[CONTRIBUTION NO. 118 FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Metathebainone[1]

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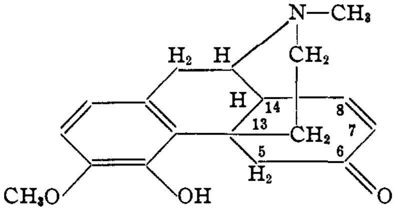
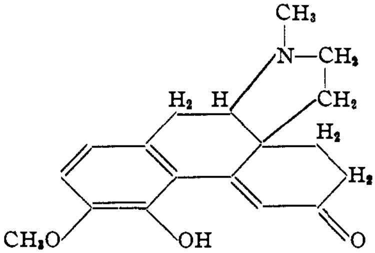
When thebaine is heated in concentrated hydrochloric acid with stannous chloride,[2] two phenolic ketones of the empirical composition $C_{18}H_{21}O_3N$ are formed. The structure of one of these, the "true" thebainone (Formula I)[3] is evident from the fact that it can be hydrogenated to the same dihydrothebainone as is obtained from the catalytic hydrogenation of thebaine.[4] The second of these phenolic ketones, metathebainone, for which Formula II has recently been proposed,[5] contains an alicyclic double bond which is indifferent to catalytic hydrogen[6] but is saturated by reduction with sodium amalgam in alkaline solution. The product, dihydrometathebainone (III),[7] is isomeric with the above-mentioned dihydrothebainone.



I. "True" Thebainone



II. Metathebainone

While the Schöpf metathebainone formula (II) offers the only satisfactory explanation of these facts, the point of attachment of the nitrogen-containing ring and the location of the double linkage rests almost entirely upon speculative evidence, namely, exclusion of other positions, and the extraordinary resemblance of metathebainone to α,β-unsaturated ketones of the type of salicylidene acetone.[5,8] The isolation from a reduction of metathebainone of a diastereomer of the known dihydrometathebainone would constitute a direct proof of the position of the metathebainone double linkage at C-5, C-13 (*i. e.*, at a carbon atom which becomes asym-

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[1] This investigation was supported by a grant from the Committee on Drug Addiction of the National Research Council from funds provided by the Bureau of Social Hygiene, Inc., and the Rockefeller Foundation.

[2] Pschorr, Pfaff and Herrschmann, *Ber.*, **38**, 3160 (1905).

[3] Schöpf and Hirsch, *Ann.*, **489**, 224 (1931).

[4] Freund, Speyer and Guttmann, *Ber.*, **53**, 2250 (1920); Skita, Nord, Reichert and Stukart, *ibid.*, **54**, 1560 (1921).

[5] Schöpf and Borkowsky, *Ann.*, **458**, 148 (1927).

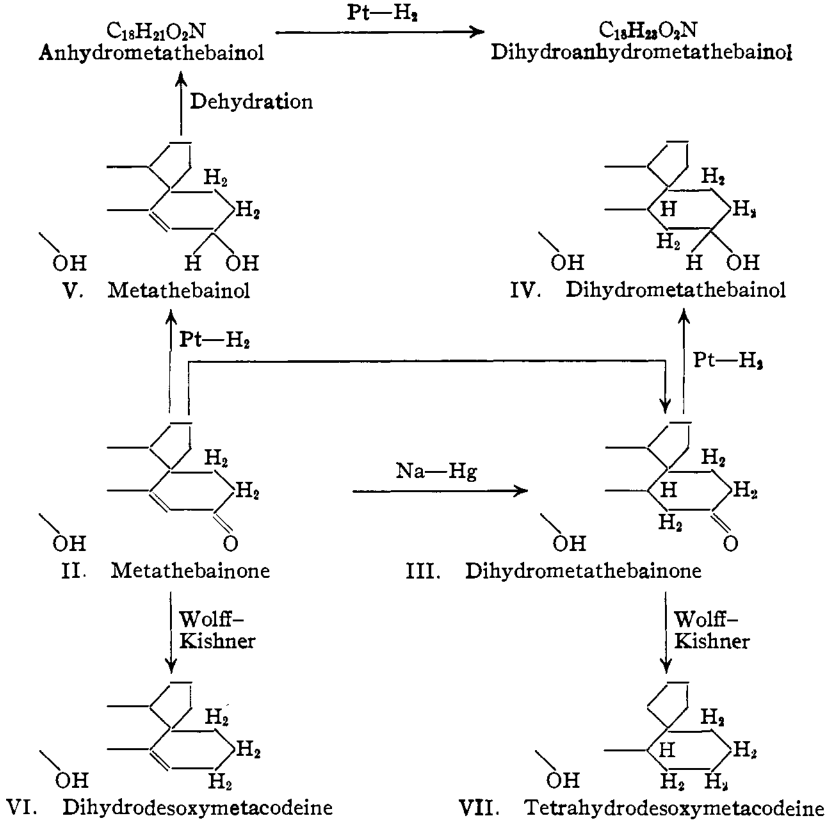
[6] Heinz Hoek, Dissertation, Munich, 1926.

[7] The thebainol of Pschorr,[2] who believed it to be a secondary alcohol; its ketone nature was demonstrated by Gulland and Robinson.[8] A recent review of the chemistry of metathebainone may be found in the "Chemistry of the Opium Alkaloids," by Small and Lutz, U. S. Government Printing Office, 1932, pp. 308–321.

[8] Gulland and Robinson, *J. Chem. Soc.*, **123**, 998 (1923).

metric on reduction),[9] and hence of the ethanamine side chain at C-14.[10] Such a diastereomer, designated as β-dihydrothebainone, from catalytic hydrogenation of metathebainone, was described by Kondo and Ochiai[11] without mention of its significance for the metathebainone formula. The present investigation was undertaken with a view to obtaining by reductive methods more definite evidence on the structure of metathebainone; while the desired proof of structure has not been obtained, nothing has been found which is not in accord with Schöpf's formula.

Metathebainol.—Under the conditions imposed by Hoek (base in alcohol or in excess of dilute acetic acid), metathebainone takes up no hydrogen



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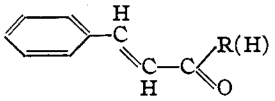
[9] The dihydro-epi-thebainone of Schöpf and Winterhalder [*Ann.*, **452**, 239 (1927)], which must still contain the thebaine nitrogen ring system, is apparently the stereoisomer on C-14 [compare, however, Small and Cohen, This Journal, **53**, 2237 (1931)] of dihydrothebainone, and is different from dihydrometathebainone; it may therefore be assumed that dihydrometathebainone does not represent one of the two diastereomers which might be derived from the saturation of a hypothetical double linkage at C-8, C-14. See Schöpf and Borkowsky, *Ann.*, **458**, 155 (1927).

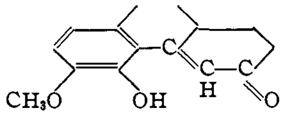
[10] Schöpf and Borkowsky, *ibid.*, **458**, 159 (1927). The morphol degradation of methylmetathebainonemethine [Knorr and Pschorr, *Ber.*, **38**, 3172 (1905)] makes attachment of the ethanamine chain at other than a tertiary carbon atom unlikely.

[11] Kondo and Ochiai, *J. Pharm. Soc. Japan*, No. **549**, 913 (1927); *Ann.*, **470**, 232 (1929).

with palladium or platinum. When hydrogenation is carried out under the conditions of Kondo (base neutralized with dilute hydrochloric acid), or as we later found, on an aqueous solution of the base, one mole of hydrogen is absorbed readily. The product is a mixture of two substances, as might be suspected from the constants given by Kondo for the supposed β-dihydrothebainone. The main product (65% or more) is not a dihydro ketone, but the isomeric α,β-unsaturated alcohol (V) which we have named metathebainol. It is obtained in quantitative yield when metathebainone is hydrogenated in the presence of platinum oxide at two to three atmospheres pressure. The second product isolated from hydrogenation at atmospheric pressure is a ketone, obtained in about 5% yield as the semicarbazone. This was dextrorotatory, and proved to be identical with the already-known semicarbazone of dihydrometathebainone (III).

While these findings invalidate any support which may have been lent to the C-5, C-13 location of the double linkage by the supposed existence of a second dihydrometathebainone, the formation of the same dihydro ketone as in the sodium amalgam reduction does not necessarily weigh against the Schöpf formula. It seems not improbable that the catalytic saturation of the double bond has been accomplished through the same mechanism which we believe functions in the sodium amalgam reduction, namely, a primary 1,4-addition of hydrogen.[12] Metathebainol, which does not present this opportunity for a 1,4-addition, is completely indifferent to sodium amalgam or catalytic hydrogen. The predominating 1,2-addition at the carbonyl group recalls the hydrogenation of α,β-unsaturated ketones and aldehydes containing a system not dissimilar to that of metathebainone





where it could be demonstrated, particularly in the case of cinnamic aldehyde, that the course of normal hydrogenation consisted of a primary reduction of the carbonyl oxygen to hydroxyl.[13]

Metathebainol does not give any of the characteristic reactions for the keto group. The presence of two hydroxyl groups is shown by the formation of a diacetyl derivative, which may be saponified to yield metathebainol and a small amount of a new base of unknown nature. The acetyl group on the phenolic hydroxyl of metathebainol, while stable toward alcoholic potassium acetate at 140°, is split off easily by an aqueous solu-

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(12) A prediction from Skita's rule [Skita, *Ann.*, **431**, 1, 15 (1923); Skita and Faust, *Ber.*, **64**, 2878 (1931)] that diastereomeric compounds should appear in the two types of reduction involved, does not seem warranted where the possibility of 1,4-addition is present.

(13) Straus and Grindel, *Ann.*, **439**, 276 (1924); compare Tuley and Adams, THIS JOURNAL, **47**, 3061 (1925).

tion of hydroxylamine hydrochloride at room temperature.[14] The resulting compound is phenolic and still contains one acetyl group; whether other changes in the molecule take place was not investigated. Monoacetylthebainol shows marked thermochromism;[15] the colorless solution in cold alcohol or bromobenzene gives a reversible change to pink on warming. The colored solution is apparently not affected by oxygen, and the monoacetyl compound can be recovered unchanged from the experiment.

Metathebainol shows no halochromism with cold hydrochloric acid, but is changed slowly to a substance which gives a highly-colored solution; the color disappears on dilution with water, and a new halogen-containing base can be isolated. The monoacetyl and diacetyl derivatives likewise show no immediate halochromism, but are converted to halochromic compounds on standing in acid solution.

Metathebainol crystallizes associated with one molecule of methanol or chloroform. While, as noted above, the alkaloid or its compound with methyl alcohol is indifferent to catalytic hydrogenation, the compound with chloroform was observed to absorb one molecule of hydrogen. The product was pure metathebainol hydrochloride. The hydrogen chloride was obviously derived from catalytic hydrogenation of the chloroform of crystallization, and experiments have shown us that chloroform, in the presence of such a saturated base as dihydrocodeine, can be hydrogenated with ease, one molecule of hydrogen being absorbed for each molecule of base present.[16]

Anhydrometathebainol.—When metathebainol is heated to 160° with alcoholic potassium hydroxide, it loses one molecule of water to give a new base, $C_{18}H_{21}O_2N$, which we shall designate as anhydrometathebainol. It must contain two alicyclic double bonds, one of which apparently still occupies the metathebainol C-5, C-13 position, for it is possible to effect addition of but one mole of hydrogen catalytically. The second double linkage might be expected at C-6, C-7; the hydrogenation product, dihydroanhydrometathebainol is, however, different from the dihydrodesoxymetacodeine (VI) to be described below. It is probable, therefore, that the formation of anhydrometathebainol has involved a deeper-seated structural change (perhaps to a morphothebaine type) than mere dehydration in ring III.

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(14) A similar saponification by cold hydroxylamine hydrochloride was observed by Pschorr[2] in the case of acetylmetathebainone.

(15) A recent account of thermochromic phenomena is given by Bergmann and Corte, *Ber.*, **66**, 39 (1933). The hypothesis of Bergmann that the presence of a cross-conjugated system is necessary for thermochromism leads us to suspect that the saponification with hydroxylamine hydrochloride may have been accompanied by other structural changes.

(16) Catalytic hydrogenation of carbon tetrachloride, bromoform and iodoform in the presence of sodium ethylate has been described by Kelber, *Ber.*, **50**, 305 (1917); Busch and Stöve, *ibid.*, **49**, 1063 (1916). Borsche and Heimbürger, *ibid.*, **48**, 850 (1915), cite the experiment of Ottmers, who could reduce the halogen out of isopinol dibromide only when the hydrogen bromide formed was taken care of by piperidine or quinoline.

Dihydrometathebainol.—The alicyclic double bond of metathebainol resists reduction, but the saturated alcohol, dihydrometathebainol, (IV) may be prepared indirectly from metathebainone through dihydrometathebainone (III). The last-named compound adds one molecule of hydrogen readily in the presence of platinum (oxide), yielding a secondary alcohol, which is isomeric with the two known epimeric dihydrothebainols derived from the dihydrothebainone series.[17] The isomerism might be due: (a) to a difference in the ring position (at C-6 or C-8) of the alcoholic hydroxyl (most improbable, because of the relationship of metathebainone to codeinone[18] (*cf.* also Schöpf[19]); (b) to a difference in the point of attachment of the ethanamine side chain (the question of the generation of a new asymmetric center at C-14 has already been considered[9]).

The Hydrodesoxymetacodeines.—We have attempted to eliminate consideration (a) of the preceding paragraph through the preparation of hydrogenated derivatives of a hypothetical desoxymetacodeine. When metathebainone is heated with hydrazine hydrate and sodium ethylate (method of Wolff–Kishner), reduction of the keto group takes place[20] and a good yield of a new base, $C_{18}H_{23}O_2N$, is obtained. Dihydrodesoxymetacodeine (VI) is isomeric with the dihydrodesoxycodeines derived from the normal codeine series.[21] Like its parent substance, metathebainone, it resists hydrogenation, but since the α,β-unsaturated ketone system postulated by the Schöpf formula has been destroyed, it shows no halochromism.

Under the same conditions of reduction, dihydrometathebainone is converted in about 80% yield to the corresponding saturated tetrahydrodesoxymetacodeine (VII). The new base is different from its well-known isomer tetrahydrodesoxycodeine,[22] and must owe its isomerism to a difference in point of attachment of the nitrogen-containing side chain.[23]

It is a pleasure to acknowledge here the generosity of Merck and Co , Rahway, N. J., in supplying the thebaine used in this research.

Experimental

Metathebainone.—This base was prepared according to the directions of Gulland and Robinson.[8] By this method, which involves a final neutralization with sodium

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[17] Speyer and Siebert, *Ber.*, **54**, 1519 (1921); Kondo and Ochiai, *J. Pharm. Soc. Japan*, No. **538**, 99 (1926); *Ann.*, **470**, 224 (1929).

[18] Knorr, *Ber.*, **38**, 3171 (1905).

[19] Schöpf and Hirsch. *Ann.*, **489**, 229, Note 3 (1931).

[20] Clemmensen reduction of metathebainone or of dihydrometathebainone results in dark resinous products; our experiments in this line agree with those already reported by Hoek.[6]

[21] Small and Cohen, THIS JOURNAL, **53**, 2227 (1931).

[22] Small and Cohen, *ibid.*, **54**, 802 (1932).

[23] The possibility that rearrangement may have taken place under the vigorous conditions imposed must be mentioned, since metathebainone and dihydrometathebainone heated with sodium ethylate alone at 180° were found to be altered. The products in this case, however, were disagreeable resins, and the good yield of clean crystalline products from the Wolff–Kishner conditions speaks for a rapid primary formation of the hydrazone and transformation of the latter to the completely alkali-stable desoxy product.

bicarbonate, a yellow metathebainone, as the compound is described throughout the literature, was always obtained. The crystals were of a color close to that of picric acid, and retained this color unchanged through very numerous recrystallizations. When the final neutralization was carried to distinctly alkaline reaction with sodium hydroxide or ammonia, the crude metathebainone was only faintly yellow, and after several crystallizations from ethanol by addition of methanol was obtained as white crystals which showed no tinge of yellow when compared with pure anhydrous sodium sulfate. The white and yellow specimens have the same melting point. Both give yellow solutions in ethanol or water, colorless solutions in benzene or chloroform. For the yellow specimen, in benzene, $[\alpha]_D^{24}$ $-419°$ ($c = 1.966$); for the white specimen, $[\alpha]_D^{25}$ $-417°$ ($c = 1.802$).

Metathebainol (V).—Ten grams of metathebainone was neutralized with 0.2 *N* hydrochloric acid and reduced in the presence of 0.15 g. of platinum oxide at 2 to 3 atmospheres gage pressure until no further absorption took place (three to twelve hours). After removal of catalyst the solution was made ammoniacal and the clear liquid extracted with 30 cc. of chloroform. From the chloroform 7 to 8 g. of the metathebainol–chloroform addition product crystallized after short standing. The mother liquor from this crystallization was combined with the chloroform from two more extractions, evaporated nearly to dryness, and taken up in a little methanol. Four to five grams more of a somewhat less pure product was thus obtained.

Metathebainol crystallizes from chloroform in white crystals which melt at 87–88° with loss of chloroform. In absolute alcohol $[\alpha]_D^{25}$ -45.3, $-45.9°$ ($c = 3.490, 2.525$) was observed. The chloroform compound loses a portion of its chloroform on exposure to air and combustion analyses were not consistent; direct determination of chloroform was difficult on account of the ease with which the base distils.

Anal. Calcd. for $C_{18}H_{23}O_3N + CHCl_3$: $CHCl_3$, 28.4. Found: $CHCl_3$, 27.1, 30.2.

The solvent-free base could be obtained only as a faintly yellow resin ($[\alpha]_D^{25}$ $-66.7°$ in absolute alcohol, $c = 2.781$) which gave with chloroform the crystalline addition compound again, or gave with methanol white crystals of m. p. 92–93°. These showed $[\alpha]_D$ -60.3, $-61.2°$ (absolute alcohol, $c = 2.134, 2.043$; $t = 24, 27°$). The solvated crystals as brought to analysis always contained less than one molecule of methanol.

Anal. Calcd. for $C_{18}H_{23}O_3N + CH_3OH$: C, 68.43; H, 8.16; CH_3OH, 9.6. Calcd. for $C_{18}H_{23}O_3N + 0.8CH_3OH$: C, 69.04; H, 8.08; CH_3OH, 7.8. Found: C, 68.83; H, 8.13; CH_3OH, 7.6. Calcd. for $C_{18}H_{23}O_3N$: C, 71.71; H, 7.70. Found: (dried at 120°) C, 71.70; H, 8.03.

Metathebainol was regained unchanged from shaking in alkaline solution for seven hours with sodium amalgam; from boiling in alcohol solution with sodium amalgam, with occasional addition of glacial acetic acid; from treatment with sodium in alcohol; from shaking the chloroform-free base in alcohol with platinum oxide under hydrogen. When metathebainol containing crystal-chloroform was hydrogenated in alcohol with platinum oxide catalyst, one mole of hydrogen was absorbed. The product was isolated by evaporating the solution to a small volume and adding warm ethyl acetate. White crystals were obtained, which melted at 162° (gas evolution), resolidified and decomposed above 220°. The compound proved to be metathebainol hydrochloride containing one molecule of ethyl acetate.

Anal. Calcd. for $C_{21}H_{32}O_5NCl$: C, 60.92; H, 7.79. Found: C, 60.95; H, 7.57.

Metathebainol is exceedingly stable toward alkali. It was recovered unchanged after boiling with 25% potassium hydroxide for fifteen minutes, or from heating six hours with sodium ethylate solution at 125° (sodium ethylate or alcoholic potassium hydroxide at 160° effects dehydration, see anhydrometathebainol). Metathebainol in concentrated hydrochloric acid gives a colorless solution which slowly (rapidly at 60°) becomes green and finally a pure blue halochromic solution results. The blue color disappears with reducing agents, as zinc or stannous chloride, and if these are present at the beginning no color develops. Stannous chloride or salts of other heavy metals yield insoluble double salts. The base isolated from the halochromic solution was not crystalline; it contained halogen, and on catalytic hydrogenation took up one molecule of hydrogen to give the hydrochloride of a new (amorphous) base. Metathebainol gave no oxime or semicarbazone, but appeared to be decomposed by the reagents. With nitrous acid it gave an intense red color.

Metathebainol hydriodide was prepared in the usual way and purified from water.

Anal. Calcd. for $C_{18}H_{23}O_3N \cdot HI + H_2O$: I, 28.38. Found: I, 28.25, 28.11.

Metathebainol methiodide was prepared in the usual way and purified from alcohol; m. p. 225°.

Anal. Calcd. for $C_{19}H_{26}O_3NI$: I, 28.65. Found: I, 28.67.

Diacetylmetathebainol.—A solution of 1 g. of metathebainol in 4 cc. of acetic anhydride was allowed to stand for two hours at room temperature, poured into water, made ammoniacal, and the precipitate extracted with ether. The product obtained weighed 0.75 g. and after recrystallization from dilute methyl alcohol melted at 140°. It was non-phenolic; the solution in hydrochloric acid was colorless, but exhibited strong green-blue halochromism on standing. Diacetylmetathebainol in alcohol with platinum oxide could not be hydrogenated.

Anal. Calcd. for $C_{22}H_{27}O_5N$: C, 68.53; H, 7.06. Found: C, 68.78, 68.49; H, 7.29, 6.96. Calcd. for $C_{18}H_{21}O_3N(COCH_3)_2$: $COCH_3$, 22.4. Found: (Freudenberg) $COCH_3$, 22.1.

Diacetylmetathebainol was recovered unchanged after heating in absolute alcohol with potassium acetate for one hour at 130°. For saponification, 2.9 g. of diacetylmetathebainol was boiled for ten minutes with 20 cc. of 25% aqueous alcoholic potassium hydroxide. The solution was diluted, ammonium chloride added, and the precipitate extracted with chloroform. The residue from distillation of the chloroform was taken up in 20% acetic acid and a concd. solution of 2 g. of potassium iodide added. A crystalline hydriodide, 0.7 g., separated, from which small amounts of a new base of m. p. 150° were obtained. This gave a mixed melting point depression of 30° with monoacetylmetathebainol of the same melting point, and its nature is unknown. From the mother liquor of the hydriodide precipitation, 1 g. (= 32% of the calculated amount) of metathebainol-chloroform could be isolated.

Monoacetylmetathebainol.—A solution of 1 g. of diacetylmetathebainol and 0.4 g. of hydroxylamine hydrochloride in a little water was allowed to stand for one hour. Sodium carbonate was added and the precipitated base extracted into ether. On evaporation of the solvent and addition of warm ethyl acetate, white crystals were obtained which could be purified from ethyl acetate. The compound turns pink at about 143° and melts to a red liquid at 150°. A solution of acetylmetathebainol in alcohol or bromobenzene becomes pink on heating, and the color disappears on cooling; this may be repeated many times. No sensitiveness to oxygen was noted, and the compound was regained unchanged. Acetylmetathebainol has the properties of a phenol. It does not show immediate halochromism in concentrated hydrochloric acid, but is slowly changed by the acid so that a green-blue solution results. The base gave values for nitrogen which were consistently too high, and we do not consider the structure we have given it to be certain.

Anal. Calcd. for $C_{20}H_{25}O_4N$: C, 69.93; H, 7.34; N, 4.08. Found: C, 69.60, 69.76; H, 7.42, 7.39; N, 4.91, 4.78. Calcd. for $C_{18}H_{22}O_3N(COCH_3)$: $COCH_3$, 12.54. Found: (Freudenberg) 12.81.

Hydrogenation of Metathebainone. Method of Kondo and Ochiai.[11]—Two grams of metathebainone, neutralized with dilute hydrochloric acid, with 0.5 g. of charcoal (Eastman Kodak "Special") and 2 cc. of 1% palladous chloride solution absorbed 140 to 150 cc. of hydrogen (several experiments). The solution was made ammoniacal, the bases extracted into chloroform, and the extract concentrated to a small volume; on addition of methanol and cooling 1.5 to 1.6 g. (60–65%) of metathebainol–chloroform separated. The mother liquor (which contained more metathebainol) was treated with dilute acetic acid, and sodium acetate and semicarbazide hydrochloride added. After twelve hours sodium carbonate was added and the white precipitate extracted with chloroform. This yielded 0.1 g. (5% of the calculated amount) of a semicarbazone of m. p. 217–218° and $[\alpha]_D^{25}$ +88.4° (10% acetic acid, c = 1.289). When mixed with dihydrometathebainone semicarbazone of m. p. 232° and $[\alpha]_D^{27}$ +109.8°[24] it melted at 226°.

Dihydrometathebainol (IV) was obtained by hydrogenation (1 mole of hydrogen) of dihydrometathebainone in alcohol with platinum oxide. The free base, which formed poorly defined crystals of m. p. about 120°, gave a well-defined hydriodide having $[\alpha]_D^{30}$ +16.4° (water, c = 4.128).

Anal. Calcd. for $C_{18}H_{26}O_3NI + 2H_2O$: C, 46.24; H, 6.47; I, 27.17; H_2O, 7.7. Found: C, 46.40; H, 6.14; I, 27.35; H_2O, 7.7.

Dihydrodesoxymetacodeine (VI).—A solution of 1.5 g. of metathebainone and 1 cc. of hydrazine hydrate in 15 cc. of absolute alcohol containing 0.7 g. of sodium was heated in a sealed tube to 180° for three hours. The nearly colorless solution was poured into water, ammonium chloride added, and the precipitated base extracted with ether. The residue from distillation of the ether yielded 0.8–0.9 g. (56–63% of the calculated amount) of crystals on treatment with a little methanol. As recrystallized from methanol the base sinters at 65°, melts at 72°, but soon becomes amorphous through loss of methanol. It distils readily at 130–135° at 0.001 mm., forming a colorless resin which becomes crystalline with methanol. Analysis and rotation were made on the distilled solvent-free product. In absolute alcohol, $[\alpha]_D^{24}$ −93.8° (c = 1.109) was found.

Anal. Calcd. for $C_{18}H_{23}O_2N$: C, 75.74; H, 8.12. Found: C, 75.43; H, 7.95.

An alcoholic solution of dihydrodesoxymetacodeine absorbed no hydrogen (platinum oxide catalyst). The base gave no halochromism with concentrated hydrochloric acid, even on heating. In one attempted preparation of the desoxy compound, insufficient heating resulted in the formation of a bright yellow compound, sparingly soluble in alcohol or ether, m. p. 200–210° with decomposition, which was apparently the ketazine of metathebainone.

Tetrahydrodesoxymetacodeine (VII).—A solution of 1.8 g. of dihydrometathebainone (solvent-free) and 1 cc. of hydrazine hydrate in 15 cc. of absolute alcohol containing 0.9 g. of sodium was heated in a sealed tube at 170–180° for six hours. The light yellow liquid was diluted with water, the base precipitated with ammonium chloride and extracted into ether. The product was amorphous, but gave 2.1 g. of well crystallized hydriodide (80% yield). In aqueous solution the hydriodide showed $[\alpha]_D^{28}$ −12.5° (c = 1.928).

Anal. Calcd. for $C_{18}H_{26}O_2NI$: C, 52.03; H, 6.31; I, 30.58. Found: C, 52.11; H, 6.55; I, 30.12.

Anhydrometathebainol.—Three grams of solvated metathebainol was freed from chloroform at 100° and 15 mm. pressure and dissolved in 20 cc. of 95% alcohol containing 0.7 g. of potassium hydroxide. After heating at 160° for one and one-half hours in a

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[24] From sodium amalgam reduction of metathebainone; Gulland and Robinson[8] give the melting point of the semicarbazone as 216–218°, specific rotation not given.

sealed tube the solution was poured into water, treated with ammonium chloride and extracted with ether. The brown residue from evaporation of the ether became crystalline with warm methanol; yield 1.2 to 1.3 g. (53–57%). The base melts at 106–107° with decomposition; it distils at 130° and 0.001 mm. as a colorless resin, which yields the crystals of m. p. 107° with methanol. The solvent-free base turns quite brown in twenty-four hours. It dissolves colorless in concentrated hydrochloric acid, then develops a green-blue halochromism. For the solvent-free base the specific rotation was $[\alpha]^{25}_{D}$ −201° (absolute alcohol, c = 1.813).

Anal. Calcd. for $C_{18}H_{21}O_2N$: C, 76.28; H, 7.47. Found: C, 76.15; H, 7.73.

Acetylanhydrometathebainol was prepared by the method used for diacetylmetathebainol. It was purified from methanol and melted at 166°. In alcohol with platinum oxide it absorbed one mole of hydrogen.

Anal. Calcd. for $C_{20}H_{23}O_3N$: C, 73.80; H, 7.13. Found: C, 73.35, 73.46; H, 7.23, 7.36.

Dihydroanhydrometathebainol was prepared by hydrogenation of anhydrometathebainol in alcohol with platinum oxide. It crystallizes from methanol in white crystals which are stable only while in contact with the solvent. It distils at 130° and 0.001 mm. as a colorless stable resin, which crystallizes in contact with methanol. In concentrated hydrochloric acid a green-blue halochromism slowly develops.

Anal. Calcd. for $C_{18}H_{23}O_2N$: C, 75.74; H, 8.12. Found: C, 75.63; H, 8.39.

Summary

1. Hydrogenation of metathebainone in aqueous solution or as the hydrochloride results in formation of a secondary alcohol, metathebainol, together with a small amount of dihydrometathebainone.

2. The so-called β-dihydrothebainone of Kondo is a mixture of metathebainol and dihydrometathebainone. The existence of a diastereomer of dihydrometathebainone, which could serve as proof of the Schöpf metathebainone formula, has not yet been demonstrated.

3. Catalytic hydrogenation of dihydrometathebainone leads to a saturated secondary alcohol, dihydrometathebainol.

4. Metathebainone and dihydrometathebainone can be reduced by the method of Wolff–Kishner to desoxy derivatives isomeric with the dihydrodesoxycodeines and tetrahydrodesoxycodeine, respectively.

5. Through dehydration of metathebainol an anhydrometathebainol of uncertain structure is obtained.

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