THE PREPARATION AND SOME REACTIONS OF 2,3,5,6-TETRACHLORO-PHENYLMAGNESIUM CHLORIDE *

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(Received December 11th, 1980)

Summary

The reaction of pentachlorobenzene with metallic magnesium in THF at 10—15°C gives after hydrolysis 1,2,4,5-tetrachlorobenzene (76%) and pentachlorobenzene (8%); after trimethylsilylation, 1,2,4,5-tetrachloro-3-(trimethylsilyl)benzene (74%), pentachloro(trimethylsilyl)benzene (8%) and 1,2,4,5-tetrachlorobenzene (6%); after iodination, 1,2,4,5-tetrachloroiodobenzene (44%), pentachloroiodobenzene (12%) and 1,2,4,5-tetrachlorobenzene (9%); and finally after carbonation, 2,3,5,6-tetrachlorobenzoic acid (58%). These products indicate that in the Grignard reaction a mixture of largely 2,3,5,6-tetrachlorophenylmagnesium chloride and some pentachlorophenylmagnesium chloride is formed. The formation of pentachlorophenylmagnesium chloride is explained on the basis of metal—hydrogen exchange reaction between 2,3,5,6-tetrachlorophenylmagnesium chloride and the unreacted pentachlorobenzene.

Introduction

We reported recently that 2,3,4-trichlorothiophene (I) reacts in THF with metallic magnesium in the presence of 1,2-dibromoethane as an entrainer to give an equimolar mixture of trichloro-2-thienylmagnesium halide (II) and 3,4-dichlorothiophene (III) [1]. There is some evidence to indicate that 3,4-dichloro-2-thienylmagnesium halide (IV) is formed as an intermediate which undergoes metal—hydrogen exchange with the rest of I to give II and III [1] (Scheme 1). ***
The facile nature of this metal—hydrogen exchange as compared to that involving unsubstituted thiophene under similar conditions is believed [2] to be due

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* In honor of Professor Henry Gilman for his many years of outstanding research and teaching in the field of organometallic chemistry.
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*** Cl indicates that all ring positions not masked with a substituent have a chlorine atom as substituent.
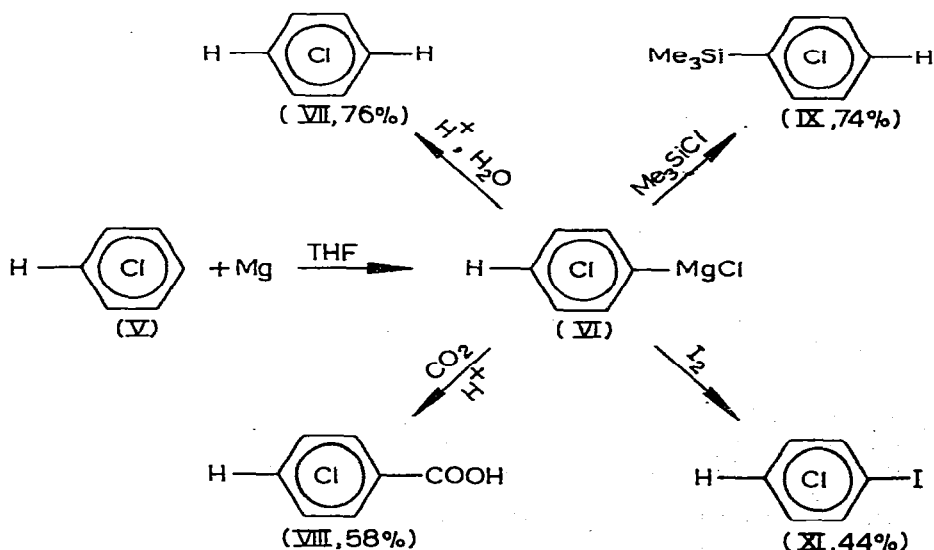
SCHEME 1
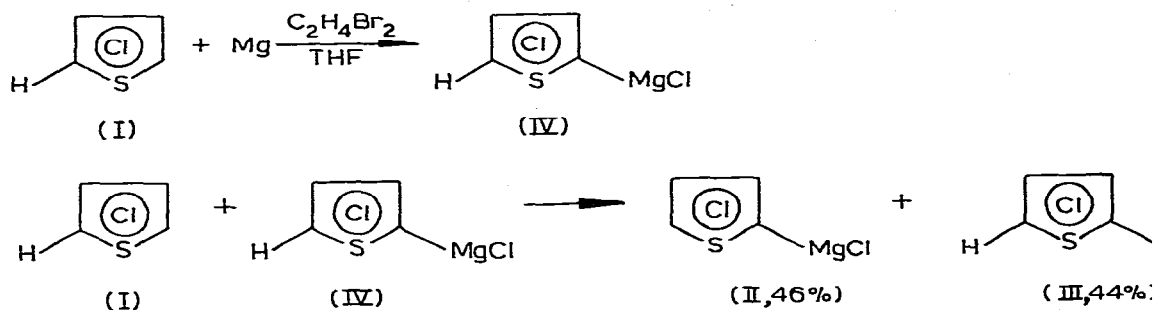
to the electron-withdrawing effect of the three nuclear chlorine atoms in I. In order to appreciate the influences of the nuclear sulphur atom in the metalation reaction, it was thought of interest to investigate a comparable reaction involving pentachlorobenzene and metallic magnesium.

We report here that the reaction of metallic magnesium with pentachloro-benzene (V) gives mainly 2,3,5,6-tetrachlorophenylmagnesium chloride (VI) and small amounts of products resulting from the metalation reaction viz., pentachlorophenylmagnesium chloride (XIII) and 1,2,4,5-tetrachlorobenzene (VII).

Results and discussion

Pentachlorobenzene (V) (x mol) reacts with magnesium (x g-at) in THF at 10—15°C to give, subsequent to hydrolysis, 1,2,4,5-tetrachlorobenzene (VII) and pentachlorobenzene (V) in 76 and 8% yield, respectively. Trimethylsilyla-tion of the reaction mixture affords 1,2,4,5-tetrachloro-3-(trimethylsilyl)-benzene (IX), pentachloro(trimethylsilyl)benzene (X) and VII in 74, 8 and 6%
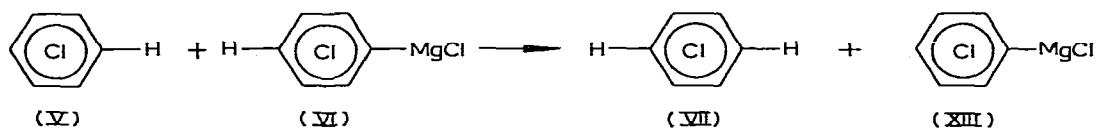
SCHEME 2

yield, respectively. Similarly, carbonation of the reaction mixture gives 2,3,5,6-tetrachlorobenzoic acid (VIII) as the only major product (58%) and iodination, 1,2,4,5-tetrachloro-3-iodobenzene (XI) and pentachloroiodo-benzene (XII) in 44 and 12% yield, respectively, and, additionally, 9% of VII. The formation of VII in the hydrolysis experiment, and of VIII, IX and XI in the other experiments, indicates that pentachlorobenzene reacts with magnesium to give 2,3,5,6-tetrachlorophenylmagnesium chloride (VI) in good yield (Scheme 2).

On the other hand the formation of X and XII indicates that some penta-chlorophenylmagnesium chloride (XIII) must also have been formed during the reaction of pentachlorobenzene with magnesium metal.
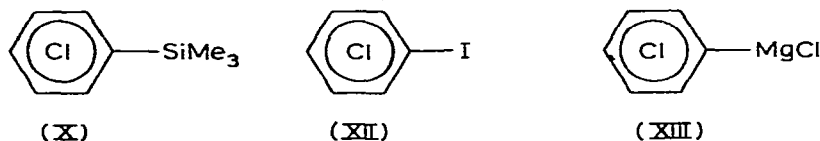
The formation of XIII may be explained by proposing a metal—hydrogen exchange reaction between V and VI as shown in Scheme 3.

SCHEME 3

We believe that the small amounts (6—9%) of 1,2,4,5-tetrachlorobenzene iso-lated from the various derivatization reactions, were formed by the metalation reaction shown in Scheme 3. This is supported by the observation that the treatment with an excess of D$_2$O of the mixture obtained from the reaction of pentachlorobenzene with magnesium gives three products, viz., VII, XIV and

XV and a small quantity of unreacted V. Doubtless, XIV and XV have origi-nated from the action of deuterium oxide on the corresponding Grignard reagents, VI and XIII, respectively, and XIII and VII from the metal—hydrogen exchange reaction shown in Scheme 3. This indicates that the true yield of 2,3,5,6-tetrachlorophenylmagnesium chloride (VI), as determined by hydrolyz-ing it to VII, is less than 76% (Scheme 2). This is because a part of this 1,2,4,5-tetrachlorobenzene (roughly 9%) would be expected to be formed by the metal—hydrogen exchange reaction. A similar exchange reaction has recently been observed by Anton, Coronas and Sales [3] and is in line with our previous observations with 2,3,4-trichlorothiophene [1] (I). However, the extent of the metalation reaction observed during the reaction of I with magnesium is

greater than that with V and magnesium, presumably because the acidity of the nuclear hydrogen in I is greatly increased by the proximity of the nuclear sulfur atom.

It is evident that the reaction of pentachlorobenzene with magnesium gives a mixture of Grignard reagents VI and XIII. However VI, prepared in this way, may still be useful in synthesis since its yield is fair (58%, yield of carboxylic acid derivative). The corresponding lithium reagent, 2,3,5,6-tetrachlorophenyl lithium, is prepared [4] in somewhat lower yield (48%) and as a 1.8 : 1 mixture with 1,2,4,5-tetrachloro-3,6-dilithiobenzene. In our system, however, no di-Grignard reagent was observed to have formed even when two equivalents of magnesium metal were used. This means that in preparative work, if a 2,3,5,6-tetrachlorophenylmetallic reagent is required and the presence of a 2,3,5,6-tetrachlorophenyldimetallic reagent needs to be avoided, then 2,3,5,6-tetra-chlorophenylmagnesium chloride, prepared by our method, offers a favorable alternative to the corresponding lithium reagent.

Experimental

All reactions were conducted under a positive pressure of dry, oxygen-free nitrogen. THF was dried over sodium wire and then distilled from sodium-benzophenone ketyl before use. IR spectra were recorded on a Perkin-Elmer Model 21 spectrometer. GLC analyses were carried out on an F and M Model 500 Gas Chromatograph using a $4' \times \frac{1}{4}''$ column packed with 15% Silicon Gum Rubber on Chromosorb W (60—80 mesh). The yields were based on the starting pentachlorobenzene. The temperatures quoted are uncorrected.

Reaction of pentachlorobenzene and magnesium: Preparation of 2,3,5,6-tetra-chlorophenylmagnesium chloride and its reaction with carbon dioxide

To Grignard grade magnesium turnings (0.055 g-at) contained in a three-necked flask fitted with a reflux condenser whose open end was connected to N_2-line, a pressure-equalizing dropping funnel and a mechanical stirrer, was added 10 ml of a solution of pentachlorobenzene (0.05 mol) in THF (120 ml). A few drops of 1,2-dibromoethane were added to initiate the reaction. When the reaction started, as evidenced by the color change, the rest of the penta-chlorobenzene solution (approx. 110 ml) was added dropwise over a period of 3 h. During addition the temperature of the mixture was maintained between 10 to 15°C. (At higher reaction temperatures the yield of 2,3,5,6-tetrachloro-phenylmagnesium chloride tended to be lower.) The mixture was stirred for another hour at that temperature after the addition. Gilman Test I [5] was positive. n-Docosane (2.015 g) in dry benzene (100 ml) was added as the internal standard for GLC study. The mixture was stirred for $\frac{1}{2}$ h and then an aliquot was withdrawn, hydrolysed with dil. HCl, extracted in ether and examined by GLC. 1,2,4,5-Tetrachlorobenzene (VII) and pentachlorobenzene (V) were formed in 76 and 8% yields, respectively. Traces of two other low boiling products (probably di- and tri-chlorobenzenes) were also formed.

The rest of the Grignard reagent was carbonated by bubbling in dry gaseous CO_2. Gilman Test I [5] was negative within 1 h. The bubbling of CO_2 was continued for another $\frac{1}{2}$ h and the mixture was hydrolyzed with dil. HCl and the

acidic material was extracted in 5% NaOH solution. The alkali extract was acidified with dil. HCl and the organic matter was extracted into diethyl ether. Removal of ether gave a brown solid which on recrystallization from CCl_4 gave 2,3,5,6-tetrachlorobenzoic acid (VIII), 58%, m.p. 179—182°C, identical (IR and mixed m.p.) with an authentic sample prepared by a published procedure [4]. No attempt was made to isolate any 1,2,4,5-tetrachlorobenzene or pentachlorobenzoic acid which might have been present as by-products.

Reaction of 2,3,5,6-tetrachlorophenylmagnesium chloride with chlorotrimethylsilane

An excess of chlorotrimethylsilane was added to 2,3,5,6-tetrachlorophenylmagnesium chloride (prepared from pentachlorobenzene (0.01 mol) and magnesium (0.01 g-at) in THF (100 ml) and the mixture was stirred for 1 h at room temperature. Gilman Test I [5] was negative at this stage. The mixture was heated at reflux for 1 h and the internal standard, *n*-docosane, in 100 ml benzene was added. The mixture was stirred at room temperature for ½ h, hydrolyzed with dil. HCl and extracted with ether. GLC analysis of the ether extract indicated that 1,2,4,5-tetrachloro-3-(trimethylsilyl)benzene (IX), (trimethylsilyl)pentachlorobenzene (X) and 1,2,4,5-tetrachlorobenzene (VII) were formed in 74.8 and 6% yields, respectively.

In another experiment, the above reaction was conducted with pentachlorobenzene (0.05 mol) and magnesium (0.1 g-at) in THF (100 ml) at 15°C and subsequently derivatized with an excess of chlorotrimethylsilane as before. GLC analysis indicated that (trimethylsilyl)pentachlorobenzene (10%) and 1,2,4,5-tetrachloro-3-(trimethylsilyl)benzene (77%) were formed. 1,2,4,5-Tetrachlorobenzene was present but its yield was not quantitatively estimated. No bis(trimethylsilyl)-1,2,4,5-tetrachlorobenzene was detected. For comparison purposes, authentic samples of the silylated polychlorinated benzenes were prepared by published procedures [6,7].

Reaction of 2,3,5,6-tetrachlorophenylmagnesium chloride with iodine

A filtered solution of 2,3,5,6-tetrachlorophenylmagnesium chloride (prepared from 0.2 mol of pentachlorobenzene and 0.2 g-at of magnesium in 200 ml of THF) was added dropwise to iodine (0.2 mol) in benzene (100 ml) at 10°C. Gilman Test I [5] was negative within 1 h. The mixture was then refluxed for 1 h, cooled, hydrolysed with dil. HCl and finally extracted with pet. ether (b.p., 60—80°C). Removal of the solvent gave a brown solid which when chromatographed on a silica gel column with pet. ether (b.p., 60—80°C) as an eluant gave (i) 1,2,4,5-tetrachlorobenzene (9%), m.p. 139—140°C, identical (GLC, IR, mixed m.p.) with an authentic sample; (ii) pentachloroiodobenzene, 12%, m.p. 210°C (cited [8]: 207.5—208°C), identical (IR, mixed m.p.) with an authentic sample and (iii) 1,2,4,5-tetrachloroiodobenzene (XI) (44%), m.p. 82—83°C; analysis found, C, 20.97, calcd. for C_6HCl_4I: C, 21.06%. The IR spectrum (Nujol mull) had the following absorption frequencies (cm^{-1}): 3050vw, 1545w, 1515w, 1307vs(sh), 1210w, 1192w, 1163vs, 1061s, 867vs, 812w(br), 755s, 723w(br), 692m(sh) and 669vs. The ^1H NMR spectrum (Varian A 60 spectrometer using TMS as internal standard in CCl_4) showed a singlet at $\delta = 7.57$ ppm. The mass spectrum showed the following important clusters of

peaks at m/e 348, 346, 344, 342 and 340 (M^+); 311, 309, 307 and 305 ($M^+ - $ Cl); 274, 272 and 270 ($M^+ - $ 2 Cl); 237 and 235 ($M^+ - $ 3 Cl); 221, 219, 217, 215 and 213 ($M^+ - $ I); 184, 182, 180 and 178 ($M^+ - $ ICl) and 183, 181, 179 and 177 ($M^+ - $ IHCl). All the above clusters had the characteristic isotope distribution pattern for the appropriate number of chlorine atoms.

Deuterolysis experiment

Deuterium oxide (0.10 mol) was added to a preparation of 2,3,5,6-tetra-chlorophenylmagnesium chloride (from pentachlorobenzene, 0.01 mol and magnesium, 0.01 g-at in 50 ml of THF), the mixture stirred until Gilman Test I [5] was negative ($\frac{1}{2}$ h), then refluxed for $\frac{1}{2}$ h and finally cooled to room temperature. The organic matter was extracted into diethyl ether. Removal of ether gave a white solid. GLC study of this solid showed it to be a mixture of two compounds, the retention volumes of which corresponded with those of 1,2,4,5-tetrachlorobenzene and pentachlorobenzene on a 5%, 5' OV-17 column. The mixture was separated by preparative GLC and the constituent compounds, fractions 1 and 2, were subjected separately to mass spectroscopic study. The mass spectrum (200°C, 70 eV) of fraction 1 showed two clusters of peaks centering around m/e 216 and 217 (the most intense peak of the respective cluster) and corresponding to the molecular ions $(C_6H_2Cl_4)^+$ and $(C_6HDCl_4)^+$, respectively. Both clusters had the characteristic isotope pattern for four chlorine atoms. Similarly, the mass spectrum of fraction 2 showed the clusters of molecular ions due to $(C_6HCl_5)^+$ and $(C_6DCl_5)^+$, both having the appropriate isotope pattern for five chlorine atoms and centering, respectively, around m/e 250 and 251.

Thus deuteration of the reaction mixture obtained from the reaction of pentachlorobenzene with magnesium in THF gave 1,2,4,5-tetrachlorobenzene, 1,2,4,5-tetrachloro-3-deuteriobenzene and pentachlorodeuteriobenzene, along with some unreacted pentachlorobenzene.

Acknowledgement

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