

tion of the pancreas is distinctly acid. This confirms and extends the conclusions of our former paper regarding the pancreases of the hog, beef and sheep.

2. The quantitative relations were studied on organs collected from September to December to cover possible seasonal or feeding variations, and results were found which show that the reactions of the pancreases of the three animals are essentially as reported before, with the P_H values running between 5.5 and 5.7. There appears to be no seasonal effect, and the condition of the animal was evidently without influence. This ion concentration is then nearly a constant and is undoubtedly a factor of physiological importance.

3. Similar experiments were made on the organs of other animals. It was found that the parotid glands, the liver and the spleen were acid in reaction, but not to the extent found for the pancreas, while the bile was slightly alkaline or neutral and the thyroid gland practically neutral, as might be expected from the location and relations of the gland.

4. In searching for the cause of the reaction of the pancreas a complete analysis of the salts of the press juice was made. The juice is rich in phosphates, while sulfates are absent and chlorides present only in traces. Of the metals, potassium is the most abundant and the relations of all the metals to the phosphoric acid is such as to give rise to a slightly acid reaction.

5. In addition to this reaction of the inorganic salts it is found that the nucleoproteins present have an acid reaction, and that one of them, at least, the α -proteid of Hammarsten, goes readily into solution with secondary sodium phosphate, in which solution the reaction of the phosphate changes from alkaline to acid, apparently from the formation of primary phosphate.

6. It appears that the marked acid reaction of the pancreas, which is stronger than found for other organs, may be accounted for through the presence of acid phosphates and acid nucleoproteins. The alkali salts of the nucleoproteins are readily soluble in water and therefore pass into the centrifugal or press juice.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF WISCONSIN.]

THE INFLUENCE OF SOME SOLVENTS ON THE RATE OF ACTION OF SODIUM WITH ISOAMYL BROMIDE.

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Three types of solvents, ether, tertiary amines, and hydrocarbons, have particular interest because of their relation to the formation of the

Grignard reagent. In ether and tertiary amines this reagent forms by the action of magnesium on the organic haloid. A hydrocarbon solution of the haloid is not thus acted upon at ordinary temperatures. Tschelinzeff¹ has found that small amounts of ether or tertiary amine in the hydrocarbon solution cause the formation of the reagent at a lower temperature. The catalytic action² of the ether or tertiary amine he explained by the dissociating effect of these substances on the organic haloids.

It was considered of interest to see whether an alkyl haloid in ether solution would react with sodium faster than when dissolved in benzene. With this in mind, attempts were made to obtain comparative measurements for the rates of reaction between sodium and isoamylbromide when the latter was dissolved to a 0.1 *N* solution in ether, in benzene, and in dimethyl aniline.

Purification of Reagents.—The ether was shaken out with water three times, dried with fused calcium chloride, then with finely divided sodium and was finally distilled from phosphorus pentoxide. It was kept in the dark with sodium. The benzene was shaken with concentrated sulfuric acid several times, with sodium hydroxide solution and then with water. It was dried with fused calcium chloride and then finely divided sodium, was refluxed and distilled from sodium. It was kept in the dark with sodium in it. The dimethyl aniline was dried with sodium and distilled. The xylene was boiled with sodium, the gasoline was shaken out with concentrated sulfuric acid, and fractionated. The hydrogen was passed through water, sulfuric acid, phosphorus pentoxide, and sodium.

Plan of Experiment.—Twenty cc. of 0.1 *N* isoamylbromide solution were shaken for a definite length of time with a large excess of finely divided sodium in a stoppered flask in a thermostat. The flask was then opened and the sodium was filtered off, washed with pure solvent and then treated with alcohol. The alcoholic solution was diluted and after proper treatment titrated to determine the amount of sodium bromide formed. This gave in cc. 0.1 *N* silver nitrate solution a measure of the amount of isoamylbromide which had reacted in any way with sodium.

Apparatus.—The shaker was a piece of two-inch plank made to carry four samples. It had two holes on each side in which the necks of the flasks fitted, being held in place by wooden clips. This plank was pushed back and fourth on the surface of the water in the thermostat. The bulb of the flask was immersed, leaving only the top of the neck exposed. The shaking was efficient as could be seen by the distribution of the sodium over the inside of the flask. The temperature of the thermostat was 25°.

¹ *Ber.*, 37, 4537-4538 (1904).

² Stadnikoff (*J. prakt. Chem.*, [3] 88, 1 (1913)) denies this role for the ether. See in reply Tschelinzeff (*J. prakt. Chem.*, [3] 89, 86 (1914)).

Experimental.

The sodium (5 or 7.5 g. weighed to 0.01 g.) was melted under boiling xylene in the flask in which the reaction was to take place, which was a 100 cc. round bottom, long-necked, Jena flask. The flask was stoppered and shaken vigorously, then opened and cold xylene poured in. This method, a modified suggestion of Brühl,¹ gave the metal in a finely divided condition. The particles in any one sample were not uniform in size, but the different samples were very similar even upon close examination. The flask containing the xylene and finely divided sodium was attached to an apparatus so arranged that it could be filled with dry hydrogen, or that diminished pressure could be maintained by a water pump. It was also possible, without admitting air, to draw a liquid first into the flask to rinse it and then into a catch bottle. Hydrogen was used when necessary to increase the pressure within the system. A sulfuric acid wash bottle just before the pump kept out moisture from this source. When the flask was first connected with this apparatus the air in it was replaced by hydrogen and the xylene was drawn over into the catch bottle. The sodium was washed twice with gasoline boiling below 75° and once with petroleum ether boiling below 50°. After most of this had been removed, the small amount remaining was evaporated under diminished pressure by immersing the flask in hot water. The flask was several times alternately filled with hydrogen and evacuated to get rid of traces of hydrocarbon. In this way sodium was washed free from xylene in an atmosphere of hydrogen and was finally obtained perfectly dry in a finely divided condition with a bright metallic surface. There was usually present a trace of sodium hydroxide formed during weighing. Hydrogen was then admitted to the full pressure of the generator and the sodium was ready for use.

The average size of the sodium particles was not greater than 0.1 to 0.2 mm. in diameter, and in no case were there any particles larger than 1 mm. It did not seem practicable to try to obtain more uniform material than this, since so large an excess of sodium was used (100 to 150 atoms).

The surface exposed is an important factor in a heterogeneous reaction. The large amount of sodium was chosen to make the surface relatively enormous, 7.5 g. of sodium in spheres having a diameter of 0.3 mm. would have a surface of over 1500 sq. cm. The actual surface exposed could not have been smaller, as the average diameter must have been less than 0.3 mm. The particles were compared with a scale ruled in millimeters in order to know their approximate size. This surface (1500 sq. cm. for 7.5 g. or 1000 sq. cm. for 5 g.) was available for reaction with 20 cc. 0.1 *N* solution of isoamylbromide (0.302 g.).

¹ *Ber.*, 35, 3516 (1902), footnote.

In order to reduce the evaporation on pouring the ether solution into the buret, the volumetric flask was closed with a two-holed rubber stopper carrying a long and a short piece of glass tubing. On inverting the flask, ether flowed out the short tube into the buret, while air entered the flask through the long tube without bubbling through the solution.

For measuring the isoamylbromide solution a buret was used which was drawn out to a long capillary below the glass stopcock. This capillary entered the flask through a glass tube in the stopper and extended almost down to the sodium. Twenty cc. of the 0.1 *N* isoamylbromide were added, and the flask was withdrawn from the rubber stopper, closed by a solid rubber stopper and shaken in the thermostat.

The reaction was stopped by filtering the sodium and washing it three times with the solvent, except in the case of dimethyl aniline. When this was used as the solvent, if sufficient time were allowed for the reaction, there was present a whitish flocculent suspension. On exposure to air, this was rapidly discolored to a brown slime which hindered filtration very much, even when suction was used. It was necessary to remove the dimethyl aniline as completely as possible, because of the color which even small amounts of it caused in the solution during titration. The final method was to dilute with gasoline before filtering off the sodium, then filter and wash with gasoline. Even with this modification, however, special treatment was necessary before the bromide could be titrated.

The sodium from benzene or ether experiments was treated with alcohol, the flask and filter were washed into this solution with water, and the solution was diluted, acidified with nitric acid, and titrated according to the Volhard method. A few of the solutions, after being exactly neutralized with 0.5 *N* nitric acid, were titrated, using potassium chromate as indicator.

The procedure when dimethyl aniline had been used was as follows: The sodium alcoholate was neutralized by cold alcoholic nitric acid, the solution filtered, and the filtrate evaporated to dryness, leaving a dark residue. This was triturated with pure benzene to dissolve the colored substance which was filtered off. The sodium bromide obtained by both procedures was dissolved in water and titrated according to the Mohr method. In the earlier cases, titrated by the Volhard method because of the color caused by traces of dimethyl aniline, it was necessary to approach the end point several times from each direction and take the average of these as correct.

The results in Table I fairly represent those obtained. In the case of the ether solution the figures given include all of the results from the last solution used, with those for 30, 72 and 96 hours from a previous solution. 7.5 g. of sodium were used in all of the experiments with ether save the last three where 5 g. were used. All of the data obtained using

dimethyl aniline and benzene as solvents are not included, as they merely emphasize the results given in the table. With benzene and dimethyl aniline solutions 5 g. of sodium were used save in the last two experiments with dimethyl aniline where 7.5 g. were used. A large number of experiments were made with ether as the solvent, in some of which 7.5 g. of sodium were used, in others 5 g., but no difference in results due to this change could be detected. The results are expressed in cc. of 0.1 *N* silver nitrate required to titrate the sodium bromide formed. Isoamylbromide was dissolved to 0.1 *N* solution in these solvents. The time is expressed in hours.

TABLE I.

Cc. of 0.1 *N* AgNO₃ required for NaBr formed from C₈H₁₁Br in solvents named.

Time, (hours).	Solvents.				Time, (hours).	Solvents.		
	Ether.		Dimethylaniline.	Benzene.		Ether.	Benzene.	
1	0.9	1.0	18.7	0.5	18	1.0	
2	0.7	1.0	18.2	0.7	30	15.0	...	
3	0.6	2.0	0.95	18.6	0.8	47	0.8
4	7.1 ¹	0.8	18.6	0.8	72	18.9	...	
5	1.1 (B)	21.2 ¹	96	20.4	...	
6	1.5	3.1	20.6	0.8	358	1.9	

These results show that the reaction in benzene does not complete itself within a reasonable length of time. In ether the reaction goes to completion within four days, while in dimethylaniline it is complete in a few hours. The solubilities concerned are not known.

That the rates of reaction do not bear any simple relation to the dielectric constants of the solvents is not surprising, since different reactions take place. In dimethylaniline the ammonium salt (dimethyl isoamyl phenylammonium bromide) is formed and sodium reacts with it as a positive metal replacing a less positive radical.²

A similar sort of reaction is possible also with the ether solution, but must be a minor reaction, as the formation of the oxonium salt is very slight. This kind of reaction is not possible in benzene solution.

As stated before, Table I does not give all the results. Many attempts were made, especially with ether solutions, to find the cause for the lack of agreement. It was the intention to obtain comparable results, and as far as the appearance of the sodium was concerned, this seemed to be accomplished. Uniform results were not obtained even with improvements in apparatus and technic. An unsuccessful attempt was made

¹ The sodium in these cases seemed more oxidized. Although in the case of (B) 21.2 cc. air was admitted by mistake, it could hardly have caused this deviation. See the later air experiments. The excess of 1.2 cc. in (B) is due to 21 cc. of 0.1 *N* C₈H₁₁Br being used by mistake.

² See E. E. Blaise, *Bull. soc. chim.*, [3] 35, 93 (1906), and Grignard, *Ibid.*, [4] 1, 260 (1907), who found tetraalkyl ammonium iodides did not react with magnesium.

to connect this lack of agreement with the effect of light by noting whether the day was cloudy or clear. This was thought of, since the trials started at any one time agreed, while those of different days did not. It has been stated that no difference in results was detected when 7.5 g. of sodium were used in place of 5 g., hence the comparatively small variation in amount of surface exposed could have had no marked effect.

The reaction resulting in the formation of sodium bromide did not uniformly attack the whole surface of the metal. The blue form of sodium bromide, which was not noticeable until equivalent to about 4 cc. of 0.1 *N* silver nitrate, was present as little blue balls scattered throughout the mass; the rest of the metal was not visibly changed. It was suspected that these particular bits of sodium might have been oxidized to sodium hydroxide, but the experiments with moist air and moist ether described later did not justify this. When a trace of alcohol was added, the blue was uniformly distributed over the whole surface.

The difficulty cannot be due to halogen in the sodium, since several blanks using large weights of substance showed none. What should cause such a result as total reaction in five hours in ether solution (B) in Table I is not known.

In order to find the effect of air and other gases on the rate of reaction, the following experiments were tried, using 0.1 *N* ether solution of isoamylbromide. The results are expressed as cc. of 0.1 *N* silver nitrate required to titrate the sodium bromide formed.

TABLE II.
The effect of enclosed gas.

Time (hours).	Cc. 0.1 <i>N</i> AgNO ₃ .	Enclosed gas.
3	0.95	Hydrogen (as usual).
3	1.0	Air-dried by H ₂ SO ₄ passed through about a minute.
3	1.5	Undried air, same length of time.
3	1.4	Dried carbon dioxide, same length of time.

Although there are small variations here, the differences are not such as were obtained in the regular series. The following data show the variations in the results for three hours—all the data for this length of time with ether solution are given here (expressed as cc. of 0.1 *N* silver nitrate solution).

TABLE III.
The results are arranged in chronological order.

						g. Na.
Solution A.....	3.4					7.5
Solution B.....	1.5	0.9				5.0
Solution C.....	0.4	0.45	2.2	4.2	1.0	5.0
Solution D....	0.6	2.0	0.95			7.5

TABLE IV.
Effect of moisture and alcohol when benzene is solvent.

Wt. of sodium.	Time, (hrs.).	Cc. 0.1 <i>N</i> AgNO ₃ required.	Impurity.
7.5	2	3.7	0.1 cc. alcohol in 1 cc. benzene.
7.5	2	2.7	1 cc. benzene satd. water.
7.5	2	0.7	None.

The sodium used in the first two trials given with Solution C had stood in hydrogen five days dry in powder form.

That the air admitted in quickly withdrawing one stopper and inserting another would not seriously affect the results, is shown by Table II. These data also eliminate the variation in the surface of the sodium as a determining factor in variation of results.

Another factor, moisture, was investigated as follows: 5 g. of sodium with 20 cc. of 0.1 *N* ether solution of isoamylbromide and 0.1 cc. of ether saturated with water after shaking three hours required, after the usual treatment, 1.1 cc. 0.1 *N* silver nitrate for the sodium bromide present. In another case 7.5 g. of sodium with similar solutions except that 1 cc. of wet ether was used and the mixture was shaken two hours, required 1.1 cc. 0.1 *N* silver nitrate. These trials were carried out four months apart with different solutions and different preparations of reagents. They show that moisture has no accelerating effect on the reaction, perhaps a surprising fact, and eliminate the presence of the sodium hydroxide as the disturbing agent.

When benzene was the solvent, moisture increased the speed of reaction. 7.5 g. of sodium were shaken for two hours with 20 cc. of 0.1 *N* benzene solution of C₅H₁₁Br plus 1 cc. of benzene saturated with water and sodium bromide equivalent to 2.7 cc. 0.1 *N* AgNO₃ was formed. This is a greater value than any with dry benzene.

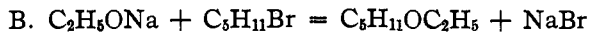
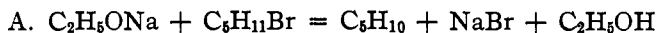
The influence of small amounts of other impurities on the speed of reaction (as indicated by the sodium bromide) was studied. The experiments are given with the blank run at the same time for the reason, previously stated, that trials made at the same time usually gave concordant results. In the following table the weight of sodium given was shaken with 20 cc. of 0.1 *N* ether solution of isoamylbromide plus 0.1 cc. of ether containing the amount of impurity stated. The sodium bromide formed required the volume of 0.1 *N* AgNO₃ solution given.

Part A of the table shows that the impurities there introduced have no marked effect in the three hours which the reaction is allowed to go. That the reaction is slower is noticeable in Part B. The impurities used in C have also no decided influence. Alcohol and acetone in Part D cause the reactions to go to completion in three hours. This is not unexpected, but these experiments show very clearly the importance of freeing the ether from the last traces of alcohol for uses of this kind.

0.01 cc. of alcohol corresponds to 0.05% alcohol in the ether, and with this purity the reaction goes 85% in two hours and 100% in three hours. With pure ether the reaction has gone about 5% in two and 10% in three hours.

The acceleration caused by alcohol is, of course, due to the fact that different reactions are taking place. Sodium with alcohol forms sodium ethylate, which reacts with the alkyl bromide. The sum of reactions involving sodium ethylate as well as metallic sodium is being measured.

The following additional reactions then take place:



Reaction A is much faster than that of sodium on the alkyl haloid. The data in Table V do not indicate how much faster Reaction A is, for the total amount of alcohol is less than one-tenth of a molecule compared to the alkyl bromide, and yet although both Reactions A and B are taking place, only A regenerates alcohol to form more sodium ethylate and react with more alkyl bromide, thus finally yielding sodium bromide equivalent to all of the isoamylbromide present. In the ether filtrate from the sodium and sodium bromide, when 0.01 cc. of alcohol had been added before the reaction, unsaturation was detected by the disappearance of bromine color, while the color in the blank remained. In another case where no alcohol had been used, unsaturation was not detected.

The effect of alcohol when benzene was the solvent was tested. 7.5 g. of sodium powder were shaken with 20 cc. of 0.1 *N* benzene solution of isoamylbromide and the impurity stated.

TABLE V.
The effect of some impurities.

Grams of sodium.	Time in hours.	Cc. 0.1 <i>N</i> AgNO ₃ required.	Impurity.	Grams of sodium.	Time in hours.	Cc. 0.1 <i>N</i> AgNO ₃ required.	Impurity.
Series A:				Series D:			
5	3	3.6	0.01 cc. benzene (dry)	5	3	22.2	0.01 cc. abs. alcohol
5	3	3.3	0.01 cc. xylene (dry)	5	3	22.3	0.01 cc. anhyd. acetone
5	3	4.0	0.05 cc. pentane	5	3	4.4	0.01 cc. ethyl acetate, dry, alcohol free
5	3	4.2	Blank	5	3	2.2	Blank
Series B:				Series E:			
5	10	0.95	0.01 cc. benzene (dry)	7.5	2	21.0	1 cc. ether contg. 0.1 cc. abs. alcohol
5	10	2.25	Blank	7.5	2	16.8	0.1 cc. ether contg. 0.01 cc. abs. alcohol
Series C:							
5	3	1.05	0.1 cc. ether satd. water				
5	3	0.85	0.01 cc. acetoacetic ester				
5	3	1.16	0.01 cc. malonic ester				
5	3	1.0	Blank				

These results, when compared with those obtained in using an ether solution, show clearly that the sodium ethylate reactions with the alkyl haloid also go much slower in benzene solution.

Summary.

1. An attempt has been made to measure the rate of reaction of metallic sodium in powder form with isoamylbromide dissolved in ether, in dimethylaniline and in benzene.
2. The rate in ether was faster than in benzene, while in dimethylaniline the rate was much greater than in either of the other two.
3. This can be explained by the formation of ammonium and oxonium (very slight) salts and by the sodium replacing the less positive organic basic radical in the salt. It cannot be explained if dissociation of the alkyl haloid alone is used and if the dissociating power of a solvent is proportional to its dielectric constant.
4. Chemically this result would be expected, as the dimethylaniline would certainly add the haloid and the ether would tend to do so, while benzene would not.
5. The effect of some impurities on the rate of reaction has been shown. That of alcohol and acetone is enormous.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA.]

THE DETERMINATION OF ACETONE IN SYSTEMS OF METHYL ALCOHOL, WATER AND POTASSIUM FLUORIDE, AND EQUILIBRIA IN SYSTEMS OF METHYL ETHYL KETONE, WATER AND INORGANIC SALTS.

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In the study of the equilibria in the systems water, acetone and inorganic salts, it was found that the amount of acetone present in an aqueous solution can be determined. It was also found that methyl alcohol cannot be salted out of an aqueous solution by means of potassium fluoride. It was thought that acetone could be then accurately determined in the presence of methyl alcohol. When the methyl alcohol did not exceed 5%, its function was found to be the same as water, and from a study of the binodal curve, the amount of acetone in a solution could be determined. It was found, however, that when larger amounts of methyl alcohol were used the alcohol did not act the same as the water, and loci of points found by experiment did not fall on the binodal curve. A more or less comprehensive study of the effect of the alcohol was then made. Solutions containing from 5-95% methyl alcohol in water were made up and the salting out effect of potassium fluoride was again tried. The