32. On the Alkaline Decomposition of Codeinone Methiodide and of 1-Bromo-sinomenine Methiodide.

By Kakuji GOTO.

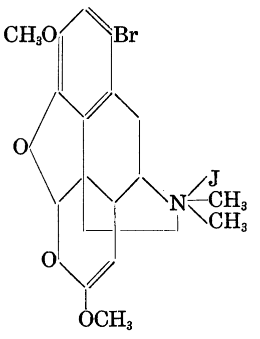
Kitasato Institute.

(Comm. by U. SUZUKI, M.I.A., March 12, 1942.)

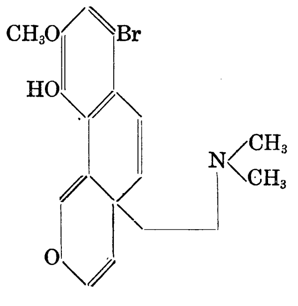
Codeinone methiodide is very unstable against alkali. Thus, Knorr[1] stated that he could not isolate any crystalline methine base from its alkaline decomposition products.

Now, 1-Bromo-sinomenine (I) is a base, very similarly constituted to codeinone. It gives, when treated with dimethyl sulphate and alkali, sometimes 1-Bromo-3-methyl-6, 7-dimethoxy-morphenol as main product and sometimes 1-bromo-3, 6-dimethyl-sinomenol exclusively[2]. This peculiarity led the present author to study the action of caustic alkali on its methiodide more minutely.

When 1-bromo-sinomeneine methiodide is dissolved in a large excess of water and added with a calculated quantity of 10 proc. caustic alkali (conc. of alkali about 0,07% in the mixture) at 20° C, a brown, cloudy precipitate is formed, which, however, quickly dissolves away. Chloroform extracts therefrom yellow prisms of m. p. 201° C and of $[\alpha]_D = +180,5°$. It shows a deep violet halochromie with sulphuric acid. From the following consideration, the formula II is assigned to this new methine base and it is named des-N-methyl-1-bromo-dehydro-meta-sinomenine[3].



I



II

The chief reasons, which may be advanced for the constitution above (II), are summerised as follows.

(i) In this substance, the original oxyde ring must have been opened. It is soluble in alkali and gives a green ferric chloride reaction.

---

[1] Ach, Knorr: Berichte d. deutsch. Chem. Ges. **36** (1903), 3073.

[2] K. Goto: Liebig's Annalen, **489** (1931), 93.

[3] For the nomenclature meta, see Schöpf, Borkowsky: Liebig's Annalen, **458** (1927), 148.

By dimethyl sulphate and alkali, it forms monomethyl ether methylmethosuphate (isolated as methiodide.

(ii) The substance must be a methine base. This is known from the strong halochromie in sulphuric acid, and the quantitative yield of 1-Brom-diacetyl-sinomenol when the above monomethyl-ether-methiodide is acetolysed.

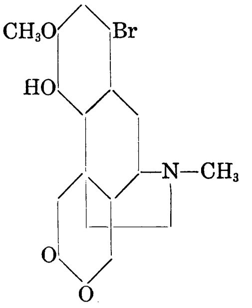
(iii) The hydrolytic scission of oxyde ring must be accompanied by a loss of a molecule of water. This is made clear from its elementary analysis.

(iv) It has very likely a chinonoid structure, as the free base is coloured yellow and forms an intensely red sodium salt. This necessitates the elimination of water at C (5) and C (13) with the shifting of the N-containing side-chain.

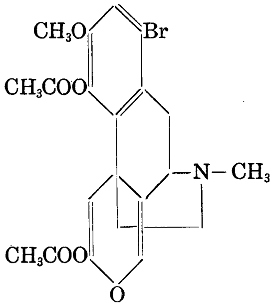
(v) The shifting must be occurred to C (14), otherwise it cannot be so easily eliminated by acetolysis.

It is rather remarkable that such complex transformation is accomplished so quickly with such dilute caustic alkali at ordinary temperature. But an indirect support for our view has been obtained by the acetolysis of 1-bromo-sinomeneine ketone (III), which gives also a base of chinonoid structure, but with the carbonyl group in a different position. The formation of this latter base elucidates somewhat the opening of the oxyde ring and the introduction of a new ethylene linkage.

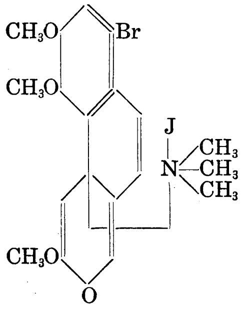
1-Bromo-sinomeneine ketone was boiled with acetic anhydride for 4 hours and after the acetic anhydride was removed in vacuum at 100° C as far as possible, the residue was treated with methanol and filtered into a large quantity of 3 proc. acetic acid. The clear solution was made alkaline with sodium carbonate and the precipitate was quickly extracted with ether. The residue of ether was not liable to crystallisation, but was turned into beautiful crystalline methiodide, when added with methyl iodide. M. p. 199° C from methanol, $[\alpha]_D = -19°$. The substance is coloured faintly yellow even after several recrystallisation and shows almost no halochromise with conc. sulphuric acid. We assign the constitution (IV) to this substance and call it Diacetyl-1-bromo-dehydro-sinomeninone, from the following facts and consideration.



III



IV



V

(i) In diacetyl-1-bromo-dehydro-sinomeninone, the original oxyde ring must have been opened hydrolytically and an ethylenic linkage must have been introduced with the loss of water, since the same diacetyl substance was obtained by the acetolysis of 1,5-dibromo-sinomeninone[1].

(ii) The two acetyl radicals in this substance are easily hydrolysable, namely none of them is attached to the nitrogen atom. This means that the substance is not a methine base. This conclusion coincides well with the fact that the substance is basic and it does not show halochromie.

(iii) The methyl-amino-ethyl side-chain is easily removed by the further acetolysis of this methiode. This fact proves that the substance did not underwent neither morphothebaine nor thebenine rearrangement.

(iv) By treating this methiodide with dimethyl sulphate and alkali at 80° C, it gave a des-N-methyl-base, in which the two acetyl radicals were substituted with two methyl radicals (isolated as des-N-methyl-1-bromo-dehydro-meta sinomeninone (V)). But the acetolysis of this trimethyl substance gave a quite different bromo-acetoxy-trimethoxy-phenanthrene from the 1-bromo-4-methyl-6-acetyl-sinomenol[2], obtained from 1-bromo-methyl-sinomenine. As a phenolic hydroxyl is very easily methylated by dimethyl-sulphate and alkali, the difference between these two brome-phenanthrene must have its cause in the reversed position of the ketonic group in the original alkaloids, and, moreover, in the alkaloid in question, this ketonic group must be in a position, which does not allow an easy enolisation. These condiserations are well expressed by the constitution (IV) and the introduction of a new ethylene linkage between C (8) and C (14) can easily be accounted for, if we assume the transitory formation and rupture of a tricyclene ring among C (13), C (14) and C (8) or of a tetracyclene ring among these three carbon atoms and C (7).

Codeinone methiodide seems to undergo the same decomposition and rearrangement in presence of alkali as 1-bromo-sinomeneine, but the isolation of the des-N-methyl-dehydro-methathebainone is far more difficult. Once, using stronger alkali (11%) and heating 10 minuites at 100° C, a substance supposed to be des-N-methyl-dehydro-meta-thebainone was isolated in a yield more than 50%. The substance crystallises in yellow needles, melts at 169° C and has specific rotatory power $[\alpha]_D = -832°$. It shows red halochromie, gives green ferric chloride reaction, and dissolves in dilute caustic alkali with red colour. But the experimental condition could never have been retraced. In spite of numerous repetitions, the yield was always scanty. Previous removal of the iodine atom with silver nitrate or acetate improved the yield somewhat, but in these cases, the product melted at 185° C and showed a lower specific rotation.

Yet, we believe that by these experiments the cause of the excessive instability of codeinone methiodide was at least partly elucidated. Namely it is deprived of its iodine atom by very dilute alkali even at ordinary temperature, opened of its oxyde ring and undergoes a very

---

[1] K. Goto, H. Shishido, K. Takubo: Liebig's Annalen, **495** (1932), 125.

[2] Sinomenol is 4, 6-dihydroxy-3, 7-dimethoxy-phenanthrene.

complex rearrandement subsequently. Only when this rearrangement goes in a favourable condition, des-N-methyl-dehydro-meta-thebainone may be obtained in a quantity.

Lastly, des-N-methyl-dehydro-meta-thebainone is strongly laevarotatory. As in this substance the asymmetric centre is only one single atom C (14), it may throw some light on the sense of rotation of each asymmetric centre of morphine alkaloids1). In this respect, the weak leavo-rotation of diacetyl-1-bromo-dehydro-sinomeninone and the strong laevo-rotation of des-N-methyl-1-bromo-dehydro-sinomeninone seems to give a clue on the sense of rotation of C (9) and C (13) in sinomenine, since these facts can be taken as an indication that in sinomenine C (9) is dextro- and C (13) leavo-rotatory against polarised light. The dextro-rotation of C (19) in sinomenine can naturally be seen from the sense of rotation of des-N-methyl-1-bromo-dehydro-meta-sinomenine. The decisive conclusion can, however, be given, only when more facts are gathered to eliminate the influence of ring-formation, ethylene linkage etc.

---

1) H. Ende, Helv. Chim. Avta, **13** (1930), 1044; K. Goto, Liebig's Annalen, **485** (1931), 252.