A New Synthesis of N-Methylmyosmine

Sir:

From several transformation studies on nicotine^{1,2,3}, it has been shown that N-methylmyosmine is an important intermediate in the degradation of this alkaloid.

Pseudoöxynicotine (III) was first described by Pinner and Wolfenstein⁴. More recently, Haines and Eisner⁵ have re-examined the earlier work and proved the compound (III) to be an open chain hydrolytic product of N-methylmyosmine (IV). By exactly following the previous method, the latter workers heated oxynicotine (I) in a sealed tube with hydrochloric acid at 140° for several hours and obtained dihydrochloride of N-methylmyosmine (IV) in a yield of 12%.

The authors have found a new synthetic method for compound (III) which also started with oxynicotine (I) under a very much milder condition and gave a yield of 60~70%. In this study, oxynicotine (I), formerly known only

ing at 198–202°/3.0 mm. which was shown to be 1-(3'-pyridyl)-3-(N-acethylmethylamino)-1-propanone (II); yield, 22.15 g., n_D^{20} = 1.5397.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 64.94; H, 7.10; N, 12.63.

The infrared spectrum of the compound exhibited two strong absorptions at 1680 and 1630 cm^{-1} . The ultraviolet absorption spectra of the compound showed λ_{max} 268 $m\mu$ (ϵ = 3000), λ_{max} 230 $m\mu$ (ϵ = 7400) and λ_{min} 252 $m\mu$ (ϵ = 2360).

1) E. Wada and K. Yamasaki, *J. Am. Chem. Soc.*, **76**, 155 (1954).

2) E. Wada, T. Kasaki and K. Saito, *Arch. Biochem. Biophys.*, **79**, 124 (1959).

3) W. G. Frankenburg, A. G. Gotscho, A. A. Vaitekunas and R. M. Zacharius, *J. Am. Chem. Soc.*, **77**, 5730 (1955).

4) A. Pinner and R. Wolfenstein, *Ber.*, **25**, 1428 (1892).

5) P. G. Haines and A. Eisner, *J. Am. Chem. Soc.*, **72**, 1719 (1950).

in aqueous solution and λ_{max} 263 $\text{m}\mu$ ($\epsilon=4360$) and λ_{min} 241 $\text{m}\mu$ ($\epsilon=1620$) in 0.03 N HCl aqueous solution.

The N-acethylamino ketone (II) (1.0 g.) in 12 ml. of ethanol was refluxed with 2,4-dinitrophenylhydrazine (1.0 g.) and 4 ml. of conc. hydrochloric acid. The reaction mixture was kept in the refrigerator and gave the 2,4-dinitrophenylhydrazone monohydrochloride, m.p. 213–214° (dec.), yield, 1.83 g.

The N-acethylamino ketone (II) (12.59 g.) was dissolved in 30% sodium hydroxide solution and steam-distilled into a flask containing a small volume of hydrochloric acid. The distillate was concentrated under diminished pressure to yield light yellow needles. The needles were recrystallized from a mixture of methanol-ethanol (1:6 V/V) and gave colorless needles melting at 196–198°. Yield, 14.04 g. The melting point was not depressed upon admixture with pseudoöxynicotine dihydrochloride prepared by Pinner and Wolfenstein's method⁴.

Anal. Calcd. for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}\cdot 2\text{HCl}$: C, 47.82;

H, 6.42; N, 11.15. Found: C, 47.57; H, 6.40; N, 11.22.

(II) was also obtained by refluxing the dihydrochloride of (III), prepared by Pinner and Wolfenstein's method⁴, with acetic anhydride and anhydrous sodium acetate. This compound (II), boiled at 208–210°/4.5 mm.

Anal. Calcd. for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 64.98; H, 7.53; N, 12.78.

The 2,4-dinitrophenylhydrazone of this compound (II) was prepared in the same way as described above and melted at 213–214° (dec.). The mixed melting point with the hydrazone obtained above showed no depression.

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