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STRUCTURES AND ABSOLUTE STEREOCHEMISTRY OF (−)-ECHITOVENILINE, (−)-11-METHOXYECHITOVENILINE AND (−)-11-METHOXYECHITOVENEDINE—NEW INDOLE ALKALOIDS OF *ALSTONIA VENENATA* R.BR.

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Abstract—Structures and absolute stereochemistry of (−)-echitoveniline, (−)-11-methoxyechitoveniline and (−)-11-methoxyechitovenedine, three new indole alkaloids of the vincadifformine type, isolated from the fruits and leaves of *Alstonia venenata* R.Br., have been established as **3b**, **3c** and **3d**, respectively, on the basis of spectral and chemical evidence. A plausible mechanism of the LAH reduction of the δ-lactones **8b** and **8c** to the corresponding diols **9b** and **9c** has been discussed.

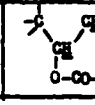
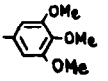
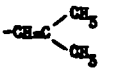
In earlier communications[1-14] the isolation and structure determination of fourteen new indole alkaloids and a monoterpenoid pyridine base, venoterpine,[5,6] in addition to the characterization of kopsinine, reserpine and trimethylgallamide,[14] isolated from different parts of *Alstonia venenata* R.Br., were reported. Structurally these new indolic bases of *A. venenata* represent distinctly three skeletal patterns,[15] *viz.* yohimbine, refractine-pleiocarpine and vincadifformine. Our continued search for alkaloidal principles in this plant has now culminated in the isolation of three more new basic constituents of the vincadifformine type. Spectral and chemical evidence establishing the structures and absolute stereochemistry of these alkaloids designated as (−)-echitoveniline (**3b**), (−)-11-methoxyechitoveniline (**3c**) and (−)-11-methoxyechitovenedine (**3d**) are summarised in the present communication.

(−)-Echitoveniline (**3b**), $C_{31}H_{36}N_2O_7$ ($M^{+\cdot}$ 548), amorph., $[\alpha]_D$ −263° ($CHCl_3$), (−)-11-methoxyechitoveniline (**3c**), $C_{32}H_{38}N_2O_8$ ($M^{+\cdot}$ 578), amorph., $[\alpha]_D$ −388° (EtOH) and (−)-11-methoxyechitovenedine (**3d**), $C_{27}H_{34}N_2O_5$ ($M^{+\cdot}$ 466), m.p. 140°, $[\alpha]_D$ −325° ($CHCl_3$), were all first isolated from the fruits of *A. venenata* in poor yields. **3c** was subsequently found to occur in the leaves in relatively better yield. Because of their close association with a number of structurally related compounds which are difficult to resolve into the pure components, the isolation of the aforesaid alkaloids involved tedious and painstaking steps of initial pH gradient fractionation, followed by partial resolution by column chromatography, the final separation being achieved through preparative TLC using multiple-run technique.

The characteristic high specific rotations together with typical IR absorptions of the alkaloids (**3b**: ν_{max} 3400, 1675 and 1605 cm^{-1}; **3c**: ν_{max} 3390, 1680 and 1615 cm^{-1}; **3d**: ν_{max} 3365, 1672 and 1610 cm^{-1}) clearly indicated the presence of β-anilinoacrylate chromophore[16] in all of them. But their UV spectra displayed a divergent pattern. Thus the spectrum of **3b** showed an additional band at 269 nm (log ε 4.12) besides the characteristic absorption maxima at 216, 297 and 330 nm (log ε 4.55, 4.09 and 4.17). The band at 269 nm is presumably associated with an additional conjugated ester carbonyl, the presence of which was revealed by the IR spectrum (ν_{max} 1712 cm^{-1}) of **3b**. On the other hand, the UV spectra of **3c** [λ_{max} 255–56 and 327 nm (log ε 4.21 and 4.18)] and **3d** [λ_{max} 225, 245 inf. and 324 nm (log ε 4.57, 4.17 and 4.24)] are complex in nature and do not resemble those of the alkaloids bearing the simple β-anilinoacrylate chromophore **1a**. Although some similarity of the UV spectra of **3c** and **3d** to those of the 11-methoxylated alkaloids bearing the chromophore **1b**, e.g. 11-methoxytabersonine[17] and echitovenaldine,[8] could be recognised, the overall nature of the spectra of **3c** and **3d** appeared to be additively modified by the presence of at least another isolated chromophoric system. The presence of the IR absorption band at 1715 cm^{-1} for **3c** and those at 1690 and 1647 cm^{-1} for **3d** clearly demonstrated that while the former contains an additional chromophoric system as in **3b**, the latter in all probability contains an α,β-unsaturated ester system having a trisubstituted double bond.

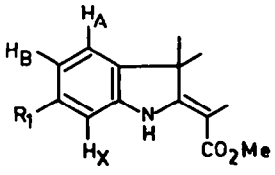
The 60 MHz PMR spectral data (Table 1) of the alkaloids **3b**, **3c** and **3d** while providing adequate support to the foregoing conclusions, disclosed further significant structural information. The aromatic proton resonances together with the indoline >NH and the carbomethoxyl signal, confirming the presence of the system **1**, and the low-field methine quartet coupled with a three-proton doublet assignable to the system **2**, are common to all the three PMR spectra which also provided further evidence regarding the precise nature of R_1 and R_2 in the systems **1** and **2**. The spectra of both **3b** and **3c** showing the presence of a benzenoid residue in addition to that in **1**, have signals for two aromatic protons together with three aromatic methoxyls characteristic of a 3,4,5-trimethoxy-

Table 1.*

Chromophore →	1				2	
Signals assigned to →	Ar-H	>NH‡	$-CO_2Me$	R_1=OMe		R_2
(-)-Echitoveniline	6.45-7.2, 4H, m	8.97, 1H, br. s	3.45, 3H, s	-	1.05, 3H, d, J 7 Hz; 4.95, 1H, q, J 7 Hz	5.94, 9H, s; 7.05, 2H, s 
(-)-11-Methoxy-echitoveniline	6.13, 1H, d, J 2.5 Hz (H_X); 6.52, 1H, dd, J_1 8 Hz, J_2 2.5 Hz (H_B); 7.02, 1H, d, J 8 Hz (H_A)	8.98, 1H, br. s	3.49, 3H, s	3.71, 3H, s	1.07, 3H, d, J 7 Hz; 4.99, 1H, q, J 7 Hz	5.92, 9H, s; 7.05, 2H, s 
(-)-11-Methoxy-echitovenedine	6.40, 1H, br. signal (H_X); 6.55, 1H, dd, J_1 8 Hz, J_2 3 Hz (H_B); 7.03, 1H, d, J 8 Hz (H_A)	9.05, 1H, br. s	3.70, 3H, s	3.78, 3H, s	0.97, 3H, d, J 7 Hz; 4.78, 1H, q, J 7 Hz	1.70, 3H, d, J 2 Hz; 2.01, 3H, d, J 2 Hz; 5.05, 1H, m 

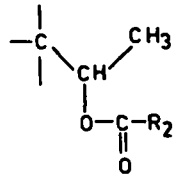
*Chemical shifts are expressed as δ(ppm) using TMS as internal standard.

‡Signals disappear on deuterium exchange with D_2O.

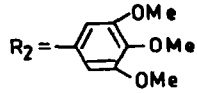


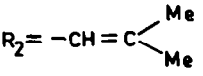
1

a: R_1 = H
b: R_1 = OMe



2

a: R_2 = 

b: R_2 = 

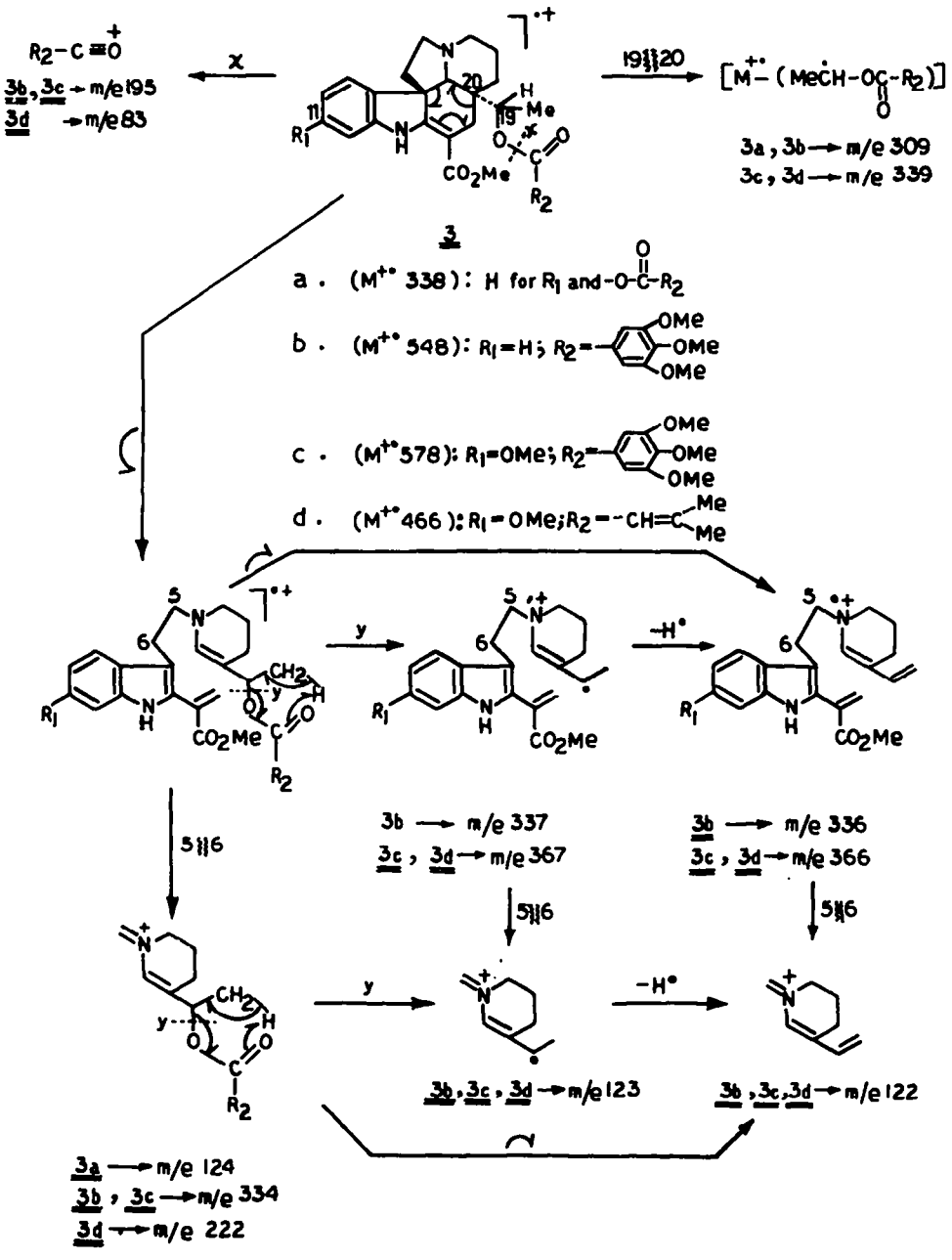
phenyl group occurring as 2a. The PMR spectrum of 3d, on the other hand, shows signals for two nonequivalent vinyl methyls and an olefinic proton, which could be attributed to a β,β-dimethylvinyl group representing R_2 (as in 2b). Moreover, the aromatic methoxyl signals and the strikingly similar splitting pattern of the aromatic protons in the system 1, attributable specifically to 1b, are common only to 3c and 3d, while 3b contains the system 1a.

The modified natures of the UV spectra of the three alkaloids (compared to those of alkaloids bearing the chromophore 1a or 1b alone) now find a rational explanation in terms of the additive contribution of a trimethylgalloyl residue to the chromophore 1a in 3b and to the chromophore 1b in 3c, and similar contribution of the β,β-dimethylacryloyl moiety to the absorption of 1b in 3d. This has been amply substantiated by the differential UV spectra of 3b and 3c against methyl trimethylgallate, which exactly correspond to those expected for 1a and 1b, respectively. Similarly, the differential UV spectrum of 3d against β,β-dimethylacrylic acid (DMAA), as well as the UV spectrum of the catalytic hydrogenation product (3e) of 3d was found to correspond to that for the chromophore 1b.

A clear picture of the skeletal structures of these alkaloids was available from their mass spectra, all showing typical vincadifformine-like fragmentation pattern[18,19] (Scheme 1). Comparison of the significant peaks appearing in their MS with those for vincadifformine (3a) revealed:

(a) For both 3b and 3c the base peaks appearing at *m/e* 334 indicated the presence of a substituent of composition $C_{10}H_{11}O_5$ (211 amu) in the piperidine-bearing part of these molecules. That this substituent is a trimethylgalloyloxy moiety was evident from the appearance of a strong peak at *m/e* 195 for both the compounds. The peaks at [M-239] in the MS of both 3b and 3c (*m/e* 309 and 339, respectively) indicate the loss of the C-20 Et side chain bearing the trimethylgalloyloxy substituent which is located at C-19 according to the PMR spectral data. Similarly, the appearance of the base peak at *m/e* 222 in the MS of 3d coupled with the peaks at *m/e* 83 and 339 [M-127] suggested the presence of a β,β-dimethylacryloxy moiety at C-19 in its molecule.

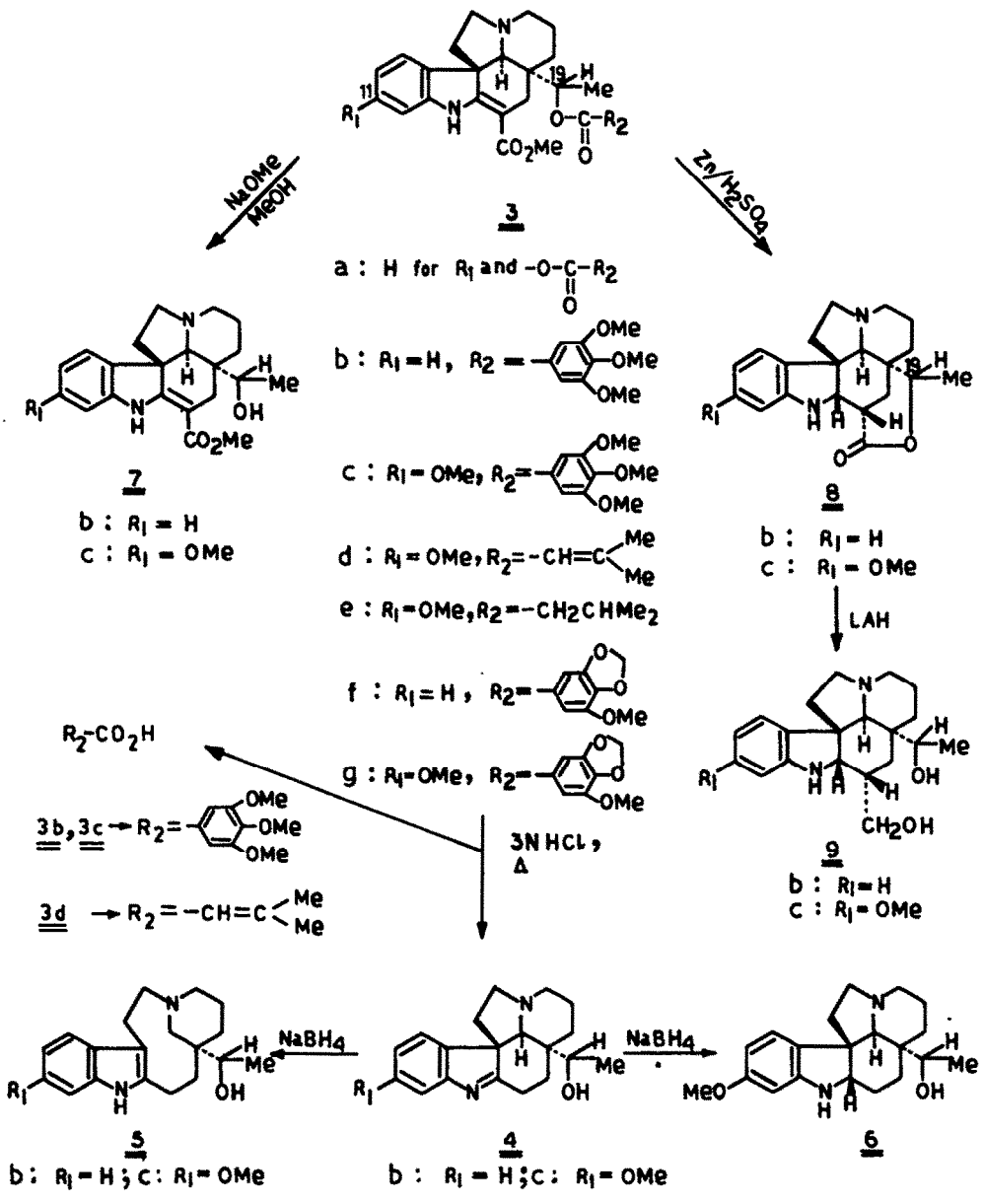
(b) For 3b the base peak corresponds to [M-214] as for vincadifformine itself, which established the unsubstituted nature of the indole part of its molecule. In the case of 3c and 3d, however, the base peaks correspond to [M-244] indicating the presence of a methoxyl group in the indole part of their molecules, presumably at C-11. These observations along with the PMR data led to the postulation of the structures 3b, 3c and 3d for (-)-echitoveniline, (-)-11-methoxyechitoveniline and (-)-11-methoxyechitovenedine, respectively.



Scheme 1.

Confirmation of the above structures and the determination of the absolute stereochemistry of the alkaloids were finally achieved through the following transformation reactions (Scheme 2). Thus 3b on acid-catalyzed hydrolysis afforded, besides trimethylgallic acid (TMGA), an indolenine base, $C_{19}H_{24}N_2O$ ($M^{+\cdot}$ 296), m.p. 180°, λ_{max} 223 and 265 nm (log ϵ 4.35 and 3.71), which on reduction with alkaline methanolic $NaBH_4$ gave an indolic base, $C_{19}H_{26}N_2O$ ($M^{+\cdot}$ 298), $[\alpha]_D$ + 125° ($CHCl_3$), λ_{max} 229, 284 and 290 nm (log ϵ 4.42, 3.80 and 3.79). The above indolenine and indole derivatives were shown to be identical in all respects with 19R - 19 - hydroxy - 1,2 - dehydroaspidospermidine (4b) and 19R - 19 - hydroxy - (+) - quebrachamine (5b), respectively, obtained from echitoserpidine[10] (3f), a fruit alkaloid of *A. venenata*. This, therefore, conclusively established the structure and absolute stereochemistry of (−)-echitoveniline to be 19R - 19 - trimethylgalloyloxy - (−) - vincadifformine (3b).

(−)-11-Methoxyechitoveniline (3c), on similar sealed-tube acid-catalysed hydrolysis furnished, besides TMGA, an indolenine derivative, $C_{20}H_{26}N_2O_2$ ($M^{+\cdot}$ 326), m.p. 199°, λ_{max} 230, 255 and 282 nm (log ϵ 3.43, 3.53 and 3.49), which on reduction with alkaline methanolic $NaBH_4$ afforded an indolic base, $C_{20}H_{28}N_2O_2$ ($M^{+\cdot}$ 328), $[\alpha]_D$ + 125.5° ($CHCl_3$), λ_{max} 230, 270 and 300 nm (log ϵ 4.37, 3.64 and 3.64) together with an isomeric indoline, λ_{max} 242 inf. and 300 nm (log ϵ 3.73 and 3.56). The same indolenine, indole and indoline compounds were obtained from (−)-11-methoxyechitovenedine (3d) under similar experimental conditions although, instead of TMGA, DMAA resulted in the first step. The indolenine, indole

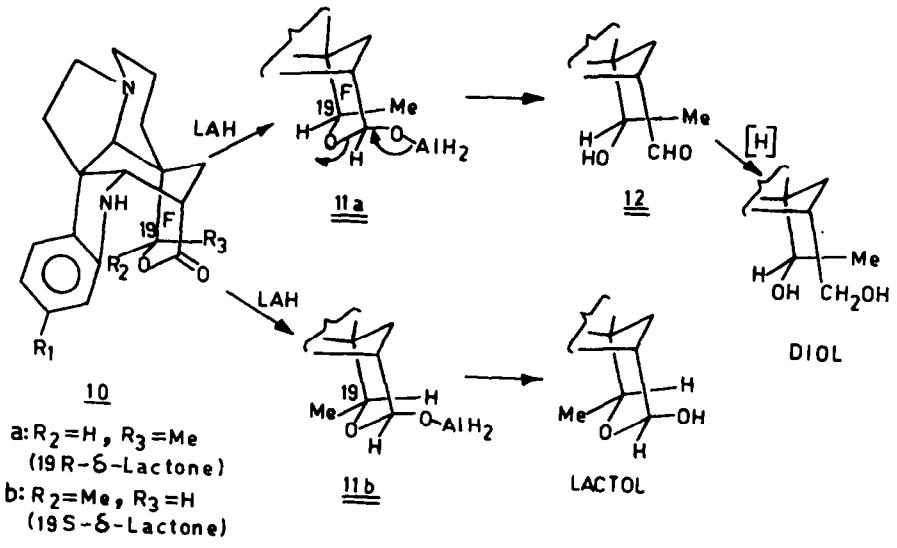


Scheme 2.

and indoline compounds as obtained above were found to be identical with 19R - 19 - hydroxy - 11 - methoxy - 1,2 - dehydroaspidospermidine (4c), 19R - 19 - hydroxy - 11 - methoxy - (+) - quebrachamine (5c) and 19R - 19 - hydroxy - 11 - methoxyaspidospermidine (6), respectively, derived from echitoserpine[11] (3g), another fruit alkaloid of *A. venenata*. This chemical correlation thus settled the structure and absolute stereochemistry of (−)-11-methoxyechitoveniline and (−)-11-methoxyechitovenedine as 11 - methoxy - 19R - 19 - trimethylgalloyloxy - (−) - vincadifformine (3c) and 11 - methoxy - 19R - 19 - β,β - dimethylacryloxy - (−) - vincadifformine (3d), respectively.

The above conclusions regarding the stereostructures of these three alkaloids are also in conformity with the fact that the physical constants of the basic product obtained from 3b and of that obtained from both 3c and 3d (preferably from 3c) by methanolysis (NaOMe in dry MeOH), compare excellently with those reported for (−)-19R-minovincinine[20] (7b) and (−) - 11 - methoxy - 19R - minovincinine[21] (7c), respectively. These are also obtainable from 3f[10] and 3g,[11] respectively, by similar methanolysis.

Further evidence in support of the absolute stereochemistry of the alkaloids as deduced above was provided by the LAH reduction of the δ-lactone 8b obtained from 3b and the δ-lactone 8c obtained from both 3c and 3d by reduction of the alkaloids with Zn and 10% methanolic H_2SO_4 followed by heating with aqueous H_2SO_4. Reduction of 8b and 8c with LAH afforded the diols, $C_{20}H_{28}N_2O_2$ ($M^{+\cdot}$ 328), m.p. 127–32°, and $C_{21}H_{30}N_2O_3$ ($M^{+\cdot}$ 358), m.p. 180°, which from their various spectral data were shown to have the structures 9b and 9c, respectively. The structures of the diols are in accord with the fact that the δ-lactones 8b and 8c, from which they are derived, are also obtained from echitoser-



Scheme 3.

pidine[10] [as well as 19R-(−)-minovincinine[20]] and echitoserpine,[11] respectively. It may be recalled that Döpke *et al.*[20] observed that the δ-lactone derived from (−)-minovincinine yielded upon reduction with LAH, a diol or a lactol depending upon whether the configuration at C-19 is, respectively, R or S. Therefore, by analogy, a 19R-configuration of the alkaloids is postulated. Although the formation of a diol or a lactol was found to depend on the C-19 configuration of the 19-hydroxy (or acyloxy) alkaloids of the (−)-vincadifformine series, no explanation has so far been offered for this observation. A plausible rationale may be as follows: Examination of Dreiding models showed that the δ-lactones (**8b** and **8c**) derived from the three alkaloids have the conformation **10a**. The corresponding 19S-δ-lactones are expressed by **10b**. The first step of the reduction process appears to be the formation of a lactol derivative (**11a** or **11b**) (Scheme 3) irrespective of the C-19 configuration (R or S). In **11a** which has a 19R configuration, the 1:3 diaxial interaction between the C-19-Me and the $OAlH_2$ group presumably forces open the ring F generating an intermediate aldehyde (**12**) which is further reduced to the corresponding diol. On the other hand, a 19S δ-lactone (**10b**) would give the intermediate **11b** which is apparently free from any significant interaction and hence the reaction stops at the lactol stage.

EXPERIMENTAL

Unless otherwise stated, column chromatography was carried out over Brockmann alumina (activity-1) and tlc over silica gel G. All analytical samples were routinely dried over P_2O_5 at 55–138° (depending upon the m.p. of the compounds) for 24 hr *in vacuo* and were tested for purity by tlc and mass spectrometry. Unless otherwise stated, IR spectra were run in Nujol mulls, optical rotations were measured in $CHCl_3$ and UV spectra were recorded in 95% EtOH (aldehyde free). The petrol used boiled in the range 60–80°. All non-hydroxylic organic solvents were dried over anhydrous Na_2SO_4. Identity of known compounds were established by mixed m.p., co-tlc and superimposable IR spectra.

Isolation of (−)-echitoveniline (3b), *(−)-11-methoxy-echitoveniline* (3c) *and (−)-11-methoxyechitovenedine* (3d) *from the fruits of* A. venenata *R.Br.* Air-dried finely ground fruits (1 kg) of *A. venenata* R.Br. were extracted with petrol in a soxhlet apparatus for 48 hr. The extract (~4 l.) was concentrated to ~200 ml, churned with 5% aq. citric acid (1 l.) for 6 hr and filtered. The filtrate was repeatedly extracted with $CHCl_3$. The $CHCl_3$ extract was washed with dil. NH_4OH aq followed by water. It was then dried, concentrated and chromatographed using as eluents petrol, mixtures of petrol/C_6H_6, and C_6H_6. The petrol/C_6H_6 (2:1) eluate gave a mixture (1:1) of echitovenedine[4b] and **3d**. Repeated chromatography of the above mixture over silica gel using as eluents different mixtures of petrol/EtOAc in order of increasing polarity furnished in the later fractions of the eluates mixtures enriched with respect to **3d** (up to ~70%). These fractions were combined and subjected to preparative tlc with silica gel G as the adsorbent (0.1 mm) and petrol/EtOAc (2:1) as the developer (R_f: echitovenedine 0.5; **3d** 0.4), which afforded pure **3d** (yield 0.005%) crystallising from methanol in rectangular plates, m.p. 140°. (Found: C, 69.75; H, 7.22; N, 5.95. $C_{27}H_{34}N_2O_5$ requires: C, 69.53; H, 7.30; N, 6.01%). $[\alpha]_D$ −325°; differential UV spectrum against DMAA: λ_{max} 245 and 328 nm (log ε 3.98 and 4.15); *m/e* (relative intensity): 466 ($M^{+\cdot}$, 27.5), 436 (1.2), 383 (1.2), 367 (25), 366 (10), 339 (2), 307 (1.8), 258 (2), 244 (1.2), 222 (100), 198 (2.5), 184 (2.5), 183 (2.5), 123 (10), 122 (5), 110 (2.5) and 83 (33); m* 287 and 67.

The total benzene washings of the main chromatogram on evaporation gave a residue which contained a mixture of echitoserpidine,[10] echitoserpine,[11] **3b** and **3c**. This on repeated chromatography afforded a mixture of **3b** and **3c** which was free from echitoserpidine but still contained some echitoserpine. This mixture was then subjected to preparative tlc as above with petrol/EtOAc (3:1) as the developer using multiple run technique (*vide* isolation of **3c** from the leaves of *A. venenata*) to give **3b** (0.001%) and **3c** in pure but amorphous state, the latter being obtained in amounts just sufficient to record its UV, MS and $[\alpha]_D$. **3b**: (Found: C, 67.3; H, 6.5; N, 5.06. $C_{31}H_{36}N_2O_7$ requires: C, 67.88; H, 6.57; N, 5.11%). $[\alpha]_D$ −263°; differential UV spectrum against methyl trimethylgallate: λ_{max} 228, 300 and 330 nm (log ε 3.90, 3.92 and 4.15); *m/e* (relative intensity): 548 ($M^{+\cdot}$, 47.2), 338 (16.7), 337 (72.4), 336 (16.7), 335 (23), 334 (100), 309 (11.5), 228 (13.1), 214 (11.5), 212 (13.1), 195 (77.1), 181 (22), 169 (13.1), 168 (31.1), 167 (21.3), 154 (19.7), 153 (11.5), 152 (11.5), 139 (11.5), 124 (19.7), 123 (32.8) and 122 (44.3); m* 206 and 44.5. **3c**: $[\alpha]_D^{EtOH}$ −388°; differential UV spectrum against methyl trimethylgallate: λ_{max} 242 and 327 nm (log ε 3.62 and 3.95); *m/e* (relative intensity): 578 ($M^{+\cdot}$, 45.7), 367 (73.7), 366 (67), 339 (3.71), 334 (100), 258 (9.39), 244 (2.14), 212 (7.39), 195 (33.2), 167 (4.61), 154 (3.29), 153 (2.65), 152 (4.18), 124 (4.78), 123 (22.6) and 122 (14.9); m* 232 and 44.5.

Isolation of **3c** *from the leaves of* A. venenata *R.Br.* Air-dried, finely ground leaves (1 kg) of *A. venenata* R.Br. was extracted with petrol and processed exactly in the same manner as in the case of the fruits. The $CHCl_3$ extract of the aq. citrate soln was washed with dil. NH_4OH aq followed by water. It was dried,

concentrated and chromatographed over silica gel, using as eluents petrol and mixtures of petrol/EtOAc in order of increasing polarity. The end fractions of petrol/EtOAc (10:1) elute contained comparable amounts of echitoserpine[11] (3g) [previously isolated from the fruits] and 3c as revealed by tlc showing mainly two nearly overlapping spots in all the three developers used (petrol/EtOAc = 3:2, 2:1 and 3:1). Repeated chromatography of this mixture over silica gel column failed to yield any significant amount of 3c, ending up only with fractions containing varying proportions of 3c and 3g. The two spots on a thin layer chromatogram could be resolved only after five successive runs in petrol/EtOAc (3:1) as developer using a 0.1 mm thick layer of adsorbent of silica gel G. Accordingly, preparative tlc was resorted to using the above set of conditions and 3c was ultimately isolated in a pure but amorphous state (yield 0.001%). (Found: C, 66.6; H, 6.47; N, 4.79. $C_{32}H_{36}N_2O_8$ requires: C, 66.44; H, 6.57; N, 4.84%).

Catalytic hydrogenation of **3d**. A soln of **3d** (0.1 g) in EtOAc (25 ml) was stirred for 3 hr in an atmosphere of H_2 in presence of Adam's platinum oxide catalyst (0.02 g). The solution was then filtered and the filtrate on evaporation gave pure **3e** in amorphous state. (Found: C, 69.1; H, 7.8; N, 6.05. $C_{27}H_{36}N_2O_5$ requires: C, 69.23; H, 7.69; N, 5.98%). λ_{max} 246 and 324 nm (log ϵ 3.93 and 4.08); ν_{max} 3400 (NH), 1472 (satd. ester >C=O), 1625 and 1690 (Ar–N–C=C–C(=O)OR) cm^{-1}.

TMGA and indolenine **4b** *from* **3b**. A soln of **3b** (0.1 g) in 10 ml 3 N aq. HCl was heated in an evacuated sealed-tube at 110 ± 2° for 7 hr. The mixture was extracted with ether, washed with water, dried and evaporated to give a residue which crystallised in stout needles of TMGA (0.03 g), m.p. 168°. (Found: C, 56.4; H, 5.75. $C_{16}H_{12}O_5$ requires: C, 56.6; H, 5.66%). The aq. acidic layer was basified with dil. NH_4OH aq, extracted with $CHCl_3$, washed with water, dried, concentrated and chromatographed. The benzene eluate on evaporation gave a residue (0.03 g) which on repeated crystallisation from petrol/C_6H_6 mixture afforded an indolenine in fine needles, m.p. 180°, identical with **4b** obtained from echitoserpidine.[10]

TMGA and indolenine **4c** *from* **3c**; *DMAA and indolenine* **4c** *from* **3d**. A soln of **3c** (0.1 g) in 15 ml 3 N aq. HCl and a soln of **3d** (0.25 g) in 25 ml 3 N HCl were separately treated exactly as above. In case of **3c** the ether extract of the products afforded TMGA (0.025 g), while in case of **3d** there was obtained DMAA (0.045 g) which crystallised from petrol in needles, m.p. 68° (Found: C, 60.1; H, 8.09. $C_3H_9O_2$ requires: C, 60.0; H, 8.0%). The aq. fraction of the products from **3c** after usual work up as in the case of **3b** furnished an indolenine (0.03 g) which crystallised from ether, m.p. 199°, identified as **4c** obtained from echitoserpine.[11] Similar work up of the aq. fraction of the mixture from **3d** afforded a solid (0.125 g) which crystallised from ether, m.p. 199°, identical with **4c** obtained from **3c**.

(+)-19-*Hydroxyquebrachamine* (**5b**) *from* **4b**. The indolenine **4b** (0.025 g) was refluxed with $NaBH_4$ (0.05 g) in 1 N MeOH–KOH (10 ml) for 3 hr. The mixture was worked up following the method reported[10] earlier to give a residue (0.02 g) which crystallised from MeOH in fine plates, m.p. 112°, $[\alpha]+125°$, identical with **5b** derived from echitoserpidine.[10]

(+)-11-*Methoxy*-19-*hydroxyquebrachamine* (**5c**) *and the indoline* **6** *from* **4c**. The indolenine **4c** (0.1 g) was reduced with $NaBH_4$ (0.15 g) in MeOH–KOH (25 ml) under reflux for 3 hr. The mixture was worked up in a previously described manner.[11] Tlc of the products revealed the presence of two compounds which were separated by preparative tlc to give an indole (0.06 g) and an indoline (0.015 g) derivative identical with **5c** and **6**, respectively, obtained from echitoserpine.[11]

(−)-19R-*Minovincinine* (**7b**) *and TMGA from* **3b**. Metallic Na (0.06 g) was added portionwise to anhydrous MeOH (20 ml). After the Na had completely dissolved, **3b** (0.1 g) was added to the soln and the mixture was refluxed for 8 hr in an atmosphere of N_2. The products were worked up following the method[10] used for similar reaction of echitoserpidine to give TMGA (0.02 g) and a basic compound (0.02 g), m.p. 135°, $[\alpha]_D^{EtOH}$ − 580°, identical with **7b** obtained also from echitoserpidine.[10]

(−)-19R-11-*Methoxyminovincinine* (**7c**) *from* **3c**, **3d** *and* **3e**. Methanolysis of **3c** (0.05 g) was carried out using 0.03 g Na in 15 ml of dry MeOH. The products were worked up following the same procedure as used for similar reaction of echitoserpine[11] to give TMGA (0.01 g), and a basic compound (0.01 g) identified with **7c** obtained by methanolysis of echitoserpine.[11] Similar methanolysis of **3d** gave only traces of DMAA and **7c**. However, treatment of **3e** (0.06 g) with 0.04 g Na in 15 ml dry MeOH under the conditions used for **3c**, followed by usual work up of the basic fraction gave **7c** (0.025 g).

δ-(delta)-Lactone **8b** *and TMGA from* **3b**. A soln of **3b** (0.1 g) in 10% MeOH–H_2SO_4 (15 ml) was refluxed with excess of Zn dust (0.5 g) for 8 hr. Unreacted Zn was filtered off and the products were further treated and worked up following the method used for echitoserpidine[10] to give TMGA (0.035 g) as the acid component and, as the basic component, a compound (0.04 g) identical with **8b** derived from echitoserpidine[10] under similar conditions.

δ-(delta)-Lactone **8c** *and TMGA from* **3c**, *and* **8c** *and DMAA from* **3d**. **3c** (0.075 g) in 10% MeOH–H_2SO_4 (12 ml) containing 0.25 g Zn dust and a soln of **3d** (0.2 g) in 10% MeOH–H_2SO_4 (30 ml) containing 0.6 g Zn dust were separately treated and worked up exactly as described above in the case of **3b**. Besides TMGA (0.025 g) and DMAA (0.01 g) obtained from the ethereal extracts of the acidic mixtures from **3c** and **3d**, respectively, in each case was obtained the same δ-lactone (0.03 g from **3c**, 0.09 g from **3d**) which was identified with **8c** derived from echitoserpine.[11]

Diol **9b** *from* **8b**. The lactone **8b** (0.03 g) was reduced with LAH (0.2 g) in THF (15 ml) under reflux for 3 hr. The mixture was worked up in the usual manner to give a product which on chromatography gave **9b** (0.02 g) in petrol/EtOAc (2:1) eluate. It crystallised from petrol/EtOAc mixture, m.p. 127–32° (Found: C, 73.25; H, 8.49; N, 8.45. $C_{20}H_{28}N_2O_2$ requires: C, 73.17; H, 8.54; N, 8.54%), $[\alpha]_D^{EtOH}$ +69°; λ_{max} 248 and 302 nm (log ϵ 3.85 and 3.47); ν_{max}^{KBr} 3480 (OH), 3300 (NH), 2780 and 2720 (Bohlmann bands) cm^{-1}; *m/e* (relative intensity): 328 ($M^{+\cdot}$, 22.6), 283 (4.2), 271 (3.6), 270 (20.6), 198 (4.9), 141 (8.2) and 140 (100); m* 222.3 and 72.6.

Diol **9c** *from* **8c**. The δ-lactone **8c** (0.1 g) was treated with LAH (0.5 g) in THF (25 ml) as above and the mixture was worked up as usual and chromatographed. This furnished **9c** (0.065 g) which crystallised from petrol/EtOAc mixture in rectangular plates, m.p. 189° (Found: C, 70.45; H, 8.36; N, 7.75. $C_{21}H_{30}N_2O_3$ requires: C, 70.39; H, 8.38; N, 7.82%) $[\alpha]_D^{EtOH}$ + 62.5°; λ_{max} 247 and 304 nm (log ϵ 3.76 and 3.69); ν_{max}^{KBr} 3530 (OH), 3400 (NH), 2775 and 2715 (Bohlmann bands) cm^{-1}; *m/e* (relative intensity): 358 ($M^{+\cdot}$, 43), 313 (8), 300 (12.7), 198 (6), 174 (3.6), 173 (2), 160 (5), 141 (12.7), 140 (100) and 122 (3.6); m* 265, 251 and 65.3.

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REFERENCES

[1]A. B. Ray and A. Chatterjee, *J. Indian Chem. Soc.* **40**, 1044 (1963); **41**, 638 (1964).
[2]T. R. Govindachari, N. Viswanathan, B. R. Pai and T. S. Savitri, *Tetrahedron Letters* 901 (1964); *Tetrahedron* **21**, 295 (1965).
[3]A. Chatterjee, P. L. Majumder and A. B. Ray, *Tetrahedron Letters* 159 (1965).
[4a]B. C. Das, K. Biemann, A. Chatterjee, A. B. Ray and P. L. Majumder, *Ibid.* 2239 (1965); [b]*Ibid.* 2483 (1966).
[5]A. B. Ray and A. Chatterjee, *Ibid.* 2763 (1968).
[6]L. A. Mitscher, A. B. Ray and A. Chatterjee, *Experientia* **27**, 16 (1971).
[7]A. Chatterjee, P. L. Majumder and B. C. Bas, *Chem. Ind.* 1388 (1969).
[8]P. L. Majumder, T. K. Chanda and B. N. Dinda, *Ibid.* 1032 (1973).
[9]A. B. Ray and S. C. Dutta, *Experientia* **29**, 1337 (1973).

[10]P. L. Majumder and B. N. Dinda, *Phytochemistry* **13**, 645 (1974).
[11]P. L. Majumder, B. N. Dinda, A. Chatterjee and B. C. Das, *Tetrahedron* **30**, 2761 (1974).
[12]S. C. Dutta and A. B. Ray, *Indian J. Chem.* **13**, 98 (1975).
[13]A. Chatterjee and S. Mukhopadhyay, *Ibid.* **15B**, 183 (1977).
[14]A. Chatterjee, S. Mukhopadhyay and J. N. Shoolery, *Ibid.* **16B**, 67 (1978).
[15]M. Hesse, *Indolalkaloide in Tabellen.* Springer, Berlin (1964, 1968).
[16]N. Neuss, *Physical Data of Indole and Dihydroindole Alkaloids*, Edn, Ely Lilly, Indianapolis, Indiana (1962).
[17]B. Pyuskyulev, I. Kompiś, I. Ognyanov and G. Spitteller, *Coll. Czech. Chem. Commun.* **32**, 1289 (1967).
[18]H. Budzikiewicz, C. Djerassi and D. H. Williams, *Structure Elucidation of Natural Products by Mass Spectrometry*, Vol. 1, p. 133. Holden-Day, San Francisco (1964).
[19]C. Djerassi, H. Budzikiewicz, J. M. Wilson, J. Gosset, J. Le Men and M.-N. Janot, *Tetrahedron Letters* 235 (1962).
[20]W. Döpke and H. Meisel, *Ibid.* 749 (1970).
[21]W. Döpke, H. Meisel and G. Spiteller, *Ibid.* 6065 (1968).