

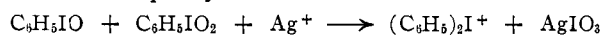
[CONTRIBUTION FROM THE INSTITUTE FOR NUCLEAR RESEARCH, AMSTERDAM]

Mechanism of the Formation of the Diphenyliodonium Ion

By J. B. TH. ATEN AND A. H. W. ATEN, JR.

The mechanism of the reaction between a mixture of iodosobenzene and iodoxybenzene with silver hydroxide has been investigated by means of a radiochemical technique. It is shown that the iodine of the diphenyliodonium ion formed is derived from the iodosobenzene and the iodine of the silver iodate from the iodoxybenzene.

It has been shown by Hartmann and Meyer¹ that the reaction of a mixture of iodosobenzene and iodoxybenzene with silver hydroxide leads to the formation of diphenyliodonium ion and silver iodate



In principle two different ways can be imagined in which this process might take place. First the iodine of both starting materials could be divided equally over the two products of the reaction, which would mean that at some intermediate stage of the process the two iodine atoms of the participating molecules would be equivalent. On the other hand the iodine of one of the original substances could go into the diphenyliodonium ion and the iodine of the other into the silver iodate. In this case one would, of course, expect the iodosobenzene to provide the diphenyliodonium-iodine and the iodoxybenzene the iodate-iodine, as was suggested by Masson, Race and Pounder.²

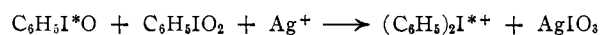
To settle this question the reaction was carried out using iodosobenzene labeled with radioactive I^{131} and inactive iodoxybenzene. The experiment was performed three times and the results were shown in Table I. Specific activities are expressed in counts per minute per milligram of iodine. All figures, including those given in the text, have been corrected for radioactive decay to the same moment. In calculating the specific activity of the diphenyliodonium iodide one iodine atom per molecule has been taken into account. This is justified by the results obtained by Juliusburger, *et al.*,³ who demonstrated the absence of exchange between the two iodine atoms in diphenyliodonium iodide. Their conclusions were confirmed by our own measurements which showed that no activity occurred in the excess of iodide used to precipitate the radioactive diphenyliodonium ions.

TABLE I

Experiment	Specific activity of the iodine in the diphenyliodonium ion of the diphenyliodonium iodide	Specific activity of the iodine in silver iodate	Specific activity of the iodine in iodosobenzene
1	375	1.2	335
2	361	2.7	335
	312		
3	374	6.9	344*

It is seen that the activity per milligram of iodine is about equal in the iodosobenzene used as a starting material and in the diphenyliodonium ion obtained. On the other hand, the specific activity of the silver iodate is negligible compared to that

of the diphenyliodonium iodide and the specific activity of the original iodoxybenzene was zero. The course of the reaction was therefore



In the second experiment the weak activity present in the iodate fraction was investigated further. Ninety-five per cent. dissolved in ammonium hydroxide and was assumed to consist of AgIO_3 . The specific activity of the iodine in this fraction was found to be 0.3. Of the residue about one-half was soluble in a sodium cyanide solution. This was supposed to be silver iodide. The rest, which had a specific activity of about 1.4—assuming the iodine content to be equal to that of iodoxybenzene—probably consisted mainly of unchanged starting material, which in that case must have been almost exclusively iodoxybenzene.

The slight activity of the silver iodate can be explained by the known fact that iodosobenzene decomposes into iodobenzene and iodoxybenzene. This means that during the reaction the iodoxybenzene is already slightly radioactive. This explanation is supported by the regular rise in the specific activity of the silver iodate from the first experiment to the third.

Experimental

Preparation of Radioactive Iodosobenzene.—Radioactive iodobenzene was synthesized by adding iodide ions labeled by addition of I^{131} ,⁴ to a solution of benzene diazonium ion. From the iodobenzene radioactive iodosobenzene was prepared by treating the former in chloroform with chlorine followed by hydrolysis in aqueous solution with sodium hydroxide.⁵

Preparation of the Diphenyliodonium Ion.—Equivalent amounts of radioactive iodosobenzene (5 g.) and of inactive iodoxybenzene (5.3 g.) were stirred vigorously at room temperature for 4–5 hours with the theoretical quantity of freshly precipitated silver hydroxide in about 500 ml. of water. The yield of the reaction is unknown.

Determination of the Specific Activity of the Samples.—Silver iodate was filtered off. The diphenyliodonium ions were precipitated with an excess of potassium iodide. Both substances were washed with water and dried with ethanol and ether.

The radioactivity of the samples was determined by β -measurement under a mica-window counter. Corrections for self-absorption were made by means of the graphical method using absorption measurements in aluminum foil.⁶ We were unable to make the organic samples quite uniform in thickness, which tends to make the accuracy of our figures somewhat low.

Acknowledgments.—We wish to thank the "Nederlandse Organisatie voor Zuiver Wetenschappelijk Onderzoek" and the "Stichting voor Fundamenteel Onderzoek der Materie" for their support of this investigation.

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We are also grateful to Dr. G. J. M. van der Kerk (Organisch Chemisch Laboratorium, Rijksuniversiteit, Utrecht) who very kindly prepared the sam-

ples of inactive iodoxybenzene used in this investigation.

AMSTERDAM, NETHERLANDS

RECEIVED JULY 18, 1951

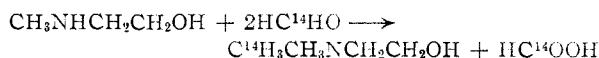
[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, BOWMAN GRAY SCHOOL OF MEDICINE, WAKE FOREST COLLEGE]

Preparation of C¹⁴-Methyl Labeled Dimethylaminoethanol

BY CAMILLO ARTOM AND MARIETTA CROWDER

2-Methylaminoethanol (1 mM./ml.) is refluxed for 6 hours with C¹⁴-formaldehyde (1 mM./ml.). Unreacted 2-methylaminoethanol and formaldehyde are destroyed with nitrous acid and alkaline iodine, respectively. C¹⁴-Dimethylaminoethanol is recovered by two successive steam distillations (yield 40% based on the isotopic formaldehyde). The solution is of isotopic purity sufficient for biological experiments. No dimethylaminoethanol is formed at pH < 7, unless formic acid is also added.

In the course of our studies on the role of dimethylaminoethanol (DMA) as a likely intermediate in choline metabolism,¹⁻³ C¹⁴-methyl-DMA was prepared by refluxing 2-methylaminoethanol (MMA) with C¹⁴-formaldehyde (FA) in alkaline solution.



The highest yield, based on the FA, was obtained with about 1 mM. each of FA and MMA per ml. of solution, and was but very slightly increased by addition of formate. No DMA was formed at pH < 7, unless formic acid was also added. A comparison between these conditions and those of other methods for the reductive methylation of amines⁴⁻⁷ may be of some theoretical interest. From the practical viewpoint, the present procedure, in spite of its lower yield, is extremely simple and the product is of a sufficient isotopic purity to be used directly for most biological experiments.

Experimental

For the radioactive measurements (thin mica window or Q-gas flow counter), both standard and unknown samples were brought to a uniform weight by adding the proper amounts of inactive materials (egg lipides), and were spread as thin films onto aluminum dishes covered by lens paper.

2-Dimethylaminoethanol.—Into a small flask fitted with a ground glass condenser, 2 ml. of a 2.5 M solution of 2-methylaminoethanol, b.p. 158–160° (5 mM.), 1.8 ml. of a solution of C¹⁴-labeled formaldehyde⁸ (300 microcuries, 4.6 mM.) and 0.7 ml. of alkaline borate, pH 10.0 (6.2 g. of boric acid in 100 ml. of N NaOH) are added. The mixture

is refluxed for 6 hours, cooled and neutralized with 2 N HCl. The unreacted 2-methylaminoethanol is destroyed by adding 10 ml. of 30% sodium nitrite and 5 ml. of glacial acetic acid. After 10 minutes in ice, the mixture is made alkaline with saturated NaOH, aerated vigorously for 0.75 hour (to remove the oxides of nitrogen), then steam distilled (Parnas-Wagner apparatus⁹) for 0.5 hour into 4 ml. of N HCl. To eliminate traces of C¹⁴-formaldehyde which may be carried over in the distillate, 1 ml. of 1% inactive FA, 1 ml. of N iodine and a slight excess of N NaOH are added. After acidification, the excess iodine is reduced with 5% NaHSO₃. The solution is concentrated to a few ml., made alkaline and steam distilled again into 4 ml. of N HCl. The distillate contained 1.87 mM. of DMA (by titration: a 40.6% yield, based on the added FA) and 41.0% of the counts introduced as C¹⁴-FA.

The extent to which other isotopic products, introduced or formed during the reaction, had been eliminated was determined. Inactive formaldehyde, formic acid, or methanol was added to separate aliquots of the solution of isotopic DMA. The mixtures were acidified and distilled. In the distillates the per cent. recoveries of C¹² and C¹⁴ (measured as BaCO₃ after oxidation with cold alkaline KMnO₄) were, respectively, formaldehyde, 97 and 0.08; formic acid, 90 and 0; methanol, 99 and 0.09.

From both active and inactive materials the picrolonic acid derivative was prepared¹⁰ with variable yields (60–95%, depending on the amounts of DMA present or added as a carrier). The m.p. was 196° (unchanged by admixture with an authentic sample of DMA picrolonate; reported,¹¹ 197°). Within the limits of error of our measurements, the specific activity of the picrolonate was the same as that calculated for the DMA in solution and was not changed after several recrystallizations from water and alcohol.

Anal. Calcd. for C₁₄H₁₉N₅O₆: C, 47.59; H, 5.42; N, 19.82. Found: C, 47.48, 47.69; H, 5.35, 5.58; N, 19.45, 19.71.

Acknowledgment.—This work was done under contract No. AT-(40-1)-288, Title II, between the Bowman Gray School of Medicine and the U. S. Atomic Energy Commission. The authors wish to express their appreciation to Mr. H. Wainer for technical help and to Dr. C. Tiedcke for the microanalyses on the DMA picrolonate.

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RECEIVED AUGUST 22, 1951

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