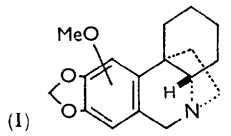
225. *The Alkaloids of the* Amaryllidaceae. *Part VIII.*[1] *The Structure of Buphanitine.*

By A. Goosen and F. L. Warren.

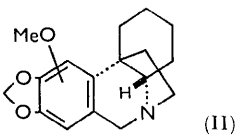
Experiments with buphanitine (dihydroxybuphanitane) indicate that it has the previously unknown 5 : 10b-ethanophenanthridine skeleton (II) with *cis*-B/C rings.

Buphanitine, $C_{17}H_{21}O_5N$, a major alkaloid from *Boöphone disticha*, contains a tertiary nitrogen atom and the formula has been expanded to $C_{15}H_{14}N(O_2CH_2)(OMe)(OH)_2$.[1,2] The methoxyl and the methylenedioxy-groups were seemingly in a benzene ring since the alkaloid showed strong absorption at 1622 cm.$^{-1}$.[3] Proof of this was obtained by treatment with sodium in butan-1-ol to give demethoxybuphanitine, $C_{16}H_{19}O_4N$.

Buphanitine is not reduced by hydrogen and Adams's catalyst and so it is tetracyclic (plus the methylenedioxy-ring.). To establish the nature of the basic ring system, the two hydroxyl groups have been eliminated to yield a new compound buphanitane, $C_{17}H_{16}N(O_2CH_2)\cdot OMe$, which was different from powellane (I).



(I)

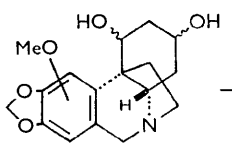


(II)

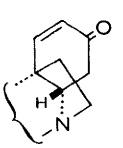
Two tetracyclic ring structures are known for this series of alkaloids, namely, pyrrolo[*de*]phenanthridine and 5,10b-ethanophenanthridine. The alkaloid seemingly had not the pyrrolo[*de*]phenanthridine structure since it was stable to oxidation with potassium ferricyanide and mercuric acetate,[4] and both the Hofmann and the von Braun reaction gave back the starting material. The alkaloids known to have the 5,10b-ethanophenanthridine structure were recently shown to have *trans*-B/C rings and to include both enantiomorphic forms.[5] It seemed likely that buphanitane possessed the previously unknown structure (II) (or its mirror image) with *cis*-B/C rings.

The hydroxy-groups in buphanitine (dihydroxybuphanitane) were secondary in that the alkaloid gave a diacetate [2] and was not readily dehydrated.

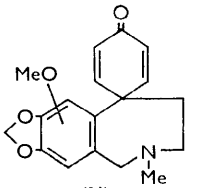
Buphanitine (III) possesses 1,3-dihydroxy-groups since it is unattacked by periodic acid and oxidation with Meerwein–Pondorff reagent gave buphanitenone (IV), which showed in the infrared spectrum a conjugated carbonyl group.



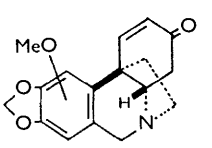
(III)



(IV)



(V)



(VI)

Buphanitenone on catalytic reduction with 10% palladium–charcoal gave buphanitanone, whose infrared spectrum showed a non-conjugated ketone in a six-membered ring. By the Huang-Minlon modification of Wolff–Kishner reaction this ketone gave buphanitane (II), m. p. 143—144°, yielding a picrate, m. p. 210—213°. This substance was different

[1] Part VII, Goosen and Warren, preceding paper.
[2] Bates, Cooke, Dry, Goosen, Krüsi, and Warren, *J.*, 1957, 2537.
[3] Fales and Wildman, *J. Amer. Chem. Soc.*, 1958, **80**, 4397.
[4] Fales, Warnhoff, and Wildman, *J. Amer. Chem. Soc.*, 1955, **77**, 5885.
[5] Jeffs, Warren, and Wright, *J.*, 1960, 1090.

from powellane (I), m. p. 113—115° (picrate 213—215°), which for comparison was prepared from buphanidrine.[6]

Buphanitenone gave a methiodide which readily underwent the Hofmann reaction to give an optically inactive methine, m. p. 131—132°, showing a strong band at 1663 cm.$^{-1}$. This substance has the same properties as powellenone methine which has been assigned structure (V)[6] and this confirms the stereochemistry envisaged for the skeleton of buphanitine. The Hofmann reaction on powellenone, the stereochemistry of which has recently been defined as in (VI),[5] and on buphanitenone, destroys the asymmetry to yield the same product (V). The structure of (IV) necessitates that buphanitine is 1,3-dihydroxybuphanitane (III) or its mirror image.

Reduction of buphanitenone with lithium aluminium hydride gave buphanitenol, which was reoxidised to buphanitenone with manganese dioxide, so that reduction was not accompanied by allylic rearrangement. Reduction of buphanitanone with lithium aluminium hydride, or catalytic reduction of α-buphanitenol, gave α-buphanitanol. One-stage catalytic reduction of buphanitenone in the presence of platinum gave β-buphanitanol.

Experimental

Optical rotations refer to chloroform solutions unless otherwise stated.

Buphanitenone (IV).—(*a*) Buphanitine (0·5 g.), aluminium isopropoxide (3 g.), and cyclohexanone (16 ml.) were heated under reflux in nitrogen. The product was cooled, sodium hydroxide added (20 ml.), and the whole extracted with chloroform. The chloroform solution was extracted with 2N-hydrochloric acid (4 × 30 ml.). The acid solution was washed with ether (2 × 30 ml.), basified with sodium carbonate solution, and extracted with chloroform. The chloroform solution gave a gum which solidified on trituration with ether. The product in acetone was decolorised with charcoal and crystallised to give *buphanitenone* as rhombohedra, m. p. 184—185°, $[\alpha]_D^{20}$ +34° (*c* 0·5) (Found: C, 68·2; H, 6·0; N, 5·1. $C_{17}H_{17}O_4N$ requires C, 68·2; H, 5·7; N, 4·7%). A Nujol mull showed a strong band at 1670 cm.$^{-1}$.

(*b*) Manganese dioxide (1·5 g.), prepared according to Attenburrow *et al.*,[7] was stirred for 6 hr. at 20° with α-buphanitenol (100 mg.). The product was twice crystallised from acetone, to give buphanitenone, m. p. and mixed m. p. 184—185°.

β-*Buphanitanol*.—Buphanitenone (100 mg.) in methanol was shaken with hydrogen and Adams catalyst. The product crystallised from acetone to give β-*buphanitanol* as rhombohedra, m. p. 130—140° with resolidification and m. p. 209—212°, $[\alpha]_D^{22}$ (*c* 1 in EtOH) (Found, after drying at 20°/0·01 mm.: C, 63·6; H, 7·4. $C_{17}H_{21}O_4N,H_2O$ requires C, 63·5; H, 7·2%). A sample sublimed at 170°/0·01 mm. had m. p. 209—212° (Found: C, 63·8; H, 6·8%). A Nujol mull showed an absorption at 3650 cm.$^{-1}$.

Buphanitanone.—Buphanitenone (200 mg.) in ethanol (40 ml.) was shaken with hydrogen and prereduced 10% palladium–charcoal. One mol. of hydrogen was rapidly absorbed. The product crystallised from acetone to give *buphanitanone* as rhombohedra, m. p. 174—177°, $[\alpha]_D^{20}$ −5·6° (*c* 1) (Found: C, 68·0; H, 6·5. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4%). A Nujol mull showed a strong band at 1718 cm.$^{-1}$.

Buphanitenone Methiodide.—Buphanitenone (200 mg.) in methanol (10 ml.) was heated with methyl iodide (1 ml.) for 30 min. and the product crystallised from methanol to give the *methiodide* as needles, m. p. 241—243° (Found: C, 48·1; H, 5·1. $C_{17}H_{17}O_4N,CH_3I,\frac{1}{2}H_2O$ requires C, 47·9; H, 4·9%).

Buphanitenone Methine (V).—Buphanitenone methiodide (300 mg.) was heated with 3% sodium hydroxide solution (15 ml.) for 10 min., cooled, and extracted with benzene. This process was repeated until the aqueous solution gave a negative test with Meyer's reagent. The benzene extracts gave a gum which, when triturated with, and crystallised from, acetone, gave *buphanitenone methine* as rhombohedra, m. p. 131—132°, $[\alpha]_D^{20}$ 0° (*c* 1) (Found: C, 68·5; H, 6·1. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1%). A Nujol mull showed a strong band at 1663 cm.$^{-1}$.

α-*Buphanitenol*.—Buphanitenone (300 mg.) was boiled for 12 hr. with lithium aluminium

[6] Wildman, *J. Amer. Chem. Soc.*, 1958, **80**, 2567.
[7] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1104.

hydride (1 g.) in ether (100 ml.). Ethyl acetate was added, then 6N-sodium hydroxide, and the ether was distilled off. The solution was extracted with chloroform; the chloroform extract gave a gum which, when triturated with, and crystallised from, acetone, gave *α-buphanitenol*, m. p. 167—170°, $[\alpha]_D^{20}$ 0° (*c* 1) (Found: C, 67·6; H, 6·5. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4%). It showed in carbon tetrachloride a band at 3650 $cm.^{-1}$.

α-Buphanitanol.—(*a*) Buphanitenol (200 mg.) in methanol (30 ml.) was shaken with hydrogen in the presence of Adams catalyst for 3 hr. *α-Buphanitanol* crystallised from acetone as rhombohedra, m. p. 211—213°, $[\alpha]_D^{22}$ 0° (*c* 1 in EtOH) (Found: C, 63·6; H, 6·7. $C_{17}H_{21}O_4N,H_2O$ requires C, 63·5; H, 7·2%).

(*b*) Buphanitanone was reduced with lithium aluminium hydride as described above; the product, crystallised from acetone, had m. p. 211—213° alone or mixed with α-buphanitanol (identical infrared spectrum).

Buphanitane.—Buphanitanone (140 mg.), 85% hydrazine hydrate, and a solution of potassium hydroxide (0·8 g.) in diethylene glycol (5 ml.) were heated at 175—185° for 2 hr. The cooled solution was poured into water and extracted with ether. The ether extract gave a gum which, treated with picric acid and crystallised three times from ethanol, gave *buphanitane picrate*, m. p. 210—213°, $[\alpha]_D^{18}$ +3° (*c* 1) (Found: C, 53·6; H, 4·4; OMe, 5·5. $C_{23}H_{24}O_{12}N_4$ requires C, 53·5; H, 4·7; OMe, 6·0%). The infrared spectrum was similar to, but not identical with, that of powellane picrate, m. p. 213—215°. The new picrate was chromatographed in chloroform over alumina to give a gum which when lixiviated with ether gave a solid, subliming at 140°/0·01 mm. to give *buphanitane* (laminæ), m. p. 143—144°, $[\alpha]_D^{18}$ +4·6° (*c* 1) (Found: C, 70·7; H, 7·7. $C_{17}H_{21}O_3N$ requires C, 71·05; H, 7·4%). Mixed with sublimed powellane (needles, m. p. 113—115° prepared from buphanidrine) it had m. p. 102—113°.

Demethoxybuphanitine.—Buphanitine (1 g.) in boiling butan-1-ol (150 ml.) was treated with sodium (9·7 g.) during 1 hr. The product was treated with ammonium chloride, steam-distilled to remove butanol, basified with sodium carbonate, and extracted with chloroform. The chloroform extract gave a gum which, chromatographed over alumina, gave a small amount of ether-soluble material and a gum whence two crystallisations from chloroform–ether gave *demethoxybuphanitine* as needles, m. p. 258°, $[\alpha]_D^{18}$ −105° (*c* 1) (Found: C, 66·3; H, 6·8; N, 5·0; OMe, 0. $C_{16}H_{19}O_4N$ requires C, 66·4; H, 6·6; N, 4·8%). The *hydrochloride*, m. p. 304—308° (Found: C, 58·9; H, 6·7. $C_{16}H_{20}O_4NCl$ requires C, 58·8; H, 6·2%), and the *perchlorate*, m. p. 285—287° (Found: C, 48·8; H, 5·5. $C_{16}H_{20}O_8NCl$ requires C, 49·2; H, 5·2%), crystallised from methanol–ether in needles.

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