloro - 3 - iodopropane in 3 ml DME, and the mixture was stirred at −70° for 14 hr. The reaction was quenched by addition of 2 ml AcOH, and diluted with 500 ml EtOAc. The organic layer was successively washed with water and $NaHCO_3$ aq, and dried over Na_2SO_4. Evaporation of the solvent afforded a yellowish oil, which was purified by silica gel chromatography. Elution with EtOAc–hexane (1:3) gave 2.51 g (71%) of **41c** as a diastereomeric mixture: IR ($CHCl_3$) ν 1675 cm^{-1}; mass spectrum *m/e* 494, 492 (M^+), 410, 408; NMR ($CDCl_3$) δ 1.1–3.88 (m, 21H), 4.02–4.57 (m, 2H), 5.13–5.47 (m, 1H), 6.92–7.79 (m, 9H).

4 - *Oxo* - 5 - (3 - *chloropropyl*) - 8 - (2 - *tetrahydropyranyl*)-1,2,3,4,5,6,7,8 - *octahydroazonino*[5,4 - b]*indole* (**41d**). To a soln of 500 mg (1.01 mmol) of **41c** in 5 ml CH_2Cl_2 was added 1 ml *n*-propylamine, and the mixture was stirred for 1 hr. After removal of the solvent, the solid residue was collected by filtration and washed with EtOAc to afford 370 mg (94%) of pure **41d**. Recrystallization from isopropanol gave colorless prisms: m.p. 180–181°; IR (Nujol) ν 3320, 1650 cm^{-1}; NMR ($CDCl_3$) δ 1.2–3.9-m, 22H), 4.1–4.4 (m, 1H), 5.15–5.5 (m, 1H), 6.40 (br, 1H, NH), 6.9–7.3 (m, 2H), 7.3–7.55 (m, 1H) 7.77–7.82 (m, 1H). (Found: C, 67.68; H, 7.66; N, 7.38. Calc for $C_{22}H_{29}N_2O_2Cl$: C, 67.94; H, 7.52; N, 7.38%).

5 - *Desethyl* - 19 - *oxo* - 1 - (2 - *tetrahydropyranyl*) *quebrachamine* **42a**. To a suspension of 75 mg (3.13 mmol) sodium hydride washed with pentane, 20 mg KI, and a catalytic amount of 18 - crown - 6 in 2 ml THF, was added 140 mg (0.360 mmol) of **41d**, and the whole mixture was heated under reflux for 1 hr. After being cooled, the excess sodium hydride was decomposed with 3 ml water, and extracted with EtOAc. After removal of the solvent, the crude residue was purified by alumina column chromatography. Elution with EtOAc–hexane (2:1) afforded 117 mg (92%) of **42a**. Recrystallization from EtOAc gave colorless prisms: m.p. 196–198°; IR (Nujol) ν 1650 cm^{-1}; NMR δ ($CDCl_3$) δ0.8–3.90 (m, 21H), 4.08–4.50 (m, 2H), 5.41 (d, J = 12 Hz, 1H), 7.00–7.9 (m, 4H). (Found: C, 74.53; H, 8.03; N, 7.99. Calc for $C_{22}H_{28}N_2O_2$: C, 74.96; H, 8.01; N, 7.95%).

19 - *Oxo* - 1 - (2 - *tetrahydropyranyl*)*quebrachamine* (**42b**). To a soln of LDA (2.88 mmol, prepared from 0.44 ml diisopropylamine and 1.92 ml of a 15% soln of n-BuLi in hexane) in 4 ml THF and 2 ml HMPA at −78°, was added dropwise a soln of 252 mg (0.716 mmol) of **41a** in 5 ml THF. After the mixture was stirred at −78° for 1 hr, 0.2 ml EtI in 0.5 ml THF was added, and the mixture stirred at −60° for 45 min. After the usual workup, the crude product was purified by silica gel chromatography. Elution with EtOAc–hexane (1:1) afforded 230 mg (84%) of **42b**, which was recrystallized from EtOAc to give colorless prisms: m.p. 176–178°; IR (Nujol) ν 1630 cm^{-1}; NMR ($CDCl_3$) δ 0.87 (t, J = 7, Hz, 3H), 1.0–3.9 (m, 22H), 4.04–4.50 (m, 2H), 5.35 (d, J = 10 Hz, 1H), 6.9–7.9 (m, 4H). (Found: C, 75.60; H, 8.56; N, 7.47. Calc for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36%).

dl - 1,2 - *Dehydroaspidospermidine* (**8**). To a suspension of 39 mg LAH in 2 ml THF was added added 39 mg (0.10 mmol) of **42b** in 1 ml THF, and the mixture was refluxed for 1 hr. After cooling, the excess reagent was decomposed with aqueous THF and 10% NaOH aq and dried over K_2CO_3. Filtration of the solid, followed by evaporation of the solvent afforded **43a** as a colorless oil, which was dissolved in 1 ml THF and treated with 0.5 ml 10% HCl for 0.5 hr. The soln was basified with 10% K_2CO_3 aq, and the separated oil was extracted with CH_2Cl_2. Evaporation of the solvent furnished a pale yellowish oil, which was purified by alumina preparative TLC (EtOAc:hexane = 1:5) to give 14 mg (48%) of **8**: IR ($CHCl_3$) ν 1610, 1575 cm^{-1}) to give 14 mg (48%) of **8**: IR($CHCl_3$) ν 1610, 1575 cm^{-1}; UV (EtOH) λ_{min} 242 nm; mass spectrum *m/e* 280 (M^+), 251, 210; NMR ($CDCl_3$) δ 0.50 (t, J = 7 Hz, 3H), 0.6 0.84 (m, 2H), 1.01 (d–t, J = 13.5, 5 Hz, 1H), 1.4–2.05 (m, 6H), 2.05–2.35 (m, 2H), 2.35–2.7 (m, 3H), 2.78 (d–q, J = 10.5, 3.5 Hz, 1H), 2.92–2.36 (m, 3H), 7.1–7.5 (m, 3H), 7.58 (d, J = 7.5 Hz, 1H). These data are in good agreement with those reported in the lit.[6]

dl - 1 - *Acetylaspidospermidine* (**9**). To a suspension of 50 mg LAH in 3 ml THF, was added a soln of 12 mg of **8** in 1 ml THF, and the mixture was stirred for 0.5 hr. After the usual workup, the crude *dl*-aspidospermidine was acetylated with 0.1 ml Ac_2O in 0.1 ml pyridine for 0.5 hr. The mixture was concentrated to dryness *in vacuo*, and the residue was purified by alumina preparative TLC (EtOAc: hexane = 1:3) to give 7 mg (64%) of **8**: IR ($CHCl_3$) ν 1645, 1600 cm^{-1}; mass spectrum *m/e* 324 (M^+), 296, 152, 124; NMR ($CDCl_3$) δ 0.65 (t, J = 7 Hz, 3H), 2.28 (s, 3H), 2.96-3.20 (m, 2H), 4.09 (d–d, J = 11, 6 Hz, 1H), 6.96–7.45 (m, 3H), 8.20 (d, J = 8 Hz, 1H). Theses spectra were identical with those of the authentic sample synthesized by us through another route.[7d]

dl-*Quebrachamine* (**10**). Lactam **42b** (65 mg) was reduced under reflux with 100 mg LAH in 3 ml dioxane for 4 hr. After standard workup, the crude residue was dissolved in 2 ml THF, and treated with 0.5 ml 10% HCl at room temp for 14 hr. The mixture was basified with 10% NaOH aq, and extracted with CH_2Cl_2. Evaporation of the solvent gave an oily residue, which was purified by alumina preparative TLC EtOAc–hexane (1:10) to give 23 mg (48%) of **10**. Recrystallization from MeOH–hexane afforded colorless prisms, m.p. 109–112° (lit. 113–116°);[8a] IR ($CHCl_3$) ν 3480, 1460 cm^{-1}; UV (EtOH) λ_{max} 230, 287, 293 nm, λ_{min} 257 nm; mass spectrum *m/e* 282 (M^+), 253, 210, 199, 157, 144, 143, 138, 125, 124, 110; NMR ($CDCl_3$) δ 0.85 (t, J = 7 Hz, 3H), 1.02–2.60 (m, 4H), 2.60–3.08 (m, 4H), 3.27 (d–t, J = 12, Hz, 1H), 7.06–7.26 (m, 2HO, 7.28–7.47 (m, 1H), 7.48–7.66 (m, 1H), 7.77 (s, 1H, NH).

21 - *Methylene* - 19 *oxo* - (*tetrahydorpyranyl*) *quebrachamine* (**42c**). To a soln of LDA (1.50 mmol) in 1 ml THF at −78° was added a soln of 176 mg (0.5 mmol) of **42a** in 2.5 ml THF. The mixture was stirred at that temp for 1 hr to generate the carbanion, and treated with 0.1 ml allyl bromide in 0.5 ml THF. After being stirred at −78° for 0.5 hr, the mixture was quenched with 0.5 ml AcOH. After the usual workup, the crude residue was chromatographed on silica gel, eluting with EtOAc–hexane (1:1) to afford 140 mg (71%) of **42c**, which was recrytallized from EtOAc to give colorless prisms: m.p. 219–220°; IR (Nujol) ν 1630 cm^{-1}; NMR ($CDCl_3$) δ 4.04–4.45 (m, 2H), 4.9–5.2 (m, 2H), 5.36 (d, J = 11 Hz, 1H), 5.58–6.07 (m, 1H), 6.9–7.84 (m, 4H). (Found: C, 76.54; H, 8.32; N, 7.26. Calc for $C_{25}H_{32}N_2O_2$: C, 76.49; H, 8.22; N, 7.14%).

21 - *Methylene* - 1,2 - *dehydroaspidospermidine* (**12**). To a suspension of 50 mg LAH in 5 ml THF was added a soln of 20 mg of **42c** in 0.5 ml THF, and the mixture was stirred at room temp for 0.5 hr. After standard workup, the crude residue was dissolved in 3 ml THF and treated with 0.5 ml 10% HCl for 0.5 hr. The soln was basified with 10% NaOH aq and the separated oil was extracted with CH_2Cl_2. The crude residue was purified by preparative TLC on alumina (EtOAc:hexane = 1:10) to give 9 mg (60%) of **12** as a colorless oil: IR ($CDCl_3$) ν 1640, 1610, 1580 cm^{-1}; UV (EtOH) λ_{max} 223, 265 nm, λ_{min} 242 nm; mass spectrum *m/e* 292 (M^+), 251, 250, 222, 194, 136, 70; NMR ($CDCl_3$) δ 0.94–3.20 (m, 17H), 4.52 (m, J = 17, 2.5, 1.0 Hz, LH), 4.80 (d–d, J = 10, 2.5 Hz, 1H), 5.43 (m, J = 17, 10, 7.2 Hz, LH), 7.0–7.65 (m, 4H). The UV, IR, NMR spectra of this sample were superimposable on those of the authentic sample kindly provided by Dr. Trojánek.

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