Studies on Proaporphine and Aporphine Alkaloids. Part VII.[1] Stereochemistry of Reduced Proaporphines of *Croton sparsiflorus* and *C. linearis* †

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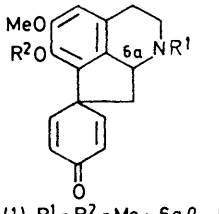
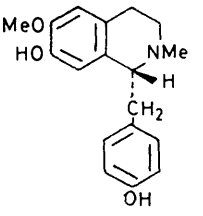
Three new alkaloids, isocrotsparinine (19a), its *N*-methyl derivative (19b), and (±)-tetraidroglaziovine (12), have been isolated from *Croton spariflorus* Morong; the stereochemistry of crotsparinine and isocrotsparinine has been defined as (6a*R*,7a*S*) and (6a*S*,7a*S*), respectively, thus pointing out the stereospecificity of the reduction of the enantiomers of crotsparine (2) during the biogenetic process. Jacularine and base E, two alkaloids of *C. linearis* Jacq., were assigned the steric formulae (20) and (21), respectively.

THE essential correlation for the absolute configuration of the C-6a asymmetric centre in proaporphine alkaloids was established by Cava *et al.*,[2] who cleaved pronuciferine (1) to give (*R*)-armepavine (6). The synthesis [1] of the diastereoisomeric (±)-8,9- and (±)-11,12-dihydroglaziovine [(7) and (8) respectively; one enantiomer shown in each case] and the *X*-ray diffraction study [3] of the hydrobromide of the latter have now provided a firm basis for studying the configuration of the reduced proaporphines having an additional asymmetric centre at C-7a, as shown for the case of amuronine in the preceding paper.[1] The stereochemistry of some reduced proaporphines of *Croton sparsiflorus* Morong and *Croton linearis* Jacq. (Euphorbiaceae) is discussed here. Bhakuni *et al.*[4] isolated the dihydronorproaporphine crotsparinine (9) and its *N*-methyl derivative (10) from *C. sparsiflorus*, along with crotsparine (crotoflorine [5]) (2) and *N*-methylcrotsparine [(−)-glaziovine [6]] (5). While reinvestigating the alkaloids of this plant in order to ascertain the configuration of (9) and (10) at C-7a, we have made some additional interesting observations.

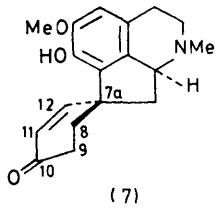
The most abundant alkaloid in the extract, crotsparine (2), was identical (t.l.c., i.r. spectrum in chloroform) with the (+)-enantiomer (3), $[\alpha]_D$ +135°, which we had isolated [7] from *Ocotea glaziovii* Mez, but showed $[\alpha]_D$ −32°; compound (2) occurs therefore as a mixture of the (±)- and (−)-forms, a situation already encountered [6] with glaziovine in *O. glaziovii*. Bhakuni and Dhar [4] reported $[\alpha]_D$ −30°, but indicated that the alkaloid was dextro- or laevo-rotatory depending on the geographical origin of the plant. After conversion of the remaining crotsparine into sparsiflorine (18),[8] an aporphine which is present in small amounts as a genuine alkaloid of the plant, by acid-catalysed dienone–phenol rearrangement, the other



(1) $R^1 = R^2 = Me$; 6aβ-H
(2) $R^1 = R^2 = H$
(3) $R^1 = R^2 = H$; 6aα-H
(4) $R^1 = CF_3{\cdot}CO$, $R^2 = H$; 6aβ-H
(5) $R^1 = Me$, $R^2 = H$; 6aα-H



(6)



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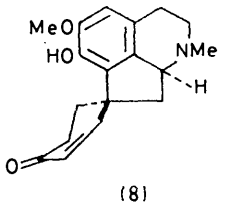
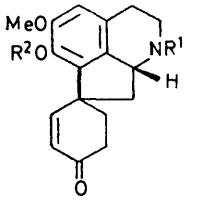
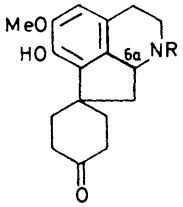


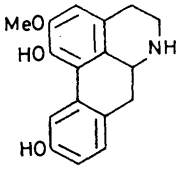
(8)



(9) $R^1 = R^2 = H$
(10) $R^1 = Me$, $R^2 = H$
(11) $R^1 = R^2 = Ac$



(12) R = Me
(13) R = Me; 6aα-H
(14) $R = CF_3CO$; 6aβ-H
(15) $R = CF_3CO$; 6aα-H



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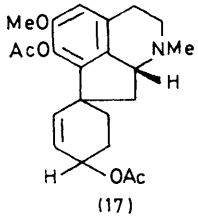


(17)

† Presented at the 167th meeting of the American Chemical Society, Los Angeles, April 1—5, 1974.

[1] Part VI, C. Casagrande, L. Canonica, and G. Severini-Ricca, preceding paper.

[2] M. P. Cava, K. Nomura, S. K. Talapatra, M. J. Mitchell, R. H. Schlessinger, K. T. Buch, J. L. Beal, B. Douglas, R. F. Raffauf, and J. A. Weisbach, *J. Org. Chem.*, 1968, **33**, 2785.

[3] A. Colombo, in preparation.

[4] D. S. Bhakuni and M. M. Dhar, *Experientia*, 1968, **24**, 10; 1969, **25**, 354; D. S. Bhakuni, S. Satish, and M. M. Dhar, *Phytochemistry*, 1970, **9**, 2573; *Tetrahedron*, 1972, **28**, 4579.

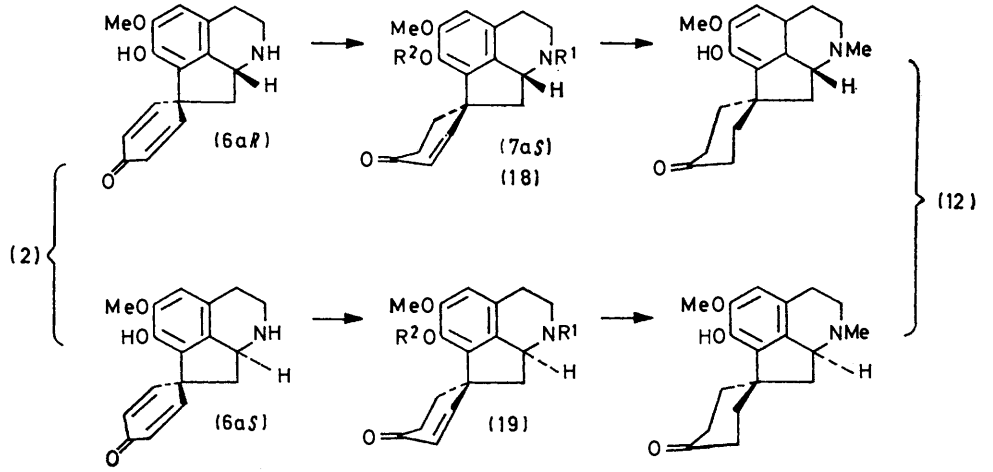
[5] A. Chatterjee and P. L. Majunder, *J. Indian Chem. Soc.*, 1968, **45**, 1087 (*Chem. Abs.*, 1969, **70**, 88,018r).

[6] G. Ferrari and C. Casagrande, *Il Farmaco, ed. Sci.*, 1970, **25**, 449.

[7] C. Casagrande and G. Ferrari, *Il Farmaco, ed. Sci.*, 1975, **30**, 479.

[8] A. Chatterjee, P. L. Majunder, R. Mukherjee, S. K. Saha, and S. K. Talapatra, *Tetrahedron Letters*, 1965, 1539.

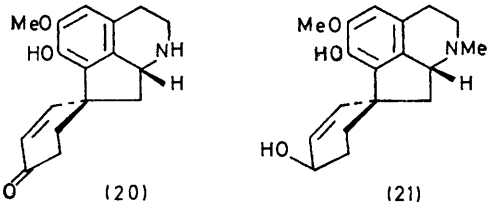
alkaloids were submitted to a preliminary chromatographic separation; this gave tetrahydroglaziovine (12) [1] in nearly racemic form, $[\alpha]_D$ +2°, as a new natural product, and revealed the presence of two pairs of very similar alkaloids. The t.l.c. behaviour of the first pair, present in trace amounts, was identical with that of (±)-8,9- and -11,12-dihydroglaziovine, (7) and (8); indeed, Eschweiler-Clarke methylation of the second, more abundant pair gave two tertiary bases which were separated by chromatography and shown to be, respectively, identical, apart from optical rotation, with the synthetic compounds (7) and (8); the characteristics of the compound eluted first, corresponding to (7), were in agreement with those reported for *N*-methylcrotsparinine



SCHEME 1

(10).[4] The chromatographic separation of the pair of diastereoisomeric secondary bases was made possible by their conversion into the corresponding *N*-trifluoroacetyl derivatives, by using a device which had proved useful in the separation of the minor alkaloids of *O. glaziovii*: [7] the secondary bases, *i.e.* crotsparinine (18a) (Scheme 1) and a new alkaloid named isocrotsparinine (19a), were thereafter regenerated by mild alkaline hydrolysis. The relative configuration of the C-6a and C-7a centres in (18a) and (19a) was inferred from the correlation with (7) and (8), respectively, and the absolute configuration of the C-6a centre was established by hydrogenation of the *N*-trifluoroacetyl derivatives (18c) and (19c) and comparison with the tetrahydro-derivative (14) of (+)-(*R*)-*N*-trifluoroacetylcrotsparine (4); this, in turn had been correlated [7] with (*R*)-pronuciferine. An overall picture of the stereochemistry of the proaporphines of *C. sparsiflorus* is given in Scheme 1, shedding some light on the biogenesis of these alkaloids; it appears likely that both enantiomers of crotsparine (2) are formed during the biosynthetic process, probably by means of a racemization at some point in the process,[2] and then one of the double bonds is reduced stereospecifically, leading to pairs of diastereoisomeric alkaloids [(18a) and (19a); (18b) and (19b)], having the same configuration at C-7a; when the second double bond is reduced and the asymmetry of the C-7a centre is lost, a pair of enantiomers is again found in (±)-tetrahydroglaziovine (12).

Jacularine [9] and base E,[10] two minor alkaloids of *C. linearis*, have been isolated as their acetyl derivatives, to which the formulae (11) and (17) have been assigned, respectively. The n.m.r. spectral data reported for diacetyljacularine are in accord with those of diacetylcrotsparinine (19d), and differ from those of diacetylcrotsparinine (18d); jacularine appears to be enantiomeric with isocrotsparinine and should therefore be



represented by formula (20). The values of the chemical shifts of the C-8 and C-12 olefinic protons are indeed the most significant spectral differences between pairs of 8,9- or 11,12-dihydro-diastereoisomers, as may be observed from the n.m.r. data collected in the Table; in

[9] K. L. Stuart, L. J. Haynes, M. Barrett, and G. E. M. Husbands, *Tetrahedron Letters*, 1968, 4473.

[10] L. J. Haynes, G. E. M. Husbands, and K. L. Stuart, *J. Chem. Soc.* (*C*), 1966, 1680; K. L. Stuart, D. Byfield, C. Chambers, and G. E. M. Husbands, *ibid.*, 1970, 1228.

both deuteriochloroform and pentadeuteriopyridine, a slightly greater chemical shift of the C-12 proton with respect to that at C-8 was constantly observed in the 10-oxo- and the 10-hydroxy-derivatives, with a difference ranging from 0.07 to 0.22 p.p.m.*

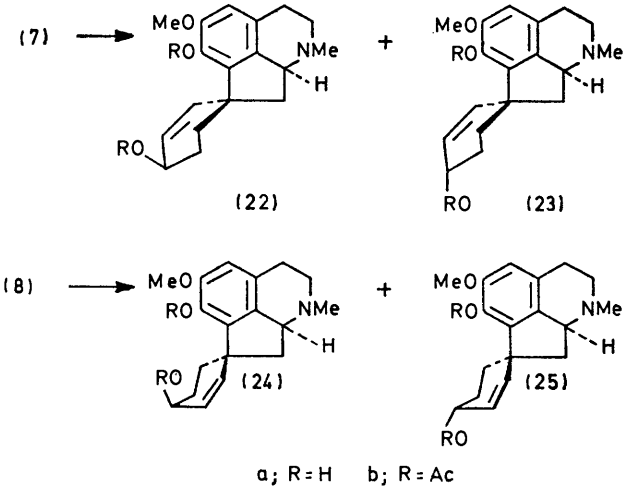
reduction of the synthetic (±)-dihydroglaziovines (7) and (8) with sodium borohydride; the pseudoaxial or pseudo-equatorial orientation of the 10-hydroxy- or acetoxy-function in these compounds was inferred from their n.m.r. spectra (Table). Base E diacetate was identical,

^{1}H N.m.r. spectra of reduced proaporphine derivatives [a]

Compound	Solvent	C(8)–H	C(9)–H	C(12)–H	C(11)–H	C(10)–H	C(10)–OAc	C(1)–OAc	C(2)–OCH_3	C(3)–H	NCH_3 or NAc	C(6a)–H
8,9-Dihydro-10-oxo-derivatives												
(7)	$CDCl_3$			6.85 [b,c]	5.94 [b]				3.82	6.54	2.36	
	C_5D_5N			7.00 [b,c]	6.13 [b]				3.62	6.68	2.30	
(18a)	$CDCl_3$			6.87 [b,c]	5.98 [b]				3.85	6.57		4.12 [d]
(18c)	$CDCl_3$			6.83 [b,c]	6.03 [b]				3.82	6.70		5.01 [d]
(18d)	$CDCl_3$			6.89 [b,c]	5.99 [b]			2.24	3.82	6.78	2.20	4.96 [d]
11,12-Dihydro-10-oxo-derivatives												
(8)	$CDCl_3$	6.75 [e,f]	5.99 [e]						3.80	6.52	2.37	
	C_5D_5N	6.92 [e,f]	6.17 [e]						3.68	6.66	2.32	
(19a)	$CDCl_3$	6.80 [e,f]	6.04 [e]						3.84	6.55		4.16 [d]
(19c)	$CDCl_3$	6.76 [e,f]	6.07 [e]						3.80	6.67		5.02 [d]
(19d)	$CDCl_3$	6.68 [e,f]	6.03 [e]					2.20	3.82	6.74	2.18	5.03 [d]
8,9-Dihydro-10-hydroxy and -10-acetoxy-derivatives												
(22a)	$CDCl_3$			5.82 and 5.84 [b]		4.16 [g]			3.82	6.52	2.36	
	C_5D_5N			5.99 [b]	6.09 [b,h]	4.47 [i]			3.64	6.60	2.30	
(22b)	$CDCl_3$			5.95 [b]	5.71 [b,j]	5.30 [g]	2.06	2.30	3.79	6.64	2.35	
(23a)	$CDCl_3$			5.70 and 5.76 [b]		4.39 [k,l]			3.82	6.55	2.35	
	C_5D_5N			5.98 [b]	6.06 [b]	4.72 [k,l]			3.64	6.62	2.26	
(23b)	$CDCl_3$			5.58 and 5.88 [b,m]		5.40 [k]	2.08	2.26	3.78	6.63	2.36	
11,12-Dihydro-10-hydroxy and -10-acetoxy-derivatives												
(24a) [n]	$CDCl_3$	5.71 [e]	5.88 [e,o]			4.20 [g]			3.80	6.48	2.33	
	C_5D_5N	5.88 [e]	6.04 [e,o]			4.41 [g]			3.60	6.56	2.26	
(24b)	$CDCl_3$	5.78 and 5.83 [e]				5.30 [g]	2.06	2.22	3.78	6.50	2.36	
(25a) [n]	$CDCl_3$	5.62 [e]	5.76 [e,p]			4.28 [k]			3.78	6.50	2.33	
	C_5D_5N	5.76 [e]	6.07 [e,p]			4.66 [k]			3.63	6.56	2.22	
(25b)	$CDCl_3$	5.68 and 5.72 [e]				5.36 [k]	2.06	2.22	3.78	6.60	2.36	

[a] Recorded at 100 MHz, unless otherwise indicated; δ values from tetramethylsilane; in footnotes J or $W_{\frac{1}{2}}$ in Hz. [b] $J_{11,12}$ 10. [c] Long-range coupling (J 1) with a methylene proton [probably C(8)–H] which by decoupling was shown to absorb at δ *ca.* 1.90. [d] $J_{6a,7}$ 12 and 6. [e] $J_{8,9}$ 10. [f] Long-range coupling (J 1) with a methylene proton [probably C(12)–H_{eq}] which by decoupling was shown to absorb at δ *ca.* 2.20. [g] Unresolved multiplet, $W_{\frac{1}{2}}$ 7. [h] $J_{10,11}$ 3.5. [i] $W_{\frac{1}{2}}$ 9; $J_{9,10}$ 4.5 (*eq,ax* and *eq,eq*) observed upon decoupling by irradiation of the olefinic proton signals. [j] $J_{10,11}$ 4. [k] Unresolved multiplet, $W_{\frac{1}{2}}$ 16—18. [l] $J_{9,10}$ 10 (*ax,ax*) and 6 (*eq,ax*) observed upon decoupling by irradiation of the olefinic proton signals. [m] The resolution of these signals was insufficient for a definite measurement of the coupling constants. [n] 60 MHz. [o] $J_{9,10}$ 4.5. [p] $J_{9,10}$ 2.

The steric structure of base E diacetate (17) was established by comparing an authentic sample with the diacetyl



SCHEME 2

derivatives (22b)—(25b) (Scheme 2; one enantiomer shown in each case) of the four alcohols obtained by

except for its rotation, with compound (24b); base E can therefore be represented by formula (21).

EXPERIMENTAL

For general methods see preceding paper.

Isolation of the Alkaloids.—Ground dried aerial parts (24 kg) of *Croton sparsiflorus* Morong were extracted by stirring at room temperature for 3 days with 120 l of ethanol, and then twice with 100 l. The extracts were evaporated under reduced pressure to 8 l, diluted with aqueous tartaric acid (5%; 15 l), stirred, and then decanted. The solution was washed with chloroform (2 × 10 l), made basic (to pH 8.5) with ammonia, and extracted with chloroform (3 × 6 l). The extracts were evaporated and the residue was taken up in ethyl acetate, giving crystalline crotsparine (2), which was recrystallized from ethyl acetate (47 g). The ethyl acetate mother liquors were combined and evaporated; the residue (135 g) was dissolved in 2N-hydrochloric acid and kept at room temperature for 2 days, thus converting the remaining crotsparine (2) into sparsiflorine (16), which crystallized as the hydrochloride (10.5 g) [identical t.l.c. behaviour with a sample obtained by treating (+)-crotsparine [7] with hydrochloric acid]. The filtrate was

* Similar differences have been observed in the ^{13}C n.m.r. spectra of these compounds (G. Severini-Ricca, in preparation).

adjusted to pH 8.5 (NH_4OH) and extracted with chloroform. The crude mixture of alkaloids (98 g) obtained by evaporation of the extracts was chromatographed (chrom. 1) on silica gel (2 kg) with chloroform and chloroform containing increasing amounts of ethanol (5—20% v/v); the elution was monitored by t.l.c. (CH_2Cl_2–CH_3OH–28% NH_4OH aq. 89 : 10.6 : 0.4) and the following fractions were collected: chrom. 1, fraction 1 (0.4 g), traces of alkaloids, including *N*-methylcrotsparinine (18b) and *N*-methylisocrotsparinine (19b); fraction 2 (3 g), (±)-tetrahydroglaziovine (12); fraction 3 (4.2 g), (12) and unidentified minor alkaloids; fraction 4 (7.2 g), minor alkaloids, crotsparinine (18a), and isocrotsparinine (19a); fraction 5 (16.5 g), (18a) and (19a); fraction 6 (9 g), (18a), (19a), and sparsiflorine (16); fraction 7 (15.5 g), (16).

A portion (3 g) of chrom. 1, fraction 5 was methylated by heating at 100 °C for 4 h with 34% aqueous formaldehyde (0.95 ml) and 85% formic acid (2.9 ml). The mixture was evaporated under reduced pressure, the residue was taken up in water, and the mixture was again evaporated; the residue was stirred with potassium hydrogen carbonate solution and chloroform. The organic extract was evaporated and the residue chromatographed (chrom. 2) on alumina (600 g; activity IV); elution with chloroform gave, in the following order, an unidentified compound (60 mg), then *N*-methylcrotsparinine (18b) (90 mg from ethyl acetate), a mixture of (18b) and (19b) (190 mg), and pure *N*-methylisocrotsparinine (19b) (88 mg from ethyl acetate). Chrom. 1, fraction 4 (7.2 g) in pyridine (35 ml) was treated with trifluoroacetic anhydride (7 ml); the mixture was kept at room temperature during the night, then diluted with water and hydrochloric acid (pH 3), extracted with chloroform, and chromatographed (chrom. 3) on alumina (activity IV; 50 : 1 ratio). Elution with chloroform gave the *N*-trifluoroacetyl derivatives of two unidentified alkaloids, followed by a mixture of *N*-trifluoroacetylcrotsparinine (18c) and *N*-trifluoroacetylisocrotsparinine (19c). The remaining portion of chrom. 1, fraction 5 and chrom. 1, fraction 6 were submitted to the same treatment [the latter after separation of a further amount of (16) as the hydrochloride]. The *N*-trifluoroacetyl derivatives obtained from chrom. 1, fractions 4—6 were combined (11.6 g), chromatographed on alumina (activity IV; 200 : 1 ratio), and eluted with chloroform (t.l.c. monitoring; benzene–ethyl acetate, 6 : 4; two runs); only 0.48 g of pure (18c) was obtained; the remaining fractions were combined in two groups, respectively enriched in (18c) and (19c), which were separately rechromatographed in the same way, affording 0.5 and 0.91 g, respectively, of pure *N*-trifluoroacetylcrotsparinine (18c) and *N*-trifluoroacetylisocrotsparinine (19c), along with a number of mixed fractions.

Crotsparine (2).—The isolated alkaloid (47 g) was slightly contaminated with crotsparinine (18a) and isocrotsparinine (19a). A pure sample was obtained by chromatography on alumina (activity IV; 50 : 1; $CHCl_3$); m.p. 188—190° (decomp.), $[\alpha]_D$ −32° (*c* 1 in $CHCl_3$); identical (t.l.c., i.r. in $CHCl_3$) with (+)-crotsparine [7] obtained from *Ocotea glaziovii*, $[\alpha]_D$ +135° (*c* 0.5 in $CHCl_3$) {lit.,[4] m.p. 193—195°, $[\alpha]_D$ −30° (*c* 1.22 in $CHCl_3$)}.

(±)-*Tetrahydroglaziovine* (12).—Further chromatography of chrom. 1, fraction 2 on alumina (activity III) gave the alkaloid in nearly racemic form, m.p. 163—164°, $[\alpha]_D$ +2° (*c* 1 in MeOH), $\nu_{max.}$ ($CHCl_3$) 3 560 and 1 708 cm^{-1}, identical (t.l.c., i.r.) with a sample obtained [1] by palladium–charcoal hydrogenation of (±)-glaziovine. Hydrogenation of (−)-glaziovine [6] in the same way gave (−)-tetrahydroglaziovine (13), m.p. 98—105 and 173—175° (from ethyl acetate), $[\alpha]_D$ −55.3° (*c* 1 in MeOH).

N-*Methylcrotsparinine* (18b).—The sample from chrom. 2, m.p. 156—158°, $[\alpha]_D$ +258° (*c* 0.33 in MeOH), was identical (t.l.c., i.r. in $CHCl_3$) with synthetic (±)-8,9-dihydroglaziovine [1] (7); $\nu_{max.}$ 3 555 and 1 665 cm^{-1} {lit.,[4] m.p. 160—161°, $[\alpha]_D$ +244° (*c* 0.92 in $CHCl_3$)}.

N-*Methylisocrotsparinine* (19b).—The sample from chrom. 2, m.p. 197—199°, $[\alpha]_D$ +111.5° (*c* 0.34 in MeOH), was identical (t.l.c., i.r. in $CHCl_3$) with synthetic (±)-11,12-dihydroglaziovine (8); $\nu_{max.}$ 3 560 and 1 665 cm^{-1}.

Crotsparinine (18a).—The *N*-trifluoroacetyl derivative (18c) had m.p. 192—194° (from ethyl acetate), $[\alpha]_D$ −22.4° (*c* 0.25 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 530, 3 440br, and 1 680br cm^{-1}. It was dissolved (100 mg in 10 ml) in a solution of sodium ethoxide (3% Na in anhydrous ethanol); after 1 h at room temperature, hydrochloric acid was added (pH 3), the solvent was evaporated off under reduced pressure, and water, ammonia (to pH 8.5), and chloroform were added. The organic extract was chromatographed on alumina (4 g) giving crotsparinine (18a) (39 mg), m.p. 122—123° (from ethyl acetate); $[\alpha]_D$ +248° (*c* 0.22 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 550—3 200br and 1 665 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 550 and 1 668 cm^{-1}; *m/e* 285 (M^+, 100%), 284 (81), 268 (10), 257 (16), 256 (80), 255 (10), 254 (11), 242 (22), 241 (19), 228 (14), 223 (10), 214 (11), 213 (17), 202 (11), 199 (10), 191 (11), and 190 (22). The observed m.p. differs from the reported [4] value of 184—185°. Some differences were also shown in the optical rotation and the n.m.r. data (*cf.* Table) {lit.,[4] $[\alpha]_D$ +215° (*c* 2.37 in $CHCl_3$), δ ($CDCl_3$; 60 MHz), 3.79 (OCH_3), 6.50 (3-H), and 6.12 and 6.94 (olefinic, *J* 10 Hz)}.

Acetylation of (18a) with acetic anhydride–pyridine gave the *NO*-diacetate (18d), m.p. 182—183° (from ethyl acetate–ether), $[\alpha]_D$ −76° (*c* 0.20 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 760, 1 670, and 1 635 cm^{-1}; *m/e* 369 (M^+).

Isocrotsparinine (19a).—The *N*-trifluoroacetyl derivative (19c) had m.p. 197—199° (from ether), $[\alpha]_D$ +257° (*c* 0.25 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 380br and 1 675 cm^{-1}. Treatment with sodium ethoxide as indicated for (18c) gave isocrotsparinine, m.p. 198—199° (from ethyl acetate), $[\alpha]_D$ +112.5° (*c* 0.23 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 480 and 1 657 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 560 and 1 668 cm^{-1}; *m/e* 285 (M^+, 100%), 284 (68), 268 (10), 257 (10), 256 (74), 255 (10), 254 (10), 242 (29), 241 (18), 228 (18), 223 (10), 214 (18), 213 (19), 202 (15), 199 (9), 191 (8), and 190 (26).

Methylation of (19a) with formaldehyde–formic acid was shown by t.l.c. to give (19b), while (18b) was formed from (18a). Acetylation of (19a) with acetic anhydride–pyridine gave the *NO*-diacetate (19d), m.p. 131—132°, $[\alpha]_D$ +239° (*c* 0.23 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 760, 1 673, and 1 635 cm^{-1}; *m/e* 369 (M^+). The reported [9] n.m.r. characteristics of *NO*-diacetyljacularine (20), δ 2.17, 2.20, 3.82, 6.03, 6.71 (9 Hz), and 6.79, are in accord with those of (19d) (Table); m.p. and $[\alpha]_D$ were not given.

Absolute Configuration of the C-6a *Centre of Crotsparinine* (18a) *and Isocrotsparinine* (18b).—(*R*)-*N*-Trifluoroacetylcrotsparine [7] (4) (50 mg) in dioxan (3 ml) was hydrogenated at 3—4 atm for 2 h over palladium–charcoal (10%; 18 mg); the catalyst was filtered off, the solution was evaporated, and the residue was recrystallized from ether–light petroleum (b.p. 60—80°), yielding the tetrahydro-derivative (14) (29 mg), m.p. 161—162.5°, $[\alpha]_D$ −133° (*c* 0.21 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 420, 1 710, and 1 680 cm^{-1}; *m/e* 383 (M^+).

Hydrogenation of *N*-trifluoroacetylcrotsparinine (18c) and

N-trifluoroacetylisocrotsparinine (19c) under the same conditions gave the dihydro-derivatives (14) and (15), showing $[\alpha]_D$ −125° (*c* 0.22 in $CHCl_3$) and +126° (*c* 0.2 in $CHCl_3$), respectively; their i.r. spectra and t.l.c. behaviour (benzene–ethyl acetate, 4 : 1; two runs) were identical with those of the sample obtained from (4).

Reduction by Sodium Borohydride of (±)-8,9- *and* (±)-11,12-*Dihydroglaziovine* [(7) *and* (8)].—Sodium borohydride (4 g) was added in 30 min at 25 °C to 11,12-dihydroglaziovine (8) (8.5 g) in methanol (280 ml). After 30 min, most of the methanol was evaporated off under reduced pressure on a bath kept at 40 °C; water was added and the solution was adjusted to pH 8.5 (HCl) and extracted with chloroform The extract was evaporated and the residue chromatographed on silica gel (900 g); elution with chloroform and chloroform–methanol (98 : 2) gave in the following order the pseudoaxial alcohol (24a) (1.3 g), some mixed fractions (2 g), and the pseudoequatorial alcohol (25a) (4.7 g). The *former* (24a) had m.p. 174—175° (from ethyl acetate) (Found: C, 71.4; H, 7.8; N, 4.5. $C_{18}H_{23}NO_3$ requires C, 71.7; H, 7.7; N, 4.6%) and gave a *diacetate* (24b) with acetic anhydride–pyridine; m.p. 165—167° (from ether), $\nu_{max.}$ ($CHCl_3$) 1 755 and 1 723 cm^{-1}. *Compound* (25a) showed m.p. 177—178° (from ethyl acetate) (Found: C, 71.7; H, 7.9; N, 4.8%), and gave a diacetate (25b), m.p. 178—179° (from ether), $\nu_{max.}$ ($CHCl_3$) 1 755 and 1 727 cm^{-1}.

Similar reduction of (±)-8,9-dihydroglaziovine (7) gave another pair of alcohols: *pseudoaxial isomer* (22a), m.p: 183—184° (from ethyl acetate) (Found: N, 4.6. $C_{18}H_{23}NO_3$ requires N, 4.6%); diacetate (22b), m.p. 158—159° (from ether), $\nu_{max.}$ (KBr) 1 770 and 1 725 cm^{-1}; *pseudoequatorial isomer* (23a), m.p. 189—190° (from ethyl acetate) (Found: N, 4.9%); diacetate (23b), m.p. 154—156° (from ether), $\nu_{max.}$ (KBr) 1 765 and 1 732 cm^{-1}.

Base E diacetate [10] (17) was studied by t.l.c. (CH_2–Cl_2–CH_3OH–28% NH_4OH aq. 89 : 10.6 : 0.4; two runs); it was identical with (24b) and different from compounds (22b), (23b), and (25b); also identical were the i.r. spectra of (17) and (24b) in $CHCl_3$ solution.

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