STUDIES ON BIMOLECULAR ALKALOIDS. PART I.
ON DISINOMENINE AND Ψ-DISINOMENINE.

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The milder action of oxidising agents, such as $AuCl_3$, $AgNO_3$, $K_3Fe(CN)_6$, $KMnO_4$, $FeCl_3$ and H_2O_2, on sinomenine leads to the formation of two isomeric, bimolecular substances, disinomenine and ψ-disinomenine in a nearly equal proportion. These two alkaloids are very similar in their behaviour, but are distinguished by the following characteristics.

	Disinomenine	ψ-Disinomenine
M. p. of free base	222°	227°
Dec. p. of free base	245°	243°
Crystal form	plates	hairy needles
M. p. of hydrochloride	>290°	>290°
Solubility of hydrochloride . . .	0.6%	∞
Dec. p. of methiodide	263°	268°
M. p. of oxim	265° (dec.)	>290°
M. p. of semicarbazone	>290°	>290°
$[\alpha]_D$	+149.98°	-127.03°
Formaldehyde-H_2SO_4.	pink	yellow

The acetolysis of the two substances gives the identical tetraacetyl-disinomenol, which is converted into the identical tetramethoxy-, tetraethoxy- and tetrabenzoyl-derivatives respectively, and these derivatives of disinomenol are again quite identical with those prepared from disinomenol, obtained by the linking together of sinomenol by the action of boiling 66% potash.⁽¹⁾

Thus, the two new alkaloids seems to be stereoisomeric, but not enantiomorphic, since they are quite easily separated from each other by the recrystallisation of their hydrochlorides. The isomerism here may have been caused by the difference in the third nucleus of phenanthrene, i.e. perhaps by the difference in the linking position of the ethanamine chain. Spectrographic study gives little clew in this respect, the curve of the absorption of ψ-disinomenine being almost identical with that of disinomenine.

As regard to the linking position of two sinomenine molecules in these substances, the position 2, opposite to the free phenolic hydroxyl may be

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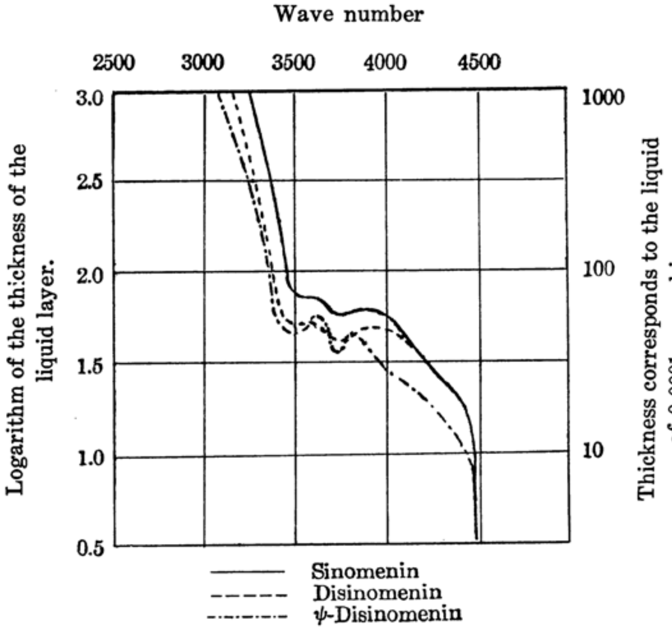
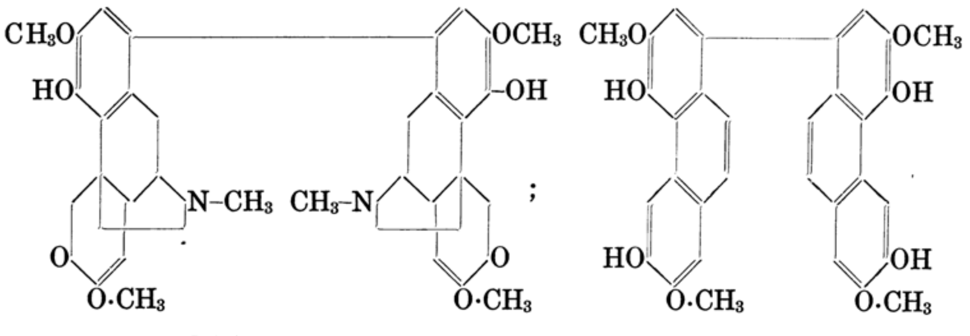
(1) See *Proc. Imp. Acad.*, **2** (1926), 414.



assumed with some certainty from the following two facts. In the first place, the strong diazoreaction of sinomenine (sensitiveness 1:2,000,000) is greatly diminished in these two substances (1:50,000). Secondly, the monobrom-sinomenine, in which the diazoreaction is similarly diminished (1 : 50,000) and on that account the bromine atom seems to occupy the position 2, does not give a bimolecular substance by the same oxidising agent and treatment.



Disinomenine Disinomenol

Disinomenine occurs in nature, accompanying sinomenine, but ψ-disinomenine has not been isolated from sinomenium acutum up to present.

Experimental.

Preparation of Disinomenine and ψ-Disinomenine. *With potassium ferri-cyanide and sodium carbonate.*—Potassium ferricyanide solution (1 mol.; 10.5 gr. in 300 c.c. water) is poured into an aqueous solution (300 c.c.) of sinomenine hydrochloride (12 gr.; 1 mol.) at 50°. The mixture is immediately made alkaline with sodium carbonate solution. The precipitates, richly formed, are collected on a filter-paper and after being washed with water, redissolved in a small quantity of dilute hydrochloric acid. After standing overnight, the hydrochlorides of disinomenine and ψ-disinomenine are deposited. By repeated crystallisation from water, the hydrochloride of disinomenine can be obtained in a pure state. From the united filtrates, the free base of ψ-disinomenine can be precipitated by ammonia, and recrystallised from methyl alcohol.

With silver nitrate. Free base of sinomenine (9 gr.) is dissolved in alcohol (100 c.c.) and water (200 c.c.) and is oxidised by silver nitrate (7 gr.) in aqueous solution (300 c.c.) The isolation of the bases, after the removal of metallic silver and silver ion, is carried out in the almost same way as above.

Properties of disinomenine.—Hexagonal plates from methyl alcohol (solubility 1:50 hot; 1:250 cold.) M. p. 222° and decomposes at 245°. With formaldehyde sulphuric acid, it takes a pink colour.

Anal. Found: C=70.07, 69,03; H=6.85, 6.89; N=4.69, 4.63%. Calc. for $(C_{19}H_{22}NO_4)_2$: C=69.68; H=6.47; N=4.28%.

Mol. wt. Found: (in glacial acetic acid) 670, 677; (in boiling acetone) 659. Calc. for $(C_{19}H_{22}NO_4)_2$: 656.

Hydrochloride: m. p. >290° (Cl=9.64, 9.66. Calc., 9.65%.)

Solubility in cold water: 0.6%; in boiling 3.3%.

Methiodide: m. p. 263° (dec.). Long prisms from water (solubility, 0.3%.)

Oxim: m. p. 265° (dec.).

Semicarbazone: m. p. >290°.

Properties of ψ-Disinomenine. Long hairy needles from methyl alcohol. It dissolves easily in cold methyl alcohol, but when once these hairy needles containing methyl alcohol are formed, it becomes as difficultly soluble as disinomenine. M. p. 228°, decomposing at 245°. In formaldehyde sulphuric acid, it dissolves with a yellowish brown colour.

Anal. Found: C=66.57, 66.99, 66.83; H=7.05, 6.56, 8.03; N=4.24%. Calc. for $(C_{19}H_{22}NO_4)_2+2CH_3OH$: C=66.66; H=7.02; N=3.78%.

Mol. wt. Found: (in glacial acetic acid) 696. Calc. for $(C_{19}H_{22}NO_4)_2$: 656.

Methoidide: Polyhedral crystal from water. M. p. 267~268° (dec.) (Found: I=26.83. Calc.: I=27.02%).

Oxim: m. p. >280°. (Found: N=7.76. Calc. for dioxim: N=8.16%).

Semicarbazone: m. p. <290°.

Acetolysis of Disinomenine and ψ-Disinomenine. Disinomenine (1 gr.) is heated with acetic anhydride (5 gr.) in a sealed tube at 180° for 8 hours. The contents are poured into water and the acetic anhydride is destroyed by boiling. The insoluble part is recrystallised from benzene (15 gr.) The crude tetracetyl-disinomenol thus obtained, amounts to 0.2 gr. and already melts at 253°. It is once more recrystallised for analysis.

The same treatment of ψ-disinomenine gives the identical tetracetyl-disinomenol.

Anal. Found: C=67.78; H=4.91%. Calc. for $C_{40}H_{34}O_{12}$: C=67.98; H=4.81%.
Mol. wt. Found: (by Rast's) 703. Calc. for $C_{40}H_{34}O_{12}$: 706.
Methoxyls. Found: 17.28%. Calc. for $4CH_3O-$: 17.56%.

Nitrogenous decomposition products were in both cases methyl-ethyl amine, as the case with sinomenine (Gold salt, m. p. 179°; Platinum salt, dec. p. 224°). Yield: 0.25 gr. as hydrochloride from 3 gr. of ψ-disinomenine, and 0.2 gr. from 3 gr. of disinomenine.

The acetyl groups are easily hydrolysed away by alcoholic sodium hydroxide, and, from the disinomenol thus formed, tetramethoxy-, tetraethoxy, and tetrabenzoyl-disinomenol can easily be prepared by the action of dimethyl- and diethyl-sulphate and benzoyl chloride respectively. In the following, these three derivatives were prepared from the tetracetyl-disinomenols obtained from disinomenine as well as from ψ-disinomenine.

Disinomenol: m. p. >310°. It takes a beautiful blue colour in an acetone solution, when oxidised by ammoniacal silver (Sensitiveness 1:50,000).

Anal. Found: C=70.24; H=5.21%. Calc. for $C_{32}H_{26}O_8$: C=71.37; H=4.83%.

Tetramethyl-disinomenol: m. p. 240°, Fine needles difficultly soluble in cold acetone.

Anal. Found: C=72.70; H=5.92%. Calc. for $C_{36}H_{34}O_8$: C=72.72; H=5.72%.
Mol. wt. Found: (by Rast's) 638. Calc. for $C_{36}H_{34}O_8$: 594.
Methoxyls. Found: 40.01%. Calc. for $8CH_3O-$: 41.75%.

Tetra-ethyl-disinomenol: m. p. 177° (184°, very pure specimen).

Anal. Found: C=74.10; H=6.64%. Calc. for $C_{40}H_{42}O_8$: C=73.84; H=6.46%.
Mol. wt. Found: (by Rast's) 624. Calc. for $C_{40}H_{42}O_8$: 650.
Methoxyls. Found: 18.70%. Calc. for $4CH_3O-$: 19.07%.

Tetrabenzoyl-disinomenol: m. p. 280°, long needles. Very difficultly soluble in ordinary solvents. Benzoylation of disinomenol can only be carried out smoothly in ethyl-benzoate solution by benzoyl chloride and aqueous sodium hydroxide. The same substance can be obtained by heating disinomenol (1 gr.) with benzoic anhydride (5 gr.) in a stoppered test-tube at 180°–200° for 6 hours.

Anal. Found: C=74.79; H=4.11%. Calc. for $C_{60}H_{42}O_{12}$: C=75.47; H=4.40%.
Mol. wt. Found: (by Rast's) 1010, Calc. for $C_{60}H_{42}O_{12}$: 954.

On Colour Reaction of Monomolecular and Bimolecular Phenanthrene. Sinomenol, 3,7-dimethoxy-4,6 dioxy phenanthrene, dissolves yellow in cold conc. sulphuric acid, but almost decolourised on the addition of water. On the contrary, disinomenol, bis-1,1′- (3,7-dimethoxy- 4,6-dioxy)-phenanthrene dissolves brown in cold conc. sulphuric acid, and gives intensely purple flocculations on diluting with water. The same behaviour was ascertained with dimethyl-, diethyl-, diacetyl- and dibenzoyl-derivatives of sinomenol and with corresponding tetravalent derivatives of disinomenol. This reaction can be utilised advantageously in the study of potash fusion of phenanthrene alkaloids, since some of them are expected to give rise to bimolecular phenanthrene derivatives in that treatment.

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