59. On Hofmann's Decomposition of Sinomenine.

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In the previous communication, it was reported that sinomenine is decomposed into sinomenol ($C_{16}H_{14}O_4$)¹⁾ and methyl-ethylamine by boiling it with a 66% solution of caustic potash. The reaction goes in the same way with sinomenine iodomethylate, only the amine liberated in this case being dimethyl-ethylamine. The latter reaction can be regarded in a sense to be Hofmann's decomposition, but the measure was too drastic and a milder reaction was desirable to allow us to get an insight into the nature of the reaction.

When sinomenine iodomethylate (1 mol.) is boiled with a 2% solution of caustic soda (2 mol.), for about one minute and the caustic soda is fixed quickly by passing carbon dioxide into it, beautiful crystals are deposited in the deeply coloured liquid. The crystals become almost colourless after repeated recrystallisation from benzene or purification through the sodium salt. The product contains no iodine, melts at 183° , almost insoluble in water, but soluble in ordinary organic solvents. Elementary analysis gave the molecular formula $C_{20}H_{26}NO_4$ (with two methoxys), The hydroxyl which replaced the iodine must have been,

1) Proceedings, 2, p. 7. There the formula of sinomenol is given as $C_{16}H_{16}O_4$ by an accidental error.

therefore, eliminated as water with one of the hydrogen atoms originally attached to the sinomenine molecule. The author proposes to call this base N-Methyl-anhydrosinomeninium base, and assign the annexed formula (I) to it.

This interpretation might seem to be somewhat singular, especially in view of the fact that in other phenanthrene alkaloids such as morphine, codeine and thebaine, such an anhydrobase has never been isolated. But the property of this new base tends to lead the author to assume the above formula. The assumption of the double bond between C(9) and N is principally based on the easy decomposition of this base with dilute acids, dilute alkalis, boiling water or alcohol and even with methyl-iodide. Particularly proving on this point is the intense blue coloration which it takes with fuming hydrochloric acid, after being added with potassium permanganate in an acetone solution. This is the colour reaction of α -sinomeninemethine, in which tetrahydropyridin nucleus is undoubtedly opened, as shown below.

N-Methyl-anhydrosinomeninium base is also easily decomposed by caustic soda and dimethyl sulphate in the cold and gives a substance (m. p. 213°), which dissolves in fuming hydrochloric acid or in concentrated sulphuric acid with beautiful blue colour. This must be one of the O-methyl-sinomenine-methine-methylsulphates (with three methoxys, formula II.). This methine is also prepared directly from sinomenine or its iodomethylate by the action of dimethyl sulphate and caustic soda, but in this case it is accompanied by a second methine, which crystallises later and dissolves in the above mentioned acids with intense orange red colour. The author proposes to distinguish them as α - and β -methyl-sinomeninemethine. Thus α -sinomeninemethine dissolves blue in fuming hydrochloric acid and the β -compound orange red in it.

α -Methyl-sinomeninemethine, which can be obtained in a 20% yield, has been decomposed in two ways. It loses trimethyl-amine in a 2%

solution of caustic soda at 100° and gives a nitrogen free substance $C_{19}H_{20}O_4$ (m.p. 310°, with three methoxyls formula III.). It gives also a tetramethoxyl substance $C_{21}H_{22}O_4$ m.p. 273°, presumably tetramethoxy-vinyl-phenanthrene-dihydride, when treated with dimethyl sulphate and caustic soda in the warm. This latter compound is obtained directly from sinomenine by treating it with dimethyl sulphate and caustic soda in the warm, but in this case it is invariably accompanied by an isomeric substance m.p. 114° (in one case, m.p. 122°), which is apparently formed from β -methyl-sinomeninemethine,

The trials to obtain anhydrobases of morphine and codeine from their iodomethylates gave only negative results. Morphine iodomethylate was not attacked by dilute caustic soda (2 mol.-4 mol.)²⁾ and codeine iodomethylate was also little attacked by dilute caustic soda (1 mol.), while the stronger (2 mol.) turned it directly into α -methyl-morphine. This ought not, however, to be regarded as a proof of impossibility of forming anhydrobases of these alkaloids or against the proposed constitution of the anhydrobase of sinomenine. For, if there is such a difference in stability against alkali in the iodomethylates of morphine and codeine, the latter being nothing but O-methyl-morphine, it is easily conceivable that there might exist a bigger difference in this respect between sinomenine and morphine or codeine.

The present investigation involved some other preparations not mentioned in the above, and the whole is, therefore, given in the following list for brevity's sake.

- 1) Sinomenine methylsulphate, m.p. 245°.
- 2) Methyl-sinomenine methylsulphate, m.p. 265°; the oxime, m.p. 252°.
- 3) α -Methyl-sinomeninemethine-methylsulphate, m.p. 213°, $[\alpha]_D^{13} = ca + 478^\circ$. (Formula II).
- 4) β -Methyl-sinomeninemethine-methylsulphate, m.p. 178°.
- 5) Substance $C_{19}H_{20}O_4$, Trimethoxy-keto-vinyl-phenanthrene-tetrahydride, m.p. 310°. (Formula III).
- 6) Substance $C_{21}H_{22}O_4$, α -Tetramethoxy-vinyl-phenanthrene-dihydride, m.p. 283°.
- 7) β -Tetramethoxy-vinyl-phenanthrene-dihydride, m.p. 122°.
- 8) N-Methylanhydro-sinomeninium base, m.p. 183°. $[\alpha]_D^{13} = ca + 31^\circ$. (Formula I).

2) Cf. BROOKMANN and PORSTORFF: Berichte d. deutsch. chem. Ges. 13, (1880), 97.

- 9) α -Sinomeninemethin, m.p. 172°; the iodomethylate, m.p. 213°. This methin base is prepared by boiling sinomenine iodomethylate in a 5% solution of caustic soda for a moment.
- 10) β -Sinomeninemethin, m.p. 263°; the iodomethylate, m.p. 287°. (Preparation same as above).

The author is still occupied with the study of sinomenine and with the formation of the anhydrobases in morphine and other similarly constituted cyclic bases.