

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY]

## The Preparation of Several Deuterium Derivatives of Pyrrole

BY FOIL A. MILLER<sup>1</sup>

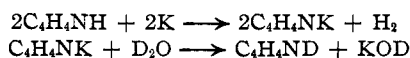
In the course of some studies on the vibrational spectrum of pyrrole<sup>2</sup> it became necessary to prepare several of the symmetrically substituted deuterium derivatives. Inasmuch as the methods of preparing these compounds add some interesting facts to our knowledge of pyrrole chemistry, and since other workers may have occasion to prepare deuteropyrroles, it seems worth while to describe the preparations in some detail.

Very little earlier research has been reported on this subject. Pyrrole-N-*d* has been prepared by Redlich and Stricks<sup>3</sup> and by Bonino and Manzoni-Ansidei.<sup>4</sup> The extent of exchange between pyrrole and heavy water has been determined by Koizumi and Titani.<sup>5</sup> They conclude that at  $pH \geq 2$  only one hydrogen exchanges, but that at  $pH \leq 1$  all five hydrogens exchange rapidly. However, no attempt was made to prepare and isolate an isotopically pure product. This paper reports the application of Koizumi and Titani's findings to the preparation of 8 ml. quantities of pyrrole-N-*d*, *sym*-pyrrole-*d*<sub>4</sub>, and pyrrole-*d*<sub>5</sub>. Spectroscopic evidence is offered as convincing proof for the course of the exchanges.

## Experimental

**Pyrrole-N-*d*. 1. Preparation from Potassium Pyrrole.**—This is the method used by both Redlich and Stricks and by Bonino and Manzoni-Ansidei. It was deemed necessary to repeat the work, however, because the Raman spectra of the two samples differed considerably,<sup>3,4</sup> and because pyrrole-N-*d* was needed for purposes of comparison in a later experiment.

The reactions involved are



Clean potassium was added slowly in slight excess to 10 ml. of freshly-distilled pyrrole<sup>6</sup> dissolved in 80 ml. of toluene.

(1) Chemical Foundation Fellow, 1938-1942.

(2) R. C. Lord, Jr., and Foil A. Miller, *J. Chem. Phys.*, **10**, June (1942).

(3) O. Redlich and W. Stricks, *Monatsh.*, **66**, 47 (1936).

(4) G. B. Bonino and R. Manzoni-Ansidei, *Ricerca sci.*, **7**, 11, Nos. 3-4 (1936); or *Atti accad. Lincei, Classe sci. fis. mat. nat.*, **25**, 494 (1937).

(5) (a) M. Harada and T. Titani, *Bull. Chem. Soc. Japan*, **11**, 465-474 (1936); (b) M. Koizumi and T. Titani, *ibid.*, **12**, 107-108 (1937); (c) M. Koizumi and T. Titani, *ibid.*, **13**, 85-94 (1938).

(6) The pyrrole was obtained through the kindness of Dr. Saul R. Buc, formerly of this Department. It had been prepared from ammonium mucate according to the method of Blicke and Powers [*Ind. Eng. Chem.*, **19**, 1334 (1927)].

The mixture was warmed and later refluxed in a water-free atmosphere until the precipitate became white. Most of the excess potassium was removed mechanically. The solid was filtered off on a sintered glass funnel in a gas box, washed with ether which was sufficiently dry to give a blue color with sodium and benzophenone, and dried; yield of potassium pyrrole, 80%. The solid was suspended in 40 ml. of dry ether, and heavy water (99.6%) was added dropwise with continued shaking until a second layer of liquid was formed. Five and one-half ml. of heavy water was used, which is about 2.5 times the theoretical amount. The ether-pyrrole-N-*d* solution was filtered through a sintered glass funnel and removed from the gas box, and the ether was evaporated with a stream of dry nitrogen. The pyrrole-N-*d* was dried over sodium carbonate and distilled four times in succession at low pressure in an all-glass apparatus; yield on the second reaction, 70%.

This synthesis, while extremely wasteful of heavy water and pyrrole, is useful because one knows that the deuterium atom introduced into the molecule has bonded to the nitrogen atom of the ring.

**Pyrrole-N-*d*. 2. Preparation by Exchange.**

—Koizumi and Titani suggest that the one hydrogen which exchanges in solutions of  $pH \geq 2$  is the N-hydrogen. It was necessary to confirm this, however, for it was hoped that the suggestion could be applied later to the preparation of *sym*-pyrrole-*d*<sub>4</sub>. One can test the suggestion by carrying out an exchange between pyrrole and neutral heavy water. Comparison of the Raman spectrum of the resulting compound with that of the pyrrole-N-*d* prepared from potassium pyrrole will show whether the exchange proceeds on the nitrogen atom alone. An experiment of this kind has been performed.

Four 2.5-ml. samples of freshly-distilled pyrrole were shaken for one hour with 2-ml. portions of heavy water (99.6%) in 6-ml. cylindrically-shaped separatory funnels. Each portion of the heavy water was used with each of the pyrrole samples in turn. The exchange was continued until calculation indicated that the deuterium content was at least 99% of the total exchangeable hydrogen. The united product was dried over sodium carbonate and distilled as before. Practically no pyrrole was lost.

The Raman spectrum of this product agreed exactly with that of the pyrrole-N-*d* prepared from potassium pyrrole. Hence exchange between pyrrole and neutral water involves only the N-hydrogen.

**Pyrrole-*d*<sub>5</sub>.**—Koizumi and Titani<sup>5c</sup> have pointed out that  $pH$  1 is optimum for exchanging

all five hydrogens of pyrrole. At  $pH > 1.5$ , all the hydrogens do not exchange; at  $pH < 1$ , acid-induced decomposition of the pyrrole becomes serious. Pyrrole- $d_5$  was prepared by an exchange between pyrrole and heavy water at this optimum  $pH$ .

Adjusting the heavy water to  $pH$  1 without contaminating it with light hydrogen required special methods. Deuterium chloride was made from heavy water and thionyl chloride, using the apparatus of Langseth and Klit.<sup>7</sup> The deuterium chloride was bubbled into heavy water to which had been added a trace of dry methyl violet, until the color of the solution matched that of a comparison solution of ordinary hydrochloric acid whose  $pH$  had been adjusted to 1.0. Trials with ordinary water and hydrogen chloride showed that the  $pH$  could readily be adjusted in this manner to  $1.0 \pm 0.2$  unit, which is sufficiently close. The procedure for exchange was similar to that for pyrrole-N- $d$ . Because decomposition of the pyrrole resulted in the formation of a scum, and because the liquids did not separate as nicely as in the former case, the separatory funnels were rotated rather slowly in a large centrifuge to hasten the separation. The product was dried and distilled as before. About 1 ml. of pyrrole was lost during the exchange.

**Symmetrical Pyrrole- $d_4$ .**—This compound was prepared from pyrrole- $d_5$  by an exchange with neutral water. It has already been shown that under these conditions only the N-deuterium will be involved. The procedure for carrying out the exchange and purifying the product was identical with that for pyrrole-N- $d$ . There was practically no loss of material.

(7) A. Langseth and A. Klit, *Kgl. Danske Videnskab Selskab. Math. fys. Medd.*, **15**, No. 13, p. 7 (1937).

**Spectroscopic Results.**—It is well known that C-H stretching frequencies in aromatic rings are in the 3000–3100  $cm^{-1}$  region, while the corresponding C-D frequencies are found at 2200–2300  $cm^{-1}$ . The N-H stretching frequency in liquid pyrrole occurs at 3400  $cm^{-1}$ , and the N-D at 2530  $cm^{-1}$ . Thus the vibrational spectrum offers a good criterion for the isotopic purity of the products. Each of the deuteropyrroles has been studied by the Raman effect.<sup>2</sup> In every case valence frequencies were found only in the expected regions; even on long exposure there was no trace of lines due to an improper isotope. This is thought to mean that the isotopic purity was at least 99%. It also offers convincing proof that exchange between pyrrole and water at  $pH$  1 involves all five of the pyrrole hydrogens, but that at  $pH$  7 only the N-hydrogen is involved.

Acknowledgment is made for a grant-in-aid from the Hynson, Westcott and Dunning Fund. The author also wishes to thank the Chemical Foundation, Incorporated, for a fellowship for graduate study.

### Summary

Simple and efficient methods of preparing pyrrole-N- $d$ , *sym*-pyrrole- $d_4$ , and pyrrole- $d_5$  are described. It is confirmed that exchange between pyrrole and water at  $pH$  1 involves all five of the pyrrole hydrogens. In neutral solution only the N-hydrogen exchanges.

BALTIMORE, MARYLAND

RECEIVED MARCH 20, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YENCHING UNIVERSITY]

## Conductivity Studies.<sup>1</sup> III. The Limiting Equivalent Conductances of Potassium Chloride in Water at Temperatures between 15 and 40°

BY NORMAN C. C. LI<sup>2</sup> AND HSING FANG<sup>3</sup>

The determination of the electrical conductivity of electrolytes has been the subject of many investigations. A search of the recent extensive literature in this field shows that many investigators study conductivity as a function of concentration at some particular temperature or conduc-

tivity as a function of temperature at some particular concentrations, and only few study the variation of the limiting equivalent conductances with temperature.

Since aqueous solutions of potassium chloride have been used as standard solutions for determining cell constants, extensive conductivity studies on these are desirable. Recently Jones and Bradshaw<sup>4</sup> and Bremner and Thompson<sup>5</sup> studied the variation in conductance of "demal"

(1) Earlier papers in this series: Li and Fang, *J. Chinese Chem. Soc.*, **6**, 32–39, 44–50 (1938).

(2) Present address: Department of Chemistry, The Catholic University, Peiping, China.

(3) British Indemnity Research Assistant in Chemistry. This article is based on part of a thesis presented by H. Fang to the Faculty of the Graduate Yuan of Yenching University in partial fulfillment for the degree of Master of Science, June, 1941.

(4) Jones and Bradshaw, *THIS JOURNAL*, **55**, 1780 (1933).

(5) Bremner and Thompson, *ibid.*, **59**, 2372 (1937).