Studies on Sinomenine. LXI.
On (+)-epi-Dihydro-thebainone.

By Kakuji GOTO and Kimiyo MICHI.

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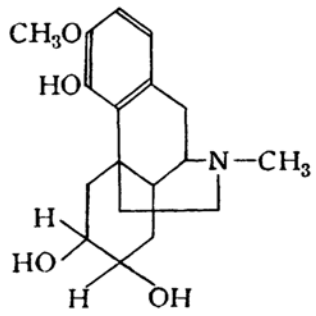
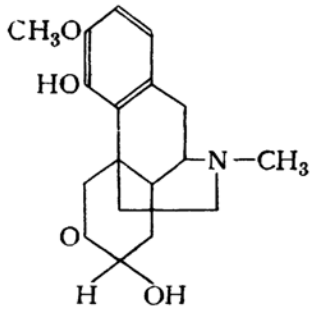
In a previous communication,[1] we reported the formation of (+)-dihydro-codeinone (III) from (+)-dihydro-sinomeninone (II) by boiling the latter in 50% sulfuric acid solution. We applied the same treatment to tetrahydro-sinomeninone (I) to see whether the base is thereby led to the formation of the oxide ring or not. We found, however, that no trace of alkali-insoluble base was formed in this case, but tetrahydro-sinomeninone was transformed into a base (IV) isomeric with the well-known dihydro-

(1) Part LX, *Acta phytochimica*, XV, 187 (1949).

thebainone. The transformation is brought about undoubtedly by a kind of semi-pinacoline rearrangement.



I



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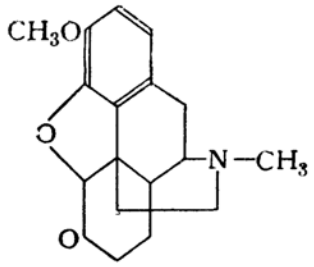
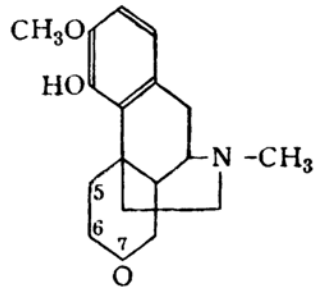
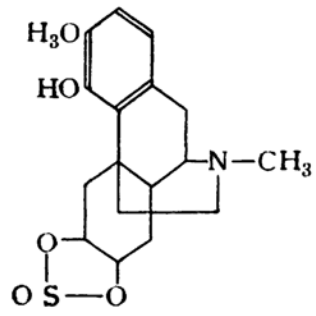


III



IV



VI

V ($C_7 = CHOH$)

The formation of (+)-dihydro-codeinone (III) from α-dihydro-sinomeninone (II) necessitates the migration of the hydroxyl groups from C (7) to C (5) around the ketonic group at C (6). This may be effected by anionotropy through the interchange of the positions between the hydroxyl group and the double linking, formed by the enolization of the ketone. The fact that tetrahydro-sinomeninone was not led to the oxide ring closure by the same treatment seems to verify the above supposition to some degree.

The new base, epi-dihydrothebainene, having the molecular formula $C_{18}H_{23}O_3N$ and being soluble in caustic alkali, gives a ferric chloride reaction and forms a monosemicarbazone. It is reduced catalytically into an alcoholic base, epi-dihydrothebainol, and shows properties quite different from dihydrothebainol. Its dibenzoyl derivative crystallizes as methiodide.

In the following table, the properties of the two pairs of the ketonic and alcoholic bases are compared.

	M. p. of free base	[α] D	M. p. of Semicarbazone	M. p. of Methiodide
(+)-Epidihydrothebainone	130°	+37.3°	205°	253°
(+)-Dihydrothebainone[2]	152°	+59.17°	235°	122°
(+)-Epidihydrothebainol	154°	+48.6°	—	282°
(+)-Dihydrothebainol[3]	165°	+31.5°	—	278°

By the way, we tried the dehydrating action of thionyl chloride on tetrahydrosinomeninone. However, the dehydration did not occur and thionyl chloride formed a cyclic sulfurous acid ester (VI) with the vicinal glycol of the base. This fact coincides well with the investigation of Kitasato and Sone.[4]

The thionyl ester gives the sodium nitro-prusside reaction and regenerates the original base, when warmed with hydrochloric acid, and gives a ferric chloride reaction, thus the phenol group seems to remain intact in the product.

Experimental (By K. M.)

(+)-Epi-dihydro-thebainone (IV). Solution of (+)-tetrahydro-sinomeninone (2 g.) in 55% sulfuric acid (15 c.c.) was boiled for 1.5 hours in an oil-bath. As the concentration of sulfuric acid plays a considerable part on the yield, it should be kept exactly 55%. The cooled solution was diluted with water, made alkaline with caustic and fixed soda, and extracted with chloroform. The chloroform residue was dissolved in acetone and the acetone solution was diluted with ether of its half volume. The precipitate was filtered off and the filtrate was concentrated, dissolved in acetone and rubbed with a glass-rod. The crude base thus crystallized out melted at 120°C. (Yield 0.5 g.). The pure epidihydro-thebainone was obtained through its semicarbazone.

Semicarbazone. To the aqueous solution of the above crude base (4 g.), a sufficient quantity of semicarbazide hydrochloride and sodium acetate was added and the mixture was heated for 15 min. on a steam-bath and left overnight. The semicarbazone was isolated with chloroform and recrystallized from alcohol and acetone. M. p 205°C. Yield 1.6 g. (Found: C, 63.70; H, 7.02; N, 15.79%. Calc. for $C_{19}H_{26}N_4O_3$: C, 63.69; H, 7.26; N, 15.64%.)

Regeneration of the free epi-dihydro-thebainone was effected by boiling the semicarbazone (0.8 g.) with 40% sulfuric acid (20 c.c.) in an oil-bath (130–135°C) for an hour. The free base crystallized out in prisms from acetone. M. p. 130°C. $[\alpha]_D^{10} = +37.3°$ (c=2.200 in chloroform). (Found; C, 72.00; H, 7.455; N, 4.595% Calc. for $C_{18}H_{23}O_3N$: C, 71.76; H, 7.64, N, 4.65%).

Methiodide. M. p. 253°C from alcohol. (Found: I, 28.59%. Calc. for $C_{18}H_{23}O_3N.ICH_3$: I, 28.70%).

(+) Epidihydro-thebainol (V). The (+)-epidihydro-thebainone (0.5 g.) was dissolved in methanol (20 c.c.), added with PtO_2 (0.05 g.) and reduced catalytically at 30°C. The

(2) K. Goto and S. Mitsui, This Bulletin, **5** (1930), 282.

(3) Prepared by catalytic reduction in the same way as is shown in the experimental part. These figures coincide well with those given by Skita and others (*Ber.*, **54** (1921), 1560) on (−)-dihydrothebainone, but somewhat differ from those of (+)-dihydrothebainone, prepared by Na-amalgam reduction.[1] A similar case is known in the catalytic reduction of cholestanone (*cis-trans* isomerism of H and OH).

(4) *Ber.*, **64** (1931), 1142.

absorption of hydrogen amounted to 50 c.c. On evaporating the methanolic filtrate, the free base crystallized out in prisms. M. p. 125°C, after sintering at 115°C. However, the dried specimen for analysis melted at 154°C. $[\alpha]_D^{17} = +48.6°$(C=1.768, chloroform). (Found: C, 71.57: H, 8.345; N, 4.49%. Calc for $C_{18}H_{25}O_3N$: C, 71.29; H, 8.25; N, 4.62%).

Methiodide. M p. 282°C from alcohol. (Found: I, 28.88%. Calc. for $C_{18}H_{25}O_3N \cdot ICH_3$: I, 28.54%).

Dibenzoyl-(+)-epidihydro-thebainol-methiodide. (+)-Epidihydro-thebainol (0.1 g.) was dissolved in dry pyridine (1 c.c.) cooled with freezing mixture and added with benzoyl-chloride (0.15 g.). The mixture was left overnight and then decanted into a saturated solution of ammonium carbonate. Two days after, the syruppy precipitate was washed with water and taken up in chloroform. The washed and dried chloroform gave an oily residue when evaporated. The dibenzoyl-derivative was too soluble in organic solvents, such as alcohol and benzene and did not crystallize from ether also. It was, therefore, turned into its methiodide in alcoholic solution. M. p. 273°C recrystallized therefrom. (Found: C, 60.53; H, 5.898; N, 2.14; I, 19.23%. Calc. for $C_{33}H_{36}O_5NI$: C, 60.64; H, 5.51; N, 2.14; I, 19.45%).

Thionyl-ester (VI) of (+) tetrahydro-sinomeninone. Dry (+)-tetrahydro-sinomeninone (1 g.) was dissolved in dry pyridine and the solution was slowly decanted into ice-cooled thionyl chloride (6 g.). After being kept standing two hours, the clear solution was poured on ice, and made alkaline with sodium carbonate. The thionylester was then extracted with chloroform. The dried chloroform was distilled off and the remaining pyridine was removed under diminished pressure. The residue crystallized on addition of methanol. Yield 0.8 g. M.p. 189°C from the same solvent. $[\alpha]_D^{22} = +71.7°$ (C=0.488, in chloroform). (Found: C, 57.27; H, 6.44; N, 3.55; CH_3OH, 7.89%. Calc. for $C_{18}H_{23}NO_5S \cdot CH_3OH$: C, 57.43; H, 6.80; N, 3.52; CH_3OH, 8.06%). The methanol free ester melted at 191°C.

As it has been already shown[5] that (—)-tetrahydrosinomeninone can be prepared from (—)-dihydrothebainone through a series of reactions, it is quite reasonable to assume that (—)-epi-dihydrothebainone and (—)-epi-dihydrothebainol can be prepared in the same way as above. This part of work must be postponed in future for the lack of materials.

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Biochemical Laboratory, Agricultural Department,
Tokyo University.

(5) K. Goto and T. Arai, This Bulletin, **17** (1942), 113.