THE REACTIONS OF ALD-CHLORIMINES WITH GRIGNARD REAGENTS

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In connection with a study of the reactions of compounds of the type RCH—NX (where X is halogen, acetate, etc.) with bases¹, it seemed of interest to investigate the reactions of these compounds with Grignard reagents. The results obtained with ald-chlorimines and certain Grignard reagents are reported in this paper.

The characteristic group of ald-chlorimines, (—CH=NCl), should be capable of undergoing at least three different types of reaction, involving, (1) the elimination of hydrogen chloride, (2) a reaction in which the nitrogen-chlorine group is attacked (as in hydrolysis), or (3) addition to the carbon-nitrogen double bond. A previous study^{1a} has shown that in the presence of certain bases, such as alcoholic alkali, only the first reaction occurs to an appreciable extent, giving in certain cases practically quantitative yields of nitrile. The present investigation shows that in the presence of Grignard reagents, the first two types of reaction occur, the second predominating; apparently, addition to the carbon-nitrogen double bond (third type) does not take place to an appreciable extent with these reagents.

The reactions of ald-chlorimines with Grignard reagents has been carried out by slowly adding the latter to the chlorimine in ether solution. In this way secondary reactions of the Grignards with the products (e. g., nitriles) was minimized. The products obtained from the reactions of aldchlorimines with ethyl-, phenyl-, or p-chlorophenylmagnesium bromide may be accounted for by equations (I) and (II). In I, the Grignard reagent removes hydrogen chloride from the ald-chlorimine to form a nitrile and R'H, while in II, the Grignard reagent is chlorinated, giving R'Cl and a nitrogen-magnesium compound.

(I) $RCH = NCl + R'MgX \rightarrow RCN + R'H + MgXCl$

(II)
$$RCH=NCl + R'MgX \rightarrow RCH=N-MgX + R'Cl$$

The yields of nitrile and of nitrogen-magnesium compound isolated are given in the accompanying table. The ald-chlorimine used up is not fully accounted for by the products isolated, but the yields given are

¹ See especially: (a) HAUSER, LEMAISTRE, AND RAINSFORD, J. Am. Chem. Soc., 57, 1056 (1935); (b) HAUSER AND JORDAN, *ibid.*, 57, 2450 (1935).

based on rather pure compounds. The identities of the nitriles were established by the mixture melting point method, those of the nitrogenmagnesium compounds by hydrolysis to the aldehydes, which were identified by mixture melting points or by derivatives. In one case the products R'H of equation I and R'Cl of equation II were isolated.

It is seen from the table that the principal reaction is II, although I occurs to a considerable extent. The quantitative relationships are probably of little significance because of the losses attendant on isolation of pure products. It is interesting however to note that in the reactions of 4-chlorobenzalchlorimine, the yield of nitrile was greater with ethylmagnesium bromide than with phenylmagnesium bromide.

Like the Grignard reagents, phenyllithium reacts with 4-chlorobenzalchlorimine to give the nitrile and a nitrogen lithium compound, which on hydrolysis yields the aldehyde.

BENZALCHLORIMINE	GRIGNARD REAGENT	TEMP. OF REACTION, °C.	PERCENTAGE YIELDS	
			RCN	RCH= NMgX
2-Chloro	C ₂ H ₅ MgBr	-45	13	43
4-Methoxy-	C ₂ H ₅ MgBr	0	17	50
4-Chloro-	C ₂ H ₅ MgBr	0	20	45
4-Chloro-	C ₂ H ₅ MgBr	23-28	34	45
4-Chloro-	C ₆ H ₅ MgBr	0	10	61
4-Chloro	p-ClC ₆ H ₄ MgBr	0	5^a	18ª

TABLE

YIELDS OF PRODUCTS FROM CERTAIN BENZALCHLORIMINES AND GRIGNARD REAGENTS

^a In addition to nitrile and aldehyde, chlorobenzene (20 per cent.) and p-dichlorobenzene (25 per cent.) were isolated.

Reaction II of the ald-chlorimines with Grignard reagents apparently involves the removal of chlorine from nitrogen with a sextet of electrons (positive chlorine). This is the characteristic manner in which chlorine is removed from nitrogen in hydrolysis and in most other reactions. Coleman² has shown that chloroamines of the type R_2NCl react with Grignard reagents predominately in this manner.³ Reaction II may involve the initial formation of a coördination compound of the type

$$\begin{array}{cc} \operatorname{Cl} & \mathrm{R}' \\ & | & | \\ \operatorname{RCH} = \mathrm{N} \rightarrow \mathrm{MgX} \end{array}.$$

² COLEMAN, *ibid.*, **55**, 3001 (1933).

³ An interesting reaction that appears to be an exception to this type of substitution is the formation of primary amines from Grignard reagents and monochloramine. In this reaction the chlorine is apparently removed from nitrogen with a complete octet of electrons. See COLEMAN AND CO-WORKERS, *ibid.*, **50**, 1193 (1928); **51**, 567 (1929). The coördination should facilitate the release of positive chlorine and of the negative R group; an α , γ shift would give the products of reaction, R'Cl and RCH=N-MgX.

Reaction I of the ald-chlorimines with Grignard reagents presumably involves the removal of the hydrogen as a proton, and of the chlorine as chloride ion, the Grignard reagent functioning as a base. While there may be an initial coördination of the chlorine of the chlorimine with the magnesium of the Grignard reagent, it is believed that this in itself would not effect the elimination of hydrogen chloride. There is evidence^{1a} that the removal of hydrogen chloride from ald-chlorimines by alkali involves a primary attack by the base on the aldehydic hydrogen atom. It is believed therefore, that the removal of hydrogen chloride from these compounds by Grignard reagents is brought about primarily by an attack of the negative R group, which is present at least potentially in these reagents, on the aldehydic hydrogen atom of the chlorimine. An initial coördination of the chlorimine and Grignard, $RCH=NCl \rightarrow MgXR$, might however, facilitate the release of the proton from the former, and of the negative R group from the latter. The elimination may be represented as follows:

$$\begin{array}{c} H \leftarrow ---- \overline{R'} \\ \downarrow \neg \\ R - C = N - C \downarrow \rightarrow Mg - \overline{X} \end{array} \rightarrow RCN + R'H + MgXCl$$

It is of interest to note that if the "syn" configuration* is assigned to ald-chlorimines,

it might appear that a cyclic mechanism⁴ would be applicable to the elimination reaction. A preliminary experiment[†] has shown, however, that an *anti* compound,

also eliminates HX in the presence of a Grignard reagent. This shows that ald-chlorimines do not need to react by a cyclic mechanism.

* No ald-chlorimine has been isolated in two geometrically isomeric forms. It seems likely that the configuration of the ald-chlorimines isolated is the more stable "syn" structure.

⁴ In this connection see JOHNSON, Gilman's "Organic Chemistry," John Wiley and Sons, **1938**, Vol. I, pp. 1636–1651.

 \uparrow A preliminary experiment with acetyl- β -3,4-methylenedioxybenzaldoxime and ethylmagnesium bromide gave a 25 per cent. yield of the corresponding nitrile.

EXPERIMENTAL

Reactions of ald-chlorimines with Grignard reagents.-In general, these reactions were carried out according to the following procedure. The ald-chlorimine (.025-.07 mole) prepared and purified as previously described,⁵ was dissolved in 100-200 cc. of dry ether and the solution brought to the desired temperature, which in most cases was 0°. To this solution was added, drop by drop, with stirring, a molar equivalent of Grignard reagent which was prepared and analyzed in the usual manner,⁶ and cooled to the temperature of the chlorimine solution. A precipitate of RCH=NMgX formed, but in certain cases, in which a rather large amount of ether was used, a portion of this nitrogen-magnesium compound remained in solution. After standing a few hours the reaction mixture was filtered, and the nitrogenmagnesium compound in the funnel was hydrolyzed to aldehyde. The filtrate usually gave a faint test for active chlorine. Analysis of the filtrate for active chlorine indicated that about 10 per cent. of the chlorimine remained. This was converted to aldehyde by shaking the solution with hydrochloric acid, which also hydrolyzed the nitrogen-magnesium compound that was present in the ether solution. The ether layer was separated and allowed to stand with saturated sodium bisulfite solution for 24-36 hours. In certain cases, the ether was first evaporated, and the residue was allowed to stand with the bisulfite solution. The aldehydebisulfite addition compound was collected by filtration and decomposed with sodium carbonate to obtain the aldehyde. Nitrile was obtained by evaporation of the ether solution. The solid nitriles and aldehydes were identified by the mixture melting point method. The liquid aldehydes were converted into their corresponding semicarbazones or phenylhydrazones. The percentage yields of nitrile and nitrogenmagnesium compound (including that isolated as aldehyde) are given in the table.

In the reaction of 4-chlorobenzalchlorimine (12 g.) with 4-chlorophenylmagnesium bromide, the ether filtrate, obtained by filtering off the nitrogen-magnesium compound from the reaction mixture, was fractionally distilled. The ether was distilled off on a water bath. The oily residue was transferred to a Claisen flask with a teninch side-neck fractionating column, and was distilled under reduced pressure. A small fraction of chlorobenzene (boiling at 130–132° at atmospheric pressure), and a higher-boiling fraction, which solidified in the condenser, were collected. The latter melted at 52°, and was identified as dichlorobenzene. A dark-colored residue was left in the flask. When this residue was fractionally crystallized from acetone, alcohol, and water, 4-chlorobenzonitrile was isolated. 4-Chlorobenzaldehyde was obtained by hydrolysis of the nitrogen-magnesium compound which was removed by filtration from the original reaction mixture. The yields of these products are given in the table. No other pure product could be isolated.

Reaction of 4-chlorobenzalchlorimine with phenyllithium.—Phenyllithium solution was prepared and analyzed according to the method of Gilman, Zoellner, and Selby.' Fifty cc. of this solution (.025 mole) was added slowly to an equivalent of the chlorimine in 100 cc. of ether at 0° . After an hour the solution, together with the small precipitate present, was shaken with acid, and the ether layer was allowed to stand with bisulfite solution for 36 hours. The aldehyde-bisulfite addition compound which formed was collected by filtration and decomposed with sodium carbonate. A yield of 34 per cent. of 4-chlorobenzaldehyde was obtained in this way. A 20 per cent. yield of the corresponding nitrile was obtained by evaporation of the ether solution.

⁵ HAUSER, GILLASPIE, AND LEMAISTRE, *ibid.*, 57, 567 (1935).

⁶ See Gilman, Zoellner, and Dickey, *ibid.*, **51**, 1577 (1929).

⁷ GILMAN, ZOELLNER, AND SELBY, *ibid.*, **54**, 1957 (1932).

SUMMARY

1. A study has been made of the reactions of ald-chlorimines with certain Grignard reagents.

2. It has been shown that in the presence of these reagents ald-chlorimines undergo two types of reaction. In one, the Grignard reagent functions as a base, removing hydrogen chloride from ald-chlorimines to form nitriles, while in the other, the chlorine of the chlorimine is substituted by --MgX.

3. These types of reaction are discussed.