SINOMENINE AND DISINOMENINE. PART XXVIII. ON HOFMANN DECOMPOSITION OF DIHYDROSINOMENINE.

By **Kakuji GOTO** and **Hideo SHISHIDO.**

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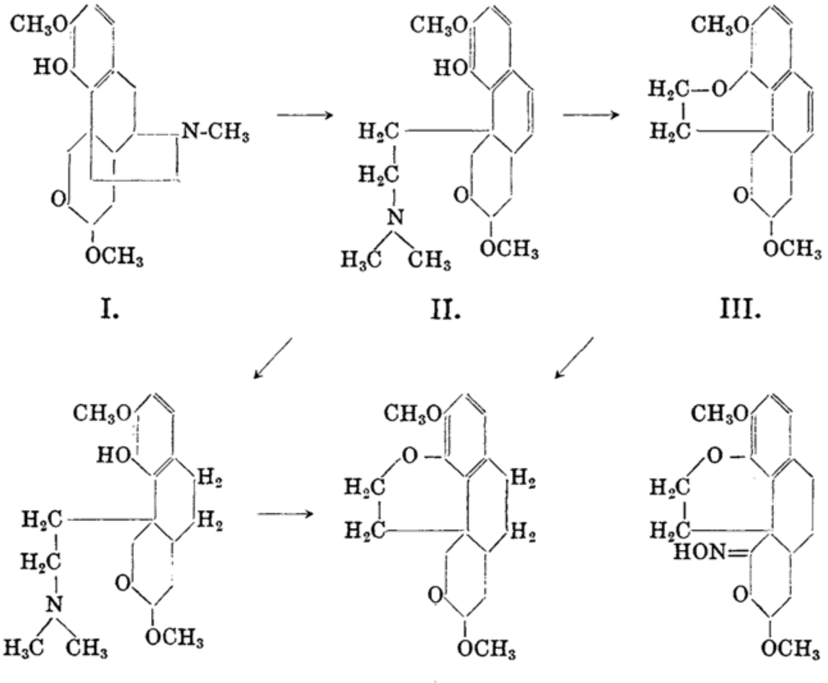
On Hofmann decomposition of sinomenine and its derivates, several communications have been published by us. In the present communication, dihydrosinomenine [I] was decomposed into the 7-methoxy-dehydro-*l*-thebenone [III] and into the 7-methoxy-*l*-thebenone [V] by the following process.



One remarkable feature in the above decomposition is that the sense of the optical rotation is inverted step by step from sinomenine to 7-methoxy-*l*-thebenone. The same phenomenon was observed in the *l*-thebenone and the *l*-thebenane series. As we have shown already, this inversion could be explained by the exalting action of the double bond only if we assume that

1. in sinomenine, $C_{(13)}$ is + and $C_{(14)}$ is −
2. the formation of an ether ring between OH in (4) and the side chain diminishes or inverts the rotatory power of $C_{(13)}$ or exalts that of $C_{(14)}$.

This hypothesis, which assumes $C_{(13)}$ to be + and $C_{(14)}$ to be − in sinomenine (hence $C_{(13)}$ to be − and $C_{(14)}$ to be + in morphine series) can be, however, applied only to the simplest cases such as the thebenone and thebenane series. In the three sinomenine methines, reported in the XXVth communication, this hypothesis is already faced with a grave difficulty. Of these three methines, sinomenine-violeo-methine seems to be most akin to the β- or δ-methylmorphi-methines, from the mode of its preparation and from its properties. But here it seems that the optical antagonisms between morphine and sinomenine series disappears or at least strongly diminishes. For, sinomenine-violeo-methine as well as its methylether-methosulphate are strongly dextrorotatory ($>300°$) just like β- or δ-methyl-morphi-methines. This may be due partly to the fact that in morphine series there are two more asymmetric carbon atoms [$C_{(5)}$ and $C_{(6)}$] than in sinomenine. Yet, the ultimate reaction, we presume, must be sought in

(1) the influence of phenyl nucleus,
(2) the influence of the ring formation, viz. the nitrogenous ring, the ether ring and the hydrated third ring of the phenanthrene and
(3) the double linking,

as we have already mentioned.

The 7-methoxy-*l*-thebenone forms an isonitroso derivative by the action of amylnitrite and Na in ether. Although this isonitroso-derivative can not be obtained in a crystallised state, yet from the determination of N and methoxyl, it is clear that the isonitroso group must have been introduced in $C_{(5)}$. Then our assumption that the side-chain in sinomenine must be attached to $C_{(13)}$, made principally from its very easy splitting off, even by boiling 2% caustic soda in case of the sinomenine-violeo-methine, seems justly to have been added with a new proof.

Experimental

1. Dihydrosinomenine-methine [II]. Dihydrosinomenine iodomethylate (5 gr.) is boiled with 16.5% KOH (30 c.c.) for 70 minutes. The liquid is then diluted with water (30 c.c.), well cooled and saturated with CO_2, by which the suspended oil drops crystallise out. The crystals are collected, washed with water and dried on a porous plate. Yield almost quantitative. Recrystallised from ether, it forms colourless long prisms. M.p. 173°C. (sintering at 160°C.).

Anal.: Subst. = 3.986; CO_2 = 10.140; H_2O = 2.806 mg. Subst. = 6.424 mg.; N_2=0.218 c.c. (12°C., 762 mm.). Found: C=69.38; H=7.82; N=4.02%. Calc. for $C_{20}H_{27}NO_4$ (345): C=69.56; H=7.82; N=4.06%.

Spec. Rotation. (0.2111 gr. Subst. in 10 c.c. chloroform, 1-dm. tube.)
$\alpha = -1.78°$ $[\alpha]_D^{18} = -84.32°$

2. 7-Methoxy-dehydro-*l*-thebenone [III]. Dihydro-sinomenine methine (6 gr.) was first turned into its iodomethylate by methyl iodide (6 gr.) in boiling methanol (30 c.c.). After the methyl iodide is perfectly evaporated off, the residue was decomposed by boiling 16.5% aqueous KOH (63 c.c.) for 35 minutes. The amine was caught in dilute HCl in this operation. The nitrogen free substance was then extracted with ether, after the free KOH was fixed with CO_2. It forms colourless prisms from ether. Yield 3.4 gr. M.p. 118°C. (Sinters at 113°C).

Anal.: Subst. = 5.989; CO_2 = 15.773; H_2O = 3.642 mg. Found: C = 71.83; H = 6.76%. Calc. for $C_{18}H_{20}O_4$ (300): C = 72.00; H = 6.67%.

Spec. Rotation. (0.2986 gr. Subst. in 10 c.c. chloroform, 1-dm. tube.)
$\alpha = -8.54$ $[\alpha]_D^{18} = -286.00°$

Oxime. 0.2 Gr. subst. was boiled in alcoholic solution (10 c.c.) with $NH_2OH \cdot HCl$ (0.4 gr.) and Na-acetate (0.4 gr.) for 2 hours. The crystals, deposited on evaporation of the alcohol, was well washed and recrystallised from alcohol. Prisms, which melt and decompose at 180°C.

Anal.: Subst. = 5.841 mg.; N = 0.213 c.c. (8°C., 760.4 mm.). Found: N = 4.38%. Calc. for $C_{18}H_{21}NO_4$ (315): N = 4.44%.

Nitrogenous substance. On evaporating the above hydrochloric acid, long needles of the hydrochloride of an amine was obtained, which was purified through absolute methanol. The chloro-aurate and the chloroplatinate melted at 246°C. and 249°C. respectively,

0.0907 Gr. chloro-aurate gave 0.0449 gr. Au. 0.0751 Gr. chloro-platinate gave 0.0278 gr. Pt. Found: Au=49.50; Pt=37.01%.

$[(CH_3)_3N \cdot HCl]\,AuCl_3$ and $[(CH_3)_3N \cdot HCl]_2\,Pt\,Cl_4$ require 49.37% Au and 36.97% Pt respectively.

3. Dihydrosinomenine-dihydro-methine [IV]. Dihydrosinomenine methine (2 gr.), dissolved in dilute HCl, was shaken in hydrogen atomosphere with $PdCl_2$ (0.1 gr.) and charcoal (1 gr.). The calculated quantity of hydrogen was absorbed in 5 minutes. The reduced methine was set free with Na_2CO_3 and extracted with ether, from which it separated out in prisms. M.p. 133°C. (sintering at 123°C.). Yield almost quantitative.

Anal.: Subst. = 3.586, 6.247; CO_2 = 9.08, 15.911; H_2O = 2.735, 4.633 mg. Subst. = 12.849 mg.; N_2 = 0.432 c.c. (12.1°C., 762 mm.). Found: C = 69.12, 69.46; H = 8.46, 8.24; N = 3.98%. Calc. for $C_{20}H_{29}NO_4$ (347): C = 69.16; H = 8.35; N = 4.03%.

Spec. Rotation: (0.4291 gr. Subst. in 10 c.c. chloroform, 1-dm. tube.)
$\alpha = +0.09 \quad [\alpha]^{18}_{D} = +2.09°$

4. 7-Methoxy-*l*-thebenone [V]. (*A*) *From the dihydromethine* [*IV*]. Dihydrosinomenine dihydromethine (1 gr.) was turned first into its iodomethylate in the same way as described in (2). The iodomethylate, which was not crystalline, was decomposed by boiling with 16.5% aqueous KOH in the same manner as described in (2). The 7-methoxy-*l*-thebenone crystallised out from ether in glistening, colourless, long prisms. Yield 0.37 gr. (ca. 50%). M.p. 128°C. (sintering at 122°C.).

The nitrogenous substance showed the same properties as that obtained in the reaction (2) and was purified in the same way.

0.0430 Gr. the chloroaurate gave 0.0212 gr. Au. 0.0585 Gr. the chloroplatinate gave 0.0216 gr. Pt. Found: Au = 49.30; Pt. = 36.92%. Calc.: Au = 49.37; Pt. = 36.97%.

(*B*) *From 7-methoxy-dehydro-l-thebenone.* 7-Methoxy-dehydro-*l*-thebenone (2 gr.) was reduced catalytically in the same way as described in (3). The calculated quantity of hydrogen was absorbed in 30 minutes. The reduced substance crystallised out from ether in glistening prisms. M.p. 128°C. (sintering at 123°C.). Yield almost quantitative.

The mixed m.p. of the substances from (A) and (B) was unaltered. Anal.: Subst. = 4.780; CO_2 = 12.526; H_2O = 3.115 mg. Found: C = 71.46; H = 7.24%. Calc. for $C_{18}H_{22}O_4$(302): C = 71.52; H = 7.28%.

Spec. Rotation. (0.2885 gr. Subst. in 10 c.c. chloroform, 1-dm. tube.)
$\alpha = -4.26 \quad [\alpha{}^{18}_{D} = -147.66°$

Oxime. Prepared quite in the same way as described in (2). Recrystallised from ethylacetate, it forms thick tetragonal plates. M.p. 168°C. (sinters at 145°C.)

Anal: Subst. = 8.739 mg.; N = 0.317 c.c. (11.2 °C, 761 mm.). Found: N = 4.31%: Calc. for $C_{18}H_{23}NO_4$(317): N = 4.41%.

5. **Isonitroso-7-methoxy-*l*-thebenone** [VI]. 7-Methoxy-*l*-thebenone (1 gr.) was dissolved in ether (50 c.c.) and ca. 1 gr. of natrium-wire was driven into it. To the ice-cooled solution, amyl nitrite (1.5 gr.) was added little by little. After standing overnight, the yellow precipitate at the bottom was collected on a glass filter and disolved in ice-water. By passing CO_2 in this solution, a resinous precipitate was formed, which was collected and dried in a vacuum-desiccator. The dried substance dissolved almost completely in ether, but showed no tendency to crystallise from it, or from ethyl alcohol. The analysis was carried out with the well dried substance.

Anal.: Subst. = 5.506 mg.; N = 0.199 cc. (18.5 °C., 758 mm.). Subst. = 9.197; AgI = 12.882 mg. Found: N = 4.13; $CH_3O-(2)$ = 18.51%. Calc. for $C_{18}H_{21}NO_5$(331): N = 4.22; $CH_3O-(2)$ = 18.73

The Department of Chemotherapy,
Kitasato Institute, Tokyo.