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ALKALOIDS FROM *ASPIDOSPERMA AUSTRALE* MÜLL. ARGOV.

THE STRUCTURE OF OLIVACINE AND *u*-ALKALOID C (GUATAMBUINE)

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Abstract—From *A. australe* the following alkaloids were isolated: from the aereal bark olivacine and (±) guatambuine; from the heartwood, olivacine and a base m.p. 186–188° present in very small amounts; from root bark, olivacine, (−) guatambuine (*u*-alkaloid C), (+) guatambuine and uleine; from root heartwood, olivacine. (±) Guatambuine is N-methyl-tetrahydro-olivacine. The products of the Hofmann degradation of the last base are identical with those obtained from uleine, a result which correlates both bases and definitely establishes the structure of (±) guatambuine (III) and olivacine (I).

Aspidosperma australe Mull. Argov. is a species with a wide distribution in South America. It is found in the northern part of Argentina, the plains of Bolivia, in Paraguay and in the Southern and Central Brazil.

The only recorded chemical study on this species is the work done by Orazi, who found aspidospermine.[1]

From plant material collected around Corumba (Brazil) and Loreto (Province of Misiones, Argentina), the following known alkaloids were isolated from *A. australe:* from the stem bark, olivacine and (±) guatambuine; from the heartwood, olivacine and a base m.p. 186–188° present in very small amounts. From root bark, olivacine, (+) guatambuine (*u*-alkaloid C) and uleine. In a new sample of root bark (−) guatambuine was found. The root heartwood yielded olivacine.

Paper chromatography showed that uleine was also present in heartwood and root wood and guatambuine in root wood. Asidospermine could not be detected in any of these sources.

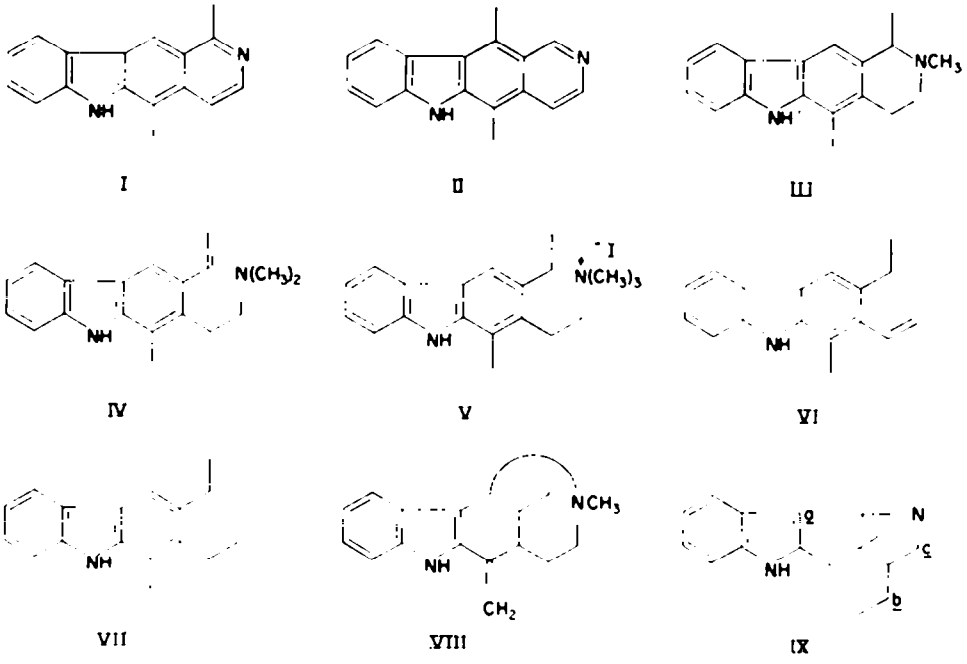
These alkaloids have been isolated from other species of Aspidosperma, olivacine from *A. olivaceum*[2] and *A. longipetiolatum*[3]; uleine from *A. ulei*[4] and *A. olivaceum*[2] and (−) guatambuine from *A. ulei* (where it was named *u*-alkaloid C)[4] and from *A. longipetiolatum*.[3]

The experiments described in this paper[5] showed that olivacine has structure (I) and is a member of the class of pyridine–carbazole alkaloids to which ellipticine (II)

[1] O. O. Orazi, *An. Asoc. Quim. Arg.* **34**, 158 (1946). Dr. Orazi has informed us that the plant specimen employed in his work has now been identified as *A. polyneuron.*
[2] J. Schmutz and F. Hunziker, *Pharm. Acta Helv.* **33**, 341 (1958).
[3] P. Carvalho-Ferreira, G. B. Marini Bettolo and J. Schmutz, *Experientia* **15**, 179 (1959); P. Carvalho-Ferreira and G. B. Marini Bettolo, *Ann. Chim.* **49**, 869 (1959).
[4] J. Schmutz, F. Hunziker and R. Hirt, *Helv. Chim. Acta* **40**, 1189 (1957); J. Schmutz and F. Hunziker, *Helv. Chim. Acta* **41**, 288 (1958).
[5] Advance information was given by M. A. Ondetti and V. Deulofeu, *Tetrahedron Letters* No. 7, 1 (1959); *Ibid.* No. 1, 18 (1960).

and methoxy-ellipticine also belong.[6] (−) Guatambuine is N-methyl-tetrahydro-olivacine (III) and is easily obtained by catalytic hydrogenation of the methiodide of olivacine.

The reverse transformation was also effected; (−) and (+) guatambuine were dehydrogenated to olivacine, by boiling with palladium in diphenyl ether, confirming again that both alkaloids have the same carbon skeleton.



The structure of guatambuine follows from its Hofmann degradation. When the methiodide of (+) guatambuine was boiled with strong alkali in ethanol, two bases were obtained that could be separated by chromatography on alumina. They were difficult to crystallize and after the separation, without any further purification, were treated with methyl iodide and transformed into two different methiodides.

One methiodide melted at 262–263° and gave a typical carbazole U.V. spectrum. The base from which this methiodide derives was a saturated compound. When it was submitted to catalytic hydrogenation prior to the treatment with methyl iodide, the same derivative melting 262–263° was obtained.

The other base gave a methiodide melting at 284–285°. This methiodide had a modified carbazole U.V. spectrum and its I.R. spectrum showed the bands characteristic of a vinyl group. When this base was first hydrogenated and treated with methyl iodide, it yielded a new methiodide, m.p. 287–288°, with a typical carbazole U.V. spectrum, showing that in the unsaturated methiodide there was conjugation between the vinyl group and the carbazol nucleus.

This new methiodide (V) was found to be identical with a methiodide m.p. 300–303°, obtained by Schmutz *et al.*[4] in their studies of the Hofmann degradation of

[6] S. Goodwin, A. F. Smith and B. C. Horning, *J. Amer. Chem. Soc.* **81**, 1903 (1959); R. B. Woodward, G. A. Iacobucci and F. A. Hochstein, *Ibid.* **81**, 4434 (1959).

uleine. The identity of both methiodides was proved in the following way: (a) a methiodide prepared by us from uleine following the method of Schmutz and co-workers[4] had a m.p. 295 296° and when mixed with that obtained from guatambuine (m.p. 287–288°) gave a m.p. 288–290°. Both methiodides gave identical U.V. and I.R. spectra; (b) the methiodide m.p. 287–288° from guatambuine, on further degradation, as described in the experimental part, loses one atom of nitrogen and gives products (VI) and (VII), identical with those obtained from the methiodide from uleine.

Büchi and Warnhoff[7] have shown without doubt that the compound obtained after two Hofmann reactions from uleine has structure (VI) and this led to the structure (VIII) for the alkaloid. This means that the structure of the methiodide, which is a common degradation product of uleine and guatambuine must be V and that the vinyl base obtained from guatambuine methiodide is IV. This is proof of structure (III) for the last alkaloid and of structure (I) for olivacine. Structure (I) has already been suggested by Woodward and Iacobucci[8] as a result of their proposal of a common intermediate (IX) in the biogenesis of ellipticine (II) and uleine (VIII). The same intermediate could play a role in the genesis of olivacine (I) (Bond *c*--N is broken, *c* joins *a*; *b* joins N). Structure (I) was also proposed by Marini Bettolo and Schmutz[9] because of the similarity of certain physical properties of olivacine (U.V. spectrum, pK) when compared to synthetic 4-methyl-pyridocarbazole, and also on biogenetical grounds, based on the open chain intermediate proposed by Wenkert[10] as a link in the formation of indole alkaloids.

Structure (I) for olivacine has been fully confirmed by its synthesis by Schmutz and Wittwer[11] and by Wenkert.[12]

Guatambuine is the product of reduction and N-methylation of olivacine. The asymmetric carbon atom is located in a position which explains why the Hofmann degradation of (±) guatambuine gives the same inactive methiodide (V) as the racemic base. It is interesting that in *A. australe* two optical isomers and the racemic form of guatambuine have been found. While reduction of the pyridine ring may be a non-enzymatic process (which could explain the formation of the racemic form), it is obvious that this is not the case for the N-methylation, which must proceed through some specific enzyme system present in the plant.

EXPERIMENTAL

All m.p. are uncorrected and were determined in the Kofler block, except when specified. Paper chromatography was employed to follow the distribution of alkaloids in the extracts and in the fractions eluted in column chromatography. The system used was a mixture of methyl-isobutyl-ketone: butanol (7:3) saturated with McIlvaine buffer, pH 4. The R_f of the alkaloids were: olivacine: 0·13; guatambuine (*u*-alkaloid C): 0·39; uleine: 0·69. Dragendorff reagent was used to develop the spots. Ultra-violet spectra, except when noted, were recorded in absolute ethanol.

Extraction of the alkaloids

Root bark. Two kilogrammes of ground root bark were well extracted with 4·5 l. methanol, repeating the extraction five times, and a sixth time with methanol containing 2% acetic acid. The

[7] G. Büchi and E. W. Warnhoff, *J. Amer. Chem. Soc.* **81**, 4433 (1959).
[8] R. B. Woodward and G. A. Iacobucci, Private communication
[9] G. B. Marini Bettolo and J. Schmutz, *Helv. Chim. Acta* **42**, 2146 (1959).
[10] E. Wenkert, *Experientia* **15**, 165 (1959); E. Wenkert and N. V. Bringi, *J. Amer. Chem. Soc.* **81**, 1474 (1959).
[11] J. Schmutz and H. Wittwer, *Helv. Chim. Acta* **43**, 793 (1960).
[12] E. Wenkert, Paper presented at the IUPAC Symposium: *The Chemistry of Natural Products*, Australia, August 1960; *J. Amer. Chem. Soc.* In press.

combined methanolic extracts were concentrated in vacuum to 600 ml and poured with good agitation into a mixture of 1200 ml water and 200 ml acetic acid. An insoluble product appeared which was filtered (Super-cel filter-aid), and the residue was washed well with 15% acetic acid.

The filtrate was extracted twice with petroleum ether (b.p. 40–60°), cooled to 5° and made alkaline to pH 10–11 with 50% sodium hydroxide, avoiding an increase of temperature. A gummy precipitate formed, which was separated from the solution. The alkaline solution was extracted with ether until it gave a negative Mayer's test.

The gummy precipitate was shaken with ether several times. The ethereal extracts were joined (6 l. in total), filtered, dried with sodium sulfate and concentrated to 400 ml. A yellow solid precipitated, which after filtering and drying weighed 4 g, m.p. 309–314°. The filtrate was again concentrated to 100 ml, when a new yellow precipitate was formed and collected, 1·1 g, m.p. 220–240°. The filtrate was then concentrated to dryness, the residue weighing 10 g.

The insoluble residue from the gummy precipitate, after the extraction with ether, was dissolved in a mixture of 600 ml water and 100 ml acetic acid, filtered from an insoluble residue and the filtrate made alkaline to pH 10–11, when a precipitate formed again. Without separation, precipitate and solution were extracted with ether and the process described above was repeated.

On concentration the ethereal extract yielded a first crop of yellow crystals that after well washing with chloroform, weighed 507 mg, and melted 308–312°. On further concentration, a second crop of 91 mg, m.p. 234–237°, was collected. On evaporation to dryness, a residue of 1500 mg was obtained.

Olivacine (I). The two batches of yellow crystals melting 308–314° were united and recrystallized several times from boiling ethanol. Yellow short prisms melting 314–316°, $(\alpha)_D^{24°}$: 0° (Pyridine). U.V. spectrum: λ_{max} 224 mμ (ε 24,300); 238 mμ (21,300); 276 mμ (50,600); 287 mμ (71,400); 292 mμ (67,000); 314 mμ (4600); 329 mμ (6250); 375 mμ (4600). In acid (HCl) absolute ethanol λ max 242 mμ (28,600); 306 mμ (77,000); 350 mμ (6200). (Found: C, 82·8; H, 5·7; N, 11·3. Calc. for $C_{17}H_{14}N_2$: C, 82·8; H, 5·7; N, 11·3).

All these data are in agreement with the properties of olivacine described by Schmutz and Hunziker.[3]

These data are almost identical with those of ellipticine, but I.R. and NMR-spectra of both bases were different.[4]

(−) *Guatambuine* (u-*alkaloid* C) (III). Recrystallization of the 1·1 g of the crude product melting 220–240° described above, from ethanol 95%, gave crystals with m.p. 235–237°. They were mixed with those melting 234–235° from the second batch and recrystallized (700 mg) several times from ethanol. Long prisms (32 mg) melting 245–248°. $(\alpha)_D^{20°}$ −112° ±3° (*c*, 0·485. Pyridine). U.V. spectrum λ_{max} 240 mμ (ε 41,300); 250 mμ (31,300); 262 mμ (22,700); 299 mμ (19,300); 330 mμ (4300). No displacement of the bands was observed in acid absolute ethanol. I.R. spectrum in potassium bromide was identical to the I.R. spectrum of (−) guatambuine (*u*-alkaloid C). (+) Guatambuine was also obtained when 10 g of the residue left on evaporation of the ethereal extracts, from which olivacine and crude (+) guatambuine have already been separated, were dissolved in 20 ml warm benzene and the solution was cooled. Two hundred and fifty miligrammes of crystals m.p. 227–231° were obtained, which on recrystallization from ethanol melted 243–244° and were characterized as (−) guatambuine.

(−) *Uleine* (VIII). The benzene solution remaining after the separation of (−) guatambuine was chromatographed on 340 g of alumina (Woelm, activity II–III) and eluted with benzene, benzene chloroform, chloroform and chloroform–methanol. When chloroform was employed, fractions giving on paper chromatography one alkaloidal spot, R_f 0·69, were collected. On concentration of those fractions, crystals melting 72–76° (Kofler) and 118–121° (capillar) were obtained. $(\alpha)_D^{24°}$ +11·5 chloroform. U.V. spectrum: λ_{max} 307–308 mμ (ε 17,000); 316 mμ (17,000). Schmutz *et al.*[4] give a m.p. 76–80° with further solidification and melting at 115–118°.

Uleine hydrochloride. Prepared as described[4] it had a m.p. 239–241° in agreement with the m.p. 241–242° given in the literature. U.V. (ethanol 95%) λ_{max} 308–309 mμ (ε 19,300). (Found: C, 68·1; H, 7·7; N, 9·2. Calc. for $C_{18}H_{22}N_2Cl_2H_2O$: C, 67·4; H, 7·8; N, 8·7).

The methiodide melted 204–206°, as described for uleine methiodide.[4]

Root wood. Olivacine. Three hundred grammes of the heartwood from the root of *A. australe* was extracted and worked as described from the root's bark. Pure olivacine (150 mg) m.p. 315–317° were isolated. The residues remaining after the removal of olivacine gave on paper chromatography spots corresponding to olivacine, guatambuine and uleine, and were not further examined.

Stem bark. Olivacine (±) guatambuine and uleine. Ground aereal bark (1·8 kg) from *A. australe* were extracted as has been described for the root's bark. The ethereal extract on first concentration gave 7·05 g of crude olivacine (m.p. 308–314°) which was identified in the usual way.

On further concentration, another crop of crystals melting 210–220° (795 mg) was obtained. Evaporation was continued to dryness, leaving a residue of 4·59 g. When this residue was treated with chloroform, the largest part dissolved, leaving an insoluble portion of 380 mg (m.p. 218–222°), which was united to the second crop. On several recrystallizations from ethanol 95%, 240 mg of long prisms, m.p. 227–228°, were obtained, $(\alpha)_D^{25°} \pm 0°$ U.V. spectrum λ_{max} 240 mμ (ε 41,000); 250 mμ (30,700); 262 mμ (22,700); 299 mμ (19,800); 330 mμ (4370). I.R. spectrum, recorded on a potassium bromide pellet, was identical to that of (+) guatambuine.

The remaining chloroform solution was then subjected to chromatography in a column containing 140 g of neutral alumina and eluted with chloroform containing increasing amounts of methanol. The first fractions eluted with chloroform 0·2% methanol, gave on evaporation and recrystallization from methanol, 14 mg of a base m.p. 74–80° (104° capillary), which gave a hydrochloride m.p. 239–241° (sintering from 234°) which did not depress the m.p. of pure uleine hydrochloride. The U.V. spectra were also identical. The middle and last fractions, eluted with chloroform 0·2% methanol, gave a spot showing the presence of guatambuine. They were collected, evaporated and recrystallized from 95% ethanol; long prisms melting 225–227°; $(\alpha)_D^{25°} \pm 0°$. U.V. spectrum identical to (±) guatambuine.

Root bark. (+) Guatambuine. A sample of 2 kg of root bark of *A. australe* collected near Corumbá (Brazil) was extracted and processed as described. The first crop of crystals from the ether extracts yielded 6 g of rather pure olivacine m.p. 316–320°, and the second crop, 1·65 g of impure crystals, melting 213–233°. The last crystals after several crystallizations from ethanol 95%, gave 520 mg of long prisms m.p. 247–248°. $(\alpha)_D^{25°}$ +106° ± 2° (Pyridine). U.V. spectrum λ_{max} 240 mμ (ε 41,000); 250 mμ (31,000); 262 mμ (22,200); 299 mμ (19,200).

Twenty-five milligrammes of the above base, mixed with the same amount of (+) guatambuine, gave on crystallization from ethanol, 35 mg of the racemic base. M.p. 224–225°. $(\alpha)_D^{25°} \pm 0°$. From the mother liquors of the obtention of (+) guatambuine, 40 mg of racemic (±) guatambuine were obtained. M.p. 224–225°; $(\alpha)_D^{25°} \pm 0°$. The residue of the ether extract, after separation of the olivacine and guatambuine, showed on paper chromatography the presence of those bases and uleine. It was not further examined.

Heartwood. Olivacine, base m.p. 186–188°. Two kilogrammes of well ground heartwood were extracted with methanol and worked up in the usual way. The ether extracts on concentration yielded 460 mg of impure olivacine, m.p. 306–312°, which after several recrystallizations from ethanol 95°, 250 mg of pure olivacine with m.p. 315–317° were obtained. After separation of the olivacine, the ether solution was evaporated to dryness and a residue of 3·5 g was obtained. This residue was treated with chloroform, filtered from an insoluble crystalline fraction, consisting of impure olivacine (217 mg, m.p. 307–310°) and the chloroform solution was chromatographed on a column of 80 g of alumina (activity II–III).

The first fractions eluted with chloroform gave on paper chromatography one spot, with R_f 0·62 which was different from the usual alkaloids. Evaporation of these fractions gave a very small amount of a base, which recrystallized several times from methanol, melted 186–188°, with λ_{max} 305 mμ (ε 17,000, calculated for a molecular weight 266 identical to uleine), which gives a yellow brown colour with Keller's reagent, a weak violet colour with ceric (III) sulphate and a permanent pink colour with concentrated sulphuric acid. U.V. spectrum and colour reactions are very similar to those of uleine.

Paper chromatography of the solutions left after separation of the crystalline alkaloids showed that uleine was present in the extracts.

Olivacine methiodide. Five hundred milligrammes of olivacine were dissolved in the minimum amount of boiling ethanol 95% and 5 ml methyl iodide added. The olivacine methiodide starts to precipitate in crystalline condition very soon. After 30 min the suspension was cooled and 600 mg of yellow long prisms collected. Recrystallization from methanol gave long prisms melting above 340°, with darkening from 315° (Found: C, 55·2; H, 4·4; N, 7·4; I, 32·1. $C_{17}H_{14}N_2.CH_3I$ requires C, 55·6; H, 4·4; N, 7·22; I, 32·6).

N-methyl-tetrahydro-olivacine or (±) guatambuine (III). Four hundred milligrammes of olivacine methiodide were suspended in 300 ml ethanol 95%, 80 mg of platinum oxide catalyst added and

reduced for 4 hr at 3 atm, the solid dissolving in about 2·5 hr. After filtering, the solution was concentrated to 25 ml, 275 ml water added, alkalinized with 2 N sodium carbonate and extracted with ether. The ether extract was well dried, evaporated, and the residue, when crystallized from ethanol 95%, gave 201 mg of a crude product melting 220–223°. After several recrystallizations from ethanol, it melted at 223–225°. Its U.V. spectrum had λ_{max} 240 mμ (ε 41,100); 250 mμ (30,700); 262 mμ (22,200); 299 mμ (19,200); 330 mμ (4120). With ethanol hydrochloric acid, the typical hyperchromic effect given by guatambuine was observed, without displacement of the maxima. I.R. spectrum identical to (±) guatambuine. (Found: C, 82·3; H, 7·9; N, 10·6; NCH_3, 5·3; $C(CH_3)_2$, 11·1; N.E., 262. $C_{18}H_{20}N_2$ requires C, 81·7; H, 7·6; N, 10·6; NCH_3, 5·6; 1 $C(CH_3)_2$, 11·3; N.E., 264).

Olivacine by dehydrogenation of (±) guatambuine. One hundred and twenty-five milligrammes of Adams platinum catalyst were suspended in 5 ml diphenyl ether and reduced. One hundred milligrammes of (±) guatambuine was added and while nitrogen was bubbled the suspension was boiled for 80 min. It was then cooled, ether and 2 N hydrochloric acid were added until two phases formed, and the water phase was well extracted with ether. It was then made alkalien to pH 11 and extracted again with ether. This second ether extract was dried, evaporated, and the crystalline residue suspended in chloroform and filtered. The 25 mg of crude crystals collected were recrystallized from ethanol; m.p. 313–316°. They were identified as olivacine by mixed m.p. and U.V. spectrum.

(±) *Guatambuine methiodide.* To 1·1 g of (±) guatambuine dissolved in boiling ethanol, 10 ml of methyl iodide were added and boiling continued for 30 min. After cooling, 1·5 g of long prisms could be collected. M.p. 299–301°, which was not changed by further crystallization. (Found: N, 6·8; I, 30·8. $C_{18}H_{20}N_2.CH_3I$ requires: N, 6·8; I, 31·2).

Hofmann degradation of (±) guatambuine methiodide. Guatambuine methiodide (1·71 g) was suspended in 400 ml ethanol containing 40 g of potassium hydroxide and boiled for 6 hr. The solution was then concentrated *in vacuo* to 50 ml, 350 ml of water were added and extracted with ether. The ether extracts, after washing with water and drying, were concentrated to dryness, when a residue of 1·24 g was obtained. Paper chromatography showed the presence of two bases, which were dissolved in chloroform and submitted to column chromatography, on 80 g of alumina.

The column was first eluted with chloroform and then with chloroform containing increasing amounts of methanol. When chloroform with 0·05% methanol was employed, the first fractions contained a base which gave a spot with R_f 0·61. When the methanol content was increased (0·5%) a new base, with R_f 0·34, was eluted.

The fractions containing the first base were joined and evaporated, giving a syrup which was dissolved in a small amount of ethanol, an excess of methyl iodide added and refluxed for 15 min. Five hundred and sixty-seven milligrammes of crude methiodide, m.p. 257–258° were obtained. After several recrystallizations from ethanol 95%, it gave long prisms melting 262–263°; λ_{max} 240 mμ (ε 44,800); 250 mμ (32,600); 260 mμ (20,900); 297 mμ (16,700). When this same base was subjected without further purification to hydrogenation with Adams catalyst in ethanol and treated with methyl iodide, the same methiodide product was obtained (Mixed m.p.; U.V. spectrum). (Found: C, 56·9; H, 6·2; N, 6·4; I, 30·5. $C_{20}H_{23}IN_2$ requires: C, 57·1; H, 6·0; N, 6·6; I, 30·1).

The fractions containing the base with R_f 0·34 were also evaporated and the residue boiled with methyl iodide in ethanol. Three hundred and ninety-two milligrammes of *methiodide* were obtained, m.p. 278–279°. Recrystallized several times from 95% ethanol, long prisms m.p. 284–285° were collected. U.V. spectrum λ_{max} 241–242 mμ (ε 39,000); 280 mμ (26,800). (Found: C, 57·4; H, 5·7; N, 6·9; I, 30·3. $C_{20}H_{23}IN_2$ requires: C, 57·1; H, 6·0; N, 6·6; I, 30·1).

When the residue obtained by evaporation of the fractions with base R_f 0·34 was hydrogenated with Adams catalyst in ethanol and then treated with methyl iodide, the methiodide (V) after several recrystallizations from ethanol melted at 287–288°. U.V. spectrum λ_{max} 240 mμ (ε 47, 500); 250 mμ (31,600); 260 mμ (20,000); 297 mμ (21,200). (Found: C, 57·1; H, 6·4; N, 6·2; I, 30·3. Calc. for: $C_{20}H_{25}IN_2$: C, 56·8; H, 6·4; N, 6·6; I, 30·0).

This methiodide did not depress the m.p. and gave a spectrum identical with that of the methiodide obtained by subjecting uleine methiodide to Hofmann degradation according to Schmutz *et al.*[4] who give m.p. 300–302°.[13]

Hofmann degradation of the methiodide m.p. 287–288°. Three hundred and fifty milligrammes of

[13] Prof. G. Büchi has kindly informed us that in his laboratory a m.p. 281–285° (Kofler) was observed for this methiodide when recrystallized from ethanol–water.

the methiodide when treated as described by the Swiss authors[4] gave 120 mg of the crystalline methine m.p. 66–68° (VI). U.V. spectrum λ_{max} 248 mμ (ε 43,300); 299 mμ (19,500). (Found: C, 85·9; H, 8·0; N, 5·9. Calc. for $C_{17}H_{17}N$: C, 86·7; H, 7·3; N, 5·9).

This compound gave no depression in the m.p. when mixed with the similar compound obtained from uleine (m.p. 69–70·5°). I.R. spectra were identical.

Hydrogenation of the last compound and purification of the reduced product by column chromatography on alumina gave a substance m.p. 83–85° (VII). λ_{max} 240 mμ (ε 45,100); 248 mμ (30,800); 261 mμ (18,700); 298 mμ (19,600).

This substance did not depress the m.p. when mixed with the compound obtained from uleine (m.p. 76·5–77°). U.V. and I.R. spectra were identical.

Hofmann degradation of (±) *guatambuine.* The methiodide of (±) guatambuine m.p. 301–302° $(\alpha)_D^{22°}$ +47·0° (Pyridine : water, 5 : 1) was treated exactly as described for the methiodide of the racemic base. Two bases were obtained with R_f 0·61 and 0·34, which on treatment with methyl iodide gave two methiodides m.p. 258–260°, $(\alpha)_D^{22°}$ ±0° and m.p. 284–285°; $(\alpha)_D^{22°}$ ±0° identical to those from the degradation of (±) guatambuine methiodide. (No depression in m.p. and identical U.V. spectra.)

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