

CXL.—*Accelerated Formation of Magnesium Alkyl and Aryl Haloids.*

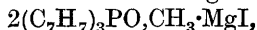
By HARRY HEPWORTH.

IN carrying out syntheses with the aid of the Grignard reagent it is customary to employ ethyl ether as the solvent medium in which the required magnesium alkyl or aryl haloid is prepared, and for a considerable period the ethers were the only class of compounds which were known to catalyse the formation of magnesium alkyl haloids from their components. From the initial analysis by Blaise (*Compt. rend.*, 1901, **132**, 839) it was concluded that these etherates were best represented by the formula $\text{RMgX}, \text{Et}_2\text{O}$. In view of the fact that Grignard showed in his

dissertation (L'Univ. de Lyon, 1901) that the whole of the ether could not be removed from the compound $\text{MgMeI}, \text{Et}_2\text{O}$ by heating for several days in a vacuum, Baeyer and Villiger (*Ber.*, 1902, **35**, 1201) regarded this compound as a true oxonium compound, $\text{Et} > \text{O} < \begin{smallmatrix} \text{MgMe} \\ \text{I} \end{smallmatrix}$. This structure admits of isomerism, and Tschelinzeff (*Compt. rend.*, 1907, **144**, 88) claimed to have obtained evidence of such isomerism. Grignard, however, has claimed (*Bull. Soc. chim.*, 1907, [iv], **1**, 256) that his formula $\text{Et} > \text{O} < \begin{smallmatrix} \text{MgI} \\ \text{Me} \end{smallmatrix}$ (*Compt. rend.*, 1903, **136**, 1260), also admits of the existence of isomerides, since the two additional valencies of the oxygen atom have not the same value as the original two.

In 1904, Tschelinzeff (*Ber.*, 1904, **37**, 4534) came to the conclusion that the ether plays the part of a catalyst, forming an additive compound with the alkyl haloid, which subsequently reacts with magnesium to form magnesium alkyl haloid with regeneration of the original ether, and further, that the ether may be replaced by tertiary amines. Somewhat later (*Ber.*, 1908, **41**, 646), he claimed to have isolated "aminates" of the general formula $\text{R}_3\text{N}, \text{MgRX}$ and "amine etherates" of the type $\text{R}_3\text{N}, \text{MgRX}, \text{Et}_2\text{O}$. The use of tertiary amines instead of ethers has not met with much success in the author's experience. Several investigators have, however, shown that tertiary bases react with magnesium alkyl haloids in the presence of ether to form double compounds containing the base, magnesium alkyl haloid and sometimes ether also (Sache, *Ber.*, 1904, **37**, 3088; Oddo, *Atti R. Accad. Lincei*, 1904, [v], **13**, 106; Houben, *Ber.*, 1905, **38**, 3017; Senier, P., 1905, **21**, 327; T., 1905, **87**, 1469).

In the course of their investigation on oxonium compounds, Pickard and Kenyon (T., 1906, **89**, 262) found that tribenzyl-phosphine oxide may replace ether in the formation of magnesium alkyl haloids, and succeeded in obtaining a compound,



in the crystalline condition. It may also be pointed out that these authors prefer to write the formulæ of the Grignard reagents as $\text{Et}_2\text{O} \dots \text{MgRX}$ in accordance with Werner's views of valency (*Annalen*, 1902, **322**, 296).

It has now been found that the alkyl sulphides accelerate the formation of magnesium methyl iodide, but not to such an extent as ether. Double compounds containing alkyl sulphide and magnesium methyl iodide are formed, but these have not been obtained in the crystalline condition. Similar results have been obtained with iodobenzene, but the reaction is very much slower than with

methyl iodide. In a similar way, it was found that diethyl selenide and dimethyl telluride accelerated the formation of magnesium methyl iodide to about the same extent as diethyl sulphide, but that all these compounds are less effective than ethyl ether.

If the accelerating action of ether is to be explained on the grounds that the oxygen atom has a tendency to become quadri-valent, and that the accelerating influence is to be measured by the relative stability of these oxonium compounds, then it would be expected that the dialkyl sulphides, selenides, and tellurides would catalyse the reaction in ascending order of magnitude. The results obtained show that the capability to form compounds of higher valency, whilst it may be the initial cause of the catalysing action, has very little effect on the speed of the reaction, and that ether is unique among these compounds as regards its marked catalytic action.

Experiments were now carried out in a similar manner in order to ascertain if the simple sulfoxides exerted a catalytic influence on the formation of magnesium methyl iodide. For this purpose, diphenyl sulfoxide and diisooamyl sulfoxide were prepared, and it was found that both these compounds were catalysts and that the double compounds formed were moderately soluble in hot benzene, but, on cooling, were deposited in an amorphous condition. From an estimation of the magnesium and the iodine content of these compounds, they would appear to conform with the general formula $2R_2SO, MgMeI$, but as the compounds were not obtained in the crystalline form, the results are not convincing. It is, however, evident that the sulfoxides are in this respect comparable with the phosphine oxides (Pickard and Kenyon, *loc. cit.*). The catalysing action of the sulfoxides is rather more pronounced than that of the sulphides, and it is suggested that this is due to the presence of an oxygen atom in the former compounds.

Similar experiments carried out with dimethylsulphone and diphenylsulphone showed that these compounds exerted no catalysing action on the formation of magnesium methyl iodide. Pickard and Kenyon (T., 1907, **91**, 896) have shown that whilst diphenyl sulfoxide readily forms additive compounds, diphenylsulphone

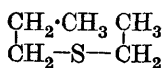
does not do so, and have suggested the formula $R_2:S \begin{array}{c} \diagup O \\ \diagdown O \end{array}$, or less

likely $R_2:S \begin{array}{c} O \\ \vdots \\ O \end{array}$ (where the dots represent subsidiary valencies) for

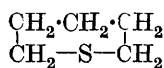
the sulphones. Since the sulphones are stable, neutral compounds, in which both oxygen atoms are firmly attached to sulphur, the

author prefers the latter formula rather than the former, which portrays the sulphones as peroxides. The inability of the sulphones to catalyse the formation of magnesium methyl iodide may be due to the influence of the additional oxygen atom, whereby the greater part of the residual affinity of each oxygen atom is mutually compensated.

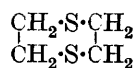
It was now decided to prepare a series of heterocyclic sulphur compounds in order to ascertain whether such substances exerted any catalysing influence, and whether any relationship existed between the structure of these compounds, containing "unsaturated" sulphur atoms, to which a large amount of residual affinity is attributed, and the property of catalysing the formation of magnesium methyl iodide. For this purpose the following substances were prepared and examined :



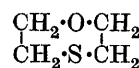
Ethyl *n*-propyl
sulphide.



Pentamethylene
sulphide.

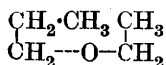


1 : 4-Dithian.

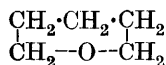


1 : 4-Thioxan.

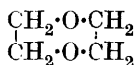
For comparative purposes, the following compounds containing oxygen in place of sulphur were prepared and examined :



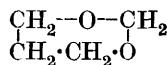
Ethyl *n*-propyl
ether.



Pentamethylene
oxide.



1 : 4-Dioxan.



1 : 3-Dioxan.

The method employed was to introduce 1 gram of the substance, 0.3 gram of magnesium, and 2 grams of methyl iodide into 50 c.c. of dry benzene, and to heat the mixture under reflux on a water-bath. A series of experiments was carried out each time, the series always including two blank experiments, with and without the addition of 1 gram of dry ether. It was found to be comparatively easy to ascertain when reaction had definitely set in, and the vigour with which decomposition ensued on the addition of ice-cold water at a constant rate gave a further confirmation as to the extent to which reaction had occurred. The results are more uniform in the case of the sulphur than the oxygen compounds, because the former react more slowly. The results obtained were as follows :

(1) It was found that the open-chain compounds, ethyl *n*-propyl ether and ethyl *n*-propyl sulphide, reacted more readily than pentamethylene oxide and sulphide respectively, from which it is evident that ring formation diminishes the catalytic activity of these compounds.

(2) 1 : 4-Dithian and 1 : 4-dioxan are more active than penta-

methylene sulphide and oxide respectively, whilst 1 : 4-dithian is almost as active as 1 : 4-dioxan, but both are much less active than ethyl *n*-propyl sulphide and oxide respectively. The marked unsaturation of 1 : 4-dithian and 1 : 4-dioxan may be attributed to the presence of two sulphur and two oxygen atoms respectively in the 1 : 4-position (Clarke, T., 1912, **101**, 1801). That the two oxygen atoms in 1 : 4-dioxan exert a mutual influence, the effect of which is to augment the basic function, has been shown by Faworsky (*J. Russ. Phys. Chem. Soc.*, 1906, **38**, 741), Paternò and Spallino (*Atti R. Accad. Lincei*, 1907, [V], **16**, 187) and others, who observed that 1 : 4-dioxan readily yields salts with sulphuric acid, bromine, iodine, picric acid, and mercuric chloride, whilst the corresponding open-chain compound, $\alpha\beta$ -dimethoxyethane, is neutral. The marked basic function of 1 : 4-dioxan does not confer any increased catalytic activity over ethyl *n*-propyl ether in the formation of magnesium methyl iodide.

(3) 1 : 4-Thioxan is more active than 1 : 4-dithian, its activity being almost equal to that of 1 : 4-dioxan. This again shows that the oxygen compounds are more active than the corresponding sulphur compounds, and that the oxygen atom is unique in its marked catalysing action. Smiles (T., 1909, **95**, 994) has shown that the sulphur atom in 3 : 5-diethoxy-1 : 4-thioxan is sluggish in its chemical functions, whilst Clarke (*loc. cit.*) has found that the velocity of reaction of bromoacetophenone with 1 : 4-thioxan is much slower than with pentamethylene sulphide and 1 : 4-dithian. If the catalysing action of 1 : 4-thioxan in the formation of magnesium alkyl haloids were due solely to the tendency of the oxygen and sulphur atoms to become quadrivalent, then it would be expected to be much less active than 1 : 4-dithian, especially since Clarke (*loc. cit.*) has shown that in compounds of the type $X < \begin{smallmatrix} \text{CH}_2 \cdot \text{CH}_2 \\ \text{CH}_2 \cdot \text{CH}_2 \end{smallmatrix} > Y$, where X and Y are both sulphur or both oxygen atoms, the effect of the mutual influence is to increase the reactivity, whilst if X and Y are sulphur and oxygen respectively, the reactivity is depressed.

(4) No difference in reactivity could be detected between 1 : 3-dioxan and 1 : 4-dioxan. The former compound only forms an unstable picrate and yields a crystalline double compound with mercuric chloride, whilst 1 : 4-dioxan is much more basic. This again indicates that the catalytic activity is not due solely to the unsaturated nature of the oxygen atoms in these compounds. Both compounds are much less active in their catalysing action in the formation of magnesium methyl iodide than is ethyl *n*-propyl ether.

It is not proposed to deal here with the voluminous literature

which has been published on the part played by ether in the formation of Grignard reagents. Although Tingle (*Amer. Chem. J.*, 1907, **37**, 483) has shown that ether is not essential, provided sufficient time is allowed, and Spencer (T., 1908, **93**, 68) has shown that magnesium and phenyl iodide react at the boiling point of the latter, yet ether does enormously accelerate the formation of Grignard compounds, and none of the sulphur compounds examined during this investigation is so effective. Tschelinzeff's view (*Ber.*, 1904, **37**, 4534) that a mere trace of ether is sufficient, has not been substantiated in the author's experience, and it should be pointed out that the fact that ether is a catalyst does not necessarily exclude the formation of "oxonium" compounds during the course of the reaction. Very little reliance can be placed on the analysis of these oxonium compounds, because, with the exception of the double compound formed between amyl ether and magnesium methyl iodide (Zerewitinoff, *Ber.*, 1908, **41**, 2244), and that between tribenzylphosphine oxide and magnesium methyl iodide (Pickard and Kenyon, *loc. cit.*), the majority of these compounds have only been obtained as amorphous solids. The results obtained in this paper show that ether is unique in its catalytic action, and that sulphur, selenium, and tellurium compounds, which show an increasing tendency to become quadrivalent, do not catalyse the formation of magnesium alkyl and aryl haloids to such an extent as the corresponding oxygen compounds.

EXPERIMENTAL.

Diethyl Sulphide.—This was prepared by the action of an excess of concentrated aqueous sodium sulphide on sodium ethyl sulphate. After removal of ethyl mercaptan by shaking with 40 per cent. aqueous potassium hydroxide, the product was dried over sodium and distilled over phosphoric oxide; b. p. 92—92.5°, d_{4}^{21} 0.8367.

Diisoamyl sulphide was prepared in a similar manner from potassium amyl sulphate and potassium sulphide; b. p. 215°, d_{4}^{20} 0.8433.

Ethyl n-propyl sulphide was prepared by the action of *n*-propyl bromide on an alcoholic solution of the sodium salt of ethyl mercaptan (Strömholm, *Ber.*, 1900, **33**, 830). After distillation in steam, the mercurichloride was precipitated as a heavy oil by the addition of an excess of dilute mercuric chloride solution. The oil, after being washed with water, was decomposed by distillation with aqueous sodium sulphide solution. The sulphide was then dried by distillation over freshly fused potassium hydroxide, and repeatedly distilled over metallic sodium; b. p. 116—117°, d_{4}^{20} 0.8446.

Pentamethylene Sulphide.—Thirty grams of α -dichloropentane, prepared by Braun's method (*Ber.*, 1904, **37**, 2918) were heated for four hours under reflux with a dilute alcoholic solution of about twice the calculated quantity of potassium sulphide. After distillation in steam, the product was precipitated as the mercurichloride, which was well washed with water and decomposed by distillation with aqueous sodium sulphide solution. The separated oil was distilled over freshly fused potassium hydroxide and then over sodium; b. p. 141—142° (Braun and Wallach, *Festschrift*, 1909, 381), d_4^{20} 0.98379.

1:4-Thioxan.—This compound was first obtained by Clarke (*T.*, 1912, **101**, 1806) by the action of dilute alcoholic potassium sulphide on $\beta\beta'$ -di-iodoethyl ether.

The thioxan used in this investigation was prepared from thiodiglycol (v. Meyer, *Ber.*, 1886, **19**, 3259) as follows: Thiodiglycol (30 grams) and concentrated sulphuric acid (1.25 grams) were heated together, when a moderate reaction ensued at 180° and the distillate obtained separated into two layers. The lower layer was removed and purified by conversion into the mercurichloride (m. p. 170°) and subsequent decomposition by potassium sulphide, followed by repeated distillation over freshly fused potassium hydroxide and sodium. The product boiled constantly at 148°; d_4^{20} 1.11744.

Diphenyl Sulphoxide.—This was prepared by the action of magnesium phenyl bromide on benzenesulphonyl chloride. The details of this preparation will be given in a later communication. After two crystallisations from benzene, the product melted at 69.8°.

Diisoamyl sulphoxide was obtained by the oxidation of diisoamyl sulphide, in acetone, with 30 per cent. hydrogen peroxide (Smiles, *T.*, 1908, **93**, 1833). After crystallisation from light petroleum, the product melted at 35°.

Diphenylsulphone was obtained by the action of benzene on benzenesulphonyl chloride in the presence of aluminium chloride (Beckurts and Otto, *Ber.*, 1878, **11**, 2066). After recrystallisation from benzene, it melted at 128° and boiled at 230°/17 mm.

Dimethylsulphone was prepared by the action of fuming nitric acid on dimethyl sulphoxide nitrate. After removal of the greater part of the nitric acid by heating on the water-bath, the syrupy mixture was solidified by cooling in a freezing mixture, pressed, crystallised from water, and the product dried in a vacuum over potassium hydroxide and phosphoric oxide; m. p. 109°, b. p. 238—240°.

Ethyl n-Propyl Ether.—Small pieces of metallic sodium were added to pure *n*-propyl alcohol until sodium *n*-propoxide began to separate. Ethyl iodide, equivalent to the sodium used, was then

added and the mixture heated under reflux for eight hours on a water-bath. On distillation, the fraction, b. p. 62—67°, was collected and repeatedly boiled with sodium until no further action took place. The pure ether distilled at 63° (Brühl, *Annalen*, 1880, 200, 177).

Pentamethylene Oxide.—Twenty grams of $\alpha\epsilon$ -dibromopentane, prepared and purified by Braun's method (*Ber.*, 1904, 37, 3210; 1905, 38, 2339), were converted into pentamethylene oxide by Clarke's method (*T.*, 1912, 101, 1802). After being dried with potassium hydroxide and sodium, it distilled at 87—88°.

1:4-*Dioxan* was prepared by heating a 4 per cent. solution of concentrated sulphuric acid in ethylene glycol on an oil-bath, according to the directions of Faworsky (*loc. cit.*). The distillate, which contained much acetaldehyde, was saturated with potassium hydroxide, the separated liquid distilled and repeatedly boiled under reflux with silver oxide. It was found necessary to treat the product repeatedly with silver oxide in order to remove the last traces of acetaldehyde. After separation and repeated distillation over freshly fused potassium hydroxide followed by distillation over sodium, a clear product, b. p. 101.5°, was obtained, which was free from aldehydes.

1:3-*Dioxan* was obtained from trimethylene glycol and trioxymethylene according to the method of Clarke (*loc. cit.*). After being repeatedly treated with silver oxide to remove aldehydes, a clear, colourless liquid, b. p. 105°, was obtained.

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