

## A New Aldehyde Synthesis

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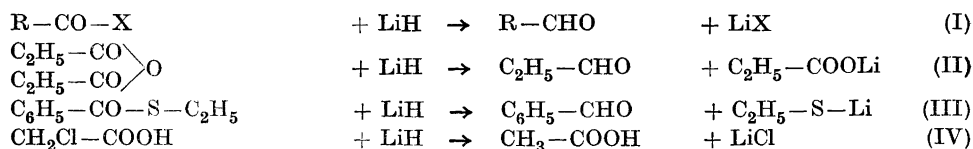
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Pure metal hydrides have hitherto not been used as reducing agents, but a mixed hydride, *i. e.* lithium aluminium hydride <sup>1,2</sup> has been used for the preparation of alcohols from organic acid halides with good results. Reduction is obtained at room temperature, and the yields are good, about 80—90 %.

The purpose of this paper is to examine whether it is possible to use metal hydrides for the preparation of aldehydes from organic acid halides, acid anhydrides or thioesters. This method of preparation will be of special interest in the preparation of unsaturated aldehydes, otherwise so difficult to obtain, as the metal hydrides, in all probability, will not react with the double bond, since lithium aluminium hydride, which is a much stronger reducing agent than the pure hydrides, usually has no effect on the double bond.

The purpose was to examine the reaction with hydrides of lithium, sodium and calcium. It has been shown that only lithium hydride gives good results.

The reaction between acid halides or the other substances used and lithium hydride takes place as follows:



where R is an organic radical (aliphatic or aromatic) and X a chlorine or bromine atom.

As lithium hydride cannot be dissolved in any medium, the reaction is necessarily heterogeneous. The reduction is carried out as follows:

A few hundred milligrams of the organic substance which is to be reduced is mixed in a 50 ml flask with about half a gram of lithium hydride and

10 ml benzene, toluene or xylene. The mixture is refluxed for some hours, and, after cooling to room temperature, is transferred to a 50 ml bottle through a filter. The best method for the determination of the aldehyde formed was found to be precipitation with methone. To the aldehyde solution in the bottle, 10 ml water, 4 ml of a 10 % sodium chloride solution, and 3 ml of a 5 % alcoholic methone solution is added. The bottle is now vigorously shaken for 12 hours, whereafter the content is poured quantitatively into a small beaker. This beaker is now left at a temperature of 30—40° C until the organic medium has completely volatilized. After filtering, the methone precipitate is washed with a small volume of 50 % alcohol and dried for four hours in a vacuum desiccator over calcium chloride, and is then weighed.

A number of experiments have been carried out with the chlorides, bromides, anhydrides and thiolesters of propionic and benzoic acid as typical examples of respectively aliphatic and aromatic substances.

The yield of aliphatic aldehydes by this method is not good when using acid halides (about 20—25 %). Much better yields are obtained, however, by using the corresponding thiolesters (about 70 %). When using aromatic substances, good yields are obtained by direct use of acid halides (about 55 %).

As to the estimation of the aldehyde formed it can be mentioned that the error is less than 1 %.

## EXPERIMENTAL

### Preparation of lithium hydride

As lithium hydride was not commercially available, it was necessary to prepare it. Sodium reagents of sodium and calcium hydride were used.

The preparation of lithium hydride is a difficult task, as the reaction between lithium and hydrogen is very vigorous and difficult to control. The hydride is obtained by passing a hydrogen current over molten lithium in a nickel boat placed in a steel tube, which, in turn, is placed inside a combustion tube of fused quartz. The pressure must not be more than 550 mm Hg, as it is otherwise impossible to control the reaction. On the other hand, the pressure must not be less than 450 mm Hg, as the metallic lithium tends to volatilize and spread into the whole tube. The temperature must also be kept under control, as the reaction starts very suddenly at about 520—530° C. The preparation of lithium hydride has been previously described by Bode<sup>3</sup>, but when carried out as mentioned in the present paper lithium hydride is obtained as a fine powder, very pure, and in a yield of about 95 %.

### Determination of aldehydes in hydrophobic solvents

The quantity of aldehyde formed in the hydrophobic medium was very difficult to determine.

First the determination of the aldehyde by titration with a sodium bisulphite solution was tried, but this method was inadequate, as the error was about  $\pm 10$  %.

The method of allowing the aldehyde formed to react with 'Girard's reagent' *i. e.* a betaine hydrazone solution<sup>4</sup> was tried. The hydrazone formed is very soluble in water, but insoluble in benzene etc., and therefore dissolves quantitatively in the aqueous phase by shaking. The latter is separated, and a solution of bismuth iodide or mercuric iodide in potassium iodide is added, whereby a complex — insoluble in water — is formed by interaction between a betaine hydrazone ion and a  $\text{BiI}_4^-$  ion or a  $\text{HgI}_3^-$  ion. The complex can be weighed directly without recrystallization.

It was shown that when using propionic aldehyde no precipitation with mercuric iodide takes place, whereas addition of potassium bismuth iodide yields a precipitate. On the other hand, mercuric as well as bismuth complex solutions gives a precipitate with benzaldehyde. The estimations were not satisfactory. The amount of aldehyde present could only be determined with an error of  $\pm 10\%$ .

The method previously mentioned, depending on the interaction between methone (5,5-dimethyl-dihydro-resorcinol) and aldehydes<sup>5-7</sup>, has been investigated. The first to investigate this method was Vorländer<sup>5</sup>, and it has turned out that it is possible to modify the method so that the error in the estimation of aldehyde is less than 1 %.

Procedure: To 5 ml of the aldehyde solution was added 5 ml of a 10 % sodium chloride solution, 10 ml of water, and 3 ml of a 5 % alcoholic methone solution. (Sodium chloride, according to Vorländer, facilitates the crystallization of the methone aldehyde complex.) The mixture was shaken for 12 hours, and then transferred to a small beaker. The organic solvent volatilizes when the beaker is heated to not more than 40° C. After cooling to room temperature the solution was filtered through an immersion filter tube. The precipitate was washed with 50 % alcohol and was dried over calcium chloride in a vacuum desiccator. The solid residue could now be weighed directly. Recrystallization did not change the m. p.

This method always yields low results, but there is a constant deviation from the true value. More than 100 analyses, with varying quantities of aldehyde (propionic and benzaldehyde) and various organic solvents (benzene, toluene or xylene) in all cases, gave results 11–12 % too low. This method is the best available to determine the quantity of aldehyde, if the found value is increased by 12 %.

In order to find out why the results are low, some experiments were carried out in which the organic liquids were volatilized at various temperatures from a mixture containing a known quantity of the pure substance formed by interaction of methone and propionic aldehyde. It was found, that if the temperature was higher than 50° C, a considerable amount of the substance disappeared together with the vapour. At room temperature, the volatilization of the solvent was extremely slow, even after a week, only half of it had vaporized. At temperatures between 30–40° C, the volatilization took place fairly quickly, and there was no detectable loss of the substance.

A probable reason for the low results might be that the aldehyde methone substance is not quantitatively formed by the interaction between the methone and the aldehyde.

### Reaction with hydrides

An attempt was made, at first, to allow lithium hydride to act on propionyl chloride (prepared from propionic acid and silicontetrachloride<sup>12</sup>) in ether. The mixture was shaken for 24 hours at room temperature. As no detectable quantity of aldehyde was formed, the experiment was repeated, with vigorous shaking for 72 hours. No positive

result was obtained in this way either, so heating the mixture for several hours in a waterbath was tried, still without obtaining positive results.

The reaction temperature was now increased by using benzene, toluene or xylene instead of ether, and considerable quantities of aldehyde were formed. The yields after boiling 20 hours, when using benzene as solvent, were 13 %, toluene, 23 %, and xylene, 2 %.

It was evident that a reaction really had taken place between the lithium hydride and the propionyl chloride according to equation I, and now the entire question was to find the best conditions for the reaction.

A number of experiments were now made to find the best reaction conditions. In most cases 0.3 g of the organic substance, 0.5 g hydride, and 10 ml of the medium were used. Some experiments were carried out with a somewhat larger quantity, *i. e.* 0.75 g of the organic substance, 1.0 g hydride, and 20 ml of the solvent.

It was necessary to distill the acyl bromides immediately before the experiments, as otherwise an oil was formed at a later stage in the procedure. The organic solvents (benzene, toluene and xylene) were distilled over metallic sodium.

#### DISCUSSION

In Tables 1, 2, and 3 are given the experimental results. It can be seen from the tables that the experiments with sodium and calcium hydride in no cases yield good results, while lithium hydride in several cases yields remarkably good results. Better results cannot be obtained by using larger amounts of the reactants.

In Table 1 the experiments with lithium hydride, acyl halides, anhydrides and thioesters are shown.

The best results from both propionyl chloride and bromide are obtained under the same conditions, namely by the use of toluene and allowing the mixture to boil for 20 hours.

The boiling time of the mixture has of course a certain effect, but not as much as would be expected. In a few experiments, where the mixture was boiled for more than 20 hours, it was impossible to determine the aldehyde formed, because during the very prolonged boiling a decomposition took place, which prevented the methone precipitate from crystallizing. At the same time the mixture became very dark.

As expected when using benzoyl chloride, a higher reaction temperature gives higher yields. When using benzene or toluene, a prolongation of the time of reaction gives a higher yield. On the other hand, when using xylene as medium, the yield is not increased. It seems as if this method is especially useful for the preparation of aromatic aldehydes, as the boiling points of the corresponding acyl halides are so high that the reaction temperature can be increased so much that the reaction can be completed in the course of a few hours with a yield of about 55 %.

Table 1. Reaction between lithium hydride and different organic substances.

Amount of organic substance (b. p.)			Medium	Hours of boiling	Yield
0.30 g	Propionyl chloride	80° C	Benzene	4	0.5 %
0.75 »	»	»	»	20	13 »
» »	»	»	Toluene	4	13 »
0.30 »	»	»	»	4	17 »
» »	»	»	»	20	18 »
0.75 »	»	»	»	20	24 »
0.30 »	»	»	Xylene	4	1.7 »
» »	»	»	»	4	2.2 »
» »	Propionyl bromide	104° C	Benzene	4	0.5 »
» »	»	»	»	20	0.9 »
» »	»	»	Toluene	4	12 »
» »	»	»	»	20	24 »
0.75 »	»	»	»	20	26 »
0.30 »	»	»	Xylene	4	2.7 »
» »	»	»	»	20	3.7 »
» »	Benzoyl chloride	197° C	Benzene	4	1.0 »
» »	»	»	»	20	10.5 »
» »	»	»	Toluene	4	4.2 »
» »	»	»	»	20	26 »
0.75 »	»	»	»	20	32 »
0.30 »	»	»	Xylene	2	59 »
0.75 »	»	»	»	4	47 »
0.30 »	»	»	»	5	57 »
0.75 »	»	»	»	20	56 »
0.30 »	»	»	»	20	52 »
» »	Propionic anhydride	196° C	Benzene	4	1.5 »
» »	»	»	Toluene	4	3.8 »
» »	»	»	»	20	3.3 »
» »	»	»	Xylene	4	4.4 »
» »	»	»	»	20	4.9 »
0.75 »	»	»	»	4	5.1 »
0.30 »	Ethyl thiolbenzoate	252° C	Benzene	4	39 »
» »	»	»	»	20	69 »
» »	»	»	Toluene	4	44 »
» »	»	»	»	20	49 »
0.75 »	»	»	»	20	51 »
0.30 »	»	»	Xylene	4	43 »
» »	»	»	»	20	44 »

Some experiments with benzoyl bromide have also been carried out, but it was impossible to determine the quantity of aldehyde formed, as an oil, which did not crystallize, was formed from the reaction with methone. From

Table 2. Reaction between sodium and calcium hydride and different organic substances.

Hydride	Amount of organic substance		Medium	Hours of boiling	Yield
NaH	0.30 g	Propionyl chloride	Benzene	20	1.2 %
»	»	»	Toluene	20	1.3 »
CaH <sub>2</sub>	»	»	Benzene	20	0.5 »
»	»	»	Toluene	20	1.0 »
NaH	»	Propionyl bromide	»	4	0.5 »
»	»	»	»	20	0.7 »
CaH <sub>2</sub>	»	»	»	4	0.5 »
»	»	»	»	20	0.6 »
NaH	»	Benzoyl chloride	»	20	1.3 »
»	»	»	Xylene	4	1.4 »
»	»	»	»	20	1.6 »
CaH <sub>2</sub>	»	»	»	20	1.1 »
NaH	»	Ethyl thiolbenzoate	Toluene	20	0.6 »
»	»	»	Xylene	20	0.4 »
CaH <sub>2</sub>	»	»	Toluene	4	0.3 »
»	»	»	»	20	0.2 »
»	»	»	Xylene	20	0.4 »

the quantity of oil formed one could get an idea of the degree of the reaction and the author presumes that the results are very near the corresponding results obtained when using benzoyl chloride.

As to the experiments with propionic anhydride the yields are very poor; only a very small amount of aldehyde was formed.

The thiolester of benzoic acid was prepared from benzoyl chloride and lead mercaptide in dry ether<sup>8</sup>. As seen from the table, the yields are good. The best (68 %) was obtained by boiling for 20 hours with benzene.

In Table 2 are given the results when using sodium and calcium hydride. Contrary to expectation, the yields in all cases were very low even the experiments with the thiolester gave poor yields. Better results were expected in this case, since the thiolester is very easily transformed into the corresponding aldehyde (by boiling with Raney nickel in 80 % alcohol, a large quantity of aldehyde is formed<sup>9</sup>).

In Table 3 some special experiments are shown. Fumaryl chloride was prepared from maleic anhydride and phthalyl chloride<sup>10</sup>. Fumaryl bromide<sup>11</sup> was prepared by passing dry hydrogen bromide through fumaryl chloride at 120° C. That a reaction really took place between fumaryl chloride (fumaryl bromide) and lithium hydride, could in this case be seen quite clearly, as the solution, after about twenty minutes of boiling, became intensely yellow. The

colour comes from fumaraldehyde (possibly from malealdehyde). The formation of an aldehyde was shown by means of the reaction with phenylhydrazin, as it was not possible to use methone in this case.

A few experiments have also been made, in which monochloroacetic acid was used. After five hours boiling in xylene, about 5 % of the chlorine atoms had been replaced by hydrogen atoms. Free chloride ions were formed by this reaction and they were determined by titration with a 0.1 *N* silver nitrate solution.

Table 3. Reaction between lithium hydride and different substances.

Substance	Medium	Hours of boiling	'Yield'
Fumaryl chloride	Benzene	4	Yellow colour
» »	»	6	» »
Fumaryl bromide	»	4	» »
» »	»	6	» »
Monochloroacetic acid	Xylene	4	4.0 %
» »	»	6	7.0 »

#### SUMMARY

It has been shown that it is possible to prepare aldehydes from acid halides by reduction with lithium hydride. The reaction gives the best results with aromatic acid halides (approx. 55 % yields). When using aliphatic acid halides the yields are not higher than 25 %, but in some cases the yield can be increased by transforming the acid halide to the corresponding thiolester, which can very easily be reduced by lithium hydride to the aldehyde stage. In this way the total yield, in proportion to the acid halide, will closely approximate that obtained with the aromatic substances.

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