

NOTES

Ionic Radii of the Histadyl and Pyrilamine Cations

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Recent studies of the physical chemistry of the antihistamines² have been valuable in the correlation of the pharmacological properties of such compounds with certain of their physical properties. It is thought that the ionic radius of an antihistamine may be important in its biological efficiency. This paper describes two techniques which were used to determine the ionic radius of the Histadyl and Pyrilamine cations. The radii obtained by the two methods for Histadyl are in close agreement; however no satisfactory radius could be obtained by the apparent molal volume method for Pyrilamine.

Experimental

Materials.—Histadyl (*N,N*-dimethyl-*N'*,2-thenyl-*N'*- α -pyridylethylenediamine hydrochloride), which was furnished by Eli Lilly and Co., carried the manufacturers specifications of HCl: 12.1–12.4%, Histadyl base: 87.0–87.5%. Pyrilamine (*N-p*-methoxybenzyl-*N'*,*N'*-dimethyl-*N*- α -pyridylethylenediamine malcate), which was furnished by Merck and Co., carried the manufacturers ultraviolet Assay of 99.8% Pyrilamine. The materials were used without further purification since conductance studies³ of recrystallized products showed no deviation from the original material received.

Methods. I. Ionic Radii from Ionic Conductances.—An equation based on Stokes law⁴ permits the calculation of ionic radii from a knowledge of the limiting ionic conductance, l° , viscosity of solvent, η , and the valence of the ion, Z . The simplified equation has the form

$$l^\circ \eta = \frac{0.8147 \times 10^{-8} |Z|}{r}$$

where r is the ionic radius in centimeters. The values for l° for the Histadyl and Pyrilamine cations have been previously reported.³ The viscosity of water was taken as 8.949 millipoises at 25°. Substituting these values into the equation gives 3.96×10^{-8} cm. and 3.75×10^{-8} cm. as the radii of the Histadyl and Pyrilamine cations, respectively.

II. Ionic Radii from Apparent Molal Volumes.—The apparent molal volumes of cesium and rubidium chlorides, bromides and iodides may be represented to a close approximation by the equation,⁵ $\phi = 6.47 (r^{3+} + r^{3-})$ where ϕ is the apparent molal volume and r is the crystallographic radius. It was assumed that this equation might be applied to Histadyl since large ions are involved in both cases. The apparent molal volume for Histadyl was evaluated from the relation⁷

$$\phi = \frac{1000}{c} - \frac{1}{d'} \left(\frac{1000d}{c} - M \right)$$

where M is the molecular weight of the solute, d' and d are the densities of the solvent and solution, respectively, and c is the concentration of solute in moles per liter.

Table I gives the apparent molal volumes of various con-

centrations of Histadyl. The densities shown were determined with a Weld pycnometer.

TABLE I

APPARENT MOLAL VOLUMES OF HISTADYL		
c	Density	ϕ (ml.)
0.13198	1.00426	243.7
.23003	1.00972	243.7
.30377	1.01397	242.8
.40761	1.01966	242.9

Using the value 243 ml. for the apparent molal volume and the crystallographic radius of the chloride ion as 1.81×10^{-8} cm.⁴ the value for the ionic radius of Histadyl is 3.84×10^{-8} cm. which agrees closely with the value obtained from ionic conductances.

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The Chemical State of F¹⁸ from the Fast Neutron Irradiation of Fluorobenzene

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Experimental

We have irradiated fluorobenzene with fast neutrons obtained by bombardment of beryllium with 26 Mev. deuterons in the Philips synchrocyclotron. The fluorobenzene was prepared from C₆H₅N₂BF₄ and had been purified by simple distillation. Before the start of the experiment the liquid had been treated with a concentrated solution of hydrofluoric acid to introduce a carrier for the inorganic radiofluorine. (The quantity of hydrofluoric acid dissolved in this way amounts to much less than 1% of the organic fluorine.)

The fluorobenzene was irradiated in a brass cylinder, which was gold-plated on the inside. It was closed by means of a disc of polyvinyl chloride with a screwed-on top on the outside and a thin gold foil on the inside. To separate the inorganic radiofluorine from the organic fraction the contents of the cylinder were poured into a brass tube which was gold-plated on the inside and mixed with a solution of sodium hydroxide and sodium fluoride. The mixing was done by means of a gold-plated silver vibrating stirrer. The liquid was then separated in a separating funnel and the two fractions collected in glass tubes. The original cylinder was rinsed with hydrogen fluoride and this liquid collected in the gold-plated tube which had served for the first separation.

All fractions were measured in their glass or brass tubes in a Philips hollow liquid γ -counter (No. 18508), which is eminently suitable for this purpose. We made sure that the sensitivity for the radiation of F¹⁸ was the same for all tubes. The activity found in the wash liquid and on the wall of the gold-plated tube, which at most amounted to about 10% of the total, was added to that of the inorganic fraction. The correct half-life for F¹⁸ was observed in all cases. We found 0.64 of the activity in the inorganic fraction with a probable error of a few per cent. (In the final series individual experiments gave the figures: 0.68, 0.64, 0.62, 0.67, 0.59 and 0.63.)

The main uncertainty lay in the danger that the radiofluorine atoms might react with the gold-plated walls. We were unable to prove that this complication did not occur, as the brass cylinder became so active that we would not have been able to recognize the F¹⁸ in its decay curve. We did, however, carry out some irradiations in which a very

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(2) A. V. Tolstoukhov, *Trans. N. Y. Acad. Sci.*, **14**, 260 (1952).

(3) A. C. Andrews and H. B. Johnson, *Trans. Kans. Acad. Sci.*, **56**, 449 (1953).

(4) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1950.

(5) "International Critical Tables," Vol. 3, McGraw-Hill Book Co., New York, N. Y., 1929, p. 10.

(6) R. H. Stokes and R. A. Robinson, *This Journal*, **70**, 1870 (1948).

(7) E. M. Baker, *ibid.*, **71**, 3336 (1949).

thin gold foil spiral was put inside the fluorobenzene. The surface of this spiral was roughly four times that of the inside of the cylinder and we were able to show by the decay of its activity that this spiral (which because of its low weight became only moderately radioactive) did not retain more than a negligible quantity of F^{18} after washing.

Discussion

The presence of hydrogen fluoride during the irradiation seemed essential to provide a scavenger for fluorine atoms. Otherwise radioactive fluorine or rather hydrogen fluoride might conceivably have reacted with the metal parts present, or with small amounts of impurities or have been adsorbed and have given rise to erroneous and irregular results.

No attempt was made to determine the chemical state of the organic fluorine. We do not know whether it was present partly as monofluorobenzene and partly as difluorobenzene or entirely as one of the two.

If the result obtained in this experiment is compared to retention values measured for other halogen benzenes several points must be kept in mind.

The addition of an inorganic scavenger for free halogen atoms increases the inorganic yield when the irradiated material is an organic compound of bromine or iodine which contains hydrogen.¹ Free radiohalogen atoms after being reduced to thermal energies, may react with an organic molecule in the absence of a scavenger, but if the latter has been added the radioactive halogen will suffer exchange and remain in the inorganic fraction. It was proved and explained by Chien and Willard² that in the case of organic chlorine compounds, which contain hydrogen atoms, the addition of a small amount of scavenger was without effect on the distribution of the radioactivity between the organic and the inorganic fraction. This is due to the fact that a free chlorine atom can take away a hydrogen atom from an organic compound. This reaction forms a hydrogen halide and an organic free radical. (In the case of the Szilard-Chalmers process the hydrogen halide is, of course, radioactive.) In a system of this second type all radioactive inorganic molecules are formed by processes in which a "hot" radiohalogen atom or ion takes part. Similar reactions are possible with an isolated fluorine atom, and therefore the addition of a small quantity of hydrogen fluoride to the fluorobenzene before irradiation should not influence the ratio of organic and inorganic radiofluorine.

It is clear that if the organic fraction in C_6H_5F is compared to the organic fraction in C_6H_5Br containing a scavenger the difference between the two fractions should be due only to the difference in the reaction between fast radioatoms and halobenzene molecules. In the case of bromobenzene the best value seems to be 0.29³ for the organic fraction (found by Chiang and Evans in the presence of 3 mole % Br_2 according to Chien and Willard) and the similarity between this figure and the value 0.36 found by us for C_6H_5F indicates that the influence of the nature of the halogen is not very great in this respect. That the organic yield in bromobenzene is much larger in the absence of a scavenger

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- (2) J. C. W. Chien and J. E. Willard, *ibid.*, **75**, 6160 (1953).
- (3) J. C. W. Chien and J. E. Willard, *ibid.*, **76**, 4735 (1954).

(from 0.63 to 0.83 according to Shaw and Collie⁴ and from 0.47 to 0.88 as reported by Chien and Willard, both with a very bad reproducibility) is not surprising.

Finally it should be kept in mind that a fluorine atom formed by an $(n,2n)$ -process has an enormous kinetic energy (of the order of one Mev.). Even a very small fraction of this energy is sufficient to tear off a number of electrons from the atom and to leave it with an appreciable positive charge.⁵ (In case the radiohalogen has been formed by neutron-capture it has much less kinetic energy and its primary positive charge is likely to be much lower, although even in this case part of it⁶ seems to be present as positive ions.) It is, however, by no means certain that the high positive charge persists till the moment the free halogen enters into its final chemical condition. In the case of methyl iodide the ratio of inorganic to organic radiohalogen was demonstrated to be the same⁷ for the products of (n,γ) - and of $(n,2n)$ -processes. (But one cannot be certain that the energy which the radioactive atoms have at the moment of formation will always be without influence on their final distribution, as the energy of the activating neutrons has been reported⁸ to influence the retention after an (n,γ) -process in solid $Na_2As_2O_4$ and Na_2HAsO_4 .) However, radiofluorine, because of the high ionization potential of the element, will lose its positive charge with exceptional ease and so it seems even more unlikely in this case than in others that an original positive charge will influence the final chemical state of the fluorine-18.

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Determination of Light Intensities with a Highly Sensitive Uranyl Oxalate Actinometer

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During the past twenty years the uranyl oxalate actinometer²⁻⁴ has been widely used in photochemical studies. The usual analytical procedure involves titration with standard permanganate or ceric solutions of the undecomposed oxalate in the irradiated sample and the total oxalate in the blank.

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