

Ethylation By Means Of Diethyl Sulphate

A Thesis Submitted in Partial Fulfillment of the
Requirements for the Degree of Bachelor of Science
in Chemistry by Robert V. Cole.

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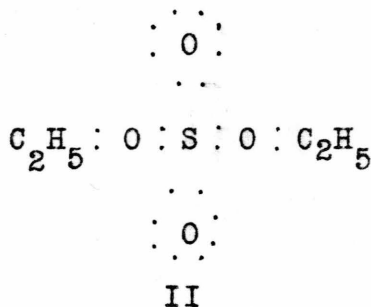
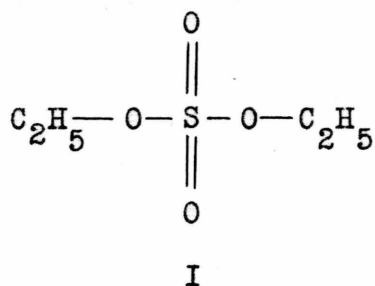
Ethylation By Means Of Diethyl Sulphate

Purpose- It appears from the literature that not a great deal of extensive work has been done on the ethylation of various compounds by means of diethyl sulphate. As a result, it was concluded that not only some very interesting, but also some very advantageous work could be performed along this line. Several types of purely organic compounds possessing the ability of being ethylated were taken, and by varying conditions of the reaction such as time, temperature, amount of water present, amount of sodium hydroxide added, etc., the yields of the resulting products under each different condition were observed and tabulated. The different types of compounds were phenols, acids, and aromatic amines.

Theoretical Considerations

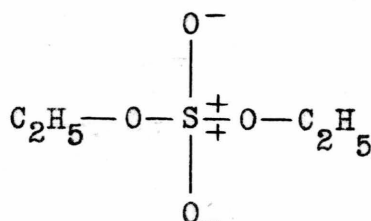
Diethyl Sulphate, $(C_2H_5)_2SO_4$, commonly known as ethyl sulphate, is a colorless, oily liquid of an agreeable peppermint like color, insoluble in water and solidifying on exposure to a low temperature, around $-24.5^\circ C$. This liquid is entirely neutral in its reaction.

The chemical structural formula for diethyl sulphate, where sulphur has a valence of six, according to the classical valence theory may be represented by the following formula I.

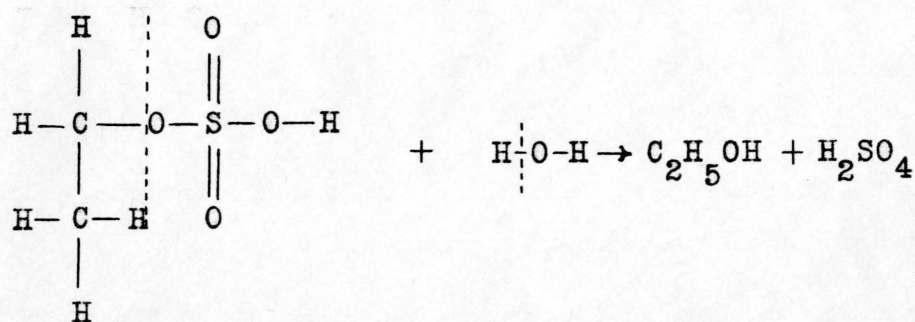
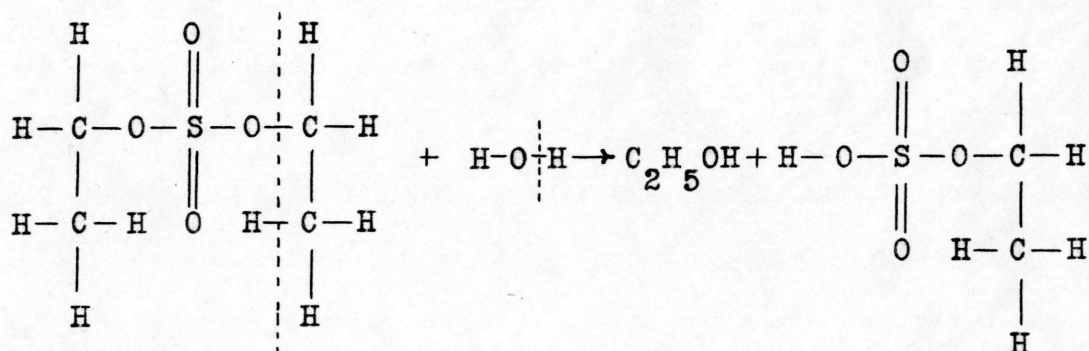


According to the new valence theory this compound may be represented by the formula II, in which the sulphur is attached to each oxygen atom by one electron pair and, therefore, has a valence of four. Of course, this is a direct contradiction of the above classical theory, but this is removed by making use of the concept of the semi-polar double bonds and writing the bonds between sulphur

and the single oxygen atoms as $\bar{O}-^+S$. This gives sulphur two electrovalences in addition so that its total valence is six as shown below.



n At temperatures around $96^\circ C$ and 15mm pressure diethyl sulphate boils without decomposition and also at temperatures around $120^\circ C$ and 45mm pressure. However, at temperatures above $150^\circ C$ it begins to decompose and boils at $208^\circ C$ with vigorous decomposition. Also it hydrolyzes in warm water and in boiling water eventually breaks up into two molecules of ethyl alcohol and one of sulphuric acid. This may be said to take place in two definite steps- the first of which forms a molecule each of ethyl alcohol and ethyl sulphuric acid, while the second results in the formation of one molecule of ethyl alcohol and one molecule of sulphuric acid. The two step reaction may be represented by the following structural equation:



There is still another reaction which occurs simultaneously with the above. It is the formation of ethyl ether and sulphuric acid from the reaction between the ethyl alcohol and the ethyl sulphuric acid in the neighborhood of the 155° C. This reaction does not proceed as readily as the one above, but it is at times used in the preparation of ethyl ether. Usually there appears a trace of ether during the ethylation with the diethyl sulphate and this reaction is responsible for its appearance.

In case water is absent decomposition occurs

above 150° C., as mentioned previously, with the formation eventually of two molecules of ethylene and one of sulphuric acid in much the same mechanism as with water, only of course in place of the ethyl alcohol ethylene is formed. If heat is applied for a sufficient length of time the sulphuric acid decomposes into SO₃.

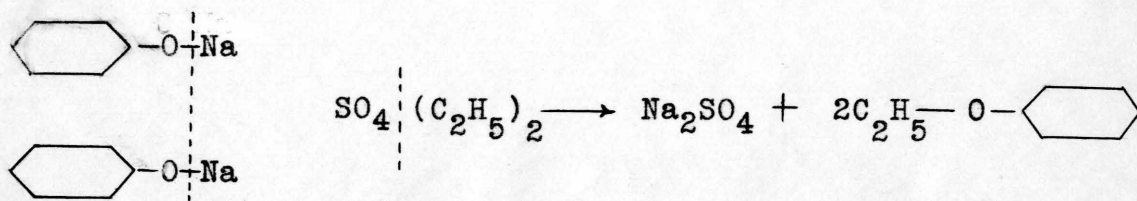
Its Preparation

Diethyl Sulphate is prepared in the laboratory by heating ethyl alcohol with fuming sulphuric acid at a temperature around 100° C. However, this method is not used in industry due to the cost and the lack of purity. The best method for its production is that patented by H.R.Crume. It consists of passing pure ethylene into commercial sulphuric acid (66° Be), a continuous cycle being established and producing directly diethyl sulphate of high purity.

Its Ethylating Ability

Diethyl Sulphate appears to be a fairly recent newcomer to the field of ethylation. As can be seen by the chemical formula, (C₂H₅)₂SO₄, there are available two ethyl groups. By means of diethyl sulphate metal alkoxides can be ethylated to form ethers, salts of organic acids can be ethylated to form esters, amines can be ethylated to form

primary and secondary ethyl amines. In the ethylation of hydroxy compounds, as for example, phenol, with diethyl sulphate the reaction is nothing more than a Williamson synthesis where, in this case, the phenoxide salt is made to react with the diethyl sulphate instead of an ethyl halide, the usual reactant. It may be represented by the following:

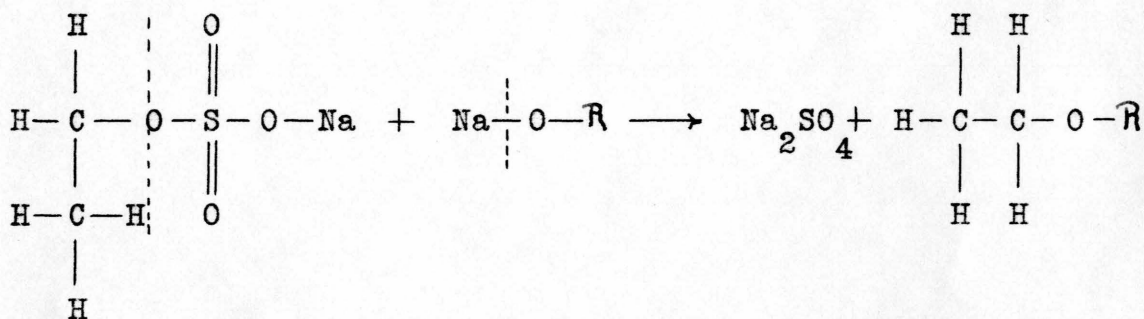
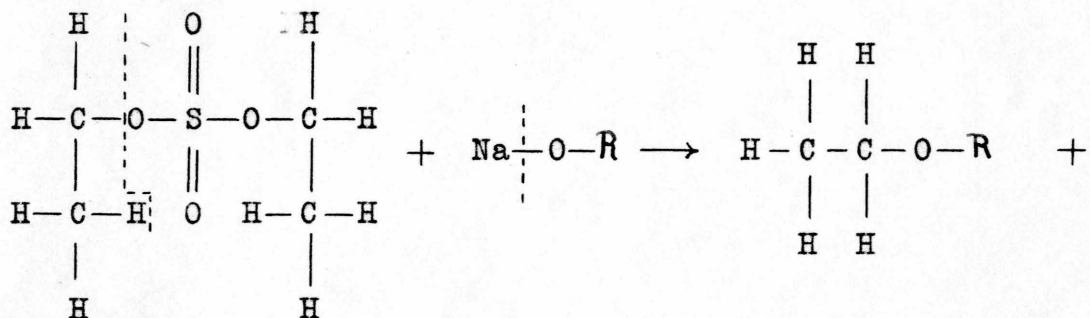


General Williamson synthesis with ethyl iodide



Theoretically, it can be seen that in the case of the diethyl sulphate there are two ethyl groups available in the reaction. Actually, it is possible to get only part of the second ethyl groups to react. This ethylation according to all indications proceeds in two distinct steps. First, the diethyl sulphate loses one ethyl group resulting in the formation of one molecule of the ether and one molecule of sodium ethyl sulphate. As the reaction progresses the remaining ethyl group in the sodium

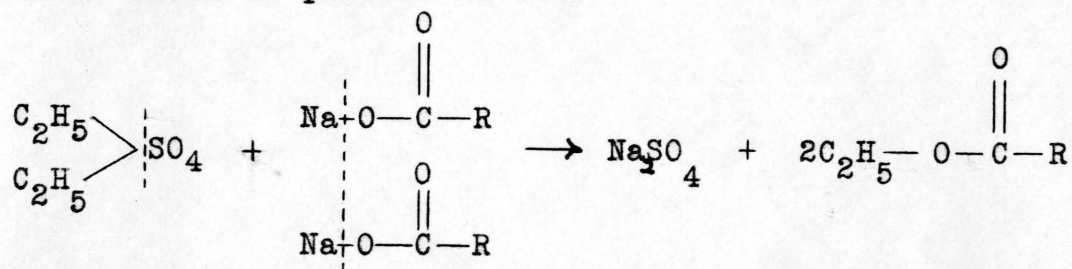
ethyl sulphate reacts. The following equation will serve to illustrate the complete reaction:



It was stated above that it was possible to get only part of the second ethyl groups to react. This is due partly, no doubt, to the fact that sodium ethyl sulphate is not nearly so reactive as the diethyl sulphate.

Carboxylic acids or preferably their alkali salts alkylate to form their respective ethyl esters by means of diethyl sulphate. It reacts with these acids in much the same way as it does with phenols, that is, a two-step reaction ensues in which, first, a molecule each of the ester and sodium ethyl sulphate is formed, and second,

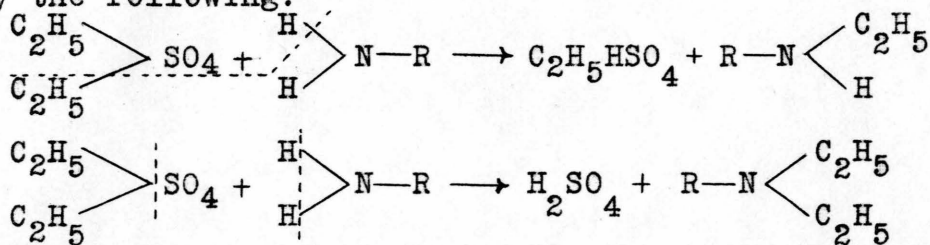
another molecule of the ester is formed and a molecule of sodium sulphate. Generally, in one step the reaction can be shown to proceed as this:



In case the carboxylic acid is used sulphuric acid is formed instead of the sodium sulphate. The sodium salt of the acid generally gives superior results. Two factors which affect the yield immensely are the amount of water and alkali present during the reaction. Of course, these two when present in excess will cause saponification of the ester and thus lower the yield considerably, so it is very important to limit their presence.

Theoretically, it appears that the ethylation of amines should be a stright-run process by which the hydrogens on the nitrogen groups are replaced by ethyl groups, and this action actually takes place. Either one of the hydrogens or both may be replaced by an ethyl group. In the former case, obviously, the product formed is a monoethyl amine, while in the latter case it is a diethyl amine. Graphically the reaction may be represented

by the following:



Along with the formation of the monoethyl amine some of the diethyl amine forms, and vice-versa. Since both boil within a few degrees of each other it is rather difficult and probably impossible to separate one from the other by distillation. Therefore, some other method had to be devised for this separation, and it was the Hinsberg reaction. In this reaction the solution is made alkaline, and to it is added benzene sulphonyl chloride, $\text{C}_6\text{H}_5\cdot\text{SO}_2\text{Cl}$, which forms the solid benzene sulphonyl derivative of any primary and secondary amine which may be present, but reacts in no way with the tertiary amine. Therefore, the solid secondary and primary amine may be filtered off from the tertiary amine. Since the sodium salt of primary amines is soluble in water, then, by the addition of sodium hydroxide and water primary and secondary amines can be separated from each other. The secondary amines, then, can be regenerated by boiling with alkali and one has accomplished the complete separation of the three amines, primary, secondary, and tertiary.

Primary amines appear to be very easily ethylated and as a result the reaction with ethyl sulphate can proceed unaided, that is, without the application of heat. In fact, at times it is necessary to control the temperature because of the high heat of reaction. With higher temperatures the diethyl amine is formed.

Experimental Work

The primary purpose of the experimental work was to ethylate certain specific types of compounds mentioned previously as phenols, carboxylic acids, and amines, and by varying conditions of the experiment observe the reactions and the yields obtained. Of the phenols phenol was taken; of the carboxylic acids benzoic and salicylic acid were taken; and of the amines aniline was taken. It was assumed that the method which gave the superior yields for one of these simpler compounds of its type would also give the superior yield for a more complex compound of the same type. Therefore, it was found advisable to take the simpler compounds of each of the three types. The various conditions of the experiment and the percentage yield have been arranged in table form.

Ethylation of Phenols

For phenol- the data is as follows:

Time of Heating	Amount of $(C_2H_5)_2SO_4$	Amount of Phenol	Water	NaOH	Percentage Yield
1 hr. @ 100°C	.3M	.3M	20.8M	.95M	60.0%
1 hr. @ 150°C	.18M	.3M	20.8M	.95M	41.1%
1 hr. @ 150°C	.18M	.3M	5.0M	.95M	59.3%
1 hr. @ 150°C	.18M	.3M	1.0M	.95M	69.4%
5 hr. @ 150°C	.18M	.3M	1.0M	.95M	75.8%
5 hr. @ 150°C	.18M	.3M	0.0M	.5M	79.2%
5 hr. @ 150°C	.18M	Na Phenoxide .3M	Enough to dis- solve it	.15M	81.1%

The general method by which the phenetole was prepared in the experiment was as follows: to the phenol was added a given amount of sodium hydroxide dissolved in the specific amount of water. The mixture was then raised to a temperature of 110°C., and to it was added the specific amount of the ethyl sulphate, very slowly from a dropping funnel. The mixture was then refluxed for the given time at 150°C., being stirred continuously by a mechanical stirrer. At the end of this time the phenetole was extracted with ether. This ethereal solution was dried by the addition of anhydrous sodium sulphate and fractionally distilled. That fraction which came over between 168°C. and 173°C was kept as the phenetole. The excess diethyl sulphate was a bit troublesome and, therefore, had to be extirpated. This was accomplished by adding sodium carbonate to the

first mixture and refluxing for one-half hour at 190°C.

The first method was adapted from "Organic Compounds" by Coghill and Sturtevant who stated that the yield should be nearly quantitative. Certainly, my results were far from being quantitative, and I took particular care to follow out their instructions exactly, even to the extent of duplicating the experiment. As can be seen by the other methods three important factors seemed to be responsible for the relatively low results. They are: too much water was added, temperature not high enough, and heat not applied long enough. One can see from the data that the less water used the better were the results even to the extent of eliminating it. This was the case with method VI in which no water was used at all, and the sodium hydroxide in a crushed form was added to the liquid phenol. A temperature of 150°C. applied for five hours is also necessary for good results. The last method was that of using sodium phenoxide instead of phenol plus sodium hydroxide. This also improved the results which no doubt was due to better contact between the reactants as mentioned in the theory.

Since diethyl sulphate has available two ethyl groups it was only necessary to use a little more than half

the molar quantity of ethyl sulphate as phenol. The slight excess was present in order to take care of that ethyl sulphate which might have decomposed.

The best general method, then, for the preparation of ethyl aromatic ethers from their phenols would be as follows: the sodium salt of the phenol should be dissolved in as little water as possible and, then, to this mixture heated up to 110°C . should be added slowly a little more than half the molar quantity of ethyl sulphate as of the sodium salt. This mixture should be refluxed at 150°C for five hours. From time to time small amounts of sodium hydroxide should be added in order to keep the solution alkaline at all times. At the end of five hours the mixture should be made very alkaline and its temperature raised to 190°C . and kept there for a half hour in order to destroy the excess ethyl sulphate. The product then should be extracted with ether and fractionally distilled or crystallized depending whether it is a solid or a liquid at normal temperatures. Vacuum distillation is preferable for high boiling liquids.

Ethylation of Benzoic Acid

The data obtained for the ethylation of benzoic

acid is as follows:

Time of Heating	Amount of $(C_2H_5)_2SO_4$	Benzoic Acid	Water	NaOH	Percentage Yield
2 hr. @ 145°C	.5M	5	.3M	.6M	50.8%
2 hr. @ 145°C	.25M	5	.3M	.6M	30.3%
4 hr. @ 145°C	.25M	5	.3M	.6M	37.3%
4 hr. @ 145°C	.25M	5	.1M	.6M	54.4%
4 hr. @ 145°C	.25M	Na Benzoate	Enough to dissolve it	.2M	60.1%
4 hr. @ 145°C	.25M	Na Benzoate	Enough to dissolve it	Kept slightly alkaline	58.0%

The general method for the preparation of ethyl benzoate by diethyl sulphate is the same as that used for the preparation of phenetole except, of course, benzoic acid was used instead of phenol. The variation in the results obtained by the addition of various amounts of water and sodium hydroxide and time of heating were very much the same as obtained with phenol. However, it was more necessary to limit the water and sodium hydroxide content due to the saponification of the ester. It will be noted in the table the great improvement in the yield when the water added was decreased by two mols, an increase of about 14% and also an increase of 8% when the addition of sodium hydroxide was limited to the extent of keeping the solution slightly alkaline at all times in order to neutralize the acid which

is formed during the reaction. Too, it will be seen that the yield is also increased by using the sodium salt of the acid as was the case with phenol. That fraction which distilled over between 209°C and 213°C was taken as the product.

Then, from the information obtained from the above experimental data it was found that the best method of ethylating a carboxylic acid would be as follows: to the sodium salt of the acid should be added just enough water to entirely dissolve it. With the temperature of the mixture at 100°C the diethyl sulphate should be slowly added, the quantity of which is a little more than one-half the molar quantity of the sodium salt. Then, the temperature should be raised to 150°C and kept at that point for four hours. During this time the solution ought to be kept alkaline by small additions of sodium carbonate from time to time. Also it is advantageous to keep the mixture thoroughly stirred during the reaction by means of some mechanical stirrer. After the four hour period the ester is extracted by ether and the solution dried by the addition of a small amount of sodium sulphate. Then, the solution is fractionally distilled or crystalized depending whether the product is

liquid or solid at normal temperatures.

Following is the data obtained from the ethylation of salicylic acid. Since the results of this ethylation correspond generally to those of benzoic acid they will not be discussed.

Time of Heating	Amount of $(C_2H_5)_2SO_4$	Salicylic Acid Amount of Na Salicylate	Water	NaOH	Percentage Yield
2 hrs. $145^\circ C$.13M	.13M	.3M	.2M	52.7%
2 hrs. "	.7M	.13M	.3M	.2M	40.0%
4 hrs. "	.7M	.13M	.3M	.2M	47.2%
4 hrs. "	.7M	.13M	Enough to dissolve it	.2M v	59.3%
4 hrs. "	.7M	.13M	Enough to dissolve it	Solution kept slightly alkaline	67.43%

Ethylation of Amines

In the ethylation of a primary amine, as mentioned in the previous section, either it can be monoethylated or diethylated forming, respectively, a secondary or tertiary amine. Which takes place depends primarily on the existing temperature during the reactions. It appears from the following data the ideal temperature for the formation of the ethyl amine is at $75^\circ C$. However, it seems that above that temperature the diethyl amine commences to form and thereby

reduces the ethyl amine yield. The data for the formation of ethyl aniline from aniline is as follows:

Time Heated	Amount of (C ₂ H ₅) ₂ SO ₄	Amount of Aniline	Temperature	Percentage Yield
To completion of reaction-	.5M	.5M	100°C	60.0%
25 minutes	.28M	.5M	100°C	35.0%
1 hr.	.5M	.5M	100°C	67.3%
2 hrs.	.5M	.5M	100°C	68.0%
1 hr.	.5M	.5M	75°C	77.5%
1 hr.	.5M	.5M	60°C	74.9%
1 hr.	.5M	.5M	90°C	72.1%
1 hr.	.5M	.5M	75°C	83.2%

In the last method one-half mol of Na₂CO₃ was used to neutralize the acid formed.

Time and temperature appear to be of first importance in this ethylation. Though the reaction is completed in about 25 minutes, as can be seen from the data, if the heating is continued for over an hour, not necessarily over, the yield is increased by about 7%. Also the temperature of 75°C, and not over, is necessary for the optimum yield. It appears that the solution should be alkaline at all times, since by the addition of one-half mol of Na₂CO₃, the yield was increased by 6%. At this point it may be added that the heat of the reaction is such in this experiment that no heat need be applied, in fact, at times the vessel must be cooled in order to maintain the correct temperature. Continuous stirring of the mixture through-

out the experiment is deemed as advisable.

As mentioned in the previous section, along with the formation of the ethyl aniline some diethyl aniline might also be produced. Since they both distill within a few degrees of each other it would be practically impossible to separate them by that means. Therefore, the Hinsberg reaction was resorted to, which was described thoroughly in the theory.

A method has been prepared for the preparation of ethyl amines which takes into consideration the conditions under which the best yields of ethyl aniline were obtained. It is as follows: to a certain amount of the primary amine is added very slowly from a dropping funnel an equimolar quantity of diethyl sulphate. The mixture is stirred constantly, preferably by an electric stirrer, and its temperature maintained very carefully between 65°C to 75°C . At times, it may be necessary to place the vessel in a cold water bath to do so, since the heat of reaction is very high. After the vigorous reaction is completed application of heat is necessary and the mixture should still be kept at the temperature indicated above for one hour. The cooled mixture is then made alkaline with sodium hydroxide solution which causes the ethyl aniline to separate to the top.

To this top layer is added an excess of sodium hydroxide and the solution is refluxed for a half hour at 100°C. This procedure destroys the excess diethyl sulphate. In order to separate any diethyl aniline, which may have formed during the reaction from the ethyl aniline, the Hinsberg reaction is applied by the addition of a small amount of benzene sulphonyl chloride. The solid material is then filtered off from the liquid, and placed in a vessel to which an excess of alkali has been added. This mixture is then boiled for fifteen minutes in order to regenerate the amine which is ^{then} extracted with ether. Fractional distillation or crystallization, depending on whether the product is liquid or solid, is resorted to in order to obtain the ethyl amine.

Diethylation of Aniline

The procedure for the diethylation of aniline is much the same as its monoethylation except the temperature is a good bit higher, at 150°C, and also the time of heating, which is in the vicinity of two hours. Following is the table of data on the diethylation of aniline:

Time of Heating	Amount of $(C_2H_5)_2SO_4$	Amount of Aniline	Temperature	Percentage Yield
1 hr.	.25M	.5M	75°C, then 115°C	40.0%
1 hr.	.25M	.5M	75°C, then 150°C	50.3%
1 hr.	.5M	.5M	75°C, then 150°C	73.1%
2 hr.	.5M	.5M	75°C, then 150°C	79.5%
3 hr.	.5M	.5M	75°C, then 150°C	80.6%
2 hr.	.5M	.5M	75°C, then 150°C	85.3%

In the last reaction one-half mol of Na_2CO_3 was added in order to neutralize the acid.

The conditions under which diethylation of aniline gives the best yield are the same as for the ethylation of aniline, as might be expected. As mentioned before, the temperature is a bit higher and time of heating a bit longer.

The best general method for the diethylation of amines is the same as that for the ethylation of amines with a few exceptions. In the first place, after the vigorous reaction has begun to subside the temperature is raised to 145°C and kept there for a two hour period. Then, in the separation of the diethyl amine from any small amount of ethyl amine which may be present the Hinsberg reaction is also used. However, instead of keeping the solid form the liquid form is kept, since it is in the form of a tertiary amine it remained unchanged despite the addition of the benzene sulphonyl chloride. Therefore, it need not be

regenerated . These are the only differences between the monoethylation and diethylation of amines.

Summary:

It is seen from the results of the experiments that there are four important factors which have a tremendous influence upon the yields of each product obtained from the ethylation. These four are: the amount of sodium hydroxide and water present during the reaction, and also the time and amount of heat applied. The amount of water and sodium hydroxide present appear to have the greatest affect upon the results, especially upon the ethylation of acids where the ethyl ester is formed, and saponification is very likely to occur. In the ethylation of phenols and carboxylic acids the best yields are obtained when their sodium compounds are dissolved in as little water as possible, the mixture kept slightly alkaline at all times, and refluxed at 150°C for a period of four hours with the diethyl sulphate. The yields obtained are about 80% of the theoretical, which might be considered as fairly good. When it comes to ethylating aromatic amines one is struck with the ease in which monoethylation takes place. All that it is necessary to do is to slowly

add the diethyl sulphate to the amine mixture maintaining the temperature between 65°C to 75°C . This latter specification is quite important since if not adhered to strictly it will result in the formation of some diethyl amine above this temperature, thus lowering the yield of the ethyl amine. This brings up the question of the diethylation of an amine. Good yields are obtained when the amine is refluxed with the diethyl sulphate at a temperature of 150°C for four hours.

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