[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND ENTOMOLOGY, IOWA STATE COLLEGE]

CATALYTIC REDUCTION OF NICOTINE AND METANICOTINE

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In the study of the toxicity to insects of compounds structurally related to nicotine, considerable quantities of the reduced derivatives of nicotine were desired. The catalytic reduction of nicotine by means of platinum-oxide platinum black and hydrogen as used by Smith[2] on the dipyridyls and by Hamilton and Adams[3] on the pyridine and quinoline derivatives was selected as the most feasible method of preparation. During the course of these investigations, this method was also used by LaForge[4] for the reduction of metanicotine to dihydrometanicotine.

Nicotine was first reduced by Liebrecht[5] by the use of sodium in absolute alcohol. Since he regarded nicotine as hexahydrodipyridyl, he described the reduction product as β,β'-dipiperidyl. Pinner,[6] after establishing the constitution of nicotine, considered that the above reduction yielded largely hexahydronicotine. Blau[7] showed the majority of the reduction products to consist of octahydronicotine (also called octahydrometanicotine by Maass and Hildebrandt)[8] together with some hexahydronicotine. Both the method of reduction and the method of separation used in these studies would preclude their use as methods of preparation for any quantity of these derivatives.

Contrary to expectations, in the catalytic reduction of nicotine, rupture of the pyrrolidine ring takes place simultaneously with the hydrogenation of the pyridine ring. Complete reduction with the absorption of 3.7 moles of hydrogen to each mole of nicotine hydrochloride gives a mixture containing 25% hexahydronicotine hydrochloride and 75% octahydronicotine hydrochloride. If the reduction is interrupted at the point where three moles of hydrogen have been absorbed for each mole of nicotine hydrochloride (theoretical amount for reduction to hexahydronicotine), the resulting mixture consists of 19% hexahydronicotine hydrochloride, 57% octahydronicotine hydrochloride and 21% unchanged nicotine hydrochloride. An efficient method of separation for such a mixture has been

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[2] Smith, THIS JOURNAL, **50**, 1936 (1928).

[3] Hamilton and Adams, *ibid.*, **50**, 2260 (1928).

[4] LaForge, *ibid.*, **50**, 2483 (1928).

[5] Liebrecht, *Ber.*, **18**, 2969 (1885).

[6] Pinner, *ibid.*, **26**, 765 (1893).

[7] Blau, *ibid.*, **26**, 628, 1029 (1893).

[8] Maass and Hildebrandt, *ibid.*, **39**, 3700 (1906).

devised by taking advantage of the differences in solubilities of the hydrochlorides and picrates.

The catalytic reduction of metanicotine to dihydrometanicotine as carried out by LaForge[4] was duplicated. The complete reduction to octahydronicotine is also reported in the experimental data.

The compounds, with their constants and a suitable derivative, are listed in Table I. The hydrochlorides are hygroscopic and as a rule not suitable for characterization of the bases. The picrates of nicotine and dihydrometanicotine melt at 162 and 163°, respectively, so that this derivative cannot be used to distinguish between these compounds. The picrate of octahydronicotine is difficult to obtain sufficiently pure so that it will not be oily, while the bis-phenylsulfone derivative is easily prepared and melts sharply.

TABLE I

CONSTANTS AND REFERENCES TO COMPOUNDS SUITABLE FOR CHARACTERIZATION OF THE REDUCED NICOTINE DERIVATIVES

		B. p. of free base, °C.	Suitable deriv.	M. p., °C.
Nicotine	$C_{10}H_{14}N_2$	246[a]	Picrate	218[b]
Metanicotine	$C_{10}H_{14}N_2$	276[c]	Chloroplatinate	255[c]
Dihydrometanicotine	$C_{10}H_{16}N_2$	259[d]	Chloroplatinate	199[d]
Hexahydronicotine	$C_{10}H_{20}N_2$	246[e]	Picrate	202[e]
Octahydronicotine	$C_{10}H_{22}N_2$	259[f]	Hydrochloride	202[f]
			Bis-phenylsulfone	143.5[e]

[a] Wolffenstein, "Pflanzenalkaloide," Julius Springer, Berlin, **1922**, 3d ed., p. 136. [b] Pinner and Wolffenstein, *Ber.*, **24**, 66 (1891). [c] Pinner, *ibid.*, **27**, 1053 (1894). [d] Löffler and Kober, *ibid.*, **42**, 3431 (1909). [e] Blau, *ibid.*, **26**, 1029 (1893). Hexahydronicotine is a solid melting at 36–37° when absolutely anhydrous. Blau gives the m. p. 198–201° for the picrate; when pure, the melting point is 202° sharp. [f] Blau, *ibid.*, **26**, 628 (1893).

Experimental

Nicotine Hydrochloride.—The standard methods of obtaining pure nicotine depend upon fractional extraction between ether and water and final purification by distillation. A more convenient method has been found in the direct crystallization of the hydrochloride salt using a commercial product containing 95% water-free nicotine as a source. When dry hydrogen chloride gas is passed into an ether solution of commercial 95% nicotine containing a small amount of acetone, crystallization of nicotine hydrochloride takes place with little difficulty. Sufficient hydrogen chloride gas should not be added to completely precipitate the nicotine as considerable amounts of the oily impurities present come down with the last portions of the nicotine hydrochloride. The small amount of acetone present in the ethereal solution serves to aid crystallization. After precipitation of the nicotine hydrochloride, it was rapidly filtered on a Büchner funnel and twice recrystallized from a mixture of absolute alcohol and acetone. This was accomplished by dissolving the hydrochloride in a small amount of hot absolute alcohol and adding acetone until the solution just became turbid. "Seeding" at this stage aided materially in crystallization. After cooling, the crystallized salt was rapidly filtered and the above procedure repeated. Because of the very deliquescent nature of nicotine hydrochloride, it was stored over calcium chloride or stick sodium hydroxide, the latter serving to remove any occluded hydrogen chloride present.

Metanicotine Hydrochloride.—Metanicotine was prepared according to Löffler's and Kober's[9] modification of Pinner's[10] method involving the formation and subsequent hydrolysis of benzoylnicotine. This method was also used by LaForge.[4]

The traces of unchanged nicotine can be removed from the benzoylnicotine by washing with dilute acetic acid, the weakly basic benzoyl derivative being only slightly soluble. The hydrochloride of the free base was prepared and recrystallized as described above for nicotine.

Catalyst and Reduction Apparatus.—The platinum-oxide platinum black was prepared from C. P. chloroplatinic acid according to the directions of Adams and Shriner.[11] The reduction was carried out in an apparatus similar to that used by Adams and students[12] in their investigations.

Reduction of Nicotine.—As a standard run 0.1 mole (23.5 g.) of nicotine hydrochloride in 150 cc. of 95% alcohol with 0.2 g. of the platinum-oxide platinum black catalyst was used. The catalyst was not reduced previous to adding the nicotine salt. The time required for complete reduction (absorption of 0.37 mole of hydrogen) varied from three to four hours when the initial pressure of hydrogen gas was 40 pounds per square inch. For the partial reduction (0.30 mole of hydrogen absorbed) two to three hours were required.

When the reduction had been carried to the point desired, the hydrogen was removed and the mixture shaken with oxygen for a short time to coagulate the colloidal catalyst. The catalyst was then removed by filtration and the solvent evaporated as completely as possible under reduced pressure. There is not sufficient difference in the boiling points of the free bases to effect a sharp separation by distillation.

The oily mixture of hydrochlorides was dissolved in a small amount of hot absolute alcohol and acetone was slowly added until the solution just became turbid. Most of the octahydronicotine hydrochloride crystallized on cooling since it is much less hygroscopic and less soluble than either nicotine or hexahydronicotine hydrochlorides; this was removed by filtration. The picrates of the hydrochlorides in the filtrate were formed by adding a saturated alcoholic solution of picric acid. Octahydronicotine picrate is very soluble in alcohol but insoluble in water, hexahydronicotine picrate is soluble in hot but relatively insoluble in cold alcohol, while nicotine picrate is comparatively insoluble in both hot and cold alcohol. The mixed picrates were extracted with hot alcohol on a hot water funnel leaving the nicotine picrate on the funnel and dissolving the hexahydronicotine picrate together with any octahydronicotine present. Upon cooling the filtrate, the hexahydronicotine picrate crystallized and was filtered from the remaining octahydronicotine picrate. By the evaporation of a portion of the alcohol and addition of water, any octahydronicotine which was not previously removed as the hydrochloride was precipitated as the picrate. The hydrochloride of octahydronicotine was recrystallized from absolute alcohol and acetone, the picrate of hexahydronicotine from alcohol. Yields were calculated on the amounts of these recrystallized salts obtained.

The free bases were obtained from the hydrochlorides by treating with sodium hydroxide and extracting with ether. The ether was evaporated and the bases distilled under reduced or atmospheric pressure. To obtain the free bases from the picrates the best procedure was found to be to treat the picrate with a small amount of 20% hydrochloric acid, which hydrolyzed the picrate almost immediately and precipitated a large

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[9] Löffler and Kober, *Ber.*, **42**, 3431 (1909).

[10] Pinner, *ibid.*, **27**, 1053 (1894).

[11] Adams and Shriner, THIS JOURNAL, **45**, 2171 (1923).

[12] Adams and Voorhees, "Organic Syntheses," John Wiley and Sons, Inc., New York, Vol. VIII, **1928**, p. 10.

part of the picric acid. This was filtered off and the remainder extracted with ether. The hydrochloride of the base was made strongly basic, the free base extracted with ether and subsequently distilled under reduced or atmospheric pressure.

Reduction of Metanicotine.—As a standard run 0.1 mole (23.5 g.) of metanicotine hydrochloride in 150 cc. of 95% ethyl alcohol with 0.2 g. of platinum-oxide platinum black was used. The time required for the reduction to dihydrometanicotine (absorption of 0.1 mole of hydrogen) was thirty minutes, while the reduction to octahydrometanicotine (absorption of 0.4 mole of hydrogen) required three to four hours. The catalyst was removed and the free bases were recovered from the hydrochlorides as in the reduction products of nicotine. The yields are practically quantitative in each case.

The ethylenic linkage in the aliphatic chain in metanicotine is much more easily reduced than the unsaturated bonds in the pyridine nucleus as practically all of the metanicotine is converted into dihydrometanicotine before the reduction of the pyridine ring is started.

Summary

Nicotine hydrochloride has been reduced to a mixture of hexahydronicotine hydrochloride and octahydronicotine hydrochloride with hydrogen using platinum-oxide platinum black as catalyst. Metanicotine hydrochloride has been reduced to both dihydrometanicotine hydrochloride and octahydronicotine hydrochloride, the yields being quantitative.

A method is given for the separation of the reduction products of nicotine involving the solubilities of the hydrochlorides and picrates.

Pure nicotine can be conveniently obtained by crystallization of the hydrochloride from an ether–acetone solution of the commercial 95% nicotine. The hydrochloride recrystallizes from hot absolute ethyl alcohol upon the addition of acetone.

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SULFUR DYES. I. PREPARATION OF A NEW SERIES[1]

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Introduction

In 1861 Troost,[2] by reducing a crude mixture of 1,5- and 1,8-dinitronaphthalenes with sodium sulfide and other reducing agents, obtained colored products. Croissant and Bretonnière[3] obtained a patent in 1873 which included the conversion to dyes of a heterogeneous collection of organic substances (animal and vegetable products, chiefly) when heated with alkali sulfides and polysulfides.

Vidal,[4] in 1893, found that certain aromatic nitrogen compounds yielded

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[1] Presented at the Atlanta meeting of the American Chemical Society, April, 1930.

[2] Troost, *Jahresber*, 958 (1861); *cf.* French Patent 244,885.

[3] Croissant and Bretonnière, English Patent 1489 (1873).

[4] H. R. Vidal, German Patent 84,632 (1893); St. Dennis and Vidal, German Patent 85,330, etc.