SINOMENINE AND DISINOMENINE
PART XIV. ON BROMO-SINOMENINONE.

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In the 12th communication(1) of this study, one of the authors (K.G.) has reported the formation of sinomenine hydrate by heating the latter with 2 n. hydrochloric acid. The assumption of a semiacetal constitution of this hydrate was there supported with several facts.

As this formation of sinomenine hydrate is, however, rather remarkable, it is desirable to repeat the same reaction with other phenanthrene alkaloid and enforce the author's conception. Thebainone may seem at first sight to be fitted for the purpose, but actually it is not, .since its preparation involves the heating with conc. hydrochloric acid at 100°C. It seems, therefore, that there is no other easily accessible alkaloid than bromo-sinomenine in this respect. That the bromo-sinomenine has exactly the same constitution with sinomenine, except one bromine atom at C_1, was indirectly proved by its catalytic reduction by K. Goto and T. Nakamura.(2) The action of hot dilute hydrochloric acid was, therefore, proved on bromo-sinomenine. The results of the experiment were, however, somewhat different from those with sinomenine. The easily crystallizable substance

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(1) Goto and Sudzuki, this Bulletin, **4** (1929), 244.

(2) This Bulletin, **4** (1929), 195.

from bromo-sinomenine, when the latter was heated two hours with 2n. hydrochloric acid, was not bromo-sinomenine hydrate, but bromo-sinomeninone itself. It has the molecular formula $C_{18}H_{19}NO_4Br$, one methoxyl group and two ketone groups, forming a dioxime and a disemicarbazone. That this bromo-sinomeninone must be corresponding to the sinomeninone, which would be formed by the hydrolysis of the semi-acetal group of sinomenine hydrate or the hydrolysis of the dioxime of sinomenine hydrate (though these reactions are not yet realised), is proved by the fact that the dioxime of the sinomenine hydrate gave on bromination the same bromo-sinomeninone dioxime as obtained from bromo-sinomeninone.

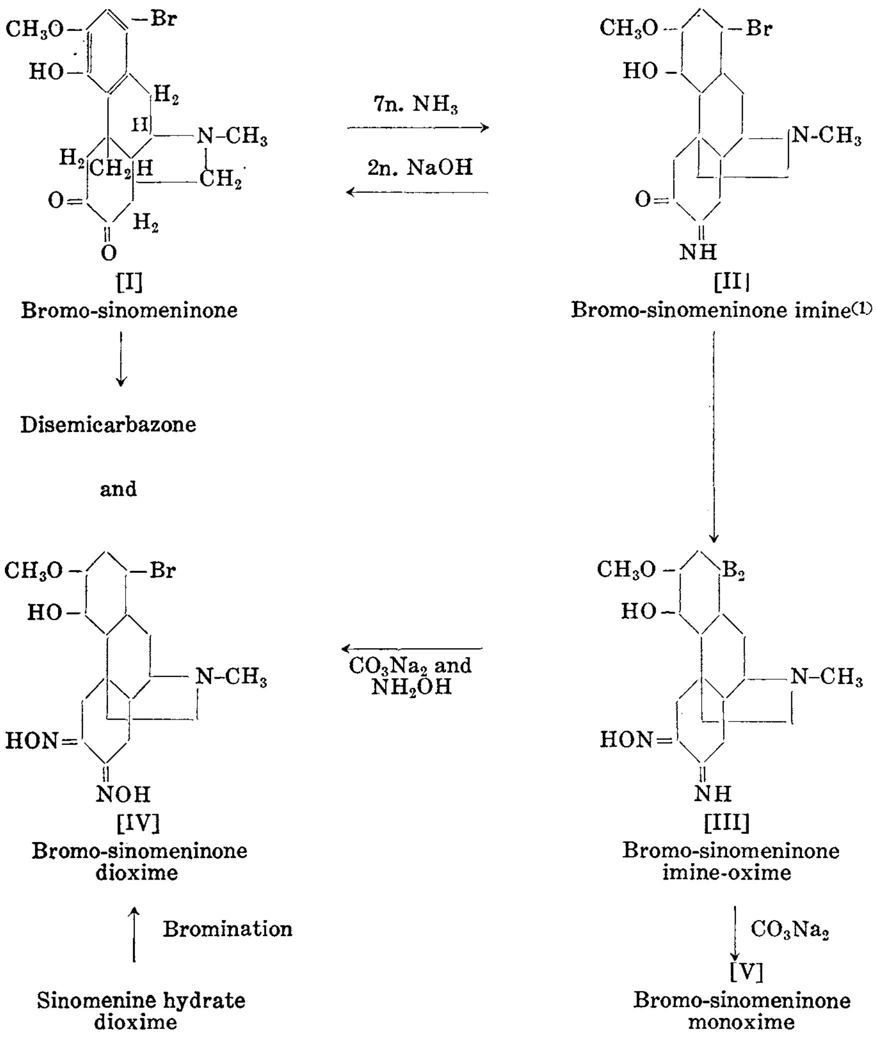
When bromo-sinomeninone was treated with 7 n. ammonia, it did not gave the expected condensation product, but a monomolecular imine $C_{18}H_{20}N_2O_3Br$. That here we treat actually an imine is shown from the following two facts. First, this bromo-sinomeninone imine is easily hydrolyzed by caustic alkali on its imino-group and gives bromo-sinomeninone and ammonia in a nearly quantitative yield. Secondly, the oxime of bromo-sinomeninone imine is easily attacked even by sodium carbonate and gave bromo-sinomeninone monoxime. This monoxime could be turned into the above bromo-sinomeninone dioxime by treating again with hydroxylamine.

The properties of the bromo-sinomeninone and its imine are summarised in the following table and the relation of these substances are shown in the annexed diagrams.

Table 1.

	Bromo-sinomeninone	Bromo-sinomeninone imine
Yield	50~70%	50°
Crystal form	long prisms	short prisms
M.p.	227°	208°
$[\alpha]_D$	+54.52°	+110.19°
M.p. of oxime	189° (dioxime)	208° (monoxime)
M.p. of iodomethylate	244°~246°	not yet crystallized
Methoxyls	one	one
$FeCl_3$ - reaction	violet (in alc.)	weak (in alc.)
Diazo - reaction	(+1,000,000th dil.)*	+50,000th dil.
$K_3Fe(CN)_6$ - reaction	no	no
Formaline - SO_4H_2	yellowish brown	yellowish brown

* This strong diazo-reaction may be due to the two methylene groups, vicinal to the 1, 2-diketone.



Experimental.

Bromo-sinomeninone (I)—Bromo-sinomenine bromohydrate (20 gr.) is heated with 2 n. HCl (200 c.c.) in a steam-bath for two hours. It is precipitated with sodium carbonate and extracted with chloroform. The bromo-sinomeninone can be recrystallised from methyl alcohol in long prisms. M.p. 227° (dec.). Yield 50%. From the free base of bromosinomenine the substance was obtained in a somewhat better yield (70%). For the properties, see the Table 1.

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(1) Mutual position of the ketone and imine groups is not yet determined.

Anal. Found: C=54.71; H=5.52; N=3.20; Br=19.62; Methoxyl=7.90%. Calc. for $C_{18}H_{20}NO_4Br=394$: C=54.82; H=5.55; N=3.28; Br=20.30; CH_3O-=7.87%.

Sp. rotatory power. 0.2421 gr. subst. was dissolved into 10 c.c. alcoholic solution. l=1dm; $\alpha=+1.32°$. $[\alpha]^{16}_{D}=+54.52°$.

Iodomethylate. Recrystallised from water; m.p. 244~246°; yield 50% (Found I=23.23%; Calc. I=23.69%).

Semicarbazone. Recrystallised from acetone. It decomposes at 118°, sintering at 98°. Yield not good. (Found: N=18.01%; Calc. for disemicarbazone: N=19.29%).

Dioxime. Prepared in ordinary way and extracted with ether, after the precipitate was dissolved in methyl alcohol and water. Beautiful prisms. M.p. 189° (dec.) Yield good. (Found: N=9.33%. Calc. for dioxime: N=9.91%).

Bromination of Sinomenine Hydrate Dioxime (IV). Sinomenine hydrate dioxime (1 gr.), dissolved in glacial acetic acid (20 c.c.) is brominated by bromine (0.5 gr.) in glacial acetic acid (5 c.c.) at the freezing point of the solvent. After being made alkaline with sodium carbonate solution, it is extracted with chloroform and obtained in crystals, when methyl alcohol is added to the residue of the chloroform evaporation. Yield almost quantitative. M.p. 189° (dec.) Admixture with bromo-sinomeninone dioxime did not lower the m.p.

Bromo-sinomeninone Imide (II). Bromo-sinomeninone (1 gr.) is dissolved in 1% hydrochloric acid (10 c.c.) and added with conc. ammonia (10 c.c.; d=0.9). After standing overnight, the precipitate is collected and dissolved in chloroform. It crystallises out in prisms, when methyl alcohol is added to the residue of the chloroform evaporation. Yield 50%. It darkes at 228°, sinters at 233°, but does not melt completely until 300°. For the properties, see Table 1.

Anal. Found: C=54.83; H=5.45; N=7.05, 7.19; Br=20.16; Methoxyl=8.01%. Calc. for $C_{18}H_{21}N_2O_3Br=393$: C=54.96; H=5.34; N=7.11; Br=20.35; CH_3O-=7.89%.

Sp. rotatory power. 0.3158 gr. subst. was dissolved into 10 c.c. chloroform solution. l=1dm; $\alpha=+3.48$. $[\alpha]^{16}_{D}=+110.9°$.

Mol. wt. Found (in glacial acetic acid): 244. (Remarkably low value is perhaps due to the partial decomposition of the imino-group).

Oxime (III). Prepared in ordinary way, and extracted without the use of sodium carbonate, i.e. methyl alcohol is added to the reaction mixture just enough to dissolve the precipitate and is shaken with ether several times, until the oxime crystallises out in colourless prisms. It sinters at 208°, but does not decomposes until 300°. (Found: N=10.23%. Calc. for $C_{18}H_{22}N_3O_3Br$: N=10.29%).

In the above reaction, when sodium carbonate is used to precipitate the oxime, sometimes bromo-sinomeninone dioxime, and sometimes bromo-sinomeninone monoxime is obtained, according to the conditions. Dioxime obtained in this case is quite identical with that obtained from bromo-sinomeninone directly. The mixed melting point remained unaltered. (Found: N=9.49%. Calc. for dioxime: N=9.88%).

Monoxime is long needles and melts at 199°, sintering first at 191°. (Found: N=7.59, 7.40%. Calc. for monoxime: N=6.83%).

Hydrolysis of Bromo-sinomeninone Imine. Bromo-sinomeninone imine is easily hydrolysed on its imino-group by warm caustic soda (10%), and bromo-sinomeninone is recovered in an almost quantitative yield by extracting with ether. By micro-Kjeldahl, the ammonia was determined up to 80% in this reaction.

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