STRUCTURES OF N-METHYLNICOTONE AND Py-N-METHYLMETANICOTONE

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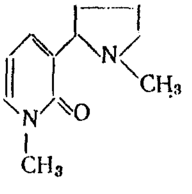
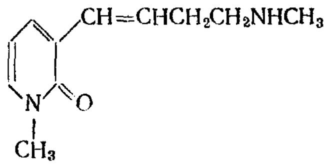
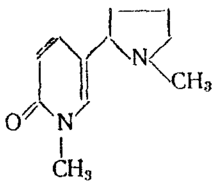
In 1925-1926 Karrer and co-workers oxidized the Py-methiodide of nicotine (Py = pyridine) and obtained the so-called N-methylnicotone (m. p. 85°), to which they assigned the structure 1-methyl-3-(1-methyl-2-pyrrolidinyl)-2-(1H)-pyridone (I) [1]. The authors based their conclusion on the identity of the chloropyridine carboxylic acid which they obtained from (I) with 2-chloronicotinic acid [2]. Guided by this, we described [3] the product of cleavage of the pyrrolidine ring in the substance of m. p. 85°, the so-called Py-N-methylmetanicotone, as a 3-substituted 1-methyl-2(1H)-pyridone (II). However, following the appearance of an abstract of a paper by Tatsuno [4], we had to return to the question of the structure of the original N-methylnicotone, and therefore to that of Py-N-methylmetanicotone. Tatsuno describes the product of the oxidation of the Py-N-methylnicotinium salt which he isolated [liquid, b. p. 165-170° (7 mm) as 1-methyl-5-(1-methyl-2- pyrrolidinyl)-2-(1H)-pyridone (III); this view is supported by the value that he found for the dipole moment and also by the fact that another analogous nicotine salt (Py-N-phenethylnicotinium bromide) gives the corresponding 5-substituted 2(1H)-pyridine (IV) when oxidized under the same conditions [5]. A similar point of view on the point of attack of the oxidizing agent on the nicotinium salt was expressed earlier by Sugasawa and Kirisawa [6], who then pointed out that the direction of the oxidation of three-substituted pyridinium salts depends on the nature of the substituent and, of course on the oxidation conditions.* In view of the above-cited facts, it was desirable to carry out the oxidation of the Py-N-methylnicotinium salt under Tatsuno's conditions and compare the compound formed with Karrer's N-methylnicotone. This became


(I)


(II)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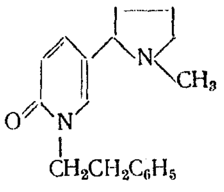
(IV)

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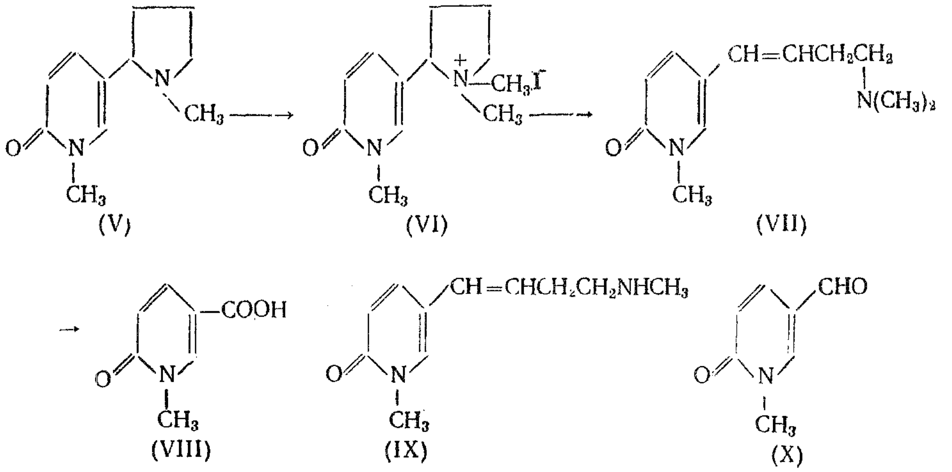
* For fuller data on this question see Thygaraian's review [7].

possible when, on our request, Tatsuno sent us a reprint of his paper, which was published in Japanese.* After vacuum distillation, the product obtained by us in this way crystallized out and was found to be identical both with respect to the melting point of the base (85°) and with respect to the melting point of the picrate with the above-mentioned Karrer's compound.

To make a final choice between formulas (II) and (III), we decided on a method of proof analogous to that used by Sugasawa and Tatsuno [5] in the investigation of the product of the oxidation of Py-N-phenethylnicotinium bromide: Hofmann cleavage of the Py-methiodide of N-methylnicotone with subsequent oxidation of the resulting dibase with potassium permanganate. We then isolated, though admittedly only in low yield, 1,6-dihydro-1-methyl-6-oxonicotinic acid (VIII), m. p. 240°, which has been described by various investigators [8, 9]. The same acid was isolated by us from the aldehyde (X), which was isolated after the ozonization of the base (IX). In this way we determined the structure (VI) for the methiodide taken in the cleavage reaction, so that the structure (V) for Karrer's N-methylnicotone is 1-methyl-5-(1-methyl-2-pyrrolidinyl)-2(1H)-pyridone. Py-N-Methylmetanicotone, which we described previously [3], must then have the structure (IX), 1-methyl-5-(4-methylamino-1-butenyl)-2(1H)-pyridone.



EXPERIMENTAL

1-Methyl-5-(1-methyl-2-pyrrolidinyl)-2(1H)-pyridone (V). 1) By the method described by Karrer [1] we prepared a crystalline product, m. p. 86° after crystallization from heptane. 2) Product (V), prepared under the conditions described by Tatsuno [4] was first obtained in the form of an oil, which was distilled twice under reduced pressure (7 mm; b. p. 168-172°), after which it crystallized out (m. p. 82-85°); after crystallization from heptane it had m. p. 85°, undepressed by admixture of the substance obtained by Karrer's method.

Methiodide of 1-methyl-5-(1-methyl-2-pyrrolidinyl)-2(1H)-pyridone (VI). This was prepared by heating 10 g of N-methylnicotone (V) with methyl iodide (4 ml) in alcohol. Crystallization from alcohol gave 14.6 g (84%) of crystals of m. p. 210-211°. Found: C 42.92; 43.08; H 5.67; 5.94; I 37.42; 37.94%. $C_{12}H_{19}ON_2I$. Calculated: C 43.11; H 5.69; I 38.02%.

5-(4-Dimethylamino-1-butenyl)-1-methyl-3(1H)-pyridone (VII). This was prepared from the methiodide (VI) (12.5 g) by the usual Hofmann cleavage. The dark-colored oil obtained was vacuum-distilled with passage of a stream of dry nitrogen. We collected 6.4 g (83%) of light-yellow oil, b. p. 163-163.5° (1 mm); on standing it darkened rapidly. Found: C 69.14; 69.09; H 8.79; 8.89; N 13.48; 13.28%. $C_{12}H_{18}N_2O$. Calculated: C 69.9; H 8.74; N 13.59%.

Oxidation of 5-(4-dimethylamino-1-butenyl)-1-methyl-2(1H)-pyridone (VII). (VII) (3.1 g, 0.015 mole) was dissolved in 300 ml of pure dry acetone and oxidized by the addition of $KMnO_4$ powder. The precipitate was filtered off, suspended in water, and brought into solution by the passage of sulfur dioxide. From the acetone filtrate we isolated 1.7 g of the original base. The aqueous solution was evaporated, and the dried residue was extracted with absolute alcohol. From the alcoholic solution we isolated 0.3 g of crystals of the acid (VIII),

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* We take the opportunity of again expressing our thanks to Tatsuno.

m. p. 234-236°; yield 25% on the amount of (VII) that reacted. After recrystallization it had m. p. 238° (needles from alcohol). For the melting point of 1,6-dihydro-1-methyl-6-oxonicotinic acid the literature gives 238° and 240° [8, 9] (the melting point of 1,2-dihydro-1-methyl-2-oxonicotinic acid is 183° [10]).

Ozonization of the dihydrochloride of 1-methyl-5-(4-methylamino-1-butenyl)-2(1H)-pyridone. The dihydrochloride of the base (IX) (2.65 g) was ozonized under the conditions described by Gol'dfarb and Karaulova for 3-[4-(acetylmethylamino)-1-butenyl]-2-aminopyridine [11]. We isolated 1,6-dihydro-1-methyl-6-oxonicotinaldehyde (0.2 g), m. p. 118.5-120° (from octane). Found: C 60.94; 60.75; H 5.25; 5.11; N 10.16; 10.31%. $C_7H_7O_2N$. Calculated: C 61.31; H 5.11; N 10.22%. The dinitrophenylhydrazone has m. p. 278-280°.

The aldehyde (X) (0.1 g) was oxidized with silver oxide in alkaline solution; after the separation of the precipitate of silver from the solution, we isolated fine needles (0.08 g), m. p. 236-237°, undepressed by admixture of the acid (VIII) obtained as described above. Found: C 54.86; 54.94; H 4.87; 4.71; N 9.05; 8.99%. $C_7H_7O_3N$. Calculated: C 54.90; H 4.58; N 9.15%.

SUMMARY

The structures of N-methylnicotone and Py-N-methylmetanicotone are, respectively, 1-methyl-5-(1-methyl-2-pyrrolidinyl)-2(1H)-pyridone and 1-methyl-5-(4-methylamino-1-butenyl)-2(1H)-pyridone.

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* Original Russian pagination. See C. B. Translation.