CONCLUSIONS

The esterification of amido- and ester-amidophosphites with 1-(2-thieny1)-2,2,2-tri-chloroethanol gave the <math>1-(2-thieny1)-2,2,2-trichloroethy1 dialkyl- and 1-(2-thieny1)-2,2,2-trichloroethy1 alkylamidophosphites, which easily add sulfur or are oxidized to the corresponding thiophosphates and phosphates.

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SYNTHESIS OF ORGANOMAGNESIUM COMPOUNDS

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In connection with developing methods for the synthesis of organic compounds, in which organomagnesium compounds (Grignard reagents) play an important role, it seems of interest to examine the reaction for the formation of RMgHal and the by-product RR as a function of the experimental conditions and the nature of the halide.

Data exist in [1] on the effect of the addition rate of RHal on the yield of RMgHal, but the yields of the RR are not indicated. The possibility of the fast preparation of PhCH₂MgCl, and also of arylmagnesium halides, without decreasing their yield noticeably, was also mentioned. The fast preparation of EtMgBr is reported in [2]. Nevertheless, it was firmly asserted in the literature [3-7] that the RHal has to be added as slow as possible to the Mg in order to obtain good yields of the RMgHal and reduce the formation of the RR by the Wurtz reaction (WR).

Up to now the formation of RR when preparing Grignard reagents was depicted as being mainly due to the reaction of RMgHal with RHal [5, 8, 9]. However, even in 1903 it was shown [10] that this reaction does not go even on long refluxing of ether solutions of these compounds (except for the reaction with a halide of the allyl or benzyl type).

Recent studies [11, 12] confirmed the proposed [13] radical mechanism for the formation of Grignard and WR compounds.

 $RHal + Mg \rightarrow [R' + MgHal] \rightarrow RMgHal$ $2R' \rightarrow RR$

According to [14], the reaction $RM + RHal \rightarrow RR + MHal$, where M is an alkali metal, which also leads to the hydrocarbon RR, must also be regarded as being a nucleophilic substitution reaction, in which R⁻ is a nucleophilic reagent that displaces the Hal⁻ anion from RHal. As a result, the hydrocarbon RR is not formed here via dimerization of the radicals, thus differing from the WR, where it is understood that dimerization of the radicals occurs independent of their paths of origin.*

We studied the effect of the nature of the halogen, the RHal concentration, the RHal:Mg ratio, and the reaction time on the yield of RR. From Table 1 it can be seen that in the case of an alkyl chloride $(C_8H_{17}Cl)$ the yield of the WR product (cetane) is low and is little dependent on the chloride concentration; in the case of an alkyl bromide $(C_6H_{13}Br)$ the yield of dodecane varies in a wide range and is quite dependent on the RBr concentration. This is explained by the difference in the rates of reaction of Mg with RCl and RB. When added at one time, $C_8H_{17}Cl$ reacts in 30-40 min, whereas in the case of $C_6H_{13}Br$ the *This difference was not mentioned in the review [15], where the WR is regarded as being reaction between the organic Na or Li compound and alkyl halide, and not as reaction between alkyl halide and either an alkali or alkaline-earth metal [16].

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Expt.	Halide	A mount of RHal, moles	Amount of Mg, g- atom	Time, min		Yield of RR	
No.				addition of RHa1	reaction	g	moles
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	$\begin{array}{c} C_8H_{17}Cl\\ The same\\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $	$\begin{array}{c} 0,5\\ 0,5\\ 1,0\\ 0,5\\ 1,0\\ 0,5\\ 1,0\\ 0,5\\ 1,0\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0$	$\begin{array}{c} 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\ 0,5\\$	75 1 1 100 1 1 120 1 1 90 1 1 60 1 1	$\begin{array}{c} 105\\ 60\\ 40\\ 120\\ 20\\ 6\\ 140\\ 20\\ 25\\ 100\\ 10\\ 5\\ 60\\ 8\\ 4\end{array}$	2,03,04,31,59152,04,013109,13109,56,03,0	0,009 0,013 0,019 0,009 0,053 0,088 0,013 0,026 0,084 0,110 0,158 0,122 0,052 0,033 0,017
16) »	0,5	1,5	1	4	0	0

TABLE 1. Yield of Wurtz Reaction Product RR as a Function of the Nature of the Halide and Experimental Conditions

reaction is ended in 5-15 min. As a result, the less active chloride extends as it were the time of reaction with Mg and in this way lowers the "acting" concentration of R[•] on its surface, which leads to a decrease in the yield of RR and its low dependence on the RC1:Mg ratio. In the case of alkyl or aryl bromides the formation of RR is directly proportional to the RBr concentration and inversely proportional to the area of the Mg surface.

Consequently, the formation of RR is not determined by the stability of the radical (for example, $C_6H_5CH_2^{\circ}$ is stable, and $C_6H_{13}^{\circ}$ is unstable, but the yields of RR are quite close for both radicals), but rather by the concentration and reaction rate of RHal on the Mg surface, which explains the highest yield of RR from RI [1].

The radical character of the reaction of RHal with Mg is especially manifest in the case of PhBr. The slow addition of 0.5 mole of PhBr to 0.5 g-atom of Mg gives a small amount of diphenyl (5.2%). The yield of diphenyl doubles when reaction is fast, while with fast reaction using a double amount of PhBr (1 mole per 0.5 g-atom of Mg) the absolute amount of diphenyl is more than 6 times the amount obtained in the case of slow reaction using an equimolar ratio of Mg and PhBr (see Table 1, Expts. 7-9). Since PhBr does not react with RMgHal, the diphenyl is formed only via the radical WR, the intensity of which is proportional to the PhBr concentration, referred to per unit area of the Mg surface. The yield of diphenyl is approximately equal to the yield of dodecane (from $C_6H_{13}Br$ and Mg).

Butylbenzene is formed when Mg reacts with a mixture of PhBr and BuBr. Isomerization of the butyl radical to the sec-butyl radical is not observed here; the reaction rates of ArBr and AlkBr with Mg are the same, since 0.25 mole of PhBr reacts when a mixture of 0.5 mole of PhBr and 0.5 mole of BuBr is reacted with 0.5 g-atom of Mg.

In the case of compounds with a benzylic Cl atom (benzyl chloride, methyl 3-chloro-3-phenylpropyl ether) the use of a double amount of Mg practically suppresses the WR and assures the formation of RMgCl under very fast conditions in $\sqrt{90\%}$ yield: the reaction with 0.5 mole of the chloride is ended in 3-4 min.

The formation of dibenzyl from $PhCH_2Cl$ and Mg under mild conditions (ether, 5 min) proceeds by the radical mechanism, inasmuch as reaction by the S_N^2 mechanism does not occur since when an ether solution of BuMgBr is refluxed with $PhCH_2Cl$ for 5 min the latter was recovered unchanged.

In the synthesis of olefins from RMgHal and CH_2 =CHCH₂Hal (reaction of the SN^2 type) it is necessary to use allyl bromide, which permits ending the reaction within 15 min (including the addition time). In the synthesis of diallyl it was recommended in [5] to add the allyl chloride (1 mole) to the Mg (0.5 g-atom) as fast as possible, in 1 h*; in our opinion this rate is very slow.

^{*}The indicated yield of diallyl of 46-48 g does not correspond to reality, since it exceeds the theoretical yield by 12-17%.

The brisk reaction of allyl bromide with Mg is caused to equal degree by the formation of $CH_2=CHCH_2MgBr$ and its subsequent conversion to diallyl, since α -nonene is formed in 87% yield when an ether solution of allyl bromide is heated with $C_6H_{1.3}MgBr$ for 5 min.

An examination of the obtained data permits changing the held opinion as to how the reactions of alkyl(aryl) halides with Mg should be run. Here it is desirable to run the Grignard reaction at the fastest possible rate of adding the halide (0.5-2 moles in 1-10 min). The process is controlled by periodic cooling of the flask, not permitting too violent ether reflex. If solid CO₂ is lacking for the preparation of the cooling mixture it is possible to use an ice-salt mixture, in which connection the reaction is extended somewhat. However, also in this case the time of forming the Grignard reagent and, in many cases, the time of running the second phase of the reaction, lie within 10-30 min for the amounts of reactants usually used in the laboratory (0.5-2 moles). The easiest to control are the alkyl chlorides, but they require up to 30 min for complete reaction if they are added at one time; alkyl bromides, aryl bromides, and benzyl chloride and its α -alkyl derivatives are added as fast as possible in one to several minutes.

The proposed intensification is not suitable for running the "Grignard reaction with association," since the rapid addition of an inactive halide as a mixture with an equimolar amount of an active halide does not lead to the formation of RMgHal from the inactive halide. As a result, the role of the active component does not consist in a mechanical cleansing of the Mg surface.

EXPERIMENTAL

Reaction of Hexylmagnesium Bromide with Allyl Bromide. To 0.45 mole of $C_6H_{13}MgBr$ in 200 ml of ether was added at one time 60.5 g (0.5 mole) of $CH_2=CHCH_2Br$. Vigorous reflux of the reaction mixture was continued for 5 min (the reaction was controlled by periodic cooling with a solid CO_2 -acetone mixture), and then the mixture was cooled, decomposed rapidly with 1:1 HCl solution, and distilled. We obtained 50 g (87%) of 1-nonene with bp 147°C (78°/80 mm).

<u>Reaction of Butylmagnesium Bromide with Benzyl Chloride.</u> To 0.5 mole of BuMgBr in 200 ml of ether was added at one time 63 g (0.5 mole) of PhCH₂Cl, after which the mixture was refluxed for 5 min, decomposed with 1:1 HCl solution, and distilled. We recovered 60 g of PhCH₂Cl.

<u>6-Methoxy-4-phenyl-1-hexene.</u> To 26 g (1.1 g-atoms) of Mg in 200 ml of abs. ether was added 1 ml of MeI and, after reaction had started, 100 g (0.545 mole) of $C_{6}H_{5}CHC1CH_{2}CH_{2}OCH_{3}$ in 100 ml of abs. ether was added in several minutes. The reaction was controlled by periodic cooling with a solid CO_{2} -acetone mixture. The reaction was ended in 10 min after starting to add the chloride; the solution was decanted from the Mg, the Mg was washed with 2×40 ml of ether, and to the obtained Grignard reagent was added in several minutes 99 g (0.8 mole) of CH_{2} =CHCH₂Br (periodic cooling with a solid CO_{2} -acetone mixture was required). After 10 min the mixture was decomposed with 1:1 HCl solution and then distilled to give 64 g (62%) of 6-methoxy-4-phenyl-1-hexene.

<u>Fast Reaction of Chlorobenzene and Butyl Bromide with Mg.</u> To 30 g (1.25 g-atoms) of Mg in 100 ml of abs. ether was added 1.5 ml of MeI and, after reaction had started, a solution of 56 g (0.5 mole) of PhCl and 69 g (0.5 mole) of BuBr in 200 ml of abs. ether was added in 1 min. Brisk reaction ended within 10 min (periodic cooling with a solid CO_2 -acetone mixture was required). After decomposing with 1:1 HCl solution and distillation we obtained 55 g of PhCl; diphenyl was not detected.

<u>Reaction of Phenylmagnesium Bromide with Bromobenzene.</u> To 0.5 mole of PhMgBr, obtained as described in Expt. 7 (see Table 1), was added 78 g (0.5 mole) of PhBr and the mixture was heated for 30 min at 80°. After decomposing with 1:1 HCl solution and distillation we obtained 3 g of diphenyl (cf. with Expt. 9).

<u>Reaction of Hexylmagnesium Bromide with Hexyl Bromide.</u> A mixture of 0.5 mole of C_6H_{13} -MgBr, obtained as described in Expt. 4 (see Table 1), and 83 g (0.5 mole) of C_6H_{13} Br was heated for 30 min at 55°. After the usual workup we obtained 4 g of dodecane (cf. with Expt. 6).

Butylbenzene by the Wurtz Reaction. To 12 g (0.5 g-atom) of Mg in 100 ml of abs. ether was added in 2 min (with periodic cooling using a solid CO_2 -acetone mixture) a solution of

78 g (0.5 mole) of PhBr and 68 g (0.5 mole) of BuBr in 100 ml of abs. ether. All of the Mg reacted in 8 min (including the time of adding the halides). After the usual workup we obtained 36 g (0.23 mole) of the starting PhBr and 1 g of a heavy, partially crystalline residue. After filtering the diphenyl (0.5 g), analysis of the filtrate by GLC disclosed the presence of butylbenzene and the absence of sec-butylbenzene. For comparison 0.5 mole of PhMgBr, obtained as described in Expt. 7 (see Table 1), was heated for 8 min with 68 g (0.5 mole) of BuBr, after which the mixture was decomposed with 1:1 HCl solution, the ether was distilled off, the residue was filtered from the diphenyl, and the absence of butylbenzene in the filtrate was established by GLC.

CONCLUSIONS

1. The radical character of the reaction of Mg with RHal, and also of the formation of RR by the Wurtz reaction, was confirmed.

2. The dependence of the yields of RR on the RHal:Mg ratio, the nature of the halide, and the reaction time was studied, and it was shown that the process for the preparation of organomagnesium compounds can be hastened.

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