785. *The Alkaloids of the Amaryllidaceae. Part IX.* Racemisation of Buphanitine (Nerbowdine) during Oppenauer Oxidations.*

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Buphanitine (nerbowdine) and *ar*-demethoxybuphanitine (*ar*-demethoxynerbowdine) on Oppenauer oxidation give powellenone and crinenone, respectively, which racemise. The racemisation of the unsaturated β-aminoketones, which also occurs on quaternisation, is discussed. These rearrangements invalidate the B/C-ring fusion previously reported for buphanitine.

Buphanitine, isolated by Tutin in 1910,[1] was later characterised fully [2] and assigned an ethanophenanthridine structure with rings B/C *cis*-fused.[3] In an effort to establish the absolute configuration we prepared " buphanitanone methine " which, contrary to expectation, was optically inactive, whereas powellanone methine was optically active. This observation and further investigations have now shown that the product from the Oppenauer oxidation, namely, " buphanitenone," is racemic powellenone and that racemisation had occurred during this reaction. The conclusion advanced previously concerning the ring fusion is invalid and buphanitine is powellane-1,3-diol (I).

Wildman and his collaborators recently isolated nerbowdine [4] which they showed was powellane-1,3-diol [5] and, from a comparison with samples sent by us, was identical with buphanitine.[6]

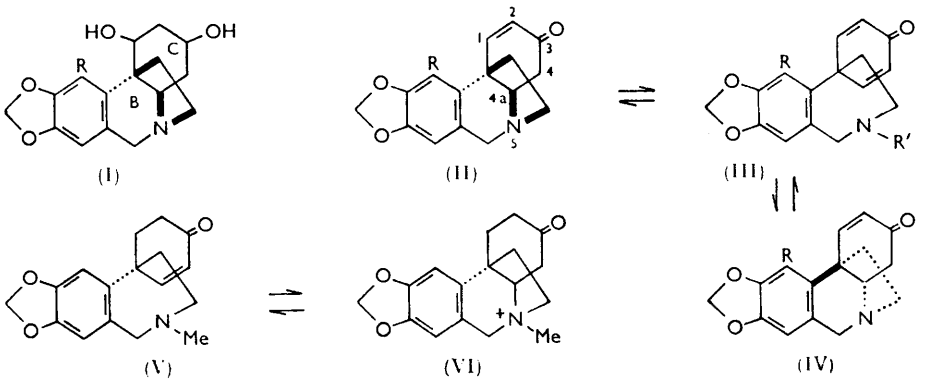
The infrared spectra of " buphanitenone " and powellenone in the solid state were

* Part VIII, *J.*, 1960, 1097.

[1] Tutin, *J.*, 1910, 1240.
[2] Goosen and Warren, (*a*) *Chem. and Ind.*, 1957, 267; (*b*) *J.*, 1960, 1094.
[3] Goosen and Warren, *J.*, 1960, 1097.
[4] Lyle, Kielar, Crowder, and Wildman, *J. Amer. Chem. Soc.*, 1960, **82**, 2620.
[5] Wildman and Manske, " The Alkaloids," Academic Press, London, 1960, Vol. VI, p. 362; Jeffs, Warren, and Wright, *J.*, 1960, 1090; Fales and Wildman, *J. Amer. Chem. Soc.*, 1960, **82**, 3268.
[6] Wildman, personal communication.

different, whilst the spectra of these substances in chloroform solution were identical. This is to be expected if " buphanitenone " is racemic powellenone [equimolecular mixture of (II) and (IV), R = OMe], and excludes the alternative explanation of inversion at position 4a to give the *cis*-B/C ring structure.

The Oppenauer oxidation is envisaged as proceeding by way of powellenone (II; R = OMe), and then the nitrogen ring opens to give an intermediate (III; R = OMe, R′ = H) which can cyclise again at $C_{(4a)}$ to give powellenone (II; R = OMe) and at $C_{(1)}$ to give the enantiomorph of powellenone (IV; R = OMe), resulting in the formation of the racemic compound. In both cases the *trans* ring-B/C is formed.



This mechanism was confirmed when heating powellenone [7] (II; R = OMe) with aluminium isopropoxide in cyclohexanone gave the racemate. Wildman [7] has shown an interesting transannular equilibrium between crinanone methine (V) and the quaternary ion (VI) which was influenced by dilution and pH of the solution. Following this lead we have found that powellenone methiodide, m. p. 266—267°, on repeated crystallisation gave the racemic methiodide, m. p. 243°, which was identical with (±)-powellenone methine hydriodide. Accordingly " buphanitenone " (reported [3] with positive rotation and now found to have $[\alpha]_D$ 0°), " buphanitanone," " buphanitane," " α- and β-buphanitanol " are racemic modifications of the corresponding substituted powellanes.

In a similar series of experiments *ar*-demethoxybuphanitine (*ar*-demethoxynerbowdine) (I; R = H) has now been oxidised to racemic crinenone [equimolecular mixture of (II) and (IV), R = H], m. p. 172—173°, whose infrared spectrum in chloroform solution was identical with that of (—)-crinenone,[7] m. p. 184°, $[\alpha]_D$ −300°, whilst in Nujol the spectra were different. Further, racemic crinenone methiodide gave a methine (III; R = H, R′ = Me) identical with that from crinenone.

The ease with which the nitrogen–carbon bond is broken and re-formed is of significance in that the 5,10b-ethanophenanthridine alkaloids are known to occur as modifications of both enantiomorphic forms, and the biosynthetic route envisaged in Barton and Cohen's [8] theory involves this ring closure.

In working up more material for these studies it has been possible to demonstrate the presence in *B. disticha* of the minor alkaloids, crinine, powelline, and ambelline (trace), in addition to those previously reported.[2b]

Experimental

Optical rotations refer to chloroform solutions.

Extraction.—The extraction procedure used was the same as in a previous report.[2b] The acetone mother-liquors from the separation of buphanitine (nerbowdine) gave a gum which

[7] Wildman, *J. Amer. Chem. Soc.*, 1958, **80**, 2567.

[8] Barton and Cohen, " Festschrift Arthur Stoll," Birkhäuser, Basle, 1957, p. 122; Barton and Kirby, *Proc. Chem. Soc.*, 1960, 392.

was chromatographed in chloroform over alumina. Elution of the column with chloroform gave buphanamine,[2b] ambelline, m. p. 265—267° (Found: C, 65·5; H, 6·5; OMe, 18·9%; *M*, 328. Calc. for $C_{18}H_{21}NO_5$: C, 65·2; H, 6·4; OMe, 18·7%; *M*, 331), crinine, m. p. 210—213° (Found: C, 70·7; H, 6·3. Calc. for $C_{16}H_{17}NO_3$: C, 70·8; H, 6·3%), and powelline, m. p. 199—201° (Found: C, 67·8; H, 6·3. Calc. for $C_{17}H_{19}NO_4$: C, 67·8; H, 6·4%).

Ambelline formed a hydrochloride, m. p. 230° (decomp.) (Found: C, 57·0; H, 6·4. Calc. for $C_{18}H_{22}ClNO_5,\frac{1}{2}H_2O$: C, 57·3; H, 6·1%), a perchlorate, m. p. 200—202° (Found: C, 49·9; H, 5·1. Calc. for $C_{18}H_{22}ClNO_9$: C, 49·8; H, 5·3%), a methiodide, m. p. 295—298° (decomp.) (Found: C, 48·4; H, 5·3. Calc. for $C_{19}H_{24}INO_5$: C, 48·2; H, 5·1%), and a monoacetate which, distilled at 120°/0·01 mm., gave a glass (Found: C, 64·1; H, 6·2. Calc. for $C_{20}H_{23}NO_6$: C, 64·3; H, 6·2%). Ambelline was hydrogenated over palladium–charcoal to dihydroambelline, m. p. 192—197° (Found: C, 64·6; H, 6·9. Calc. for $C_{18}H_{23}NO_5$: C, 64·85; H, 6·95%).

The physical properties are in agreement with those recorded for ambelline,[5] crinine,[5] and powelline.[5]

(±)-*Powellanone Methiodide.*—(±)-Powellanone (450 mg.), methanol (20 ml.), and methyl iodide (2 ml.) were refluxed for 30 min. The product, recrystallised from methanol, gave (±)-*powellanone methiodide* (500 mg.) as needles, m. p. 290—293° (decomp.) (Found: C, 48·9; H, 5·0. $C_{18}H_{22}INO_4$ requires C, 48·75; H, 5·0%).

(±)-*Powellanone Methine.*—(±)-Powellanone methiodide (500 mg.), hot water (15 ml.), and 10% sodium hydroxide solution (10 ml.) were heated on a water-bath for 10 min. and then extracted with ether. After each extraction the mixture was again heated and re-extracted, the process being repeated five times. The combined ether extracts, when washed with water and dried, gave a gum (150 mg.), $[\alpha]_D$ ±0° (*c* 1). The infrared spectrum (in Nujol) showed a strong band at 1663 cm.$^{-1}$. The gum (150 mg.) in benzene was chromatographed on alumina (5 g.). Elution with 1 : 19 methanol–chloroform yielded a yellow gum (70 mg.), $[\alpha]_D$ ±0° (*c* 1). The addition of picric acid gave (±)-*powellanone methine picrate* which recrystallised from ethanol as yellow needles (64 mg.), m. p. 230—232°, $[\alpha]_D$ ±0° (*c* 1), $\nu_{max.}$ 1663s cm.$^{-1}$ (Found: C, 53·2; H, 4·25. $C_{24}H_{24}N_4O_{11}$ requires C, 52·9; H, 4·4%).

(−)-*Powellanone Methine.*—(−)-Powellanone methiodide (100 mg.) in hot water (3 ml.) was warmed with 10% aqueous sodium hydroxide (1·5 ml.) and worked up as above. The product was a gum, $[\alpha]_D^{10}$ +82° (*c* 1).

(−)-*Powellenone Methiodide.*—(−)-Powellenone in acetone was treated with an excess of methyl iodide. The *methiodide*, recrystallised from methanol, had m. p. 266—267° (Found: C, 49·1; H, 4· . $C_{18}H_{20}INO_4$ requires C, 49·0; H, 4·7%). Repeated recrystallisations from methanol gave (±)-powellenone methiodide, m. p. 243°, having an infrared spectrum identical with that of (±)-powellenone methiodide, m. p. 243°.

(±)-*Powellenone Methine Hydriodide.*—(±)-Powellenone methine in methanol was treated with hydriodic acid, and the precipitate recrystallised from methanol to give (±)-*powellenone methine hydriodide*, m. p. 242—243° (Found: C, 47·5; H, 5·0. $C_{18}H_{20}INO_4,\frac{1}{2}H_2O$ requires C, 47·9; H, 4·9%). The infrared spectrum was identical with that of (±)-powellenone methiodide, m. p. 243°.

Rearrangement of (−)-*Powellenone.*—(−)-Powellenone (100 mg.), aluminium isopropoxide (600 mg.), and cyclohexanone (10 ml.) were heated under reflux in nitrogen for 18 hr., then treated with aqueous sodium hydroxide and extracted with chloroform. The chloroform solution was extracted with 2N-hydrochloric acid. The acid extract was washed with chloroform, basified, and extracted with chloroform. This chloroform extract gave a gum which, when chromatographed with chloroform on alumina and crystallised from ether, gave (±)-powellenone, m. p. 184°, $[\alpha]_D^{20}$ ±0° (*c* 0·36), $\nu_{max.}$ (in Nujol) 823, 807, 780, and 730 cm.$^{-1}$, identical with an authentic specimen. The solid-state infrared spectrum of (−)-powellenone had bands at 828, 775, and 738 cm.$^{-1}$.

(±)-*Crinenone.*—*ar*-Demethoxybuphanitine was oxidised with boiling cyclohexanone in the presence of aluminium isopropoxide. The product crystallised from ether to give (±)-*crinenone*, as needles, m. p. 172—173°, $[\alpha]_D$ 0° (*c* 1) (Found: C, 71·3; H, 5·6. $C_{16}H_{15}NO_3$ requires C, 71·4; H, 5·6%), $\nu_{max.}$ (in Nujol) 1240, 1222, 926, 770 cm.$^{-1}$, which differed from those of (−)-crinenone (1235, 943, 781, and 778 cm.$^{-1}$).

(±)-*Crinenone Methiodide.*—(±)-Crinenone in methanol was treated with methyl iodide. The *methiodide* crystallised from methanol as rhombohedra, m. p. 300° (decomp.) (Found: C, 49·2; H, 4·3. $C_{17}H_{18}INO_3$ requires C, 49·6; H, 4·4%).

(±)-*Crinenone Methine*.—(±)-Crinenone methiodide was treated with sodium hydroxide and extracted with benzene. The product, crystallised from ether, gave the *methine* as needles, m. p. 120°, which when recrystallised after seeding with crinenone methine, m. p. 125—127°, had m. p. 125—127°. The solid-state infrared spectrum of the crystals, m. p. 120°, differed from the spectra of crinenone methine and the crystals, m. p. 125—127°, which were identical.

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