The Morphine–Thebaine Group of Alkaloids. Part IV. The Structure of the Thebainone Methines and of Thebainone-C.*

By K. W. BENTLEY and H. M. E. CARDWELL.

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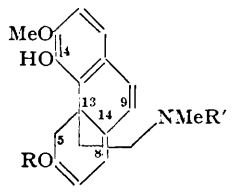
The products of hydrolysis of β-dihydrothebaine methine (I; R = R′ = Me) with mineral acid, and of dihydrothebaine-ϕ methiodide (cf. VIII; R = H) with sulphurous acid, originally thought to be the same substance (III; R = Me) (Bentley, Robinson, and Wain, *J.*, 1952, 958) have been shown to be two isomers (III and V; R = Me). A third isomer (VI; R = Me) has been prepared by Hofmann degradation of thebainone-B methiodide. Structures have been allotted to the isomers on the basis of infrared and ultraviolet absorptions. Catalytic hydrogenation of both (III; R = Me) and (V; R = Me) gives β-dihydrothebainone dihydromethine (XII). All three methines are converted into highly coloured substances by aerial oxidation.

The structure allotted by Bentley and Wain (Part I, *J.*, 1952, 967) to thebainone-C has been disproved. This base has been shown to be a cyclic base with the ethanamine chain bridging positions 13 and 8. The steric arrangement of groups at $C_{(14)}$ in thebainone-C has been proved to be the same as in morphine by reduction, degradation, and further reduction to dihydrothebainone dihydromethine.

ALTHOUGH in all other known cases catalytic hydrogenation of substances in the morphine group containing a 8 : 14-double bond leads exclusively to the same steric arrangement at $C_{(14)}$ present in morphine itself, the hydrogenation of thebainone-B methine, hitherto allotted the constitution (III; R = Me), affords β-dihydrothebainone dihydromethine (XII), epimeric at $C_{(14)}$ with the general morphine series (Bentley, Robinson, and Wain, *J.*, 1952, 958). We have investigated this anomaly by preparing the four isomeric thebainone methines (III—VI; R = Me), interconvertible through the common enol (I; R = H, R′ = Me), and we have prepared some of the tautomerides by methods not involving the common enol as an intermediate.



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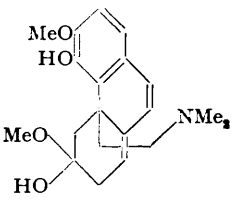

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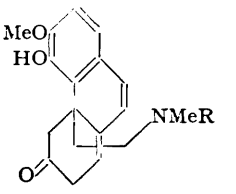

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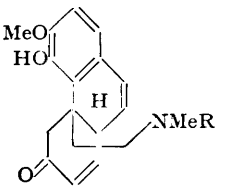

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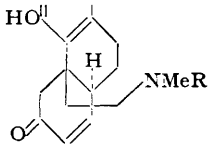

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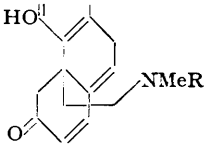

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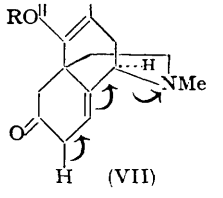

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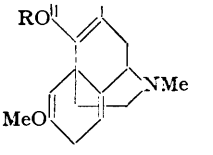


(VIII)

The $\Delta^{8(14):9}$-methine (III; R = Me) was prepared by mild hydrolysis of β-dihydrothebaine methine (I; R = R′ = Me) (Bentley, Robinson, and Wain, *loc. cit.*) with mineral acid: hydration of the most basic end of the conjugated system leads directly to the hemiketal (II) and thence to the methine (III; R = Me), whose structure was established by the similarity of its ultraviolet absorption to that of β-codeimethine (XVII) and confirmed by the presence of saturated carbonyl stretching bands and the absence of strong C:C bands

* Part III, preceding paper.

characteristic of double bonds conjugated with carbonyl groups in the infrared spectra of the hydriodide and hydrobromide. Ultraviolet extinction curves for the isomeric methines are given in Fig. 1, and optical rotations and infrared data in the Table.

The methines are oxidised so rapidly that optical measurements were made on salts; this precluded infrared solution measurements. Both the hydriodide and the hydrobromide of each tautomeride were prepared by methods that minimised interconversion. The examination of two series of salts was necessary, as in one case the carbonyl band of one salt, but not of both, was sufficiently shifted by polarisation in the crystal for its position not to allow unambiguous decision as to its significance. Optical rotations and ultraviolet absorptions were measured in the presence of sodium dithionite to minimise oxidation.

FIG. 1. FIG. 2.

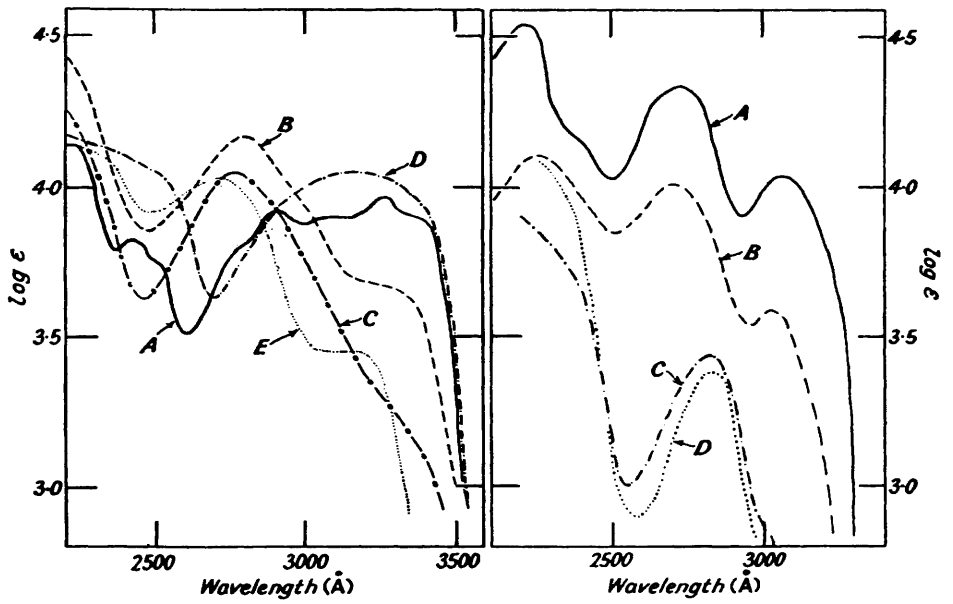


FIG. 1. *A*, $\Delta^{8(14):9}$-*Thebainone methine hydrobromide*; *B*, $\Delta^{7:9}$-*thebainone methine hydrobromide*; *C*, $\Delta^{7:9(14)}$-*thebainone methine hydrobromide*; *D*, β-*codeimethine*; *E*, α-*codeimethine*.

FIG. 2. *A*, *Thebainone-C perchlorate* (cf. XIII); *B*, α-*codeimethine hydrochloride*; *C*, *dihydrothebainone-C* (XIV); *D*, *thebainone-A dihydromethine* (XV).

The $\Delta^{7:9(14)}$-methine (VI; R = Me) was prepared from thebainone-B (VII; R = H) methiodide. Bentley *et al.* (*loc. cit.*) remarked on the instability of thebainone-B and its methiodide. It is possible to prepare the latter in dry, non-polar solvents and to measure its optical rotation rapidly in cold water, but attempts to recrystallise it always lead to partial formation of the methine hydriodide, and the methine is immediately precipitated when an aqueous solution of the methiodide is treated with aqueous sodium carbonate or ammonia. The free base is extremely unstable and the methine was isolated as the hydrobromide and hydriodide. The structure of this methine was clear from its method of preparation and was confirmed by the ultraviolet and infrared absorption spectra.

The hydriodide of the $\Delta^{7:9(14)}$-methine, on treatment with hot sulphurous acid, afforded a different hydriodide, the infrared spectrum of which was distinct from those of the starting material (the $\Delta^{7:9(14)}$-methine) and the $\Delta^{8(14):9}$-methine. Bentley *et al.* (*loc. cit.*) prepared a hydriodide by the action of hot sulphurous acid on the dihydrothebaine-ϕ methiodide. This was presumed, from lack of mixed melting point depression, to be identical with the hydriodide of authentic $\Delta^{8(14):9}$-methine (III; R = Me). However, from its method of preparation it is identical with the new hydriodide prepared from the $\Delta^{7:9(14)}$-methine, and this was confirmed. The infrared and ultraviolet spectra demonstrate that

this substance is the $\Delta^{7:9}$-methine. It was this methine (prepared from dihydrothebaine-ϕ methiodide) that was used in the hydrogenation experiment described by Bentley *et al.*; hence the reductive anomaly was removed as the starting material (V; R = Me) already had the anomalous configuration at $C_{(14)}$. The anomaly returned, however, when we found that the hydrobromide of authentic $\Delta^{8(14):9}$-methine (III; R = Me) on hydrogenation also gave β-dihydrothebainone dihydromethine (XII), but with much less force for our experiments show that (V) is thermodynamically the most stable of the four isomerides. Conversion into the stable isomeride is extremely easy and takes place more rapidly than reduction. Similarly the variability in melting points, which are very sensitive to the rate of heating, and the failure to observe any mixed melting point depressions are probably due to inter-

Diagnostic infrared bands (μ) *and* $[\alpha]_D$ *of thebainone methines.*

Unsaturation	Hydrobromides				Hydriodides			
7 : 9(14)	5·87 [a]	6·01 [c]	6·07 [f]	+ 87°	5·84 [a]	5·97 [c]	6·06 [f]	+ 7·9°
7 : 9	5·83 [a]	5·96 [c]	6·06 [f]	+114	5·90 [a]	6·03 [d]	6·08 [f]	+115
8(14) : 9	5·82 [b]	5·96 [a]		+324	5·82 [b]			+300

[a] Weak bands due to traces of other isomerides or thebainone-B. [b] Saturated ketone group. [c] αβ-Unsaturated ketone group. [d] αβ-Unsaturated ketone group shifted by polarisation in the crystal. [e] αβγδ-Unsaturated ketone group. [f] Double bond conjugated with carbonyl group.

conversion of isomerides. The $\Delta^{8(14):9}$-methine is converted into the $\Delta^{7:9}$-methine by hot sulphurous acid.

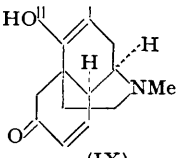
By the severe criterion of carbonyl stretching bands in the infrared spectra each of our products contained *traces* of the other tautomerides, but this does not in any way invalidate our conclusions. More serious was the contamination of the substances (especially the free bases) by coloured oxidation products. This sensitivity precluded lengthy equilibration experiments to determine the relative stability of the various tautomerides.

The methines (III and V; R = Me) appear to form mixed crystals. (We are grateful to Dr. John Robertson, of the Department of Chemical Crystallography in Oxford, who took powder photographs of several preparations. The photographs were very similar and contained many common spacings.) This suggests that in both molecules the three rings are coplanar and further diminishes the remote possibility that the stable tautomeride is the missing methine (IV; R = Me). Although the latter has eluded isolation, indirect proof of its existence was obtained.

Small and Browning (*J. Org. Chem.*, 1939, **3**, 618) found that hydrolysis of dihydrothebaine-ϕ (VIII; R = H) by sulphurous acid gave a sensitive phenolic ketone "α-thebainone." This substance was re-examined by Bentley and Wain (Part I, *J.*, 1952, 967) and renamed thebainone-C. As at that time hydrolysis of dihydrothebainone-ϕ methiodide by sulphurous acid was thought to give the $\Delta^{8(14):9}$-methine (III; R = Me), the equivalent structure (III; R = H) was assigned to thebainone-C. This assignment was supported by the presence of a saturated carbonyl group (infrared spectrum) and the existence of a long-wavelength ultraviolet absorption band of the same $\varepsilon_{max.}$ and $\lambda_{max.}$ as the main absorption band of β-codeimethine (XVII). Our present work, however, suggests the production of one of the other isomerides (V or VI; R = H). The ultraviolet spectrum of thebainone-C, although of much greater intensity than that of α-codeimethine (XVI), shows a striking coincidence of wavelength of the main absorption bands (Fig. 2). The presence of a saturated carbonyl group and a styrenoid chromophore in thebainone-C is only consistent with cyclisation of (III, IV, and V; R = H) at position 8 to give a structural isomeride of the thebainones. This hypothesis has now been established, thebainone-C being the isomeride (XIII) with the usual morphine configuration at position 14.

The structure of thebainone-C was proved by hydrogenation to dihydrothebainone-C (XIV) with uptake of one mol. of hydrogen and disappearance of the styrenoid chromophore (ultraviolet spectrum; Fig. 2). This saturated ketone readily gave a methiodide which was more stable than that of thebainone-B but on treatment with cold aqueous sodium carbonate immediately gave a precipitate of the basic αβ-unsaturated ketone (XV), thebainone-A dihydromethine (Δ^7-dihydrothebainone methine) (CO absorption at 5·97 μ). This on hydrogenation yielded dihydrothebainone dihydromethine (XI).

In the preparation of thebainone-C a colourless crystalline solid separates; this is probably the bisulphite betaine (XVIII) of thebainone-B. On its dissolution in hot water sulphur dioxide is evolved and none of the adduct is recovered. On neutralisation the solution readily becomes coloured through aerial oxidation and thebainone-C slowly crystallises. On careful recrystallisation thebainone-C is obtained as colourless prisms that show none of the characteristic instability of the methines. The sensitivity of thebainone-C commented on by Small and Browning is presumably due to *N*-normethines resulting from the decomposition of thebainone-B.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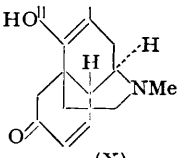
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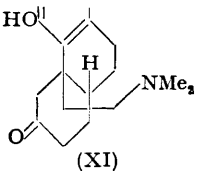
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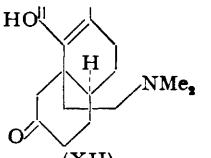
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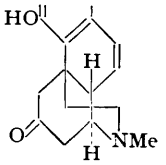
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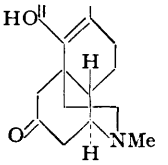
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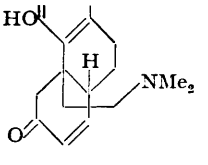
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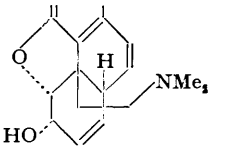

(XVI)

The mode of formation of thebainone-C is now clear. Thebainone-B, first formed by the hydrolysis of dihydrothebaine-ϕ, decomposes to the methine (VI; R = H). If the conditions are not sufficiently vigorous to rearrange this to the more stable (IV and V; R = H), recyclisation takes place by two processes: first, a rapid *trans*-addition of the ethanamine chain and proton, to give β-thebainone-A (IX) and, secondly, by a less rapid, non-stereospecific reaction to give the betaine (XIX) from which thebainone-A (X) is formed by direct transfer of a proton to $C_{(14)}$. If the conditions are more vigorous the methine (VI) is converted into a mixture (IV and V; R = H), these then cyclising at $C_{(8)}$ to give a mixture of thebainone-C and β-thebainone-C, the latter so far having eluded isolation. This mechanism explains our observation that the hydrolysis to thebainone-C is much more reliable if the sulphurous acid treatment is carried out at 40°. The erratic yields (10—30%) of thebainone-C are probably due to the presence of β-thebainone-C [$C_{(14)}$ epimeride of (XIII)]. The formation of β-thebainone-A (IX) in good yield rather than the more stable tautomeride thebainone-A (X) during the treatment of dihydrothebaine-ϕ and thebainone-B with cold aqueous potassium hydrogen sulphate is inexplicable on the basis of the common enol as an intermediate, but is readily explained on the basis of a rapid stereospecific cyclisation.

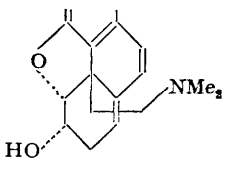
The increasing ease of ring opening in the series thebainone-A, thebainone-C, thebainone-B, parallels the acidity of the enolisable hydrogen atom, which is tertiary in the first case, secondary in the second, and flanked by a carbonyl group and double bond in the last. These observations provide the long-sought degradative evidence for the attachment of the nitrogen atom at $C_{(9)}$ rather than $C_{(10)}$ in the morphine alkaloids.

The immediate liberation of a ring-opened base on treatment of thebainone-B methiodide with aqueous sodium carbonate removes the previously valid argument (Bentley, Robinson, and Wain, *loc. cit.*) that the perchlorate obtained by the brief treatment of the methiodide of dihydrothebaine-ϕ methyl ether (VIII; R = Me) with perchloric acid was the perchlorate of a base. The infrared and ultraviolet spectra have now established that it is the metho-perchlorate of thebainone-B methyl ether (VII; R = Me).

Our experiments suggest that the order of stability of the various tautomeric methines is (V) > (IV) > (III) > (VI). When the nitrogen ring is intact the *cis*-octalone (X) is more stable than the *trans*-octalone (IX) (Gates and Helg, *J. Amer. Chem. Soc.*, **1953**, **75**, 379) and this inversion of the normal order of stability of octalones has been ascribed by Bose (*Chem.*

and Ind., 1954, 130) to interference between the 4-hydroxyl OH group and a hydrogen atom at $C_{(5)}$ in the *trans*-isomer (IX). A similar explanation involving the hydrogen at $C_{(15)}$ may be advanced for the preferential formation of thebainone-C. In the ring-opened isomerides (IV and V; R = Me) there is no longer this radical difference between the two forms, hence the observation that the *trans*-isomeride is the more stable is to be expected and is convincing evidence for the soundness of Bose's ingenious suggestion.

The oxidative instability has precluded any attempt to prepare the missing methine (IV; R = Me) by preparation of the corresponding alcohol followed by oxidation. The colours developed during oxidation are spectacular. The salts in aqueous solution are oxidised even in the presence of sulphurous acid to deep blue and finally black solutions. In non-aqueous solvents the sequence is deep red ⟶ violet ⟶ black. In one case the methiodide of the methine (VI; R = Me) was allowed to oxidise for several weeks, giving a black amorphous solid. This showed a succession of intense absorption bands in the ultraviolet and visible region, extending beyond 6000 Å. It is clearly a mixture, the analysis indicating the addition of up to two atoms of oxygen. The methine (V; R = Me) was oxidised in 2-ethoxyethanol and to aliquot parts of the resulting deep purple solution diluted with ethanol (*a*) sodium dithionite and (*b*) ferric chloride were added until straw-coloured solutions were obtained. These on mixing developed a purple colour. With the methyl ether of (V; R = Me) oxidation also occurs, but the resulting solution is brown, not blue-purple. These preliminary experiments suggest the formation of intermolecular and/or intramolecular quinhydrones, the common enol oxidising at positions 7 and/or 10 and to some extent also in the aromatic ring, giving substances such as (XX), (XXI), and (XXII).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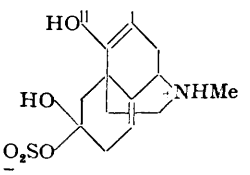
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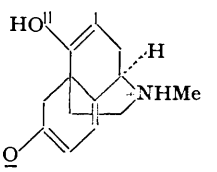
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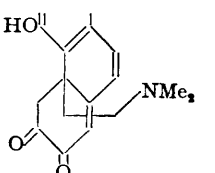
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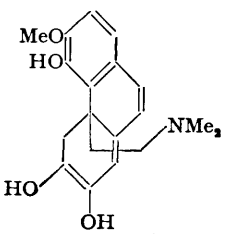
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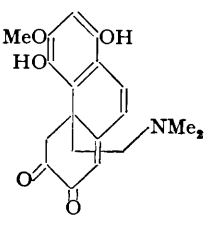
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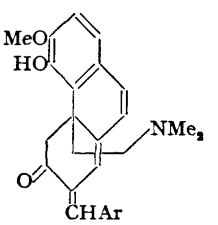
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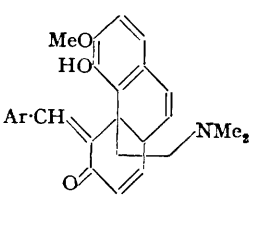
(XXIV)

These changes are doubtless accompanied by some self-coupling as in the decomposition of the sinomenine methines (Goto and Takubo, *Bull. Chem. Soc. Japan*, 1931, **6**, 126). Our observation that the pure piperonylidene derivative (XXIII) of (III; R = Me) is quite stable to aerial oxidation, whilst the piperonylidene derivative prepared by Bentley *et al.* from (V; R = Me), which differed in crystal form from the derivative of (III; R = Me) but gave identical infrared and ultraviolet spectra, was readily oxidised [possibly owing to the presence of traces of 5-piperonylidene derivative (XXIV)], taken together with the fact that marked colour changes on oxidation have not been reported for the sinomenine methines, suggests that a potential CH_2 group at $C_{(7)}$ is essential for the production of the brilliant colours here described. We plan to investigate the oxidation in more detail, the analogy to melanin formation being suggestive.

This work required the preparation of considerable quantities of dihydrothebaine-ϕ. Stork (*J. Amer. Chem. Soc.*, 1952, **74**, 768), contrary to Bentley and Robinson (*Experientia*, 1950, **6**, 353), found it necessary to add ethanol in the reduction of thebaine with sodium

and liquid ammonia, and implied that the ethanol was mechanistically required as a proton source. The rate of reduction of thebaine by sodium and liquid ammonia, without added ethanol, is dependent on the state of subdivision of the thebaine crystals. *Ethanol is never mechanistically required*, but if the crystals are large their rate of solution, and hence the rate of reduction, is increased by the addition of ethanol. When finely divided thebaine (80-mesh sieve) is used, reduction in the absence of ethanol is extremely rapid.

Experimental

Dihydrothebaine-ϕ was prepared by the method of Bentley, Robinson, and Wain (*loc. cit.*). It was advantageous to precipitate the base from alkaline solution by the addition of saturated aqueous ammonium chloride and to extract it *rapidly* with the minimum of quantity of ether. A large quantity of the pure base crystallised from the extract in 45 min. This was collected and a further quantity of slightly less pure material was recovered by concentration of the dried mother-liquors to small bulk. The yield was up to 95%.

The *methobromide* was prepared in toluene (5 parts) at $-20°$ (3 hr.) and recrystallised from water in the presence of sodium dithionite; it was obtained as colourless solvated prisms, m. p. *ca.* 120° with loss of solvent (Found, in material dried at 120°/*in vacuo*: C, 56·5; H, 6·4. $C_{20}H_{26}O_3NBr,H_2O$ requires C, 56·3; H, 6·6%).

Thebainone-B was prepared as the hydrobromide by the hydrolysis of dihydrothebaine-ϕ with alcoholic hydrobromide acid as described by Bentley and Wain (*loc. cit.*). The salt (5 g.) was dissolved in water and shaken with aqueous sodium carbonate and benzene. The organic layer was separated, clarified with anhydrous magnesium sulphate, and treated with methyl iodide, the whole operation being complete within 10 min. After 30 min. the pale yellow flocculent methiodide was collected. (Further quantities of solid separated from the filtrate but were contaminated with methine hydriodide and methiodide.) *Thebainone-B methiodide*, $[\alpha]_D^{18}$ $+21° \pm 8°$ (*c* 1·4 in aqueous sodium dithionite) (Found: C, 52·3; H, 5·8. $C_{18}H_{21}O_3N,CH_3I$ requires C, 51·7; H, 5·8%), could not be recrystallised without the formation of appreciable quantities of $\Delta^{7:9(14)}$-thebainone methine hydriodide; the resulting mixed material, m. p. 200—205° (decomp.), from ethanol was partially solvated (Found: C, 51·0; H, 5·6; N, 2·6. Calc. for $C_{19}H_{24}O_3NI$: C, 51·7; H, 5·8; N, 3·2%).

$\Delta^{8(14):9}$-*Thebainone Methine* (*Thebainone-B Methine*).—β-Dihydrothebaine methine (1 g.) was treated in ethanol (10 ml.) with hydriodic acid (1 ml.). After 10 min. the hydriodide was collected and recrystallised twice from water in the presence of sodium dithionite, forming almost colourless prisms, m. p. 230° (Bentley, Robinson, and Wain give m. p. 214°) (Found: C, 51·6; H, 5·7. Calc. for $C_{19}H_{23}O_3N,HI$: C, 51·8; H, 5·5%). The hydrobromide, prepared similarly, had m. p. 232° (Bentley *et al.* give m. p. 234°). The *piperonylidene derivative* was prepared by the addition of sodium ethoxide to an alcoholic suspension of the hydriodide and piperonaldehyde. After 10 min. the blood-red solution was diluted with water, and the precipitate collected and recrystallised from ethanol; it was obtained as orange felted needles, m. p. 196° (Found: C, 72·8; H, 6·2. $C_{27}H_{27}O_5N$ requires C, 72·8; H, 6·1%).

β-$\Delta^{7:9}$-*Thebainone Methine* (β-*Thebainone-A Methine*).—The hydriodide was prepared as described by Bentley, Robinson, and Wain by the hydrolysis of dihydrothebaine-ϕ methiodide by hot sulphurous acid. The *hydrobromide* was prepared similarly: Dihydrothebaine-ϕ methobromide (4 g.) was dissolved in boiling water (25 ml.) and sulphur dioxide passed through the solution for 10 min., during which it became dark blue. The solution was rapidly evaporated to dryness. The residue recrystallised from ethanol in presence of sodium dithionite as colourless prisms, m. p. 235°, $[\alpha]_D^{20}$ $+114°$ (*c* 1·8 in EtOH) (Found: C, 57·5; H, 6·0. $C_{19}H_{23}O_3N,HBr$ requires C, 57·9; H, 6·1%).

$\Delta^{7:9(14)}$-*Thebainone Methine*.—Thebainone-B methiodide (5 g.), dissolved in cold aqueous sodium dithionite (20 ml.), was treated with aqueous sodium carbonate. The white precipitate, which separated immediately, was rapidly collected and transferred at once into aqueous hydrobromic acid containing sodium dithionite (the base began to become brown in air even with the most rapid manipulation). On trituration hydrated $\Delta^{7:9(14)}$-*thebainone methine hydrobromide* separated. This crystallised from ethanol–ether in pale pink needles, m. p. 217—223° (decomp.) alone or when mixed with the $\Delta^{8(14):9}$-methine hydrobromide (Found: C, 55·4; H, 6·2. $C_{19}H_{23}O_3N,HBr,H_2O$ requires C, 55·3; H, 6·3%). It had $[\alpha]_D^{18}$ $+87° \pm 14°$ (in aqueous sodium dithionite). The aqueous filtrate from the hydrobromide was poured into saturated aqueous potassium iodide. The crystals that separated were then collected and recrystallised from ethanol–ether; $\Delta^{7:9(14)}$-*thebainone methine hydriodide* was obtained as blue needles, m. p.

221—226°, $[\alpha]_D^{18}$ +79° ± 30° (in aqueous sodium dithionite) (Found: C, 51·5; H, 5·3. $C_{19}H_{23}O_3N$,HI requires C, 51·7; H, 5·4%).

Conversion of $\Delta^{7:9(14)}$*-Thebainone Methine into the* $\Delta^{7:9}$*-Methine.*—$\Delta^{7:9(14)}$-Thebainone methine hydriodide was dissolved in hot water through which a stream of sulphur dioxide was continuously bubbled for 20 min. on the water-bath. The mixture was then heated to expel this gas. On cooling, the deep blue solution deposited the $\Delta^{7:9}$-methine hydriodide, which formed prisms, m. p. 215—225°, from water. As the isomeric methines cannot be differentiated by m. p. this salt was identified as the $\Delta^{7:9}$-methine hydriodide by its infrared spectrum in a paraffin mull.

Reduction of $\Delta^{8(14):9}$*-Thebainone Methine* (*Thebainone-B Methine*).—$\Delta^{8(14):9}$-Thebainone methine hydrobromide (1 g.) in water (35 ml.) was shaken under hydrogen in presence of platinum oxide (60 mg.) until absorption of hydrogen ceased (2·05 mols.). The catalyst was removed, and the base precipitated with sodium carbonate, washed, and recrystallised from 50% ethanol; β-dihydrothebainone dihydromethine was obtained as almost colourless needles, m. p. and mixed m. p. 179° (Small and Browning, *loc. cit.*, give m. p. 177—179°; Bentley, Robinson, and Wain, *loc. cit.*, m. p. 179°).

Oxidation of Methines.—(*a*) $\Delta^{7:9(14)}$-Thebainone methine hydrobromide was shaken with aqueous sodium carbonate and ether, the ether layer separated, dried ($MgSO_4$), diluted with ethanol and treated with methyl iodide. The solution was then left for 2 months exposed to air. The solution became red, then violet, and finally deposited a black semicrystalline substance. This *substance* was dissolved in ethanol and partially reprecipitated on addition of ether (Found: C, 49·1; H, 5·5; I, 24·1. $C_{20}H_{24}O_5NI$ requires C, 49·5; H, 5·0; I, 26·2%). In water a deep purple solution was obtained, which was immediately decolorised on addition of aqueous sodium dithionite, ferric chloride, or chromic acid.

(*b*) $\Delta^{7:9}$-Thebainone methine (1 g.) was dissolved in 2-ethoxyethanol (5 ml.) and air bubbled rapidly through the solution for 24 hr., during which the solution became very deep purple. Equal portions were diluted with ethanol until the depth of colour was considerably reduced. One portion was then treated with aqueous sodium dithionite, and the other with warm alcoholic ferric chloride until the colour was just discharged. The two solutions were then mixed; a purple solution was obtained.

Thebainone-C.—This was prepared by a modification of Small and Browning's method (*loc. cit.*). Dihydrothebaine (5 g.) was dissolved in water (75 ml.) saturated with sulphur dioxide and the solution set aside at 40° for 1 hr. In all experiments after the fourth, a colourless crystalline *compound* separated after 10—15 min. When separated this was found to be very sparingly soluble in cold water but readily soluble in hot water, though it could not be recovered by cooling the solution [Found: C, 52·5; H, 6·5. $C_{18}H_{23}O_6NS,2H_2O$ (*i.e.*, XVIII) requires C, 53·0; H, 6·6%]. The yield of thebainone-C was not noticeably affected whether the solid alone or the whole reaction mixture was worked up. The mixture was neutralised with ammonia in the presence of sodium dithionite, the precipitated gummy base was extracted with ether, and the extracts were washed with water and decanted from gum, dried, and evaporated under hydrogen. The residue was dissolved in alcohol (6 ml.), and water containing a small amount of sodium dithionite was added to the resulting dark brown solution (which then became pale yellow) until precipitation of a yellow oil just began. A few drops of alcohol were then added and the mixture set aside under hydrogen for one week during which colourless prisms separated together with some brown resinous material. Crystallisation was much more rapid if methanol containing two drops of aqueous sodium dithionite was used instead of aqueous ethanol at this stage. Of sixteen experiments carried out at 40° none was unsuccessful. Thebainone-C so obtained was washed with methanol (which removed the resinous material) and recrystallised from methanol. The first recrystallisation removed most of the impurities and the mother-liquors quickly became dark violet. A second recrystallisation yielded thebainone-C as colourless prisms, m. p. 190° (Small and Browning, *loc. cit.*, give m. p. 185—186°; Bentley and Wain, *J.*, 1952, 967, m. p. 186—187°), stable in air. The perchlorate was obtained as colourless leaflets, m. p. 201° (Bentley and Wain give m. p. 200°); the *picrate* was prepared in ethanol and recrystallised from 2-ethoxyethanol as canary-yellow plates, m. p. 186° (decomp.), darkening in strong sunlight (Found: C, 54·6; H, 4·4; N, 10·1. $C_{24}H_{24}O_{10}N_4$ requires C, 54·5; H, 4·55; N, 10·6%).

Dihydrothebainone-C.—Thebainone-C (550 mg.) was shaken in glacial acetic acid (15 ml.) under hydrogen in the presence of platinum oxide (60 mg.) until absorption of hydrogen ceased (0·98 mol.). The solution was filtered, the acetic acid removed by distillation *in vacuo*, the residue dissolved in water, and the base precipitated with ammonia, washed with water, and dried. It was dissolved in hot 1 : 1 benzene–light petroleum (b. p. 80—100°), but crystallisation did not occur until water was added or was absorbed from the atmosphere. A hemihydrate of

dihydrothebainone-C then separated as colourless prisms, m. p. 143°, $[\alpha]_D^{20}$ −70° (*c* 2·0 in $CHCl_3$) (Found : C, 69·3; H, 7·6. $C_{18}H_{23}O_3N,\frac{1}{2}H_2O$ requires C, 69·6; H, 7·7%). Anhydrous material did not crystallise. (Thebainone-A behaves in the same way; Gates and Helg, *J. Amer. Chem. Soc.*, **1953**, **75**, 380, footnote 2.) The base is readily soluble in organic solvents except petroleum, and in ethanol gives a blue colour with ferric chloride. The *perchlorate*, prepared in ethanol, crystallised from 95% ethanol as colourless elongated prisms, m. p. 260° (decomp.) (Found : C, 54·0; H, 5·9; Cl, 8·8. $C_{18}H_{23}O_3N,HClO_4$ requires C, 53·8; H, 6·0; Cl, 8·8%). The *picrate*, prepared in ethanol, crystallised from aqueous 2-ethoxyethanol as canary yellow plates, m. p. 205—206°, darkening in strong sunlight (Found : C, 54·3; H, 4·8; N, 10·3. $C_{24}H_{26}O_{10}N_4$ requires C, 54·3; H, 4·9; N, 10·5%).

Thebainone-A Dihydromethine (*Δ^7-Dihydrothebainone Methine*) (XV).—Dihydrothebainone-C (4 g.) was dissolved in benzene (20 ml.), and methyl iodide (5 ml.) added. After 3 hr. the methiodide was collected and dissolved in water (55 ml.). Adding 10% aqueous sodium carbonate (15 ml.) produced an immediate precipitate. This was extracted with hot benzene and the extract allowed to cool. Colourless needles which separated recrystallised from benzene, giving *thebainone-A dihydromethine* (*Δ^7-dihydrothebainone methine*) as felted colourless elongated needles, m. p. 153·5°, $[\alpha]_D^{20}$ +40° (*c* 1·9 in $CHCl_3$) (Found : C, 72·1; H, 8·2. $C_{19}H_{25}O_3N$ requires C, 72·4; H, 7·9%); there was a carbonyl absorption band at 5·97 μ. The *methoperchlorate* was obtained as colourless prisms, m. p. 234°, from water containing 5% of ethanol (Found : C, 55·5; H, 6·3. $C_{20}H_{28}O_7NCl$ requires C, 55·8; H, 6·5%).

Reduction of Thebainone-A Dihydromethine.—The methine (1·5 g.) in glacial acetic acid (50 ml.) was shaken under hydrogen in presence of platinum oxide (60 mg.) until absorption of hydrogen ceased (0·97 mol.). The catalyst and solvent were removed, the residue dissolved in water, and ammonia added. The precipitated base was washed with water and recrystallised from 25% ethanol, giving dihydrothebainone dihydromethine as colourless needles, m. p. 138°. The picrate was obtained as rosettes of yellow needles, m. p. 185—186°, from aqueous 2-ethoxyethanol (lit., m. p. 185—187°). The methiodide was converted into thebenone by Wieland and Kotake's method (*loc. cit.*) and the product obtained as colourless needles, m. p. and mixed m. p. 136° (lit., m. p. 136°).

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