

of about 10 cc. per minute by admitting mercury from B to A. In order to maintain atmospheric pressure mercury is added to B through M. The liquid air trap at E condensed the methyl iodide formed and unused tritium was returned through B eventually to I.

The active methyl iodide containing tritium was made in about 2 g. quantities in better than 75% yield. The crude material of d^{20} 1.5268 melted at about -60° . It was redistilled and the vapor passed over phosphorus pentoxide *in vacuo*.

Preparation and Use of Catalyst.—The catalyst was prepared by dissolving 120 g. of cupric nitrate in 100 cm. of water and adding a saturated solution containing 60 g. of potassium carbonate at about 50° . The precipitated basic copper carbonate was filtered off, washed well and dried; 45 g. of the pulverized material was added to 100 cc. of quartz chips (0.5 to 1 mm.) and 50 cc. of chromic acid

solution containing 2 g. of CrO_3 . The mixture was well stirred and dried on a steam-bath. The catalyst chamber of 3.5-cc. capacity was filled with this material and the catalyst reduced by passing about 20 cc. of hydrogen per minute over it at a temperature of 325° for six hours. Tank hydrogen was passed over the catalyst at 160° , the temperature used for the reduction of the ester, for two hours before each preparation.

Summary

Radioactive methyl iodide has been prepared by two processes, the one leading to a compound containing short-lived C^{11} , the other to a compound containing radioactive hydrogen. Each process is designed for small amounts of material.

BERKELEY, CALIFORNIA

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

A Study of the Menschutkin Reaction Using Radioactive Hydrogen as a Tracer

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The reaction between amines and organic halides



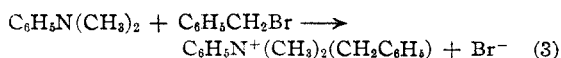
has been the subject of considerable experimentation and speculation.¹⁻¹⁰

The kinetics of this reaction are of particular interest because the probability factor in the rate expression

$$\frac{d(\text{I}^-)}{dt} = k(\text{R}_3\text{N})(\text{RX}) = PZe^{-E/RT} (\text{R}_3\text{N})(\text{RX}) \quad (2)$$

is unusually low, and, moreover, markedly affected by the solvent. For example, in the reaction between $\text{C}_6\text{H}_5\text{NH}_2$ and $\text{C}_6\text{H}_5\text{COCH}_2\text{Br}$ the factor P varies from 4×10^{-11} in benzene to 5×10^{-5} in benzyl alcohol.¹⁰

The values of $\log P$ and E in different solvents for the reaction



as given by V. A. Gol'tschmidt and N. K. Vorob'ev⁹ are reproduced in Table I.

- (1) N. Menschutkin, *Z. physik. Chem.*, **6**, 41 (1890).
- (2) Moelwyn-Hughes and Hinshelwood, *J. Chem. Soc.*, 239 (1932).
- (3) G. E. Edwards, *Trans. Faraday Soc.*, **33**, 1294 (1937).
- (4) R. G. W. Norrish, *ibid.*, **33**, 1521 (1937).
- (5) C. N. Hinshelwood, *ibid.*, **33**, 970 (1937).
- (6) Moelwyn-Hughes and Sherman, *J. Chem. Soc.*, 101 (1936).
- (7) Stern and Eyring, *J. Chem. Phys.*, **5**, 113 (1937).
- (8) Scatchard, *ibid.*, **2**, 657 (1934).
- (9) V. A. Gol'tschmidt and N. K. Vorob'ev, *J. Phys. Chem. (U. S. S. R.)*, No. 4, 473 (1939).
- (10) R. G. Cox, *J. Chem. Soc.*, 119, 142 (1921).

TABLE I

THE ACTIVATION ENERGY AND PROBABILITY FACTOR FOR THE REACTION OF EQUATION 3

Solvent	$(\text{CH}_3)_2\text{-CO}$	$\text{C}_6\text{H}_5\text{-COCH}_3$	$\text{C}_6\text{H}_5\text{NO}_2$	$\text{C}_2\text{H}_5\text{OH}$
$k \times 10^4$ (30°)	80.5	84.5	118	650
E	9747	9929	11,200	13,800
$-\log P$	4.94	5.08	6.16	8.78

For other types of reaction the value of P is usually close to unity; the very low values in the Menschutkin reaction imply that very few "activated" collisions result in reaction. Many theories have been advanced to account for this abnormality and the present paper presents experimental results which offer a test of some of these explanations.

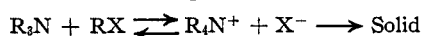
Moelwyn-Hughes and Sherman⁶ have assumed that at least one of the reactants forms an unstable complex with the solvent and that the true reactant is this solvated portion. In such a case the evaluation of the product $(\text{R}_3\text{N})(\text{RX})$ of the rate expression is in error and the true value of P could be unity.

Hinshelwood,⁵ from a consideration of Eucken's¹¹ work on the variation of the velocity of sound with frequency in the gas phase, and Norrish,⁴ by analogy with a number of photochemical reactions, account for the apparent inefficiency of the activated collisions by assuming an intermediate collision complex which can yield the

(11) Eucken and Jaacks, *Z. physik. Chem.*, **B30**, 85 (1935).

final products only if conditions are favorable for stabilization of the products. Otherwise the complex reverts to the reactants. Norrish, in his explanation, invoked the hypothesis of the Franck-Rabinowitch cage effect. While this hypothesis is very helpful to an understanding of what happens before highly activated intermediates (free radicals, etc.) can permanently separate, it seems doubtful if it is important in considering processes where there is very little thermodynamic tendency for recombination of the initial products of dissociation, *i. e.*, where the equilibrium state is far toward dissociation.

Edwards³ has postulated for benzene solutions, in which the product of the Menschutkin reaction is sparingly soluble, that the reaction is primarily rapid and reversible. He presumes that the rate of the over-all reaction is governed by the rate of formation of the solid product.



The equilibrium in solution favors the original reactants. This hypothesis takes the form of those above, in that a reversibly formed intermediate is involved in the net process.

Experimental Results and Discussion

It is possible to test the theory of a reversibly formed intermediate in the Menschutkin reaction by allowing an amine to react with an alkyl halide which contains a radioactive hydrogen or carbon atom. If the nature of the intermediate is such that the alkyl groups become spatially equivalent with respect to the halide ion before reversion to the initial reactants occurs, radioactivity should be found in the experimentally unreacted amine as well as in the alkyl halide salt. With this in mind, methyl iodide containing radioactive hydrogen or tritium (H^3) was allowed to react with trimethylamine and dimethylaniline, respectively, in both alcohol and benzene solutions.

Two equivalents of trimethylamine stood for three hours in 95% ethanol solution, with one equivalent of methyl iodide containing tritium. The reaction went to completion and the excess amine was examined for tritium content. Less than 1% of the activity to be expected on the basis of random distribution of the methyl groups between the amine and methyl iodide was obtained. An increase of amine concentration to a five-fold excess did not produce detectable interchange. The expected radioactivity appeared in the tetramethylammonium salt formed in the reaction.

Since the reaction between $C_6H_5N(CH_3)_2$ and CH_3I is very slow, the equivalent quantities of the reactants were allowed to stand for three hours at 25°, and then the unchanged $C_6H_5N(CH_3)_2$ was isolated and examined for radioactivity. No activity was found.

Ethanol as a solvent could have promoted ion separation and stabilized the initial reaction product, and, therefore, the reactions were carried out in benzene. The procedures used were the same as those employed when the reactions were carried out in ethanol except that the reaction between $C_6H_5-N(CH_3)_2$ and CH_3I was stopped after thirty minutes, which from previous experience is just prior to separation of crystals. No activity appeared in the unreacted amine in either case.

The sparingly soluble active tetramethylammonium iodide does not exchange methyl groups, at room temperature, with trimethylamine upon standing for eight hours in alcohol or for three days in benzene. The alcohol soluble tetramethylammonium chloride was prepared from the active iodide; it did not exchange with the amine in alcohol solution in eight hours.

It is evident that for the cases studied, no intermediate exists which is rapidly and reversibly formed and in which the iodide ion loses its identity with the methyl group originally present in the active methyl iodide.

Experimental

The following procedure was used for both benzene and alcohol solutions. Five cc. of 0.2 *M* radioactive CH_3I^{12} solution was added to 10 cc. of 0.2 *M* trimethylamine solution contained in a 25-cc. flask. After shaking, the mixture was placed in a bath at 25°. When the reaction was carried out in alcohol, crystals began to form in about ten minutes, but with benzene as a solvent an immediate turbidity was observed. At the end of about three hours, by which time the reaction had gone to completion, the excess of amine and the solvent were removed from the salt by first freezing the contents of the flask in liquid air, connecting the latter by a wide bore tube to another flask, evacuating the system, placing the liquid air-bath around the second flask and gently warming the reaction mixture. A quantity of concentrated hydrochloric acid sufficient to convert all of the amine to the hydrochloride was then added to the distillate and the water and solvent removed at 100° under vacuum. When benzene was used as the solvent, 10 cc. of alcohol was added so that upon addition of the hydrochloric acid a homogeneous solution resulted. The flask was then equipped with a dropping funnel, an air inlet and a tube leading to a combustion furnace.

(12) D. Harman, T. D. Stewart and S. Ruben, *THIS JOURNAL*, **64**, 2293 (1942).

Two cc. of 50% potassium hydroxide was added to the dry salt and the amine generated was swept through a drying tube to the combustion tube by a slow stream of air. Explosions resulted from the use of pure oxygen or of too rich an air mixture. The water formed was collected in a small liquid air trap and converted to hydrogen as follows, by a procedure worked out by Mr. T. H. Norris of this Laboratory. The water was transferred to the bottom of a test-tube (29 × 300 mm.) which was then filled with magnesium turnings and connected, in a vertical position, to a glass coil which in turn was attached to a high vacuum line. After placing the lower end of the tube in liquid air the system was evacuated, the glass coil also immersed in liquid air, and an electric heater placed around the top portion of the tube. When the temperature of the heater was constant, at approximately 625°, the liquid air was removed from the bottom of the test-tube which was then gently heated to vaporize the water. The hydrogen formed was collected in a 3-liter flask on the vacuum line from which it was transferred to a Geiger counter. The counting mixture was composed of about 15 mm. mercury pressure of alcohol and 20.0 cm. mercury pressure of hydrogen. This procedure required about thirty minutes.

The data on a typical experiment are

(Original reactants

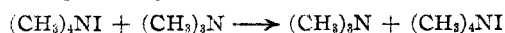
Moles methyl iodide	1.02×10^{-4}
Moles trimethylamine	2.00×10^{-3}
Equiv. of methyl group	7.02×10^{-3}

Specific radioactivity of hydrogen (counts/min./g. atom)

From initial methyl iodide	1.85×10^7
From excess trimethylamine	$<1.46 \times 10^4$
Calcd. for random distribution	$<1.58 \times 10^7$

The last figure in the above calculation gives the activity to be expected in the excess amine if, during the reaction, random distribution ($6.00 \times 1.85 \times 10^7/7.02$) were achieved; the activity found corresponds to less than 0.1% of that predicted on the assumption. Two experiments were made in alcohol and one in benzene, as described above. One was made in alcohol in which the concentration of the amine was five times as great as that of the methyl iodide. In all cases there was no exchange within experimental error.

In order to determine whether the excess amine reacts with the quaternary salt



the amine solution was added to some of the salt formed from active methyl iodide in a previous experiment and whose activity was known. After standing for eight hours in alcohol as a solvent, or for forty-eight hours in benzene, the amine was removed and its activity, determined as above, found to be negligible.

Since tetramethylammonium iodide is not very soluble in alcohol or benzene, the experiment was repeated in alcohol

using the corresponding chloride which was prepared from the same sample of iodide. No exchange was evident.

To test the possibility that, in the conversion of the amine to its hydrochloride and regeneration back to the amine, the H of the methyl groups exchanged with those of water, a 50% solution was prepared using very active water which was then used to regenerate amine from inactive trimethylamine hydrochloride. The activity of the amine was determined in the usual manner and no exchange was found.

The procedure for the reaction between dimethylaniline and methyl iodide was the same in both benzene and alcohol. Ten cc. of 0.2 M CH_3I was added to 10 cc. of 0.2 M $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$ and the resulting solution allowed to stand for three hours. A very few small crystals formed in this time, the quantity being greater in alcohol. The solvent and unreacted methyl iodide were separated from the quaternary salt and unreacted amine under vacuum as described above. The amount of methyl iodide in the distillate was determined as a measure of the extent of quaternization; about 1% reaction occurred. The amine was separated from the quaternary salt by treating the mixture with benzene and filtering through a fine sintered glass filter. Most of the benzene in the filtrate was removed by distillation, finally at 100° and 2-mm. pressure, and from a tube which could be placed in the combustion tube to burn the residual amine. The activity in the water was determined as above, and found to be zero within experimental error. While little net reaction had occurred, no exchange of the methyl groups was found.

Summary

Excess trimethylamine was quaternized by methyl iodide in which the hydrogen atoms were in part replaced by radioactive hydrogen or tritium. All the radioactivity was found in the quaternary salt, none in the excess amine. The solvents used were alcohol and benzene. Incomplete quaternization of dimethylaniline in alcohol or benzene produced no radioactivity in the unreacted base. It is concluded that for these cases there is no reaction intermediate which is reversibly formed and in which iodide ion loses its identity with the methyl group to which it was originally attached. Tetramethylammonium iodide or chloride does not methylate trimethylamine in alcohol solution at room temperature in eight hours; suspended in benzene no reaction occurs in three days.

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