SINOMENINE AND DISINOMENINE. XX. ON BENZENE-AZO-SINOMENINE.

By Kakuji GOTO and Hideo SHISHIDO.

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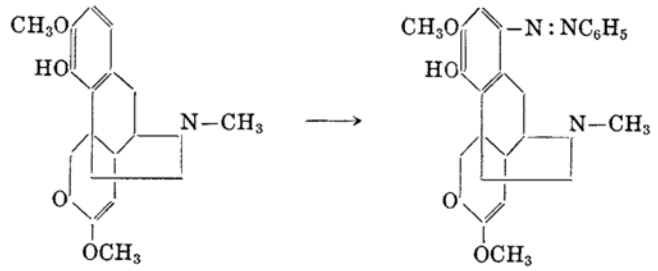
The diazo-coupling reaction of sinomenine [I] and the bases derived therefrom is as strong as the red colour produced by it is still visible in the 2,000,000th dilution of the bases.[1] This property is shared by almost all the alkaloids of phenanthrene group, in which a free phenol group situates in (4) with the unsubstituted para-position (1). Thus, thebainone, dihydro-thebainone, desoxy-codeine, β- tetrahydro-desoxy-codeine, morpho-thebaine and apomorphine give the same reaction in the same strength.[2] On the contrary, those derivatives of sinomenine and thebainone, in which the para-position (1) to the phenol group (4), may be assumed, from the nature of reaction, to be substituted, namely, bromo-sinomenine both di-sinomenines and α- and β- dithebainones give this reaction in an exceedingly diminished degree (in the 20,000th dilution or thereabout) or not.

The diazo-coupling reaction is thus very conveniently to be taken use of in judging whether the para-position (1) is substituted or the phenol group (4) is perfectly etherified or esterified in these bases.

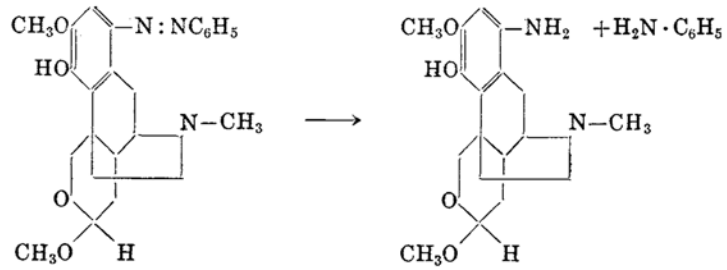
Now, the authors could, as is described in the experimental part, prepare the benzene-azo-compounds of sinomenine, hydrosinomenine and thebainone in nice crystalline form. M.p. of these coupled bases are the following.

	Benzene-azo-sinomenine	Benzene-azo-hydrosinomenine	Benzene-azo-thebainone
Solvent for recryst.	nitrobenzene	dil. methyl alc.	dil. methyl alc.
Cryst. form	hexagonal plates	prisms.	prisms.
Colour	dark red	dark red	yellowish brown
M.p.	253° (dec.)	231° (dec.)	152°

(1) *J. of Agr. Chem. Soc. Japan*, **1** (1924), 5.
(2) This Bulletin, **4** (1929), 103.



[I] [II]



[III] [IV]

By reducing benzene-azo-dihydrosinomenine [III] by sodium hydrosulphite, we could obtain l-amino-dihydro-sinomenine [IV]. The free base was rather unstable and the analysis was made with its hydrochloride, crystallised from the mixture of alcohol and chloroform.

It contained tenaciously one molecule of water and chloroform. The analytical results were, however, satisfactory as such.

The same reduction of benzene-azo-sinomenine would give rise to the mixture of l-amino-sinomenine and l-amino-dihydro-sinomenine, as the preliminary experiment with sinomenine has shown. Therefore, the reduction of benzene-azo-sinomenine was not undertaken.

Recently, G. Charrier and A. Neri reported that by dissolving benzene-azo-morphine in conc. sulphuric acid, they could transform it into benzene-azo-apomorphine.[1] The same treatment of benzene-azo-sinomenine did not give the expected results. The base did not change the shade of the colour, but became water-soluble, indicating perhaps the sulphonation of the coupled benzene-nucleus.

(1) Cited after *Chem. Zentr.*, **101** (1930), 1309; *Gazz. chim. ital.*, **59** (1929), 804.

Experimental Part.

Diazo Coupling Reaction. Five drops of N/25 sulphanilic acid solution are diazotised with two drops of 10% caustic soda solution, and 1 drop of N/5 sodium nitrite solution. To this alkaline solution of diazo-benzene sulphonic acid is added about 1 c.c. of the solution of the hydrochloride of the base in different concentration. When 1% hydrochloric acid is added to this mixture drop by drop, a beautiful red colour is produced at certain stage. Five to seven drops of the acid is enough to produce the maximum shade. Reaction still alkaline. Too much acid will decolourise the solution again.

Sinomenine and the bases of allied constitution give the red colour up to the 2,000,000th dilution.

Benzene-azo-sinomenine [II]. Anilin (1 gr.) was diazotised in acidic medium (8 c.c. of 10% HCl+92 c.c. Water) with the calculated quantity of $NaNO_2$ (0.7 gr. in 20 c.c. water) at 5–10°C. To this solution was added the aqueous solution (50 c.c.) of sinomenine hydrochloride (4 gr.). Since this mixture is still acidic, neither the red colour nor red precipitate is produced in this stage. When this solution is, however, added with sodium hydroxide solution, the red precipitate is richly formed. The latter, being redissolved in the excess of caustic soda solution, is precipitated again by CO_2 gas. The precipitates are collected, dried and recrystallised from boiling nitrobenzene. Dark red tetragonal or hexagonal plates, decomposing at 253°. Yield almost quantitative.

Anal. Found: C=69.08; H=6.05; N=9.18, 9.16; methoxyls=14.01%. $C_{25}H_{27}N_3O_4$ requires: C=69.28; H=6.23; N=9.70; methoxyls=14.31%.

Benzene-azo-dihydrosinomenine [III]. Mode of preparation is the same with the foregoing. Recrystallised from dilute methyl alcohol, it forms long, dark red prisms of m.p. 231° (dec.).

Found: N=9.41%. $C_{25}H_{29}N_3O_4$ requires: N=9.65%.

Benzene-azo-thebainone. Prepared in the same way as above. Yellowish brown prisms from dilute methyl alcohol. M.p. 152°.

Found: N=10.23%. $C_{24}H_{25}N_3O_3$ requires: N=10.42%.

Reduction of Sinomenine with Sodium Hydrosulphite. Sinomenine (10 gr.) was boiled with $Na_2S_2O_4$ (20 gr.) in aqueous solution (60 c.c.) for two hours, when a clear solution was produced. When the bases were separated in the ordinary way, the part, which was first extracted, consisted

principally of hydrosinomenine (2 gr.; 20%). Next came the unchanged sinomenine (2.5 gr.). The rest was difficultly crystallisable.

l-Amino-dihydrosinomenine Hydrochloride [IV]. When a mixture of benzene-azo-dihydrosinomenine (5 gr.), sodium hydrosulphite (12 gr.), water (50 c.c.) and methyl alcohol (20 c.c.) was boiled, the mixture was decolourised in twenty minutes. After boiling for one hour, aniline was removed by steam-distillation (until the bleaching powder reaction was disappeared in the distillate). The base was, then, set free with sodium carbonate and extracted with chloroform.

The chloroform was dried with sodium sulphate, filtered and saturated with HCl gas, by which the hydrochloride of the amino-dihydro-sinomenine was thrown down in a pale yellow mass. Ethyl alcohol was added to this chloroform in a quantity which is just enough to dissolve the precipitate away. After standing some time, the hydrochloride appears in stout prisms, collected in rosettes. This was collected, and washed with chloroform and ether.

For recrystallisation, the hydrochloride is redissolved in alcohol and precipitated with much chloroform. Yield 2 gr., m.p. $>300°$.

The free base is unstable, and accordingly, the hydrochloride was analysed, after it was left in a desiccator over H_2SO_4 for twenty days, until the weight became constant. The hydrochloride seems to contain one molecule each of chloroform and water, the former appearing as a drop when the hydrochloride is dissolved in water.

Anal. Found: C = 43.33, 43.28; H = 5.82, 6.45; N = 5.25; Cl = 31.51; Methoxyls = 11.56%. $C_{19}H_{26}N_2O_4 \cdot 2HCl \cdot CCl_3H \cdot H_2O$ requires: C = 43.12; H = 5.57; N = 5.03; Cl = 31.89; methoxyls = 11.14%.

Department of Chemotherapy,
Kitasato Institute, Tokyo.