[Contribution from the Chemical Laboratory of the University of Illinois.]

THE ACTION OF THE GRIGNARD REAGENT ON THIOCYANATES.

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In a previous paper, a review was given of the various reactions between the Grignard reagent and those organic compounds which contain a cyan radical. In addition, it was shown that cyanamides were readily converted into amidines[1] by the action of the Grignard reagent. In this communication the action of the Grignard reagent on alkyl thiocyanates is described. Two main reactions have been shown to take place according to the following equations.

$$\mathrm{RSCN + RMgBr \longrightarrow RSR + MgBrCN}$$

$$\mathrm{RSCN + RMgBr \longrightarrow \underset{\substack{\downarrow \\ RSH}}{RSMgBr} + RCN}$$

Excess (3 moles) of Grignard reagent was always used. It has been found that with aliphatic thiocyanates and the Grignard reagent, a mixture of thio-ether and mercaptan is produced. By the usual method of addition, namely, of the thiocyanate to the Grignard reagent, the yield of mercaptan is higher than when the Grignard reagent is added to the thiocyanate. In the same way, the yield of thio-ether is lower in the former and higher in the latter case. If, after the Grignard reagent and thiocyanate are mixed, the solid and the ether solution are worked up separately, as would be expected, the ether solution yields chiefly thio-ether and the solid material yields chiefly mercaptan.

If an aromatic Grignard mixture is used with the thiocyanates, the second reaction is the principal one almost to the exclusion of the first.

It might be expected that the RCN produced in the second equation would react with the excess of Grignard reagent to give an addition compound that on subsequent decomposition would yield a ketone.

$$\mathrm{RCN + RMgBr \longrightarrow RC(NMgBr)R \longrightarrow RCOR.}$$

Such a reaction was shown to take place when phenyl magnesium bromide was employed. Upon decomposition of the reaction mixture with hydrochloric acid, a solid, the hydrochloride of benzophenone-imide, separated, insoluble both in the ether and in the hydrochloric acid layers. Moreover, in the ether layer, a certain amount of benzophenone was obtained. With an aliphatic Grignard mixture, the cyanides produced would be converted into unstable imide hydrochlorides which would yield volatile ketones that could not be separated from the large amount of ether used as a solvent. None of these ketones was isolated when aliphatic Grignard reagent was used.

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[1] This Journal, 38, 2768 (1916).

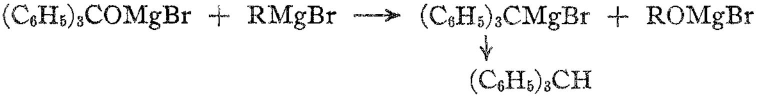
The yields of thio-ethers and mercaptans are small when the Grignard reagent and thiocyanate are of low molecular weight, due to the fact that the products are volatile with the ether which is used as a solvent and thus easily lost. However, as the molecular weights of the Grignard reagent and the thiocyanate increase, the yields of the thio-ethers and mercaptans become better. The use of this reaction for the preparation of either thio-ethers or mercaptans can hardly be recommended because mixtures are always obtained and the separation of the 2 products by fractionation is necessary.

The action of phenyl-magnesium bromide on benzoyl cyanide was studied. Several reactions took place simultaneously with the production of triphenyl-carbinol, triphenyl-methane and benzoic acid. The formation of the triphenyl-carbinol may be easily explained by the following equations.

$$C_6H_5COCN + C_6H_5MgBr \longrightarrow C_6H_5COC_6H_5 + MgBrCN$$

$$C_6H_5COC_6H_5 + C_6H_5MgBr \longrightarrow (C_6H_5)_3COMgBr \longrightarrow (C_6H_5)_3COH$$

The triphenyl methane is probably formed as follows,



$$(C_6H_5)_3COMgBr + RMgBr \longrightarrow \underset{\displaystyle (C_6H_5)_3CH}{\underset{\downarrow}{(C_6H_5)_3CMgBr}} + ROMgBr$$

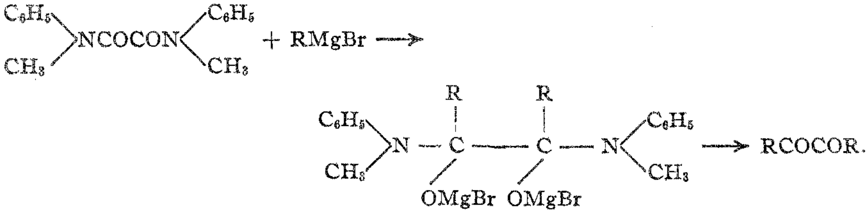
The formation of this compound in reactions of an analogous nature has been observed by previous investigators.[1] The benzoic acid probably comes from the hydrolysis of benzoyl cyanide.

If, instead of 3 moles of Grignard reagent, only one mole is used, triphenyl-acetonitrile, triphenyl-methane and benzoic acid are formed.

$$C_6H_5COCN + C_6H_5MgBr \longrightarrow (C_6H_5)_2C(OMgBr)CN$$

$$(C_6H_5)_2C(OMgBr)CN + C_6H_5MgBr \longrightarrow (C_6H_5)_3CCN + MgBr_2 + MgO.$$

Simultaneous with the study of the Grignard reagent on benzoyl cyanide, which it was hoped would yield 1,2-diketones, the action of the Grignard reagent on dimethyl-oxanilide was investigated in order to obtain diketones as follows.



$$\begin{matrix}C_6H_5\\ CH_3\end{matrix}\!\!>NCOCON<\!\!\begin{matrix}C_6H_5\\ CH_3\end{matrix} + RMgBr \longrightarrow$$

$$\begin{matrix}C_6H_5\\ CH_3\end{matrix}\!\!>N-\overset{R}{\underset{OMgBr}{C}}-\overset{R}{\underset{OMgBr}{C}}-N<\!\!\begin{matrix}C_6H_5\\ CH_3\end{matrix} \longrightarrow RCOCOR.$$

The results showed, however, that no matter how large an excess of Grignard reagent was used only one of the carbonyl groups reacted;

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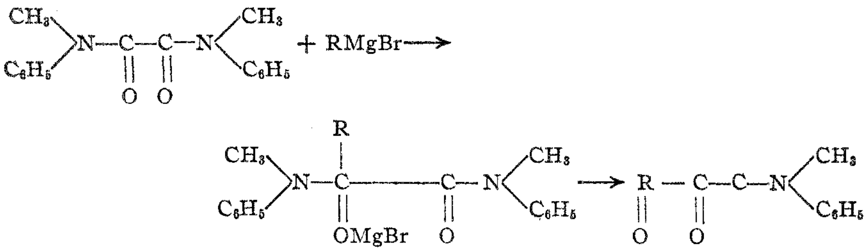
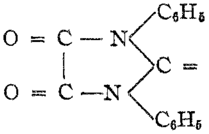
[1] This Journal, 39, 2012 (1916).

consequently, on decomposition, the methylphenyl amides of α-keto acids were produced.



The nonreactivity of the second carbonyl is probably due to steric hindrance. That both carbonyls do not react is strange, when it is considered that vinylidene-oxanilide[1]  with methyl- or ethyl-magnesium halides is reported to give, respectively, diacetyl and dipropionyl, although no details or yields are given.

Experimental.

Isoamyl Thiocyanate and Ethyl-Magnesium Bromide.

Forty g. (1 mol) of *iso*-amyl thiocyanate and an equal volume of dry ether were added slowly to a well-cooled solution of 3 moles of ethyl-magnesium bromide (2.3 g. of magnesium and 105 g. of ethyl bromide). After the reaction mixture had stood at room temperature for 2 hours, the ether was decanted from the solid material into a flask and treated with hydrochloric acid. When the ether layer, separated and dried over anhydrous sodium sulfate, was fractionally distilled, the main portion, which boiled between 158° and 161°, proved to be ethyl-*iso*-amyl sulfide. The solid material from the original reaction mixture was decomposed with hydrochloric acid and extracted with ether. By fractional distillation, the main portion boiled between 120° and 122° and proved to be *iso*-amyl mercaptan.

If the ethyl-magnesium bromide was added to the *iso*-amyl thiocyanate and the reaction mixture was allowed to stand, when it was decomposed in the usual way, fractionation of the product into definite substances was more difficult. The amount of mercaptan was very small and, in addition to the main product, *iso*-amyl-ethyl sulfide, a higher boiling portion was obtained which, on analysis proved to be di-*iso*-amyl disulfide.

Isoamyl Thiocyanate and Propyl-Magnesium Bromide.

One mole of *iso*-amyl thiocyanate was allowed to react with 3 moles of propyl-magnesium bromide as described under the reaction with ethyl-

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[1] *Ber.*, 40, 186 (1907).

magnesium bromide. The reaction mixture, without separating the solid and the ether, was then decomposed directly with hydrochloric acid and the ether layer separated, dried and fractionally distilled. Two main fractions were obtained, one boiling between 118° and 122° consisted of *iso*-amyl mercaptan; and the other boiling between 179° and 181° at 740 mm. (d_{20} 0.851; n_D^{20} 1.4495) was *iso*-amyl propyl sulfide.

Calc. for $C_8H_{18}S$: S, 21.3. Found: S, 21.9.

Isobutyl Thiocyanate and Ethyl-Magnesium Bromide.

One mole of thiocyanate and 3 moles of the Grignard reagent were allowed to react as described above. The reaction mixture was treated with hydrochloric acid. *Iso*-butyl mercaptan and ethyl-*iso*-butyl sulfide were obtained, but the volatility of these products with ether, caused the yields to be very small.

Heptyl Thiocyanate and Ethyl-Magnesium Bromide.

By the interaction of these 2 substances, heptyl mercaptan boiling between 174° and 176° and heptyl-ethyl sulfide boiling between 188° and 192° at 732 mm. (d_{20} 0.871; n_D^{20} 1.4518) were obtained.

Calc. for $C_9H_{20}S$: S, 20.0. Found: S, 20.1

Isoamyl Thiocyanate and Phenyl-Magnesium Bromide.

One mole of *iso*-amyl thiocyanate was added to 3 moles of phenylmagnesium bromide. Upon treatment of the reaction mixture with hydrochloric acid, a large amount of yellow solid still remained undecomposed. This was filtered and purified by dissolving it in chloroform and precipitating it with dry ether. It did not melt below 240°, was insoluble in water, in hydrochloric acid and in ether. Analysis showed it to be the hydrochloride of benzophenone-imide. When it was warmed with a solution of sodium hydroxide and extracted with ether, benzophenone was obtained.

The ether layer obtained by the decomposition of the original reaction mixture was dried and distilled. In this way, small amounts of *iso*-amyl mercaptan boiling between 120° and 122°, phenyl-*iso*-amyl sulfide and benzophenone were isolated.

Benzyl Thiocyanate and Isobutyl-Magnesium Bromide.

By the interaction of one mole of thiocyanate and 3 moles of the Grignard reagent, a product was obtained which, by careful fractionation, gave benzyl mercaptan boiling between 194° and 195° and benzyl-*iso*-butyl sulfide, a yellowish oil, boiling between 243° and 244° (d_{20} 0.968; n_D^{20} 1.4912).

Calc. for $C_{11}H_{16}S$: S, 17.6. Found: S, 17.0.

Benzyl Thiocyanate and Phenyl-Magnesium Bromide.

After allowing one mole of the thiocyanate and 3 moles of phenylmagnesium bromide to react, the mixture was decomposed with hydrochloric acid. An insoluble substance separated which was the hydrochloride of benzophenone-imide. Upon fractional distillation the ether solution yielded benzyl mercaptan and benzophenone.

Benzyl Thiocyanate and Ethyl-Magnesium Bromide.

When one mole of the thiocyanate and 3 moles of the ethyl-magnesium bromide reacted, and the solid and the ether were worked up separately, the substances isolated were benzyl-ethyl sulfide, boiling between 218° and 220° and benzyl mercaptan boiling between 194° and 195°.

Benzoyl Cyanide and Phenyl-Magnesium Bromide.

An ether solution of 32.5 g. (one mole) of benzoyl cyanide was allowed to run slowly into an ice-cooled ether solution of phenyl-magnesium bromide (78 g. of phenyl bromide and 12 g. of magnesium). A liter of ether was used as solvent. When this product was treated with hydrochloric acid in the usual way, the ether gave a solid which, on purification from alcohol, proved to be triphenyl carbinol, m. p. 159°. The ether mother-liquor yielded an impure solid, which on purification from benzene, melted at 93° and was triphenyl methane.

If instead of using such a large volume of ether as a solvent only 500 cc. was used, the reaction took place in a different manner; after evaporation of the ether, if the residue was fractionally distilled, an excess of bromobenzene, together with triphenylmethane and benzoic acid were the products obtained.

When benzoyl cyanide and phenyl-magnesium bromide were allowed to react in the proportion of 1 : 1, the ether solution submitted to fractional distillation, gave benzophenone, benzoic acid, and triphenylacetonitrile. The yields were poor.

Benzoic acid and a small amount of substance which was probably phenyl-diethyl-aceto-nitrile were isolated when benzoyl cyanide and ethylmagnesium bromide reacted in the proportion of one mole to 3 moles.

Derivatives of Dimethyl-Oxanilide.

Dimethyl-oxanilide.[1]—Four parts of technical monomethyl-aniline was dissolved in an equal volume of benzene. This solution in a flask attached to a reflux condenser was cooled with a slush of ice and water, and one part of oxalyl chloride dissolved in an equal volume of benzene was allowed to drop slowly from a separatory funnel through the condenser. After all of the oxalyl chloride had been added, the reaction mixture was allowed to stand in an open dish until the benzene evaporated. The solid which remained was treated with cold water to dissolve the methyl-aniline hydrochloride and the crystals remaining were filtered by suction, washed thoroughly with water and dried. The dimethyloxanilide crystallized from 75% alcohol and melted at 110°. The yield is about 95%.

[1] *J. prakt. Chem.* 90, 275 (1914).

Methylanilide of α-Ketobutyric Acid.—To 4 moles of ethyl-magnesium bromide in dry ether one mole of dry dimethyl-oxanilide was added in small portions; during the addition, the reaction mixture should be kept cold and stirred constantly. As soon as the addition was completed, ice and dil. hydrochloric acid were added until the solution was clear. The ether layer was separated, dried over calcium chloride and distilled. A clear, yellow liquid, weighing 27 g. was obtained. Distilled under reduced pressure a light yellow oil was produced; b. p., 165° at 17 mm. In every case a considerable portion of decomposition product remained in the distillation flask.

Subs., 0.2551: 16.2 cc. N_2 at 25° and 770 mm.
Calc. for $C_{11}H_{13}O_2N$: N, 7.3. Found: 7.4.

Methylanilide of Pyruvic Acid.—To 4 moles of methyl-magnesium iodide, one mole of dimethyl-oxanilide was added gradually. The reaction products were worked up in the usual way; an ether solution was obtained which, on distillation, gave a brown oil. This oil solidified to a crystalline mass after 48 hours. The crystals were filtered with suction from the oil and washed first with a little petroleum ether and ether, and finally crystallized from the same mixture. White needles, melting at 83–84° were obtained.

Subs., 0.2230: 11.6 cc. N_2 at 24° and 765 mm.
Calc. for $C_{15}H_{13}O_2N$: N, 5.8. Found: 6.0.

Methylanilide of *p*-Toluyl formic Acid.—The reaction was carried out in the same way as the preceding one except that *p*-tolyl-magnesium bromide was used. Upon decomposition with acid, a solid product separated which was insoluble both in the ether layer and in the water layer. It was filtered, dried, and recrystallized from 85% alcohol. It melted at 128–29°.

Subs., 0.2485: 12.4 cc. N_2 at 24° at 752 mm.
Calc. for $C_{16}H_{15}O_2N$: N, 5.5. Found: 5.7.

Summary.

1. Alkyl thiocyanates react with the Grignard reagent to give a mixture of thio-ether and mercaptan.

2. Benzoyl cyanide (one mole) with phenyl-magnesium bromide (2 moles) give triphenyl carbinol and triphenyl methane; in the proportion one mole to one mole, the products are benzoic acid, benzophenone and triphenyl acetonitrile.

3. Dimethyl-oxanilide with excess of the Grignard reagent yields methylphenyl amides of α-ketonic acids.

URBANA, ILLINOIS.