SINOMENINE AND DISINOMENINE. XVII.
ON METHYL-SINOMENINONE.

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One of the authors (K.G.) has reported that the action of 2*n* hydrochloric acid on sinomenine(1) at 100°C. gives rise to the formation of sinomenine hydrate (II)(1) and the same treatment of 1-Bromo-sinomenine leads to the formation of 1-Bromo-sinomeninone (III)(2) The difference in the behaviour of those two very similarly constituted bases might be due to the negativity of bromine atom in the latter. So, it was desirable to expose methyl-sinomenine to the same treatment in order to see whether it gives hydrate or diketone.

The experiment revealed that methyl-sinomenine was simply hydrolysed on its enol-ether group by the action of 2*n* hydrochloric acid at 100°C. and gave methyl-sinomeninone (III) in a yield about 70%. The hydrate was not isolated in this case, too, so it seems that the stage of hydrate was jumped over both in bromo- and methyl-sinomenine in the formation of the respective diketones.

By the action of concentrated ammonia, sinomenine hydrate was turned into a bimolecular bis-demethyl-sinomenyliden,(3) and bromo-sinomeninone into a mono-molecular bromo-sinomeninone imine,(4) but the methyl-sinomeninone was turned into an amorphous substance by the same reagent, and no base corresponding to one of the above substances could not be isolated.

By the reduction with Pd+H_2, methyl-sinomeninone absorbed two atoms of hydrogen and gave a new base $C_{19}H_{25}NO_4$, which formed a monoxime, showing that one of the two ketone groups was reduced to the alcohol group. This base should be called dihydro-methyl-sinomeninone (V).

It is interesting to examine which of the two ketone groups of the methyl-sinomeninone was reduced in this case. The clew may be obtained from the methylation of α- and β-demethoxy-sinomenine hydrate. But,

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(1) Goto and Sudzuki, this Bulletin, **4** (1929), 271.

(2) Goto and Nambo, this Bulletin, **5** (1930), 73.

(3) Loc. cit.

(4) Loc. cit.

unfortunately the reaction products of these two substances with diazomethane became syruppy and no conclusion could be obtained in this trial.

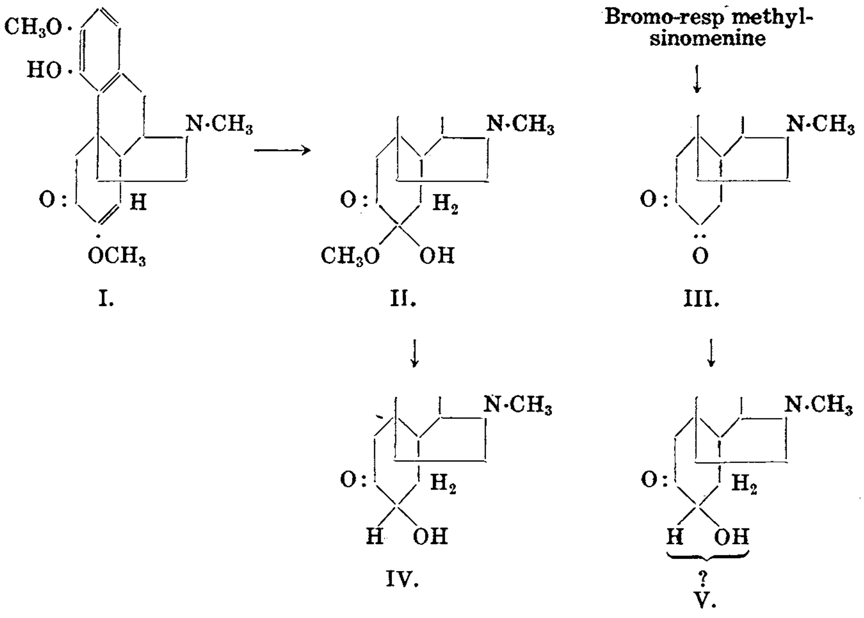
Then we tried to reduce catalytically bromo-sinomeninone and compared the reduced base with brominated α-demethoxy-sinomenine hydrate. From the mode of preparation, it is almost clear that α-demethoxy-sinomenine hydrate has its ketone group on C_6 and its secondary alcohol group on C_7 (IV). If, by the reduction of bromo-sinomeninone, the identical base was obtained as with the bromination of α-demethoxy-sinomenine hydrate, we may assume with some certainty that in the reduction of bromo-sinomeninone the ketone group situated in C_7 has been reduced. The result was affirmative. The substances prepared in these two different ways melted both at 231°C. as well as the admixture.

From these results, we should like to assume that in dihydromethylsinomeninone, the ketone group situated at C_7 is also reduced, though an exact proof is still lacking.

In these experiments, the methylation of sinomenine was again studied in a more detailed way and the yield was improved. Benzoylation of sinomenine was carried out with benzoyl chloride in pyridine solution with better yield. The detailed conditions are given in the experimental part.

Table 1.

	Methyl-sinomenine	Methyl-sinomeninone	Dihydromethyl-sinomeninone	Benzoyl-sinomenine
Yield	30–35%	70%	80%	40%
Solubility in methyl alcohol	12–52%	4.47%	—	—
M.p.	179°	188°	127° (dried) 108° (air dry)	225°
$[\alpha]_D$	−29.61°	+18.65°	+71.05°	+85.03°
Methoxyls	3	2	2	2
M.p. of oxim	139°	213°	117°	249°
M.p. of iodomethylate	157° (dec.)	225°～227°	248°	237°
$FeCl_3$-reaction	no	no	no	no
Diazo-reaction	20,000	10,000	almost no	appears slowly
$K_3Fe(CN)_6$-reaction	no	no	no	no
Formaline-sulphuric acid	yellow→green	green→bordeau	yellow	yellow



Experimental.

Note on Preparation of Methyl Sinomenine with Nascent Diazomethane. A better yield (30–35%) was attained in using methyl alcoholic solution of sodium hydroxide in an almost calculated quantity. Purification is easy, taking advantage of the facts that methyl-sinomenine is more easily soluble in ether than sinomenine itself and also that the hydrochloride of the former is less soluble in water (3.7%) than that of the latter (4.5%). Twice recrystallised from water, the methyl-sinomenine gives no ferric chloride reaction.

With diazomethane in ethereal solution, no better yield was obtained than in the above method.

The phenol-hydroxyl of sinomenine is, however, very easily methylated with dimethyl sulphate and caustic alkali, the fact being shown by the disappearance of the diazo-coupling faculty. But, the greater part of the sinomenine is splitted in its $N-C_9$ linking by this treatment.

The phenol-hydroxyl is also methylated by methyl-iodide and alkali in methyl alcoholic solution. But, the seperation of methyl-sinomenine iodomethylate from sinomenine iodomethylate gives some difficulties.

As for the properties, see the first column of the table in the theoretical part.

Anal. Found: C=70.03; H=7.49; N=4.03; methoxyl=26.51%. $C_{20}H_{25}NO_4$ requires C=69.97; H=7.29; N=4.08; Methoxyl=27.11%.

Optical rotatory power measured in chloroform:

$$[\alpha]_D^{14}=(10\times 0.52)\div(0.3515\times 0.5)=-29.61°$$

Oxim: Prepared in ordinary way. Amorphous precipitate formed with sodium carbonate becomes stout prisms, when left stand overnight under water added with ether. M.p. 139° (decomposes between 150–160°). Found: N=7.66%. Calc. for monoxime: N=7.82%.

Iodomethylate: Recrystallisable from water. Dired crystals decomposes at 151° (sintering from 141°C). Found: I=26.04% Calc. I=26.18%.

Metyl-sinomeninone. Methyl-sinomenine hydrochloride (10 gr.) is heated with 2*n* hydrochloric acid (50 c.c.) on a steam bath for an hour. Isolation was carried out in an usual way. Recrystallised from a large quantity of hot methyl alcohol, it forms large prisms. M.p. 188°. Yield ca. 70%.

See the table in the theoretical part for its properties.

Anal. Found: C=69.21; H=7.00; N=4.20; methoxyl=19.11%. $C_{19}H_{23}NO_4$ requires C=69.30; H=6.99: N=4.25; methoxyl=18.88%.

Sp. rotatory power, measured in chloroform: $[\alpha]_D^{14}=(10\times 0.30)\div(0.5\times 0.3216)=+18.65°$

Oxim: Prepared and crystallised in the same way as with methyl-sinomenine. M.p. is very unsharp, sintering above 100°, melting at 170° and decomposing completely at 213°. Found: N=11.74% Calc. for dioxime: N=11.70%.

Iodomethylate. Stout prisms, decomposing at 225~227° with yellow colour. Found: I=26.51% Calc. I=26.96%.

Dihydromethyl-sinomeninone. Methyl-sinomeninone (1.9 gr.) was reduced catalytically with palladinised charcoal and hydrogen gas in weakly acidic solution. Absorption of H_2 amounted to 50 c.c. (ca. 1 mol.) in 50 minutes. Isolation was carried out in an usual manner. It crystallises out in long prisms from the 33% methyl alcohol solution, saturated with ether. M.p. 108° (air-dry) or 128° (dried over P_2O_5 in vacuum). Yield ca. 1.5 gr. (80%).

Properties were given in the table in the theoretical part.

Anal. Found: C=68.61; H=7.62; N=4.41, 4.20; methoxyl=18.93%. $C_{19}H_{25}NO_4$ requires: C=68.84; H=7.60; N=4.25; methoxyl=18.73%.

Sp. rotatory power, measured in chloroform: $[\alpha]_D^{15}=(10\times 0.81)\div(0.2280\times 0.5)=+71.05°$

Oxim: Crystallised from methyl alcohol. M.p. 177°. Yield ca. 40%. Found: N=7.67%. Calc. for monoxime: N=8.09%.

Iodomethylate. Long needles from methyl alcohol. M.p. 248° (dec.). Yield good. Found: I=26.35%. Calc.: I=26.85%.

Benzoyl-sinomenine. Sinomenine (2.5 gr.) in a pyridine solution (12.5 gr.) was added with benzoyl chloride (3 c.c.) at 10°C. After half an hour, the pyridine solution was poured into the mixture of ice (100 gr.) and saturated ammonium carbonate solution. After standing two days, when the first appeared oil drops changed into fine solid, the latter was collected and recrystallised from the mixture of benzol and ether. M.p. 224°. Yield ca. 35%. This preparation is far more convenient than that formerly given.

Anal. Found: C=71.81; H=5.77; N=3.23; methoxyl=14.21%. Calc. for $C_{26}H_{27}NO_5$=433: C=72.05; H=6.23; N=3.23; methoxyl=14.31%.

Sp. rotatory power measured in chloroform: $[\alpha]^{4}_{D}=(10\times2.5)\div(0.294\times1)=-85.03°$

Iodomethylate: hairy crystalls from water. M.p. 237° (dec.). Found: I=22.14%. Calc.: I=22.08%.

Oxim: Prepared in ordinary way and extracted with chloroform. Prisms from methyl alcohol. M.p. 249° (dec.) Found: N=5.99%. Calc. for monoxime: N=6.25%.

Bromination of *α*-desmethoxyl-sinomenine hydrate.(1) The condition of bromination is the same as with sinomenine.(2) From a large quantity of alcohol, it forms long prisms, which melt at 231°. Yield about 50%.

Anal. Found: C=54.79; H=5.43; N=5.5. $C_{18}H_{22}BrNO_4$ requires: C=54.55; H=5.55; N=3.53; Br=20.20%.

Oxim: M.p. 147°. Found. N=6.54%. Calc.: N=6.81%.

Catalytic Reduction of Bromo-sinomeninone. Bromo-sinomeninone (2 gr.) was catalytically reduced with palladinised charcoal and molecular hydrogen. When the calculated quantity of hydrogen was absorbed the reduced base was isolated in the usual way. Yield good. It melted at 231° and the admixture with the above described specimen did not lower the melting point.

Errata.—To the constitution formula II of p. 94, this Volume, the following corrections must be given. The methoxyl on $C_{(7)}$ must be replaced by H. The—H on $C_{(8)}$ must be replaced by H and one free bond. Thus, the formula is brought in harmony with the facts and its name 1, 1′-dibromo-bis-[8, 8′]-demethoxy-dihydro-sinomenine.

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(1) Loc. cit., p. 275.

(2) Goto and Nambo, this Bulletin, **5** (1930), 167.