REACTIONS OF ACETYLENE AND ITS DERIVATIVES WITH ALDEHYDES

AND KETONES

by

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INTRODUCTION

Since no satisfactory method,in the sense of being short,simple,and resulting in high yields,has been found for the condensation of acetylene with aliphatic aldehydes, it was the purpose of this thesis to find such a method. In attempting to solve the problem two aldehydes,form-aldehyde and n-butyraldehyde were used. The former because, if the reaction proceeded in the desired manner,the result would be propargyl alcohol,and the latter because it was considered a representative saturated aliphatic aldehyde.

Our interest in propargyl alcohol($HC\equiv C-CH_2OH$) was a-roused because its structure is such that it would be very useful as a building block for many compounds,since,although it contains only three carbon atoms,it is acetylenic at one end and alcoholic at the other. Propargyl alcohol has been prepared by various methods,but these are quite tedious and thus far only small yields have been reported.[1]

A possible method of attacking this problem was suggested by the work of several research men who have worked on the condensation of sodium acetylide with ketones and aldehydes.[2] Campbell,Campbell,and Elby[2a] have used the

[1] a)Henry,B.,$\underline{5}$,453,564;$\underline{6}$,729;$\underline{14}$,404; Ann.Scient.Brux.(1878)

b)Paal,Heupel,B.,$\underline{24}$,3039

[2] a)Campbell,Campbell,and Elby J.A.C.S. $\underline{60}$,(1938),2282

b)Moreau and Desmots Bull.Soc.Chim. $\underline{27}$,(1902),360

method of preparing sodium acetylide in liquid ammonia
and adding their ketone or aromatic aldehyde directly to
the resultant solution. Hess and Munderloh[3] made the mod-
ification of evaporating off the liquid ammonia and using
a little ether to moisten the sodium acetylide before add-
ing the liquid aldehyde. Other researchers have reported
similar condensations with varying degrees of success.[4]

Another method of attack was suggested by several
other chemists[5] who prepared the mono grignard of acetyl-
ene. Dr.Thompson working during the summer of 1939 prepared
some mono grignard of acetylene and reacted it with p-form-
aldehyde,obtaining small yields of propargyl alcohol by
this very long and tedious method.

It was decided then to use metallic acetylides in
order to determine if,and under what conditions,these could
be caused to react with aldehydes to yield the correspond-
ing alcohols in satisfactory amounts. Formaldehyde was the
aldehyde mainly used,but butyraldehyde was also used.

Sodium acetylide was used in the main and it was
reacted under various conditions of temperature with gas-
eous formaldehyde and its solid polymer,p-formaldehyde,

[3] Hess and Munderloh B.,51,380
[4] a) Iotisch Bull.Soc.Chim.,(3) 34,(1905),181
   b) Nef Ann.308,(1899),264
   c) F.G.Fischer and Lowenburg Ann. 475,(1929),183
[5] a) V.Grignard,L.Lapayne,T.Faki, Comptes Rendues(187) 517 (1928)
   b) B.Oddo Gazz.Chim.Ital. 34,(1904),429
   c) Salkind,Rosenfeld B.,(1924),57,1690

and also various solvents,liquid ammonia,ether,and diox-
ane,were used.One trial was also made using calcium acet-
ylide instead of sodium acetylide,reacting this with gas-
eous formaldehyde. An attempt to make propargyl alcohol
by means of the mono grignard of acetylene,dioxane as the
solvent was also made. The result of these reactions was
a 12% maximum yield, as shown by hydrogenation, of propargyl
alcohol,and this yield was obtained using sodium acetylide,
gaseous formaldehyde,dioxane as the solvent,and with the
temperature uncontrolled.

Several trials were made with n-butyraldehyde,us-
ing sodium acetylide,dioxane as the solvent,and varying
conditions of temperature. These trials gave no measurable
amount of the desired alcohol ($CH_3-CH_2-CH_2-\underset{H}{\overset{OH}{C}}-C\equiv CH$),but did
give indications of high yields,especially at -5 degrees,
of aldol condensation products,only two molecules being
condensed.(i.e. evidently no polymers of long chains with
more than two butyraldehyde units were obtained.)

GENERAL PROCEDURE

In order to prepare the sodium acetylide the method
suggested by Campbell[2a] as modified by Miss Rovno[6] was
used. This method consists of dropping pellets of sodium
into liquid ammonia through which a stream of dry acetylene
is being constantly passed, the reaction mixture being mech-
anically stirred continuously. When the solution completely
loses its dark blue color it is considered complete.

No references could be found for a method of react-
ing formaldehyde with sodium acetylide, but, as stated pre-
viously, Campbell, whose method proves quite satisfactory
when aromatic aldehydes are used, suggested adding the al-
dehyde directly to a liquid ammonia solution of sodium a-
cetylide.

It was decided to use this method with *any* necessary mod-
ifications. Since it was soon found that liquid ammonia
was not a suitable solvent, it was necessary to turn to
other solvents.

The method used for the Grignard synthesis was a
modification of the work done by V. Grignard.[5a] He suggests
preparing phenyl magnesium *bromide* /in ethyl ether and passing in
acetylene for long periods of time at one half an atmosphere
pressure. Several men working at the Institute have found it
impossible to reproduce his work, obtaining almost entirely

[6] I. Rovno Thesis M.I.T. 1939

the di magnesium bromide compound. It was therefore decided since dioxane is often a good solvent for inorganic substances,perhaps it would bring the di magnesium bromide compound into solution to allow further reaction with acetylene.Acetylene was passed in at atmospheric pressure.

EXPERIMENTAL

A⟶ Method when using mono sodium,or calcium,acetylide.

This discussion will be limited to working with half molal quantities of acetylide,but it is applicable to larger quantities,the only difference being that proportionately larger amounts of liquid ammonia and solvent must be used.

Sodium* acetylide was made in the set-up labeled "Apparatus A" (page 6a). The three necked flask was surrounded by a dry-ice-toluene bath,and with the only opening to the atmosphere being the soda-lime drying tube,[I] 300 cc. of liquid ammonia were led into the flask through the T tube. One half a mol (11.5 grams) of sodium in the form of pellets of such a size that they will not clog the tube when attempting to shake them into the reaction mixture,were now placed in the sodium addition tube (M). The

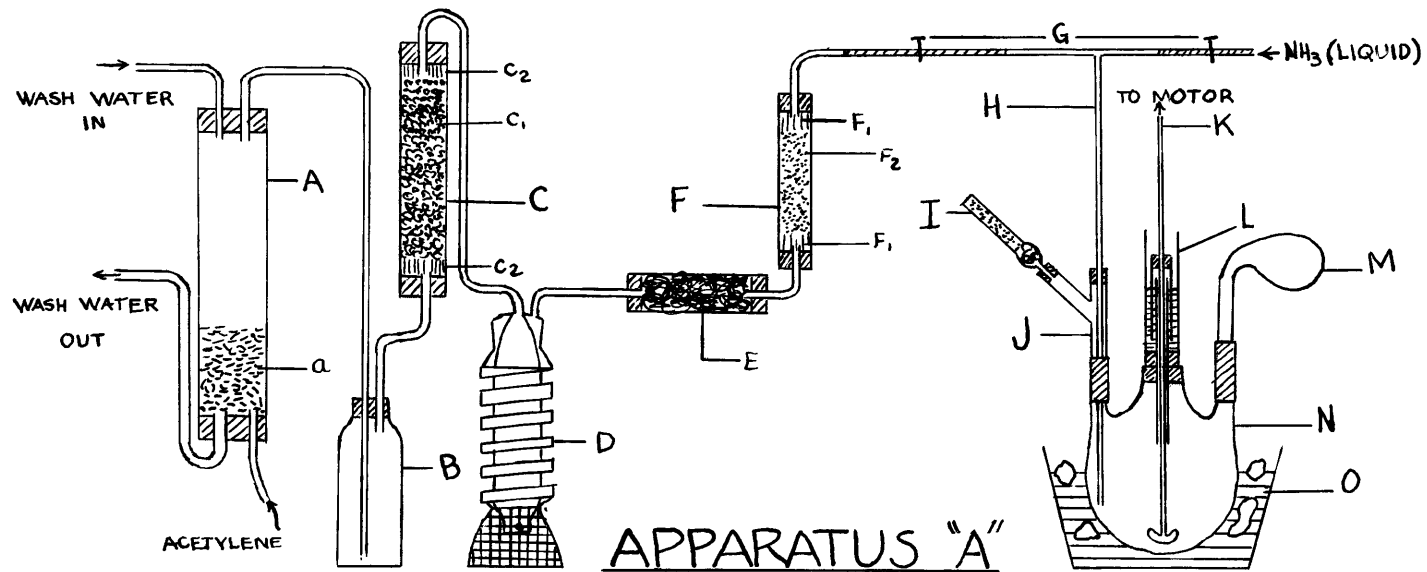* Whenever the word "sodium" is used,"calcium" may be substituted.

mechanical stirrer was set into operation,turning at quite a rapidrate,the water turned on in the gas washer,and acetylene passed into the reaction chamber at a rapid rate.*

Several pellets of sodium were dropped into the reaction chamber by tilting the addition tube. After the blue color,caused in the reaction mixture by such addition,disappeared,a few more pellets were added. Such addition and waiting for the color to be discharged were continued until all the sodium had been added. This took from fifteen to twenty minutes.

Acetylene was bubbled through the reaction mixture for from five to ten minutes longer to insure formation of the mono- rather than the di- acetylide.

The acetylene washing and drying train was now shut off from the reaction flask by means of a screw clamp placed on the rubber tubing connecting the T tube(H) with the phosphorous pentoxide drying tube(F). When liquid ammonia was used as a solvent for the subsequent reaction,the substitutions(mentioned below) for the sodium addition tube(M) were made immediately. At other times the liquid ammonia was evaporated off on a warm water bath (40-50 degrees) through the soda-lime drying tube(I) with the mechanical

* When the incoming stream of water flows at a steady and not too rapid rate,the height of the water level is automatically adjusted,since it can not rise above the level of the tube labeled "wash water out".

WASH WATER IN

A

WASH WATER OUT

a

ACETYLENE

B

c_2

c_1

C

c_2

D

E

F

F_1

F_2

F_1

G

NH₃ (LIQUID)

H

TO MOTOR

K

I

J

L

M

N

O

APPARATUS "A"

A- GAS WASHER (WATER USED)
  a- SMALL PIECES OF GLASS TUBING
B- TRAP
C- DRYING TUBE
  C_1- GLASS WOOL
  C_2- CALCIUM CHLORIDE
D - SULFURIC ACID GAS DRYER

E- GLASS WOOL TRAP
F- DRYING TUBE
  F_1 - GLASS WOOL
  F_2 - P_2O_5
G- SCREW CLAMPS
H- T TUBE

I- SODA-LIME DRYING TUBE
J- Y TUBE
K- MECHANICAL STIRRING ROD
L- MERCURY SEAL
M- SODIUM ADDITION TUBE
N - 1 LITER 3 NECKED FLASK
O- DRY ICE-TOLUENE BATH

stirrer kept in operation to avoid bumping. When the liquid
ammonia was entirely evaporated, 100-150 c.c. of solvent were
put in the reaction chamber.

When the reaction with aldehyde was carried out at an
elevated temperature, a reflux water condenser, protected by
a soda-lime drying tube, was substituted for the soda-lime
drying tube (I).

The sodium addition tube was removed and, depending
upon the state of the aldehyde, the following were substit-
uted:

1. If liquid aldehyde (butyraldehyde), a drying tube
protected dropping funnel.

2. If gaseous aldehyde (formaldehyde), a formaldehyde
gas generator. (Three types were used. For when each was
used, see table on pages 10a and b)

3. If solid aldehyde (p-formaldehyde), a large filter
funnel.

In case 1, half a mol of butyraldehyde was used, and
it was added in such a manner that the temperature variation
of the reaction was never more than one or two degrees.

In cases 2 and 3, a threefold excess (1.5 mols) of
formaldehyde was used, usually. When p-formaldehyde was
used, it was added all atonce, the funnel removed, and the
opening stoppered. An alternative method of reacting with
p-formaldehyde, that of washing the sodium acetylide into
a bottle with between 100 c.c. and 150 c.c. of solvent

stoppering the bottle tightly and shaking,was also tried.
This mixture gave a high initial heat of reaction which,
however,was of short duration.

When gaseous formaldehyde was used,three formaldehyde
generators were employed. These are shown on page8a . The
first of these was unsatisfactory because the formaldehyde
formèd by depolymerizing p-formaldehyde repolymerized in
the U tube,clogging it and causing explosions. The second
of these was so constructed that clogged material could
theoretically be pushed out manually,but this too was un-
satisfactory because explosions occurred anyhow and moist
air was admitted to the reaction chamber. The third of these
eliminated the previous difficulties since the addition
tube could be kept above 180 degrees and so prevent repoly-
merization.

The stirring rod was kept going continuosly during
the aldehyde addition.

When the reaction was complete the solution was
made slightly acid with concentrated sulfuric acid in ice,
adding the acid as rapidly as possible with mechanical stir-
ring. Two layers,organic and water,appeared at this point.

The three necked flask was removed from the rest of
the apparatus and its contents treated inthe following
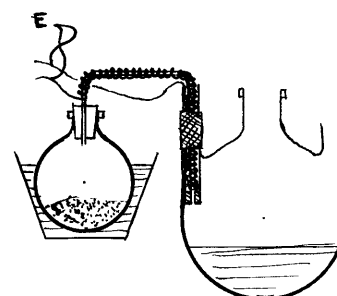manner:

The reaction mixture was neutralized with sodium
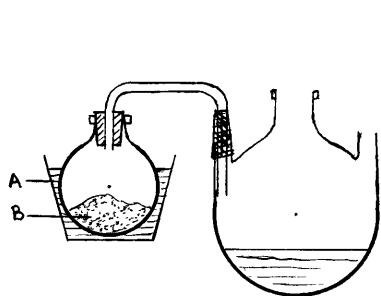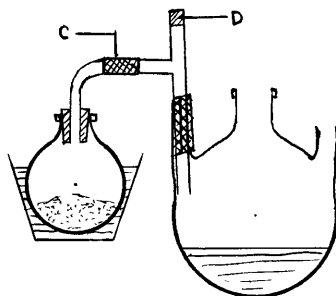
GENERATOR 1   GENERATOR 2   GENERATOR 3

A-OIL BATH   B-p FORMALDEHYDE   C. RUBBER CONNECTOR   D- STOPPER

WHICH CAN   BE REMOVED TO PUSH OUT THE REPOLYMERIZED CH_2O

E- RESISTANCE WIRE

bicarbonate. The excess bicarbonate was filtered off and washed two or three times with 10-15 cc. portions of ether, washings being returned to solution. To form the bisulfite addition product,an amount of sodium bisulfite,dissolved in the minimum amount of water,equivalent to all the aldehyde was shaken thoroughly with the organic layer(this was done only in those cases indicated by an asterisk(*) in table 1,pages 10a+b)

The water layer was saturated with sodium chloride and the organic layer separated. The water layer was extracted4-5 times with 50-60 cc. portions of ether,the extracted material being added to the organic layer. The organic layer was now dried with anhydrous magnesium sulfate, the magnesium sulfate then being filtered off and washed 3-4 times with 15-20 cc. of ether. The washings were added to the filtered organic layer. The ether was removed from the organic layer by distilling to 55 degrees using column "1" (page 9a). The residue was fractionated on the column labelled"2",page 9a.

The water layer was continuously extracted with ethyl acetate for periods of 18-24 hours in several runs without further recovery of alcohol.

At first ethyl ether was the solvent used,but later dioxane,because it was found that the latter was a better solvent for p-formaldehyde and sodium acetylide.
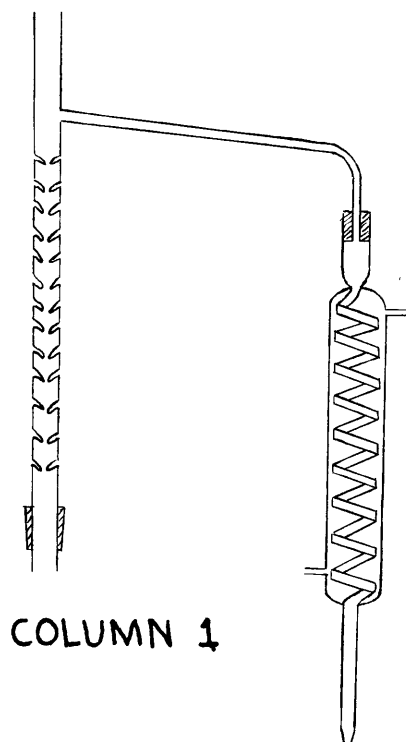
COLUMN 1
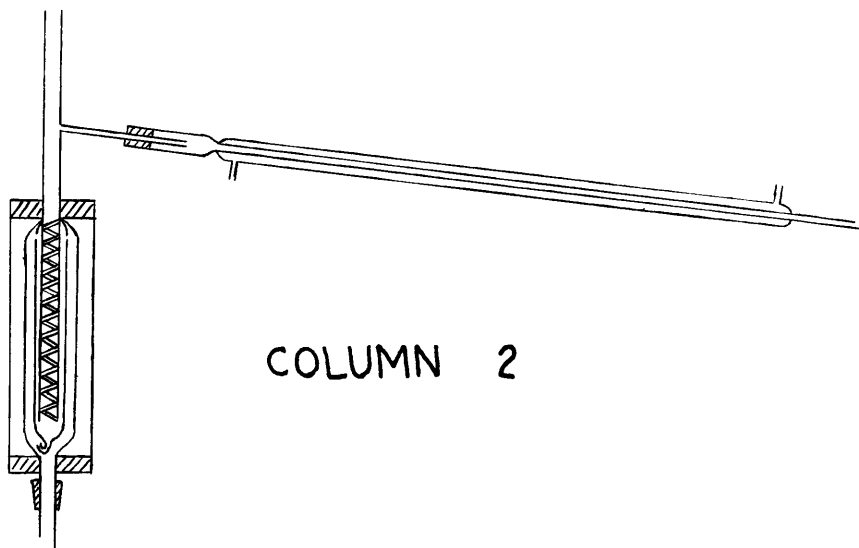
COLUMN 2

The product was tested for free acetylenic hydrogen with ammoniacal silver nitrate in almost every case and with cuprous chloride in several cases. Its unsaturation was determined by hydrogenation,using platinum oxide catalyst, whenever the silver acetylide test showed it worth while.

It was found that if much dioxane was present when attempting to make this silver acetylide test,no characteristic curdy white precipitate was obtained. Silver acetylides seem to be soluble in dioxane.

The solvents used,conditions maintained,and the results of all the runs,together with any other pertinent data are listed in table 1,pages 10a+b.

The 12% yield,as shown by hydrogenation,was made under non-reproducable conditions of explosions and foreign materials getting into the reaction chamber. Attempts to reproduce this yield under controlled conditions proved unsuccessful.

B- Attempted Grignard Synthesis

Ethyl magnesium bromide was prepared as follows in the apparatus shown on page 22a. Magnesium turnings(7.8 gm.-.32 mols) were placed in the three necked flask and 50 cc. of dry ether were added and the mechanical stirrer was started. Ethyl bromide(40 grams-.37 mols) was mixed with 200 cc. dry ether and placed in the dropping funnel. The

TABLE I

Run #	Solvent + # Mols of NaC≡CH	Reactant + How Introduced	How Run	Temp. Control	Observations	Results
1	Liquid Ammonia + 1 mol	2 mols CH_2O as p-form-aldehyde + Na addition tube	In 3 necked flask	None	Addition tube heated up and the p-formaldehyde became gummy. Reaction time = 1 hour	Positive test for hexamethylenetetramine. Slight AgC≡C-R test
2	Ether + 1 mol	4 mols CH_2O as p form-aldehyde + filter funnel	))	))	When temperature of distillation reached 41° only 20cc of material remained. Reaction time = ½ hour	
3	Ether + 1 mol	CH_2O gas ½ mol generator 1	))	))	Distilled to 44°. little remained. Many explosions	Faint AgC≡CR test
4	Dioxane + 1 mol	CH_2O gas 3 mols generator 2	))	))	Explosions occur. Final fraction = 18 gm. B.P. 103-104 (Theor = 114-115) Reaction time- generation = 3½ hrs additional = ½ hr	Strong AgC≡CR test. Hydrogenation = 11.9-12.9% yield
5	Dioxane + 2 mols	2 mols CH_2O as p form-aldehyde	Bottle	"	BP = 103 - 107 Reaction time = 20 mins. of shaking	Strong AgC≡C-R test. Hydrogenation = 5-7% yield
6	Dioxane + 3 mols	6 mols CH_2O as p form-aldehyde + filter funnel	In 3 necked flask	"	Distilled to 100°, only 10cc remained. Reaction time = 1¾ hours	Faint AgC≡CR test
7	Dioxane + ½ mol	1½ mols CH_2O as p form aldehyde	Bottle	"	Shaken for 12 hours. Everything boiled below 101°	No AgC≡CR test

10a

TABLE I CONTD.

Run#	Solvent + #Mols of $NaC\equiv CH$	Reactant	How Run	Temp Control	Observations	Results
8	Dry Dioxane + ½ mol	1½ mols CH_2O as p-form aldehyde	In 3 necked flask	Hot water bath	Everything boiled below 101° Reaction time = 2 hours	No $AgC\equiv CR$ test
*12	Dry Dioxane + ½ mol	34 gm CH_2O gas + generator 3	"	none	Material distilled to 71° + residue tested Reaction time = 1¼ hours	No $AgC\equiv CR$ test (Dioxane present) Hydrogenation = 3.5% yield
*13	Dry Ether + ½ mol	38 gm CH_2O gas + generator 3	"	Dry ice toluene bath (-80°)	Distilled to 36° when only 20cc remained Reaction time = 2½ hours	No $AgC\equiv CR$ test or $CuC\equiv CR$ test
*15	Dry Dioxane + 1 mol $Ca(C\equiv CH)_2$	90 gm CH_2O gas + generator 3	"	none	A few cc boiled between 101½ + 103½. Nothing boiled higher Reaction time = 3 hours	Faint $AgC\equiv CR$ test
9	Dry Dioxane + ½ mol	½ mol n butyraldehyde	"	none	High initial heat of reaction. Dioxane refluxes. BP - 105°-160 gives $NaHSO_3$ Addition	Faint $AgC\equiv CR$ test
*10	Dry Dioxane + ½ mol	"	"	10°	Addition time = ½ hr. Extra time = ½ hr Alkaline soln - red. Acidic soln- yellow Fraction 1- B.P. 101½ - 153 2 - (2cc) 153 -160 - gives $NaHSO_3$ add'n	No $AgC\equiv CR$ test
11	Dry Dioxane 50 parts Dry Ether 15 part + ½ mol	"	"	-5°	Addition time =1 hr Extra time =½ hr Same color changes as at 10° BP (1) 101½ - 160 (3cc (2) 160 - 170 - 28 gm - gives $NaHSO_3$ add'n	No $AgC\equiv R$ test 78% yield Aldol (?) condensation prod.

In those runs marked with an asterisk*, the reaction mixture was shaken with $NaHSO_3$ to remove any unreacted aldehyde

mixture was dropped into the flask at such a rate as to cause slow refluxing. Time required for this was $\frac{3}{4}$ of an hour. The reaction was completed by refluxing slowly for $\frac{1}{2}$ hour on a warm water bath.

The reaction flask was now connected to the acetylene washing and drying trains (see "Apparatus A",p. 6a), and 200 cc.dry dioxane were added. A finely divided white precipitate probably consisting of C_2H_5MgBr and $MgBr_2$ appeared immediately.

The mechanical stirrer was set in motion and acetylene bubbled slowly through the washing and drying train into the reaction mixture for 12 hours.

The acetylene train was then shut off from the reaction chamber by means of a screw clamp,and 45 grams of formaldehyde gas were passed in over a period of $1\frac{1}{2}$ hours using generator #3,page 8a. The reaction mixture was now made slightly acidic with concentrated sulfuric acid in ice and treated as described in the sodium acetylide runs.

Nothing distilled above 102 degrees,and the final cc. of distillate gave no silver acetylide test.

CONCLUSIONS

We have observed that when using formaldehyde no
product other than that corresponding to propargyl alcohol
was separated. The alkalinity of the reaction mixture prob-
ably caused side reactions of formaldehyde polymerizing to
ether insoluble carbohydrates,thus explaining the failure
to recover by-products. This premise seems to be substan-
tiated by the fact that when p-formaldehyde is shaken with
sodium acetylide for 12 hours,no sodium acetylide is left,
as shown by the very small heat of neutralization with
sulfuric acid and the completely negative silver acetyl-
ide test. In spite of the fact that the 12% yield could
not be reproduced,the results of the various runs seemed
to indicate that in order to make this reaction proceed
in the desired manner,the following conditions should be
maintained:

1-High concentration of formaldehyde gas.

2- Use of a solvent which will not react with sod-
ium acetylide or formaldehyde,but will dissolve these sub-
stances to a considerable extent.

3-Acidification of the reaction mixture as soon as
possible after the heat of reaction has ceased.

The reasons for specifying these conditions are sev-
eral. In the first place the only runs in which yields were
obtained at all were those in which formaldehyde gas was
used,or in which the high heat of reaction depolymerized
the p-formaldehyde. Secondly dioxane gave much better re-

sults than any other solvent used. And finally, when the reaction mixture was acidified very soon after reaction heat had ceased the highest yields of propargyl alcohol were obtained, but when allowed to react for a long time afterwards, no measurable yields were obtained.

While the yields of alcohol from the butyraldehyde runs were insignificant, if extant at all, the results showing aldol condensation may be quite significant. We have several reasons for saying that condensations took place to give the dimolecular aldol compounds. It is know that in dilute solutions of alkali, which condition is met by the dioxane solution of sodium acetylide, aldol condensations are prone to occur. Also, although when fractionating the organic layer no fraction corresponding to butyraldehyde was obtained, the organic layer always gave a sodium bisulfite addition product, indicating the presence of an aldehyde, and a fraction was obtained with a boiling point corresponding approximately to the aldol condensate of butyraldehyde. In one case the fraction gave a 78% yield, and in all cases it gave a very definite sodium bisulfite addition product. The significance of all this is that in those cases where it is difficult to make the dimolecular aldol condensation product of an aldehyde, it might be useful to go through the sodium acetylide procedure, since it is quite simple and gives no extraneous products.

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   b)Paal,Heupel,B.,24,3039

2. a)Campbell,Campbell,andElby J.A.C.S. 60,(1938),2282

   b)Moreau and Desmots Bull.Soc. Chim. 27,(1902),360

3. Hess and Munderloh B.,51,380

4. a)Iotisch Bull.Soc.Chim. (3) 34,(1905),181

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  c)F.G.Fischer and Lowenburg Ann. 475,(1929),183

5. a)V.Grignard,L.Lapayne,T.Faki Comptes Rendues(187) 517 (1928)

   b)B.Oddo Gazz.Chim.Ital. 34,(1904),429

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6. I.Rovno Thesis M.I.T. 1939

REACTION OF CERTAIN GRIGNARD REAGENTS
WITH β IONONE

INTRODUCTION

Although much work has been done with β ionone, it has not been established whether Grignard reagents react with it to give 1,2 or 1,4 addition. Knowledge of this is quite important, especially for synthetical work on Vitamin A, since if 1,4 addition predominates, there will always result a difficultly separable mixture. It was the purpose then of this research to attempt to cast more light on the subject.

Since β ionone is an α, β unsaturated ketone, it is difficult to tell beforehand just how Grignard reagents will behave with it. From the great amount of work that has been done with α, β unsaturated ketones and aldehydes, some knowledge of the peculiarities of their reactions may be gleaned. It has been found that some Grignard reagents add 1,2 to the carbonyl group, others 1,4, to the conjugated system, still others 3,4, and finally some add both 1,2 and 1,4. Unsaturated ketones give either saturated ketones or unsaturated alcohols.[1]

Kohler has done a great deal of research on α, β unsaturated ketones and the following table of his covers some of the most significant points.[2]

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[1] Gilman-Organic Chemistry- 1938 ed.,Vol 1,p.581

[2] Kohler,Am.Chem.J.,38,(1907),511

Substance	% 1,4 addition with	
	C_6H_5MgBr*	C_2H_5MgBr*
$C_6H_5CH=CHCHO$	0	0
$C_6H_5CH=CHCOCH_3$	12	60
$C_6H_5CH=CHCOC_2H_5$	40	71
$C_6H_5CH=CHCOCH(CH_3)_2$	88	100
$C_6H_5CH=CHCOC(CH_3)_3$	100	100
$C_6H_5CH=CHCOC_6H_5$	94	99
$(C_6H_5)_2C=CHCOC_6H_5$	0	18
$C_6H_5CH=C(C_6H_5)COC_6H_5$	100	100
$C_6H_5C(CH_3)=CHCOC_6H_5$	44	41

* The remainder is to be accounted for by 1,2 addition.

"It will be noted",says Gilman,"that as the activity of the carbonyl group decreases,the amount of 1,4 addition increases."[1] The mode of such addition depends upon the number,kind,and position of the substituents in the ketone and upon the Grignard reagent.[3]

Karrer tells us further that with α ionone,allyl magnesium bromide gives us an alcohol(1,2 addition),but the reaction with β ionone is not analogous(1,4 addition?)[4]

From all this it will be seen that it is not so

[3] Smith and Hanson,J.Am.Chem.Soc.,57,(1935),1326

[4] P.Karrer,H.Salomen,R.Morf,and O.Walker Helv.Chim.Acta,15 (1932),878

easy to tell just how various magnesium halides will react with β ionone. It was attempted, therefore, to take various Grignard reagents, especially those of types similar to those which will probably be used in Vitamin A syntheses, and determine if these added 1,2 or 1,4 to the ionone.

The following Grignard reagents were used: C_2H_5MgBr, $(CH_3)_2CH-CH_2-CH_2-MgBr$, $CH_3(CH_2)_3C \equiv C-MgBr$, $CH_3(CH_2)_4C \equiv C-MgBr$, $CH_2=CH-CH_2-MgBr$. To determine the amount of 1,2 addition which had occurred, a Grignard apparatus for the determination of hydroxyl and carbonyl groups proposed by Assaf and Gladding was used.[5]

The crude products were separated into three fractions under vacuum, using an oil pump. It was deemed reasonable that the highest boiling fractions should contain no ionone and consist essentially of a mixture of 1,2 and 1,4 addition products. This was born out by the practically quantitative yields of alcohols when acetylene magnesium bromide compounds were used, as shown by Grignard analysis. The percent of 1,2 addition and the percent of crude product represented by the highest boiling fractions are summarized below.

Substance Reacted With β Ionone	% of Crude Product Represented by High Boiling Fraction	% 1,2 Addition
C_2H_5MgBr	9	42
$(CH_3)_2CHCH_2CH_2MgBr$	12	30

5 A.G.Assaf,E.K.Gladding- Ind.& Eng.Chem.,Anal.Ed.,(2),164,(1939)

Substance Reacted With β Ionone	% of Crude Product Represented by High Boiling Fraction	% 1,2 Addition
$CH_2=CHCH_2MgBr$	27	27
$CH_3(CH_2)_3C\equiv CMgBr$	50	90
$CH_3(CH_2)_4C\equiv CMgBr$	36	89
* $CH_2=CHC\equiv CMgBr$		100
* $CH_2=C(CH_3)C\equiv CMgBr$		100
* $CH_3CH_2=C(CH_3)C\equiv CMgBr$		100

* Previously prepared and tested by Dr.Thompson

GENERAL PROCEDURE

The ethyl and isoamyl magnesium bromides were prepared by the standard methods. N-butyl and n-amyl acetylene were prepared by a slight modification of the method suggested by Vaughn et al.[6] Their MgBr compounds were prepared by standard methods. The allyl magnesium bromide was prepared by a modification of the method suggested by Gilman.[7] Gilman suggested placing 30 mesh magnesium metal in a long column and pouring the allyl bromide mixed with dry ether over it,but J.Burr found that he could obtain sat-

6 T.H.Vaughn,G.F.Hennion,R.R.Vogt,J.A.Nieuwland,
    J.Org.Chem.,2,1,(1937-38)

7 Gilman,Bul.Soc.Chim.,(4),43,(1928),1326

8 J.Burr Thesis M.I.T. 1940

isfactory yields by using 60 mesh magnesium and a "Morton"[9] baffled flask equipped with a high speed stirrer. Allyl bromide,magnesium,and ether were used in the molal ratio of 1:3:7.5 as suggested by Gilman,and allowed to reflux at a very slow rate.

The reaction of β ionone with the Grignard reagents were carried out by adding the ionone dropwise to give moderately slow refluxing,and completing by refluxing on a warm water bath.

EXPERIMENTAL

A- Preparation of the acetylene derivatives.

Both hexine-1 and heptine-1 were prepared in the same way. In this discussion we will limit ourselves to the preparation of the former.

Sodium acetylide($\frac{1}{2}$ mol) was prepared in the same manner as before(see page 5). The Y tube (J) with its rubber connector and the sodium addition tube with its rubber connector were removed. In their places were substituted a reflux condenser and a dropping funnel,both protected by soda-lime drying tubes and set in tin foil-collodion painted stoppers. Such stoppers are necessary because the acetylene derivatives are very volatile,and rubber absorbs many times its volume of such substances.

[9] Morton, Ind.Eng.Chem.,Anal.Ed.,(2),170,(1939)

Then n-butyl bromide($\frac{1}{2}$ mol) was dropped into the well stirred liquid ammonia solution for a period $\frac{3}{4}$ of an hour. The liquid ammonia was then evaporated off through the water condenser and enough cold water added to dissolve the sodium bromide. The organic layer was separated from the water layer,and the water layer extracted with six 20-25 cc. portions of cold ether. The extracts were added to the organic layer,and the organic layer washed twice with ice cold 15 cc. portions of 6 N HCl and once with ice water (20 cc.).

The organic layer was now dried with anhydrous magnesium sulfate,the magnesium sulfate filtered off and washed twice with ether. This layer was then distilled through a three foot fractionating column.

Six grams of a material boiling at 71.5 degrees were collected. This is a 14$\frac{1}{2}$ % yield.

B- Preparation of the Grignard compounds of hexine-1 and heptine-1.

Ethyl magnesium bromide was prepared in the apparatus illustrated on page 22a. Magnesium turnings(3.6 grams= .15 mols) were placed in the three necked flask and 50 cc. dry ether added. Ethyl bromide(16.5 grams=.15 mols) was mixed with 120 cc. of dry ether and put into the dropping funnel. The mechanical stirrer was started and the mixture added dropwise so that slow refluxing occurred. Addition

took $\frac{1}{2}$ hour and the reaction was completed $_\wedge$ stirring and re- ^by^
fluxing slowly on a warm water bath for one hour after the
last addition of EtMgBr.

The acetylene compound(.15 mols) was introduced in-
to the dropping funnel and and added dropwise to the ethyl
magnesium bromide so that slow refluxing occurred. The re-
action mixture was stirred and refluxed (water bath) for
$\frac{1}{2}$ hour after the last addition of the acetylene derivative.

C- Preparation of Ethyl and Isoamyl Magnesium Bromides.

Ethyl magnesium bromide and isoamyl magnesium brom-
ide were prepared by the method for ethyl magnesium bromide
given in the previous paragraphs. 15 grams(.14 mols) of
ethyl bromide and 20 grams(.13 mols) of isoamyl bromide
and equivalent molal amounts of/were used together with ^Mg^
150 cc. of dry ether for the former and 175 cc. for the
latter.

D- Preparation of Allyl Magnesium Bromide

This compound was prepared in an apparatus similar
to that shown on page 22ᴀ except that a"Morton" flask was
used.

28 grams(.23 mols) of allyl bromide were placed in
the dropping funnel together with 95 cc.(.865 mols= 3.75 ✗
mols of allyl bromide) of dry ether. 18 grams(.73 mols≠
3 times # mols of allyl bromide) of ground Mg turnings were
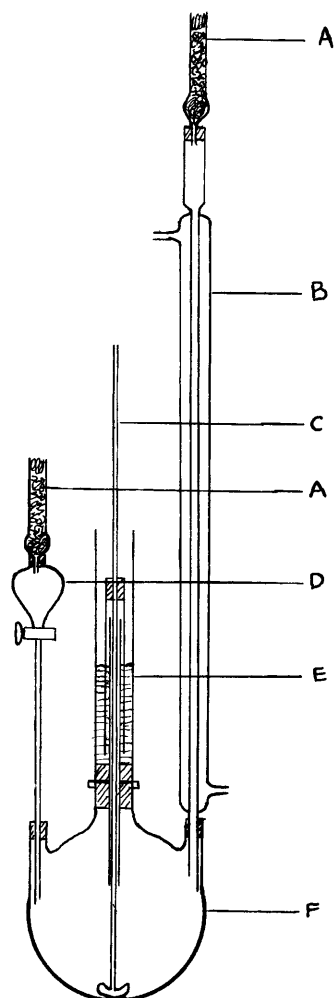
APPARATUS FOR CARRYING OUT GRIGNARD

REACTIONS

A-Calcium chloride drying tubes
B-Reflux water condenser
C-Mechanical stirring rod
D-Dropping funnel
E-Mercury seal
F-Three necked flask

were placed in the flask together with 95 cc.(.865 mols=
3.75 times the # mols of allyl bromide) of dry ether.

The motor was started at high speed and the allyl
bromide dropped in at such a rate as to give very slow re-
fluxing. Time for such addition was two hours and 50 min-
utes. The reaction mixture was stirred for ¼ hour longer
to complete the reaction. After stopping the motor and al-
lowing the Mg to settle for ¼ hour,the liquid was decant-
ed into a 1 liter three necked flask with a reflux condens-
er and a dropping funnel.

E- Reactions of the Grignard Reagents With β Ionone

β ionone was added to each of the Grignard reagents
in the same manner.

That amount of β ionone necessary to react with the
magnesium bromide compound(one mol of ionone per mol of
reagent) was placed in the dropping funnel(Apparatus p.22a)
and added at such a rate,with good stirring,that slow re-
fluxing occurred. Time for adding 0.1 mol was approximately
20 minutes. After the last drop of ionone had been added,
stirring and refluxing slowly on a water bath were contin-
ued for 1 hour. The flask was then surrounded by an ice-
water bath and the reaction mixture decomposed by making
slightly acid with ice cold sulfuric acid(1 part in 50
parts of water).

The resultant solution consisting of two layers
was treated in the following manner. After having saturated

TABLE 2

SUBSTANCE REACTED WITH β IONONE	THEORETICAL YIELD (IN GM)	FRACTION #	ACTUAL YIELD (IN GM)	VACUUM FRACTIONATION WITH OIL PUMP		REFRACTIVE INDEX*	% 1,2 ADDITION
				BATH TEMP	BOILING PT		
C_2H_5MgBr	30	1	15	160°C	105-120	1.5042	
		2	5	160	120	1.5012	
		3	2	160	120	1.5000	42
$(CH_3)_2CHCH_2CH_2MgBr$	34	1	14	150	—— 130	1.4993	
		2	8	165	130-135	1.4968	
		3	3	165	135-138	1.4880	30
$CH_2=CH-CH_2MgBr$	53	1	17	150	110-115	1.5175	
		2	12	160	115	1.5210	
		3	10	160	115-122	1.5220	2.7
$CH_3(CH_2)_3C\equiv CMgBr$	41	1	8	160-170	118-130	1.5020	
		2	7	170	130-138	1.5056	
		3	15	190	145-155	1.5160	90
$CH_3(CH_2)_4C\equiv CMgBr$	27	1	6	150-155	105-123	1.5042	
		2	4	155-190	123-152	1.5060	
		3	8	190-200	152-158	1.5170	89
† $CH_2=CH\ C\equiv CMgBr$							100
† $CH_2=CH(CH_3)C\equiv CMgBr$							100
† $CH_3CH_2=C(CH_3)C\equiv CMgBr$							100

† Substances previously prepared by Dr Thompson   * Refractive Index of β Ionone at same temp = 1.5110

23a

the water layer with sodium chloride,the organic layer was

separated. The water layer was extracted 4 times with 30-40

cc. portions of ether,the extracted material being added

to the organic layer which was now dried with anhydrous

magnesium sulfate. The magnesium sulfate was filtered

off and washed with 15-20 cc. portions of ether three times,

the washings being added to the organic layer. The ether

was removed from the organic layer through column "1",p. 9a,

up to such a temperature that decompostion began to occur.

The resultant residues were fractionated under vac-

uum,using an oil pump. Data on the fractionations are given

in table. II,page 23a.

In all cases the third fraction was analyzed to de-

termone if 1,2 or 1,4 addition had occurred. A Grignard

apparatus for the determination of the hydroxyl and car-

bonyl groups was used.The vinyl acetylene products were

those which Dr.Thompson had previously prepared. All the

results are summarized in table II,page   .

CONCLUSIONS

The results obtained from the experimental work

and from the analyses of the vinyl acetylene derivatives

of βionone indicate several interesting conclusions.

The evidence presented points strongly toward 1,2 addition occurring when β ionone is treated with acetylene magnesium bromide compounds,and 1,4 addition when treated with alkyl magnesium bromide compounds. It is interesting to note that while Karrer says allyl magnesium bromide probably does not give 1,2 addition at all,but probably does give a dimolecular hydrocarbon[4],it was found that 27% 1,2 addition was obtained by the method given in this paper. It seems reasonable to assume that the remainder of the product obtained is the 1,4 isomer because the physical properties of the products presumably eliminate any other possibilities.

The results of the various reactions carried out show further that acetylenic Grignard reagents are more reactive with reference to β ionone than alkyl reagents. It will be seen from table II that the third fractions of the former were a larger percent of the total yield than those of the latter,although conditions of reaction in each case were the same.

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