

STUDIES ON ARGENTINE PLANTS—XXXI* ALKALOIDS FROM *STRYCHNOS BRASILIENSIS*

I. IWATAKI† and J. COMIN

Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales,
Perú 222, Buenos Aires, Argentina

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Abstract—From the trunk bark of *Strychnos brasiliensis* (Spreng.) Mart., spermostrychnine (I) and six new indoline alkaloids have been isolated and their structures and configurations determined. They were named: 12-hydroxy-11-methoxyspermostrychnine (II), strychnobrasiline (III), 12-hydroxy-11-methoxystrychnobrasiline (IV), 10,11-dimethoxystrychnobrasiline (V), strychnosilidine (VI), and strychnosiline (VII).

STRYCHNOS BRASILIENSIS (Spreng.) Mart. is the southernmost of the American *Strychnos* species, growing in the northeast tropical forest of Argentina. It belongs to the section longiflorae.¹

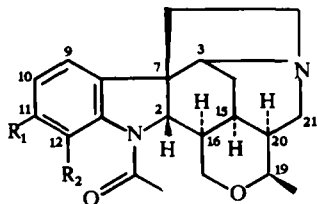
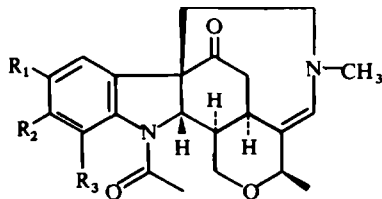
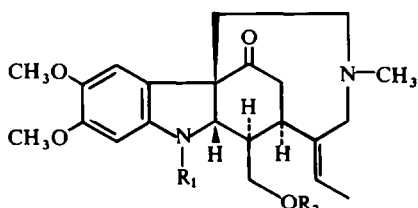
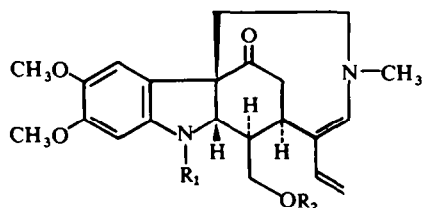
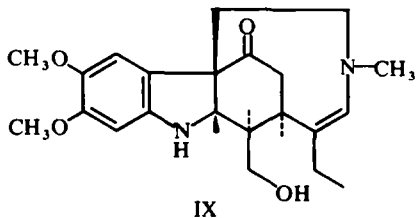
Cold water extraction of its trunk bark afforded about 1% of a complex mixture of tertiary bases from which, by chromatographic procedures, spermostrychnine² (I) and six new indoline alkaloids (II–VII) have been isolated and their structures and configurations determined. No quaternary bases were detected.

Spermostrychnine (I), m.p. 207–208°, $[\alpha]_D +83^\circ$ (CHCl₃), was identified by comparison with an authentic sample (mixed m.p., UV and IR spectra, TLC).

12-Hydroxy-11-methoxyspermostrychnine (II), C₂₂H₂₈N₂O₄, M⁺ 384, m.p. 272–273°, $[\alpha]_D -217^\circ$ (CHCl₃), shows in its mass spectrum (Table 1) the same fragmentation pattern as spermostrychnine (I) and strychnospermine³ (VIII). The UV spectrum suffers a bathochromic shift in alkaline solution, indicating the presence of a phenolic OH group. The NMR spectrum (Table 2) shows a OMe group peak and, at low field, an AB pair of doublets, indicating the presence of two vicinal aromatic protons. As the CO band of the N-Ac group is shifted from 1645 cm⁻¹ in spermostrychnine to 1630 cm⁻¹ in II, indicating H-bonding to the OH group, this has to be placed at C-12, and the OMe group at C-11, a substitution pattern confirmed by the UV spectrum.⁴ The ORD curve of II shows a positive Cotton effect between 259 and 235 nm and is very similar to the spermostrychnine curve, indicating it has the same 2β7β configuration and, accordingly, 3α15α16α20α.⁵ The β configuration (equatorial Me group) of the remaining assymmetric center (C-19) could be established by the chemical shift (δ 1.14) of the C-19 Me group doublet.⁶ The optical rotation sign is opposite to that of the unsubstituted alkaloid, a characteristic of the N-acyl-12-hydroxyindolines due to a conformational assymetry effect caused by the mentioned H-bonding.⁷ Besides, in the NMR spectrum of II, a pronounced sharpening of the

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† Present address: Nippon Soda Co., Odawara, Kanagawa, Japan.

I: $R_1 = R_2 = H$ II: $R_1 = OCH_3; R_2 = OH$ VIII: $R_1 = OCH_3; R_2 = H$ III: $R_1 = R_2 = R_3 = H$ IV: $R_1 = H; R_2 = OCH_3; R_3 = OH$ V: $R_1 = R_2 = OCH_3; R_3 = H$ VI: $R_1 = R_2 = Ac$ X: $R_1 = R_2 = H$ VII: $R_1 = R_2 = Ac$ XI: $R_1 = R_2 = H$ 

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TABLE I. MASS SPECTRA OF SPERMOSTRYCHNINE-TYPE ALKALOIDS

	M	A-42	B	C-42	D
Strychnospermine ³ (VIII)	368	160	166	174	271
	40%	20%	100%	28%	30%
Spermostrychnine (I)	338	130	166	144	241
	44%	14%	100%	54%	42%
12-Hydroxy-11-methoxy-spermostrychnine (II)	384	176	166	190	287
	100%	15%	100%	34%	53%

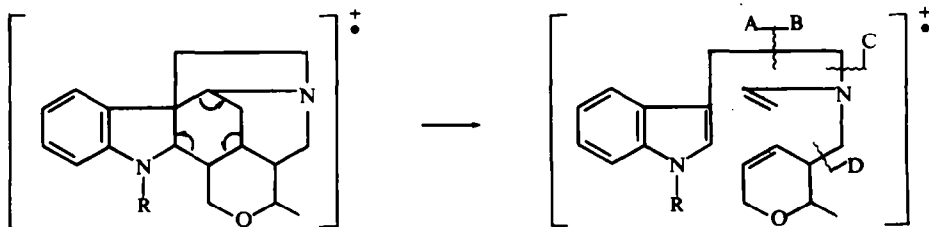


TABLE 2. NMR SPECTRA*

	H-9	H-10	H-11	H-12	H-21	H-2	OCH ₃	COCH ₃ N	COCH ₃ O	NCH ₃	CCH ₃
Spermostrychnine (I)	—	7.9 to 7.0 m	—	—	—	—	—	2.38 s	—	—	1.15 d J = 7.0
12-Hydroxy-11-methoxy- spermostrychnine (II)	6.75 d J = 8.0	6.53 d J = 8.0	—	—	—	4.50 d J = 9.0	3.87 s	2.46 s	—	—	1.14 d J = 7.0
Strychnobrasiline (III)	—	7.9 to 7.0 m	—	—	6.06 s	—	—	2.35 s	—	2.22 s	1.37 d J = 6.2
12-Hydroxy-11-methoxy- strychnobrasiline (IV)	7.00 d J = 8.0	6.71 d J = 8.0	—	—	6.03 s	4.64 d J = 11.0	3.87 s	2.40 s	—	2.22 s	1.35 d J = 6.2
10,11-Dimethoxy- strychnobrasiline (V)	7.09 s	—	—	7.6 s	6.00 s	—	3.86 s 3.87 s	2.32 s	—	2.22 s	1.37 d J = 6.1
Strychnosilidime (VI)	7.02 s	—	—	6.73 s	—	—	3.86 s 3.88 s	2.33 s	2.02 s	1.96 s	1.60 d J = 7.0
Strychnosiline (VII)	7.15 s	—	—	6.75 s	6.20 s	—	3.86 s 3.86 s	2.39 s	2.15 s	2.06 s	—

* Chemical shifts in δ units; coupling constants in Hz.

H-2 signal in comparison with the unsubstituted base is apparent, an effect also due to the fixation of the acetyl group by H-bonding to the C-12 OH group, and similar to the one found by Anet in the NMR spectrum of strychnospermine (VIII) by lowering (or rising) the temperature.⁸

Strychnobrasiline (III), $C_{22}H_{26}N_2O_3$, M^+ 366, m.p. 205–207°, $[\alpha]_D +156^\circ$ ($CHCl_3$), has an UV spectrum indicative of an N-acyl-indoline chromophore, confirmed by its change on deacetylation. The IR spectrum shows two bands in the 1600 cm^{-1} region: one at 1590 cm^{-1} due to the aromatic ring, and another at 1660 cm^{-1} due to the superposition of the absorptions of the N_a -Ac group and of the C-3 CO group, involved in transannular interaction with the N_b . In deacetylstrychnobrasiline this band is reduced to half intensity, and disappears altogether in its perchlorate, showing the formation of a carbinolamine-type salt, as, e.g. in N-methylpseudostrychnine.⁹ In the NMR spectrum of III (Table 2), the signals due to the N_b Me group and the Ac group, as well as to the four aromatic protons, are easily assigned. The doublet at δ 1.39 is identical, except a slight downfield shift, to the signal given by the C-19 Me group in the spermostrychnine-type alkaloids,^{6,8} thus allowing the formulation of ring D as a 6-membered cyclic ether. The slightly broadened singlet at δ 6.03 could be assigned to H-21 placing a double bond between C-20 and C-21. This olefinic proton is further deshielded by a supra-annular effect between the double bond and the C-3 CO group,¹⁰ and by the adjacent N_b , whose electron pair is engaged in transannular interaction with the same CO group, therefore exerting on H-21 only an exalted inductive effect, not balanced by an opposite mesomeric one. In "normal" enamines the corresponding signal appears at about δ 4.40;¹¹ in neostrychnine, where the mesomeric effect of the N_b is prohibited by the Bredt rule, it appears at δ 5.75.

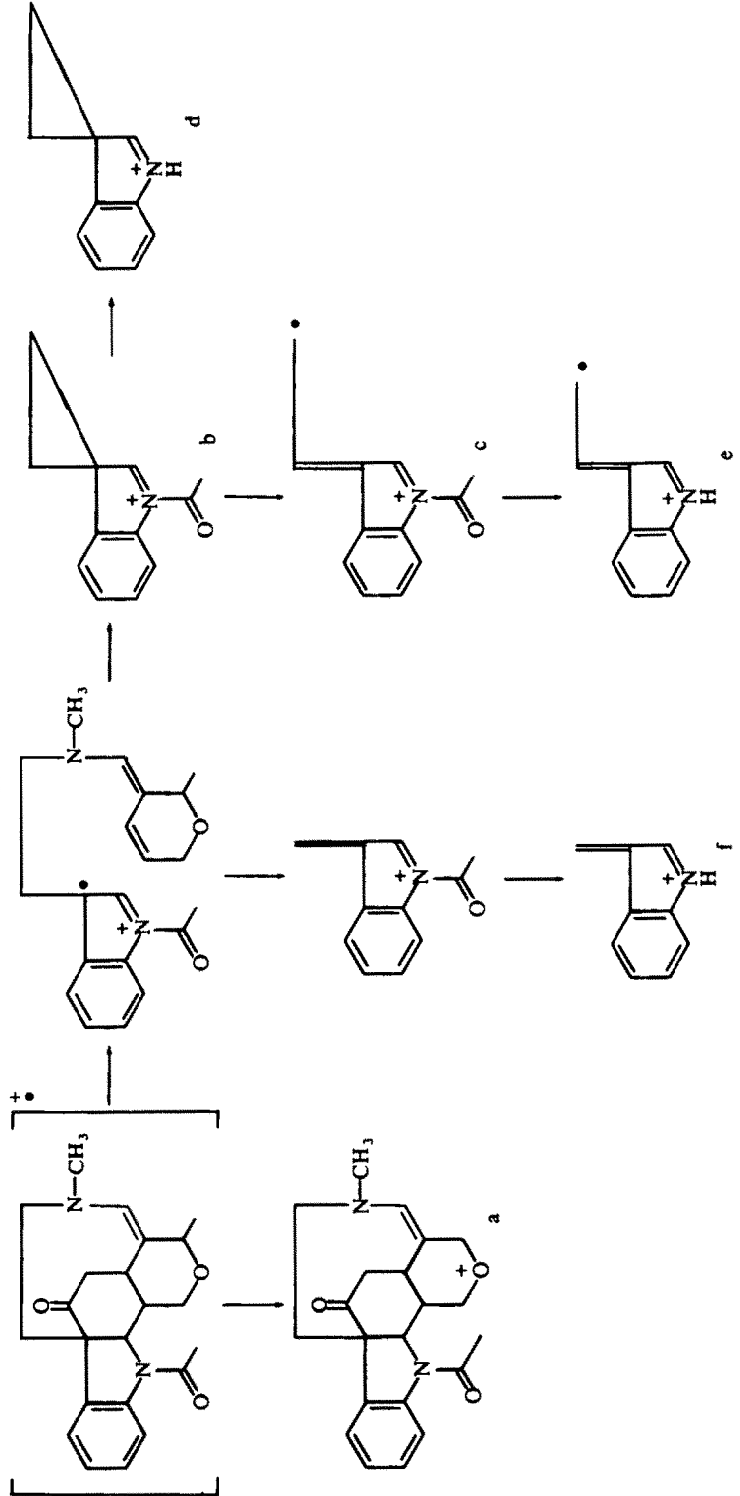
All the important peaks in the mass spectrum of strychnobrasiline (Table 3) can be rationalized from the proposed structure on the basis of known or plausible fragmentation patterns (a–p) (Schemes 1 and 2). Even more relevant are the similarities and differences with the isosplendine mass spectrum.¹² All the indoline-containing fragments (a–f) are present in similar intensities in both spectra, and the same happens with the alicyclic fragments that do not involve in their formation, directly or indirectly, the original 20–21 double bond (g–h). Instead, fragments i–p, whose relative stability depends on the presence of the double bond, appear only in the strychnobrasiline spectrum, whereas fragments q–x (Scheme 3), which involve the rupture of the 20–21 single bond or the separation of an H atom from the C-20 of isosplendine, have no counterpart in the strychnobrasiline spectrum.

12-Hydroxy-11-methoxystrychnobrasiline (IV), $C_{23}H_{28}N_2O_5$, M^+ 412, m.p. 229–230°, $[\alpha]_D -31^\circ$ ($CHCl_3$), has a mass spectrum equivalent to that of strychnobrasiline (Table 3), indicating the presence of the same basic skeleton. This is apparent also from the NMR spectrum (Table 2), that has the same features in both alkaloids. The nature and position of the substituents could also be deduced from spectral data. The bathochromic shift of the UV spectrum in alkaline solution detected the presence of a phenolic OH group, which could be placed at C-12 on account of the IR band of the N_a -acetyl CO group, which appears at 1630 cm^{-1} , due to intramolecular H-bonding. The singlet at δ 3.87 in the NMR spectrum of IV determined the presence of an OMe group, which, considering the UV spectrum and the AB system given by the aromatic protons, could be placed at C-11. The same effect

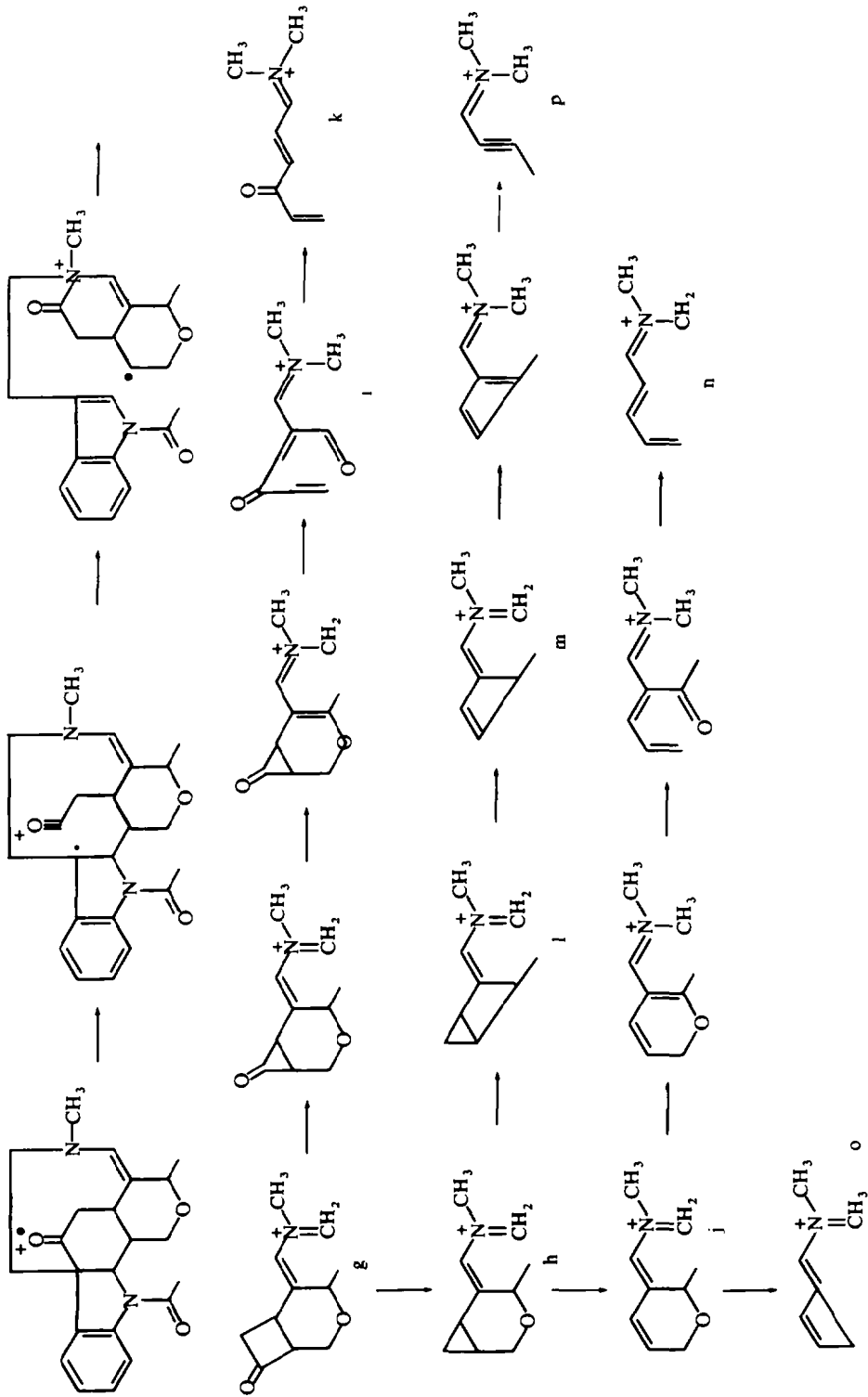
TABLE 3. MASS SPECTRA OF STRYCHNOBRASILINE-TYPE ALKALOIDS

	M	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r	s	t	u	v	x
Strychnobrasiline (III)	366	351	186	185	144	143	130	194	166	180	152	138	136	122	110	108	96							
12-Hydroxy-11-methoxystrychnobrasiline (IV)	412	397	232	231	190	189	176	194	166	180	152	138	136	122	110	108	96							
10,11-Dimethoxystrychnobrasiline (V)	426	411	246	245	204	203	190	194	166	180	152	138	136	122	110	108	96							
Isopiptendac ¹²	368	353	186	185	144	143	130	196	168	180	152	138	136	122	110	108	96	308	297	295	267	255	229	225
	44%	5%	33%	32%	100%	40%	30%	12%	15%									13%	21%	43%	22%	14%	16%	10%

SCHEME 1



SCHEME 2



observed in the NMR spectrum of 12-hydroxy-11-methoxyspermostrychnine, namely the sharpening of the H-2 signal, is apparent in the spectrum of this base.

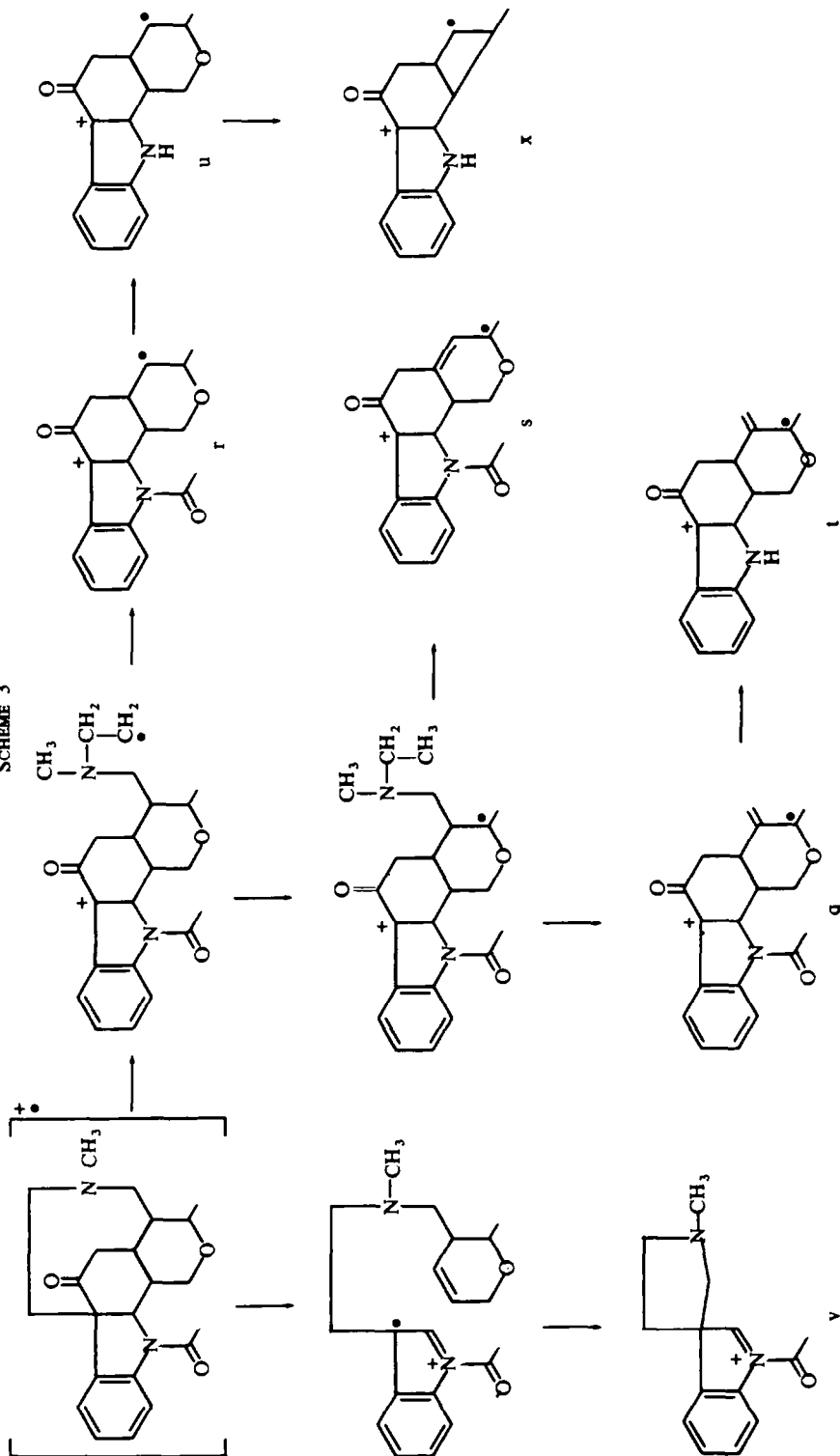
The structure of 10,11-dimethoxystrychnobrasiline (V), M^+ 426, m.p. 168–175°, $[\alpha]_D +148^\circ$ (CHCl_3), was also determined by UV, IR, NMR and mass spectral evidence (Tables 2 and 3). The position of the two OMe groups was confirmed by the NMR spectrum of the deacetyldihydro derivative IX (v.i.), in which the singlets due to H-9 and H-12 are sharp and clearly visible, not being broadened in this case by imperfect averaging of the CO group anisotropy brought about by restricted rotation of the N_a -Ac group, as it happens in the alkaloid itself and in strychnospermine.⁸

The positive main Cotton effect in the 285–250 nm region of the ORD curves of the closely related alkaloids III, IV and V, established its configuration as $2\beta 7\beta 15\alpha 16\alpha$.⁴ The C-19 configuration is independent of the other four asymmetric centres, and could be determined by measuring the N.O.E. between the C-19 Me group and the C-21 olefinic proton in IV, which is around +25%. This implies the coplanarity of both groups and, therefore, a C-19 β configuration, with an equatorial Me group. The C-19 configuration of the other two alkaloids was also established as β on account of the identical chemical shift of the Me group attached to it.⁶

An interesting feature of this group of alkaloids is the peculiar non-reactivity of the 20–21 “neo” double bond. It does not undergo any of the typical reactions of the neostrychnine double bond, from which it differs in having an allylic ether group: treatment with bromine water,¹³ nitrous acid,¹⁴ or perbenzoic acid¹⁵ gave intractable products. Intended reduction with diimide led to the recovery of starting material. Hydrogenation with different catalysts under various conditions resulted always in one or more hydrogenolysis products, as did treatment with zinc and hydrochloric acid. In the case of 10,11-dimethoxystrychnobrasiline (V) for instance, hydrogenation with 5% Pd on charcoal in 1N HCl did not reduce the double bond, producing instead hydrogenolysis of the ether linkage and hydrolysis of the N-Ac group, giving a deacetyldihydro derivative (IX), $C_{22}H_{30}N_2O_4$, M^+ 386, m.p. 250–251°, in whose NMR spectrum the C-19 Me group appears as a triplet at higher field. This lack of reactivity of the 20–21 double bond is probably due to a low π electron density in it, originated by the effects mentioned in explaining the low field position of the H-21 signal, namely a non-compensated inductive effect of N_b , and a supra-annular effect between its π -orbitals and the electrophilic C-3 CO carbon atom, which is in the appropriate position for such an interaction to occur.¹⁰

Strychnosilidine (VI), $C_{26}H_{34}N_2O_6$, M^+ 470, m.p. 236–237°, $[\alpha]_D +233^\circ$ (CHCl_3), has an UV spectrum very similar to that of 10,11-dimethoxystrychnobrasiline (V), pointing to an identical chromophoric system. This is confirmed by its NMR spectrum (Table 2), in which two OMe group signals and two aromatic proton singlets are clearly visible. The following differences with the NMR spectrum of V are noticeable: the low field singlet of the H-21 olefinic proton is absent, indicating there is no double bond between C-20 and C-21; the doublet of the C-19 Me group is shifted to δ 1.60 ($J = 7$ Hz) and somewhat broadened by long range coupling, indicating it must be attached to a disubstituted double bond between C-19 and C-20; there is a third Me group singlet at δ 1.96, that a band at 1740 cm^{-1} in the IR spectrum indicates as due to an O-Ac group. In the mass spectrum the prominent peaks are, besides those due to the indoline-containing fragments, the M-43 and M-59, produced by fragmentation of the O-Ac group. Hydrolysis of strychnosilidine gives a dideacetyl

SCHEME 3



derivative (X) in whose IR spectrum the 1740 cm^{-1} band has disappeared. The positive Cotton effect at 284–252 nm shows that the alkaloid has a $2\beta 7\beta$ configuration and, therefore, 15α . The configuration of C-16 is not linked, as in the other alkaloids, to that of the other assymmetric centres, and must be determined independently. Dideacetyl strychnosilidine (X) does not form a 6-membered isopropyliden derivative between N_8 and the alcoholic OH group, thus affording good evidence that C-16 has an α configuration, identical to that of the other alkaloids of this plant and opposite to that of geissoschizoline, where such derivatives are easily formed.¹⁶

Strychnosiline (VII), was obtained as a non-crystalline powder whose homogeneity was shown by TLC, $M^+ 468$, $[\alpha]_D +35^\circ$ (CHCl_3); on acid hydrolysis a crystalline dideacetyl derivative is obtained (XI), $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4$, $M^+ 384$, m.p. 199–201°, which on acetylation gives back the original alkaloid. UV and IR spectral data point to the same basic skeleton as strychnosilidine (VI). The NMR spectrum of VII shows no signal that could be attributed to a Me group at C-19, and the olefinic region shows, besides the H-21 proton signal, an ABX system typical of a vinyl group (δ_A 5.20, δ_B 5.51, δ_X 6.50; $J_{AX} = 17\text{ Hz}$, $J_{BX} = 11\text{ Hz}$, $J_{AB} = 1\text{ Hz}$), indicating the presence of a conjugated double bond system between C-18 and C-21. The proposed structure could be confirmed by hydrogenation of the dideacetyl derivative, when only the 18–19 double bond is reduced, the other being non-reactive as in the strychnobrasilines, and the resulting product, m.p. 250–251°, was identified as deacetyldihydro-10,11-dimethoxystrychnobrasiline (IX). The positive Cotton effect at 285–253 nm and the identity of the above two derivatives allows also to state the configuration of the alkaloid as $2\beta 7\beta 15\alpha 16\alpha$.

Alkaloids containing the hexahydropyran ring between C-15 and C-20, like bases I–V, have been found up to now in three *Strychnos* species: one Australian (*S. psilosperma*¹⁷), one African (*S. splendens*¹²) and the present American one. It is perhaps worth noting that *S. brasiliensis* is the first American species in which tertiary bases with a skeleton different from the diaboline one have been found. This could be interpreted as a further link between the several dispersion areas of the genus, but, if the absence of quaternary bases and of diaboline-type alkaloids is also taken into account, it could cast some doubts about the real geographical origin of this species.

EXPERIMENTAL

M.p.s are uncorrected. NMR spectra were determined at 60 MHz in CDCl_3 soln, with TMS as internal standard. TLC on SiO_2 and CH_2Cl_2 –MeOH 94:6 (A) and CHCl_3 –MeOH– Me_2CO 17:2:1 (B) as solvent systems; R_f values are given relative to strychnine (R_s).

Extraction and fractionation of bases

The trunk bark of *Strychnos brasiliensis* collected in January 1967 near Puerto Iguazú, Misiones, Argentina, was dried and ground. A 1.0 kg sample was percolated with 6.0 l water at room temp, and the aq soln made alkaline with conc NH_3 and extracted with CHCl_3 . The extract was dried and concentrated *in vacuo* to dryness, giving 9.7 g of a pale brown residue, which was dissolved in CHCl_3 and filtered. The clear soln was extracted first with 0.7N NaOH (Extract 1) and then with 1N HCl. The acid soln was made alkaline with conc NH_3 and extracted with Et_2O (Extract 2) and then with CHCl_3 (Extract 3).

Extract 1. The soln was acidified with 1N HCl, basified again with conc NH_3 and extracted with CHCl_3 . The extract was dried and concentrated, affording 1.0 g of a crystalline residue. It was dissolved in CHCl_3 and chromatographed on SiO_2 ; elution with CHCl_3 –MeOH 94:6 gave two main crystalline fractions: E1-1 (600 mg) and E1-2 (160 mg).

Extract 2. The ether soln was concentrated, yielding a residue (2.6 g) that was dissolved in CHCl_3 and chromatographed on SiO_2 , eluting with CHCl_3 -MeOH 96:4. Five main fractions were obtained: E2-1 (840 mg), E2-2 (500 mg), E2-3 (360 mg), E2-4 (225 mg) and E2-5 (90 mg).

Extract 3. The CHCl_3 soln was concentrated, and the residue (3.8 g) was dissolved in CHCl_3 and chromatographed on SiO_2 , eluting with CHCl_3 -MeOH 94:6 (fractions E3-1 to E3-4), 88:12 (E3-5 to E3-6) and 80:20 (E3-7 to E3-9).

Spermostrychnine (I)

Fraction E2-5 was recrystallized from Et_2O -AcOEt, affording needles, m.p. 207–208° (lit.¹⁷ 208–209°), no depression on admixture with an authentic sample; $[\alpha]_D^{25} + 83^\circ$ ($c = 0.55$, CHCl_3) (lit.¹⁷ $[\alpha]_D + 88^\circ$ (CHCl_3)); $[\phi]_{264\text{nm}}^{\text{EtOH}} + 50,400^\circ$, $[\phi]_{236\text{nm}}^{\text{EtOH}} - 89,900^\circ$; UV and IR spectra: coincident with those of an authentic sample; NMR spectrum, Table 2; mass spectrum, Table 1. R_f 0.74 (A), 0.68 (B), coincident with an authentic sample.

12-Hydroxy-11-methoxyspermostrychnine (II)

Fraction E1-2 was recrystallized from EtOH as small plates, m.p. 272–273°. $[\alpha]_D^{25} - 217^\circ$ ($c = 0.58$, CHCl_3); $[\phi]_{259\text{nm}}^{\text{EtOH}} + 10,100^\circ$; $[\phi]_{233\text{nm}}^{\text{EtOH}} - 82,700^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 225, 255, 290 nm ($\log \epsilon$ 4.36, 3.77, 2.88); $\lambda_{\text{max}}^{\text{EtOH-NaOH}}$ 235 (sh), 305 nm ($\log \epsilon$ 4.60, 3.90); $\nu_{\text{max}}^{\text{CHCl}_3}$ 1640, 1600 (sh), 1580 cm^{-1} ; NMR spectrum, Table 2; mass spectrum, Table 1. R_f 0.74 (A), 0.68 (B). (Found: C, 68.03; H, 7.56; N, 7.03. $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ requires: C, 67.78; H, 7.83; N, 7.19%.)

Methiodide. To a soln of the above base (60 mg) in 5 ml Me_2CO , an excess MeI was added and the whole refluxed for 24 hr. The ppt formed was filtered and recrystallized from Me_2CO , m.p. 289–291°. $\nu_{\text{max}}^{\text{Nujol}}$ 1630, 1590 cm^{-1} . (Found: C, 52.39; H, 5.84; N, 5.16; I, 24.16. $\text{C}_{23}\text{H}_{31}\text{N}_2\text{O}_4\text{I}$ requires: C, 52.48; H, 5.94; N, 5.33; I, 24.14%.)

Strychnobrasiline (III)

Fraction E2-3, on recrystallization from Et_2O , melted at 205–208°, $[\alpha]_D^{26} + 156^\circ$ ($c = 0.91$, CHCl_3); $[\phi]_{280\text{nm}}^{\text{EtOH}} + 43,300^\circ$, $[\phi]_{250\text{nm}}^{\text{EtOH}} - 102,000^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 247, 277 (sh), 285 (sh) nm ($\log \epsilon$ 4.15, 3.50, 3.43); $\nu_{\text{max}}^{\text{Nujol}}$ 1660, 1590 cm^{-1} ; NMR spectrum, Table 2; N.O.E. between δ 1.37 and 6.06: +25%; mass spectrum, Table 3. R_f 0.80 (A), 0.83 (B). (Found: C, 72.16; H, 7.27; N, 7.72. $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_3$ requires: C, 72.13; H, 7.10; N, 7.65%.)

Deacetylstrychnobrasiline. A soln of 40 mg of strychnobrasiline in 1.5 ml EtOH containing 100 mg KOH and 0.5 ml water was refluxed in a N_2 atmosphere for 8 hr. After working up and recrystallization from AcOEt–light petroleum, 22 mg of colourless needles were obtained, m.p. 243–244°, $[\alpha]_D^{25} + 105^\circ$ ($c = 0.85$, CHCl_3); $\lambda_{\text{max}}^{\text{EtOH}}$ 238, 302 nm ($\log \epsilon$ 3.95, 3.46); $\nu_{\text{max}}^{\text{Nujol}}$ 3250, 1650, 1590 cm^{-1} ; $\delta_{\text{ppm}}^{\text{CDCl}_3}$ 5.88 (1H, s, H-21), 2.21 (3H, s, $\text{N}_6\text{-CH}_3$), 1.33 (3H, d, $J = 6$ Hz, C-19- CH_3). R_f 0.60 (A), 0.58 (B). (Found: C, 73.82; H, 7.45; N, 8.41. $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2$ requires: C, 74.07; H, 7.41; N, 8.64%). Its perchlorate recrystallizes from MeOH, m.p. 110–114° (dec). $\nu_{\text{max}}^{\text{Nujol}}$ 1590 cm^{-1} .

12-Hydroxy-11-methoxystrychnobrasiline (IV)

Fraction E1-1 was recrystallized from MeOH, giving needles, m.p. 229–230°, $[\alpha]_D^{18} - 31^\circ$ ($c = 0.57$, CHCl_3); $[\phi]_{284\text{nm}}^{\text{EtOH}} + 10,100^\circ$, $[\phi]_{250\text{nm}}^{\text{EtOH}} - 97,200^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 227, 263 (sh), 290 (sh) nm ($\log \epsilon$ 4.65, 3.50, 3.40); $\lambda_{\text{max}}^{\text{EtOH-NaOH}}$ 235 (sh), 306 nm ($\log \epsilon$ 4.36, 4.30); $\nu_{\text{max}}^{\text{Nujol}}$ 1660, 1630, 1575 cm^{-1} ; NMR spectrum, Table 2; mass spectrum, Table 3. R_f 1.10 (A), 1.08 (B). (Found: C, 66.80; H, 6.71; N, 6.98. $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_5$ requires: C, 66.97; H, 6.84; N, 6.79%.)

10,11-Dimethoxystrychnobrasiline (V)

Fraction E3-3 (258 mg) was recrystallized from AcOEt and then from EtOH, affording small plates, m.p. 168–175°, $[\alpha]_D^{20} + 148^\circ$ ($c = 0.61$, CHCl_3); $[\phi]_{286\text{nm}}^{\text{EtOH}} + 48,000^\circ$, $[\phi]_{258\text{nm}}^{\text{EtOH}} - 89,000^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 217, 258, 297 nm ($\log \epsilon$ 4.47, 4.10, 3.67); $\nu_{\text{max}}^{\text{Nujol}}$ 1640, 1600 (sh) cm^{-1} ; NMR spectrum, Table 2; mass spectrum, Table 3. R_f 0.70 (A), 0.75 (B).

Deacetyldihydro-10,11-dimethoxystrychnobrasiline (IX). To a soln of 40 mg of V in 6 ml 1N HCl, 100 mg of 10% Pd/C was added and the mixture hydrogenated at room temp and atmospheric press for 20 hr. Filtration of the catalyst and work up of the soln gave a residue that recrystallized from Me_2CO and then from EtOH melted at 250–251°. $\nu_{\text{max}}^{\text{Nujol}}$ 3250, 1620 cm^{-1} ; $\delta_{\text{ppm}}^{\text{CDCl}_3}$ 7.23 (1H, s, H-9), 6.48 (1H, s, H-12), 5.94 (1H, s, H-21), 3.90 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 2.06 (3H, s, NCH_3), 1.02 (3H, t, $J = 7$ Hz, C-19, CH_3); mass spectrum: m/e 386 (M^+), 361, 204, 152, 138, 124 (100%), 122, 112, 110. R_f 0.40 (A), 0.33 (B). (Found: C, 68.22; H, 7.83; N, 7.41. $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_4$ requires: C, 68.37; H, 7.82; N, 7.25%.)

Strychnosilidine (VI)

The residue from fractions E3-8 and E3-9 (360 mg) was recrystallized from AcOEt as colourless needles, m.p. 236–237°, $[\alpha]_D^{25} + 233^\circ$ ($c = 0.63$, CHCl_3); $[\phi]_{284\text{nm}}^{\text{EtOH}} + 51,700^\circ$, $[\phi]_{252\text{nm}}^{\text{EtOH}} - 91,200^\circ$ (sh); $\lambda_{\text{max}}^{\text{EtOH}}$ 214, 260, 290 nm ($\log \epsilon$ 4.50, 4.14, 3.92); $\nu_{\text{max}}^{\text{Nujol}}$ 1740, 1640, 1600 cm^{-1} ; NMR spectrum, Table 2; mass spectrum: m/e 470 (M^+), 455, 427, 411, 204, 190. R_f 0.60 (A), 0.50 (B). (Found: C, 66.40; H, 7.20; N, 6.31. $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_6$ requires: C, 66.38; H, 7.23; N, 5.96%.)

Dideacetylstrychnosilidine (X). A soln of 64 mg of strychnosilidine in 7 ml 4% methanolic HCl was left at room temp for 17 hr. After working up, 40 mg of an oil, homogeneous on TLC, was obtained; $\nu_{\text{max}}^{\text{Nujol}}$ 3300, 1650, 1610 cm^{-1} ; $\delta_{\text{ppm}}^{\text{CDCl}_3}$ 6.92 (1H, s, H-9), 6.30 (1H, s, H-12), 3.78 (6H, s, OCH_3), 1.93 (3H, s, NCH_3), 1.60 (3H, d, $J = 7$ Hz, C-19, CH_3). On acetylation it gives back strychnosilidine, identified by TLC, m.p. and I.R. It yields a hydrochloride, which recrystallized from Me_2CO melts at 251–252° (dec). (Found: C, 54.35; H, 7.26; N, 5.72; Cl 14.69. $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_4 \cdot 2\text{HCl} \cdot \frac{3}{2}\text{H}_2\text{O}$ requires: C, 54.32; H, 7.20; N, 5.97; Cl, 14.61%.)

Strychnosiline (VII)

A 300 mg portion of fraction E2-1 was further purified by preparative TLC using system (B). The second band from the top was separated and eluted with CHCl_3 –MeOH 1:1, yielding 113 mg of a powder, homogeneous on TLC but not amenable to crystallization, $[\alpha]_D^{20} + 35^\circ$ ($c = 0.82$, CHCl_3); $[\phi]_{285\text{nm}}^{\text{EtOH}} + 34,400^\circ$, $[\phi]_{253\text{nm}}^{\text{EtOH}} - 91,000^\circ$; $\lambda_{\text{max}}^{\text{EtOH}}$ 217, 256, 299 nm ($\log \epsilon$ 4.47, 3.82, 3.37); $\nu_{\text{max}}^{\text{CHCl}_3}$ 1730, 1640 cm^{-1} ; NMR spectrum, Table 2; mass spectrum: m/e 468 (M^+), 453 (100%), 381, 351, 221, 204, 192, 190, 120, 108. R_f 1.20 (A), 1.33 (B).

Dideacetylstrychnosiline (XI). A soln of 210 mg of strychnosiline in 10 ml 2N H_2SO_4 was kept at 60° for 17 hr. On working up and recrystallization from AcOEt, 167 mg of needles, m.p. 199–200°, were obtained; $\lambda_{\text{max}}^{\text{EtOH}}$ 211, 238 (sh), 311 nm ($\log \epsilon$ 4.60, 4.28, 3.89); $\nu_{\text{max}}^{\text{Nujol}}$ 3430, 3300, 1650, 1630, 1600 cm^{-1} ; $\delta_{\text{ppm}}^{\text{CDCl}_3}$ 7.22 (1H, s, H-9), 6.42 (1H, s, H-12), 6.21 (1H, s, H-21), 3.88 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 2.10 (3H, s, NCH_3); mass spectrum: m/e 384 (M^+), 369, 233, 217, 204, 190, 150, 122, 120, 110, 108. R_f 0.70 (A), 0.75 (B). (Found: C, 68.89; H, 7.30; N, 7.12. $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4$ requires: C, 68.75; H, 7.29; N, 7.29%.) On acetylation it gives back strychnosiline, identified by TLC and IR.

Hydrogenation of dideacetylstrychnosiline. To a soln of 30 mg of XI in 10 ml 1N HCl, 90 mg of 10% Pd/C was added, and the whole hydrogenated at room temp and atmospheric press for 6 hr. Filtration of the catalyst and work up of the soln afforded a residue that on recrystallization from Me_2CO and then from EtOH, melted at 250–251°. no depression on admixture with IX; IR spectrum and R_f values coincident with those of IX.

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